Supplementary Data:

Development, Biological Evaluation, and Molecular Modelling of Novel Isocytosine and Guanidine Derivatives as BACE1 Inhibitors Using a Fragment Growing Strategy

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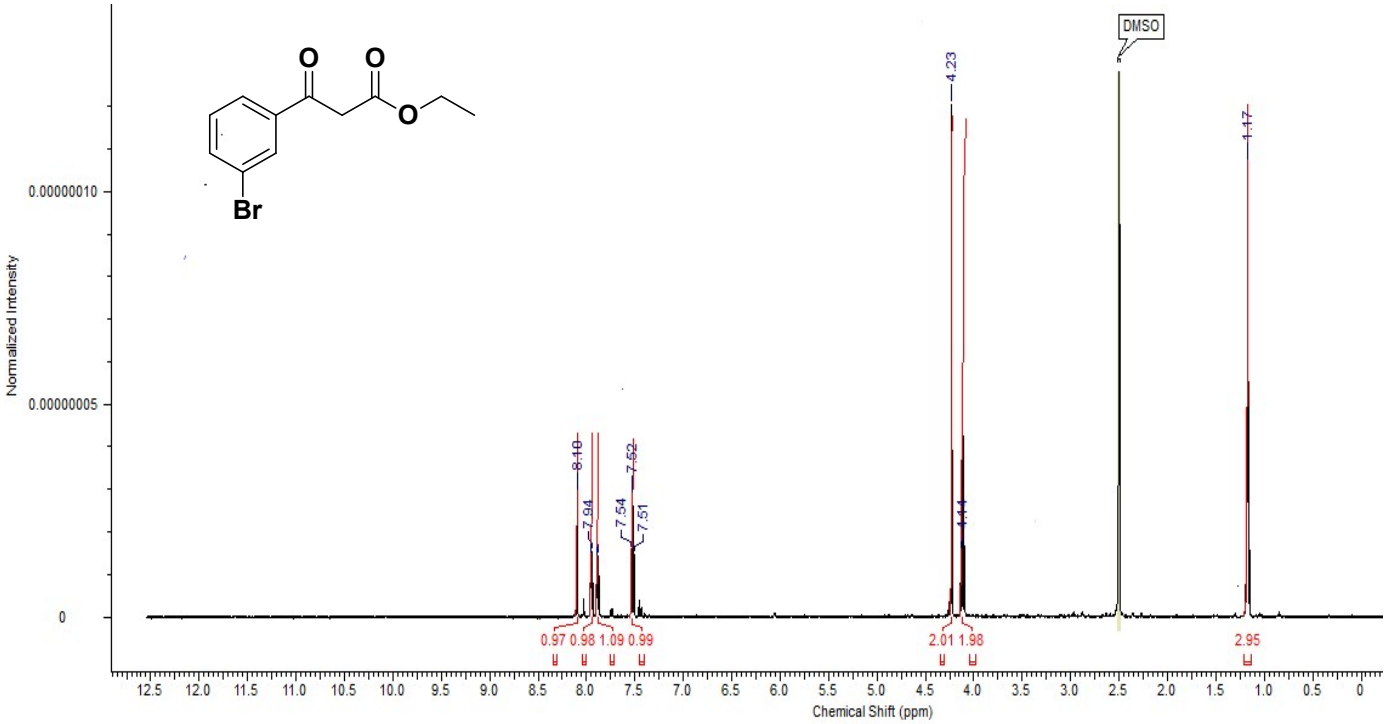


