Supplementary Information

Isatin-Based Benzyloxybenzene Derivatives as Monoamine Oxidase Inhibitors with Neuroprotective Effect Targeting Neurogenerative Disease Treatment

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[#] *Authors contributed equally to this work.*

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Contents

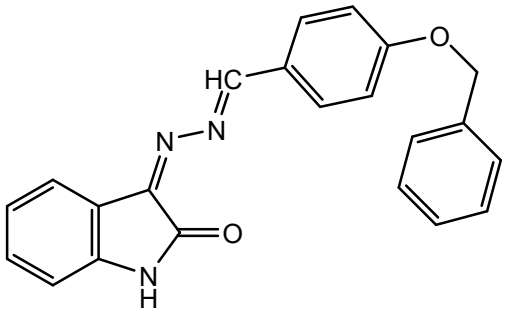

Figure S1. ISB1 structure

1.1 TLC OF ISB-1. Mobile phase is Hexane: ethyl acetate (70:30)

1.2 HPLC OF ISB-1

SHIMADZU LabSolutions **Analysis Report**

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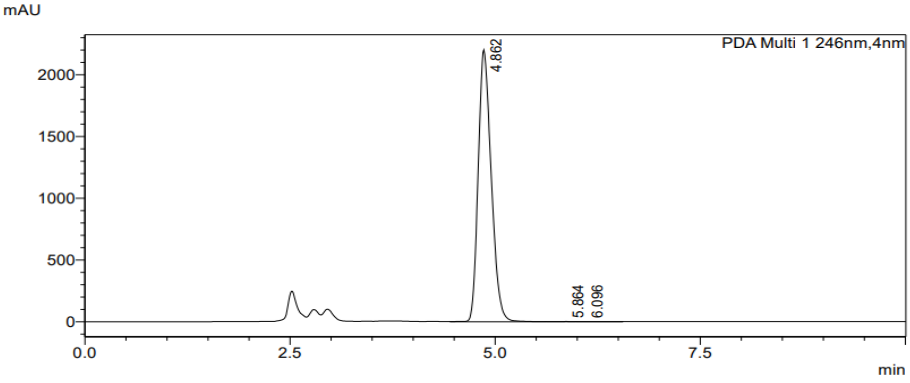

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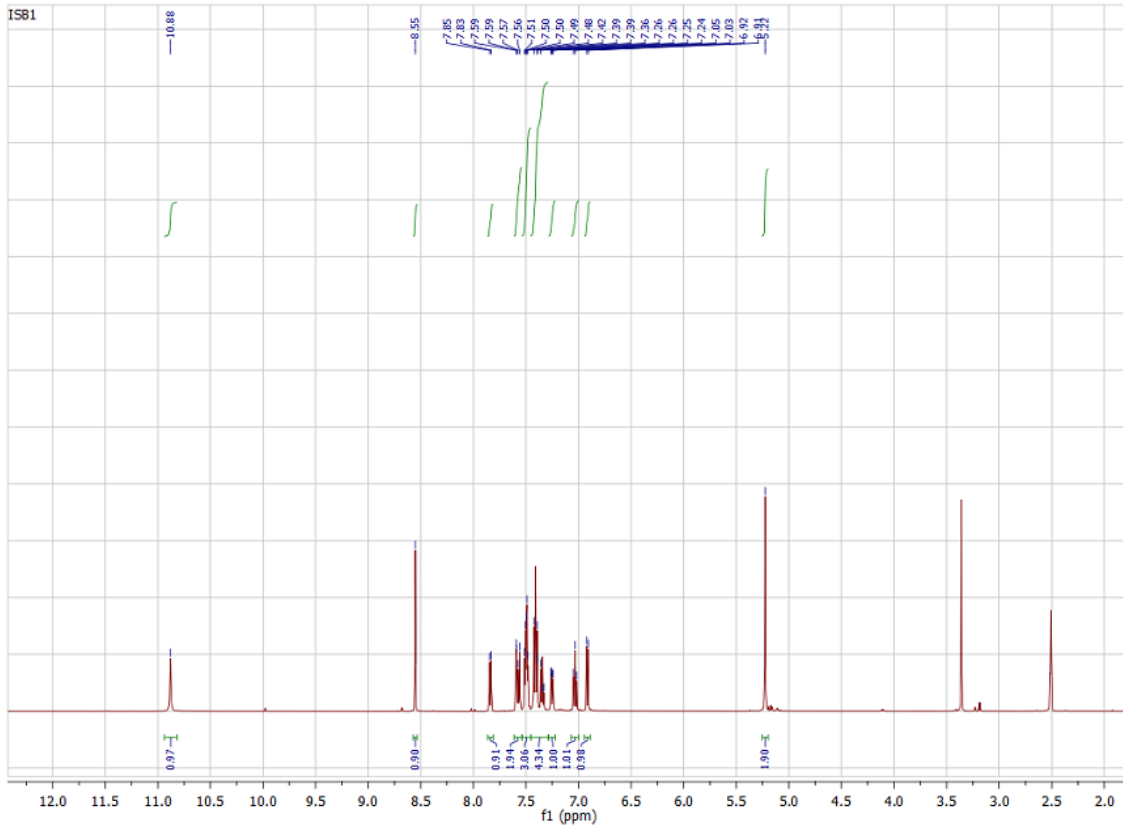
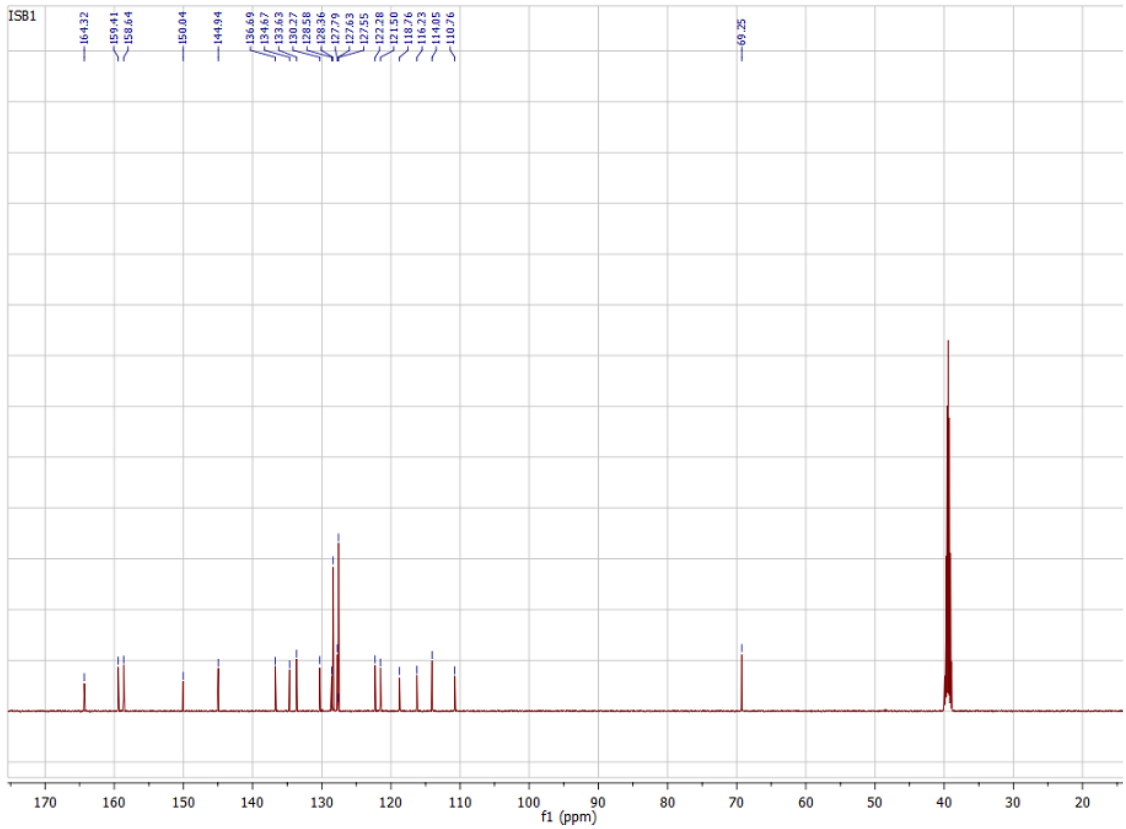
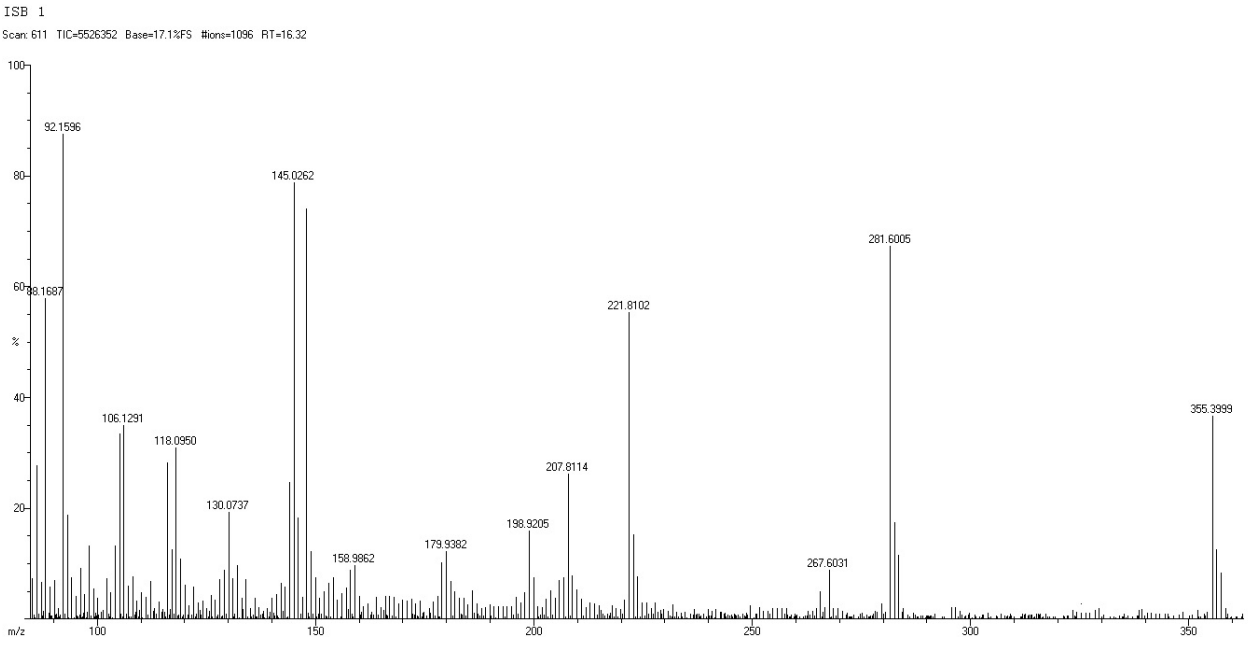
1.3 ^{1}H NMR SPECTRA OF ISB-1



1.4 ^{13}C NMR SPECTRA OF ISB-1:



1.5 MASS SPECTRA OF ISB-1



1.6 SPECTRAL INTERPRETATION:

3-((4-(benzyloxy)benzylidene)hydrazineylidene)indolin-2-one (**ISB1**): Orange, solid, 68%, melting point. 181± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.85 (s, 1H, NH), 8.55 (s, 1H, =CH-), 7.84-6.92 (m, 13H, ArH), 5.22 (s, 2H, -CH_2-). ^{13}C NMR (500 MHz, DMSO-d6) 164.32,

159.41, 158.64, 150.04, 144.94, 136.69, 134.67, 133.63, 130.27, 128.58, 128.36, 127.67, 122.28, 121.50, 118.76, 116.23, 114.05, 110.76, 69.25. Chemical Formula $C_{22}H_{16}FN_3O_2$. EI- HRMS (m/z): Calculated-355.3892, Observed-355.3999.

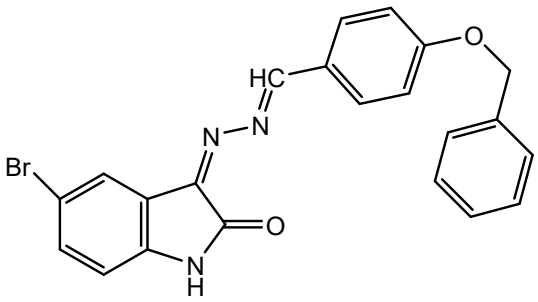
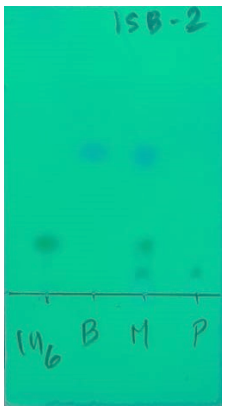


Figure S2. ISB-2 structure

2.1 TLC OF ISB-2: Mobile phase is Hexane: ethyl acetate (70:30)



2.2 HPLC OF ISB-2

SHIMADZU LabSolutions **Analysis Report**

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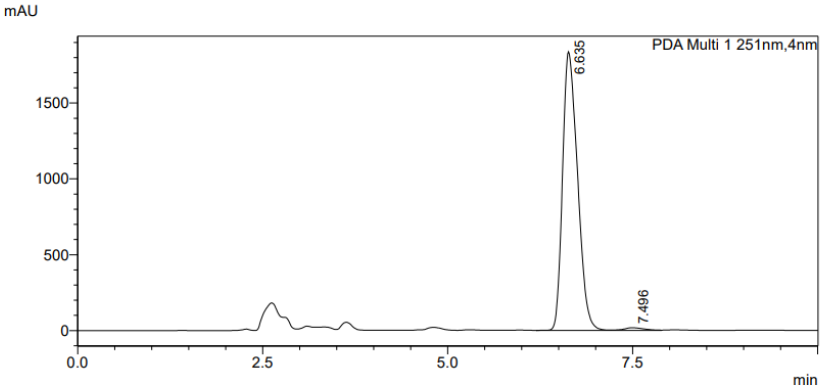

<Peak Table>

PDA Ch1 251nm

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2	7.496	367998	17950	1.396		V M
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2.3 ^{1}H NMR OF ISB-2

ISB-2
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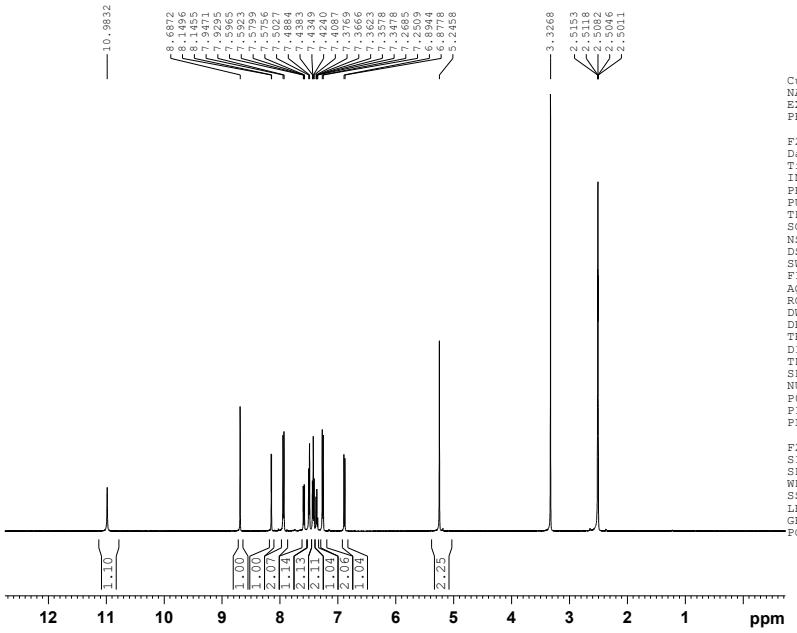


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BRUKER
AVANCE NEO
500 MHz NMR
SPECTROMETER
SAIF, P.U.

Current Data Parameters
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PROCNO                 1

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DS                     0
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FIDRES         0.448788 Hz
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RG                   101
DW                34.000 usec
DE                 6.79 usec
TE                300.2 K
D1             1.00000000 sec
TD0                    1
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NUC1                  1H
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P1                10.00 usec
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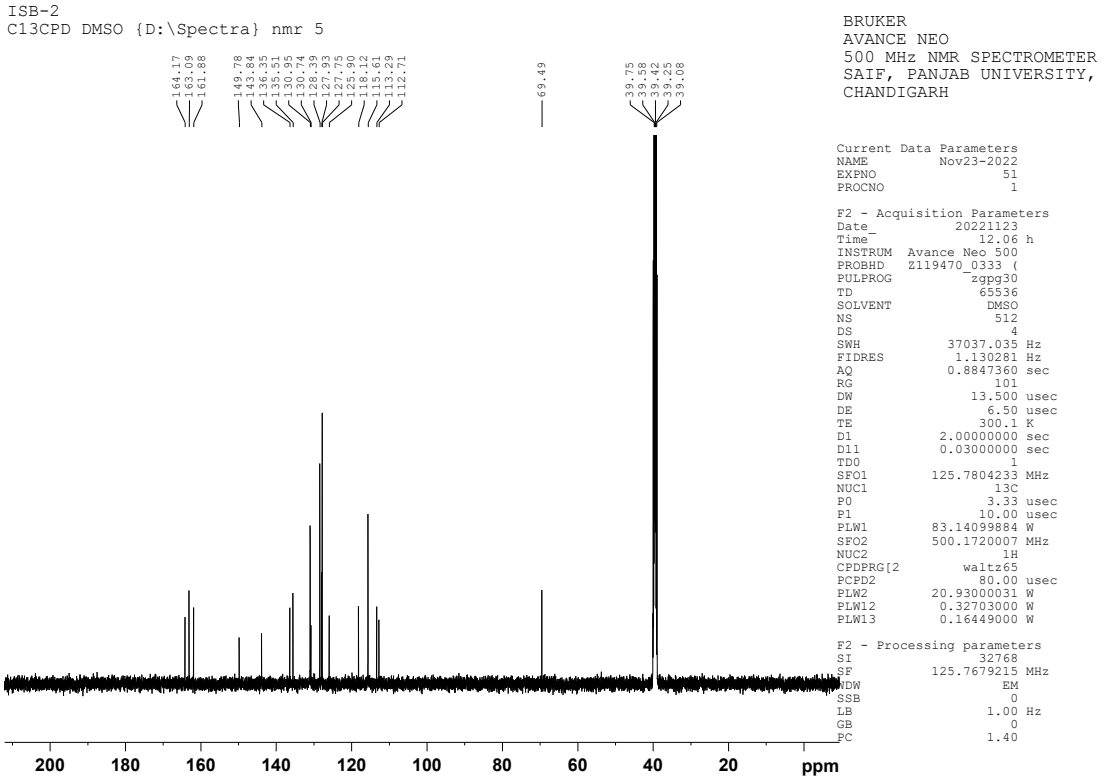
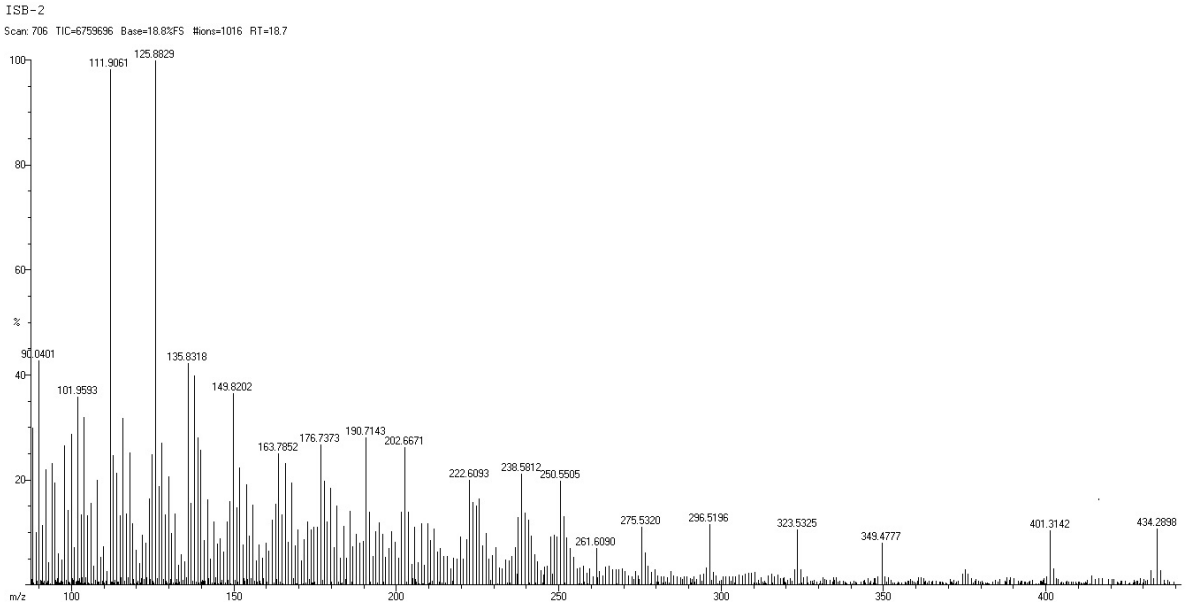
2.4 ^{13}C NMR OF ISB-2



2.5 MASS SPECTRUM OF ISB-2



2.6 SPECTRAL INTERPRETATION:

3-((4-(benzyloxy)benzylidene)hydrazineylidene)-5-bromoindolin-2-one (**ISB2**): Orange, solid, 81%, melting point. 244± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.98 (s, 1H, NH), 8.68 (s, 1H, =CH-), 8.14-6.87 (m, 12H, ArH), 5.24(s, 2H, -CH_2-) ^{13}C NMR (500 MHz, DMSO-d6) 164.17, 163.09, 161.88, 149.78, 143.84, 136.35, 135.51, 130.95, 130.74, 128.39, 127.93, 127.75, 125.90, 118.12, 115.61, 113.29, 112.71, 69.49. Chemical formula $C_{22}H_{15}BrFN_3O$ EI-HRMS (m/z): Calculated- 434.2898, Observed-434.2853.