Figure S1. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **2**

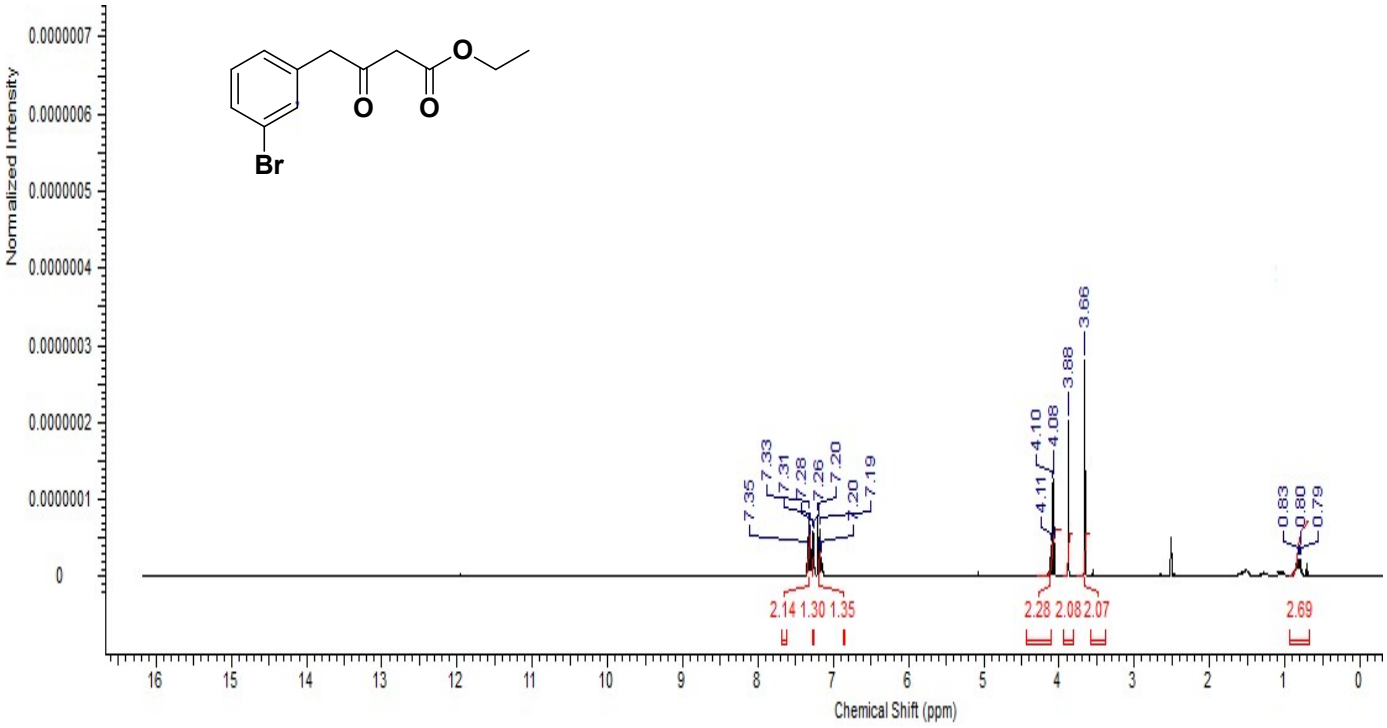


Figure S2. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **2'**

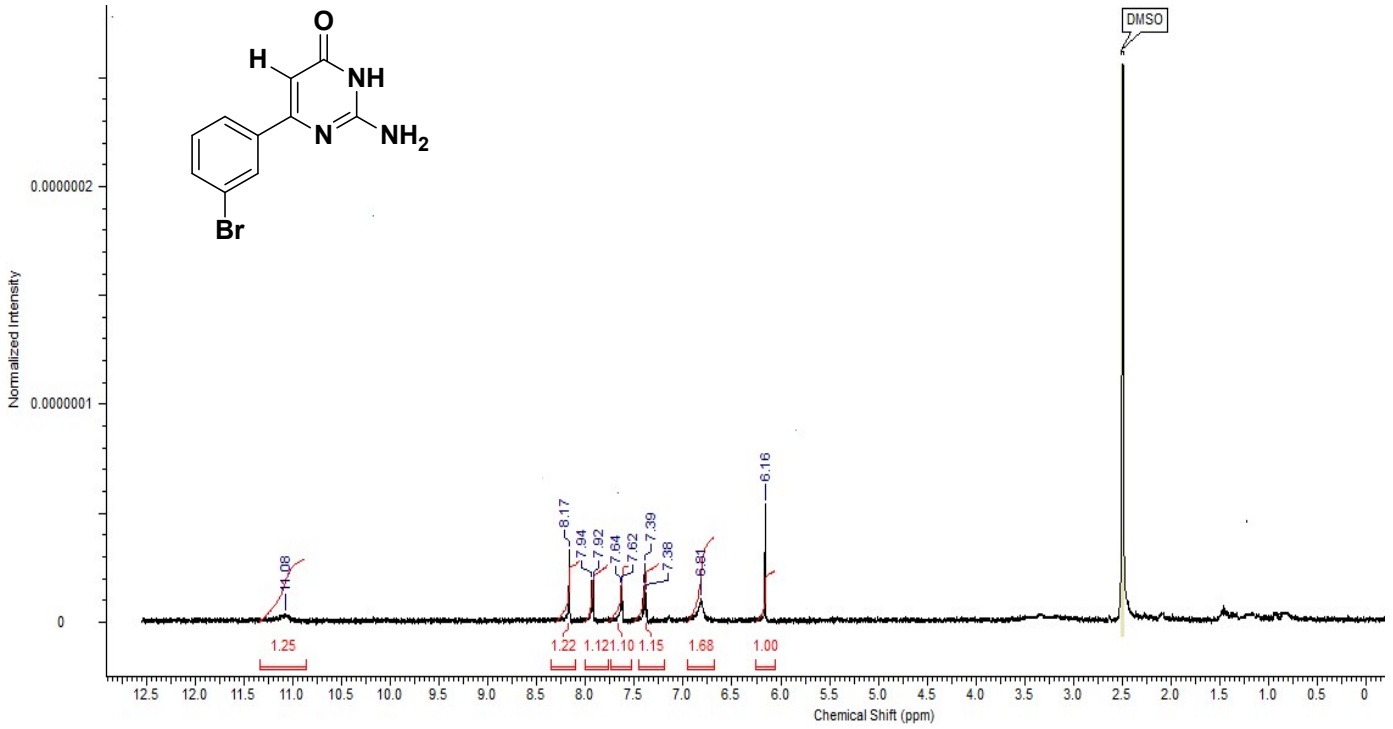


Figure S3. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **3**

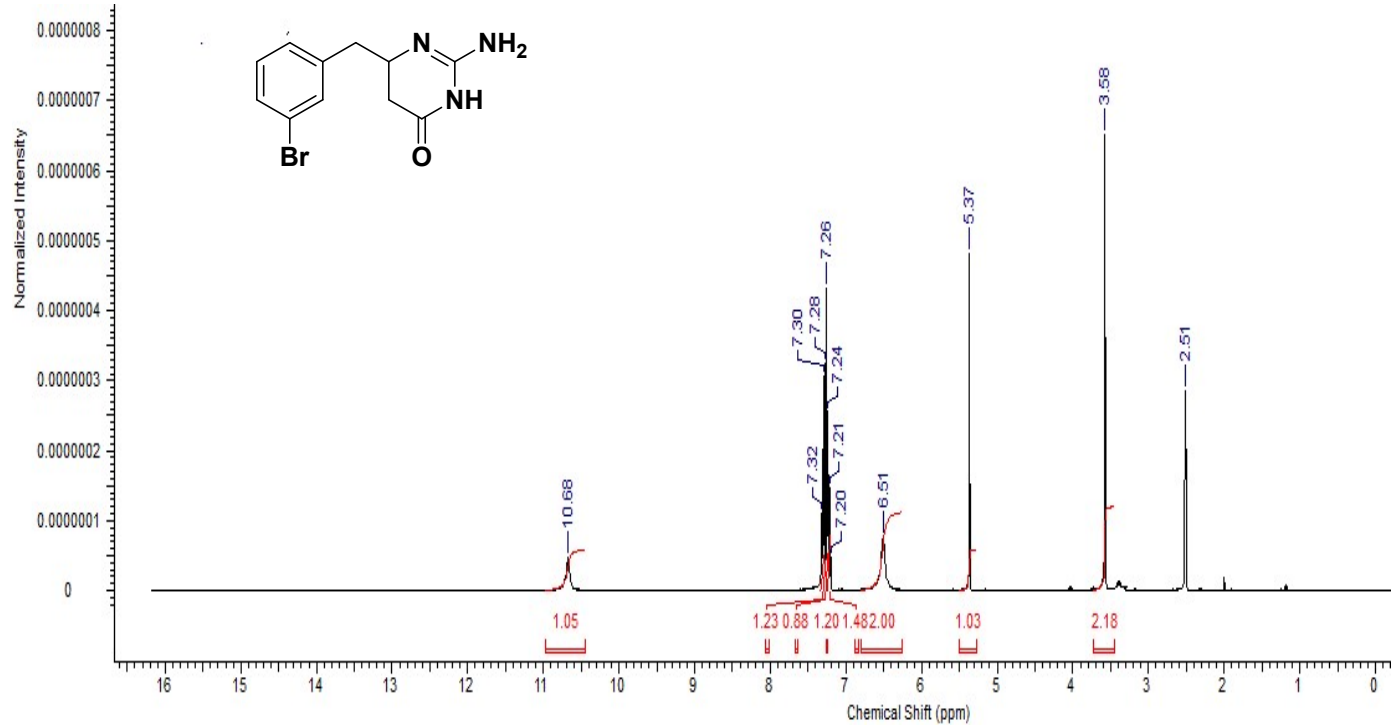


Figure S4. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **3'**

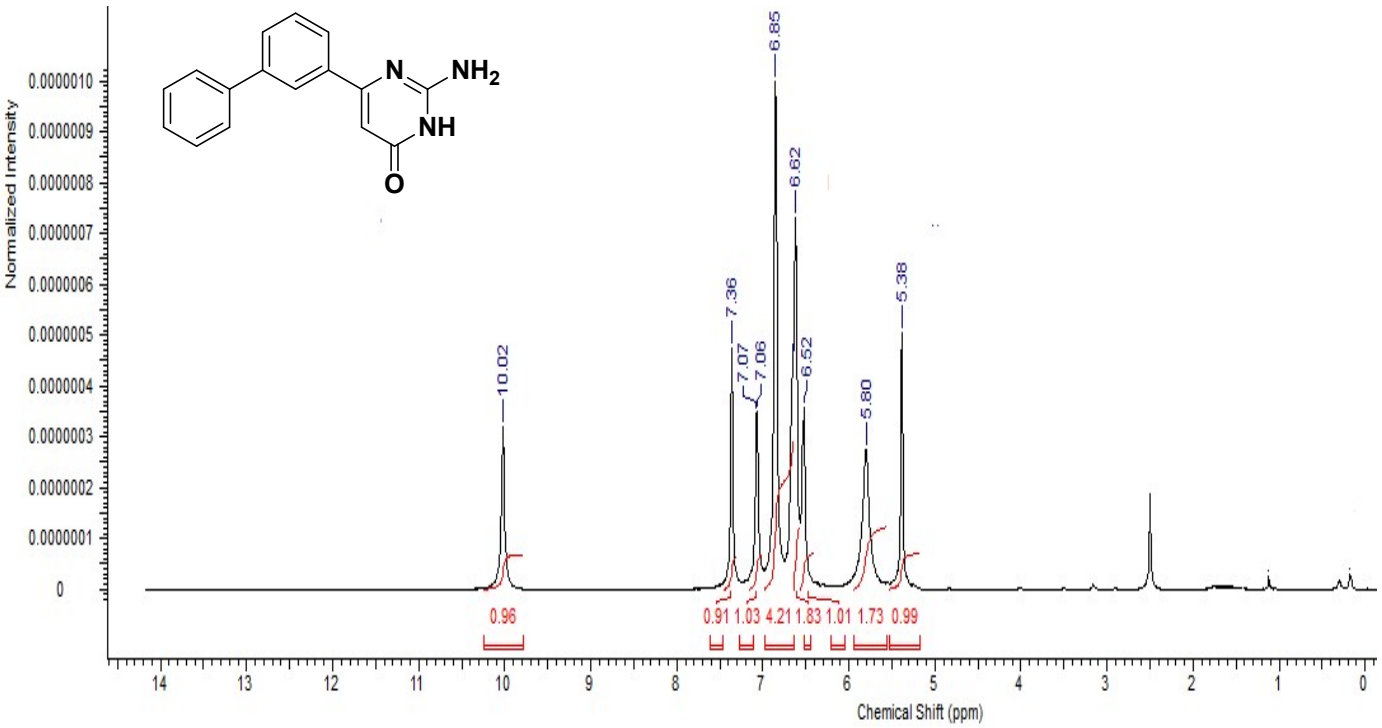


Figure S5. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4a**

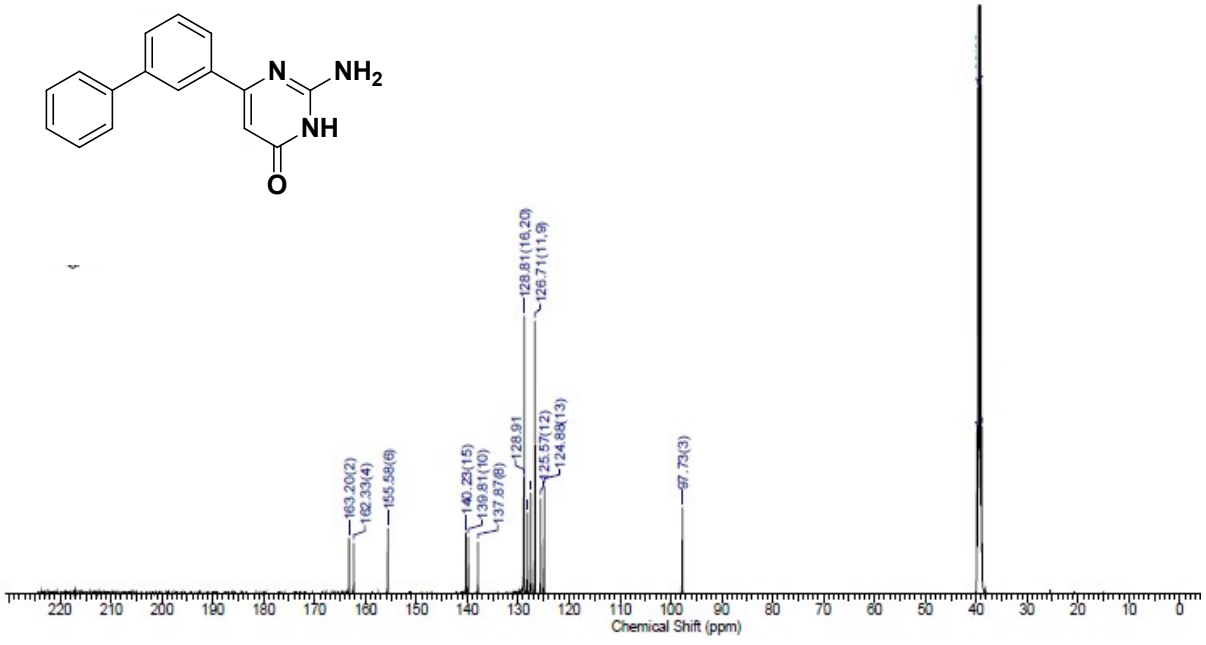


Figure S6. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4a**

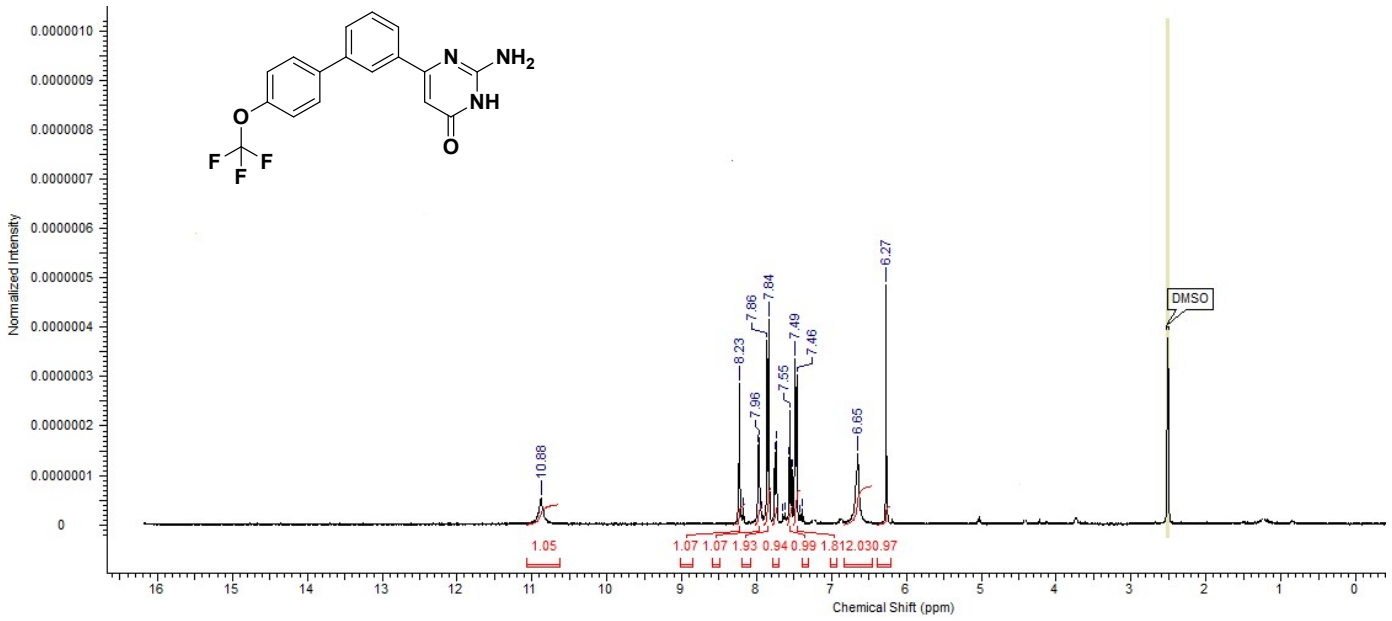


Figure S7. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4b**

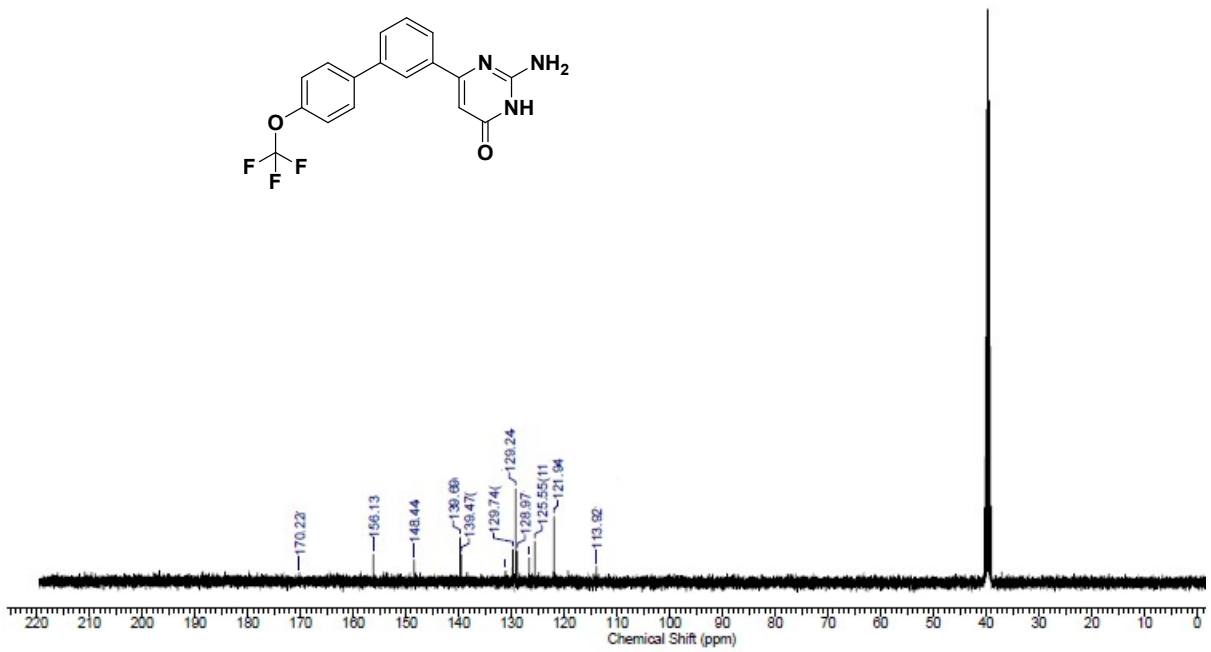


Figure S8. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4b**

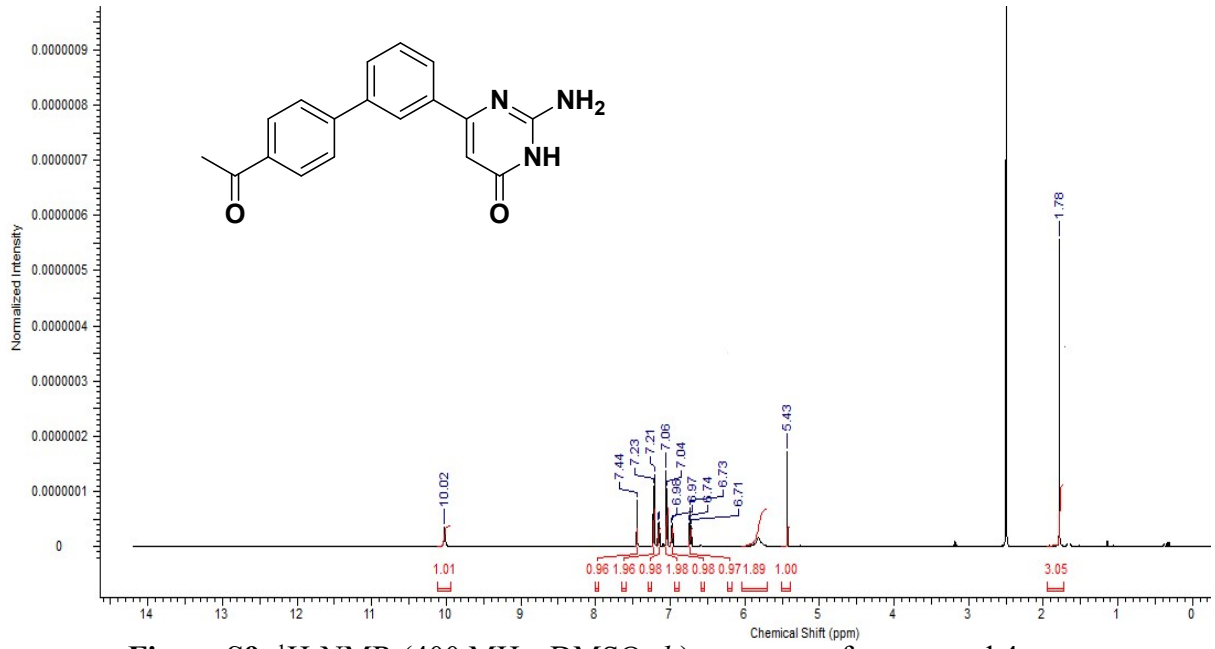


Figure S9. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4c**

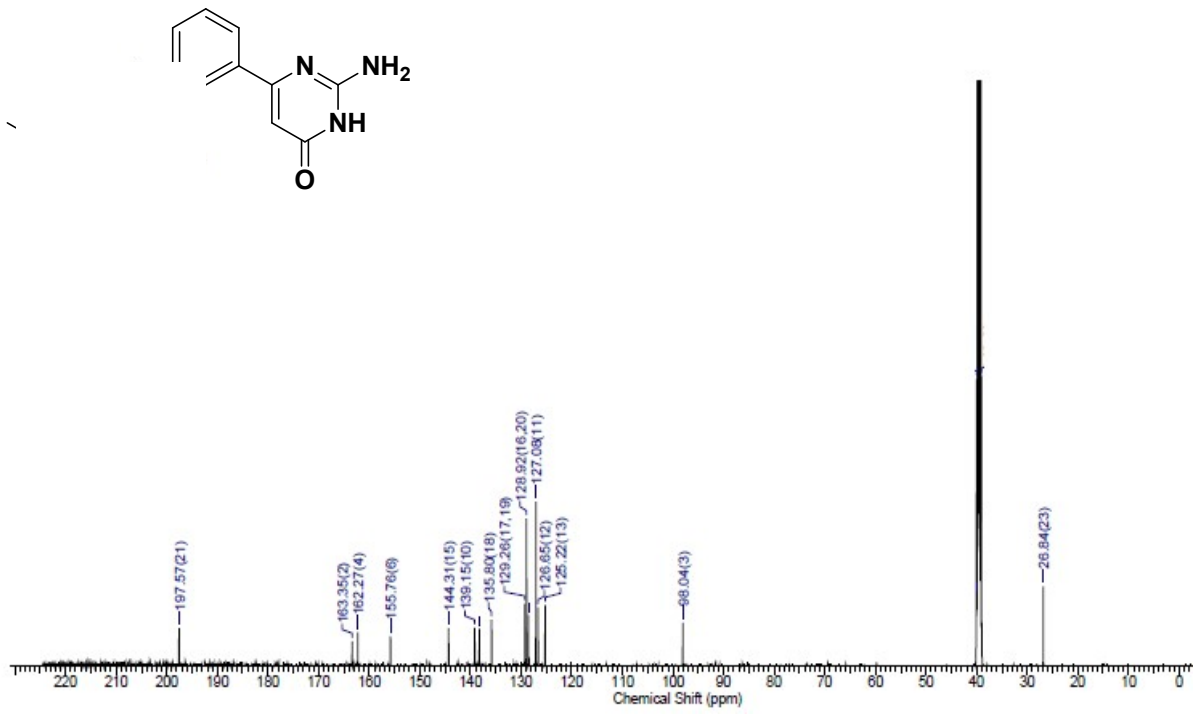


Figure S10. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4c**

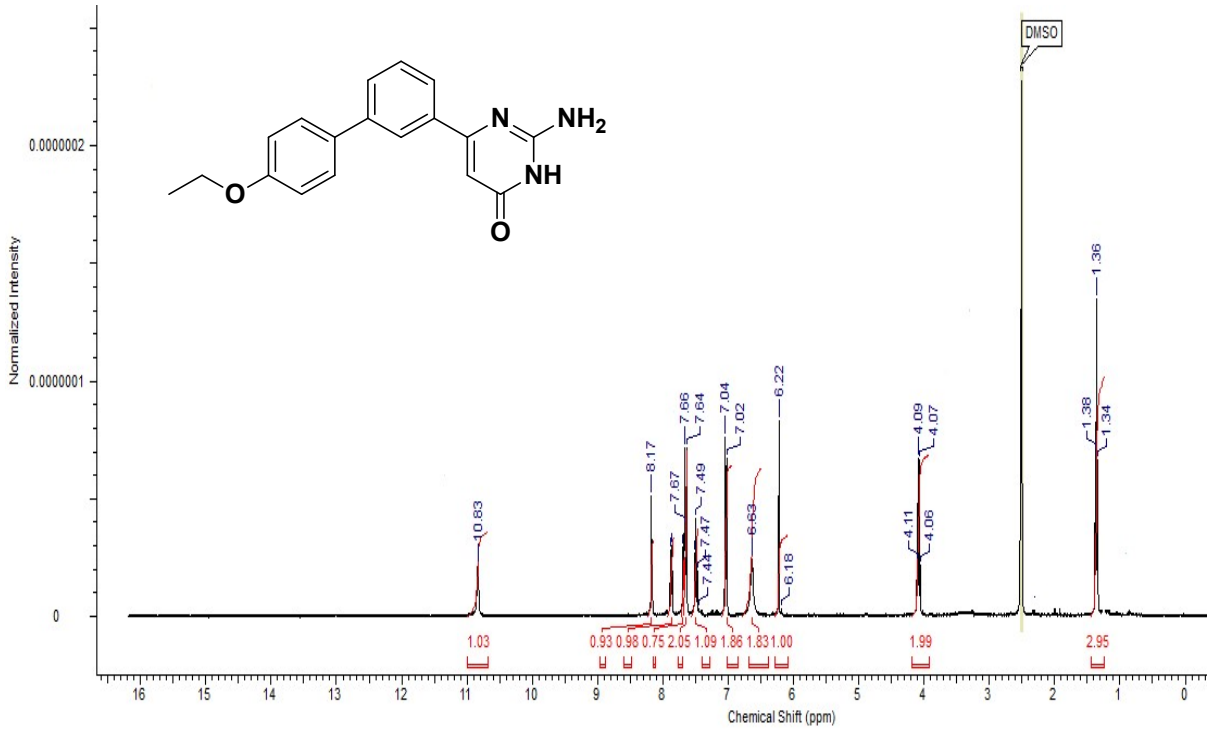


Figure S11. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4d**

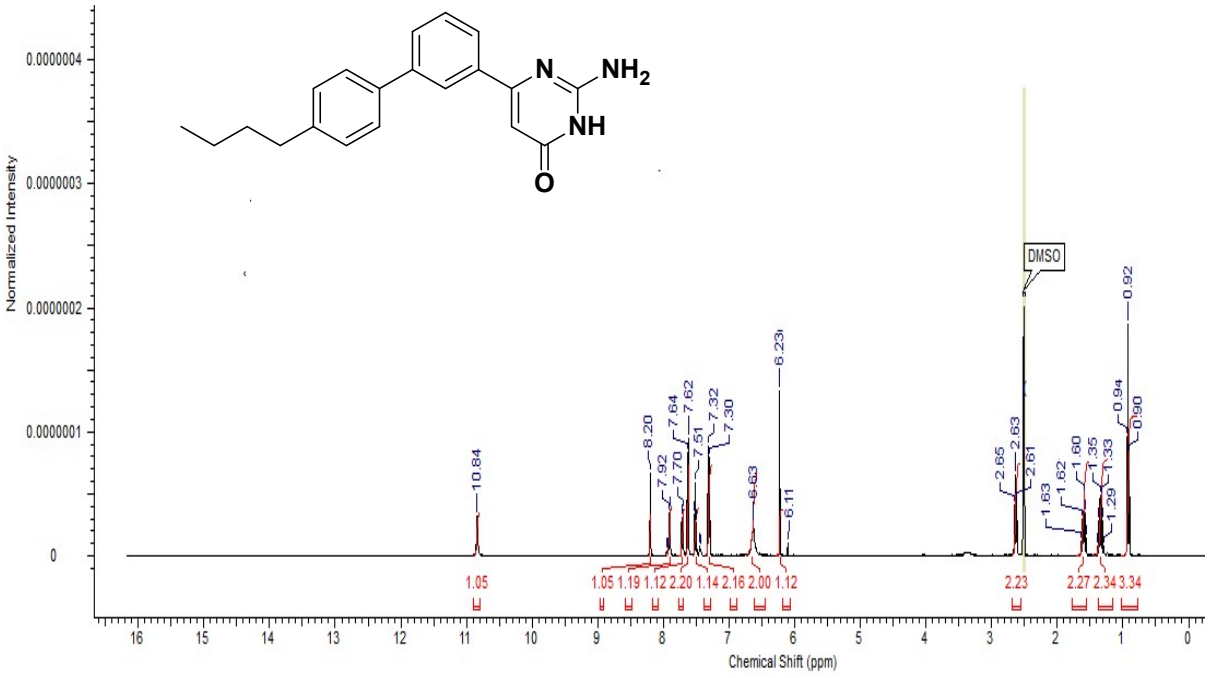


Figure S12. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4e**

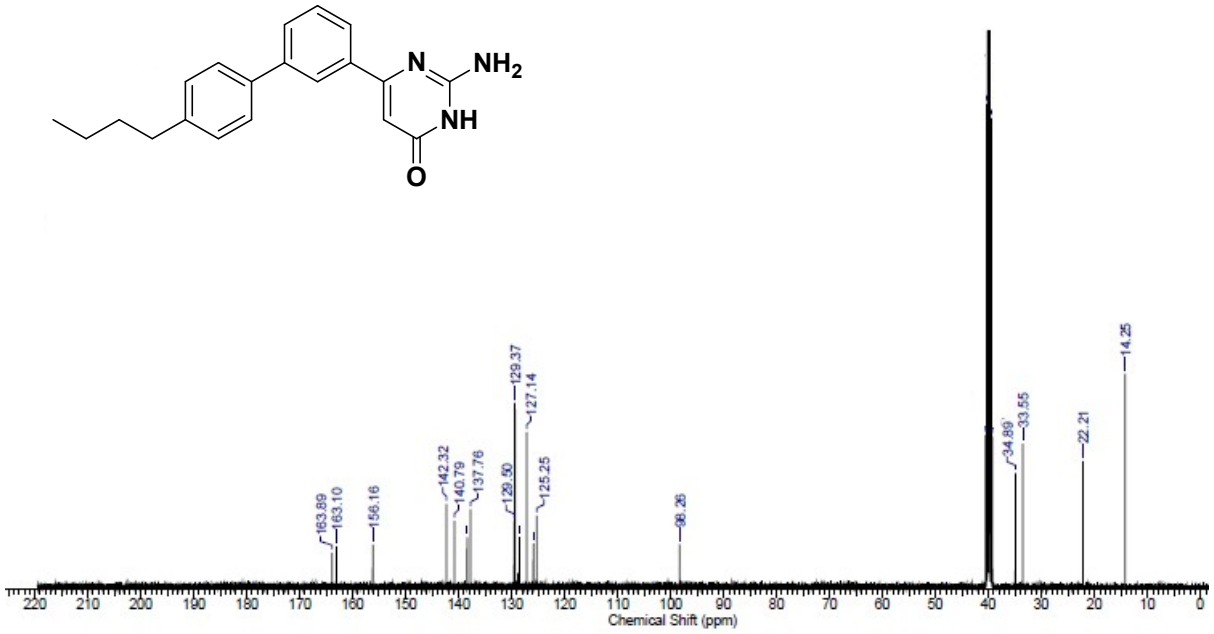


Figure S13. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4e**

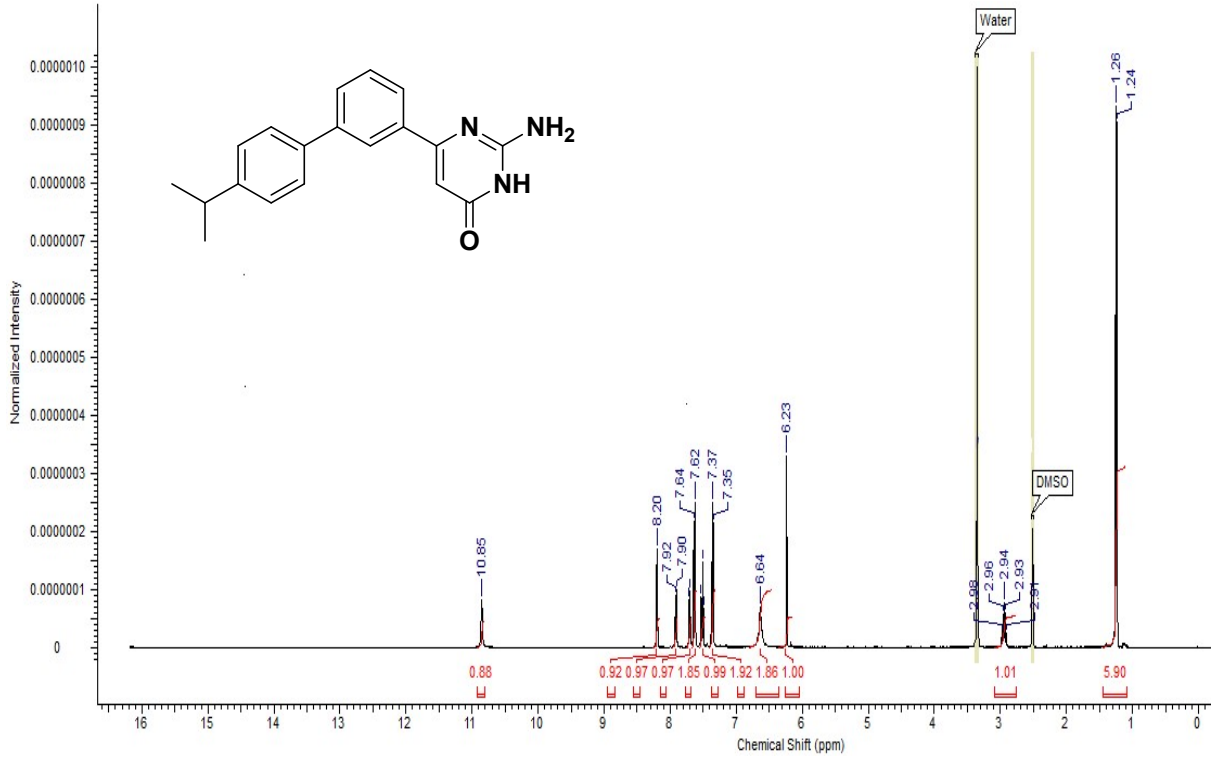


Figure S14. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4f**

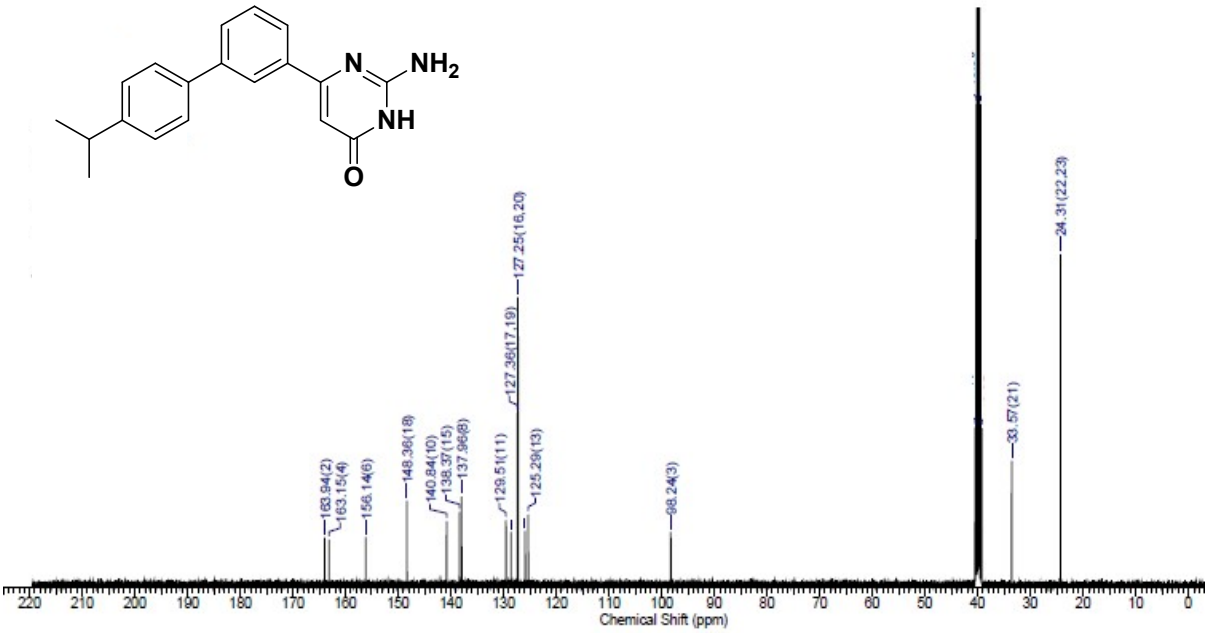


Figure S15. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4f**

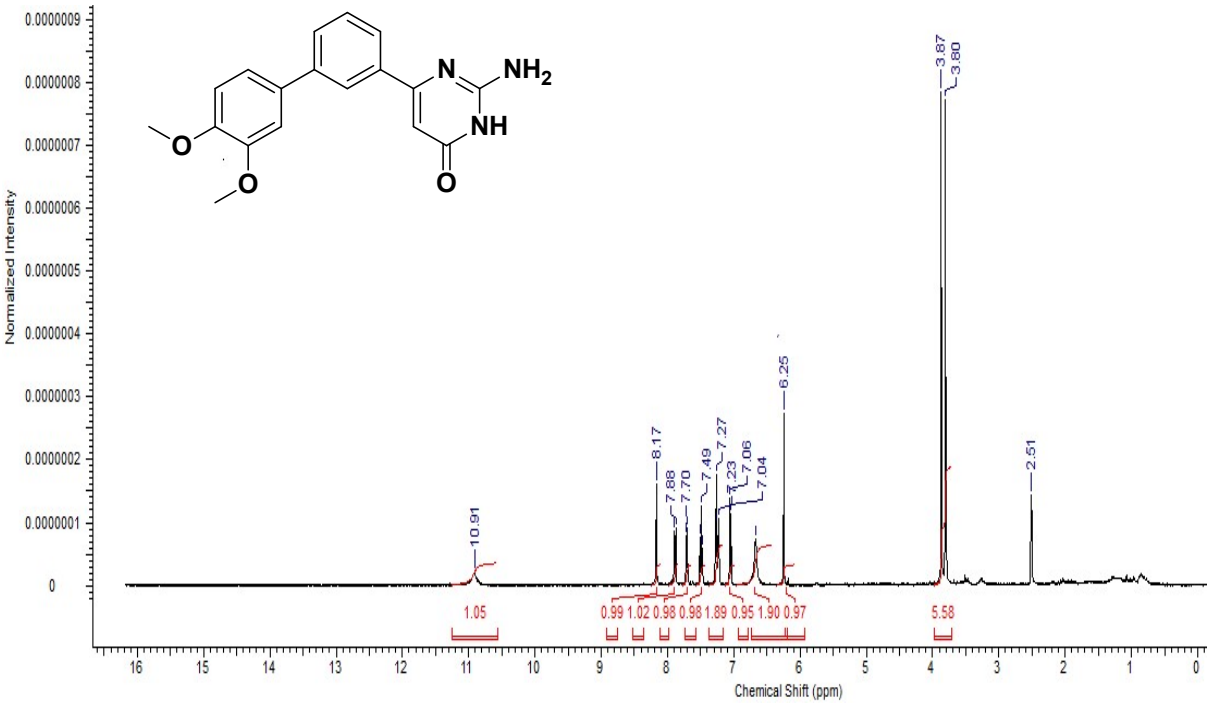


Figure S16. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4g**

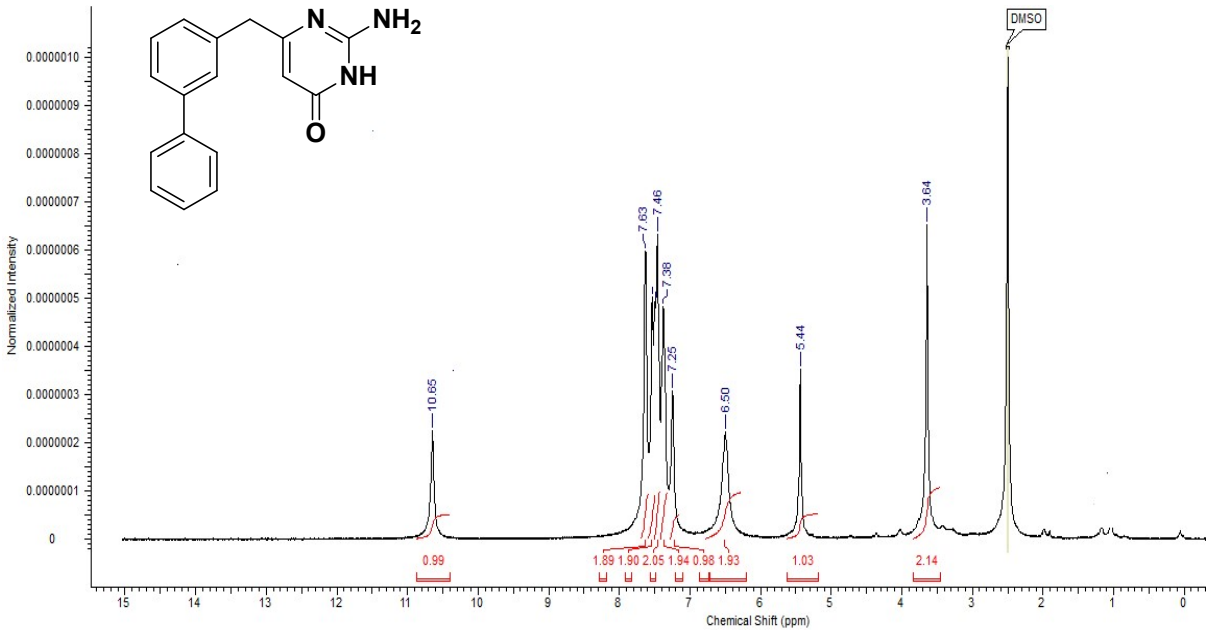


Figure S17. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4a'**

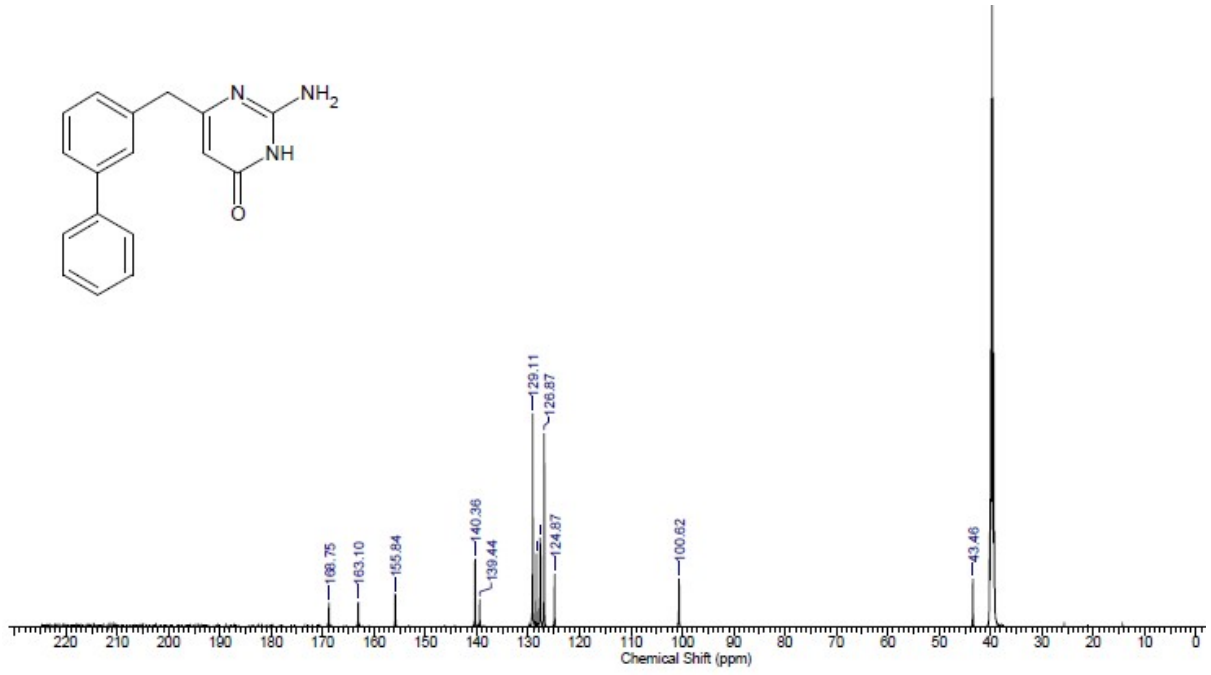


Figure S18. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'a**

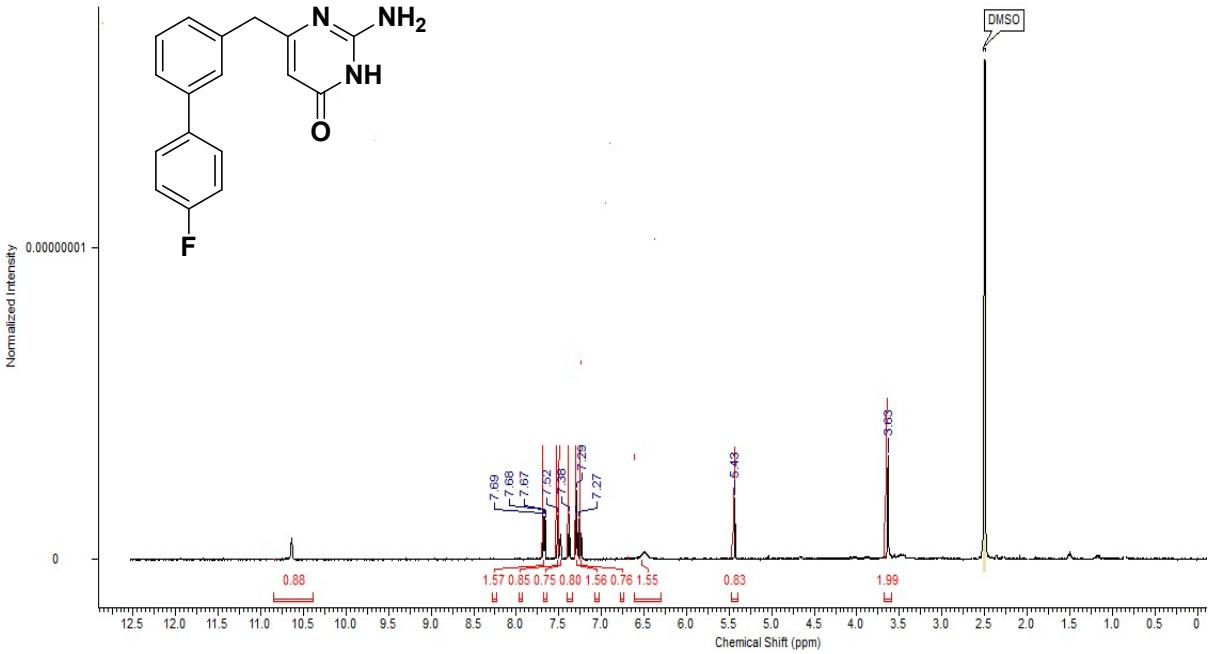


Figure S19. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'b**

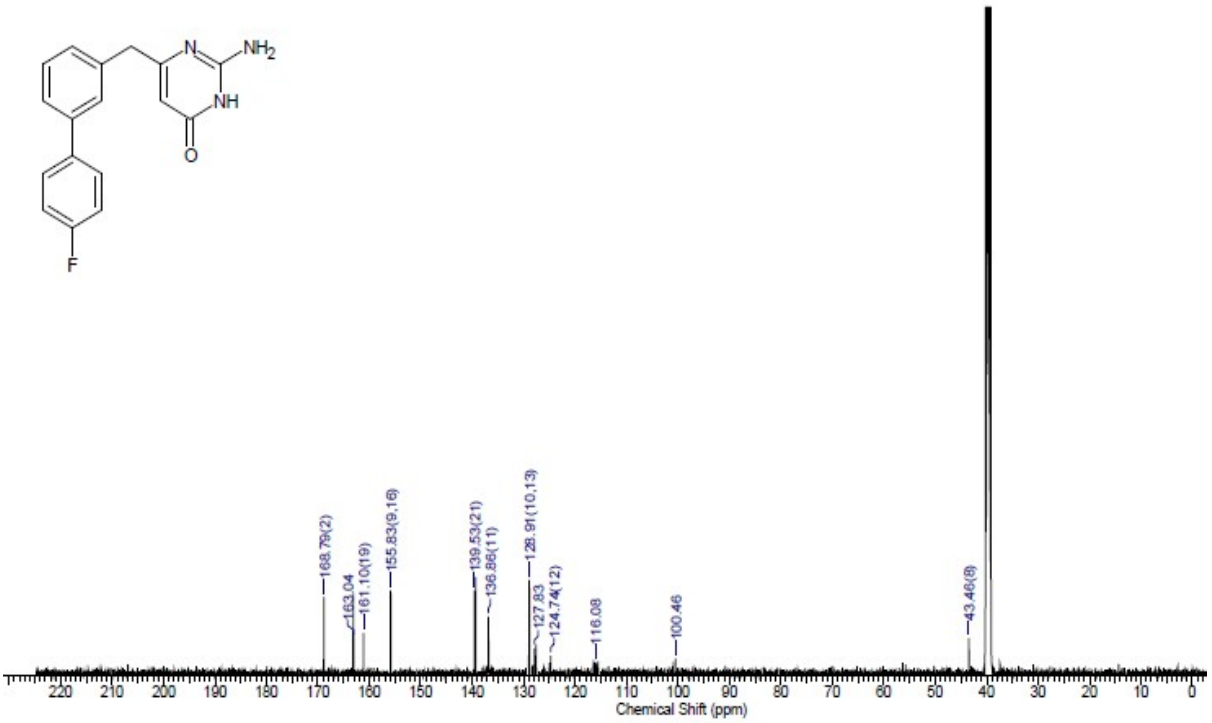


Figure S20. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'b**

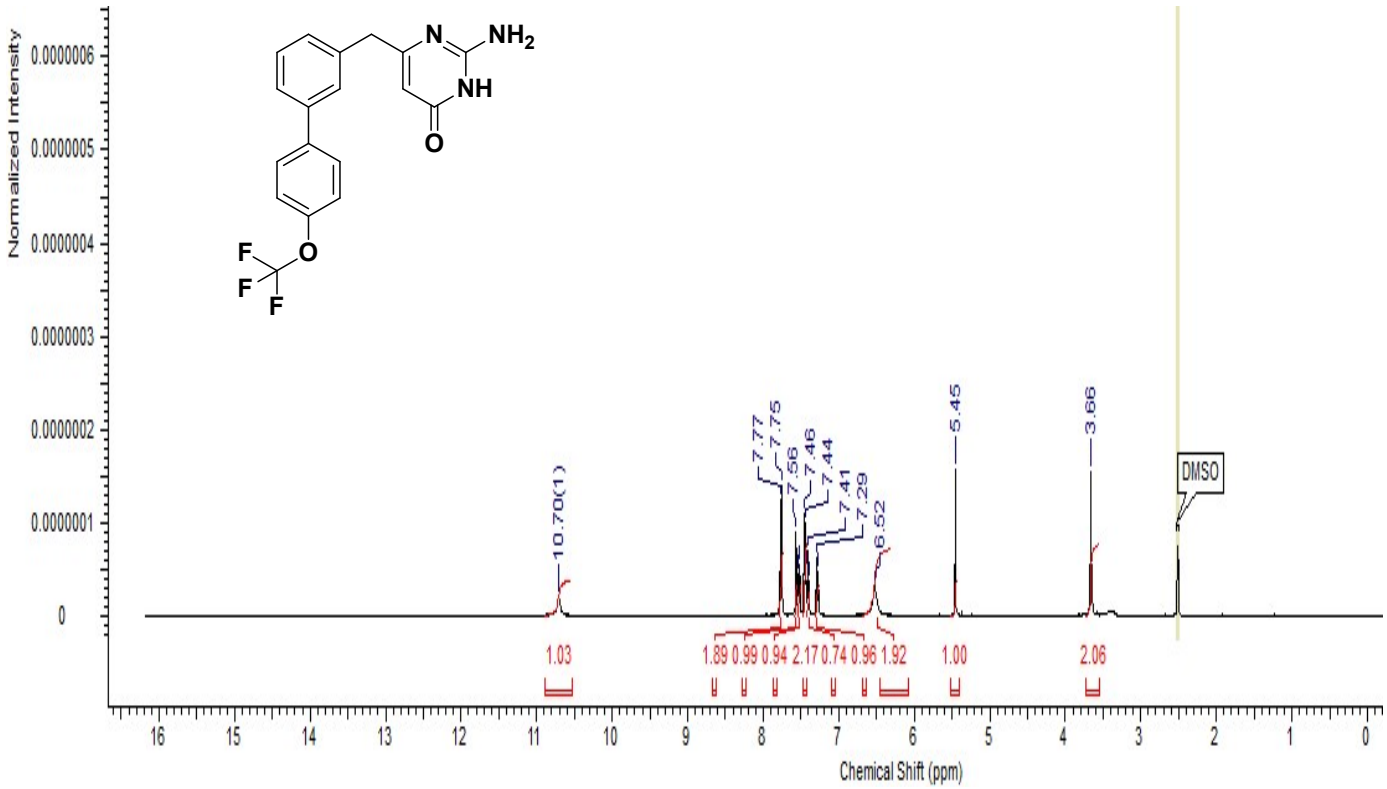


Figure S21. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'c**

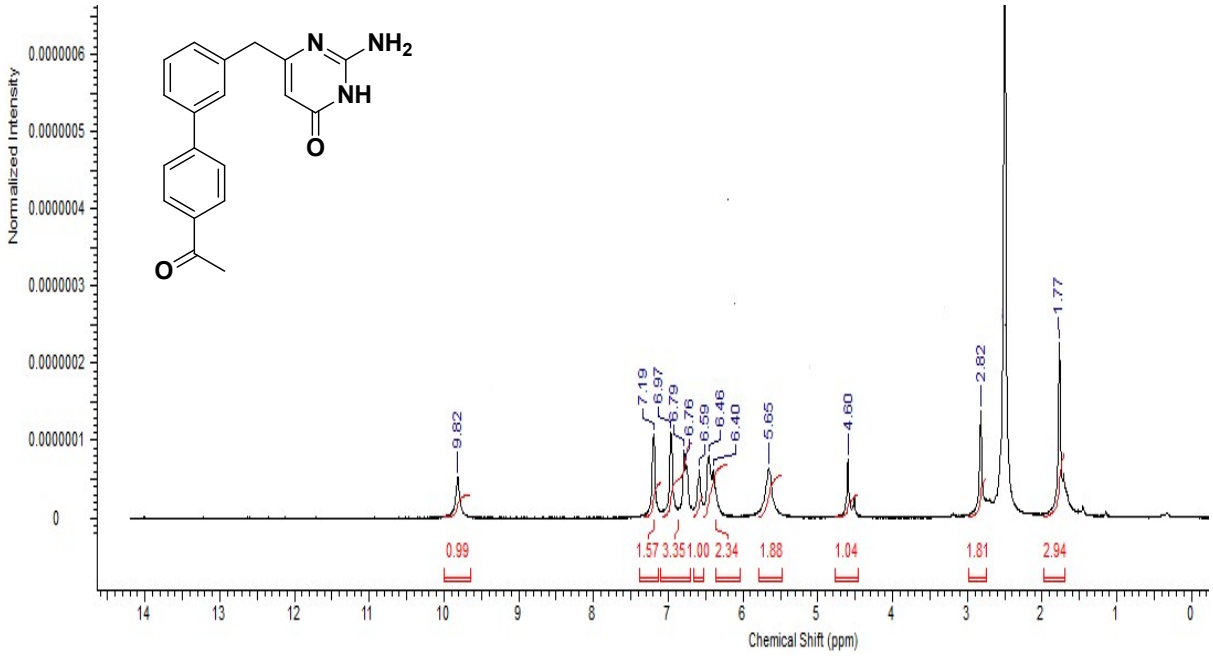


Figure S22. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'd**

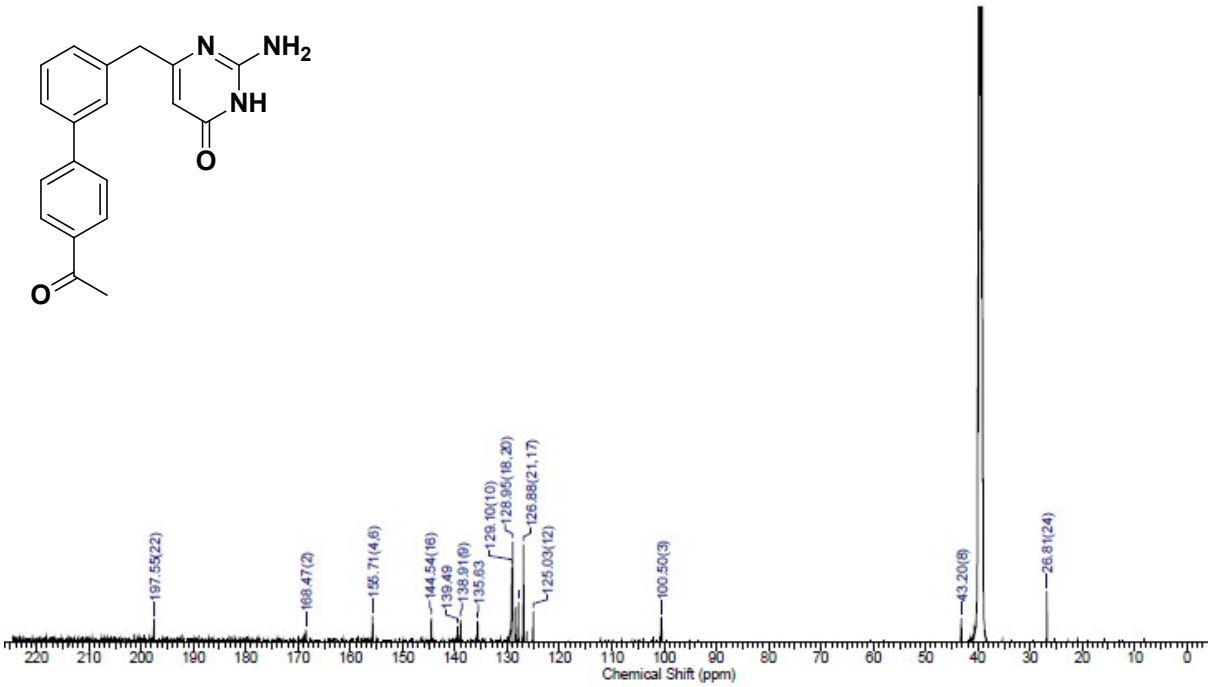


Figure S23. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'd**

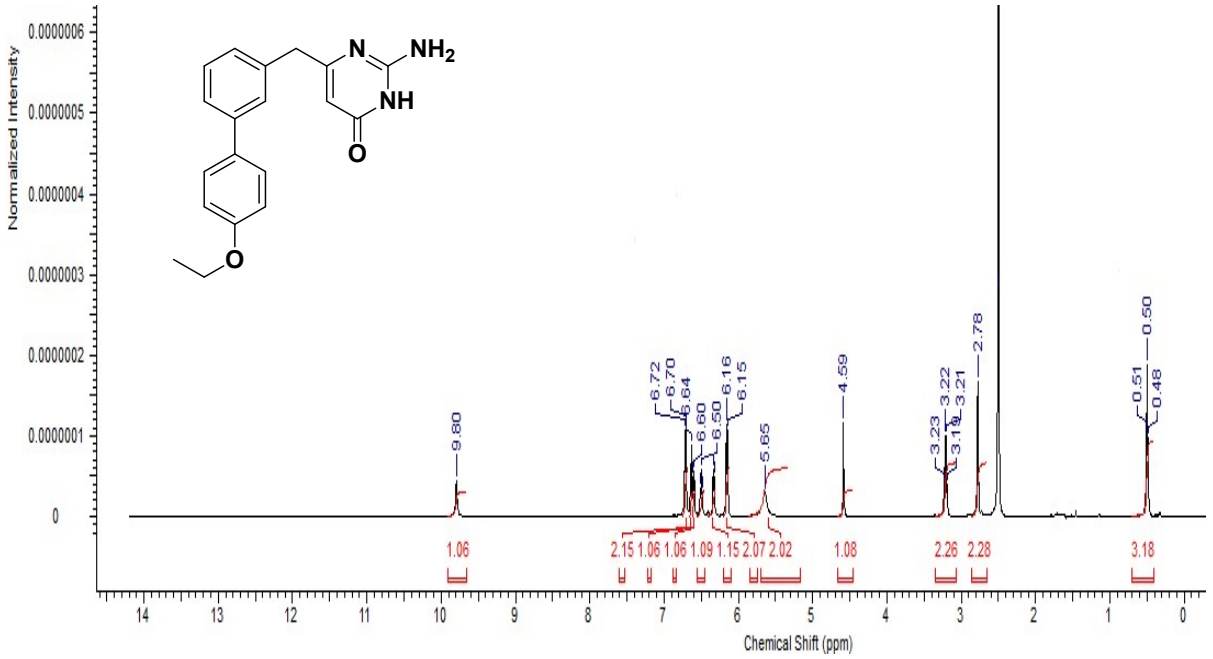


Figure S24. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'e**

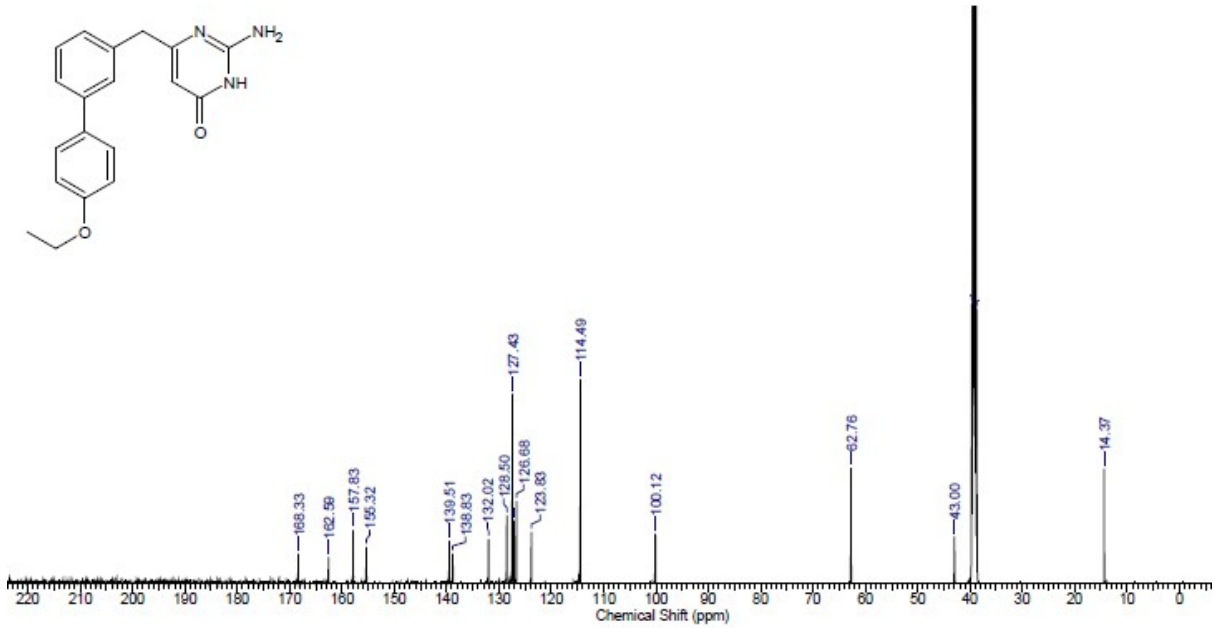


Figure S25. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'e**

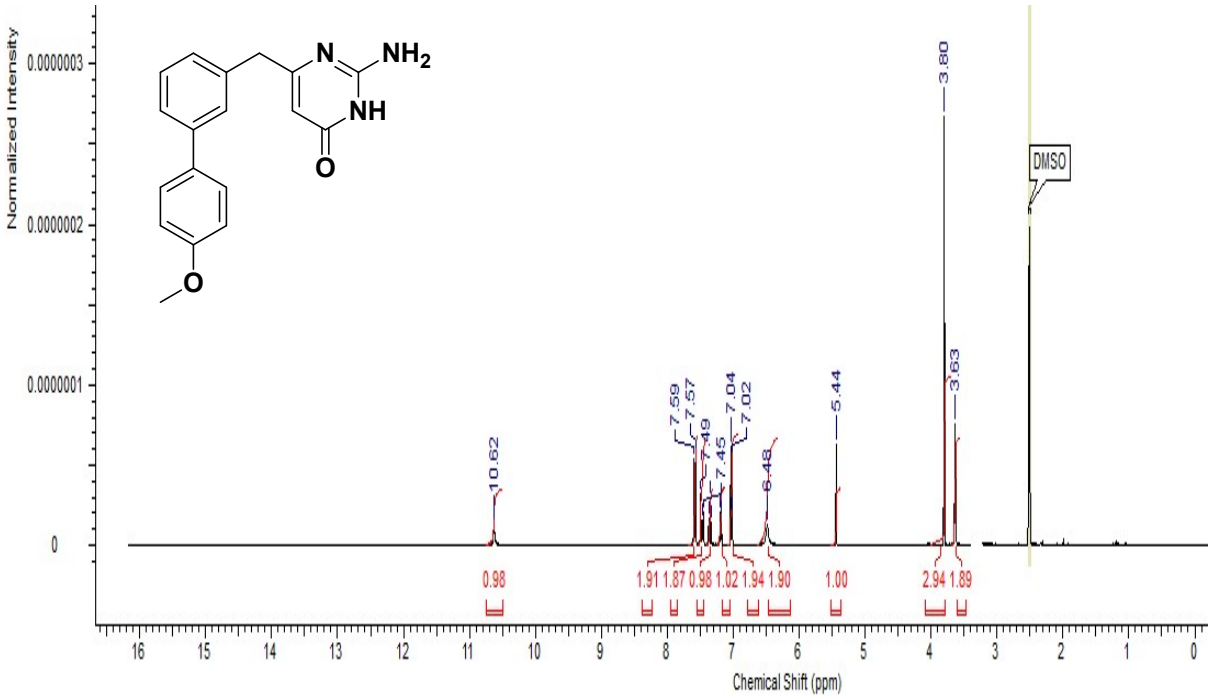


Figure S26. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'f**

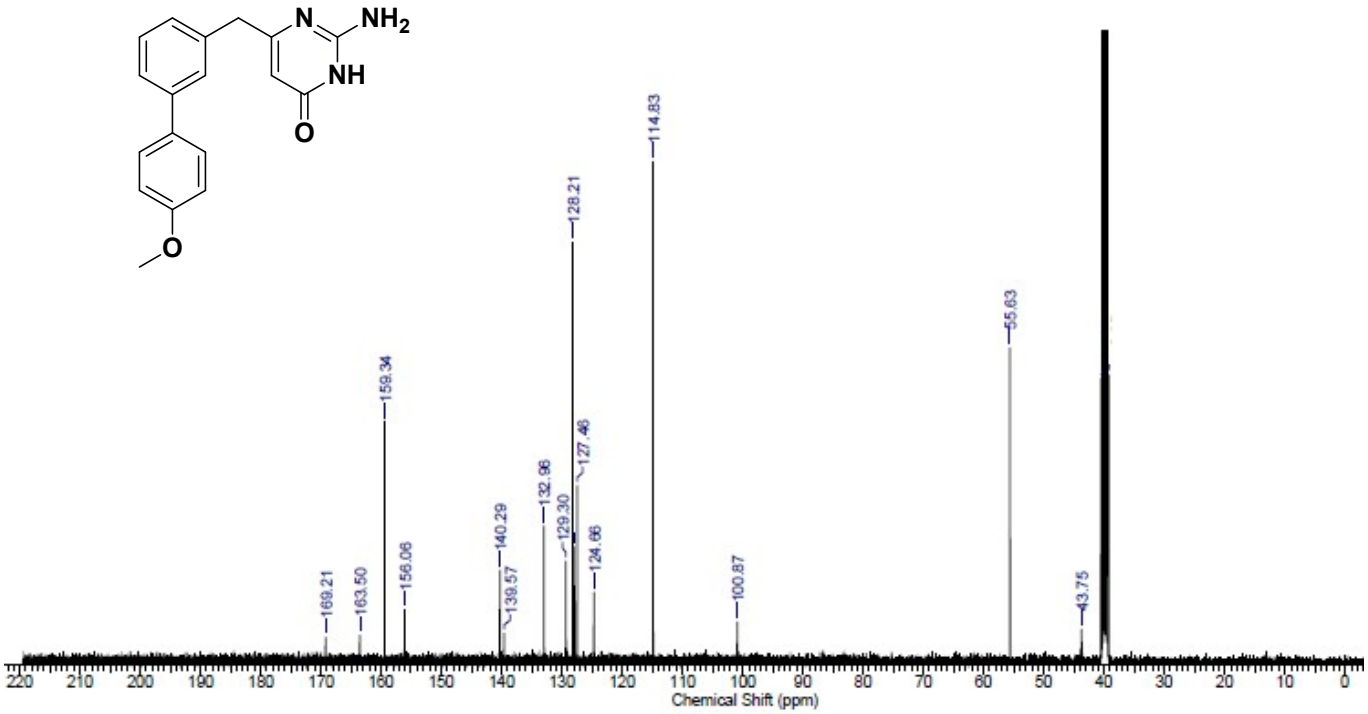


Figure S27. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'f**

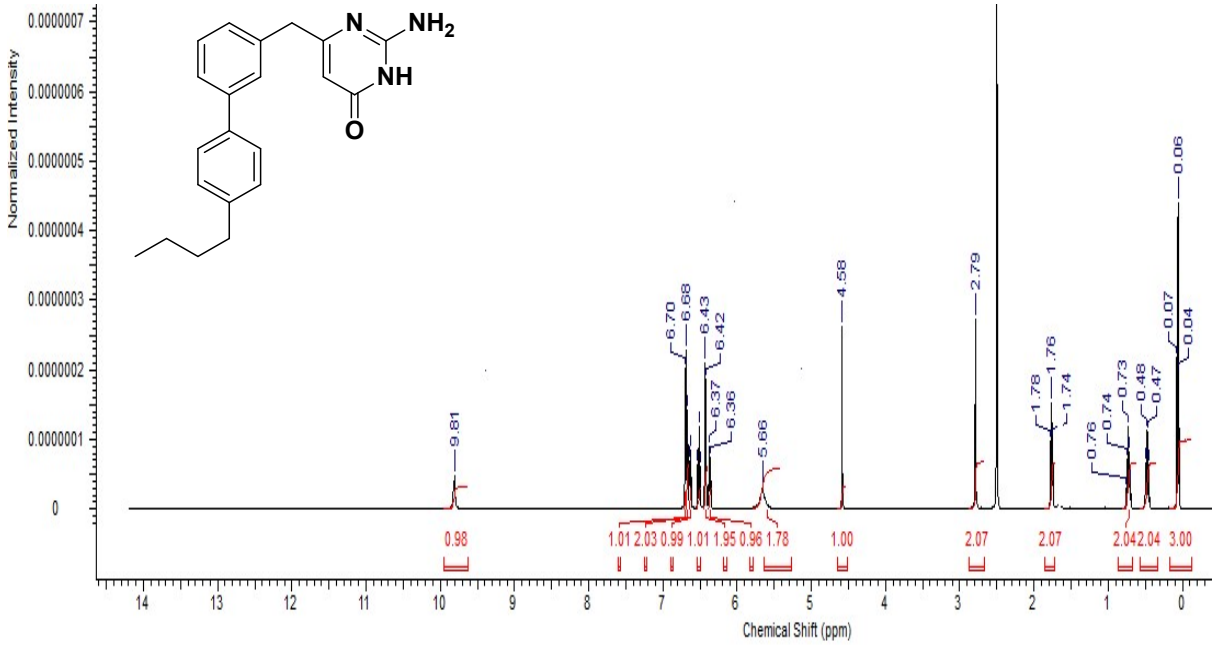


Figure S28. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'g**

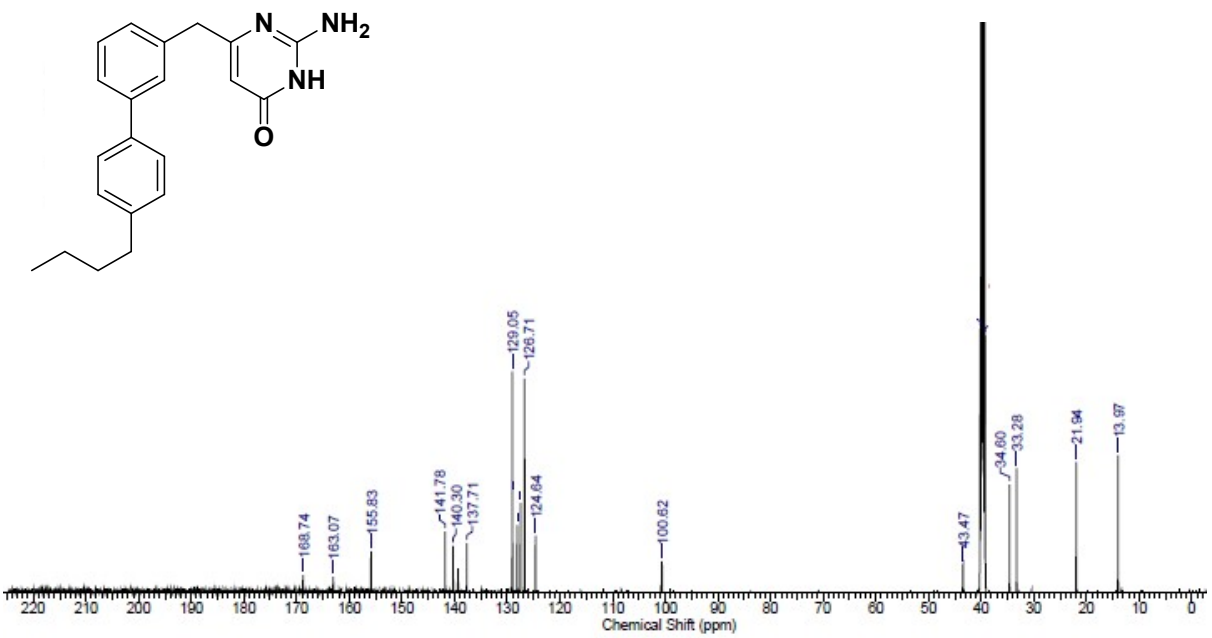


Figure S29. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'g**

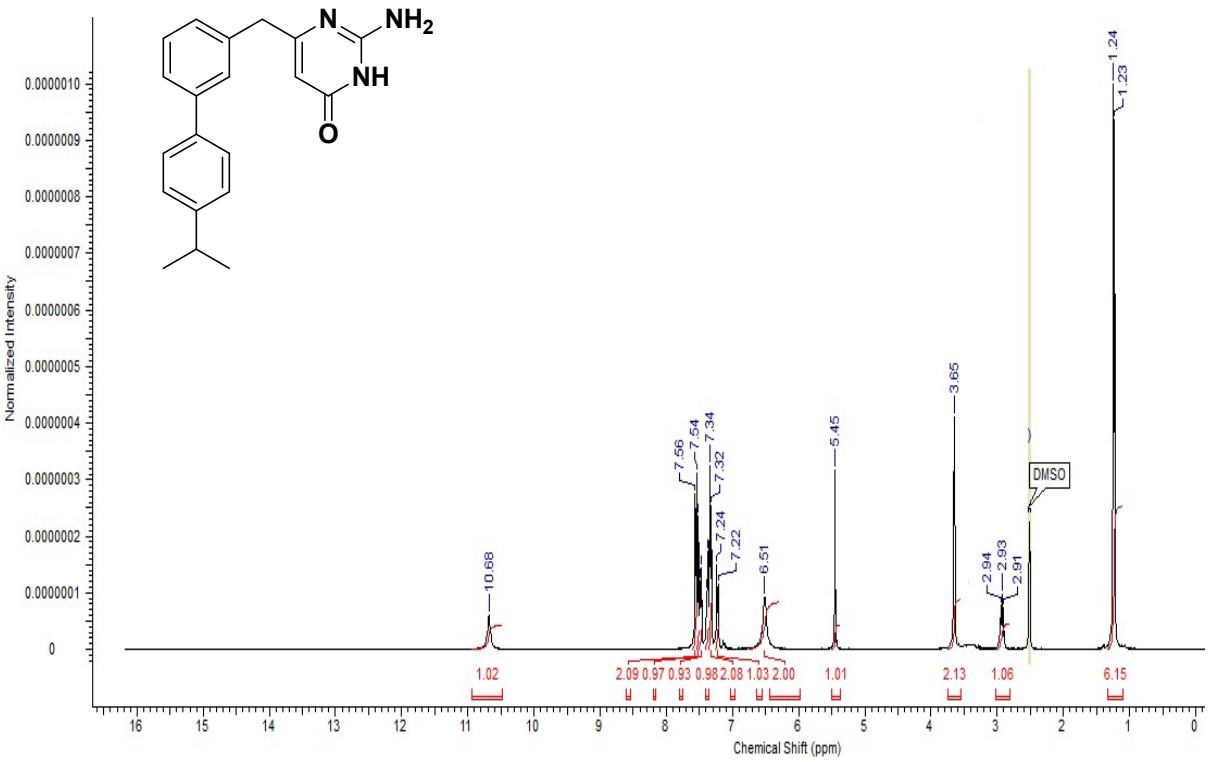


Figure S30. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **4'h**

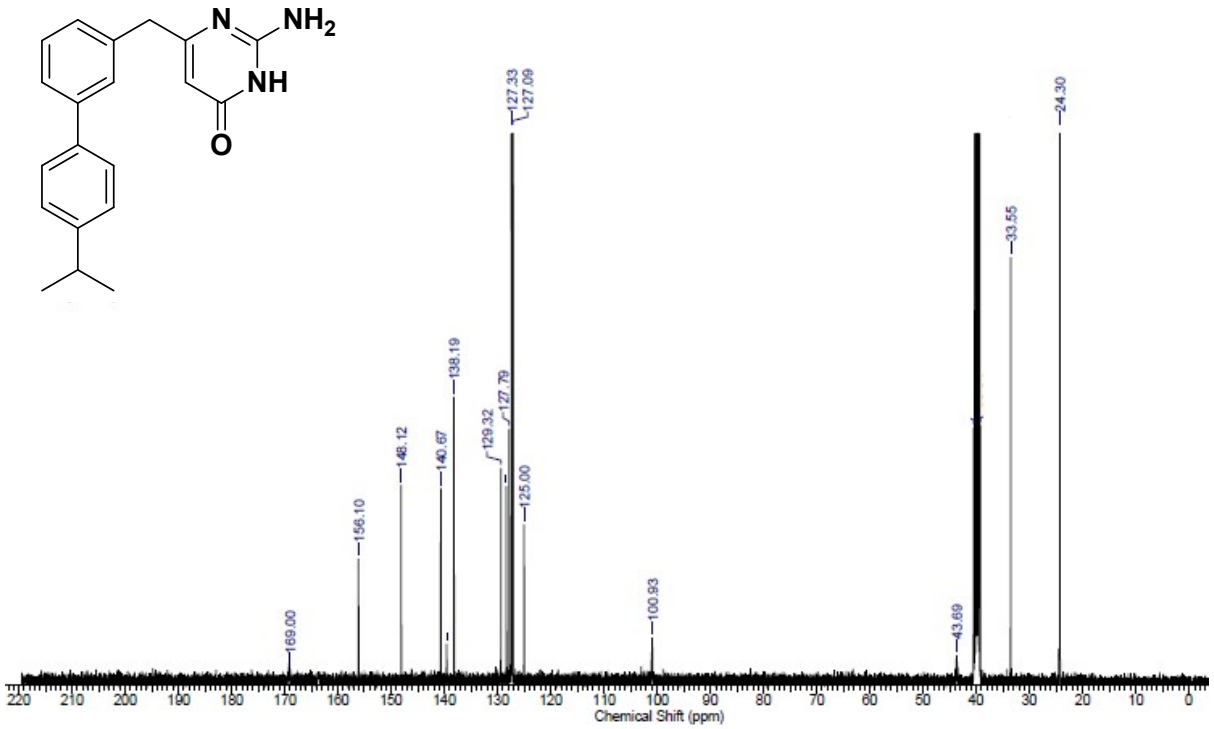


Figure S31. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **4'h**