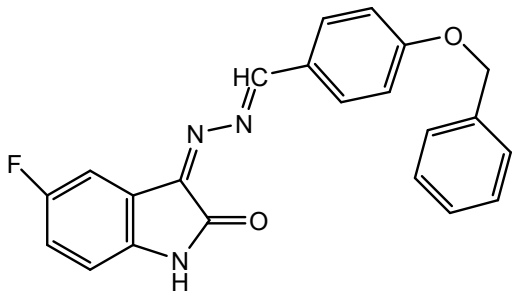
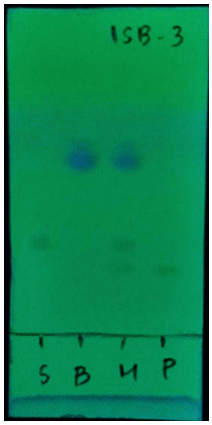


Figure S3. ISB3 structure

3.1 TLC OF ISB-3: Mobile phase is Hexane: ethyl acetate (70:30)



3.2 HPLC OF ISB-3

SHIMADZU LabSolutions **Analysis Report**

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Batch Filename	:		
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Injection Volume	: 20 uL		
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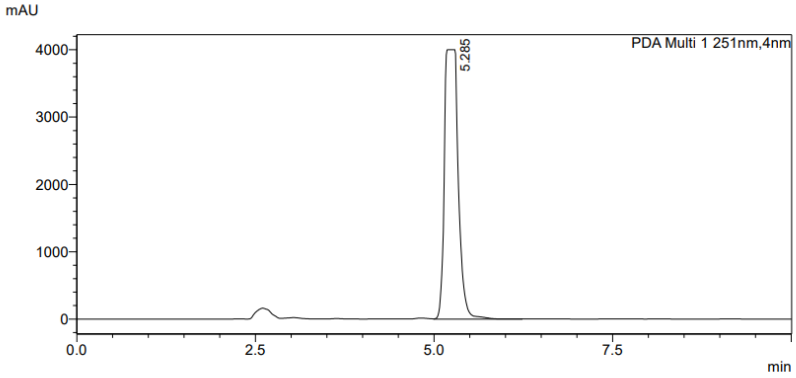

<Peak Table>

PDA Ch1 251nm

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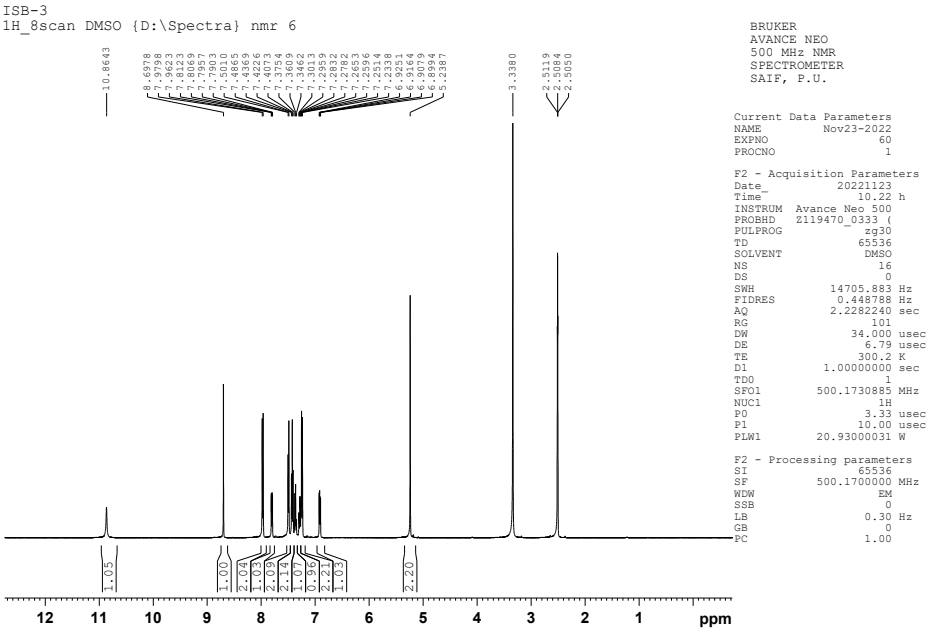
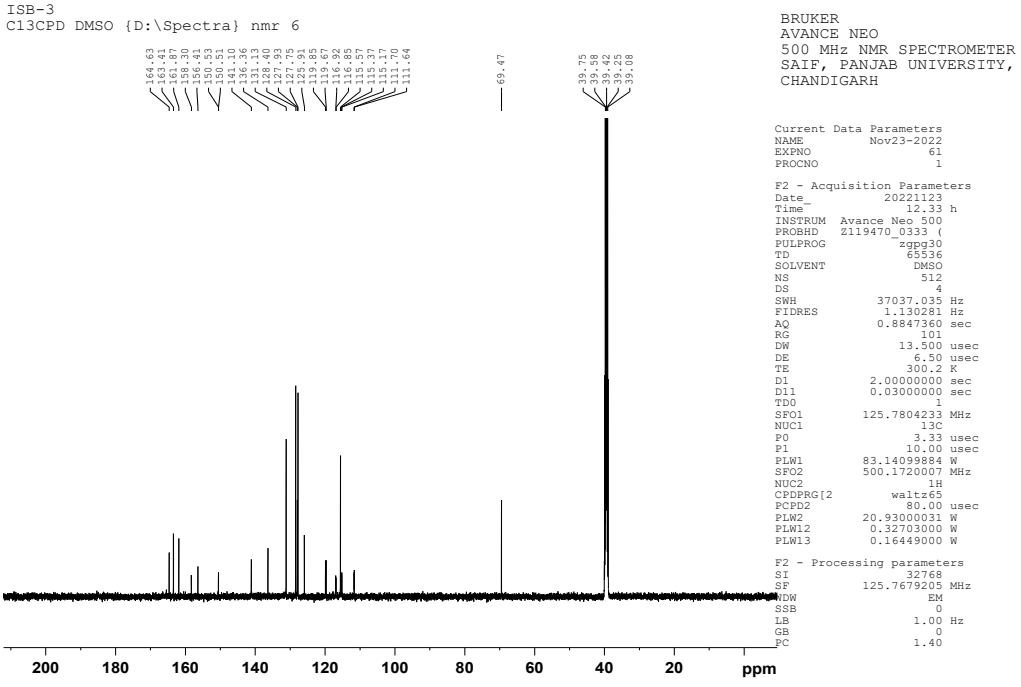
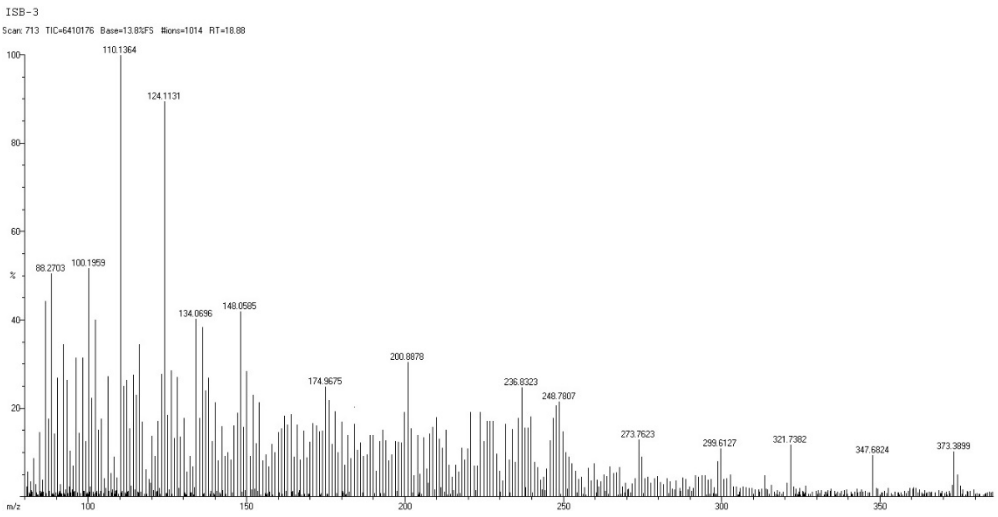
3.3 ^{1}H NMR OF ISB-3



3.4 ^{13}C NMR OF ISB-3



3.5 MASS SPECTRA OF ISB-3



3.6 SPECTRAL INTERPRETATION:

*3-((4-(benzyloxy)benzylidene)hydrazineylidene)-5-fluoroindolin-2-one (**ISB 3**):* Brick red , solid, 72%, melting point. 229± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.86 (s, 1H, NH), 8.69 (s, 1H, =CH-), 7.97-6.89 (m, 12H, ArH), 5.23 (s, 2H, -CH2-). ^{13}C NMR (500 MHz, DMSO-d6): 164.63, 163.41, 161.87, 158.30, 156.41, 150.53, 141.10, 136.36, 131.13, 128.40, 127.93, 126.91, 119.85, 116.92, 115.87, 111.70, 69.47. Chemical formula $C_{22}H_{15}F_2N_3O_2$ EI-HRMS (m/z): Calculated- 378.3899, Observed-373.3797.

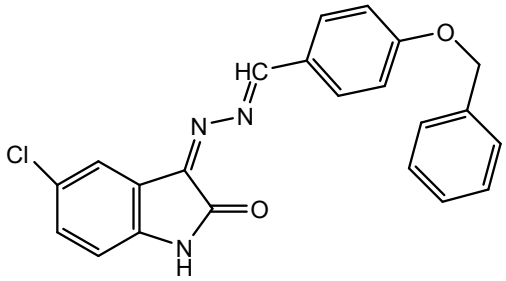
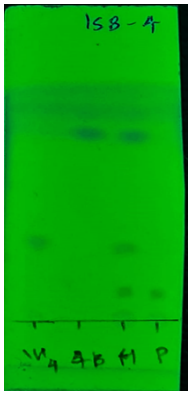


Figure S4. ISB4 structure

4.1 TLC OF ISB-4: Mobile phase is Hexane: ethyl acetate (70:30)



4.2 HPLC OF ISB-4

SHIMADZU LabSolutions **Analysis Report**

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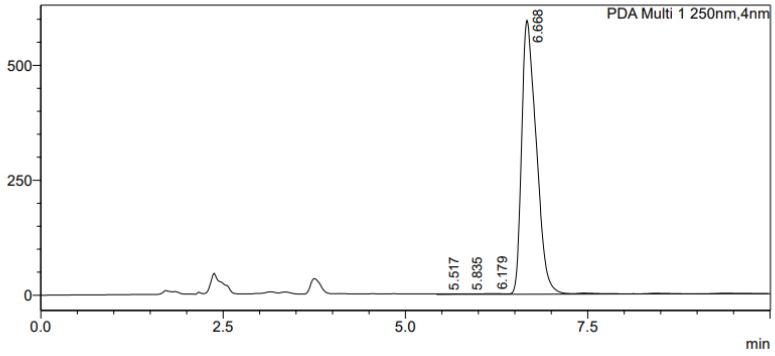

<Peak Table>

PDA Ch1 250nm

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3	6.179	28241	1507	0.332		V	
4	6.668	8435943	595104	99.275		SV	
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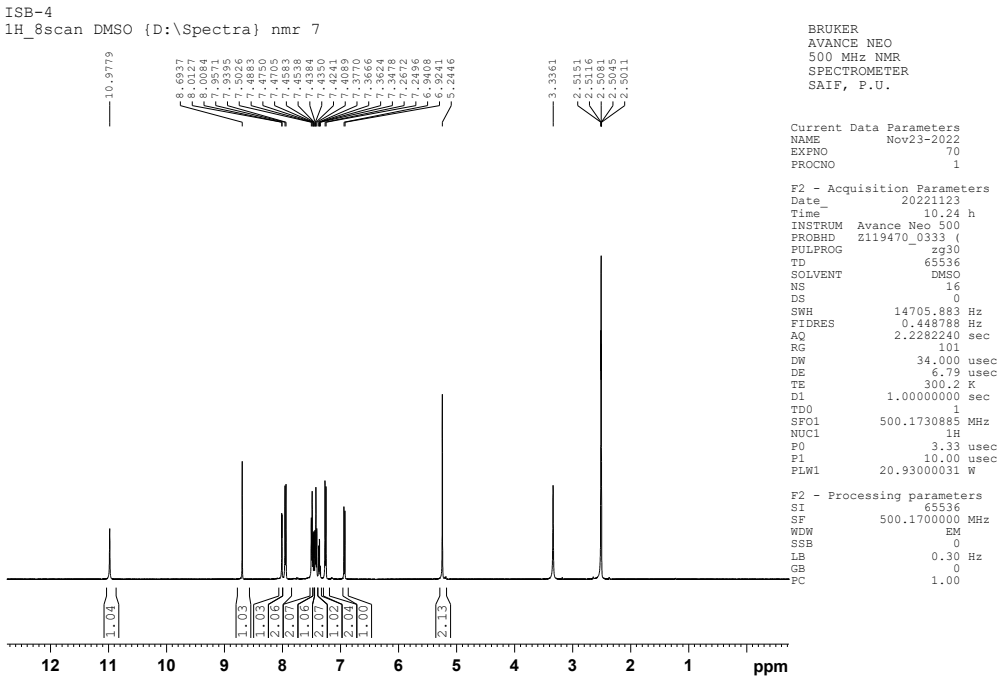
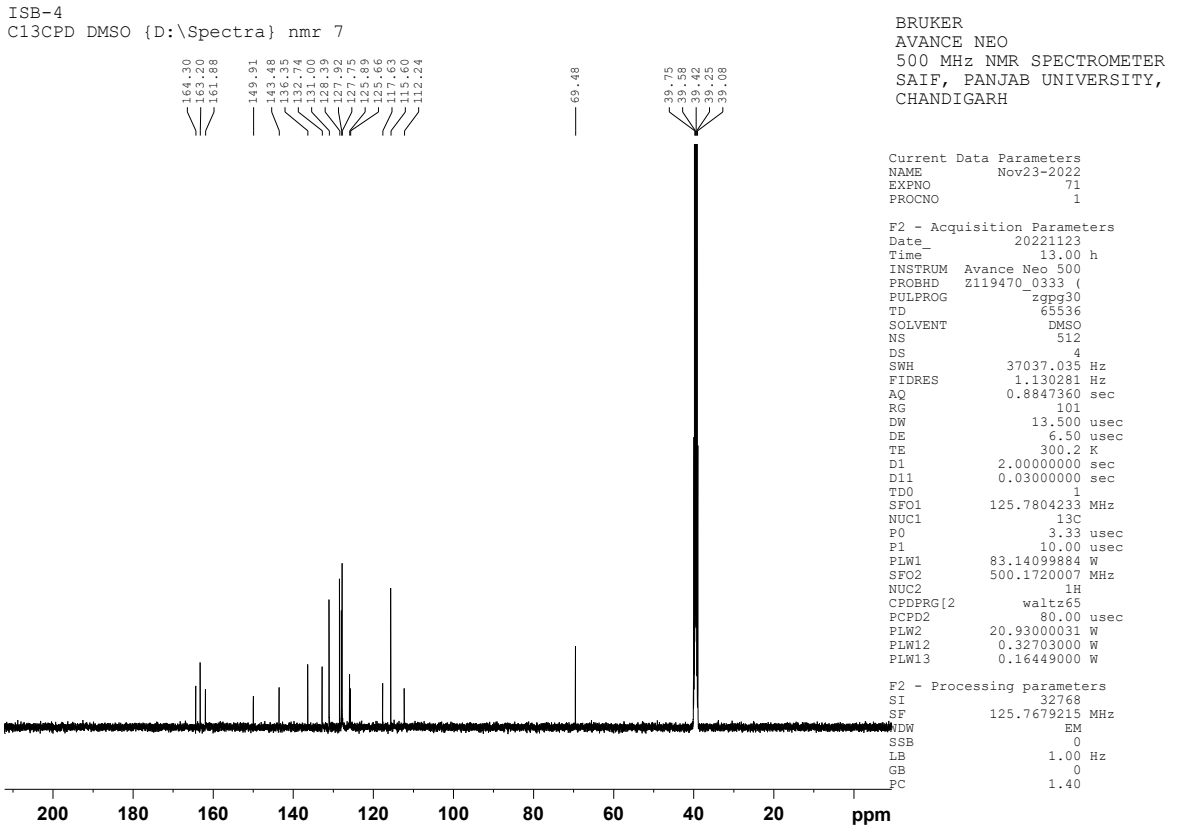
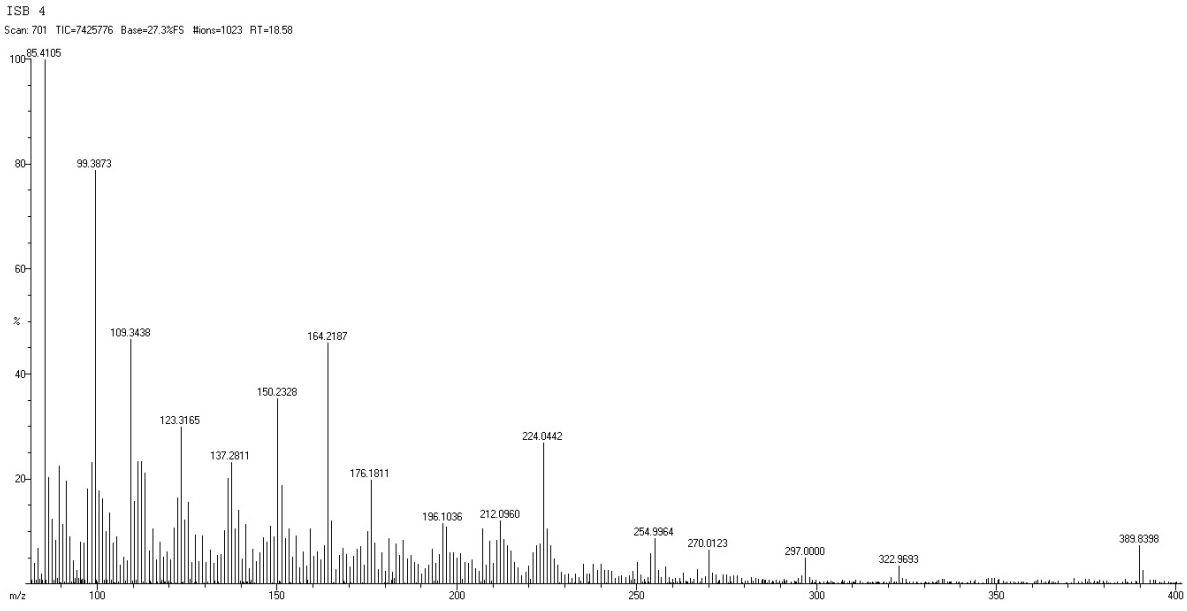
4.3 ^{1}H NMR OF ISB-4



4.4 ^{13}C NMR OF ISB-4



4.5 MASS SPECTRA OF ISB-4



4.6 SPECTRAL INTERPRETATION:

*3-((4-(benzyloxy)benzylidene)hydrazineylidene)-5-chloroindolin-2-one(**ISB 4**):* Orange , solid, 78%, melting point. 240± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.97 (s, 1H, NH), 8.69 (s, 1H, =CH-), 8.01-6.92 (m, 12H, ArH), 5.24 (s, 2H, -CH_2-) ^{13}C NMR (500 MHz, DMSO-d6) 164.30, 163.88, 161.88, 149.91, 143.48, 136.35, 132.74, 131.00, 128.39, 127.92, 126.89, 125.66, 117.63, 116.60, 112.24, 69.48. Chemical Formula $C_{22}H_{15}ClFN_3O_2$ EI- HRMS (m/z): Calculated-389.8398, Observed- 389.8343.

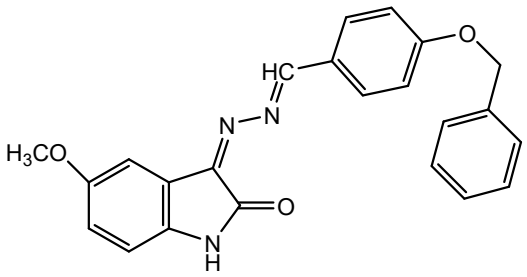
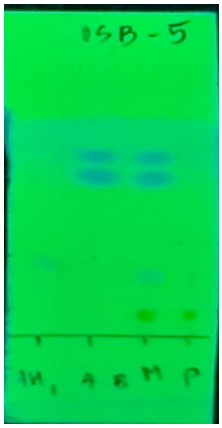


Figure S5. ISB5 structure

5.1 TLC OF ISB-5: Mobile phase is Hexane: ethyl acetate (70:30)



5.2 HPLC OF 1SB-5

SHIMADZU LabSolutions **Analysis Report**

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Batch Filename	:		
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Injection Volume	: 20 uL		
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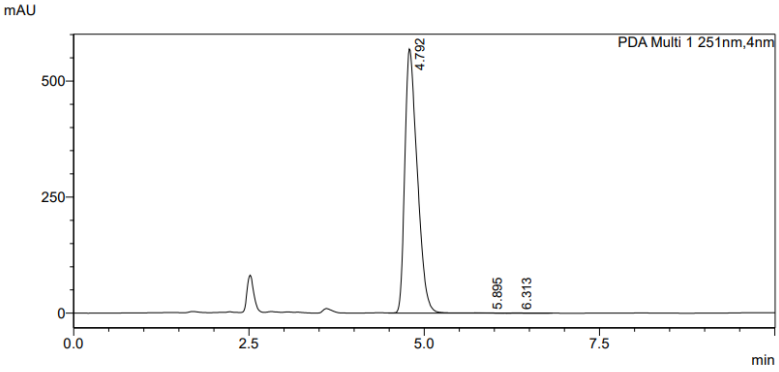

<Peak Table>

PDA Ch1 251nm

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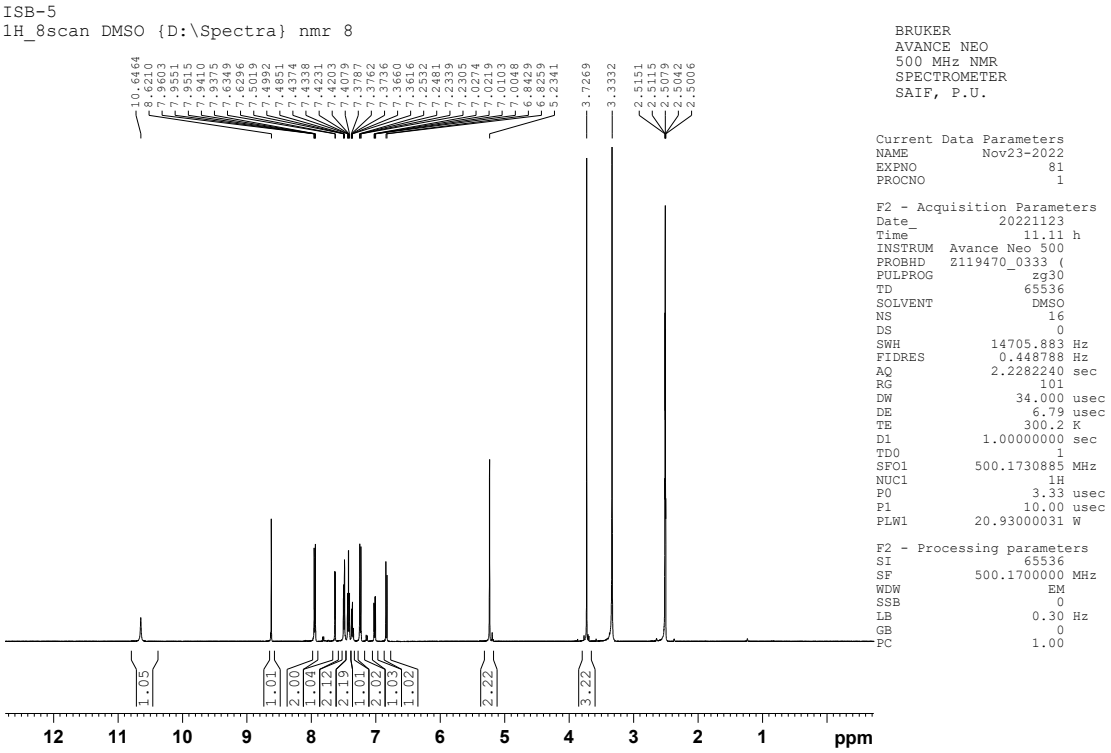
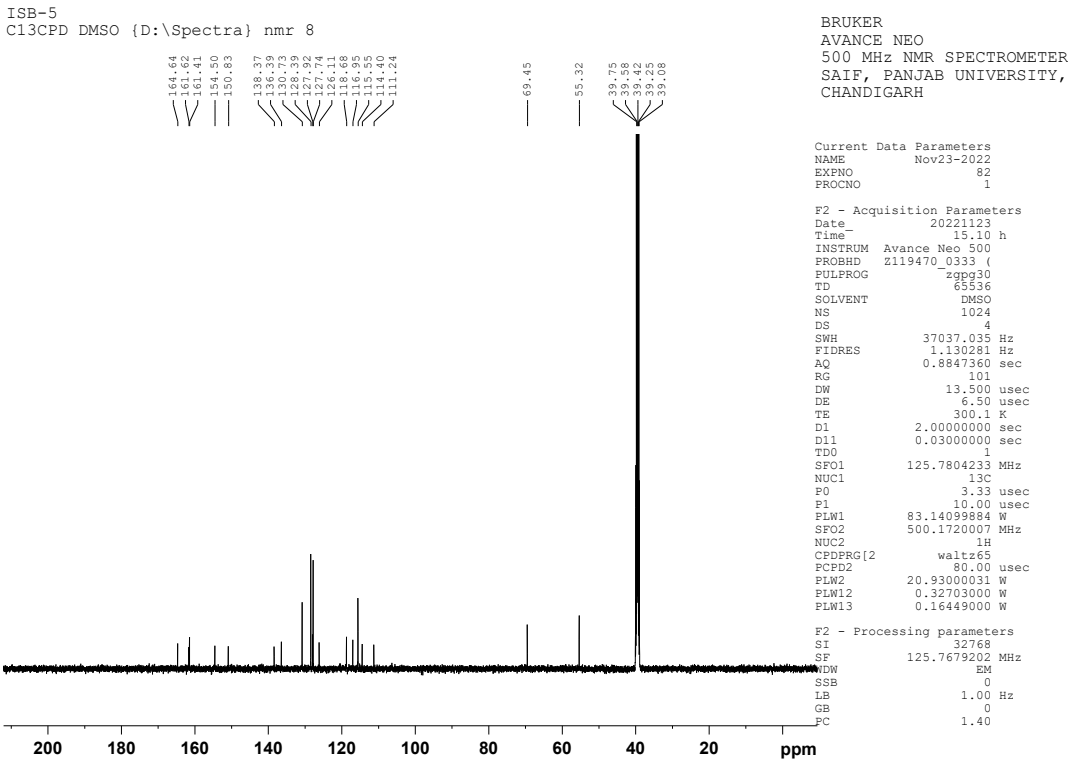
1	4.792	7049924	569118	99.894		S	
2	5.895	1977	181	0.028		T	
3	6.313	5518	338	0.078		T	
Total		7057420	569636				

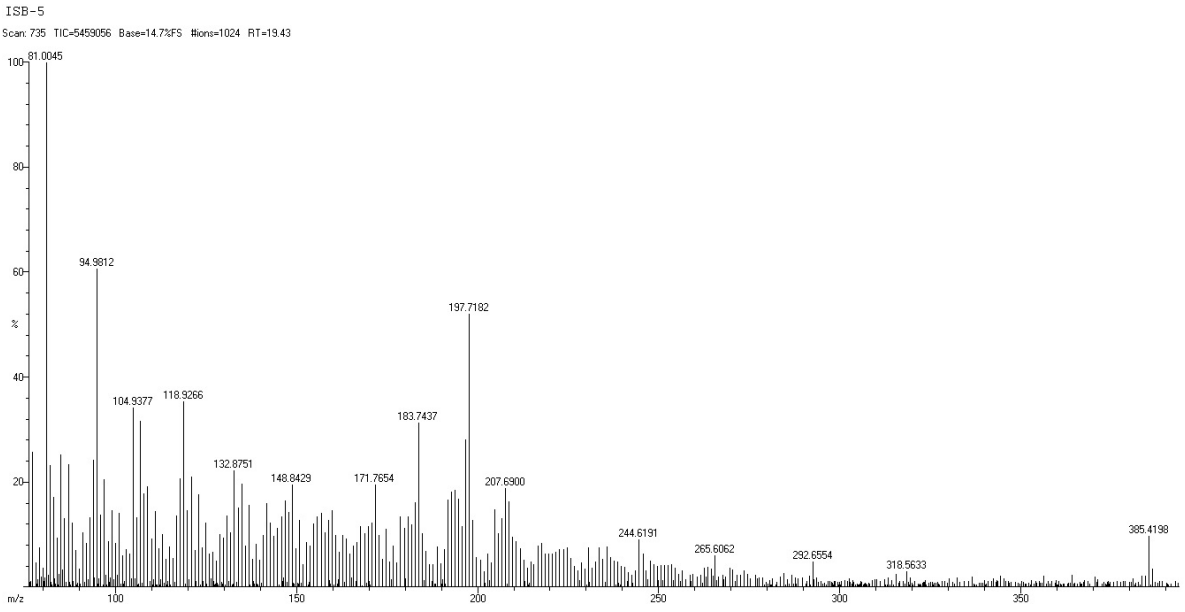
5.3 ^{1}H NMR OF ISB-5



5.4 ^{13}C NMR OF ISB-5



5.5 MASS SPECTRA OF ISB-5



5.6 SPECTRAL INTERPRETATION

*3-((4-(benzyloxy)benzylidene)hydrazineylidene)-5-methoxyindolin-2-one(**ISB5**):* Reddish brown , solid, 72%, melting point. 192± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.64 (s, 1H, NH), 8.62 (s, 1H, =CH-), 7.96-6.82(m, 12H, ArH), 5.23 (s, 2H, -CH_2-), 3.72 (s, 3H, -CH_2-Ar). ^{13}C NMR (500 MHz, DMSO-d6) 164.64, 161.62, 161.41, 154.50, 150.63, 138.37, 136.39, 130.73, 128.39, 127.92, 126.11, 118.68, 116.98, 115.55, 114.40, 111.28, 69.45, 55.32. Chemical formula $C_{23}H_{18}FN_3O_3$ EI- HRMS (m/z): Calculated-385.4198, Observed- 385.4152.