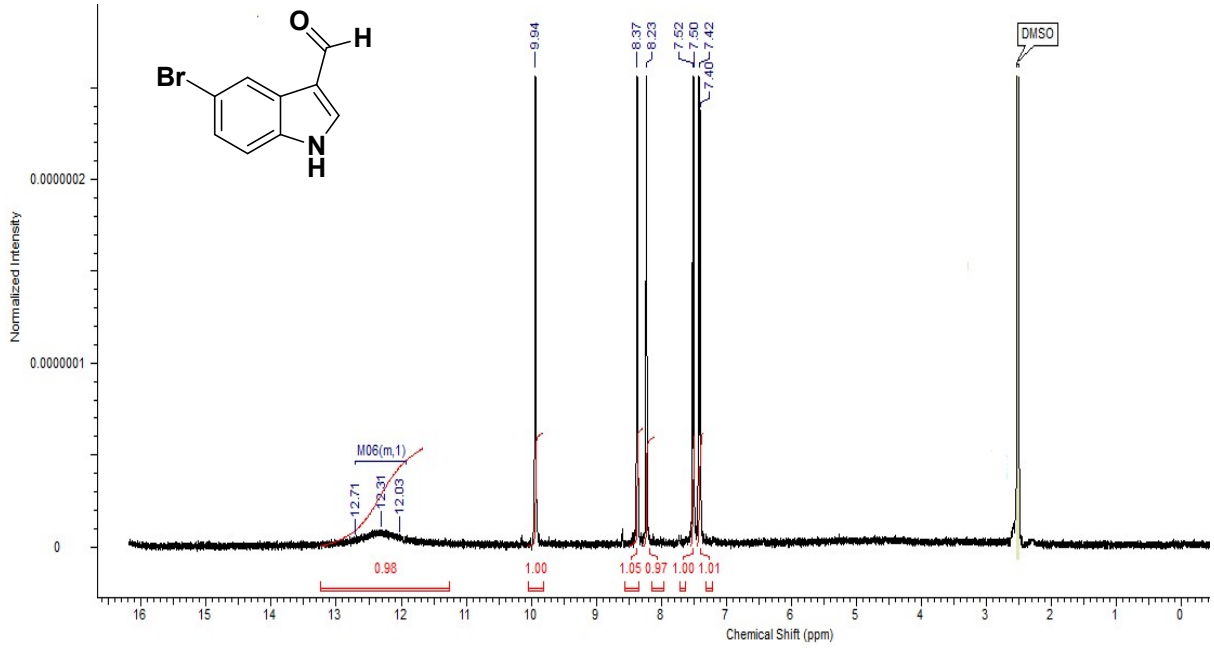


Figure S32. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **6**

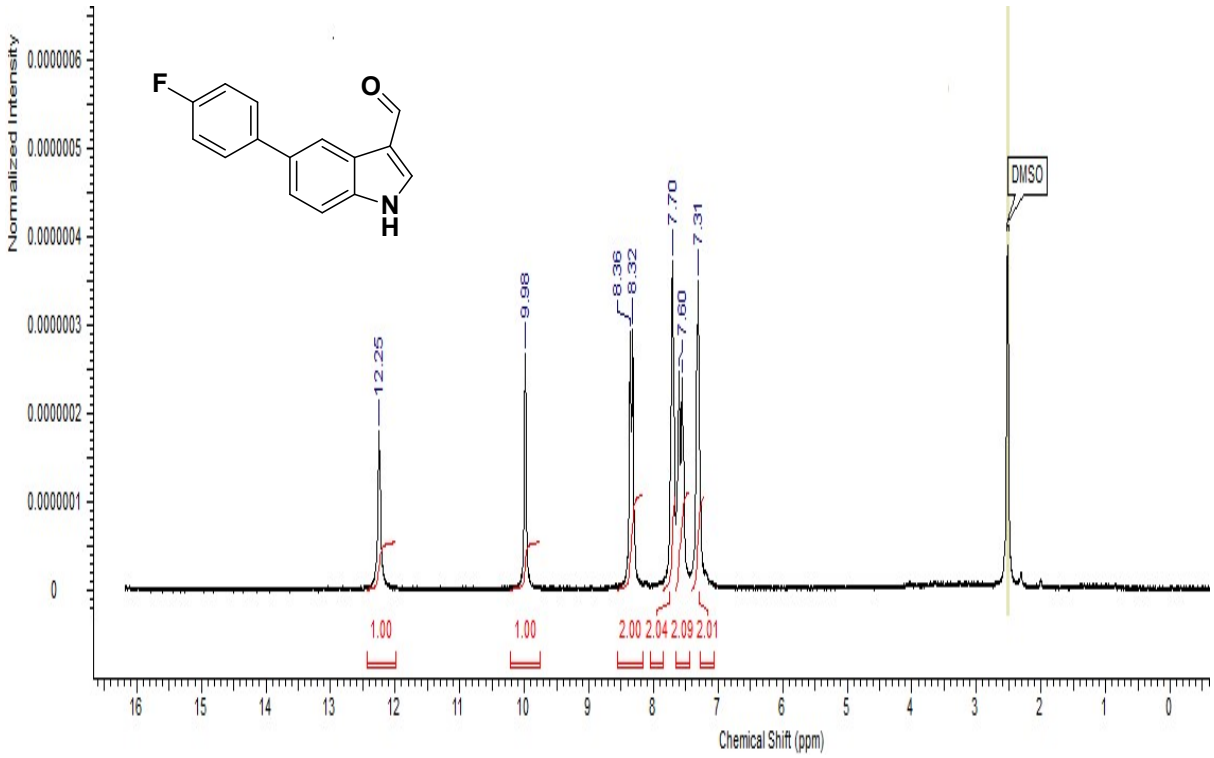


Figure S33. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **7a**

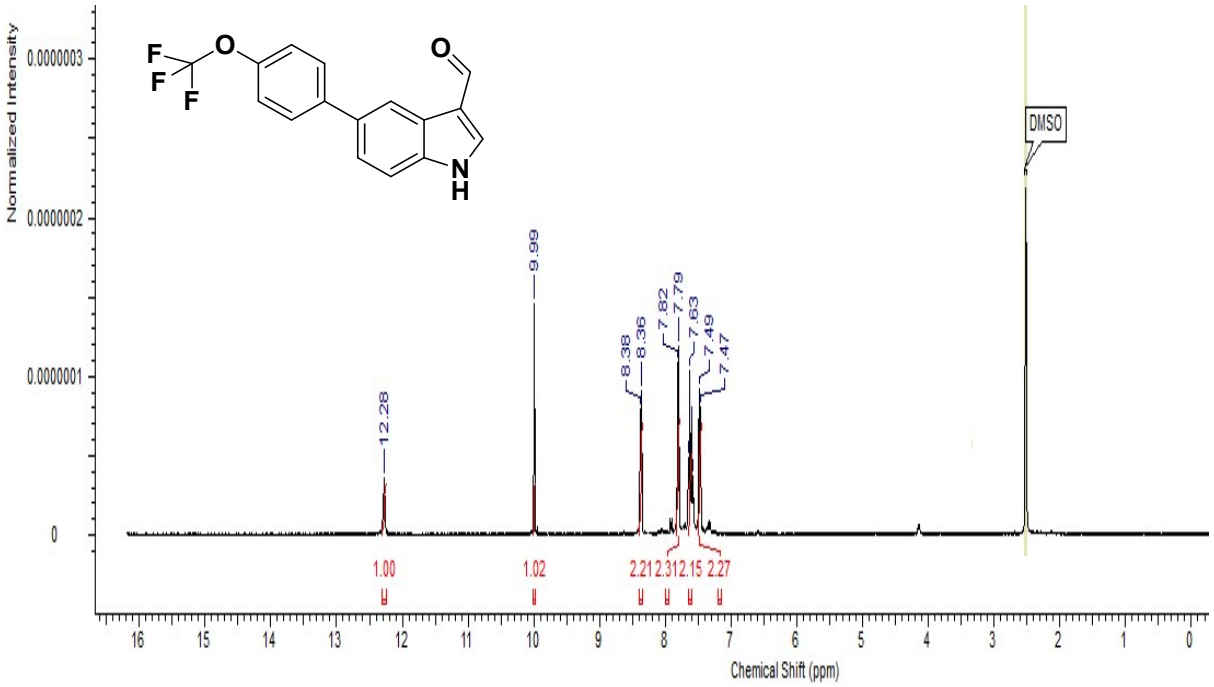


Figure S34. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **7b**

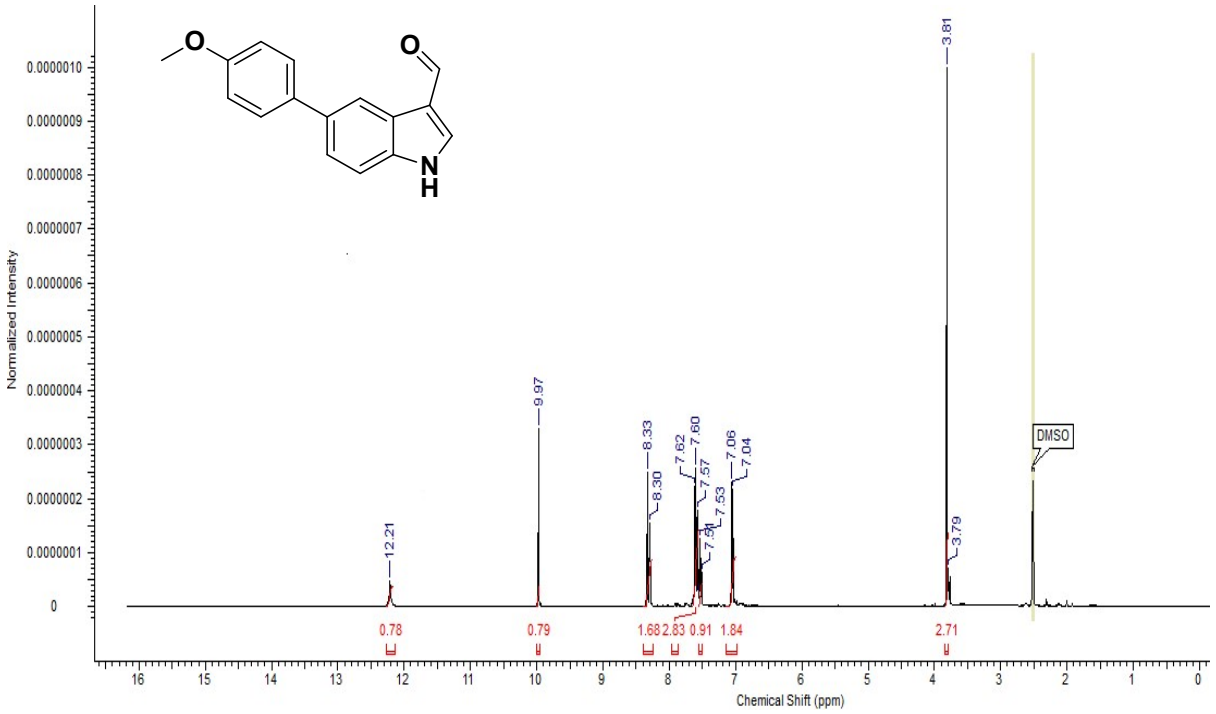


Figure S35. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **7c**

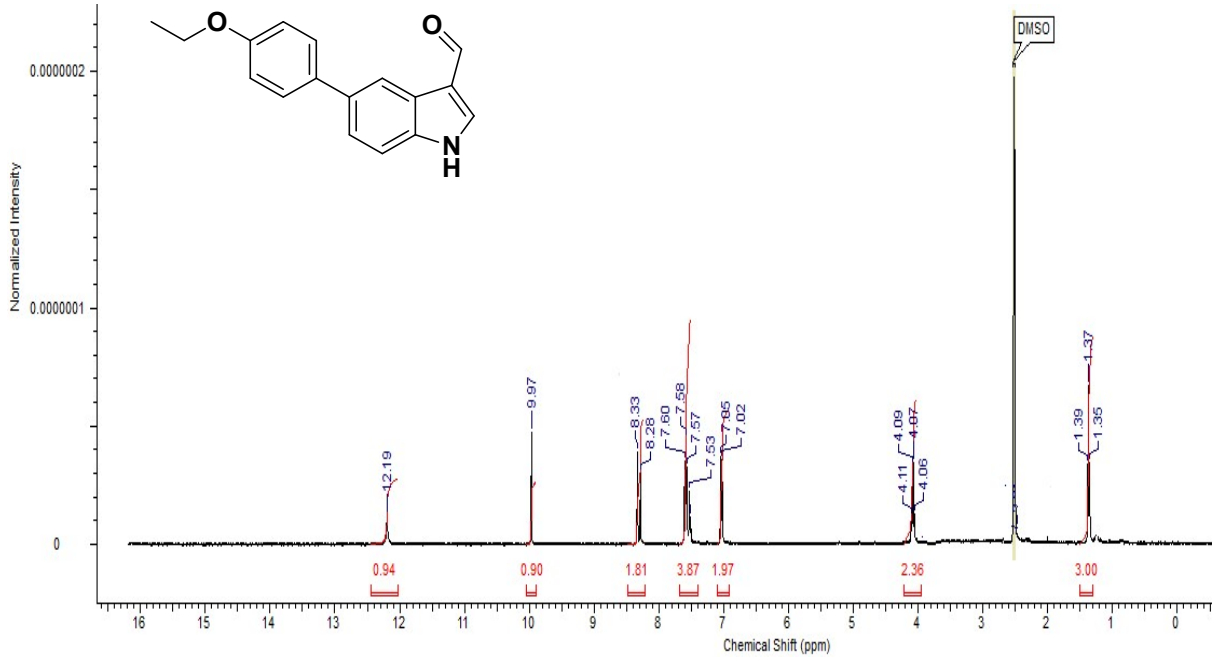


Figure S36. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **7d**

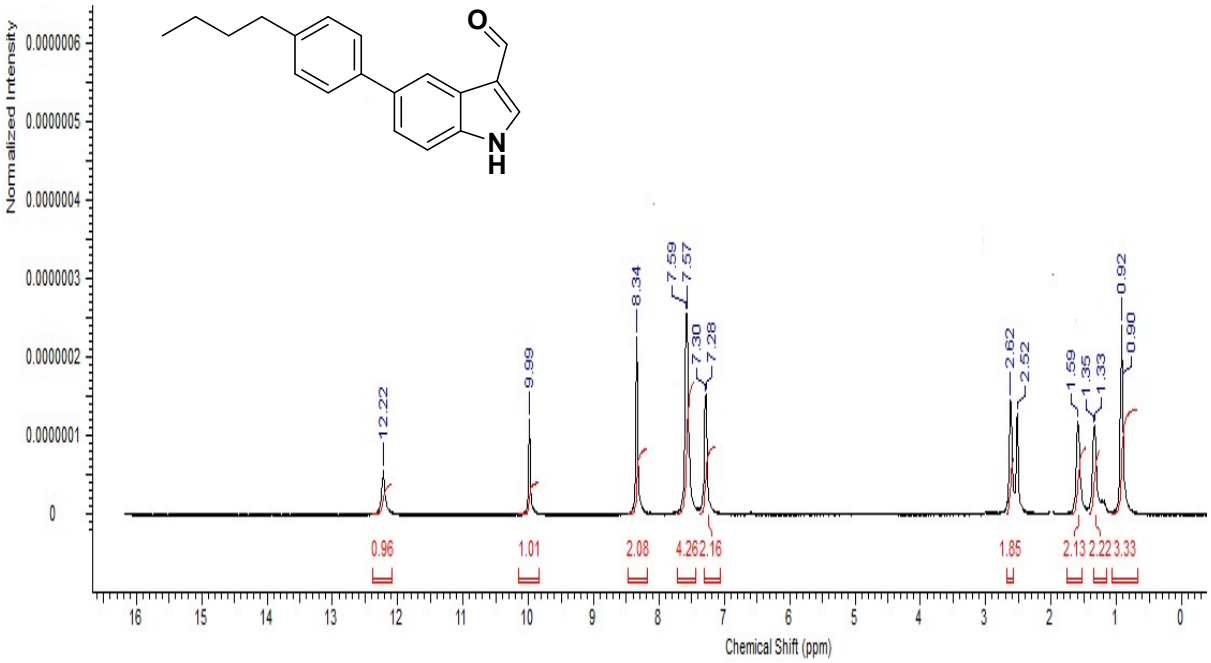


Figure S37. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **7e**

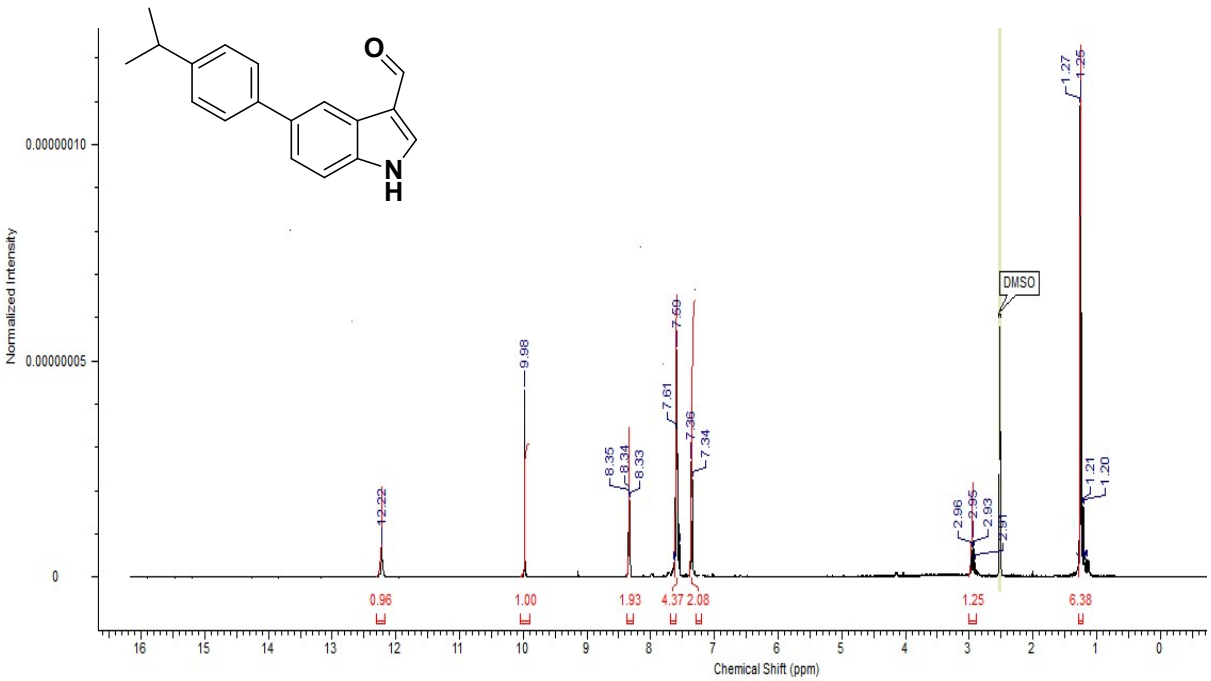


Figure S38. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **7f**

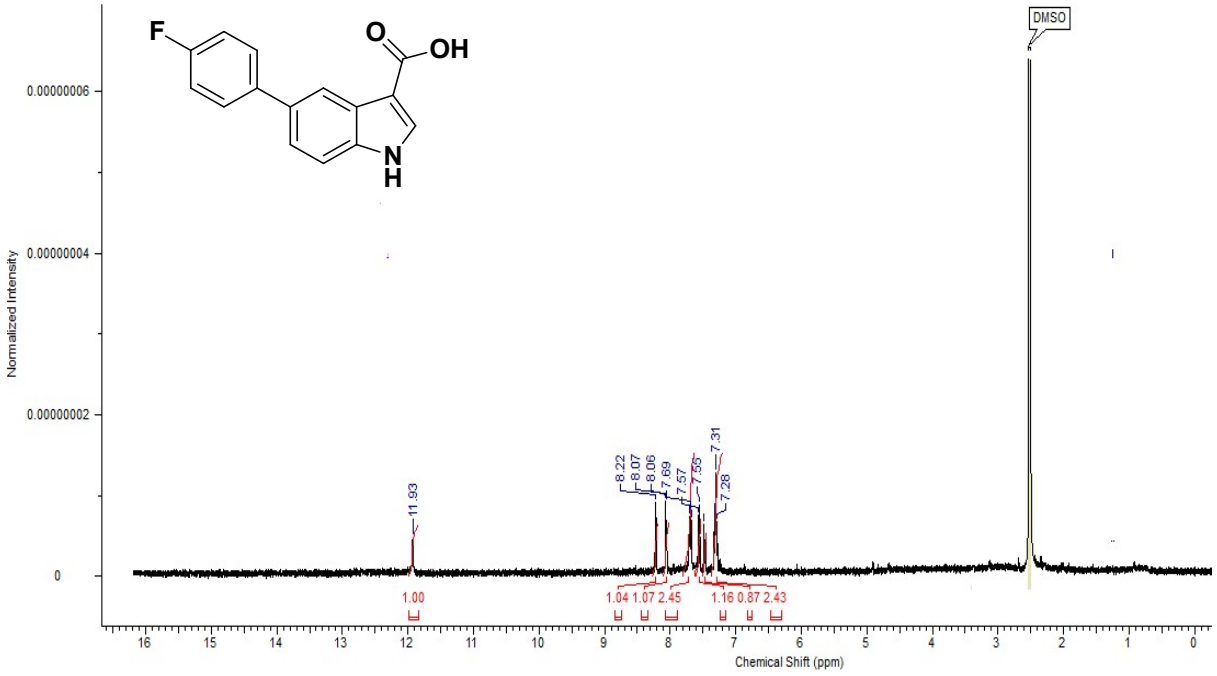


Figure S39. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **8a**

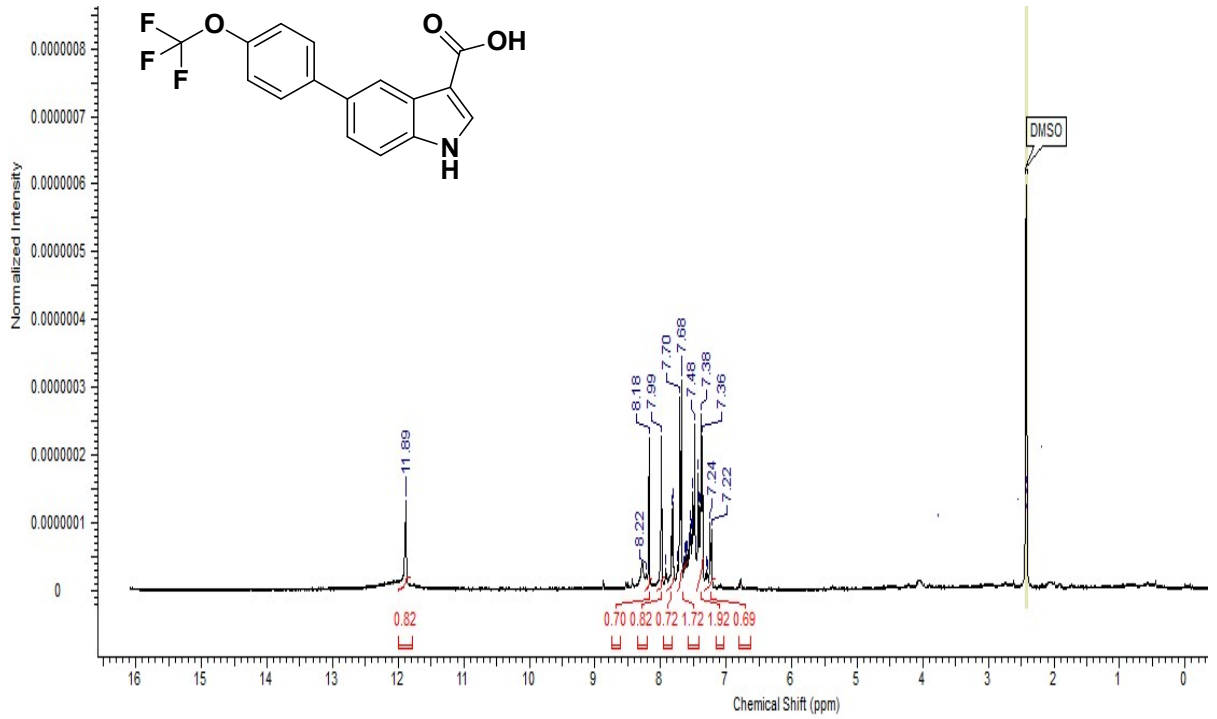


Figure S40. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **8b**

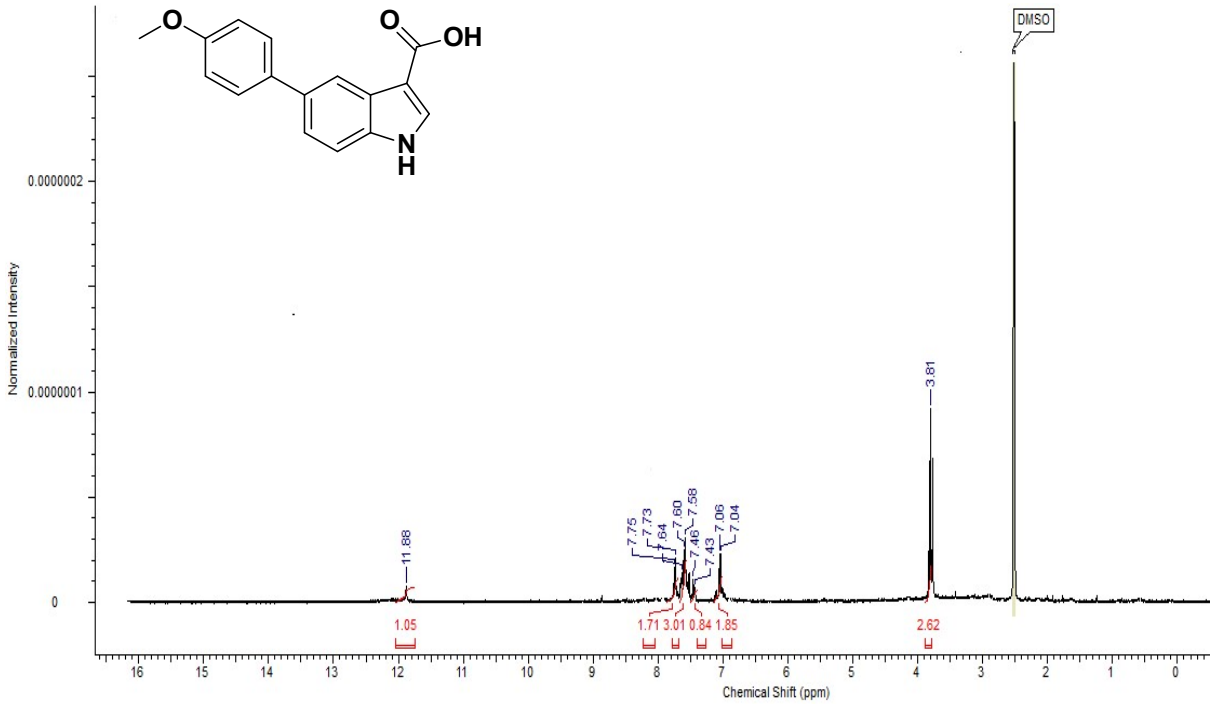


Figure S41. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **8c**

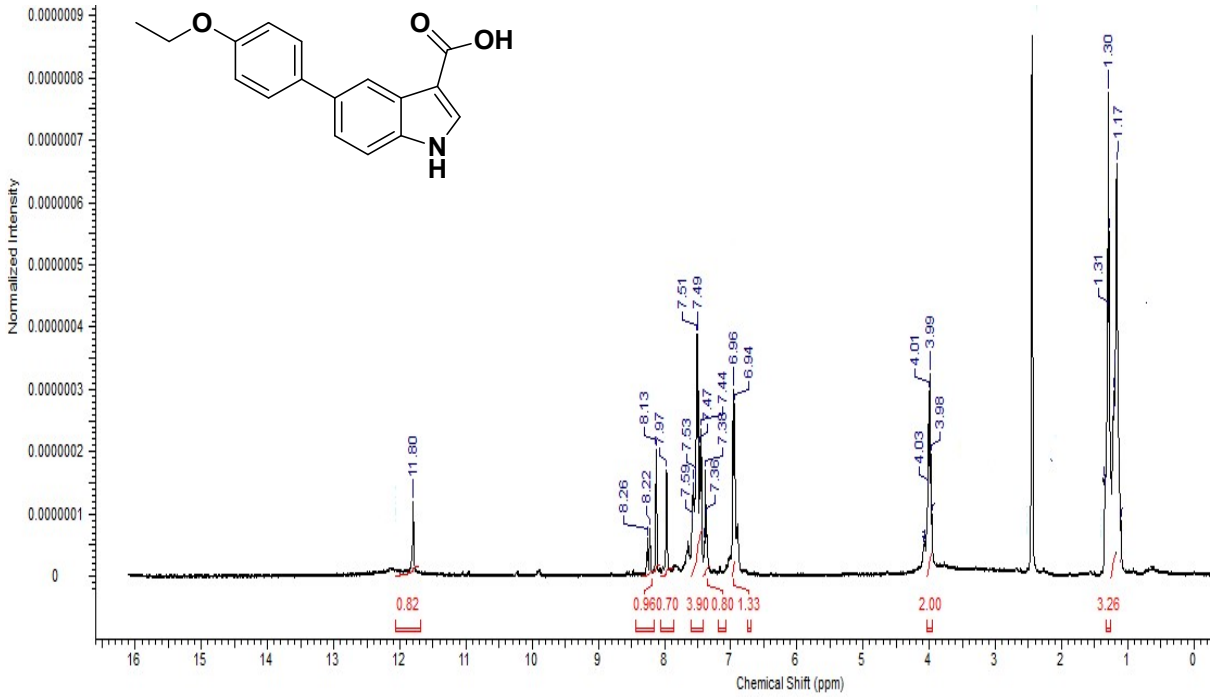


Figure S42. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **8d**

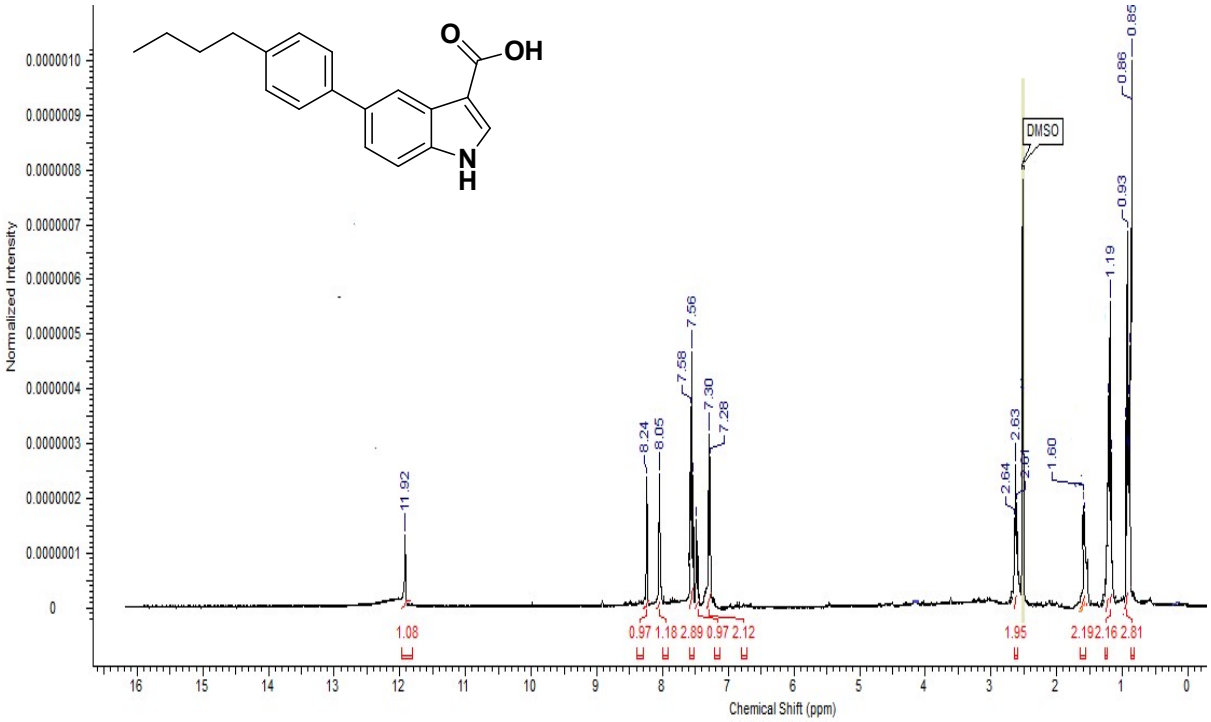


Figure S43. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **8e**

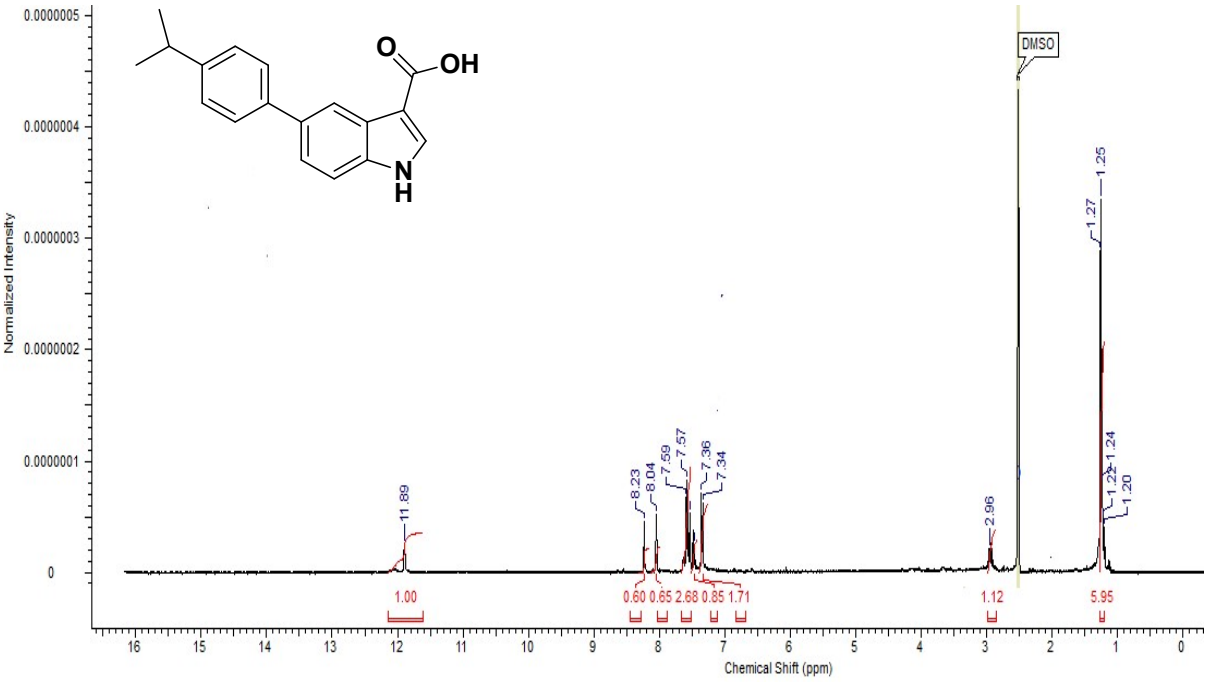


Figure S44. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **8f**

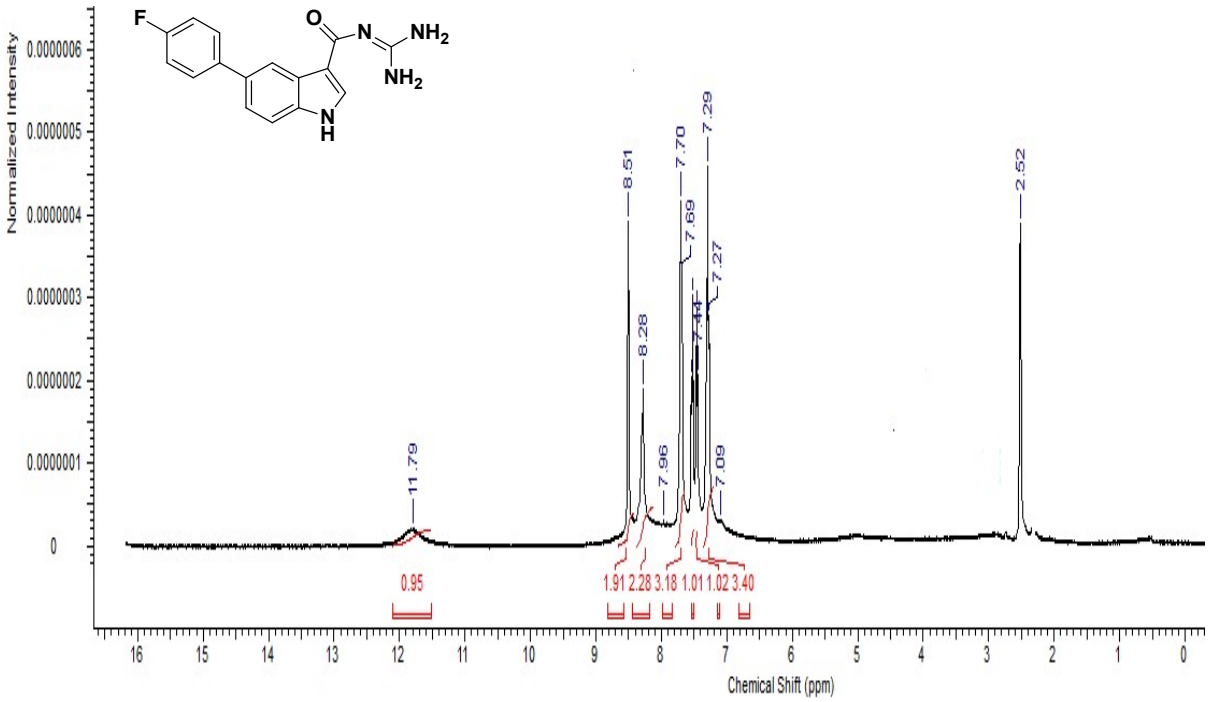


Figure S45. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **9a**

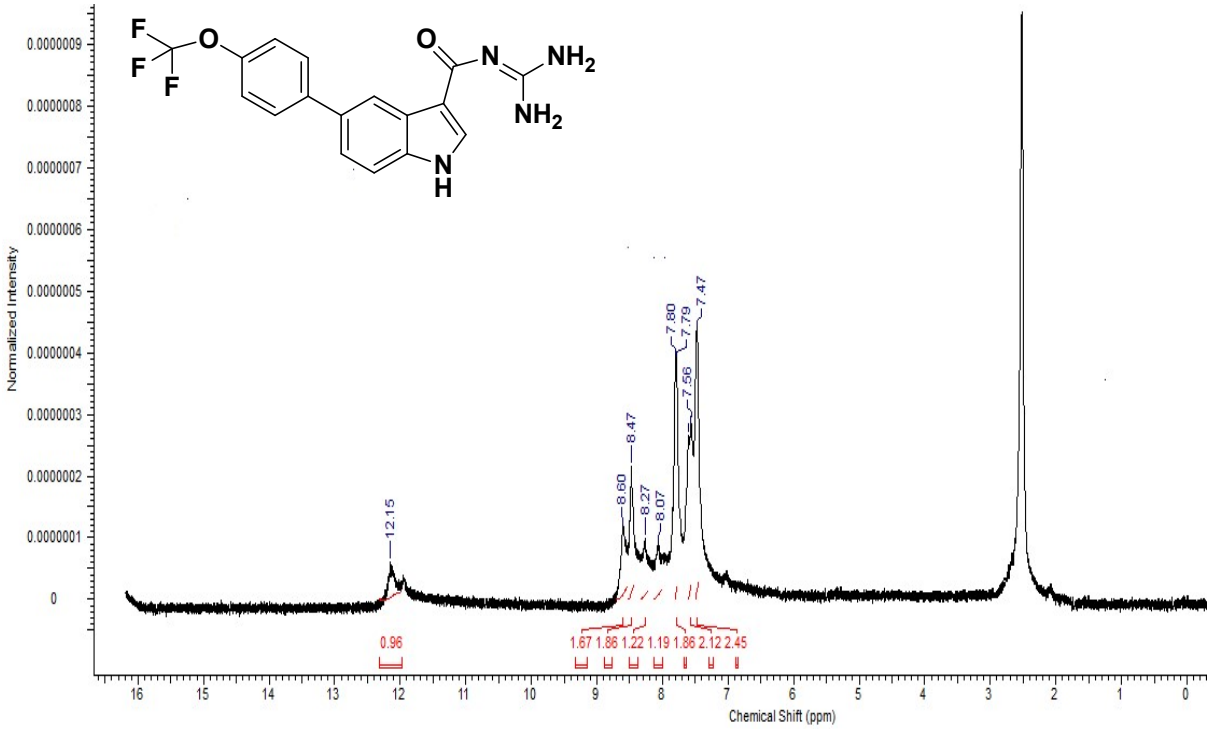


Figure S46. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **9b**

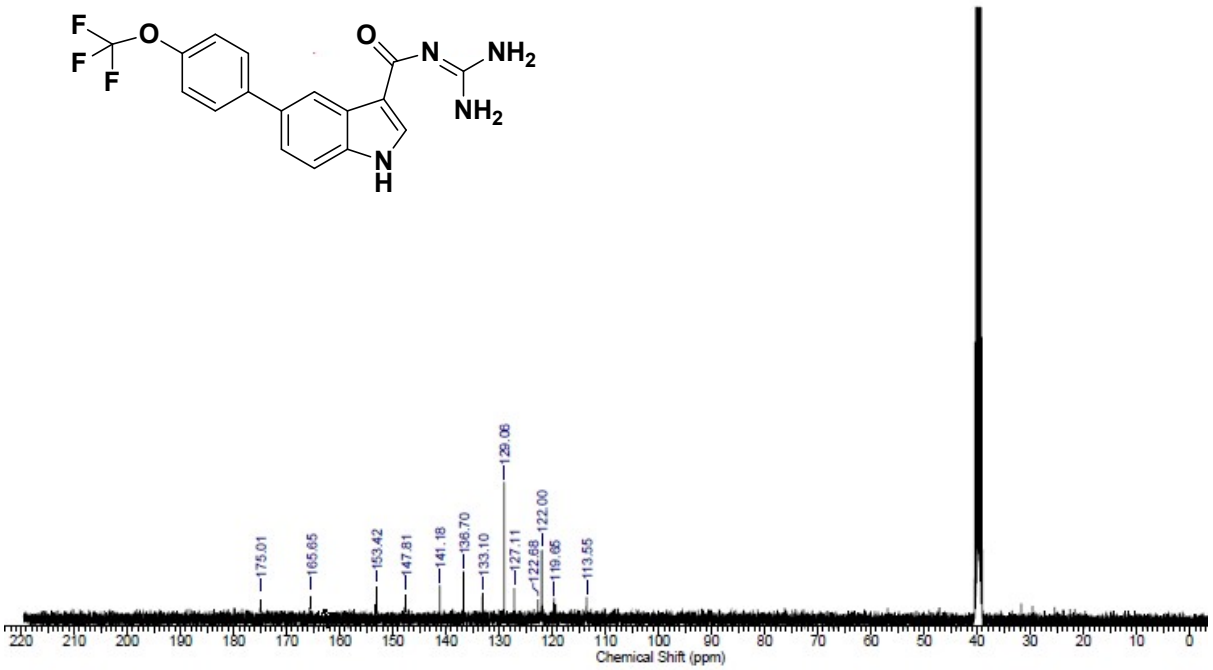


Figure S47. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **9b**

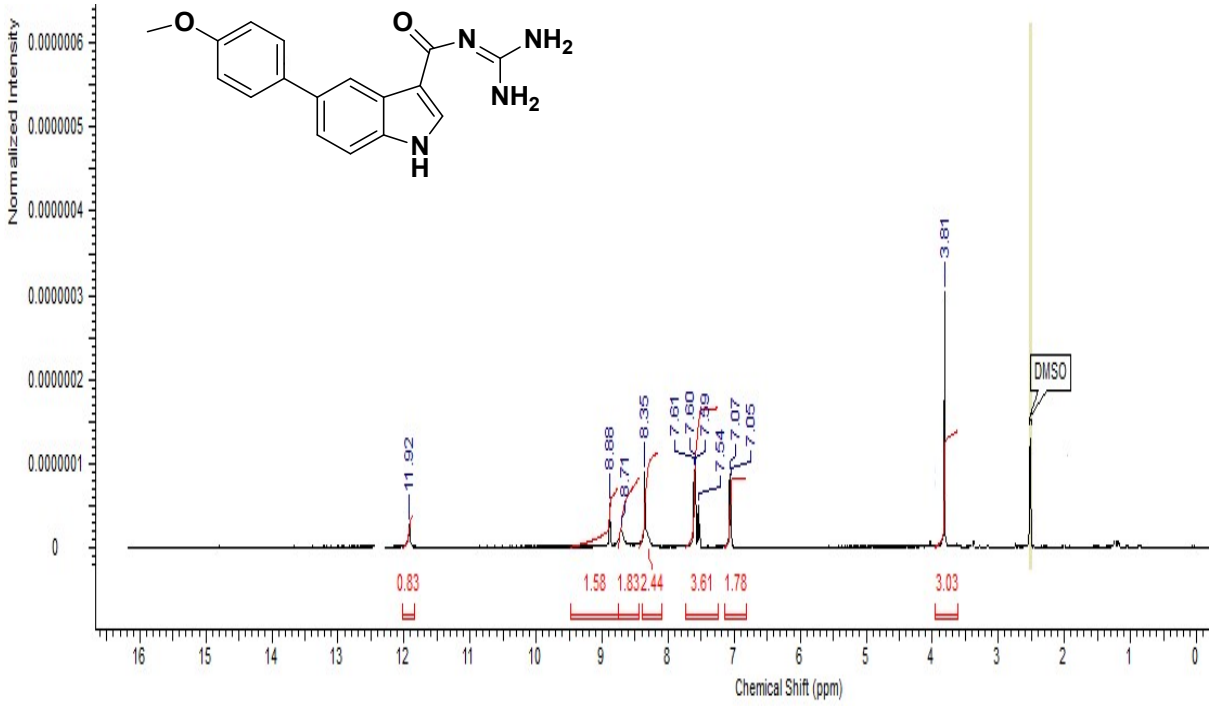


Figure S48. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **9c**

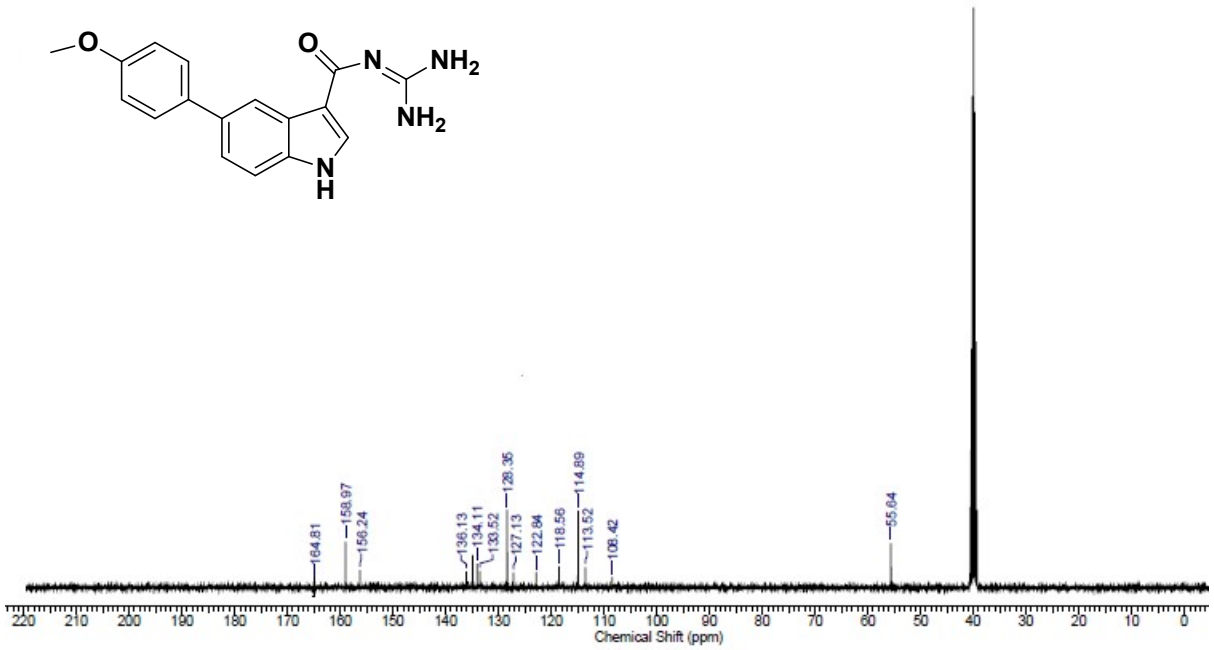


Figure S49. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **9c**

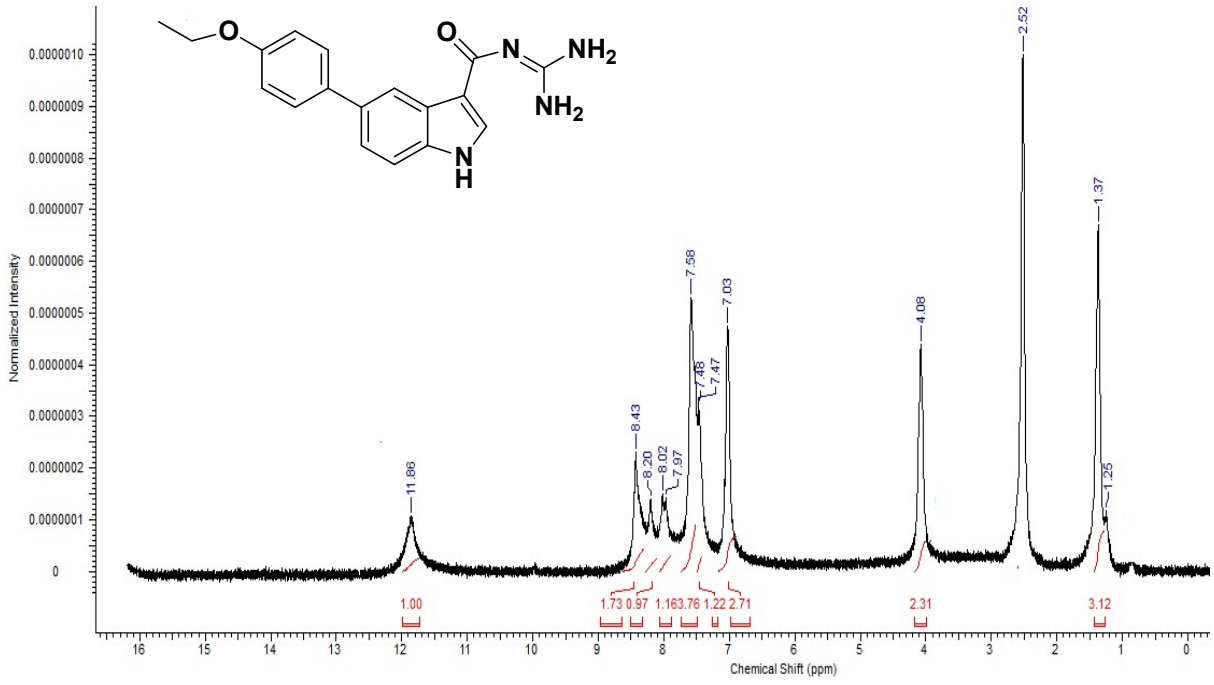


Figure S50. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **9d**

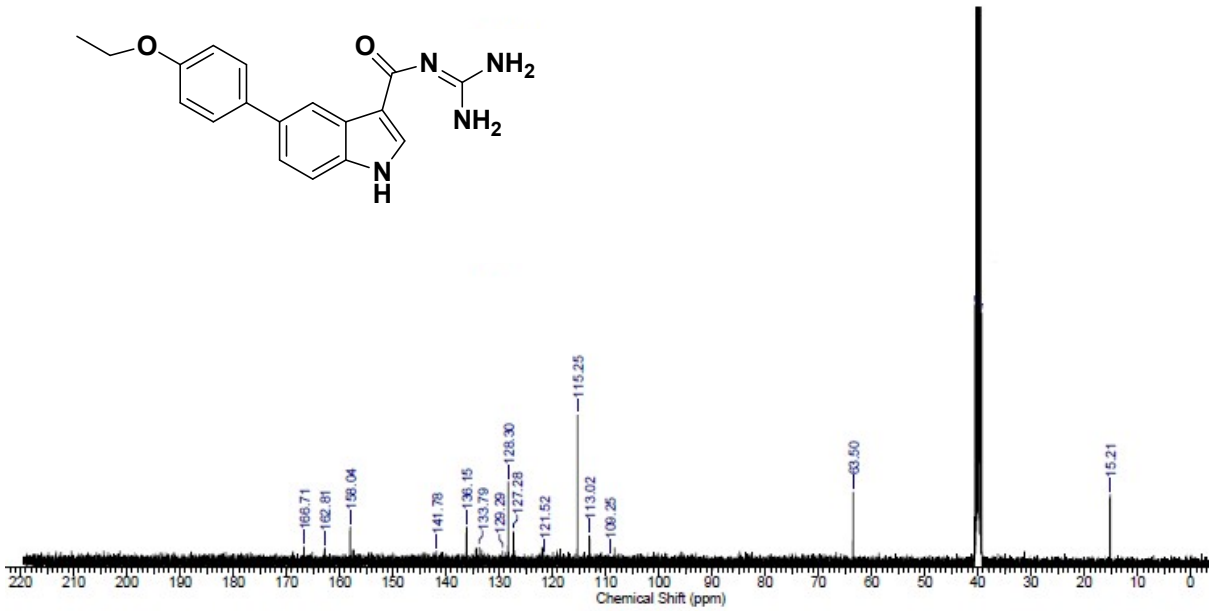


Figure S51. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **9d**

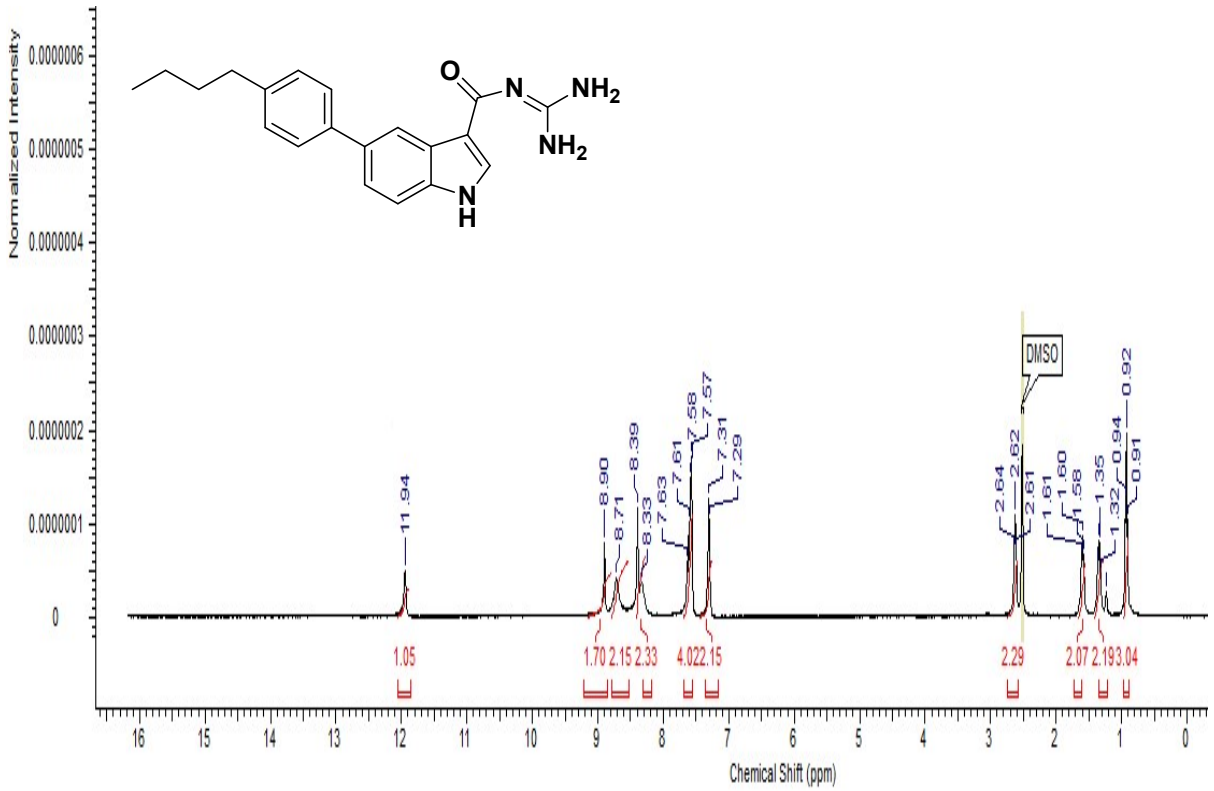


Figure S52. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **9e**

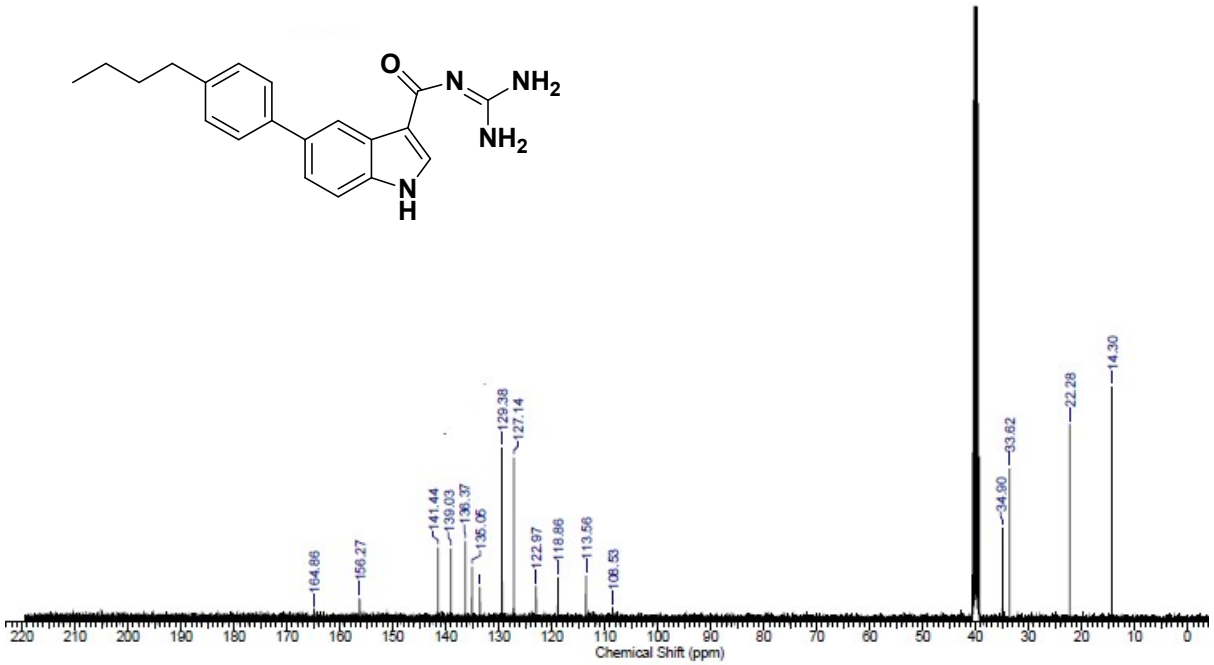


Figure S53. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **9e**

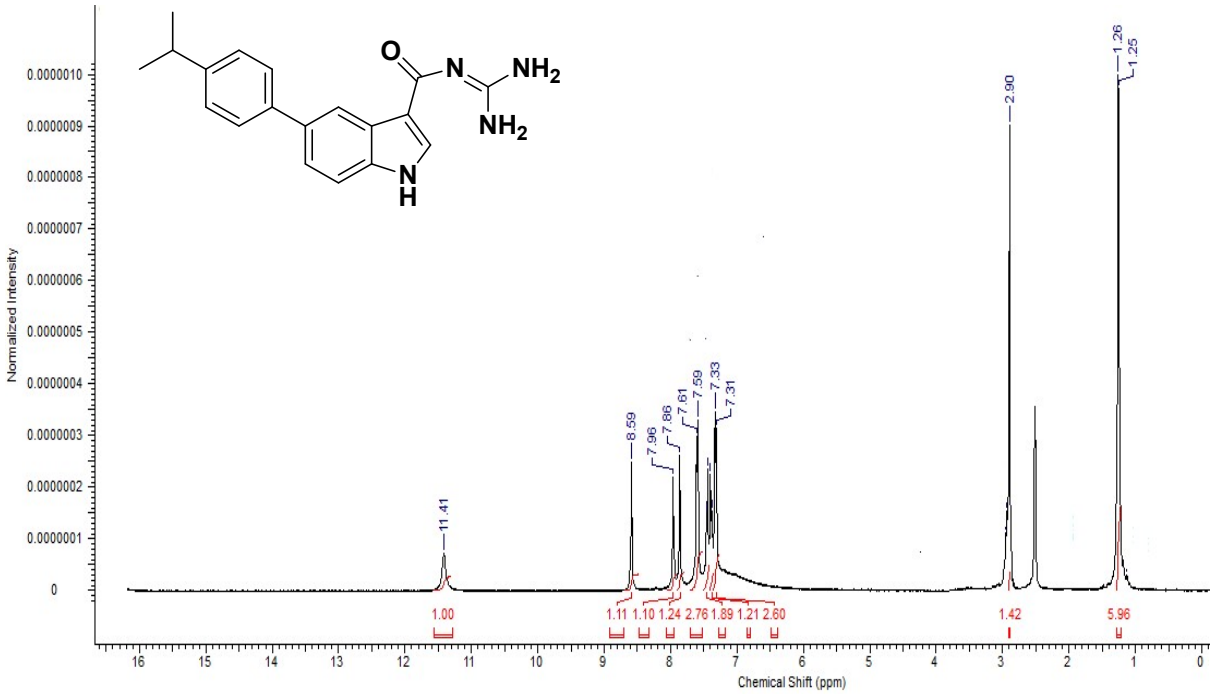


Figure S54. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **9f**

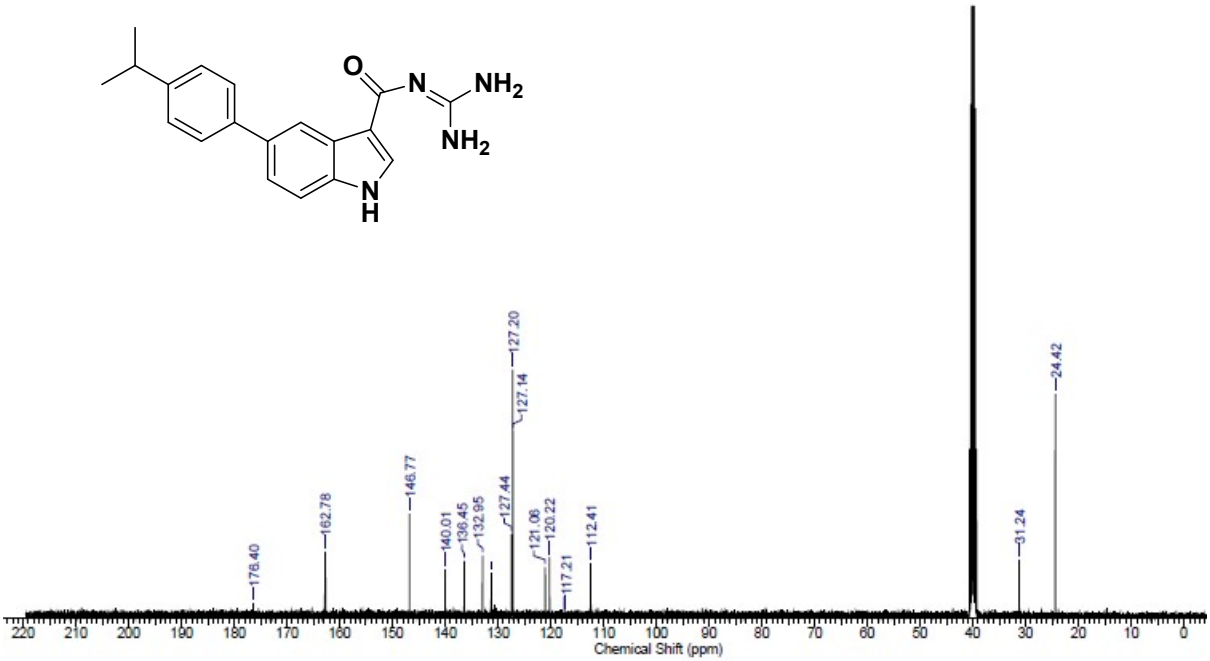


Figure S55. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **9f**

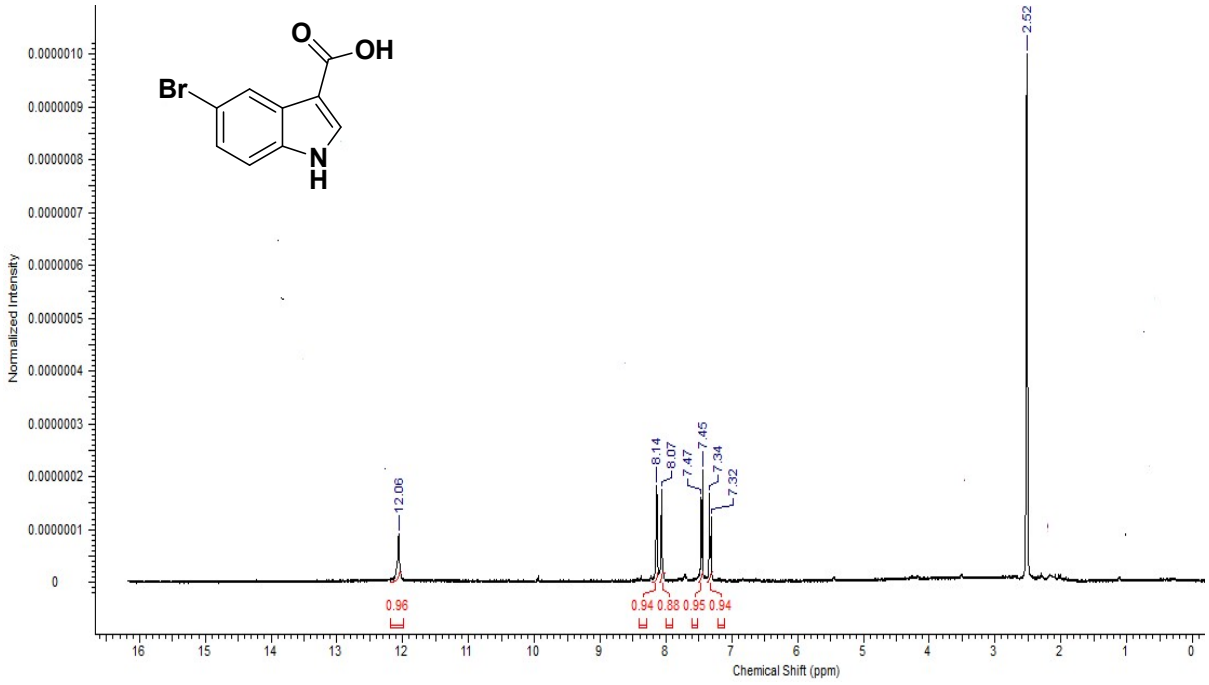


Figure S56. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **10**

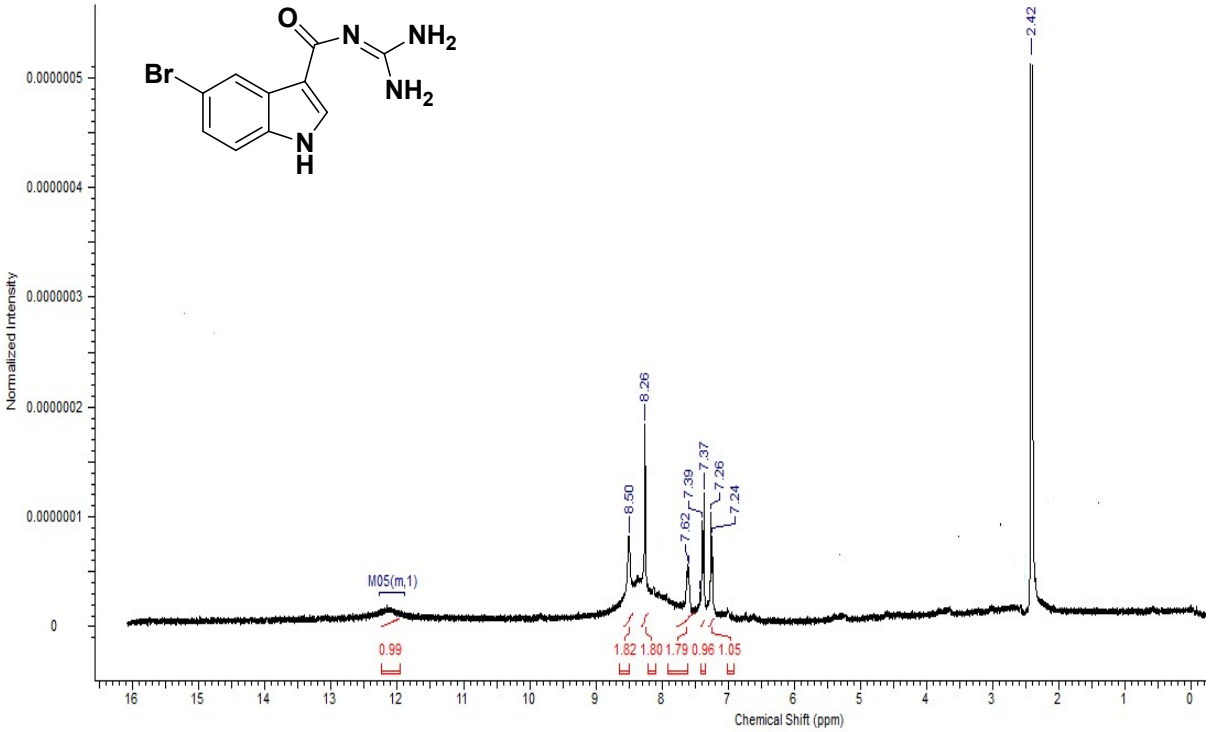


Figure S57. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **11**

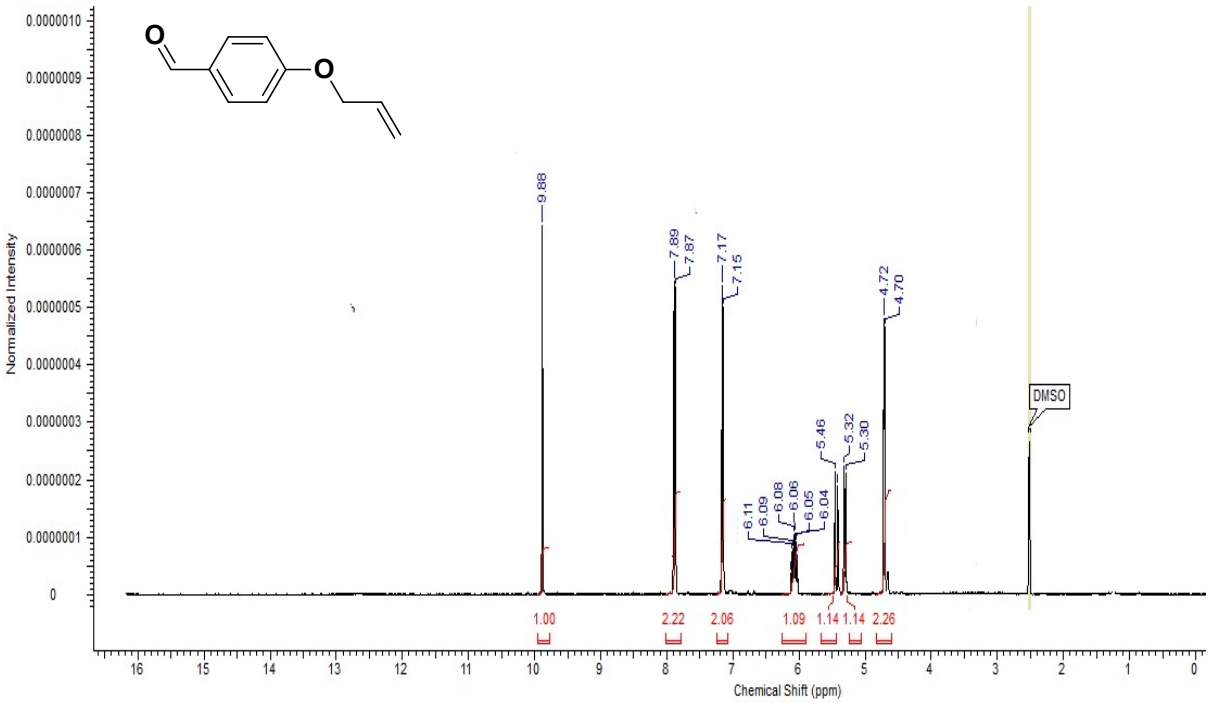


Figure S58. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13a**

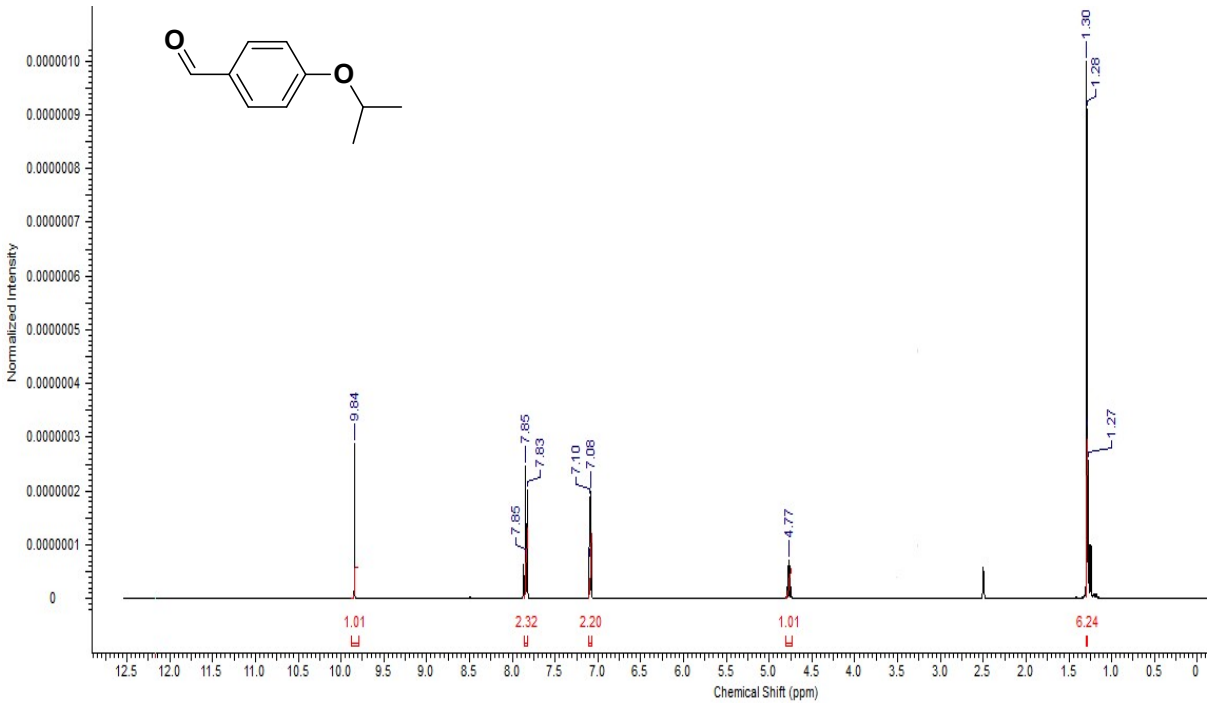


Figure S59. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13b**

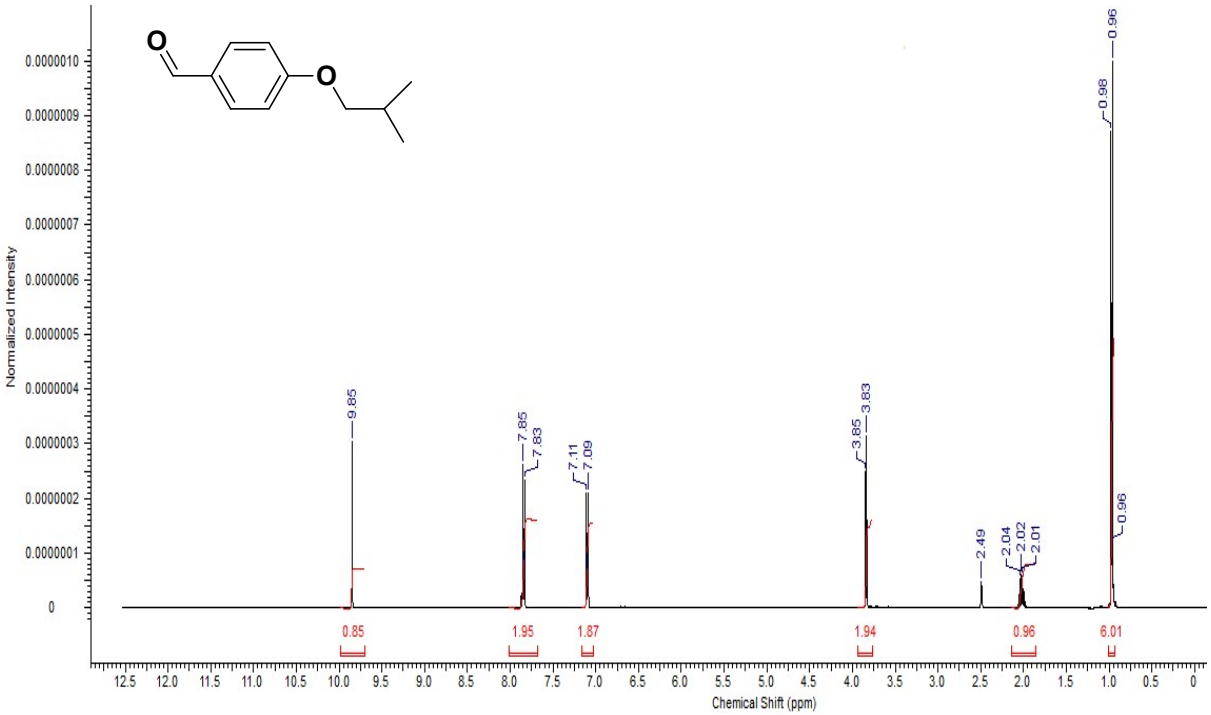


Figure S60. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13c**

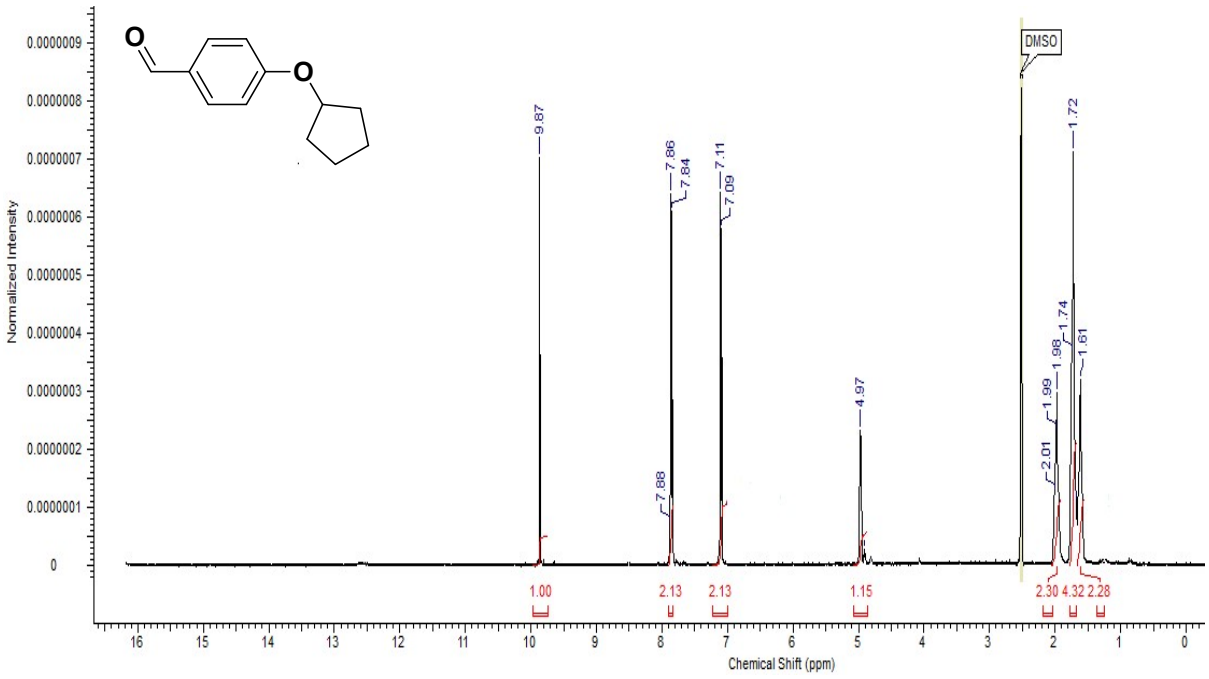


Figure S61. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13d**