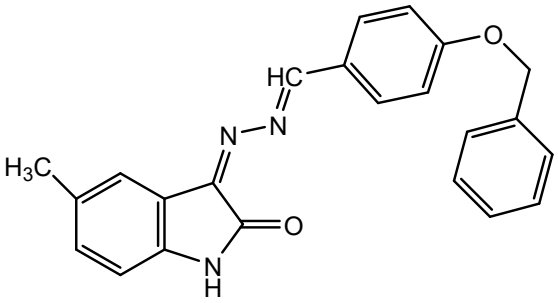
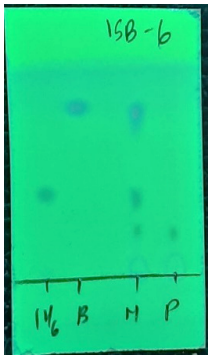


Figure S6. ISB6 structure

6.1 TLC OF ISB-6: Mobile phase is Hexane: ethyl acetate (70:30)



6.2 HPLC OF ISB-6

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: 100mcl		
Sample ID	:		
Data Filename	: ISB6.lcd		
Method Filename	: isatin.lcm		
Batch Filename	:		
Vial #	: 1-2	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 12/3/2022 4:11:05 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:55:54 PM	Processed by	: System Administrator

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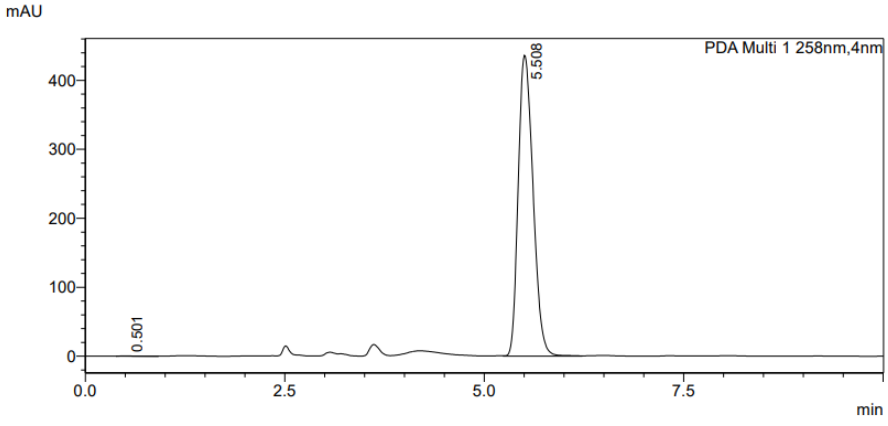
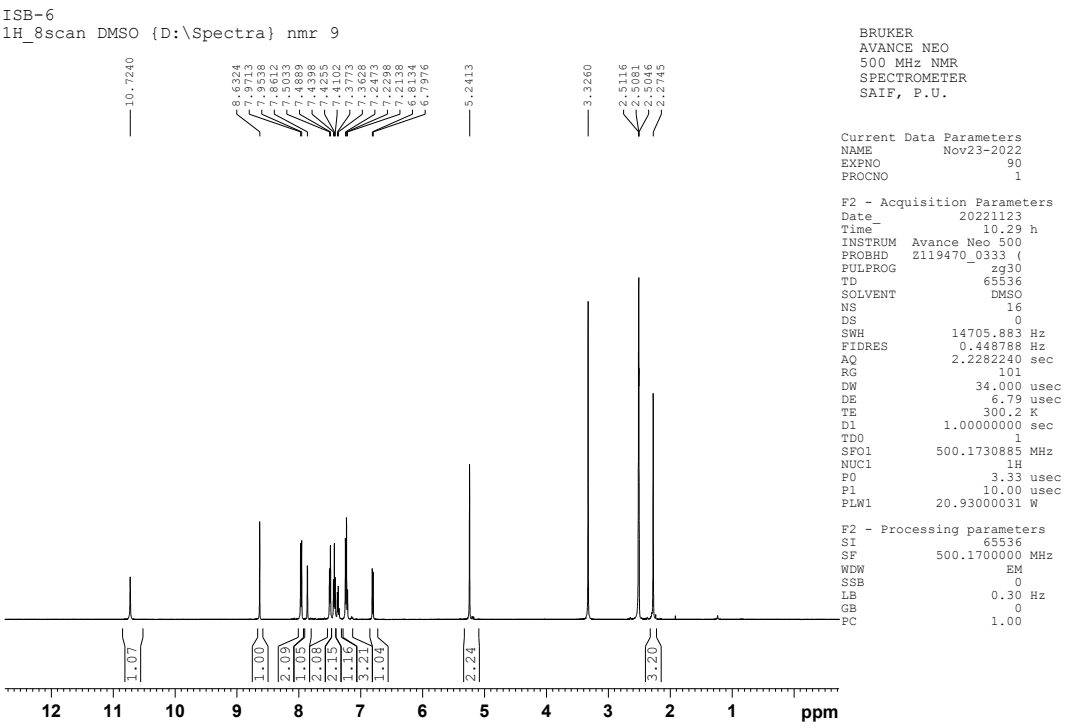


<Peak Table>

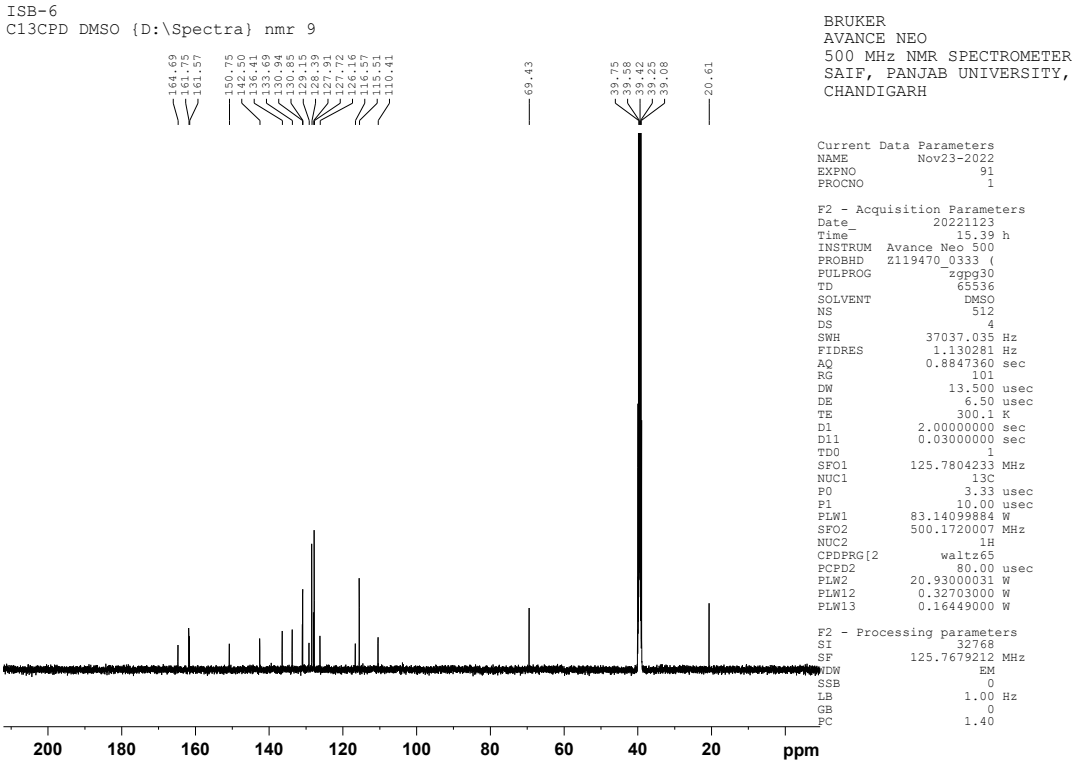
PDA Ch1 258nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	0.501	7008	324	0.124			
2	5.508	5662652	436305	99.876			
Total		5669660	436629				

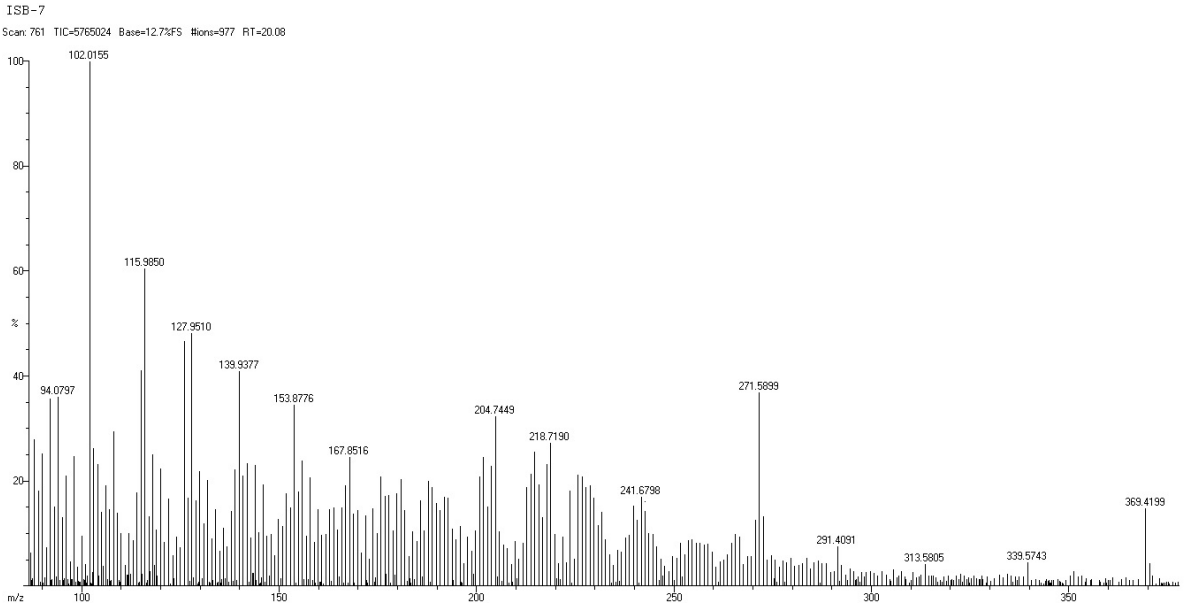
6.3 ^{1}H NMR OF ISB-6



6.4 ^{13}C NMR OF ISB-6



6.5 MASS INTERPRETATION OF ISB-6



6.6 SPECTRAL INTERPRETATION:

*3-((4-(benzyloxy)benzylidene)hydrazineylidene)-5-methylindolin-2-one(**ISB6**):* orange, solid, 68%, melting point. 210± 2˚C.^{1}H NMR (500 MHz, DMSO-d6) δ: 10.72 (s, 1H, NH), 8.63 (s, 1H, =CH-), 7.97-6.79(m, 12H, ArH), 5.24 (s, 2H, -CH_2-), 2.27 (s, 3H, -CH_2-Ar). ^{13}C NMR (500 MHz, DMSO-d6) 164.69, 161.76, 161.87, 160.75, 142.80, 136.41, 133.69, 130.94, 129.18, 128.39, 127.91, 126.16, 116.87, 115.51, 110.41, 69.43, 20.61. Chemical formula $C_{23}H_{19}N_3O_2$. EI- HRMS (m/z): Calculated-369.4199, Observed- 369.4158.

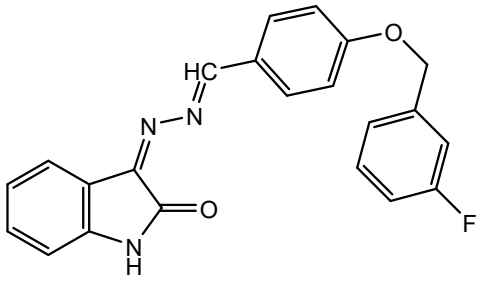
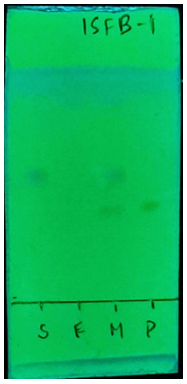


Figure S7. ISFB1 structure

7.1 TLC OF ISFB-1: Mobile phase is Hexane: ethyl acetate (70:30)



7.2 HPLC OF ISFB-1

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isfb1		
Data Filename	: fluoro and bb_05-12-2022_003.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-2	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 1:39:04 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 4:20:08 AM	Processed by	: System Administrator

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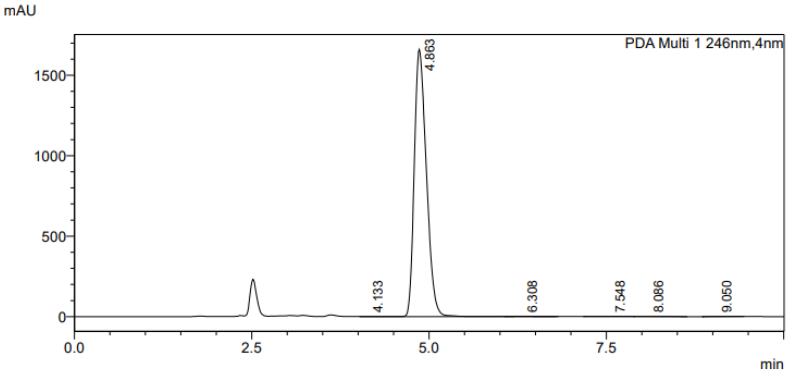
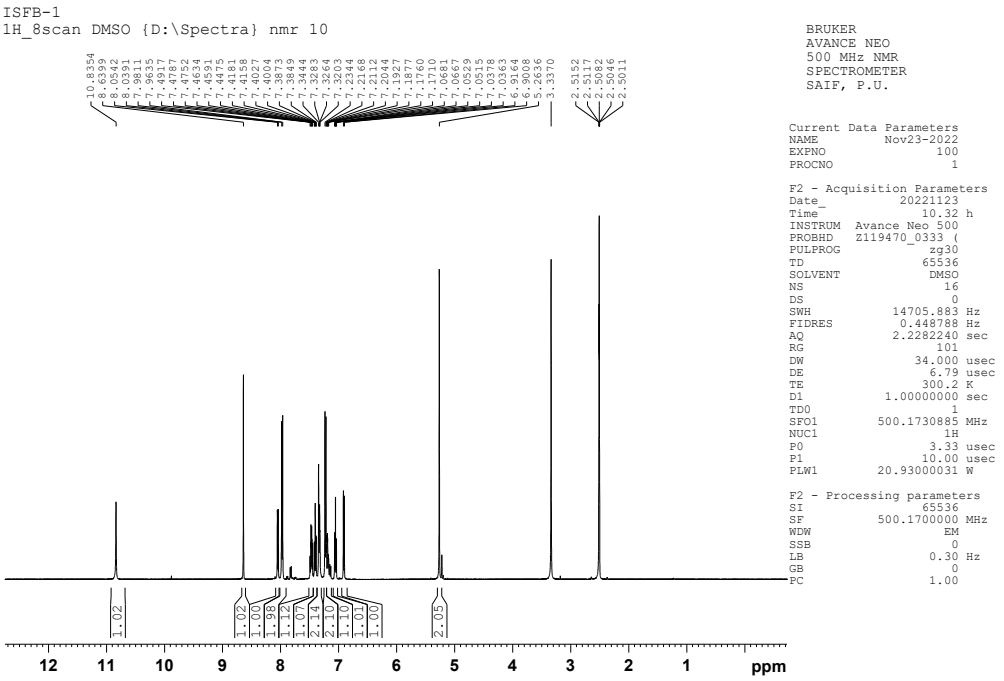


<Peak Table>

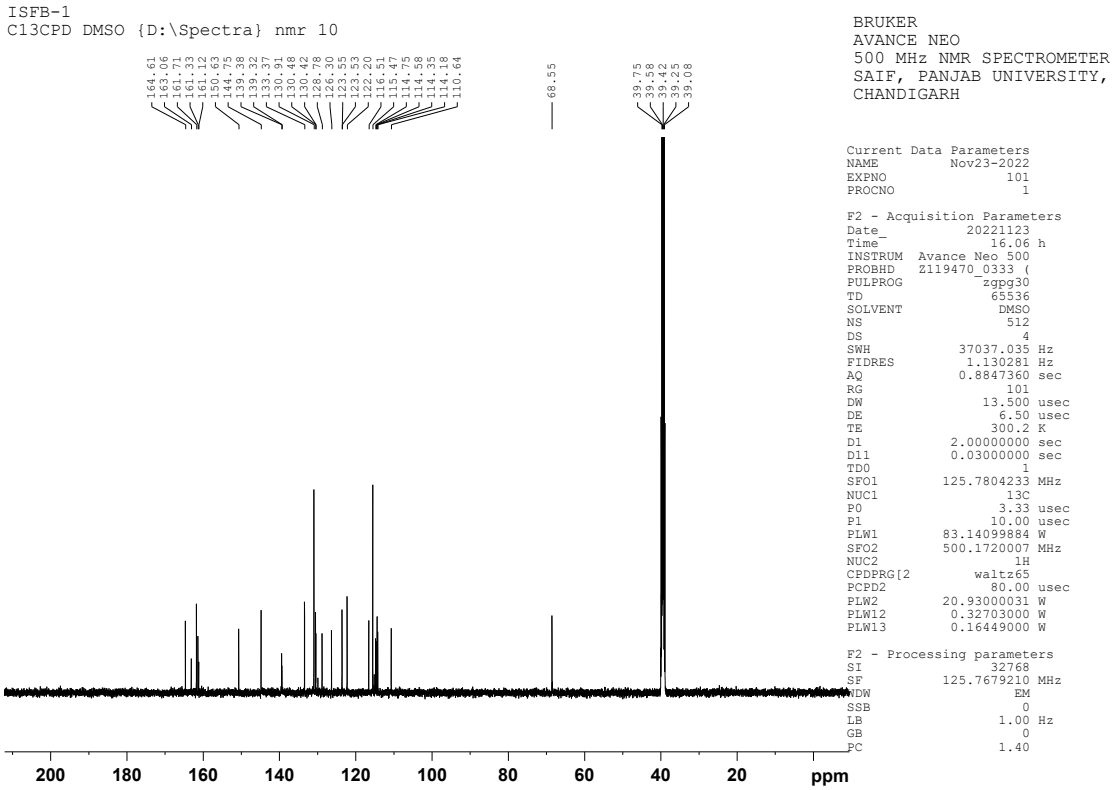
PDA Ch1 246nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.133	16616	898	0.084			
2	4.863	19734389	1659909	99.606		SV	
3	6.308	34168	1978	0.172		T	
4	7.548	12384	449	0.063			
5	8.086	11333	558	0.057		V	
6	9.050	3584	189	0.018			
Total		19812474	1663981				

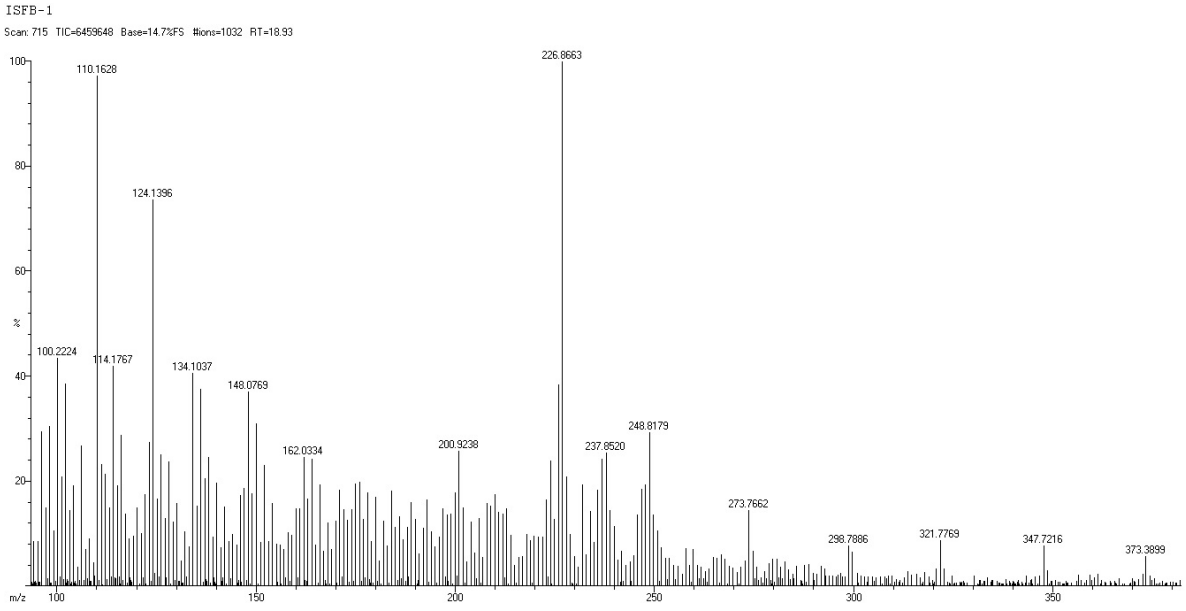
7.3 ^{1}H NMR OF ISFB-1



7.4 ^{13}C NMR OF ISFB-1



7.5 MASS SPECTRA OF ISFB-1



7.6 SPECTRAL INTERPRETATION:

*3-((4-((3-fluorobenzyl)oxy)benzylidene)hydrazineylidene)indolin-2-one(**ISFB1**):* orange, solid, 75%, melting point. 218± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.83 (s, 1H, NH), 8.63 (s, 1H, =CH-), 8.05-6.90(m, 12H, ArH), 5.26 (s, 2H, -CH_2-).^{13}C NMR (500 MHz, DMSO-d6) δ: 164.61, 163.06, 161.71, 150.63, 144.76, 139.38, 133.37, 130.91, 128.78, 126.30,123.66,122.20, 116.81, 115.47, 114.75, 110.64, 68.88. Chemical formula $C_{22}H_{16}FN_3O_2$. EI- HRMS (m/z): Calculated-373.3899, Observed- 373.3797.

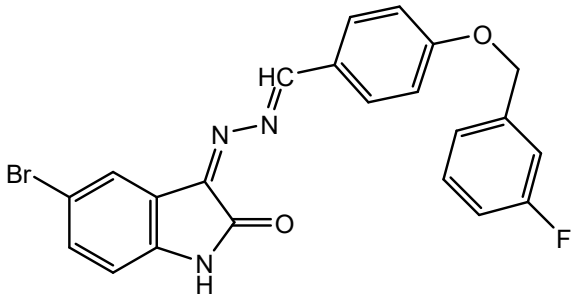


Figure S8. ISFB2 structure

8.1 TLC OF ISFB-2: Mobile phase is Hexane: ethyl acetate (70:30)

8.2 HPLC OF ISFB-2

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isfb2		
Data Filename	: fluoro and bb_05-12-2022_004.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-3	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 1:49:26 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:37:55 PM	Processed by	: System Administrator

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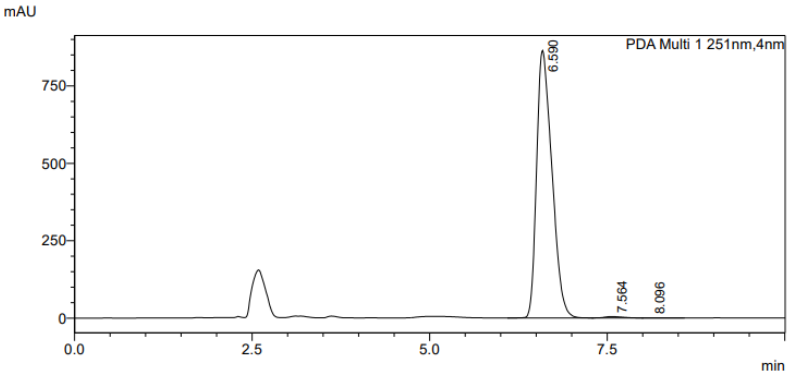


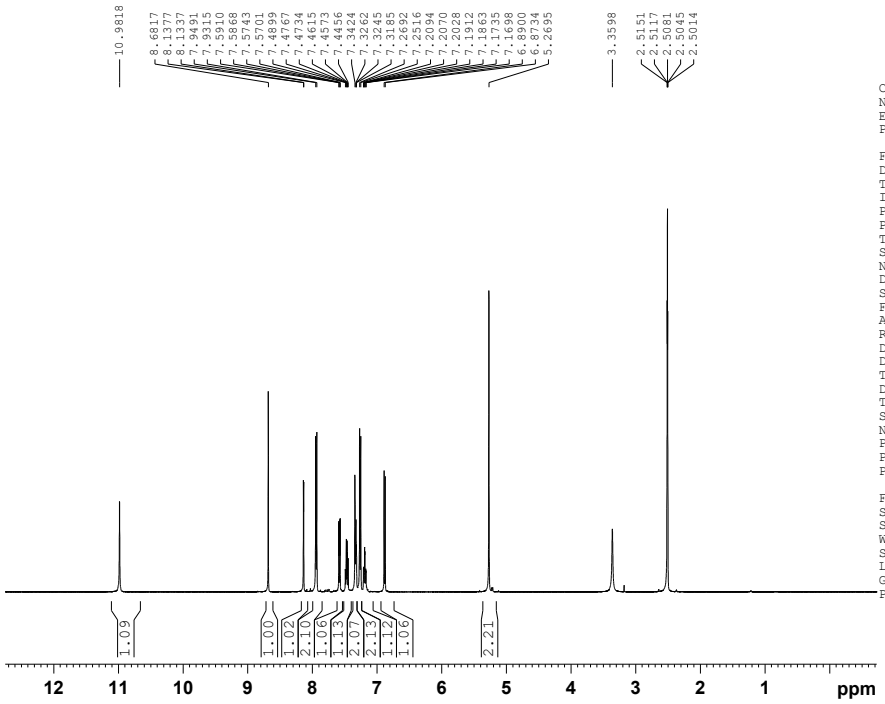
<Peak Table>

PDA Ch1 251nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.590	12988987	864298	99.271			
2	7.564	89640	4934	0.685		V	
3	8.096	5746	308	0.044		V	
Total		13084373	869540				

8.3 ^{1}H NMR OF ISFB-2

ISFB-2
1H_8scan DMSO {D:\Spectra} nmr 11

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BRUKER
AVANCE NEO
500 MHz NMR
SPECTROMETER
SAIF, P.U.

Current Data Parameters
NAME          Nov23-2022
EXPNO                110
PROCNO                 1

F2 - Acquisition Parameters
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PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     0
SWH            14705.883 Hz
FIDRES          0.448788 Hz
AQ             2.2282240 sec
RG                   101
DW                34.000 usec
DE                 6.79 usec
TE                300.2 K
D1           1.00000000 sec
TD0                    1
SFO1        500.1730885 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1        20.93000031 W

F2 - Processing parameters
SI                 65536
SF          500.1700000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
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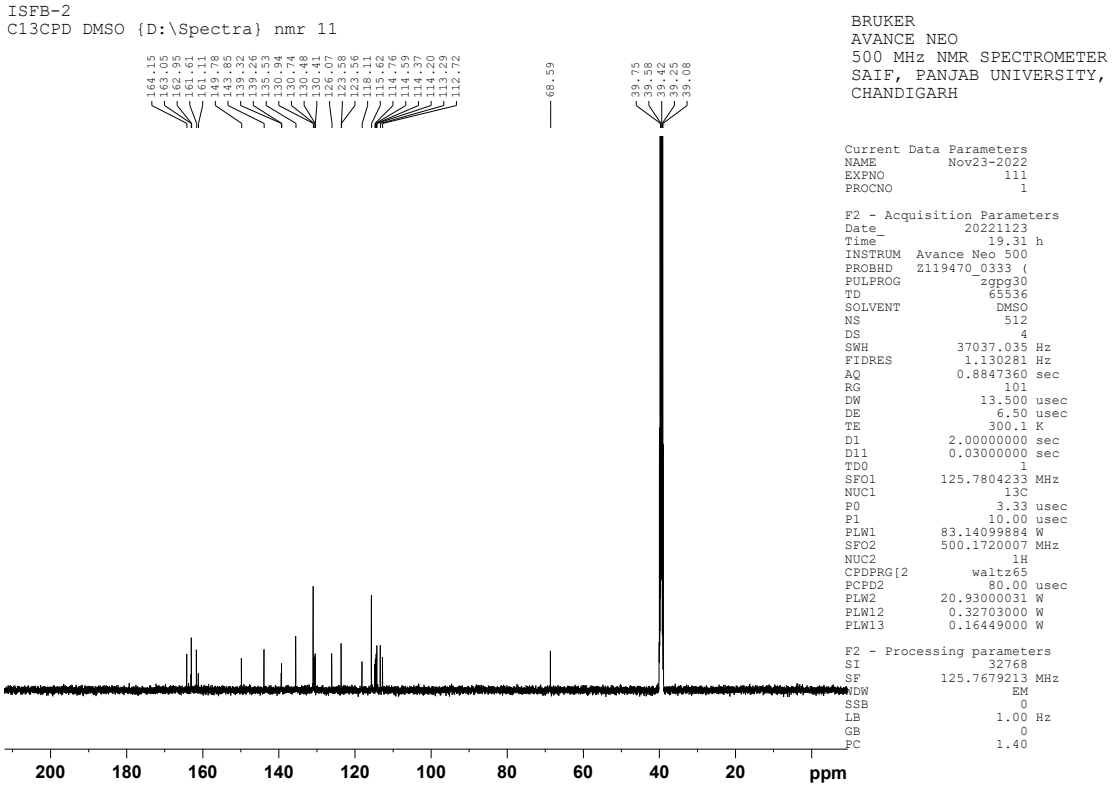
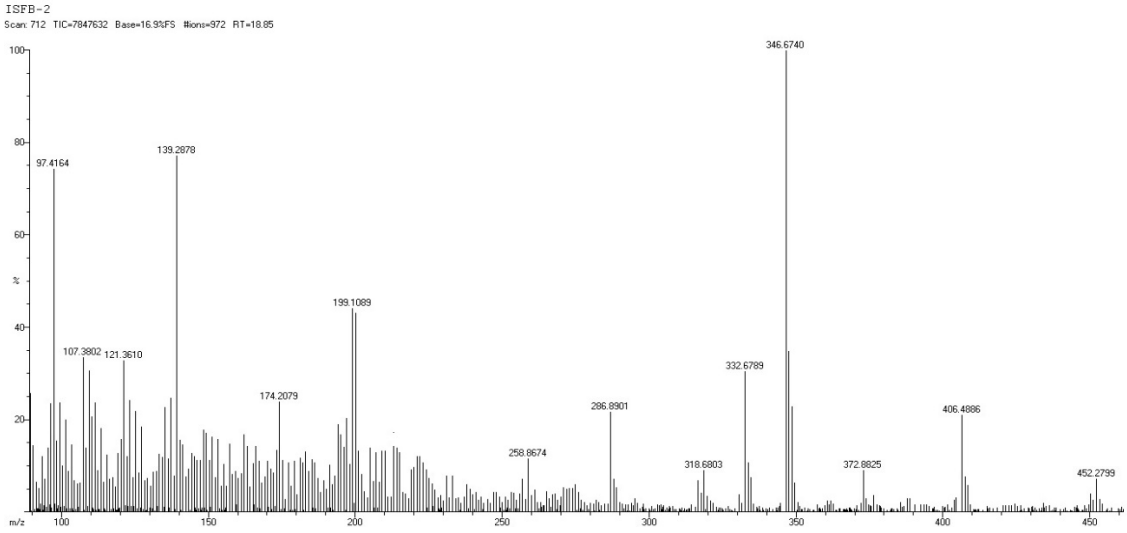
8.4 ^{13}C NMR OF ISFB-2



8.5 MASS SPECTRA OF ISFB-2



8.6 SPECTRAL INTERPRETATION:

*5-bromo-3-((4-((3-fluorobenzyl)oxy)benzylidene)hydrazineylidene)indolin-2-one(**ISFB2**)*:

Dark orange, solid, 68%, melting point. 240± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.98

(s, 1H, NH), 8.68 (s, 1H, =CH-), 8.13-6.87 (m, 11H, ArH), 5.26 (s, 2H, -CH_2-).^{13}C NMR (500 MHz, DMSO-d6) 164.18, 163.08, 162.95, 161.61, 149.78, 143.85, 139.32, 136.83, 130.94, 126.07, 123.58, 118.11, 114.76, 113.29, 112.72, 68.69. Chemical formula $C_{22}H_{15}BrFN_3O_2$. EI-HRMS (m/z): Calculated-452.2799, Observed- 452.2758.

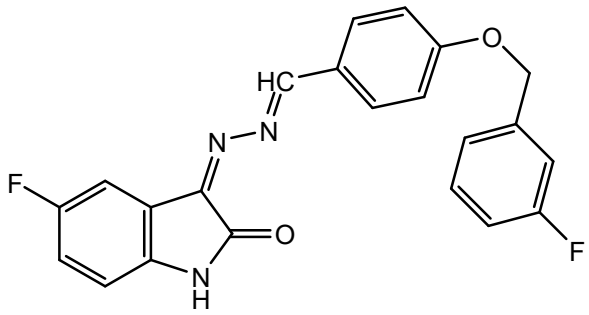
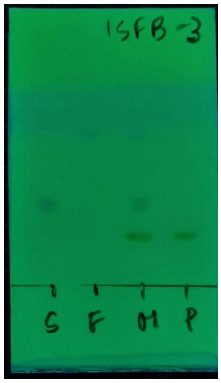


Figure S9. ISFB3 structure

9.1 TLC OF ISFB-3: Mobile phase is Hexane: ethyl acetate (70:30)



9.2 HPLC OF ISFB-3

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isfb3		
Data Filename	: fluoro and bb_05-12-2022_005.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-4	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 1:59:47 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:38:58 PM	Processed by	: System Administrator

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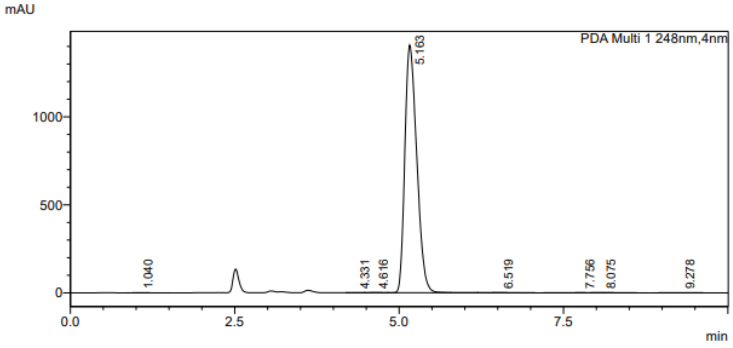
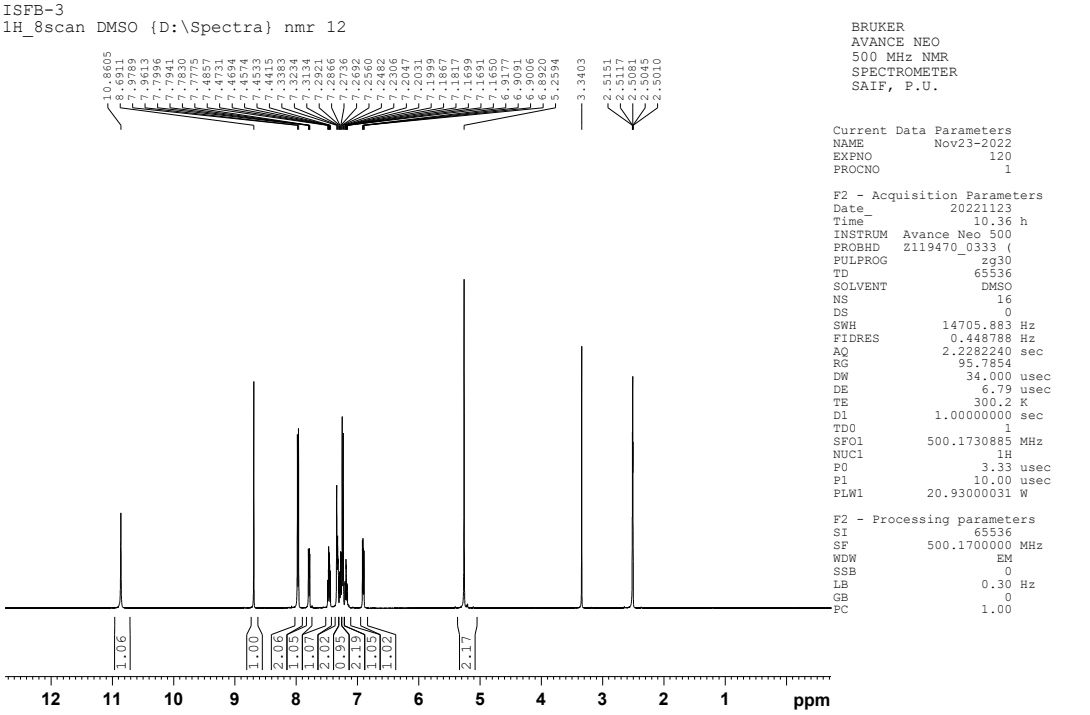


<Peak Table>

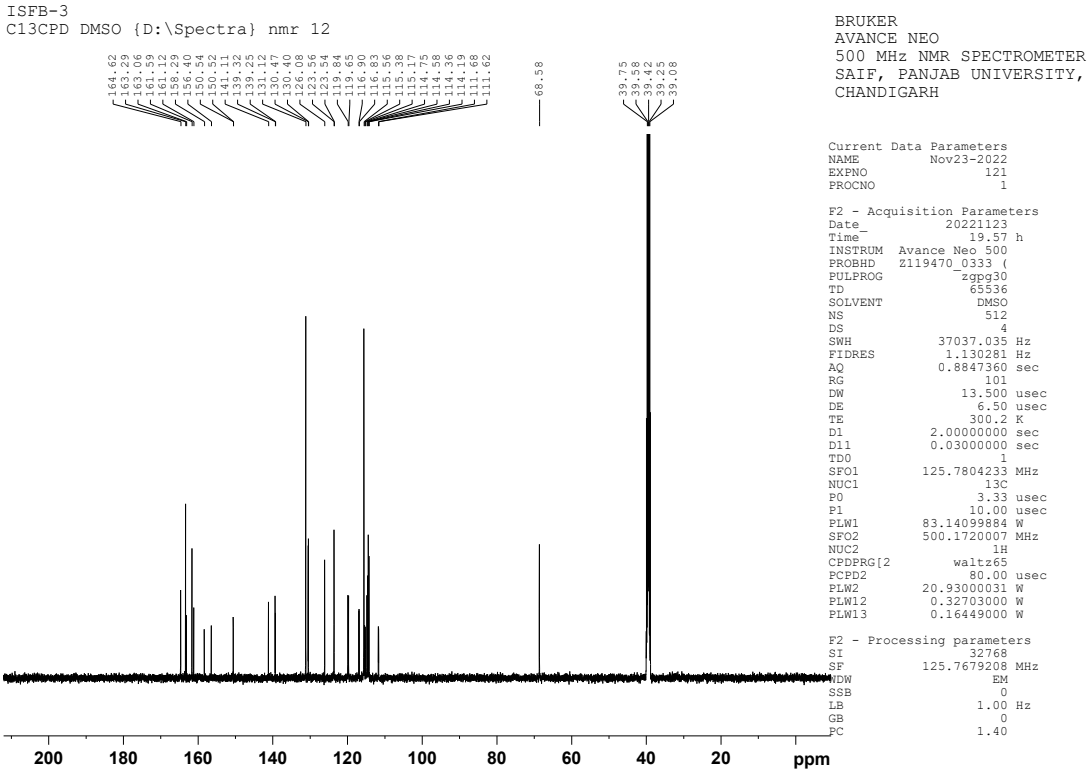
PDA Ch1 248nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	1.040	2803	136	0.016			
2	4.331	1171	138	0.007			
3	4.616	19751	1534	0.110			
4	5.163	17785891	1406472	99.151		V	
5	6.519	35192	1861	0.196		V	
6	7.756	34287	1238	0.191			
7	8.075	44788	2043	0.250		V	
8	9.278	14236	523	0.079			
Total		17938119	1413946				

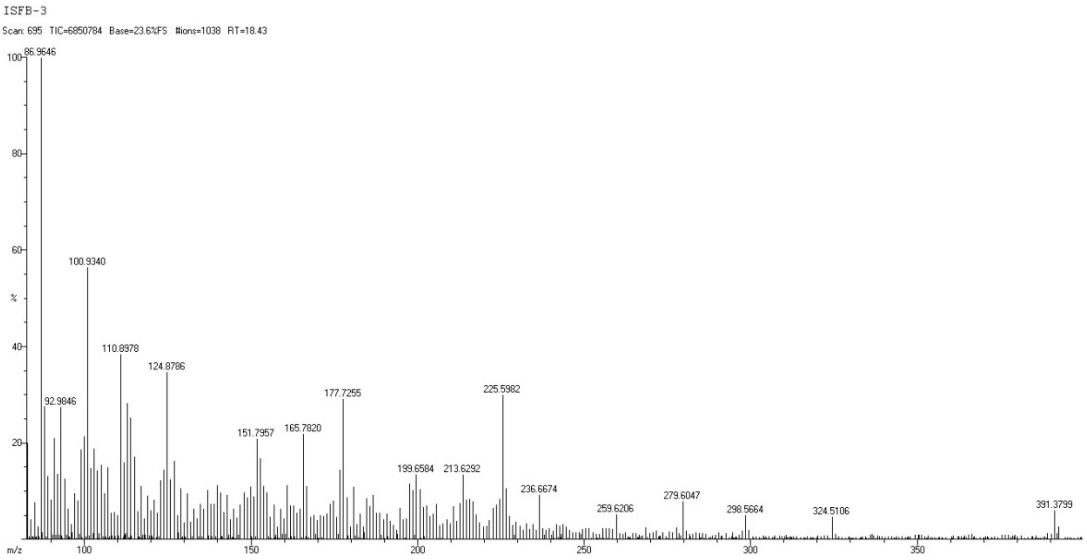
9.3 ^{1}H NMR OF ISFB-3:



9.4 ^{13}C NMR OF ISFB-3:



9.5 MASS SPECTRUM OF ISFB-3:



9.6 SPECTRAL INTERPRETATION:

5-fluoro-3-((4-((3-fluorobenzyl)oxy)benzylidene)hydrazineylidene)indolin-2-one ***(ISFB3)****:* Brick red, solid, 82%, melting point. 230± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.86 (s, 1H, NH), 8.69 (s, 1H, =CH-), 7.97-6.89(m, 11H, ArH), 5.25 (s, 2H, -CH_2-). ^{13}C NMR (500 MHz, DMSO-d6) 164.62, 163.29, 161.89, 158.29, 156.40, 150.54, 141.11, 139.32, 131.12, 130.47, 126.08, 123.86, 119.84, 116.90, 115.66, 114.75, 111.68, 68.58. Chemical formula $C_{22}H_{15}F_2N_3O_2$. EI- HRMS (m/z): Calculated-391.3799, Observed- 391.3702.

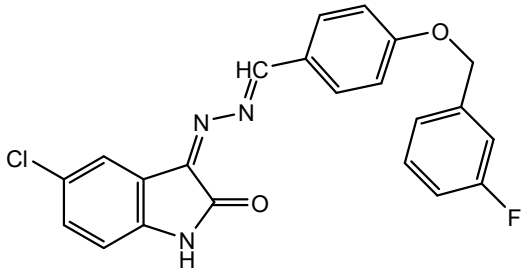
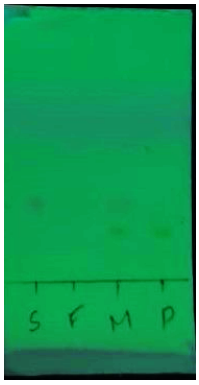


Figure S10. ISFB4 structure

10.1 TLC OF ISFB-4: Mobile phase is Hexane: ethyl acetate (70:30)



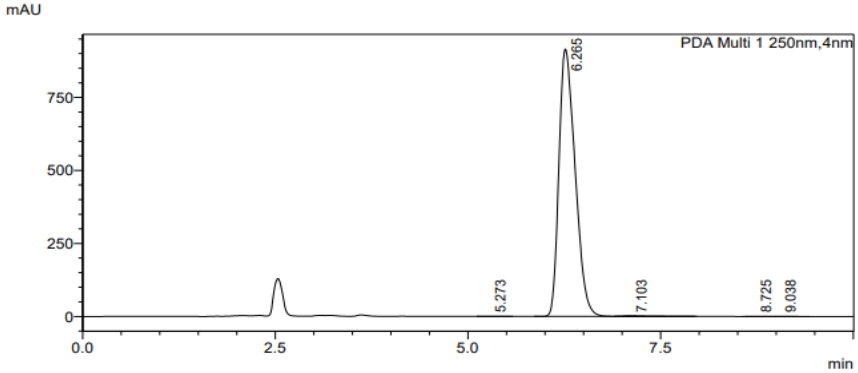
10.2 HPLC OF ISFB-4

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isfb4		
Data Filename	: fluoro and bb_05-12-2022_006.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-5	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 2:10:10 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 4:31:29 AM	Processed by	: System Administrator

<Chromatogram>

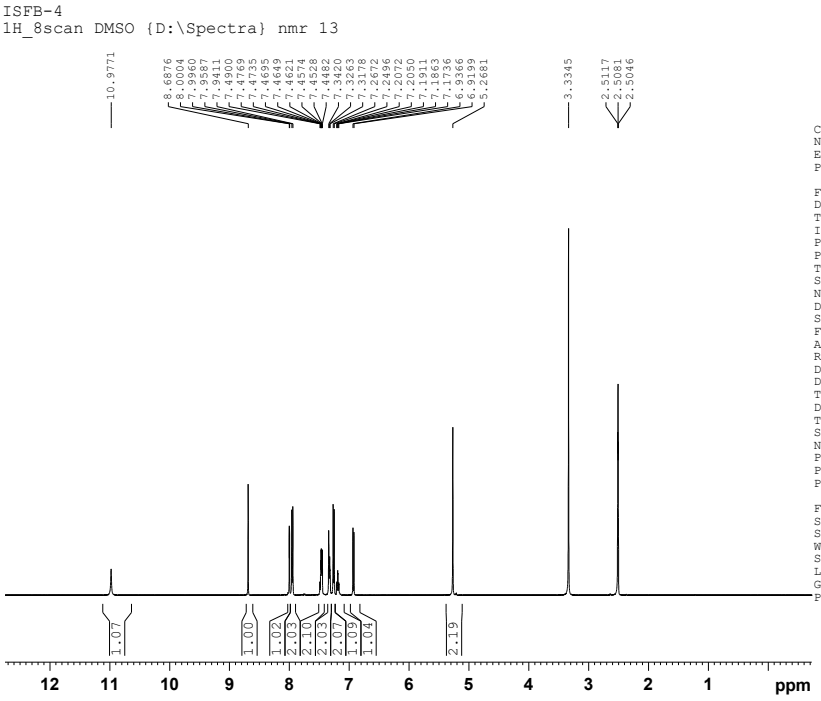


<Peak Table>

PDA Ch1 250nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.273	3583	317	0.027			
2	6.265	13393299	914624	99.620		S	
3	7.103	41061	2069	0.305		T	
4	8.725	2877	172	0.021			
5	9.038	3518	242	0.026		V	
Total		13444337	917424				

10.3 ^{1}H NMR OF ISFB-4

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BRUKER
AVANCE NEO
500 MHz NMR
SPECTROMETER
SAIF, P.U.