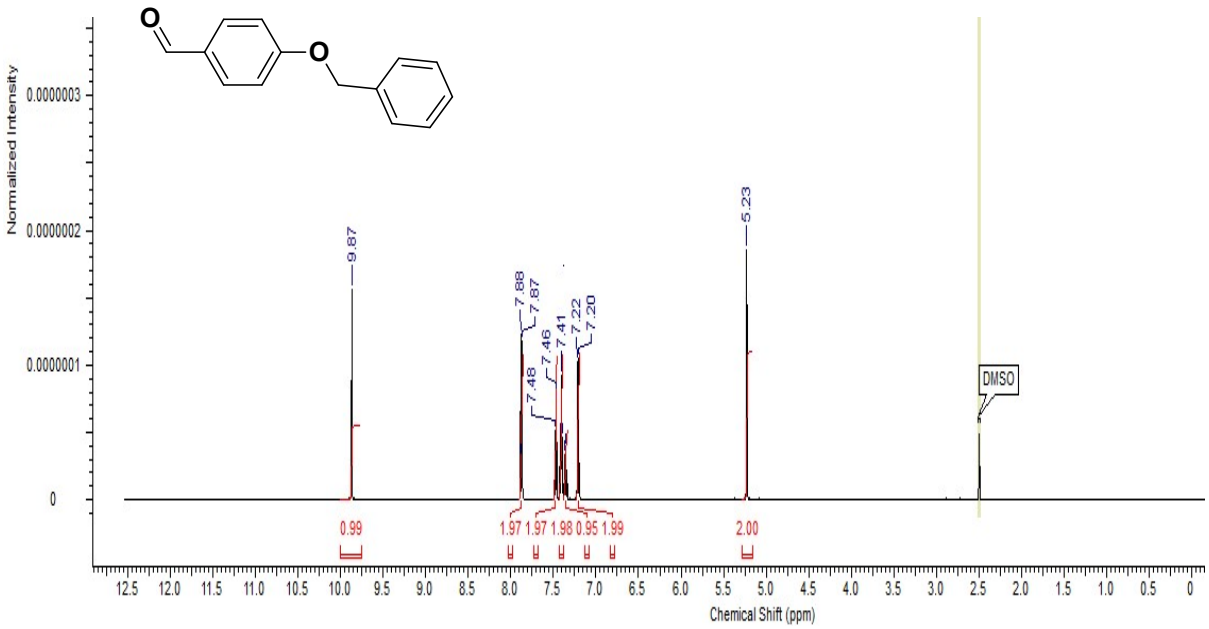


Figure S62. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13e**

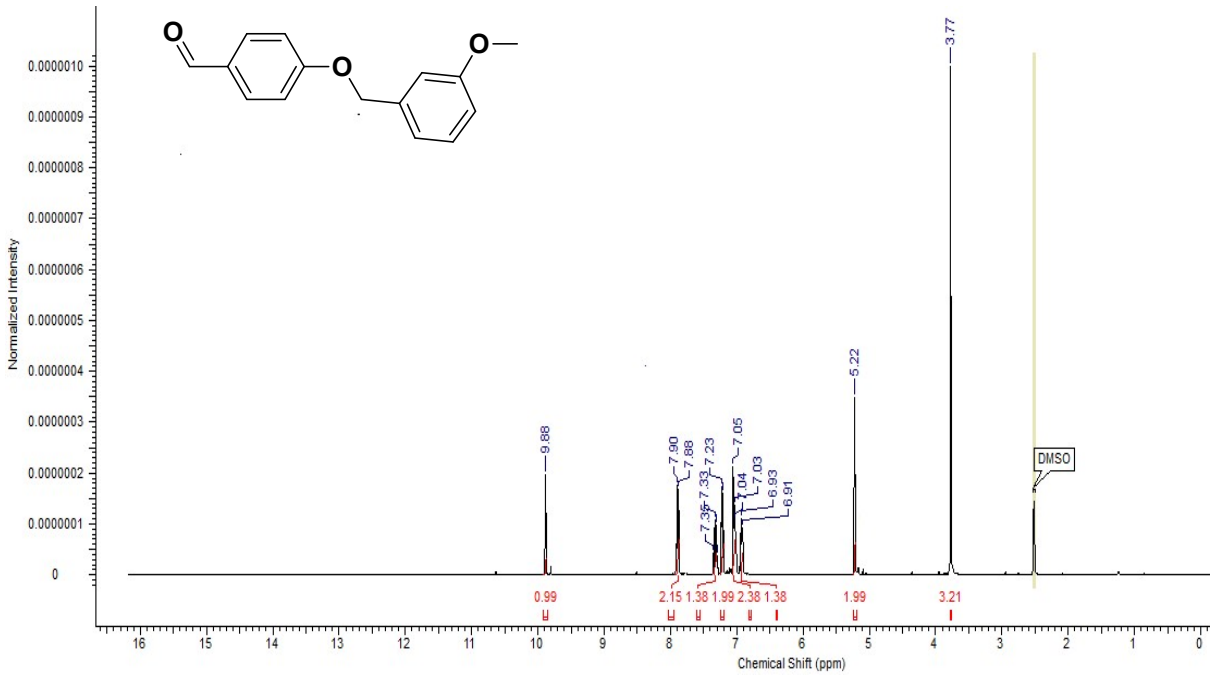


Figure S63. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13f**

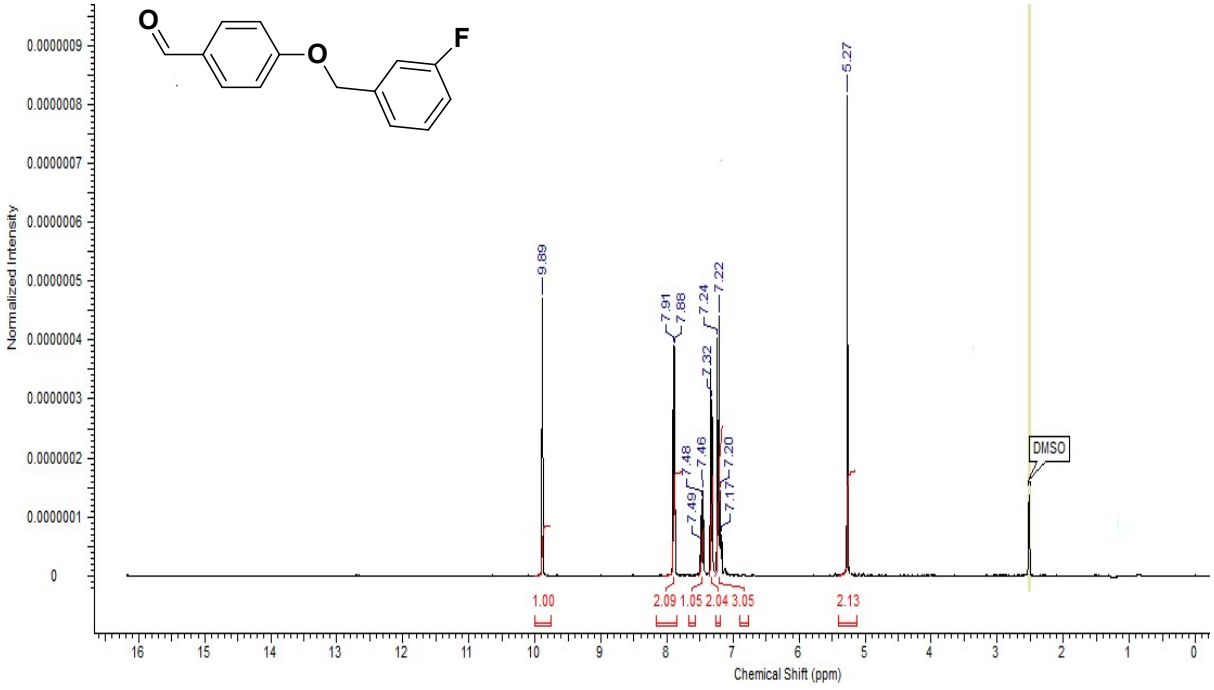


Figure S64. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13g**

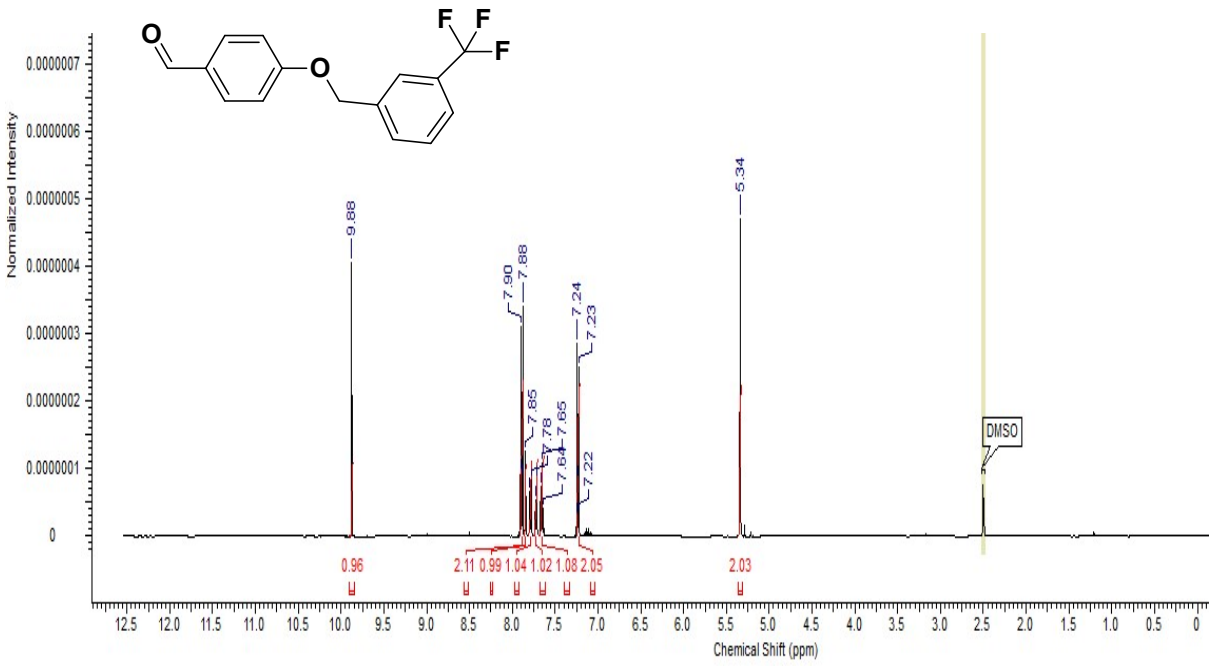


Figure S65. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13h**

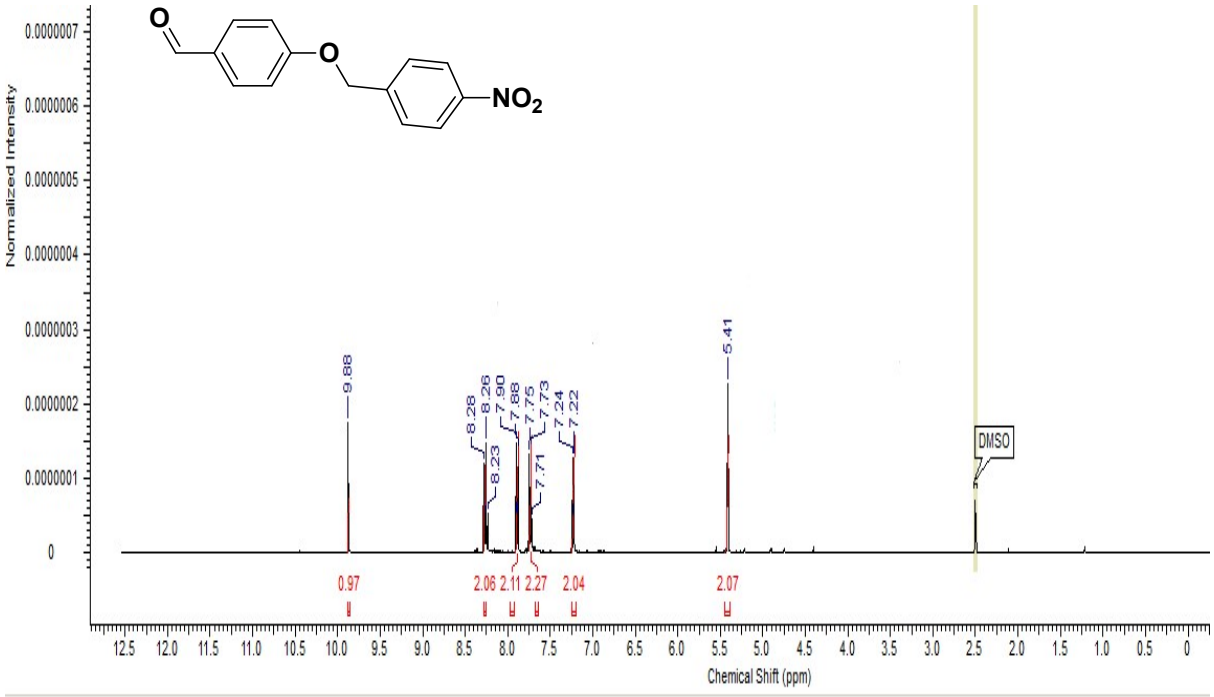


Figure S66. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **13i**

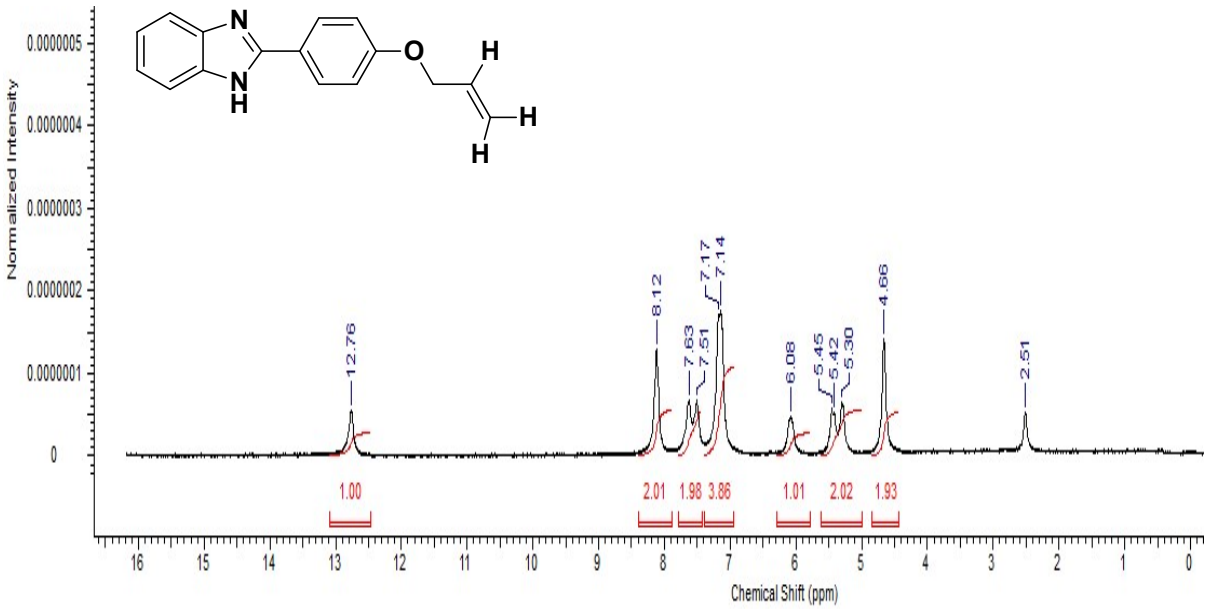


Figure S67. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14a**

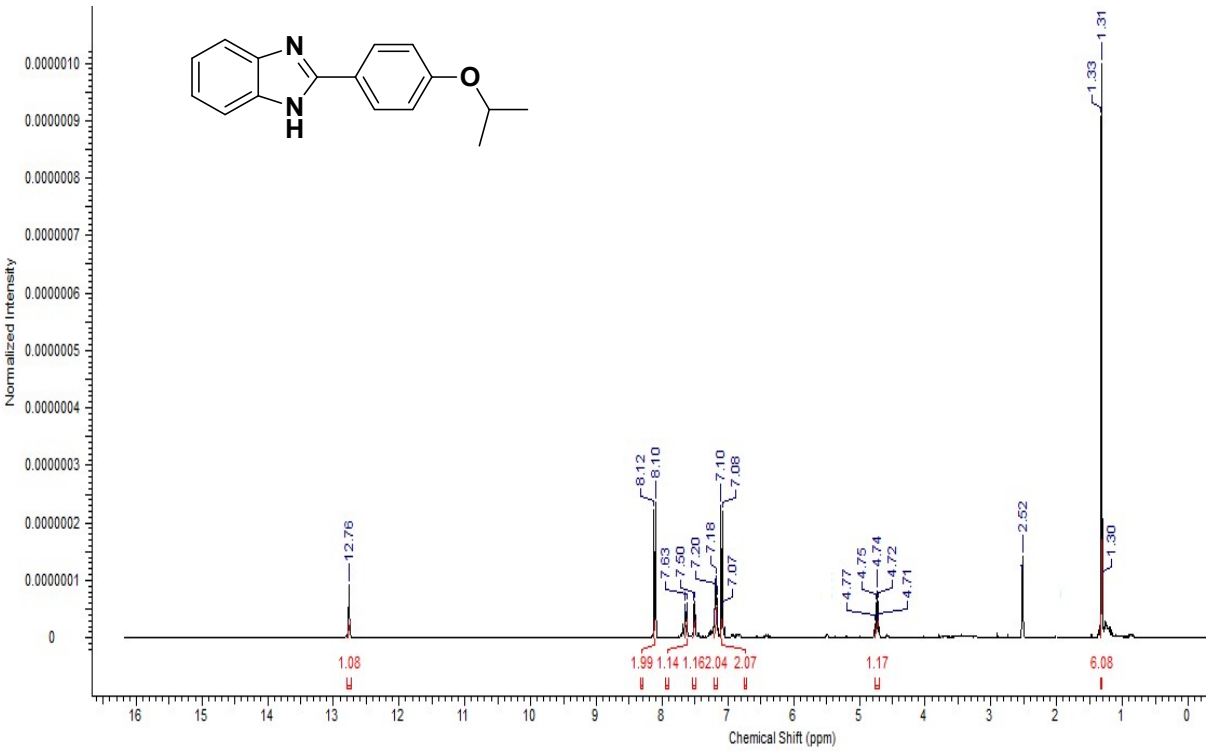


Figure S68. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14b**

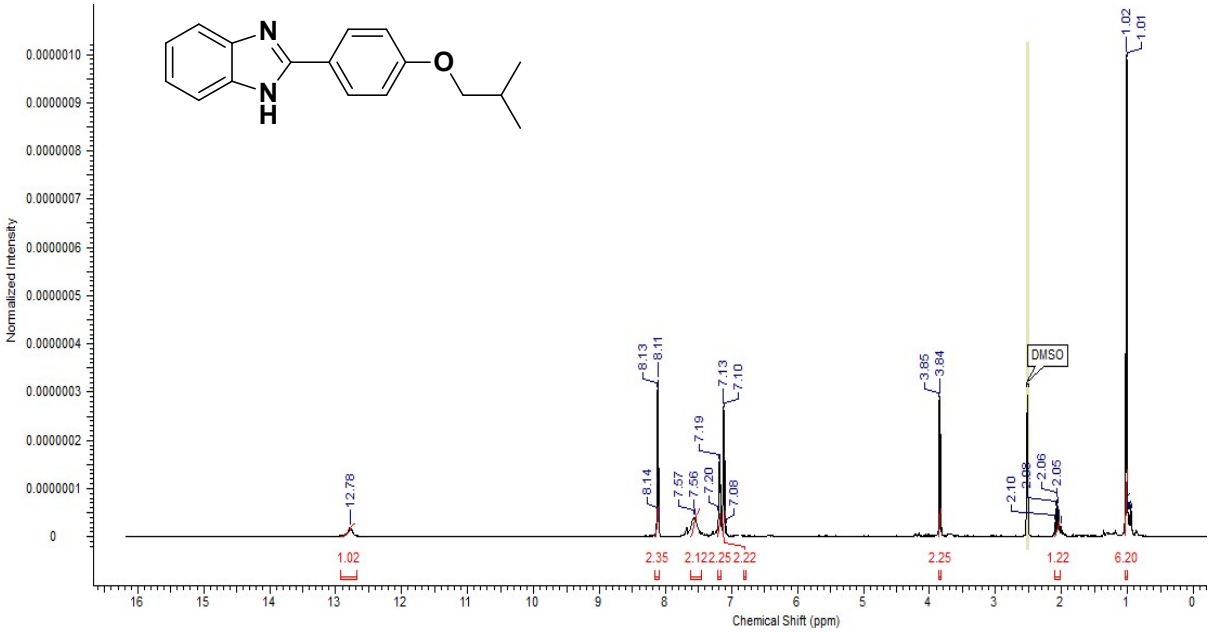


Figure S69. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14c**

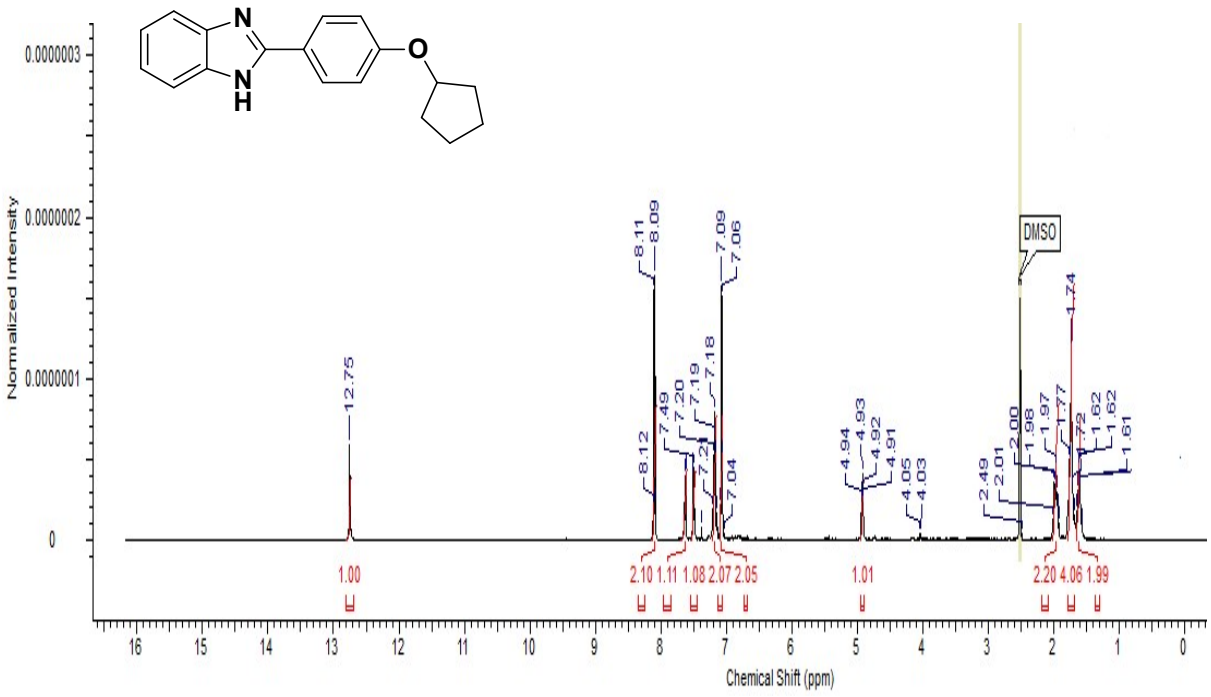


Figure S70. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14d**

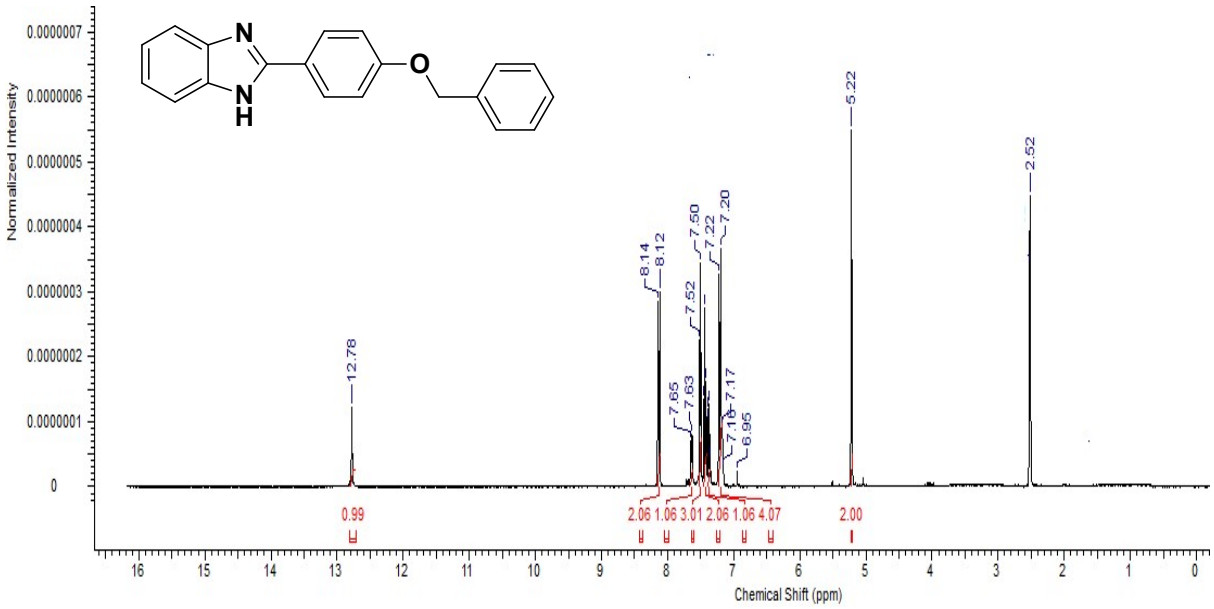


Figure S71. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14e**

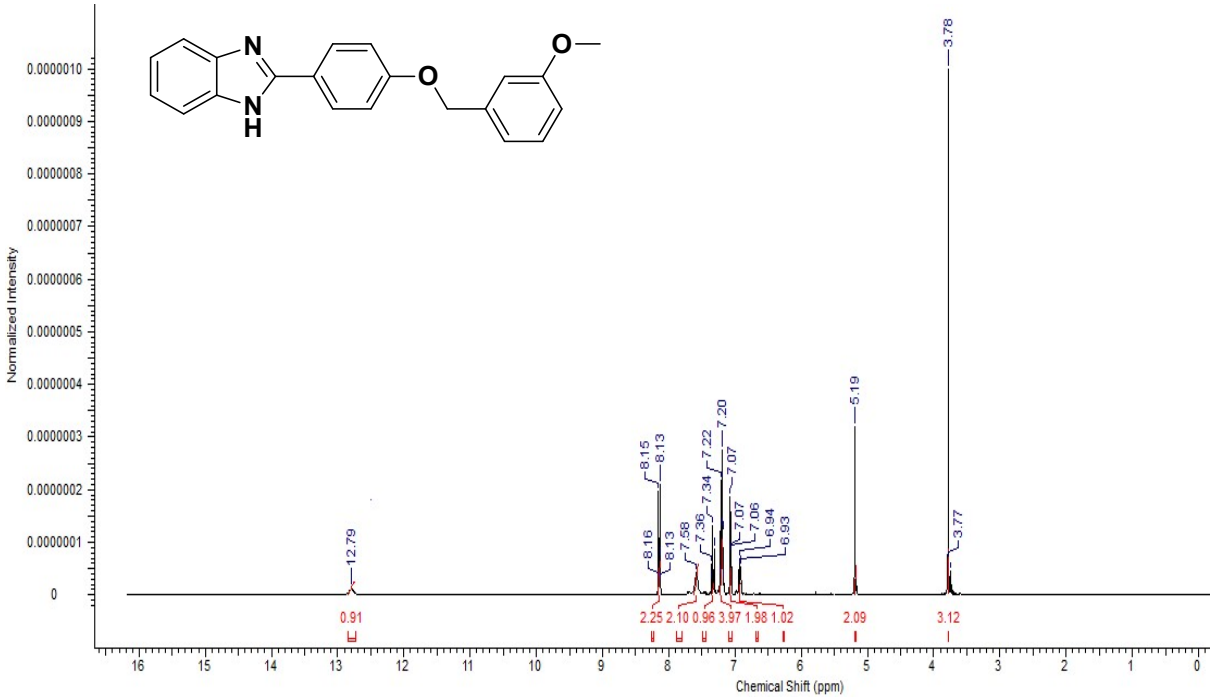


Figure S72. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14f**

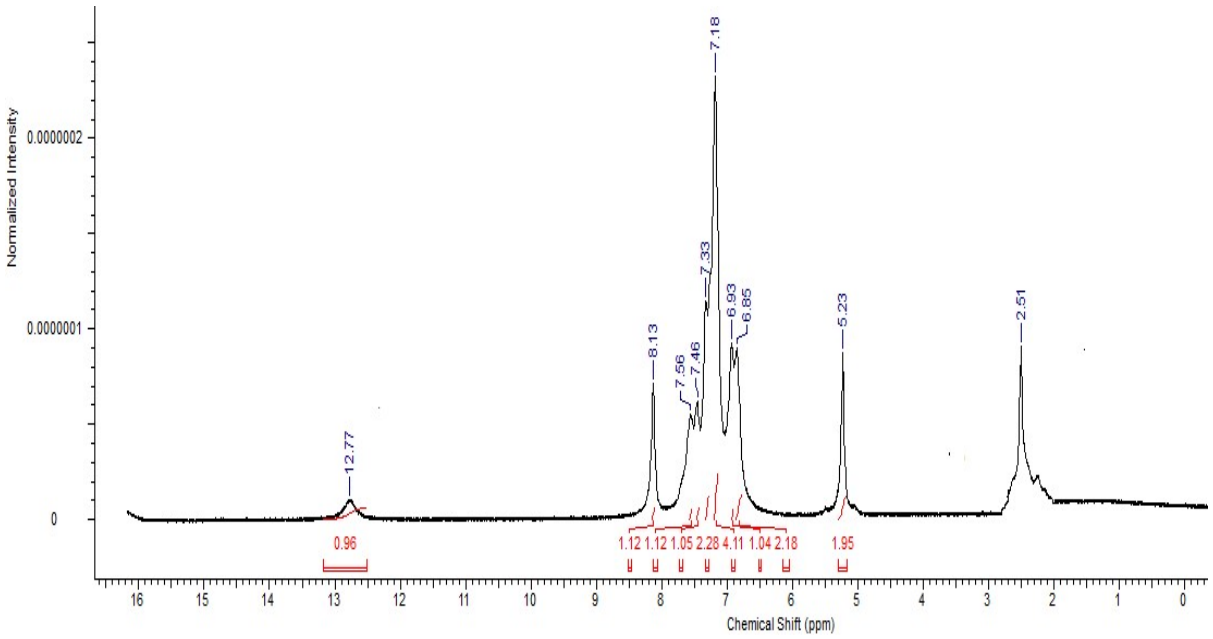


Figure S73. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14g**

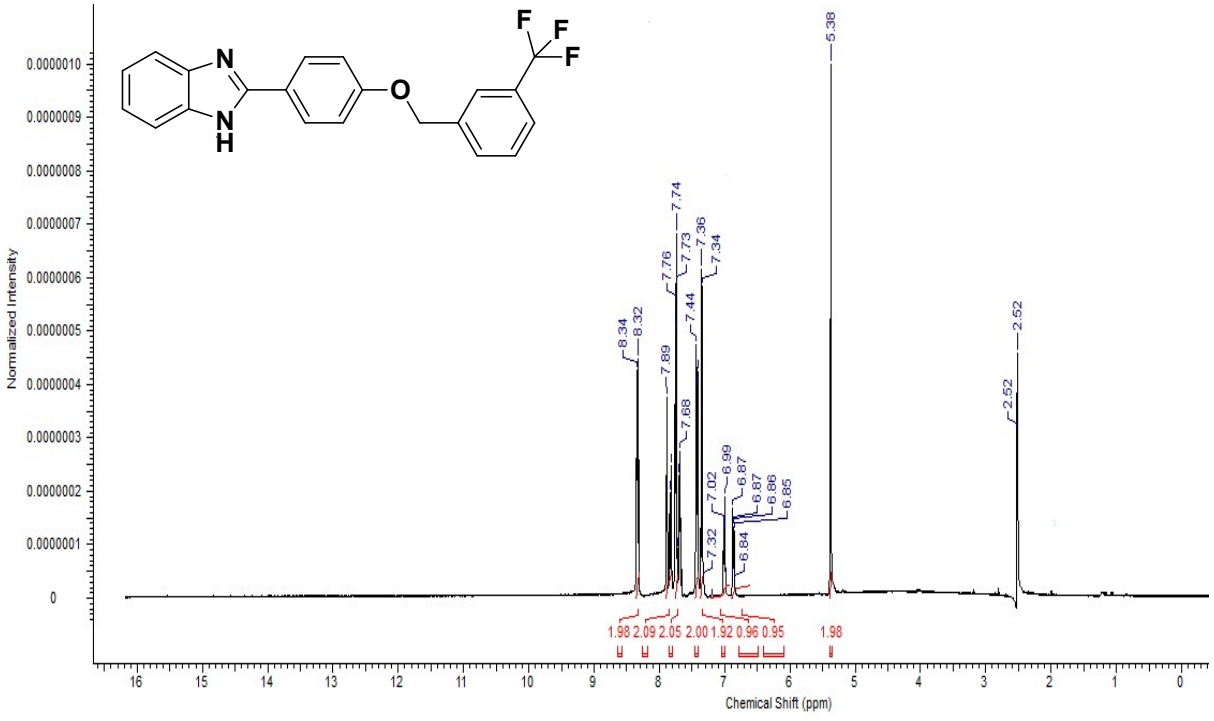


Figure S74. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14h**

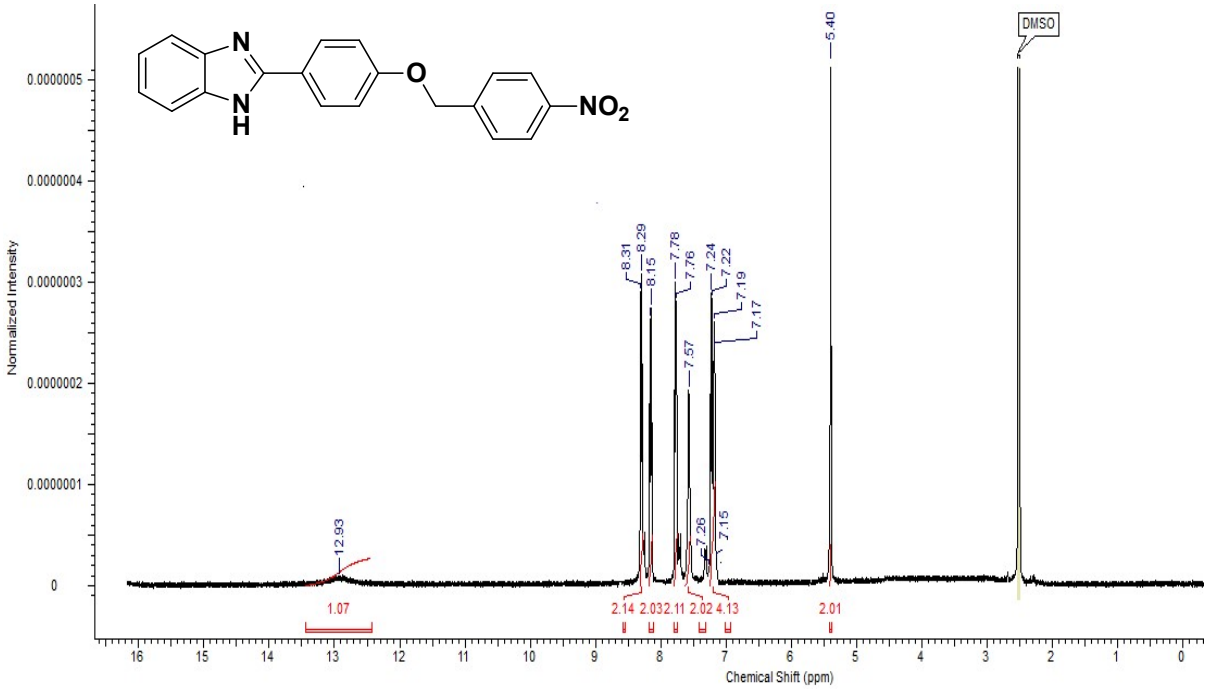


Figure S75. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14i**

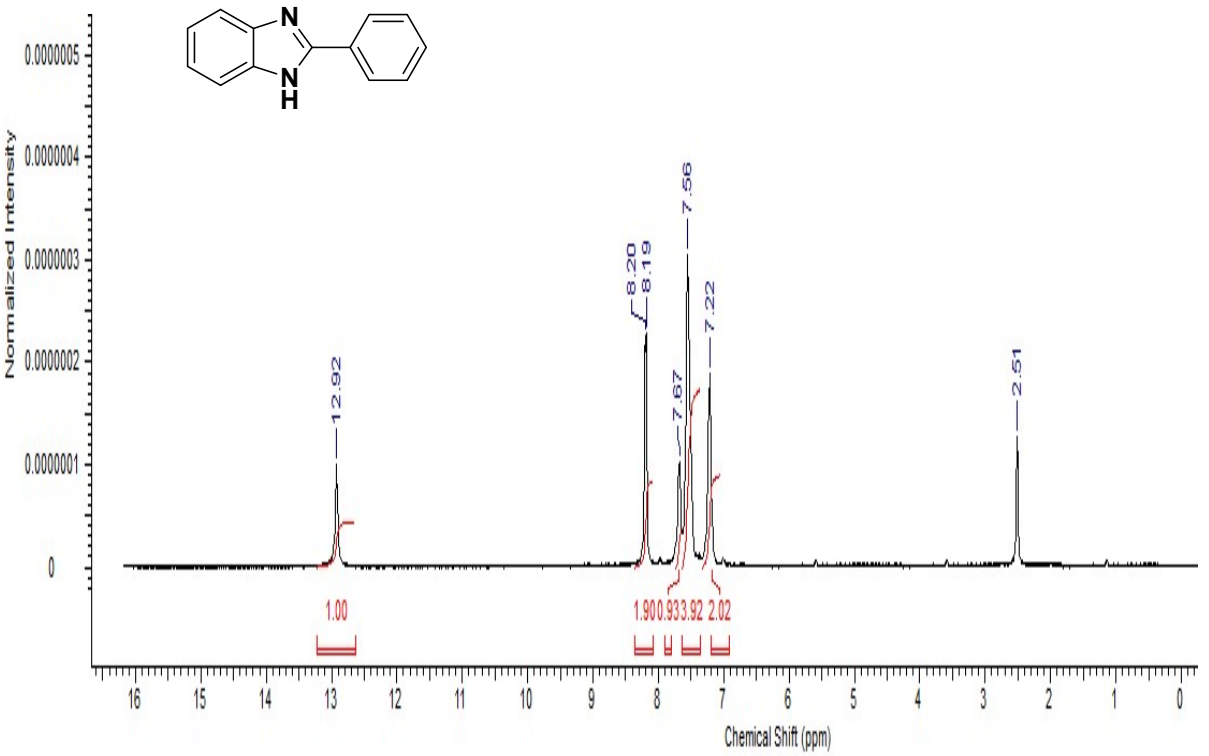


Figure S76. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14j**

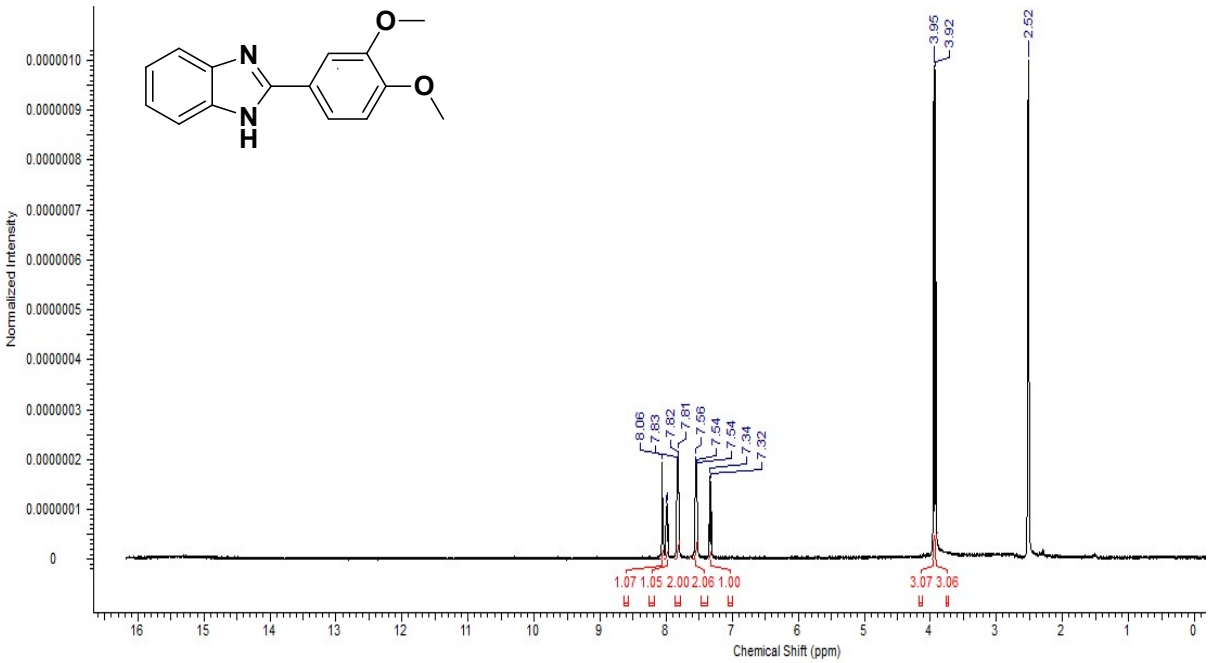