Current Data Parameters
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EXPNO                130
PROCNO                 1

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PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     0
SWH            14705.883 Hz
FIDRES          0.448788 Hz
AQ              2.2282240 sec
RG                   101
DW                34.000 usec
DE                 6.79 usec
TE                300.2 K
D1             1.00000000 sec
TD0                    1
SFO1         500.1730885 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         20.93000031 W

F2 - Processing parameters
SI                 65536
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WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
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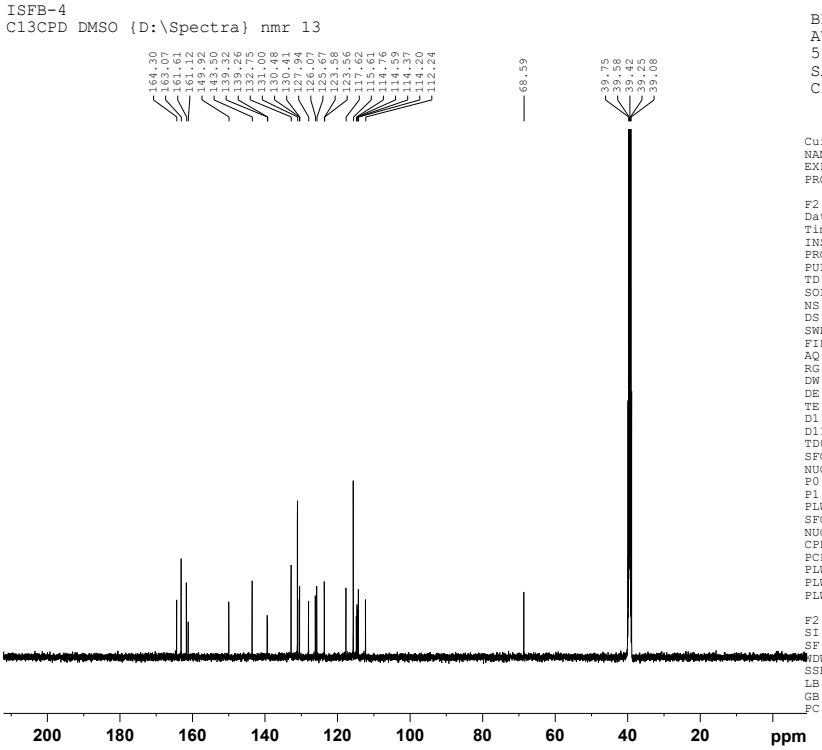
10.4 ^{13}C NMR OF ISFB-4

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BRUKER
AVANCE NEO
500 MHz NMR SPECTROMETER
SAIF, PANJAB UNIVERSITY,
CHANDIGARH

Current Data Parameters
NAME          Nov23-2022
EXPNO                131
PROCNO                 1

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PULPROG          zgpg30
TD                 65536
SOLVENT             DMSO
NS                   512
DS                     4
SWH            37037.035 Hz
FIDRES          1.130281 Hz
AQ              0.8847360 sec
RG                   101
DW                13.500 usec
DE                 6.50 usec
TE                300.1 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1         125.7804233 MHz
NUC1                 13C
P0                 3.33 usec
P1                10.00 usec
PLW1         83.14099884 W
SFO2         500.1720007 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2             80.00 usec
PLW2         20.93000031 W
PLW12         0.32703000 W
PLW13         0.16449000 W

F2 - Processing parameters
SI                 32768
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WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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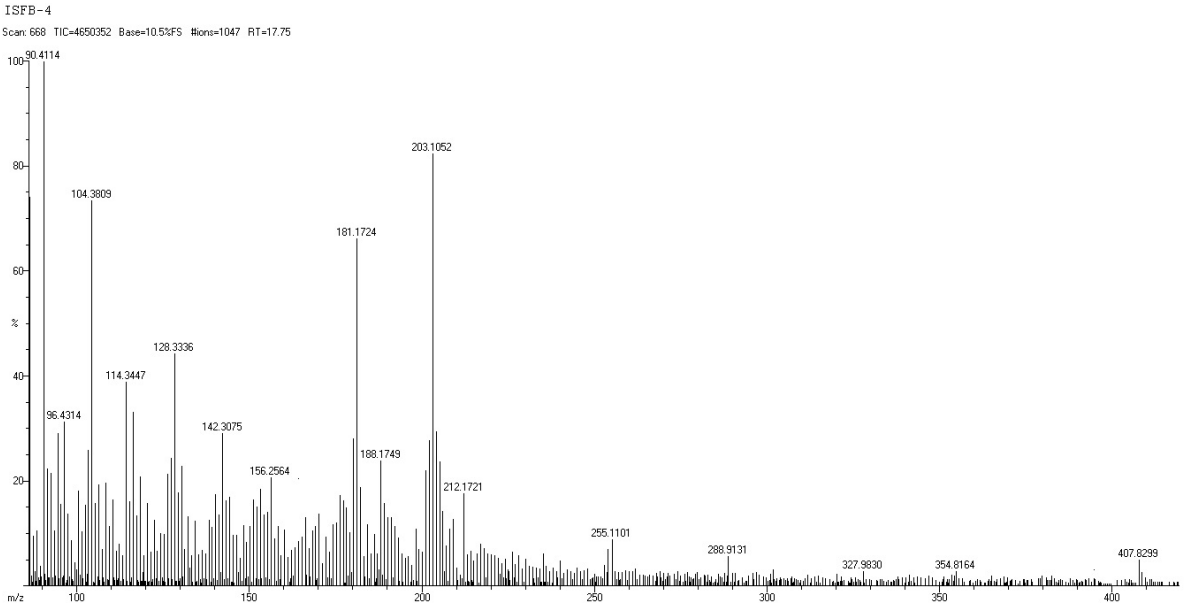
10.5 MASS SPECTRA OF ISFB-4



10.6 SPECTRAL INTERPRETATION:

5-chloro-3-((4-((3-fluorobenzyl)oxy)benzylidene)hydrazineylidene)indolin-2-one ***(ISFB4)****:* Orange, solid, 78%, melting point. 239± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.97 (s, 1H, NH), 8.68 (s, 1H, =CH-), 8.00-6.91 (m, 11H, ArH), 5.26 (s, 2H, -CH_2-).^{13}C NMR (500 MHz, DMSO-d6) 164.30, 163.07, 161.61, 149.92, 143.60, 139.32, 132.76, 131.00, 130.46, 127.94, 126.07, 125.67, 123.66, 117.62, 116.61, 114.76, 112.24, 68.69. Chemical formula $C_{22}H_{15}ClFN_3O_2$. EI- HRMS (m/z): Calculated-407.8299, Observed- 407.8248.

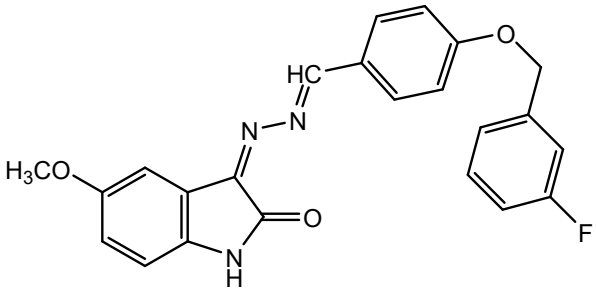
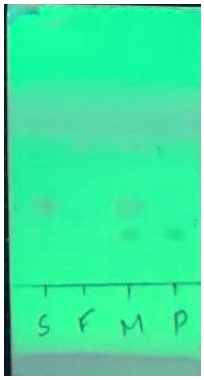


Figure S11. ISFB5 structure

11.1 TLC OF ISFB-5: Mobile phase is Hexane: ethyl acetate (70:30)



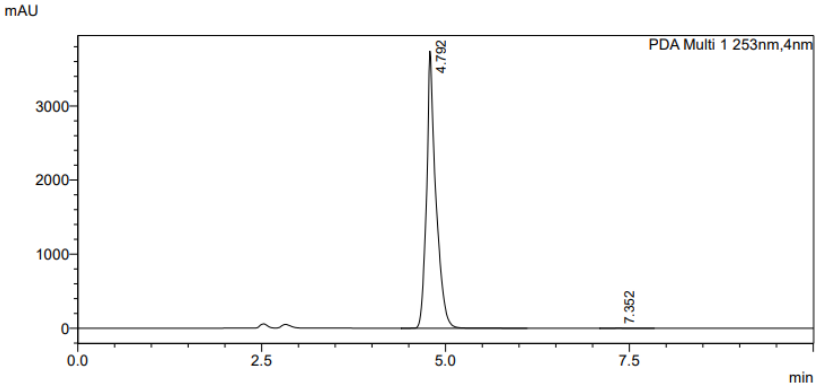
11.2 HPLC OF ISFB-5

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isfb5		
Data Filename	: fluoro and bb_05-12-2022_007.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-6	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 2:20:31 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 4:33:15 AM	Processed by	: System Administrator

<Chromatogram>

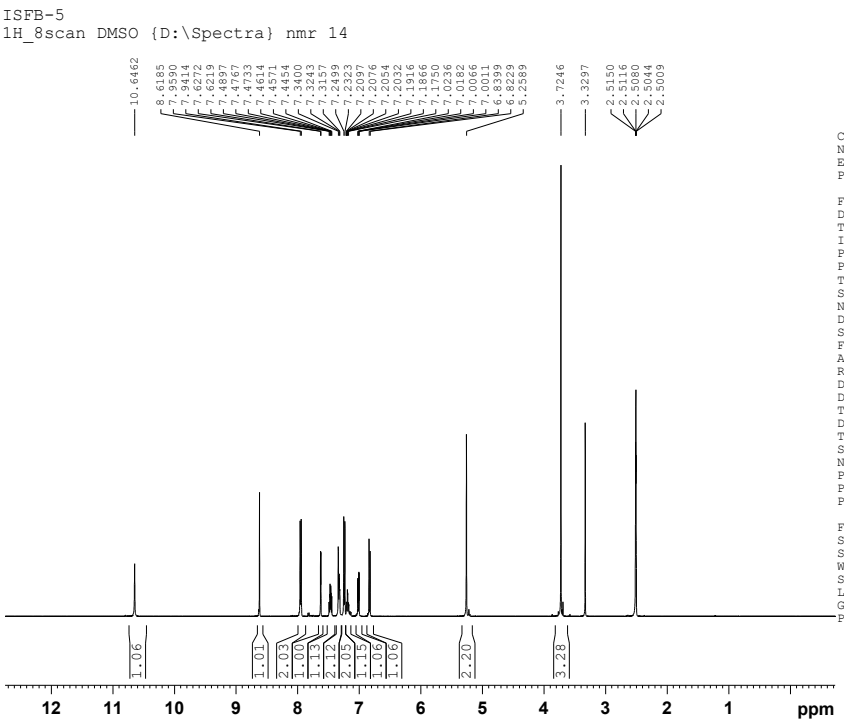


<Peak Table>

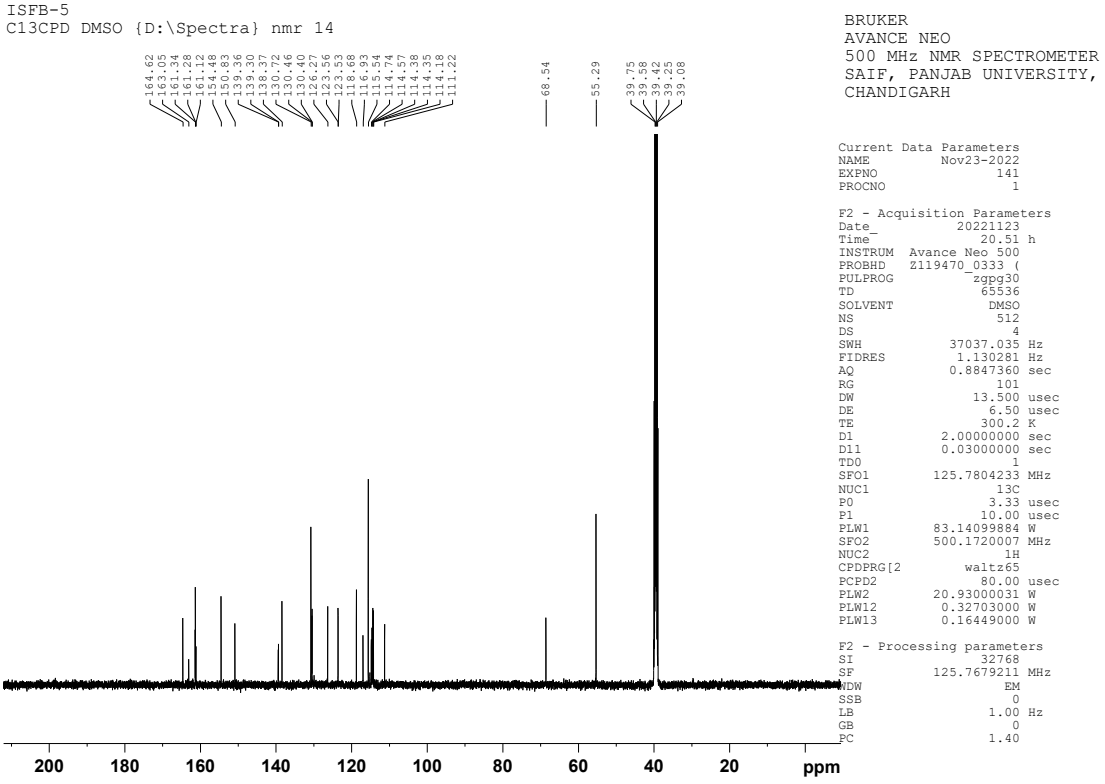
PDA Ch1 253nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.792	33082034	3741328	99.973			
2	7.352	8796	486	0.027			
Total		33090830	3741814				

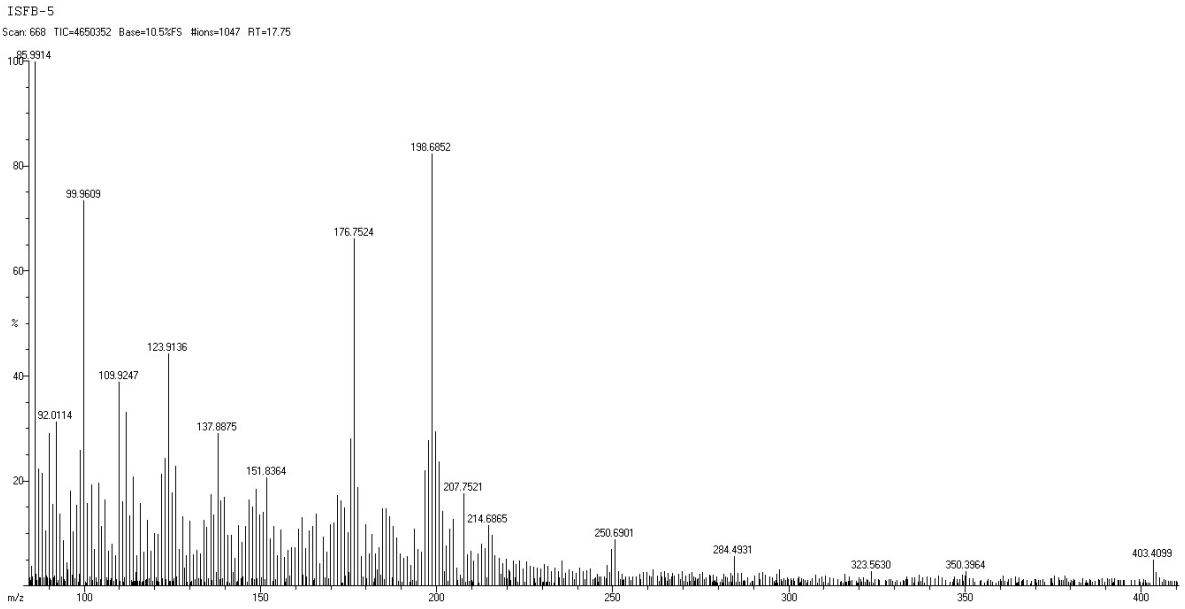
11.3 ^{1}H NMR OF ISFB-5



11.4 ^{13}C NMR OF ISFB-5



11.5 MASS SPECTRA OF ISFB-5



11.6 SPECTRAL INTERPRETATION:

3-((4-((3-fluorobenzyl)oxy)benzylidene)hydrazineylidene)-5-methoxyindolin-2-one ***(ISFB5)****:* Brown, solid, 76%, melting point. 195± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.64 (s, 1H, NH), 8.61 (s, 1H, =CH-), 7.95-6.82 (m, 11H, ArH), 5.25 (s, 2H, -CH_2-), 3.72 (s, 3H, -CH_2-Ar). ^{13}C NMR (500 MHz, DMSO-d6) 164.62, 163.05, 161.34, 154.48, 150.83, 139.36, 138.37, 130.72, 126.27, 123.56, 118.68, 116.93, 115.54, 114.74, 111.22, 68.54, 55.29. Chemical formula $C_{23}H_{18}FN_3O_3$. EI- HRMS (m/z): Calculated-403.4099, Observed- 403.4057.

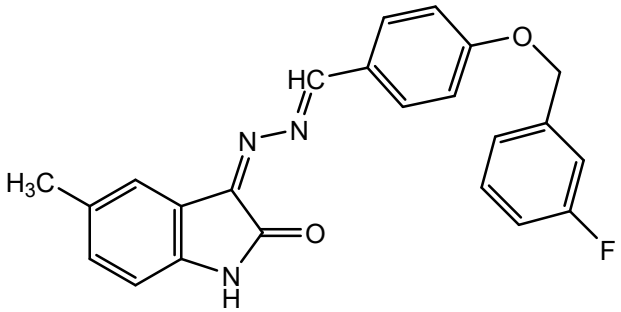


Figure S12. ISFB6 structure

12.1 TLC OF ISFB-6: Mobile phase is Hexane: ethyl acetate (70:30)

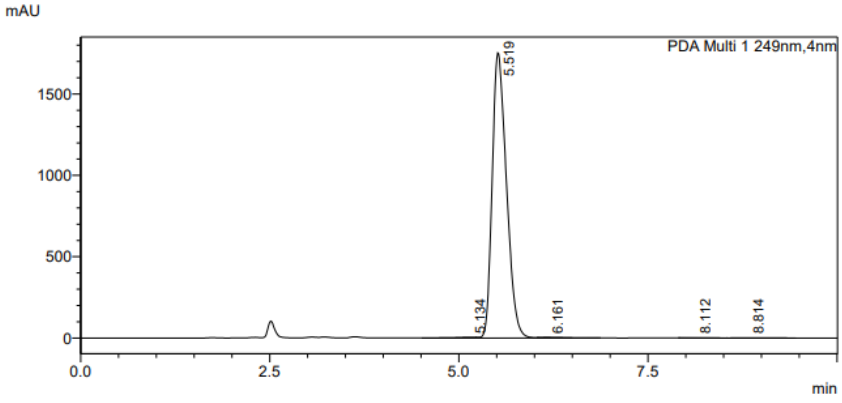
12.2 HPLC OF ISFB-6

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isfb6		
Data Filename	: fluoro and bb_05-12-2022_008.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-7	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 2:30:53 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 4:38:13 AM	Processed by	: System Administrator

<Chromatogram>



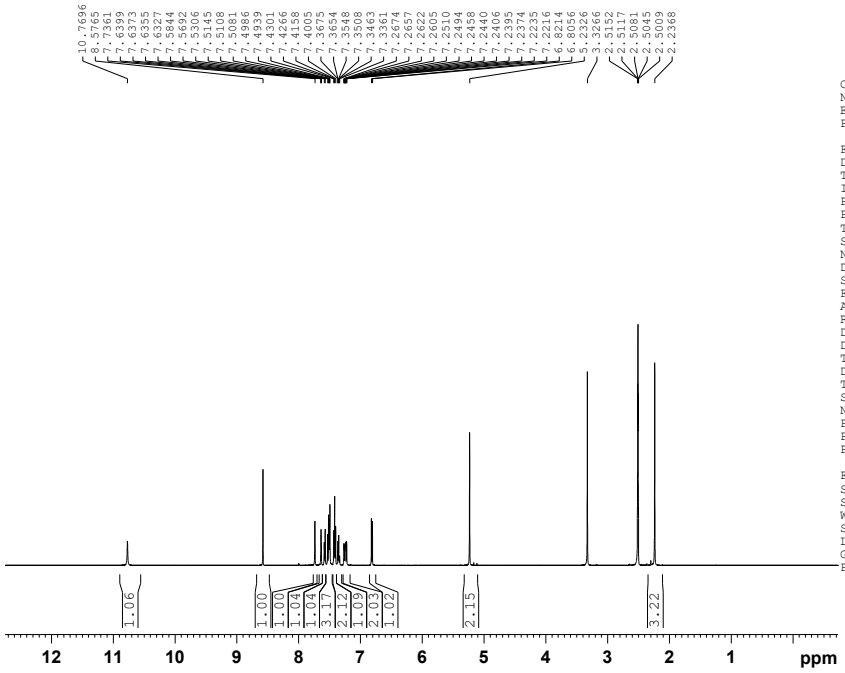
<Peak Table>

PDA Ch1 249nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.134	95496	4313	0.412			
2	5.519	23026214	1752400	99.437		SV	
3	6.161	17833	1371	0.077		T	
4	8.112	4803	293	0.021			
5	8.814	12300	497	0.053			
Total		23156646	1758873				

12.3 ^{1}H NMR OF ISFB-6

ISFB-6
1H_8scan DMSO {D:\Spectra} nmr 15



BRUKER
AVANCE NEO
500 MHz NMR
SPECTROMETER
SAIF, P.U.

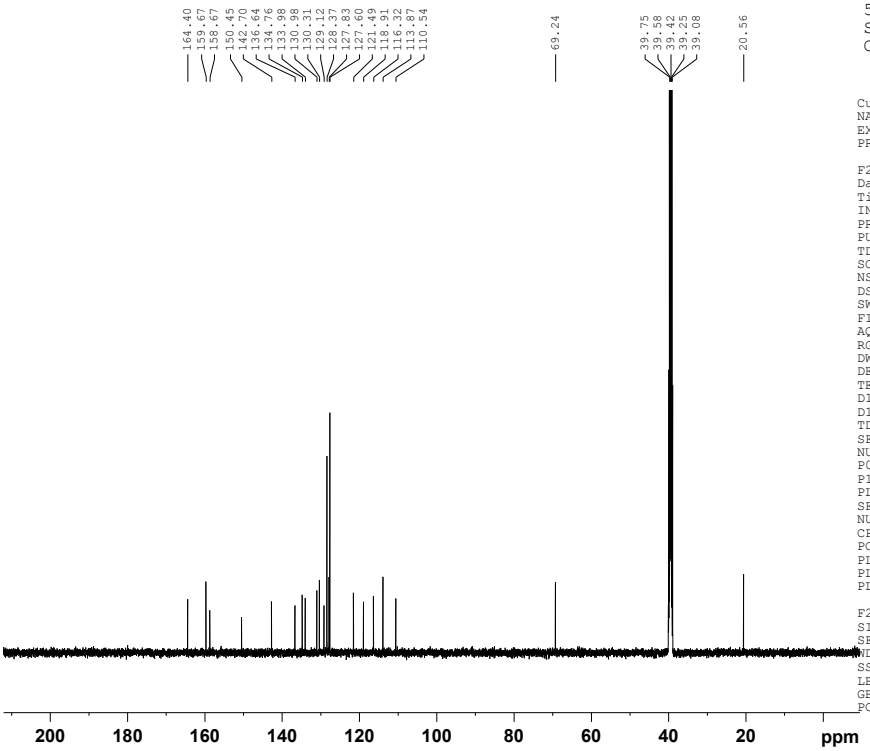
Current Data Parameters
NAME Nov23-2022
EXPNO 150
PROCNO 1

F2 - Acquisition Parameters
Date_ 20221123
Time 10.44 h
INSTRUM Avance Neo 500
PROBHD Z119470_0333 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 0
SWH 14705.883 Hz
FIDRES 0.448788 Hz
AQ 2.2282240 sec
RG 101
DW 34.000 usec
DE 6.79 usec
TE 300.2 K
D1 1.00000000 sec
TD0 1
SFO1 500.1730885 MHz
NUC1 1H
P0 3.33 usec
P1 10.00 usec
PLW1 20.93000031 W

F2 - Processing parameters
SI 65536
SF 500.1700000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

12.4 ^{13}C NMR OF ISFB-6

ISFB-6
C13CPD DMSO {D:\Spectra} nmr 15



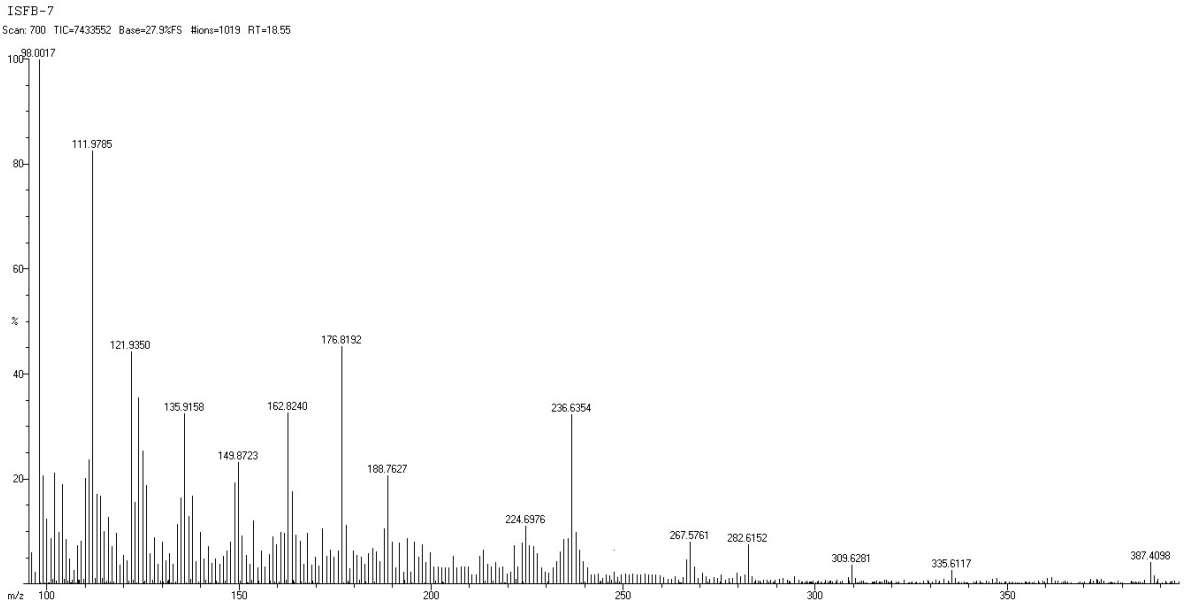
BRUKER
AVANCE NEO
500 MHz NMR SPECTROMETER
SAIF, PANJAB UNIVERSITY,
CHANDIGARH

Current Data Parameters
NAME Nov23-2022
EXPNO 151
PROCNO 1

F2 - Acquisition Parameters
Date_ 20221123
Time 21.18 h
INSTRUM Avance Neo 500
PROBHD Z119470_0333 (
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 512
DS 4
SWH 37037.035 Hz
FIDRES 1.130281 Hz
AQ 0.8847360 sec
RG 101
DW 13.500 usec
DE 6.50 usec
TE 300.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 125.7804233 MHz
NUC1 13C
P0 3.33 usec
P1 10.00 usec
PLW1 83.14099884 W
SFO2 500.1720007 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 80.00 usec
PLW2 20.93000031 W
PLW12 0.32703000 W
PLW13 0.16449000 W

F2 - Processing parameters
SI 32768
SF 125.7679213 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

12.5 MASS SPECTRA OF ISFB-6



12.6 SPECTRAL INTERPRETATION

3-((4-((3-fluorobenzyl)oxy)benzylidene)hydrazineylidene)-5-methylindolin-2-one ***(ISFB6)****:* Orange, solid, 88%, melting point. 212± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.76 (s, 1H, NH), 8.57 (s, 1H, =CH-), 7.73-6.80 (m, 11H, ArH), 5.23 (s, 2H, -CH_2-),2.23 (s, 3H, -CH_2-Ar). ^{13}C NMR (500 MHz, DMSO-d6) 164.40, 169.67, 168.67, 160.48, 142.70, 136.64, 134.76, 133.96, 130.98, 129.12, 128.37, 127.60, 121.49, 118.91, 116.32, 113.87, 110.54, 69.24, 20.56. Chemical formula $C_{23}H_{18}FN_3O_2$. EI- HRMS (m/z): Calculated-387.4098, Observed- 387.4063.

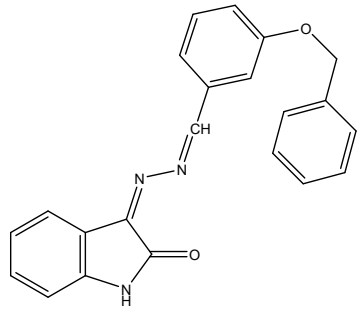
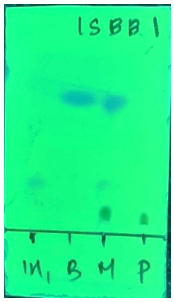


Figure S13. ISBB1 structure

13.1 TLC OF ISBB-1: Mobile phase is Hexane: ethyl acetate (70:30)



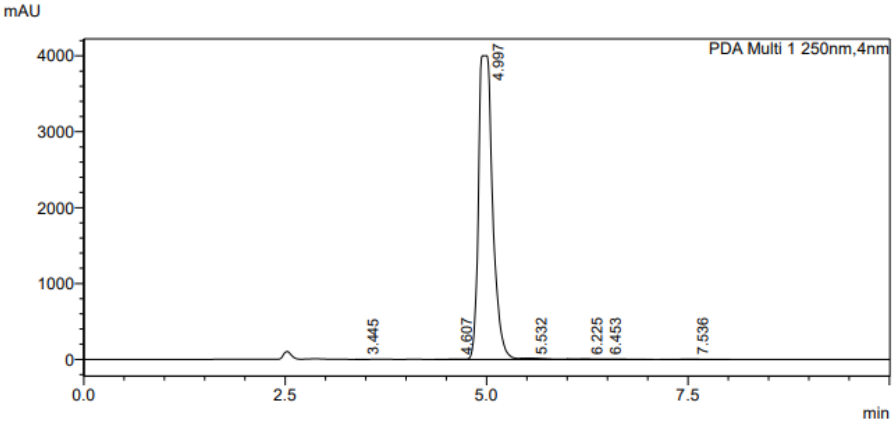
13.2 HPLC OF ISBB-1

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isbb1		
Data Filename	: fluoro and bb_05-12-2022_009.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-8	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 2:41:16 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 4:41:09 AM	Processed by	: System Administrator

<Chromatogram>



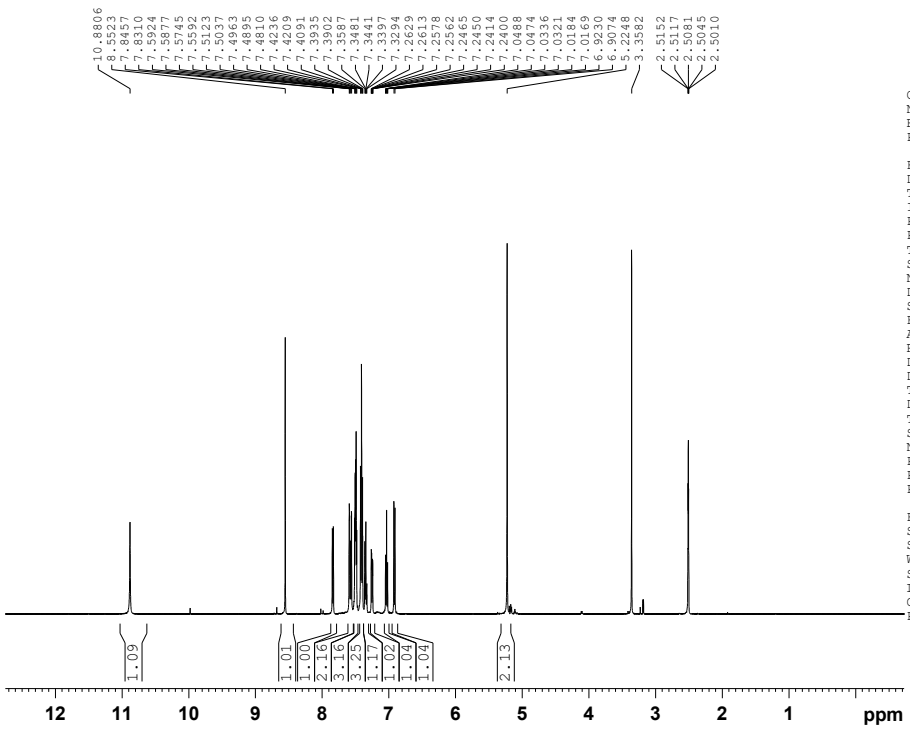
<Peak Table>

PDA Ch1 250nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	3.445	1931	228	0.004			
2	4.607	6937	500	0.014			
3	4.997	48906742	3999836	99.630		SV	
4	5.532	79091	7379	0.161		T	
5	6.225	51237	3427	0.104		T	
6	6.453	29557	2266	0.060		TV	
7	7.536	12683	558	0.026			
Total		49088178	4014195				

13.3 ^{1}H NMR OF ISBB-1

ISBB-1
1H_8scan DMSO {D:\Spectra} nmr 16

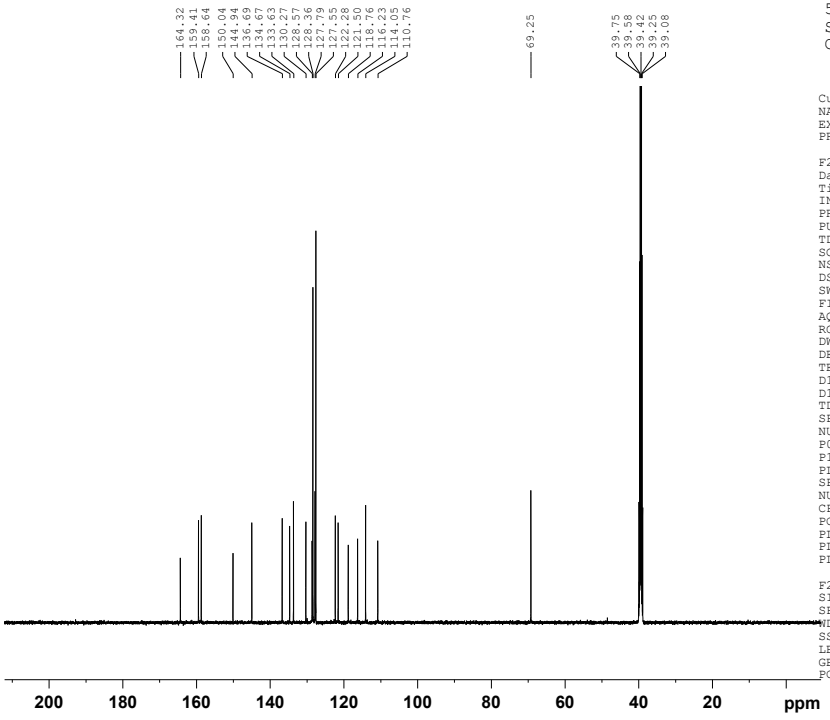


BRUKER
AVANCE NEO
500 MHz NMR
SPECTROMETER
SAIF, P.U.

Current Data Parameters	
NAME	Nov23-2022
EXPNO	160
PROCNO	1
F2 - Acquisition Parameters	
Date_	20221123
Time	10.46 h
INSTRUM	Avance Neo 500
PROBHD	Z119470_0333 (
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	16
DS	0
SWH	14705.883 Hz
FIDRES	0.448788 Hz
AQ	2.2282240 sec
RG	95.7854
DW	34.000 usec
DE	6.79 usec
TE	300.2 K
D1	1.00000000 sec
TD0	1
SFO1	500.1730885 MHz
NUC1	1H
P0	3.33 usec
P1	10.00 usec
PLW1	20.93000031 W
F2 - Processing parameters	
SI	65536
SF	500.1700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

13.4 ^{13}C NMR OF ISBB-1

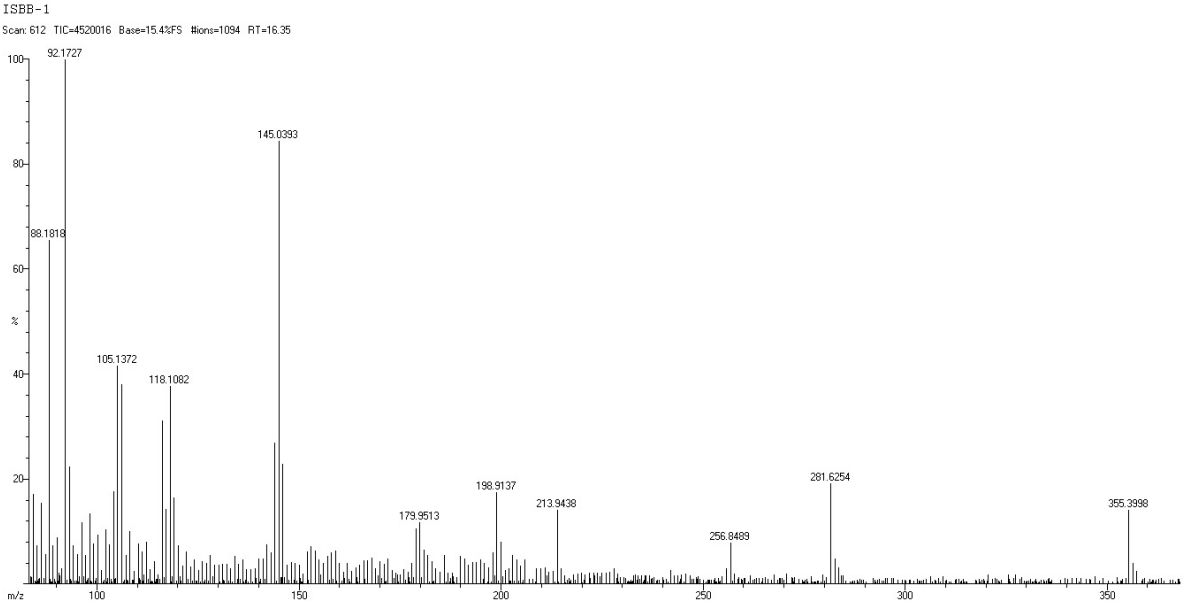
ISBB-1
C13CPD DMSO {D:\Spectra} nmr 16



BRUKER
AVANCE NEO
500 MHz NMR SPECTROMETER
SAIF, PANJAB UNIVERSITY,
CHANDIGARH

Current Data Parameters	
NAME	Nov23-2022
EXPNO	161
PROCNO	1
F2 - Acquisition Parameters	
Date_	20221123
Time	21.44 h
INSTRUM	Avance Neo 500
PROBHD	Z119470_0333 (
PULPROG	zgpg30
TD	65536
SOLVENT	DMSO
NS	512
DS	4
SWH	37037.035 Hz
FIDRES	1.130281 Hz
AQ	0.8847360 sec
RG	101
DW	13.500 usec
DE	6.50 usec
TE	300.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7804233 MHz
NUC1	13C
P0	3.33 usec
P1	10.00 usec
PLW1	83.14099884 W
SFO2	500.1720007 MHz
NUC2	1H
CPDPRG[2	waltz65
PCPD2	80.00 usec
PLW2	20.93000031 W
PLW12	0.32703000 W
PLW13	0.16449000 W
F2 - Processing parameters	
SI	32768
SF	125.7679210 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

13.5 MASS SPECTRA OF ISBB-1



13.6 SPECTRAL INTERPRETATION:

*3-((3-(benzyloxy)benzylidene)hydrazineylidene)indolin-2-one(**ISBB1**): **):*** Dark red, solid, 78%, melting point. 228± 2˚C.^{1}H NMR (500 MHz, DMSO-d6) δ: 10.88 (s, 1H, NH), 8.55 (s, 1H, =CH-), 7.84-6.90 (m, 13H, ArH), 5.22(s, 2H, -CH_2-). ^{13}C NMR (500 MHz, DMSO-d6) δ: 164.32, 159.41, 158.64, 160.04, 144.94, 136.69, 134.37, 133.63, 130.27, 128.57, 127.79, 122.28, 121.80, 116.76, 114.06, 110.76, 69.28. Chemical formula $C_{22}H_{17}N_3O_2$. EI- HRMS (m/z): Calculated-355.3998, Observed- 355.3998.

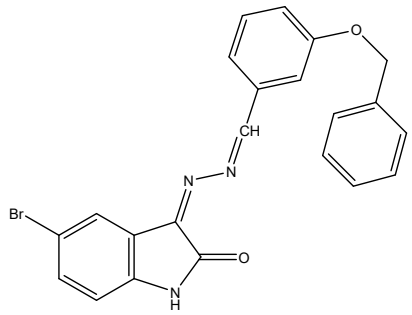


Figure S14. ISBB2 structure

14.1 TLC OF ISBB-2: Mobile phase is Hexane: ethyl acetate (70:30)

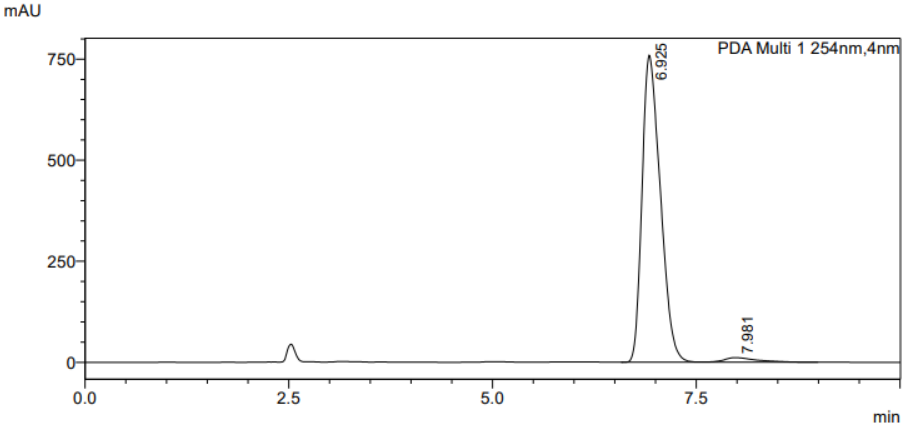
14.2 HPLC OF ISBB-2

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isbb2		
Data Filename	: fluoro and bb_05-12-2022_010.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-9	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 2:51:39 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:45:14 PM	Processed by	: System Administrator

<Chromatogram>

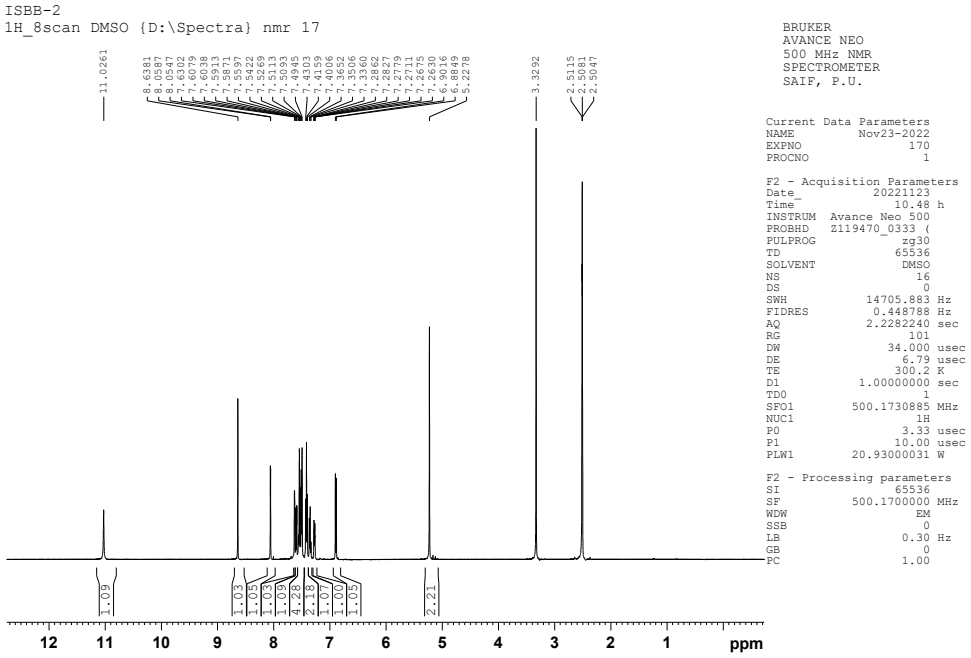


<Peak Table>

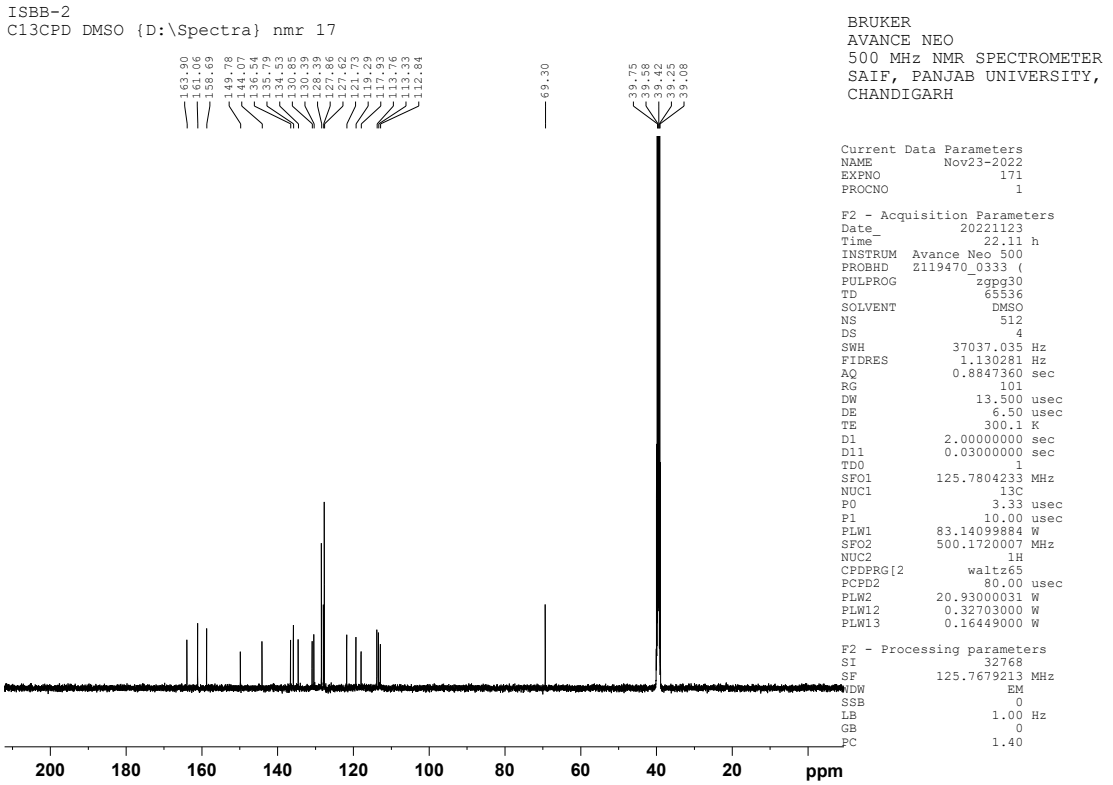
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.925	11885761	759058	97.327			
2	7.981	326456	11494	2.673		V	
Total		12212217	770551				