Figure S77. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **14k**

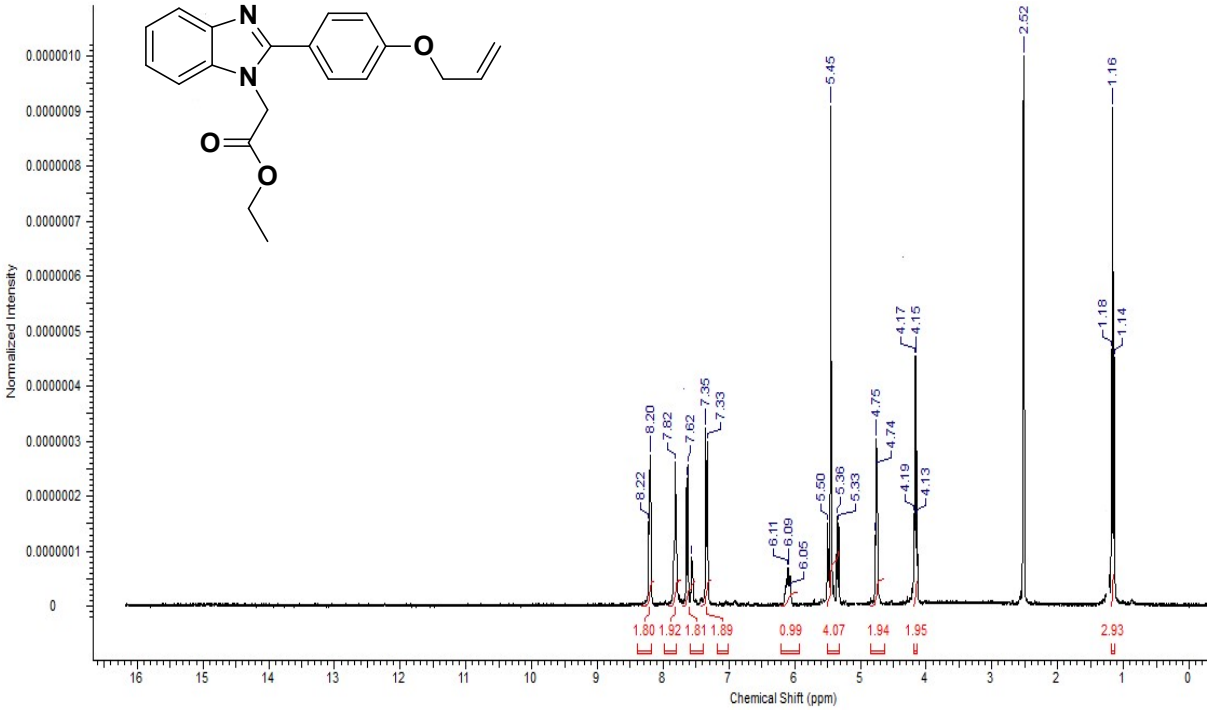


Figure S78. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15a**

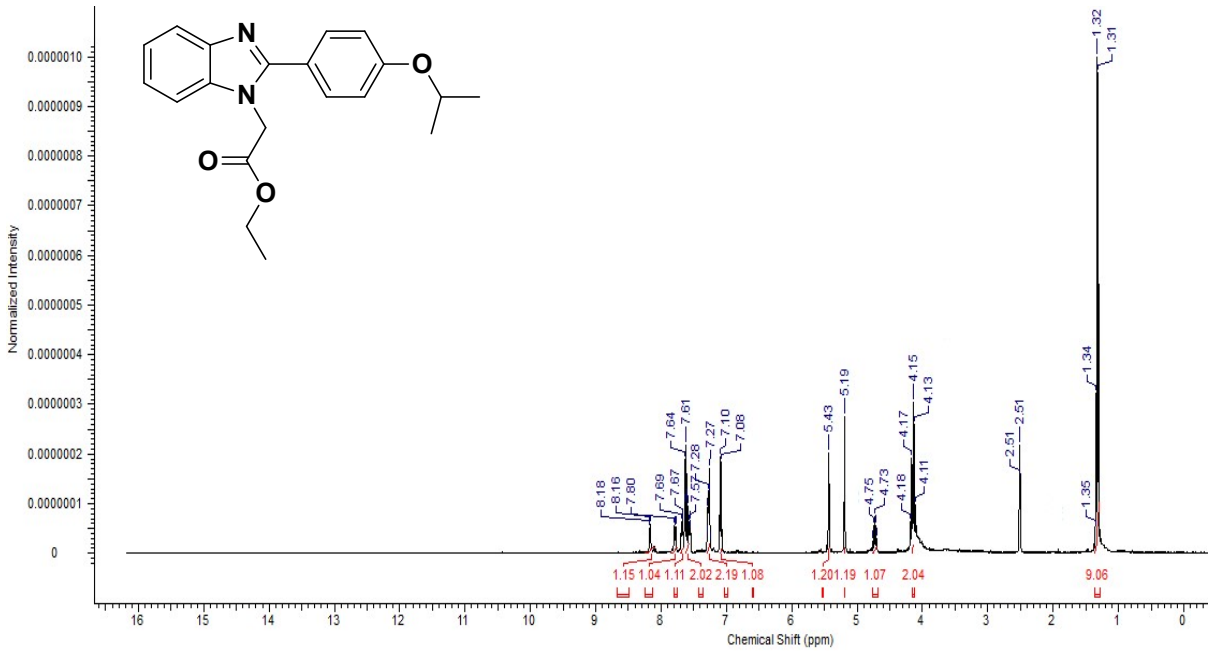


Figure S79. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15b**

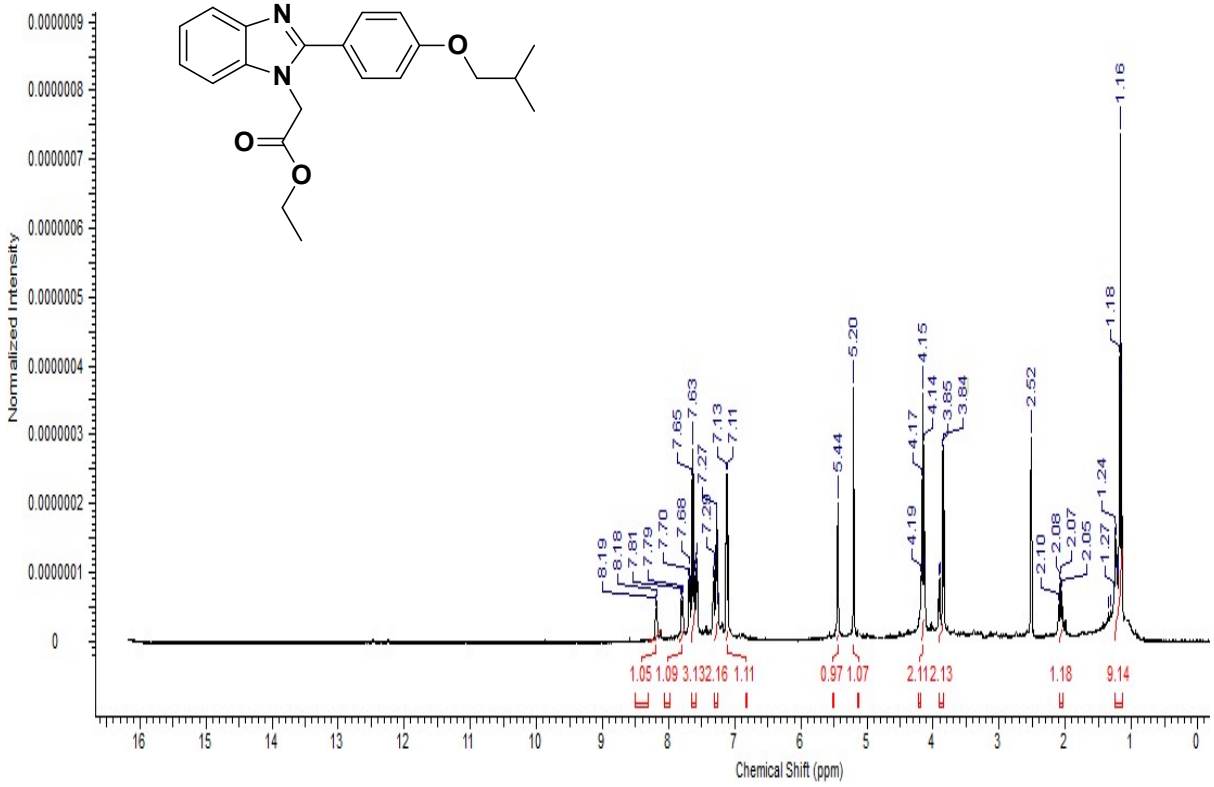


Figure S80. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15c**

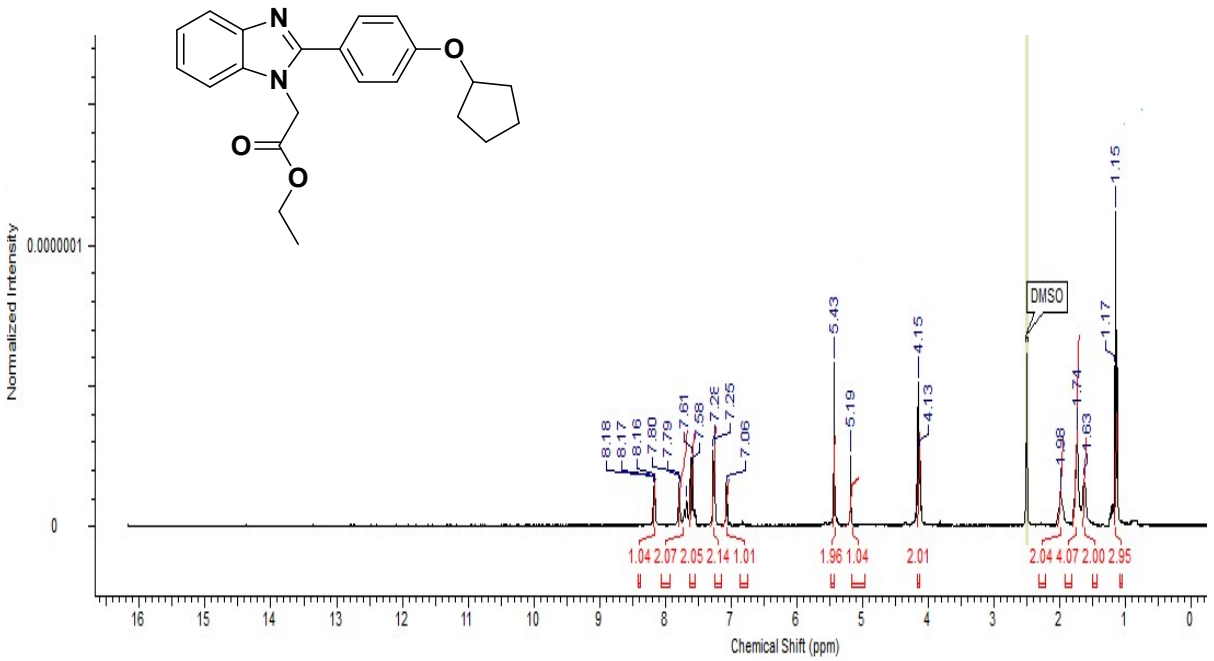


Figure S81. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15d**

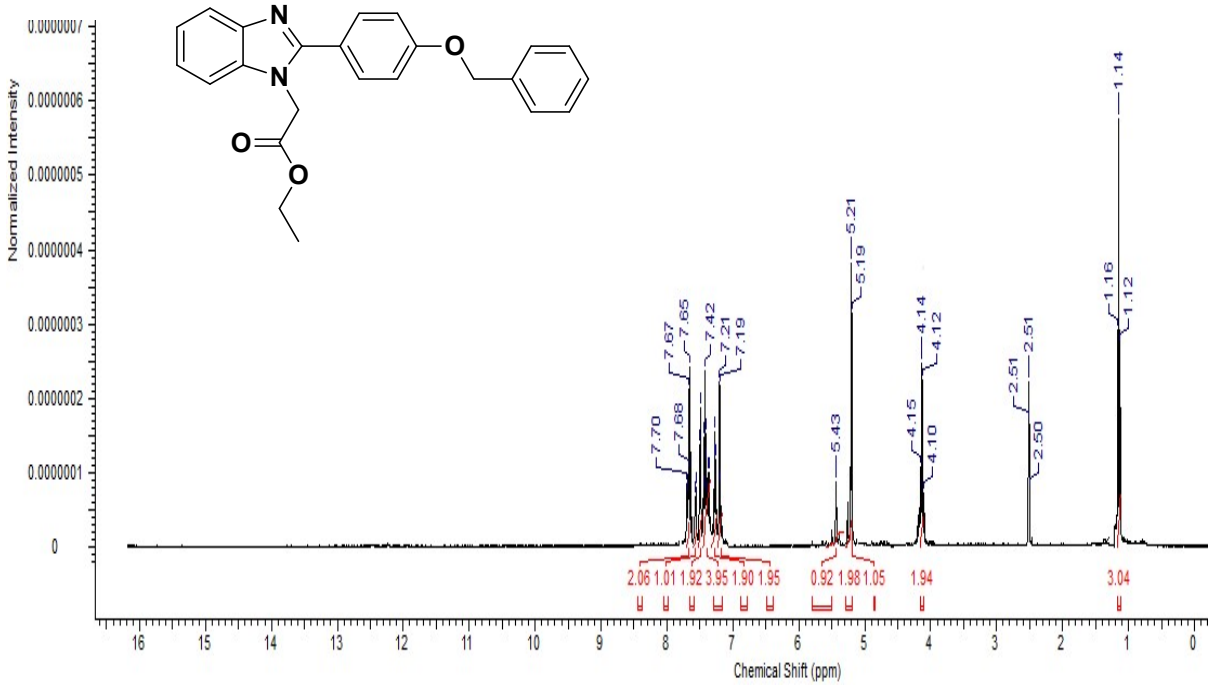


Figure S82. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15e**

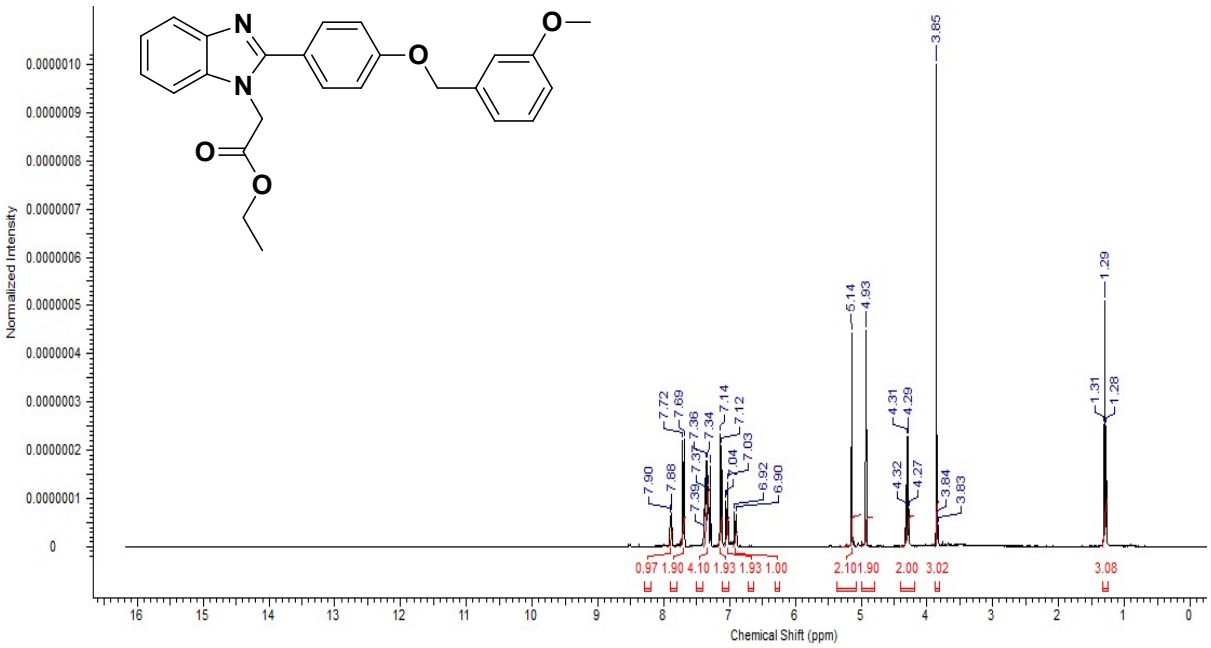


Figure S83. ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **15f**

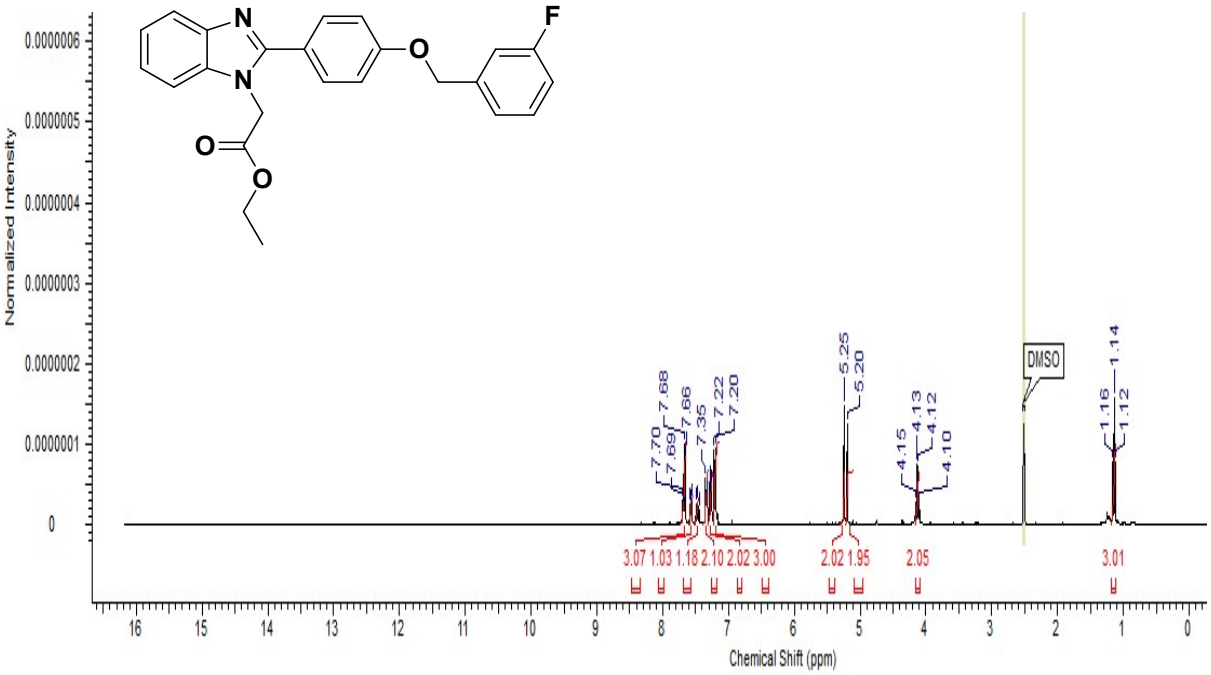


Figure S84. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15g**

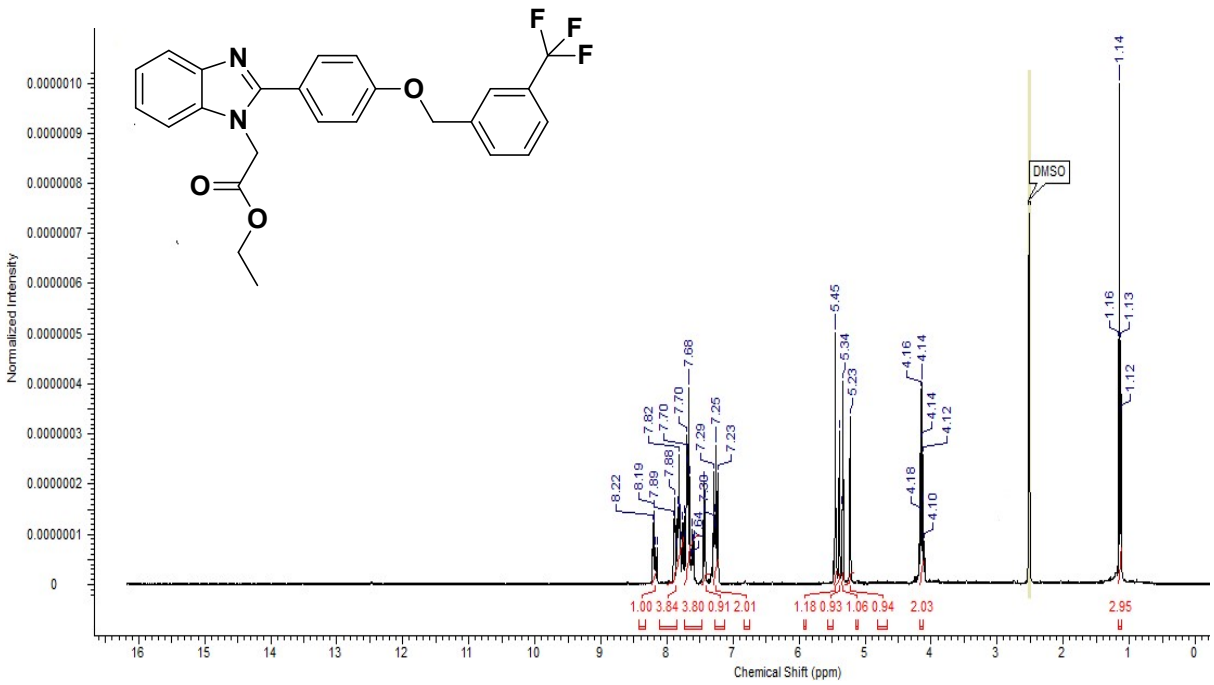


Figure S85. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15h**

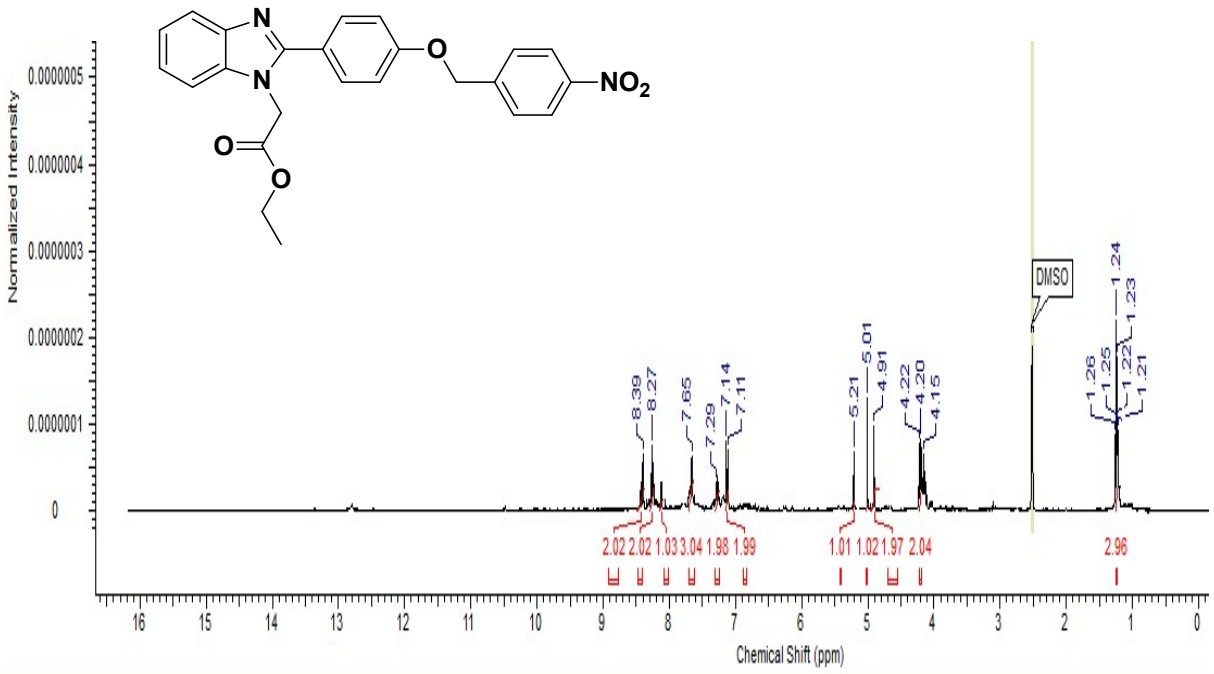


Figure S86. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15i**

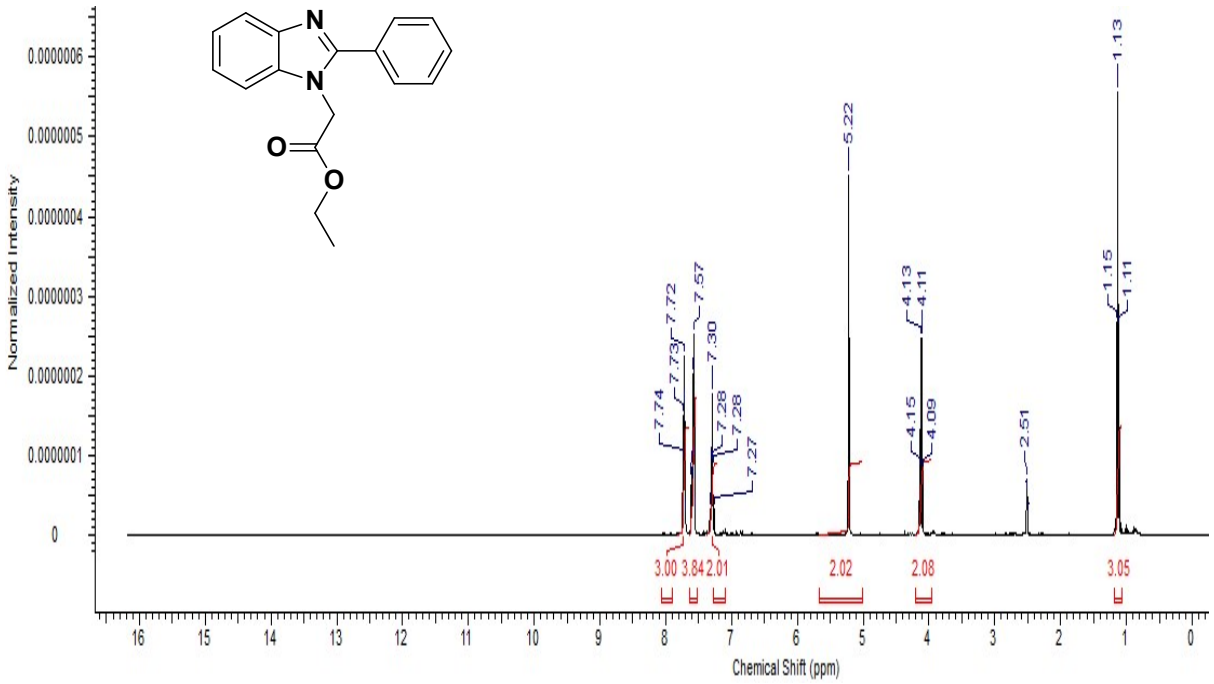


Figure S87. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **15j**

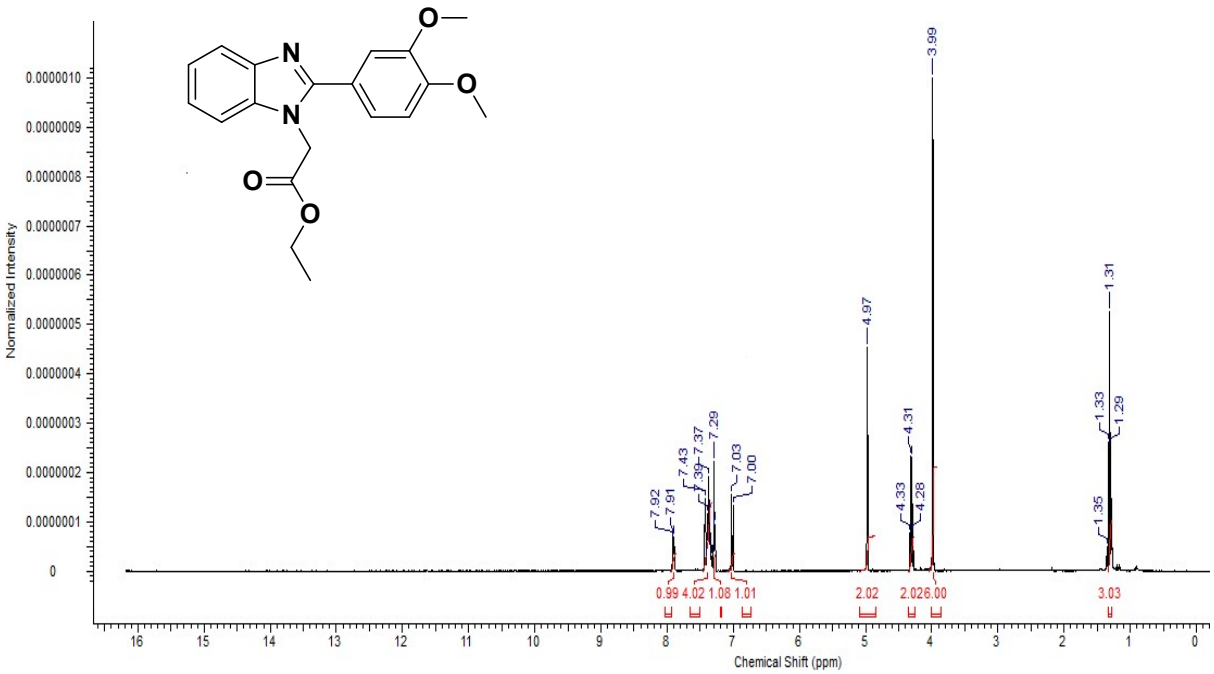


Figure S88. ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of compound **15k**

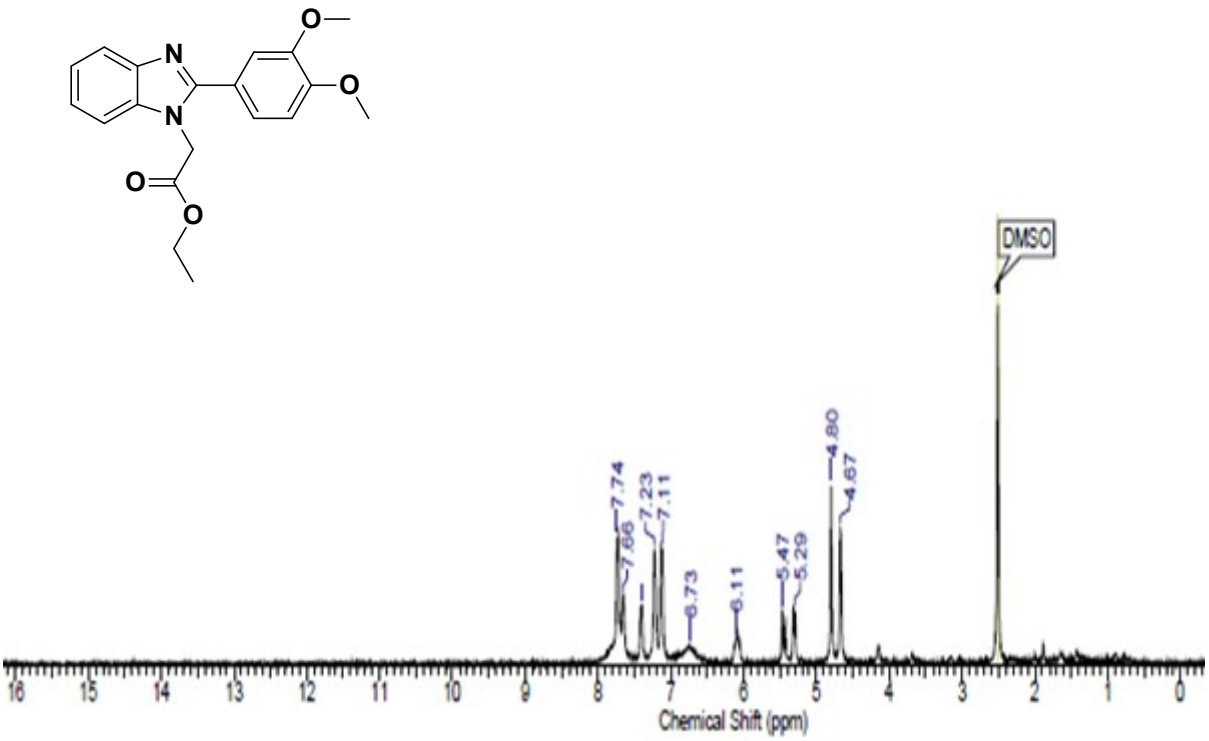


Figure S89. [1]H-NMR (400 MHz, **deutroated** DMSO-d_6) spectrum of compound **15k**

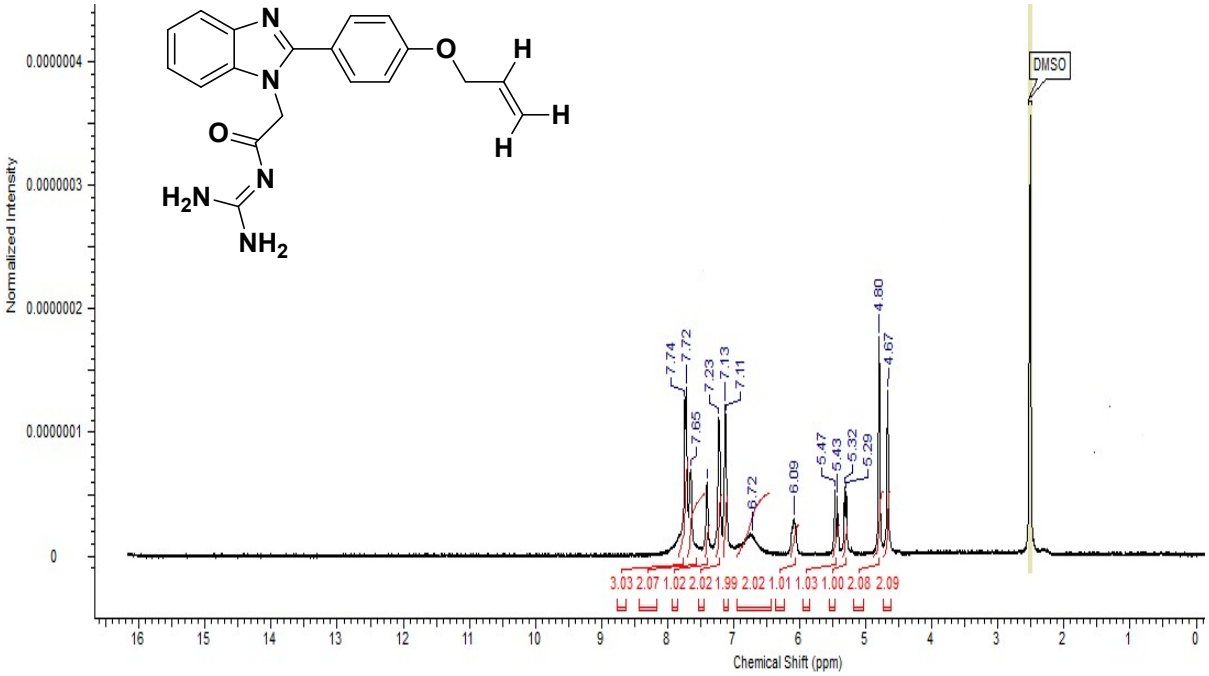


Figure S90. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16a**

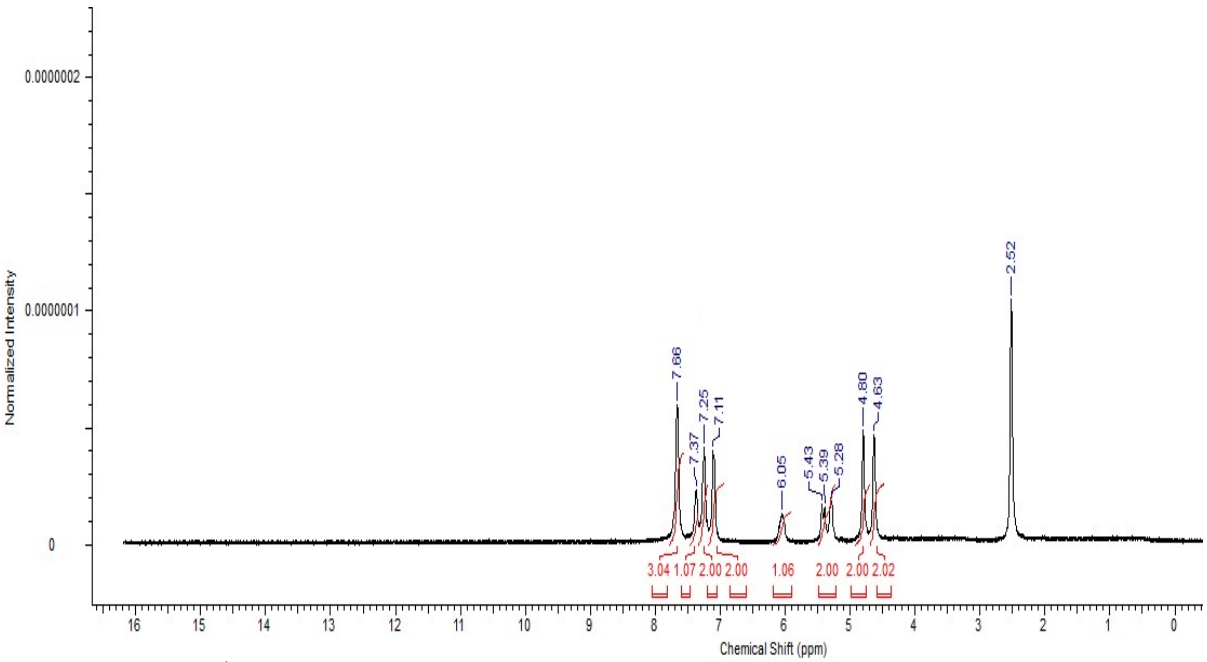


Figure S91. [1]H-NMR (400 MHz, **deutroated** DMSO-d_6) spectrum of compound **16a**