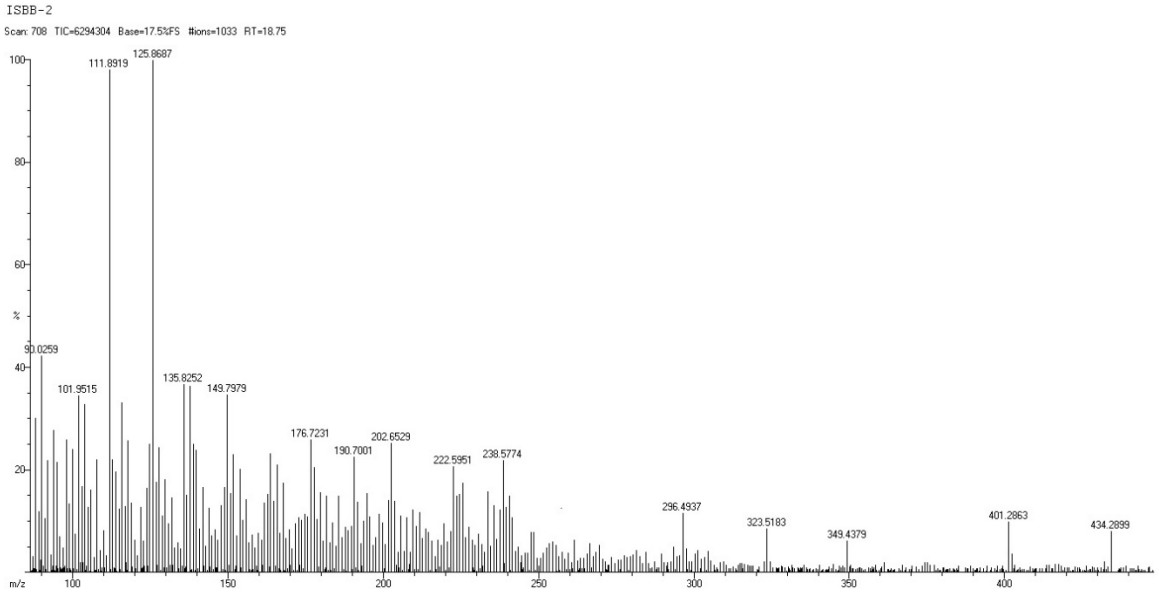
14.3 ^{1}H NMR OF ISBB-2



14.4 ^{13}C NMR OF ISBB-2



14.5 MASS SPECTRA OF ISBB-2



14.6 SPECTRAL INTERPRETATION:

*3-((3-(benzyloxy)benzylidene)hydrazineylidene)-5-bromoindolin-2-one(**ISBB2):*** Orange, solid, 69%, melting point. 235± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 11.02 (s, 1H, NH), 8.63 (s, 1H, =CH-), 8.05-6.88 (m, 12H, ArH), 5.22(s, 2H, -CH_2-)^{13}C NMR (500 MHz, DMSO-d6) 163.90, 161.06, 158.69, 149.78, 144.07, 136.64, 135.79, 134.53, 130.85, 128.39, 127.62, 121.62, 119.29, 117.93, 113.76, 112.84, 69.30. Chemical formula $C_{22}H_{16}BrN_3O_2$. EI- HRMS (m/z): Calculated-434.2899, Observed- 434.2853.

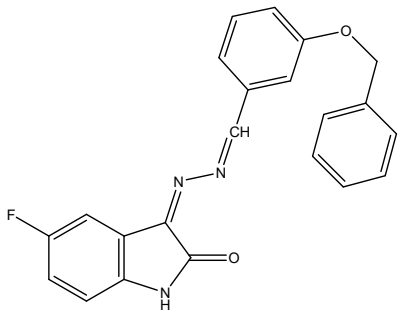
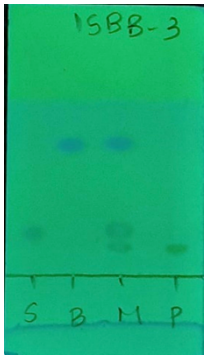


Figure S15. ISBB3 structure

15.1 TLC OF ISBB-3: Mobile phase is Hexane: ethyl acetate (70:30)



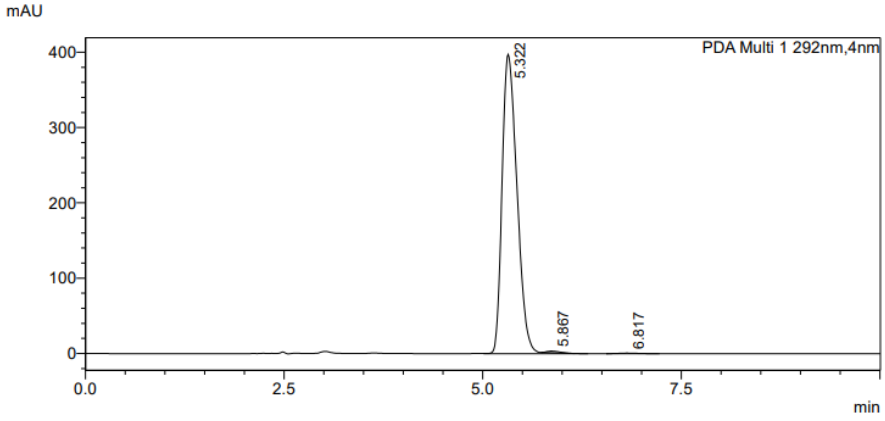
15.2 HPLC OF ISBB-3

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isbb3		
Data Filename	: fluoro and bb_05-12-2022_011.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-10	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 3:02:02 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:25:05 PM	Processed by	: System Administrator

<Chromatogram>



<Peak Table>

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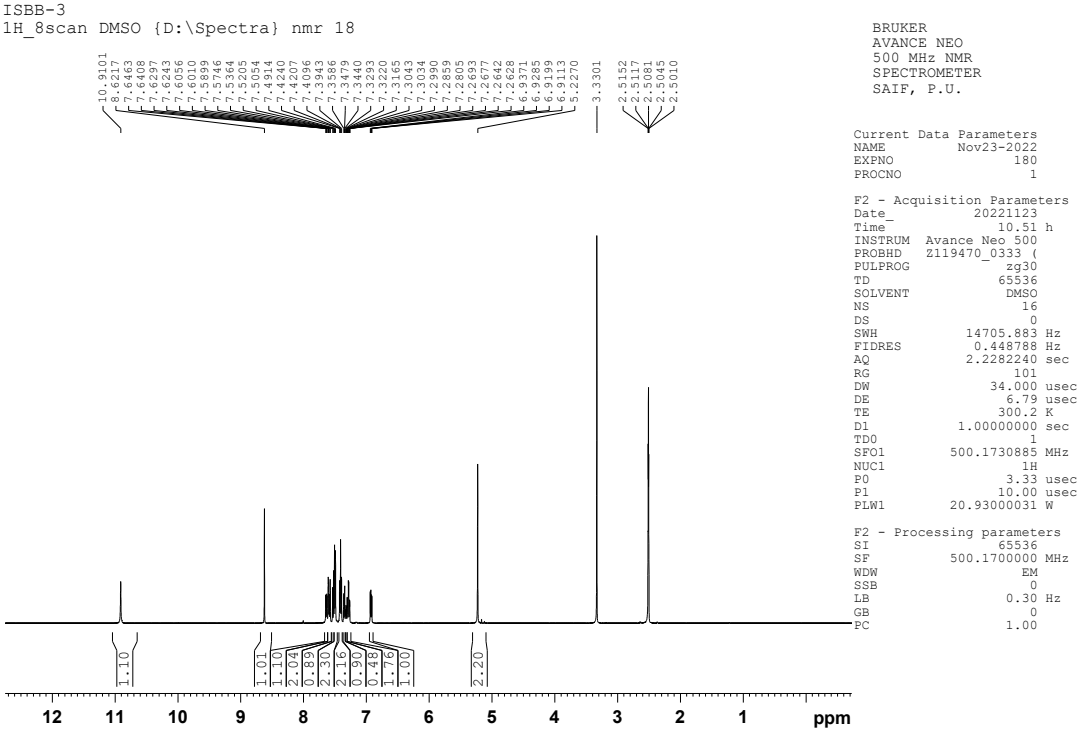
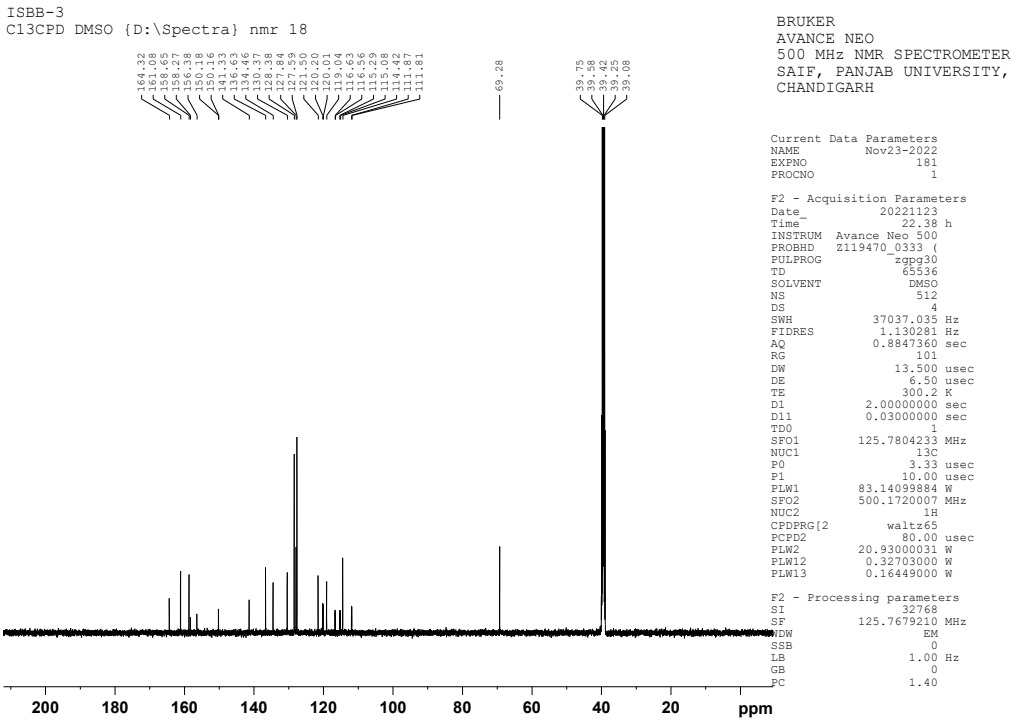
2	5.867	24549	2149	0.470		T	
3	6.817	10723	673	0.205			
Total		5222621	399970				

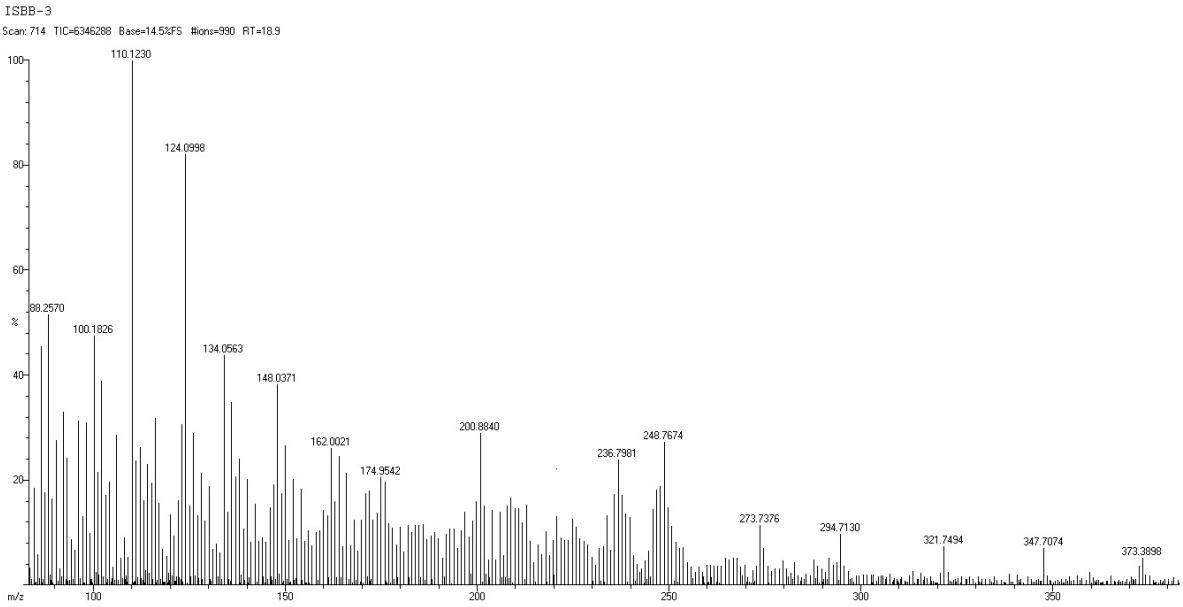
15.3 ^{1}H NMR OF ISBB-3



15.4 ^{13}C NMR OF ISBB-3



15.5 MASS SPECTRUM OF ISBB-3



15.6 SPECTRAL INTERPRETATION

3-((3-(benzyloxy)benzylidene)hydrazineylidene)-5-fluoroindolin-2-one***(ISBB3):*** Orange, solid, 86%, melting point. 210± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 11.02 (s, 1H, NH), 8.63 (s, 1H, =CH-), 8.05-6.88 (m, 12H, ArH), 5.22(s, 2H, -CH_2-). ^{13}C NMR (500 MHz, DMSO-d6) 164.32, 161.08, 158.68, 156.38, 150.18, 141.33, 136.63, 134.46, 130.37, 128.38, 127.64, 121.50, 120.20, 119.04, 116.63, 115.29,114.42, 111.87, 69.28. Chemical formula $C_{22}H_{16}FN_3O_2$. EI- HRMS (m/z): Calculated-373.3898, Observed- 373.3898.

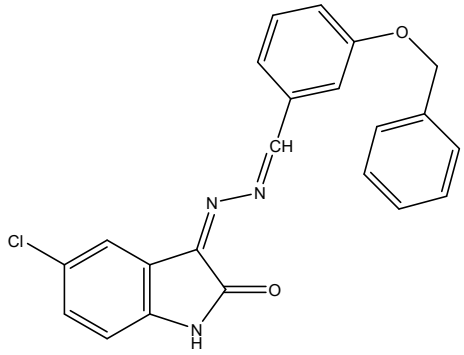
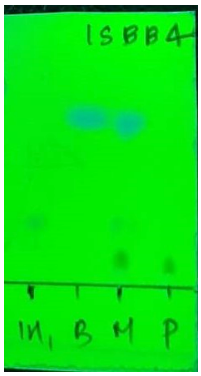


Figure S11. ISBB4 structure

16.1 TLC OF ISBB-4: Mobile phase is Hexane: ethyl acetate (70:30)



16.2 HPLC OF ISBB-4

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isbb4		
Data Filename	: fluoro and bb_05-12-2022_012.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-11	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 3:12:23 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:28:55 PM	Processed by	: System Administrator

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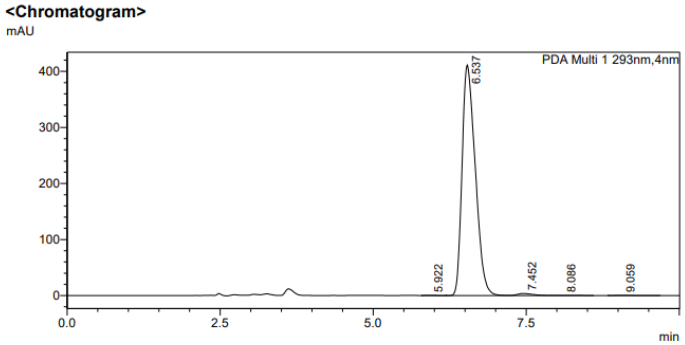
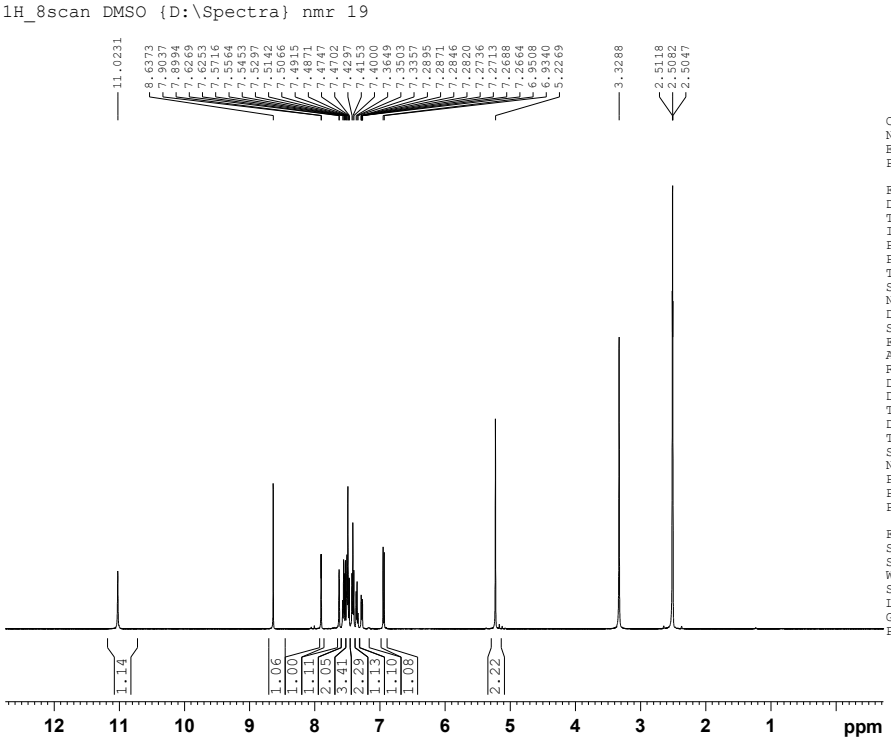


<Peak Table>

PDA Ch1 293nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.922	1629	151	0.026			
2	6.537	6186172	411063	98.701			
3	7.452	66173	3677	1.056		V	
4	8.086	8112	374	0.129		V	
5	9.059	5478	256	0.087			
Total		6267564	415521				

16.3 ^{1}H NMR OF ISBB-4

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BRUKER
AVANCE NEO
500 MHz NMR
SPECTROMETER
SAIF, P.U.

Current Data Parameters
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EXPNO                190
PROCNO                 1

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TD                 65536
SOLVENT             DMSO
NS                    16
DS                     0
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FIDRES          0.448788 Hz
AQ              2.2282240 sec
RG                   101
DW                34.000 usec
DE                 6.79 usec
TE                300.2 K
D1             1.00000000 sec
TD0                    1
SFO1         500.1730885 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         20.93000031 W

F2 - Processing parameters
SI                 65536
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WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
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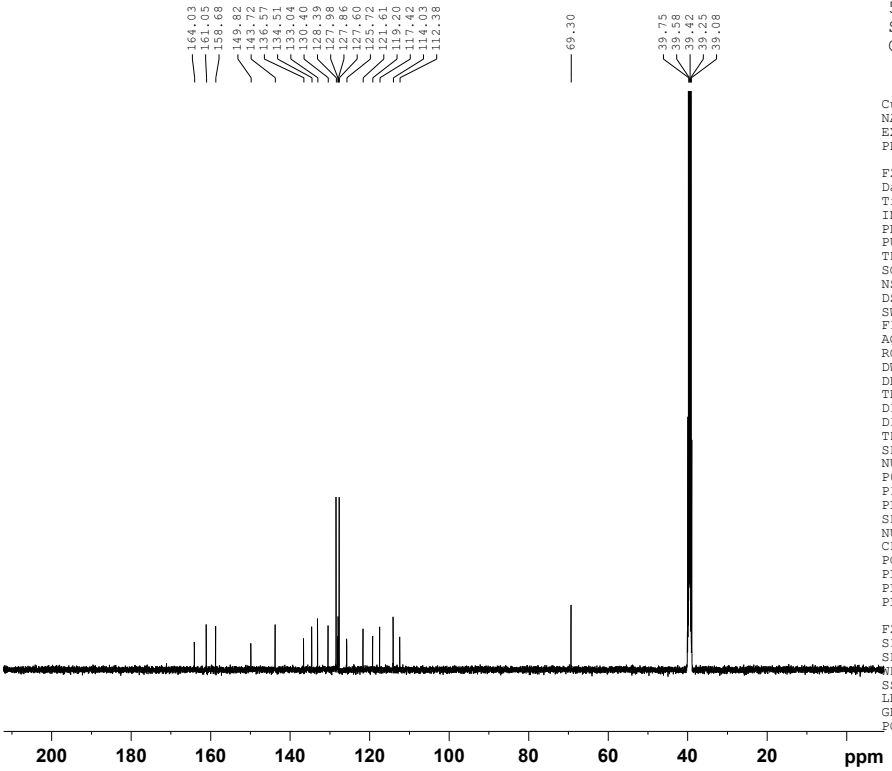
16.4 ^{13}C NMR OF ISBB-4

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BRUKER
AVANCE NEO
500 MHz NMR SPECTROMETER
SAIF, PANJAB UNIVERSITY,
CHANDIGARH

Current Data Parameters
NAME          Nov23-2022
EXPNO                191
PROCNO                 1

F2 - Acquisition Parameters
Date_           20221123
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PULPROG          zgpg30
TD                 65536
SOLVENT             DMSO
NS                   512
DS                     4
SWH            37037.035 Hz
FIDRES          1.130281 Hz
AQ              0.8847360 sec
RG                   101
DW                13.500 usec
DE                 6.50 usec
TE                300.2 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1         125.7804233 MHz
NUC1                  13C
P0                  3.33 usec
P1                 10.00 usec
PLW1         83.14099884 W
SFO2         500.1720007 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              80.00 usec
PLW2         20.93000031 W
PLW12         0.32703000 W
PLW13         0.16449000 W

F2 - Processing parameters
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WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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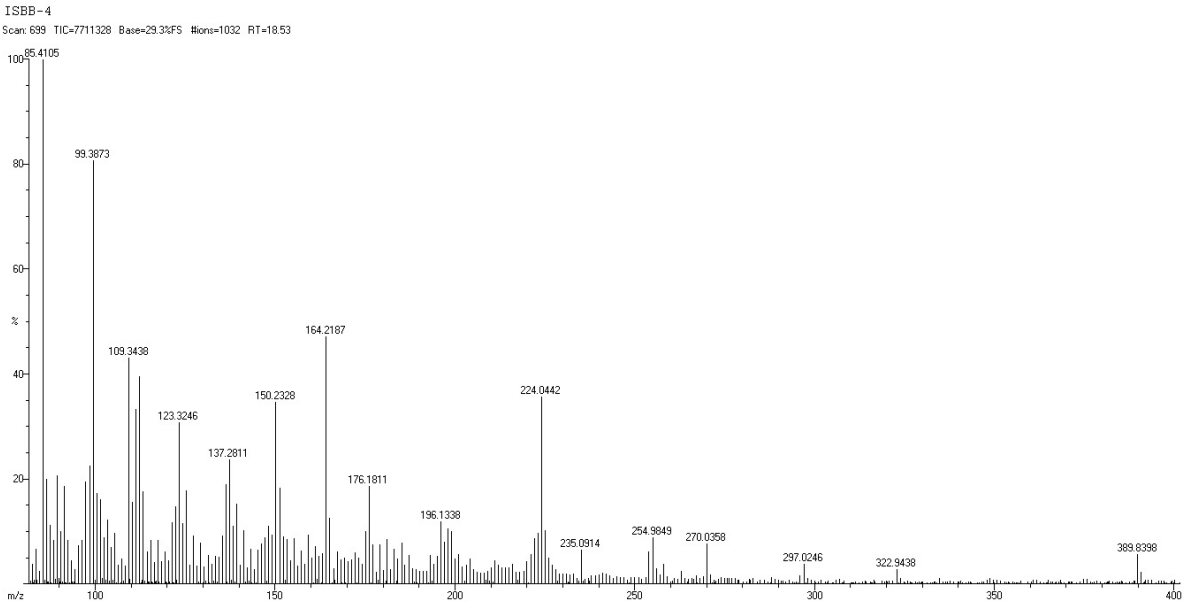
16.5 MASS SPECTRA OF ISBB-4



16.6 SPECTRAL INTERPRETATION

*3-((3-(benzyloxy)benzylidene)hydrazineylidene)-5-chloroindolin-2-one(**ISBB4):*** Orange, solid, 84%, melting point. 240± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 11.02 (s, 1H, NH), 8.63 (s, 1H, =CH-), 7.90-6.93 (m, 12H, ArH), 5.22(s, 2H, -CH_2-) ^{13}C NMR (500 MHz, DMSO-d6) 164.03, 161.05, 158.68, 149.82, 143.72, 136.67, 134.51, 133.04, 130.40, 128.39, 127.98, 126.72, 121.61, 119.20, 117.42, 114.03, 112.36, 69.30. Chemical formula $C_{22}H_{16}ClN_3O_2$. EI- HRMS (m/z): Calculated-389.8398, Observed- 389.8343.

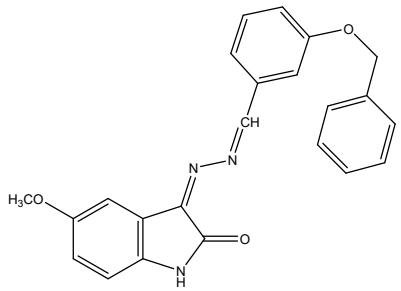


Figure S17. ISBB5 structure

17.1 TLC OF ISBB-5: Mobile phase is Hexane: ethyl acetate (70:30)

17.2 HPLC OF ISBB-5

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isbb5		
Data Filename	: fluoro and bb_05-12-2022_013.lcd		
Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-12	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
Date Acquired	: 12/5/2022 3:22:44 AM	Acquired by	: System Administrator
Date Processed	: 12/6/2022 10:32:39 PM	Processed by	: System Administrator

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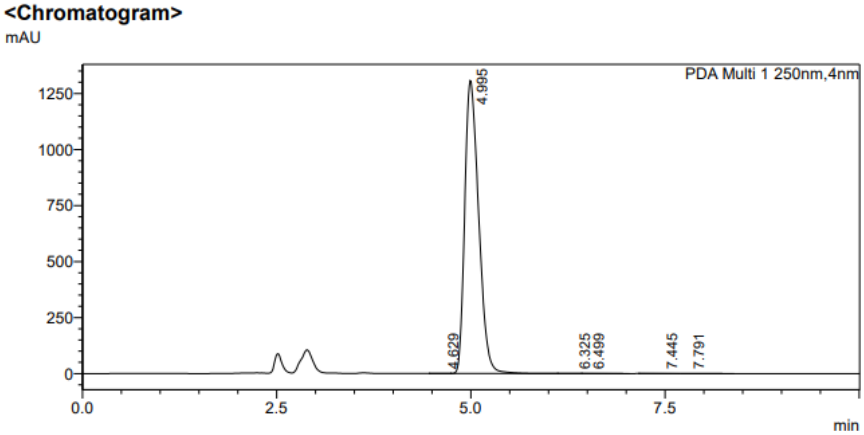
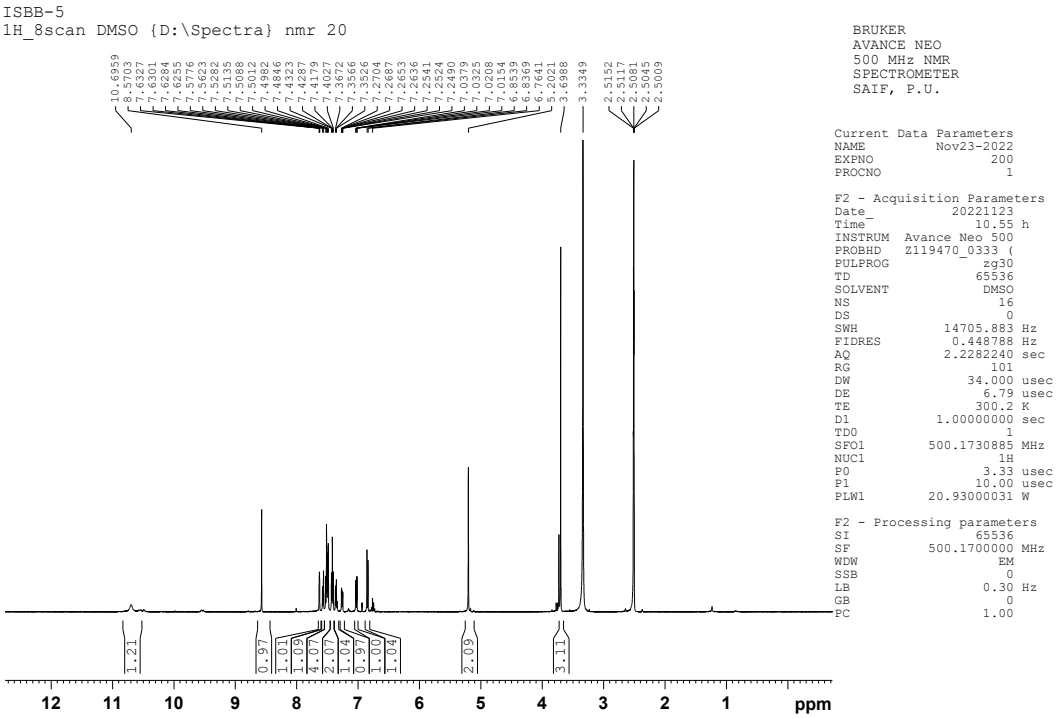


<Peak Table>

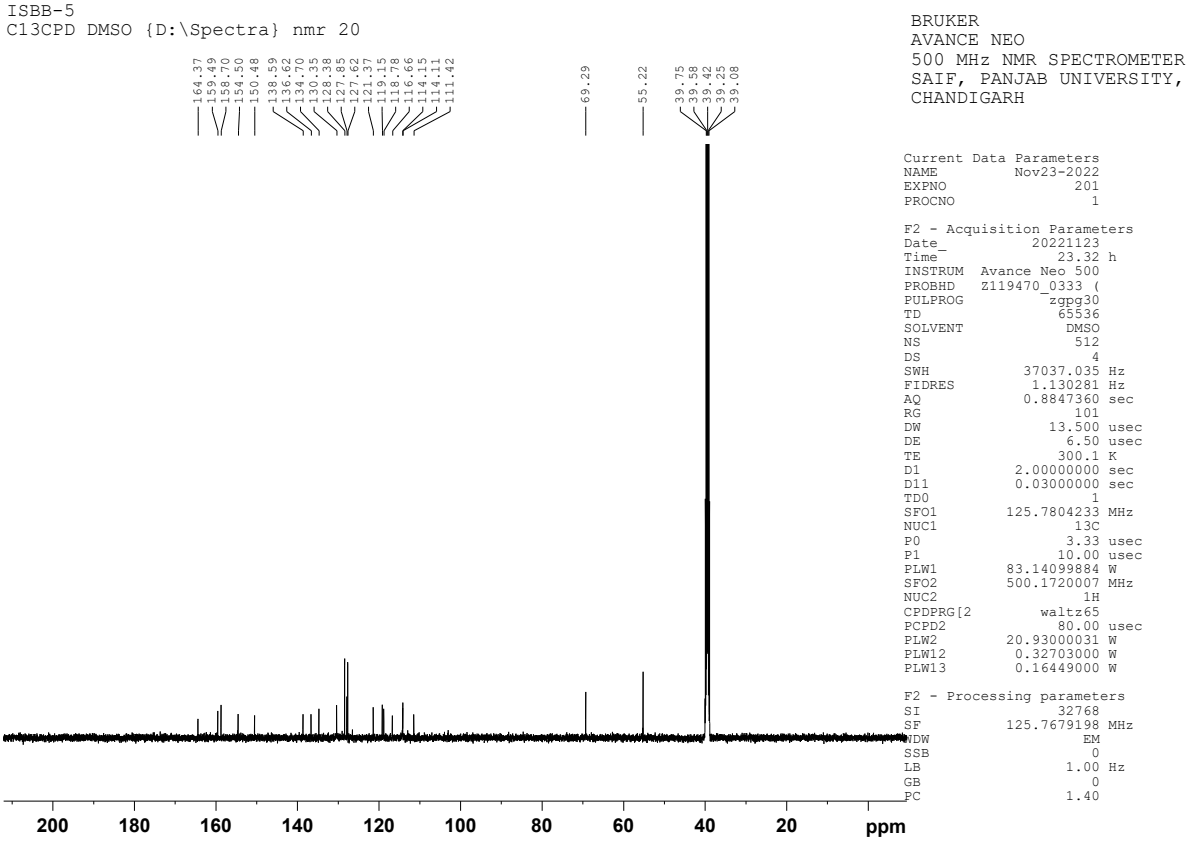
PDA Ch1 250nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4.629	1507	161	0.009			
2	4.995	16269042	1306541	99.815		V	
3	6.325	4976	433	0.031			
4	6.499	7545	537	0.046		V	
5	7.445	7884	340	0.048			
6	7.791	8321	429	0.051		V	
Total		16299275	1308441				

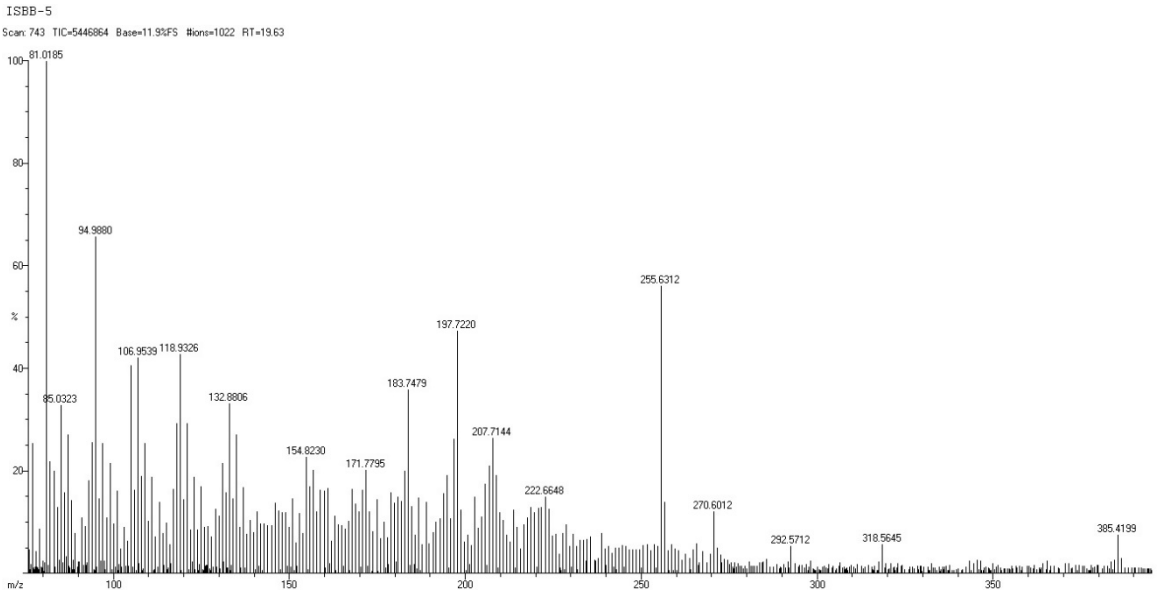
17.3 ^{1}H NMR OF 1SBB-5



17.4 ^{13}C NMR OF ISBB-5



17.5 MASS SPECTRA OF ISBB-5



17.6 SPECTRAL INTERPRETATION

*3-((3-(benzyloxy)benzylidene)hydrazineylidene)-5-methoxyindolin-2-one(**ISBB5**):* Dark brown, solid, 68%, melting point. 218± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.69 (s, 1H, NH), 8.57 (s, 1H, =CH-), 7.63-6.76(m, 12H, Ar-H), 5.20 (s, 2H, -CH_2-), 3.69 (s, 3H, -CH_2-Ar).). ^{13}C NMR (500 MHz, DMSO-d6)164.37, 159.49, 158.70, 154.80, 150.48, 138.89, 136.62, 134.70, 130.36, 128.36, 127.85, 121.37, 119.18, 118.78, 116.66, 114.15, 111.42, 69.29, 55.22. Chemical formula $C_{23}H_{19}N_3O_3$. EI- HRMS (m/z): Calculated-385.4199, Observed- 385.4152.

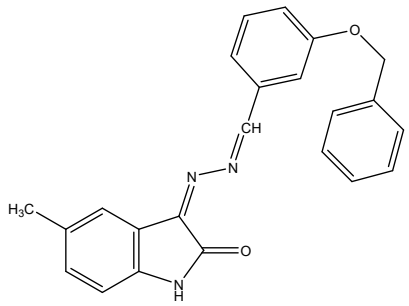
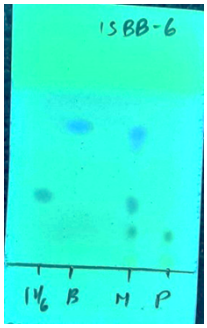


Figure S18. ISBB6 structure

18.1 TLC OF ISBB-6: Mobile phase is Hexane: ethyl acetate (70:30)



18.2 HPLC OF ISBB-6

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: isatin001		
Sample ID	: isbb6		
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Method Filename	: isatin.lcm		
Batch Filename	: fluoro and bb.lcb		
Vial #	: 1-13	Sample Type	: Standard
Injection Volume	: 20 uL	Level	: 1
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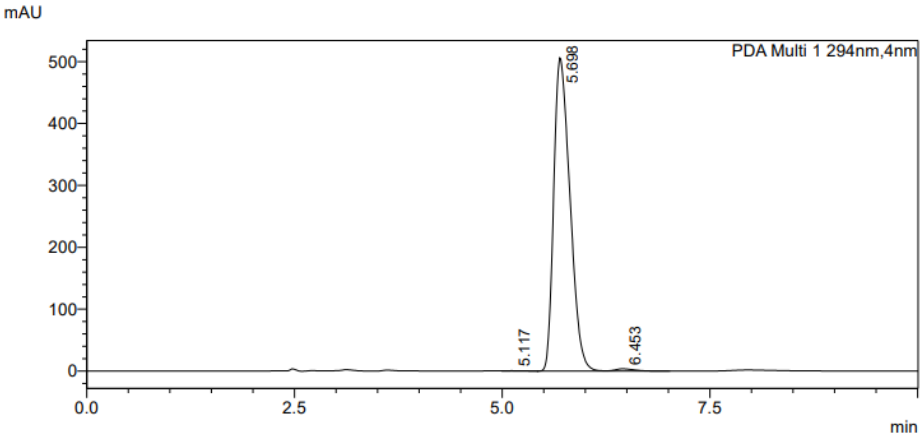
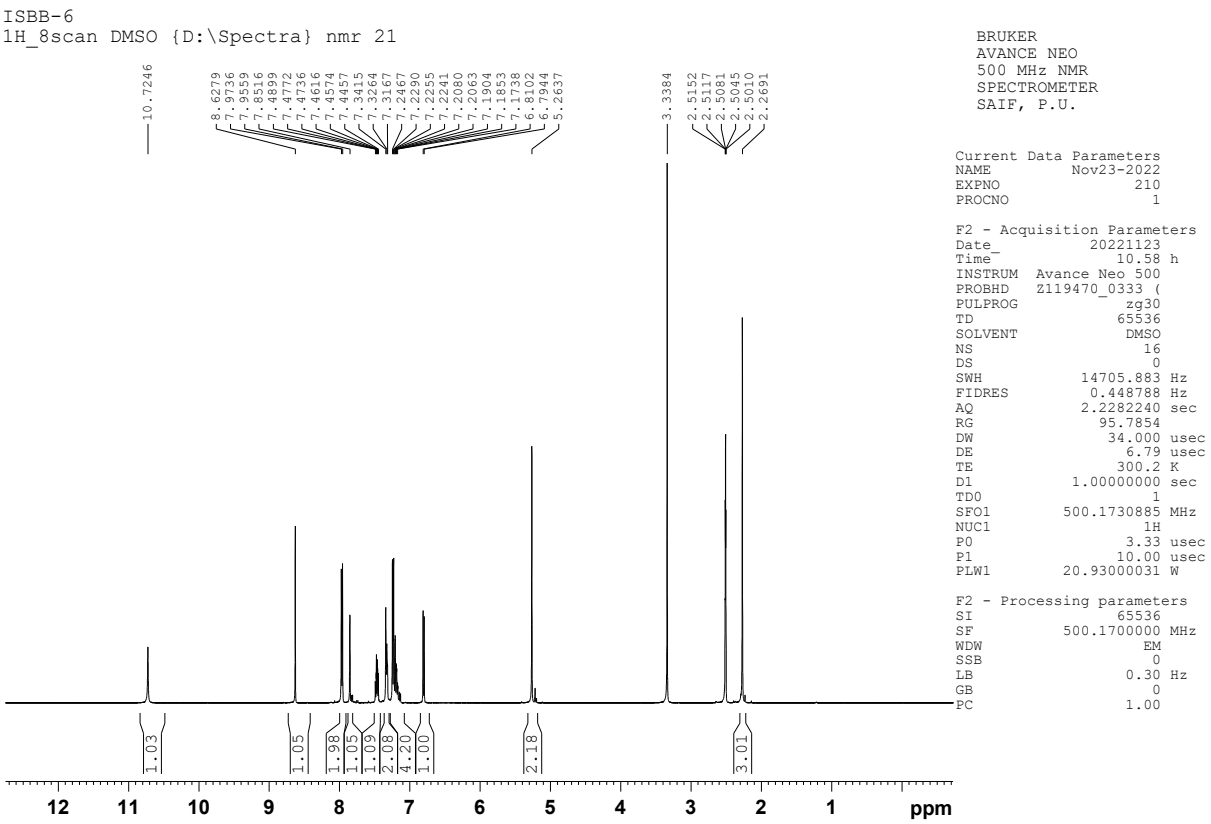


<Peak Table>

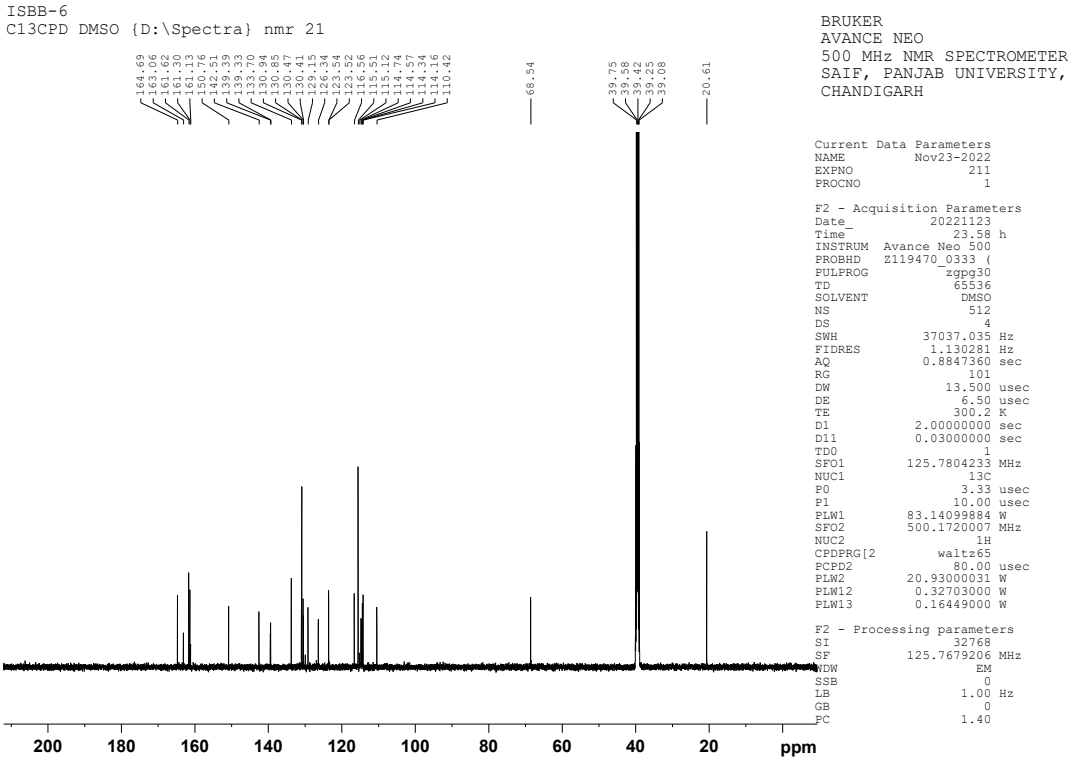
PDA Ch1 294nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.117	7527	509	0.108			
2	5.698	6879649	505641	99.070		V	
3	6.453	57057	3639	0.822		V	
Total		6944233	509789				

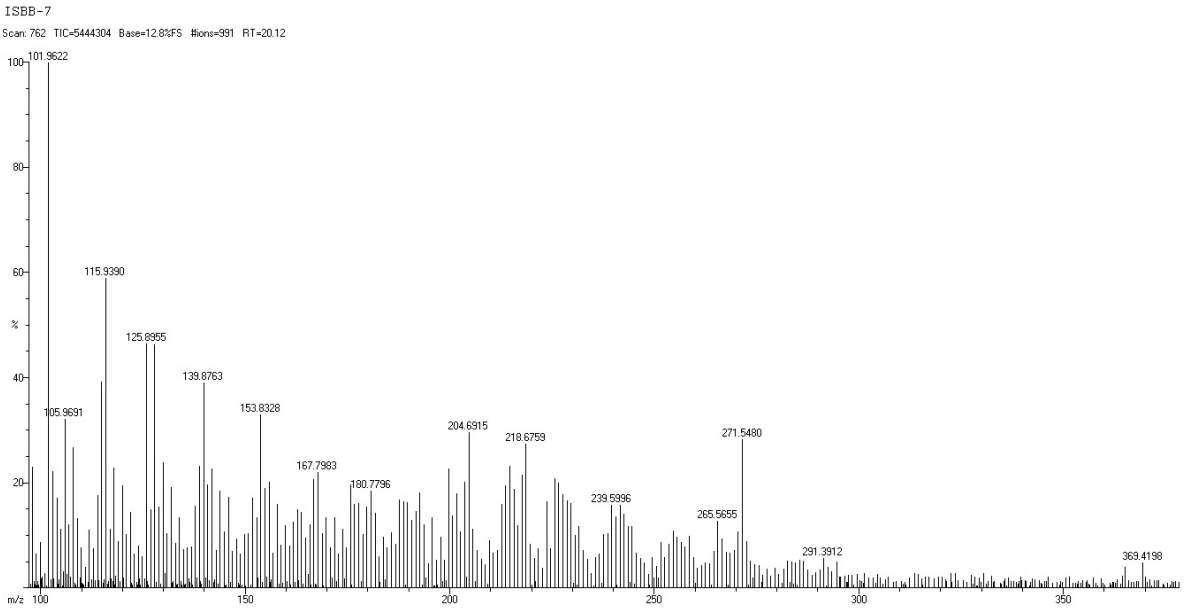
18.3 ^{1}H NMR OF ISBB-6



18.4 ^{13}C NMR OF ISBB-6



18.5 MASS SPECTRUM OF ISBB-6



18.6 SPECTRAL INTERPRETATION:

*3-((3-(benzyloxy)benzylidene)hydrazineylidene)-5-methylindolin-2-one(**ISBB6**):* orange solid, 81%, melting point. 238± 2˚C. ^{1}H NMR (500 MHz, DMSO-d6) δ: 10.72 (s, 1H, NH), 8.62 (s, 1H, =CH-), 7.97-6.79(m, 12H, ArH), 5.26 (s, 2H, -CH_2-), 2.26 (s, 3H, -CH_2-Ar). ^{13}C NMR (500 MHz, DMSO-d6) 164.69, 163.06, 161.62, 150.76, 142.61, 139.39, 133.70, 130.70, 129.15, 126.34, 123.54, 116.86, 115.12, 114.57, 110.42, 68.54, 20.61. Chemical formula $C_{23}H_{19}N_3O_2$ EI- HRMS (m/z): Calculated-369.4198, Observed- 369.4158.