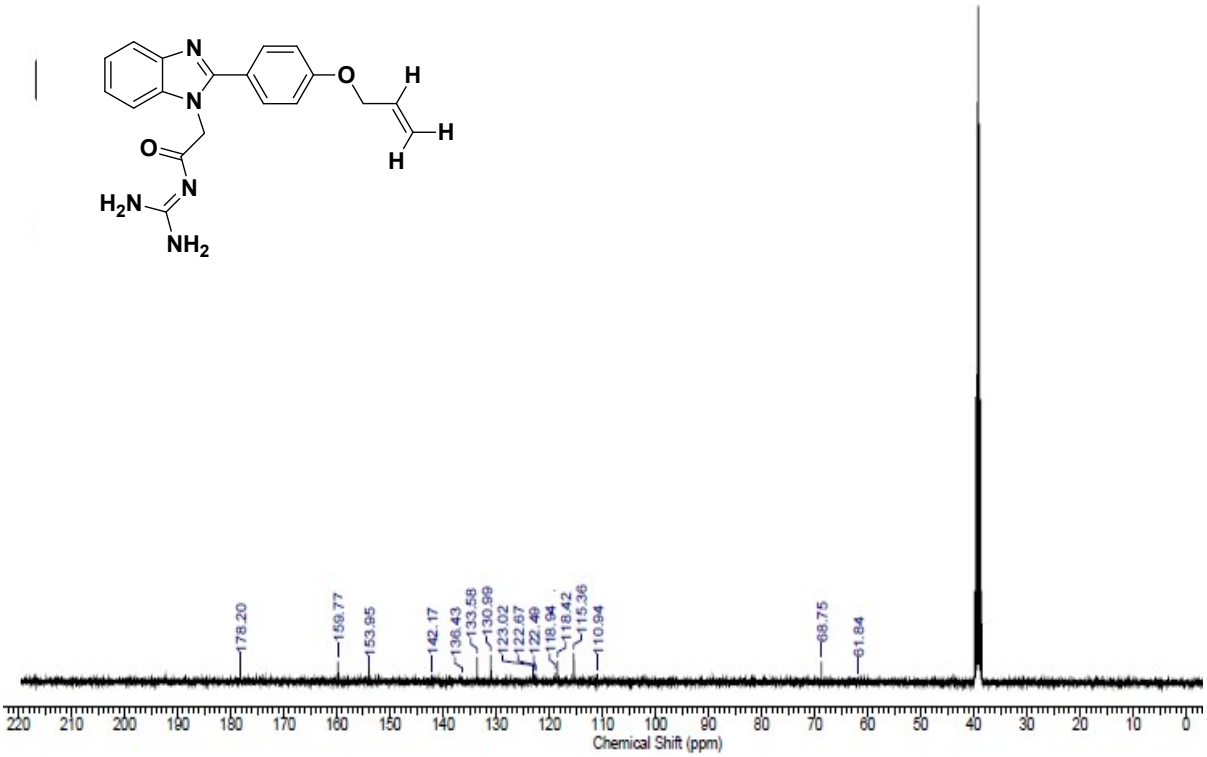


Figure S92. [13]C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16a**

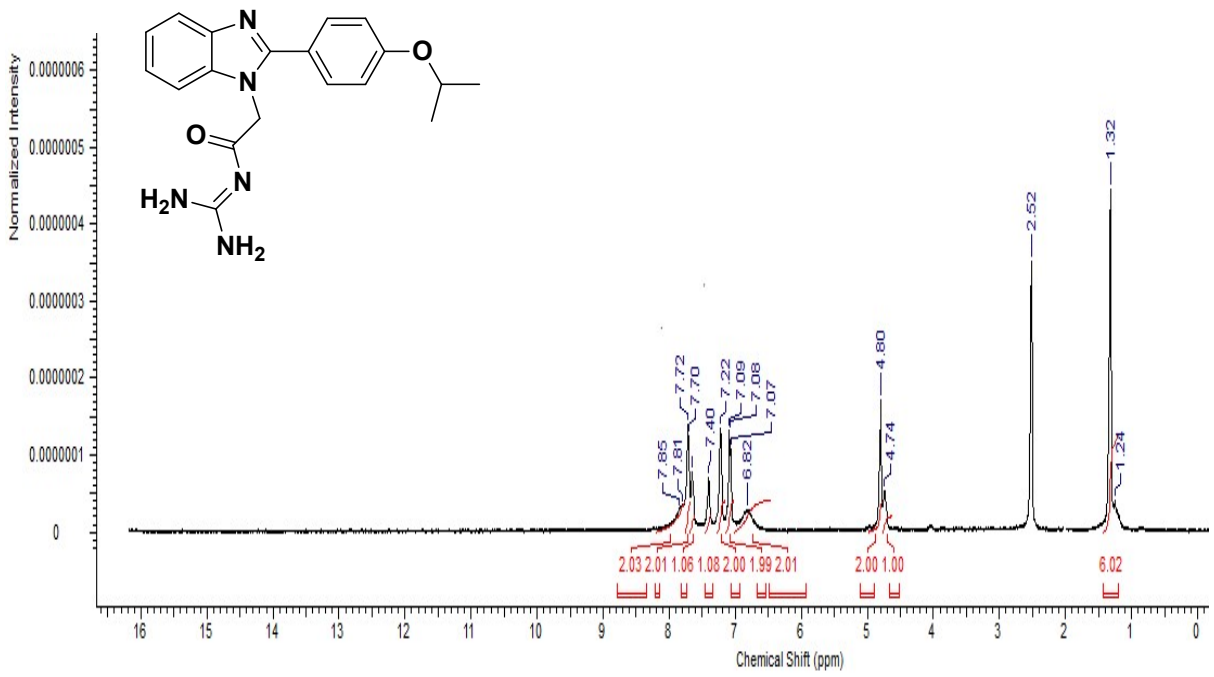


Figure S93. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16b**

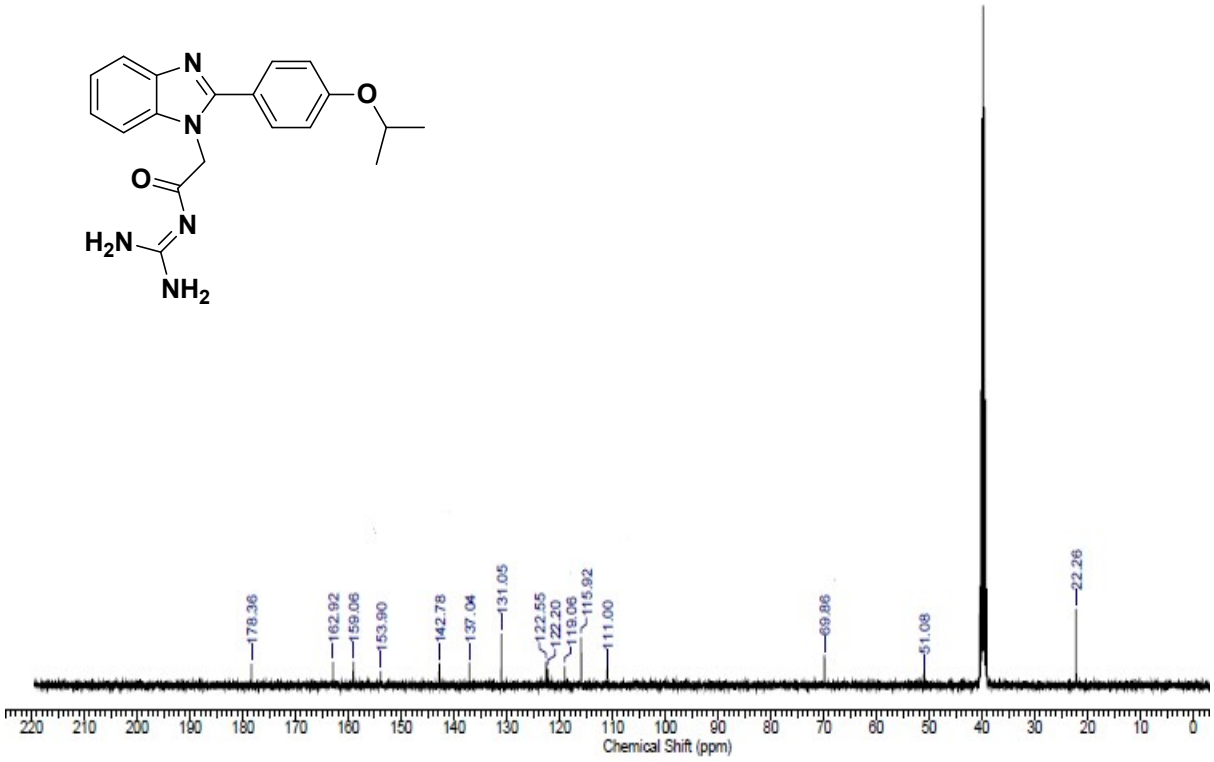


Figure S94. [13]C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16b**

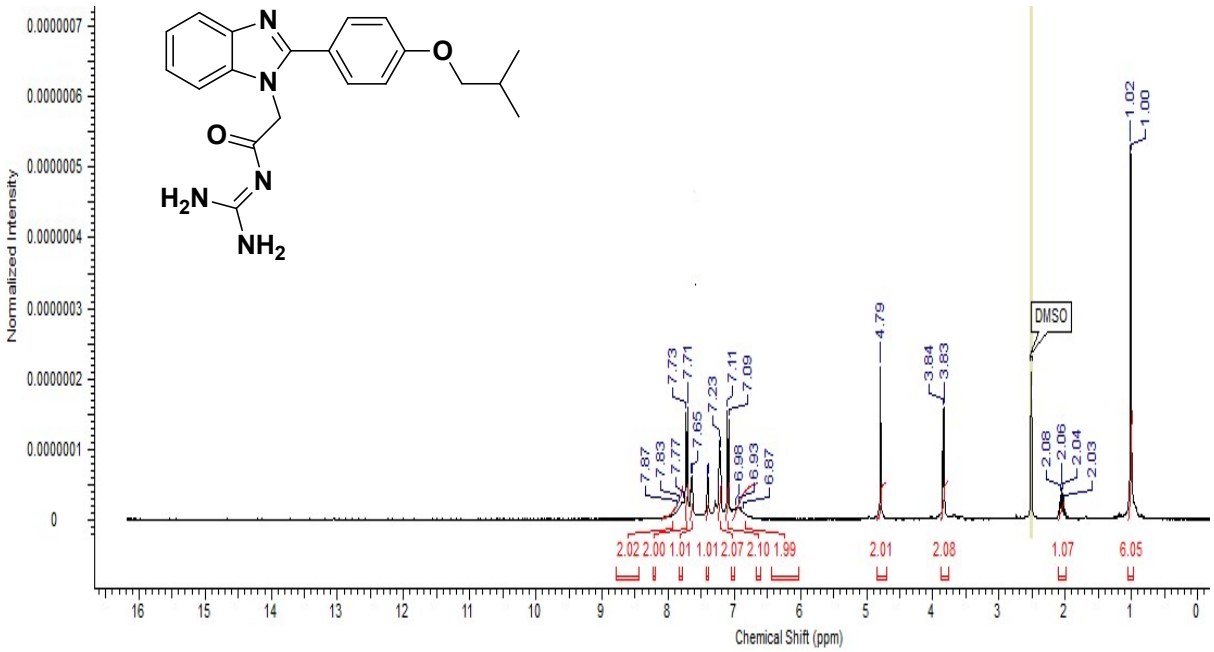


Figure S95. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16c**

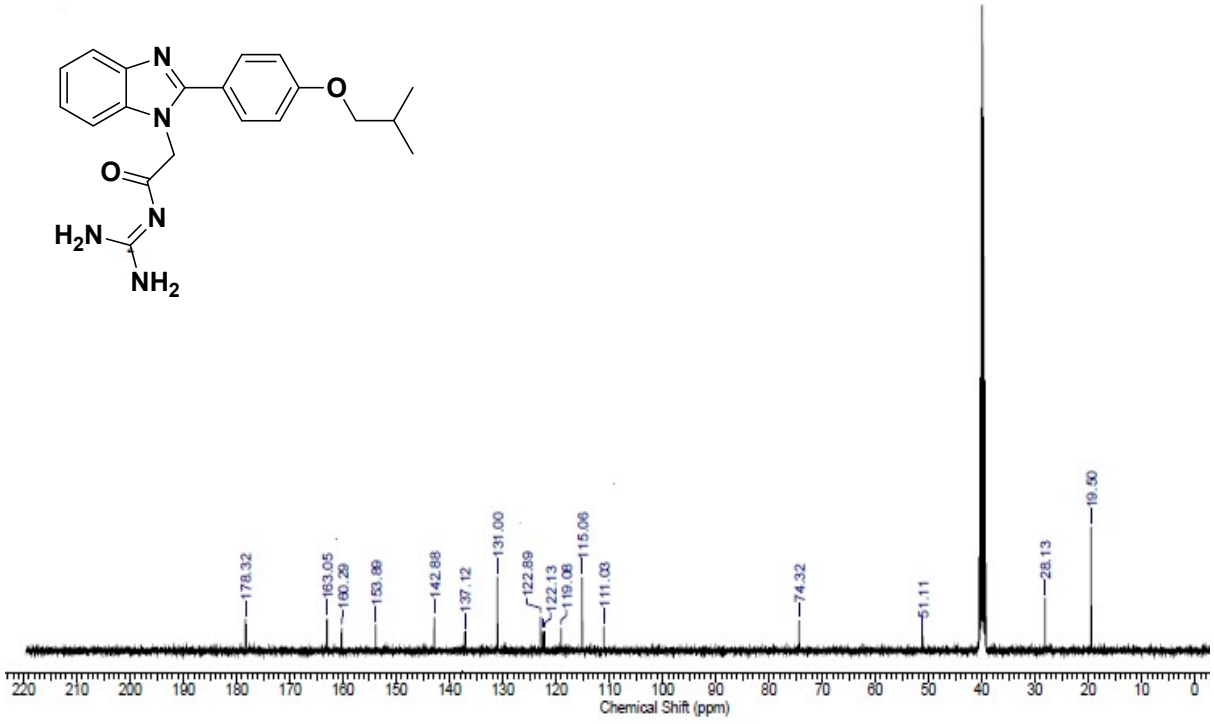


Figure S96. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16c**

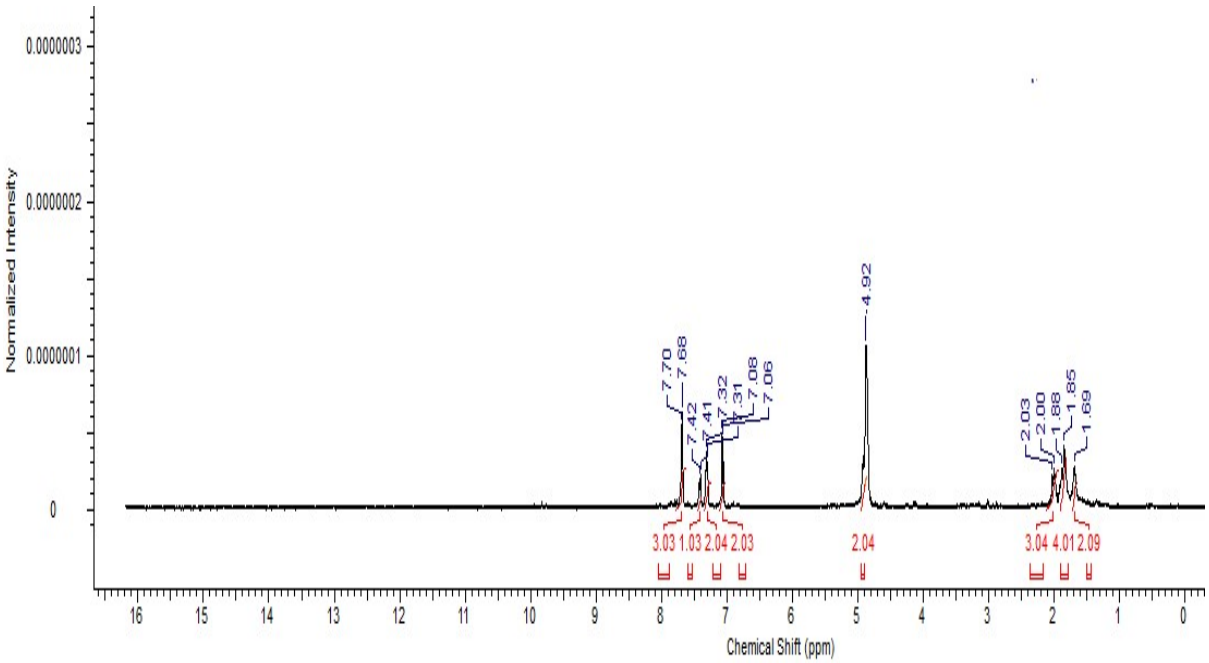


Figure S97. ^{1}H-NMR (400 MHz, CH_3OH-d_4) spectrum of compound **16d**

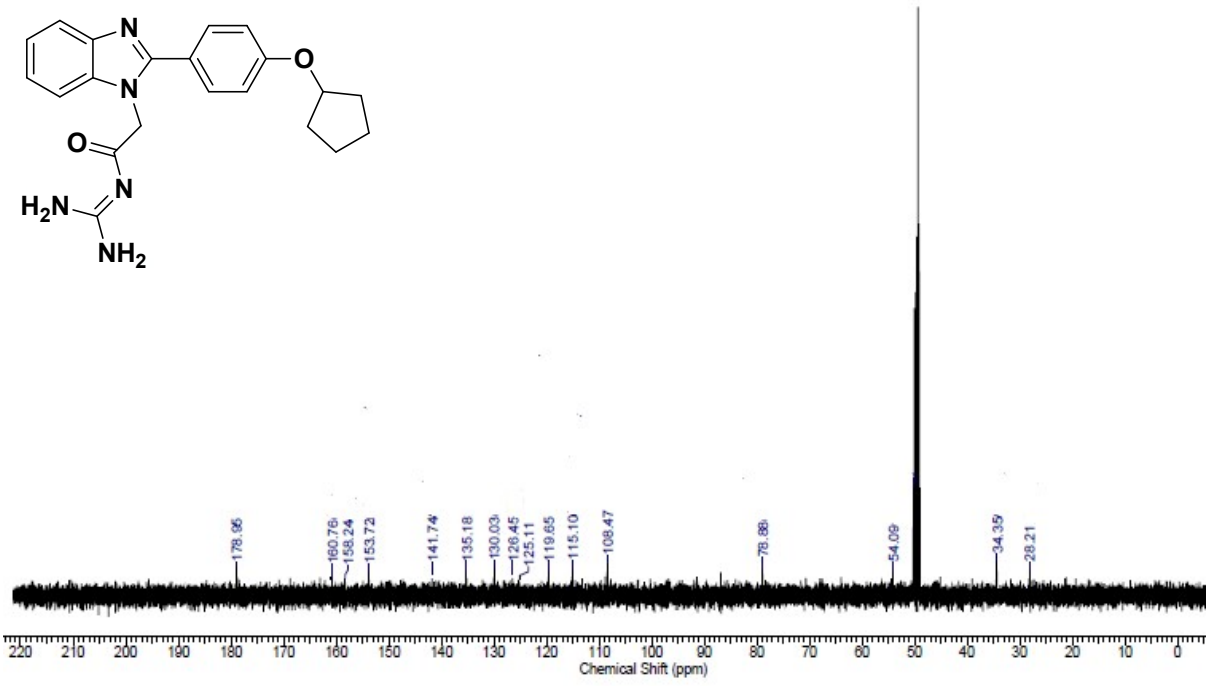


Figure S98. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16d**

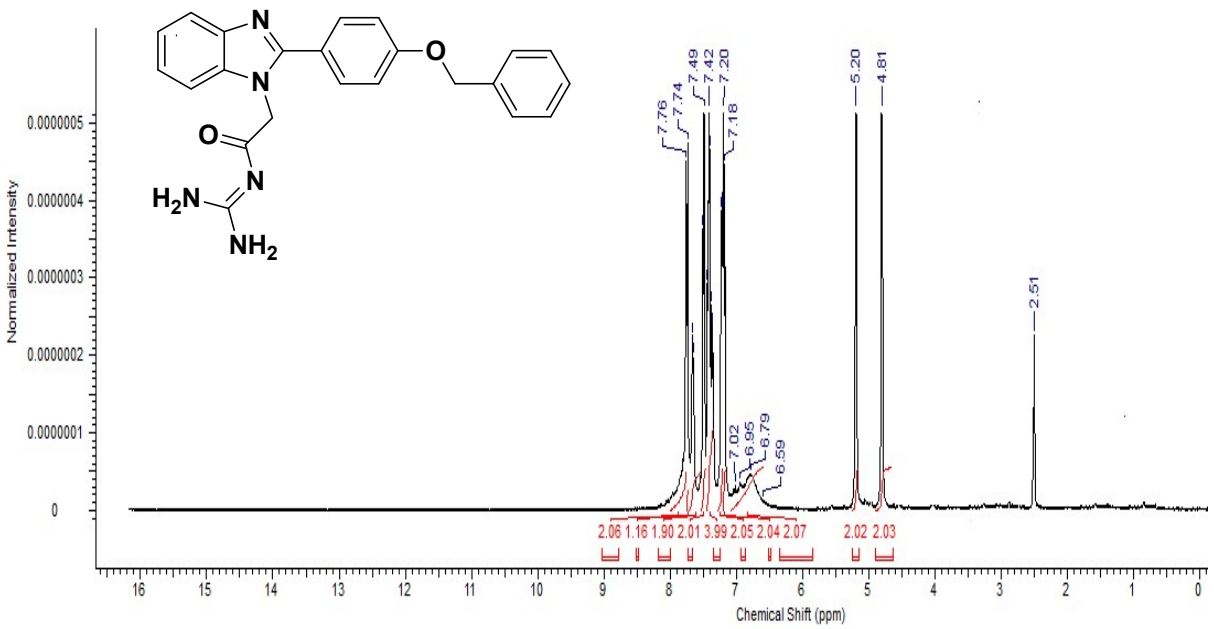


Figure S99. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16e**

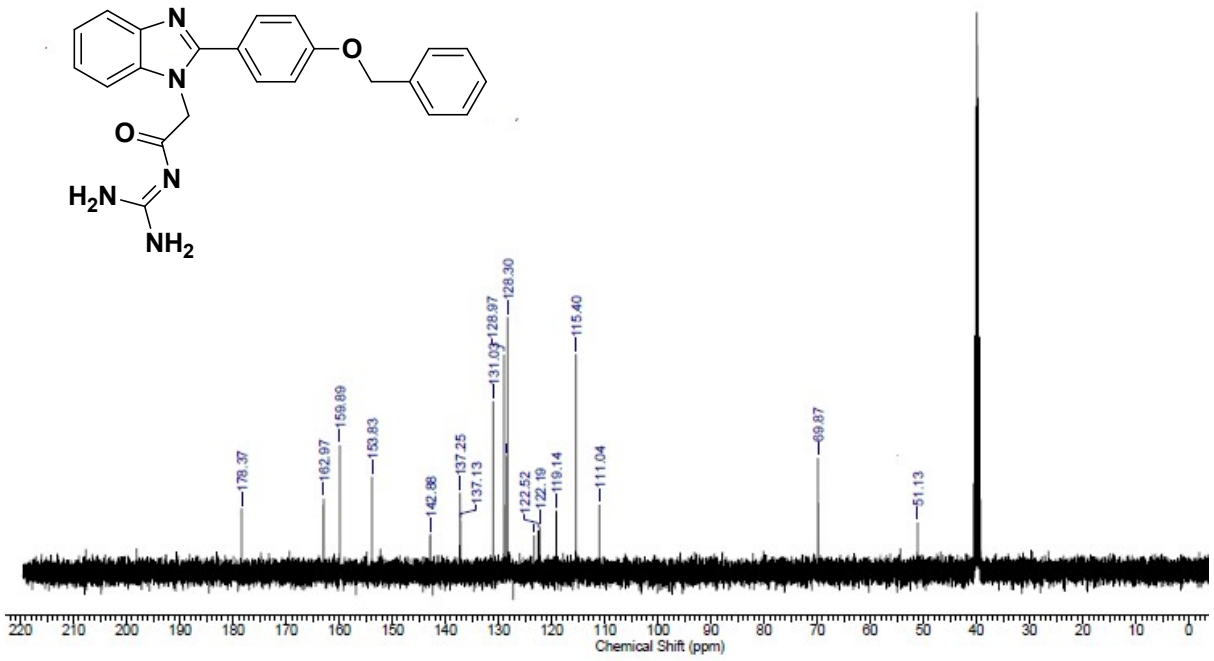


Figure S100. [13]C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16e**

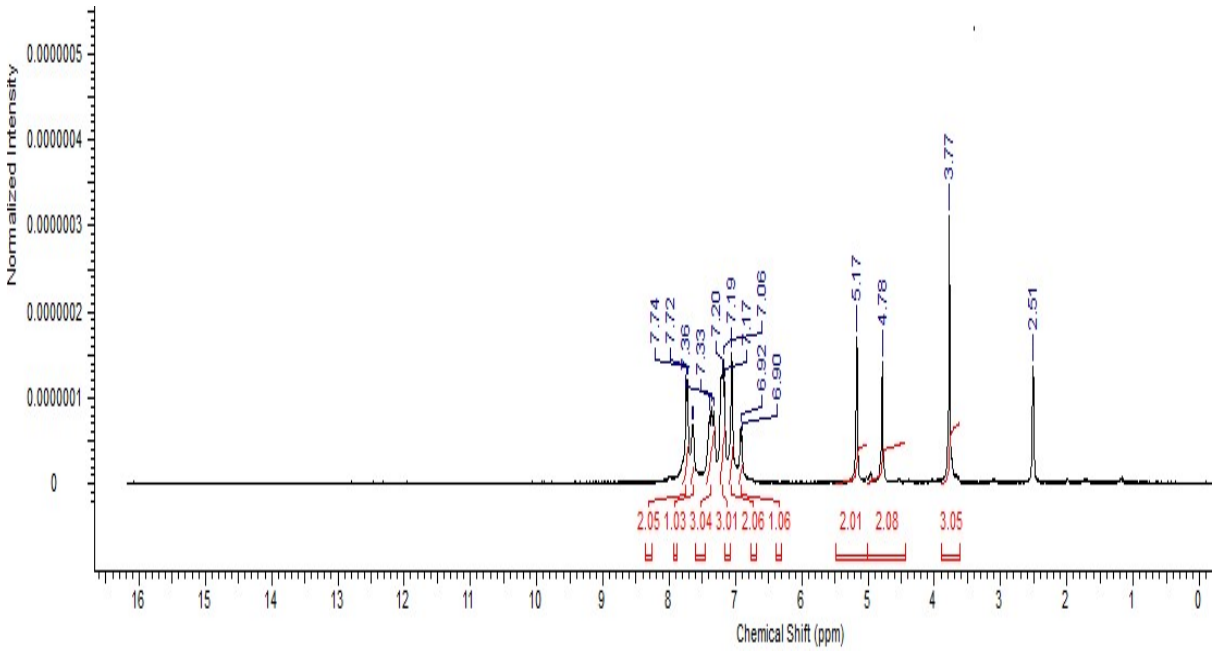


Figure S101. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16f**

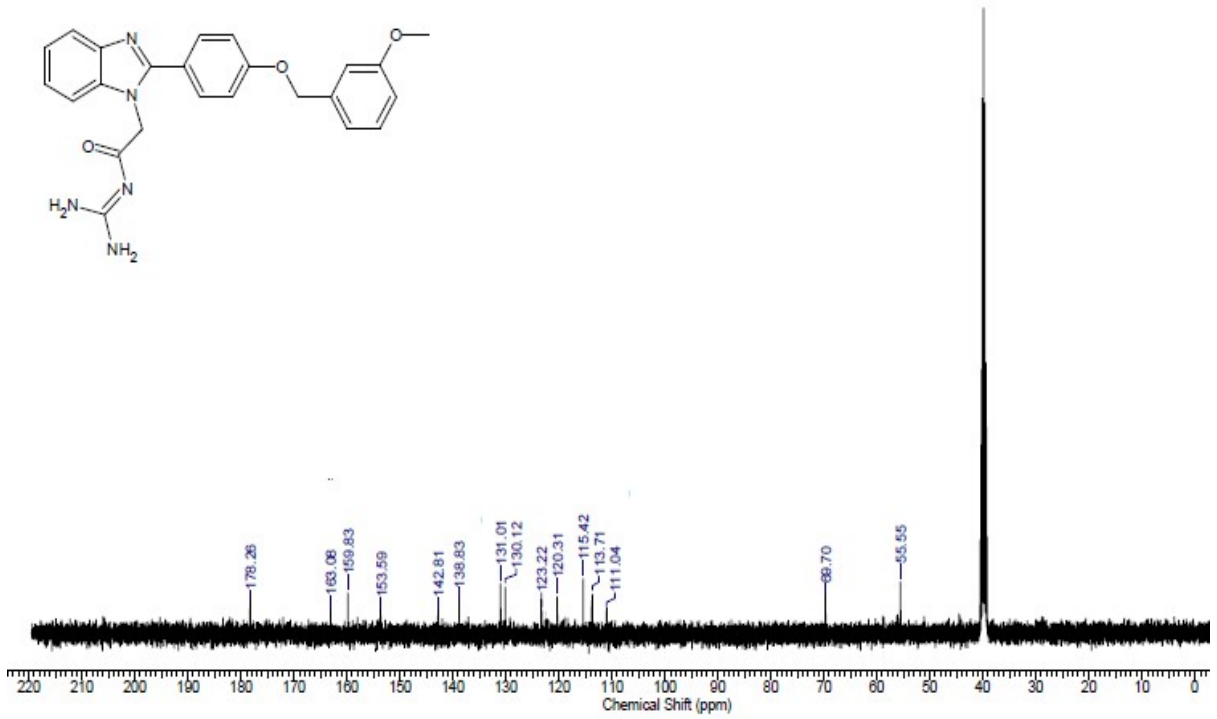


Figure S102. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16f**

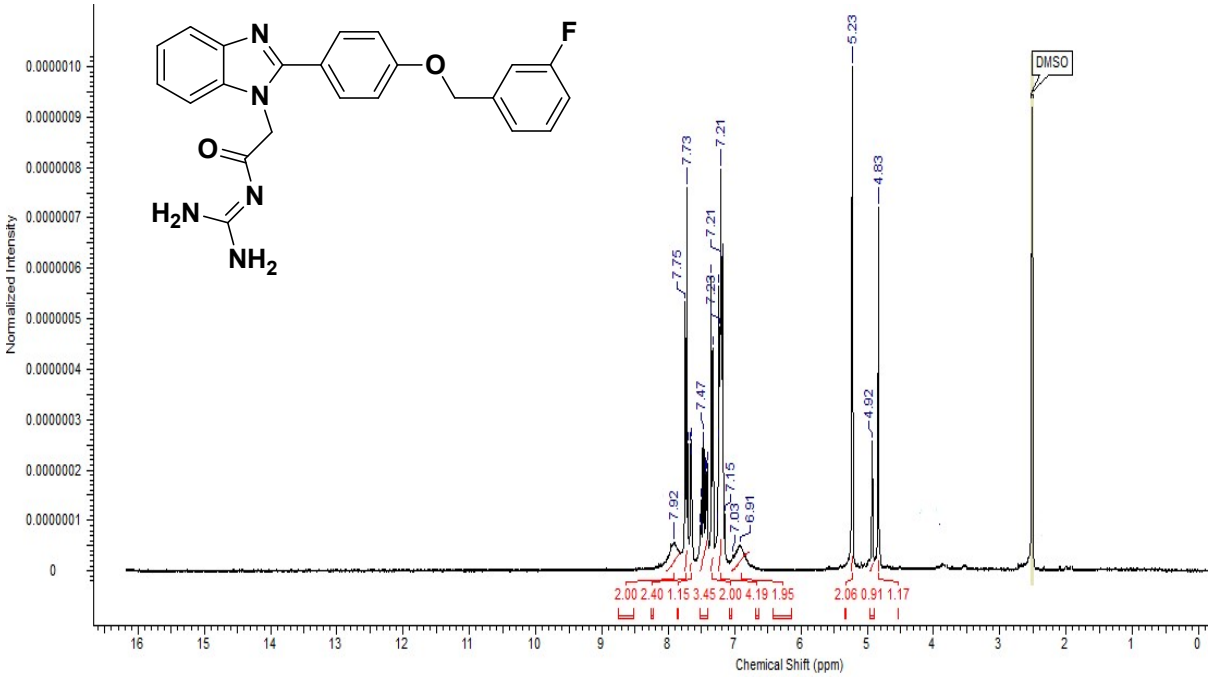


Figure S103. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16g**

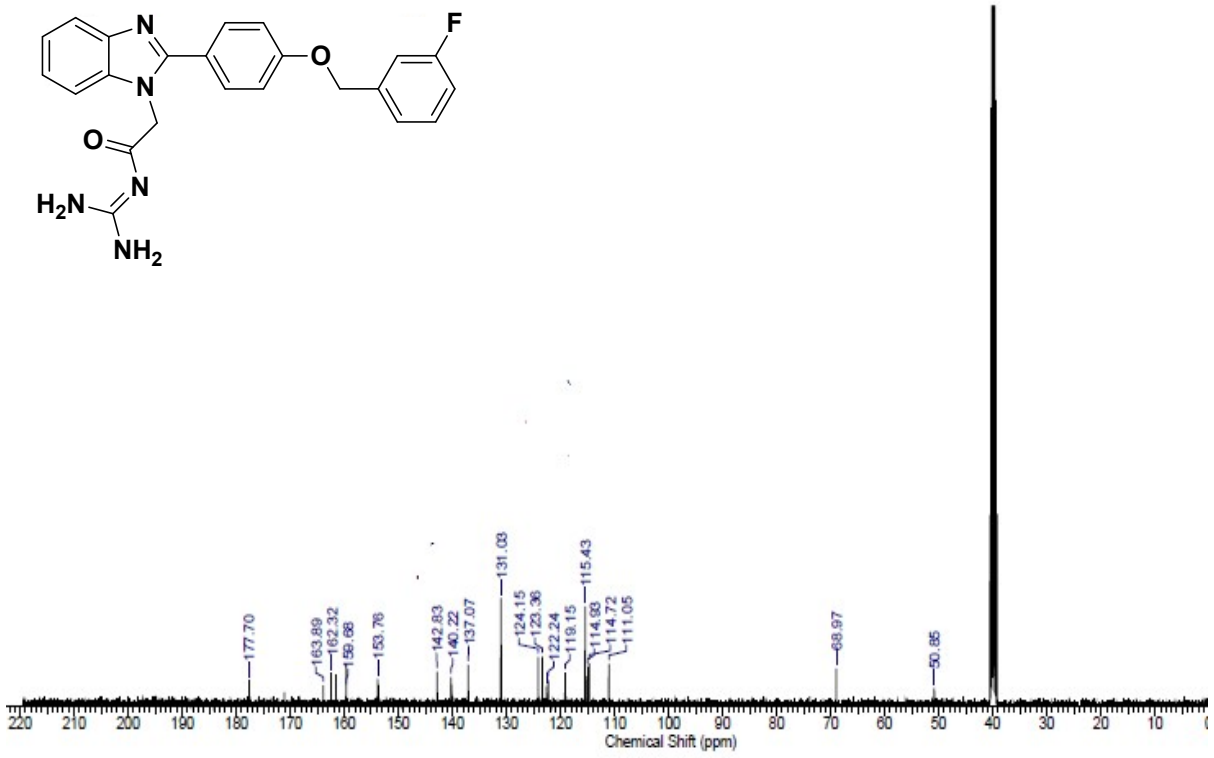


Figure S104. [13]C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16g**

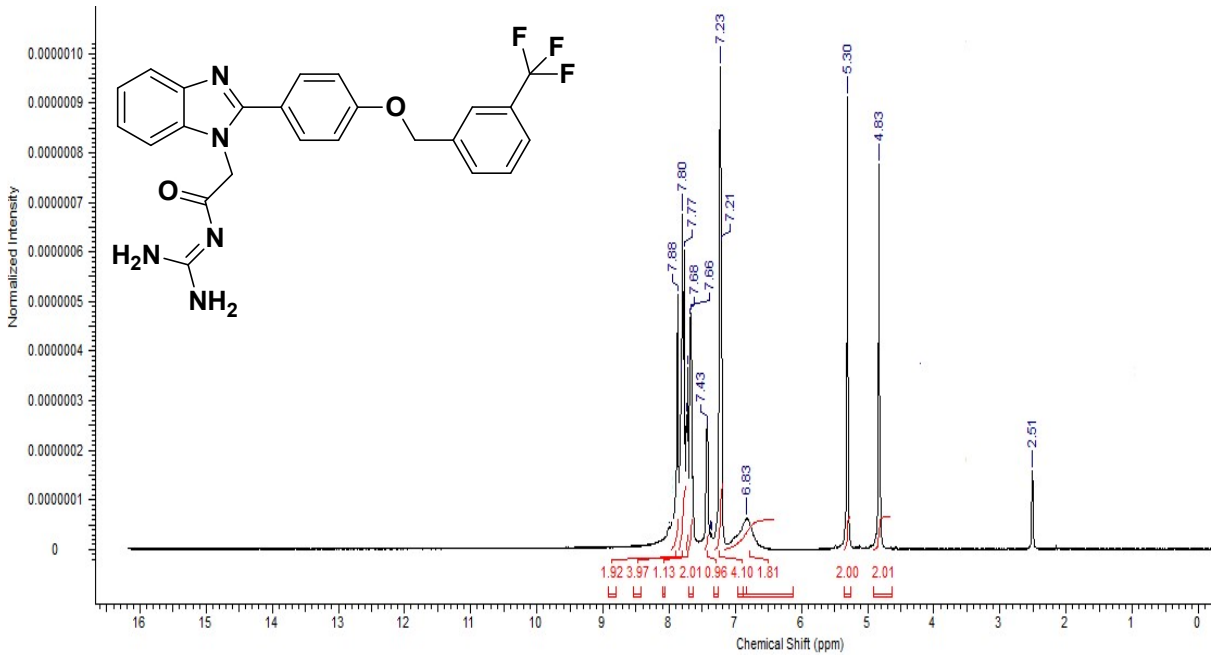


Figure S105. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16h**

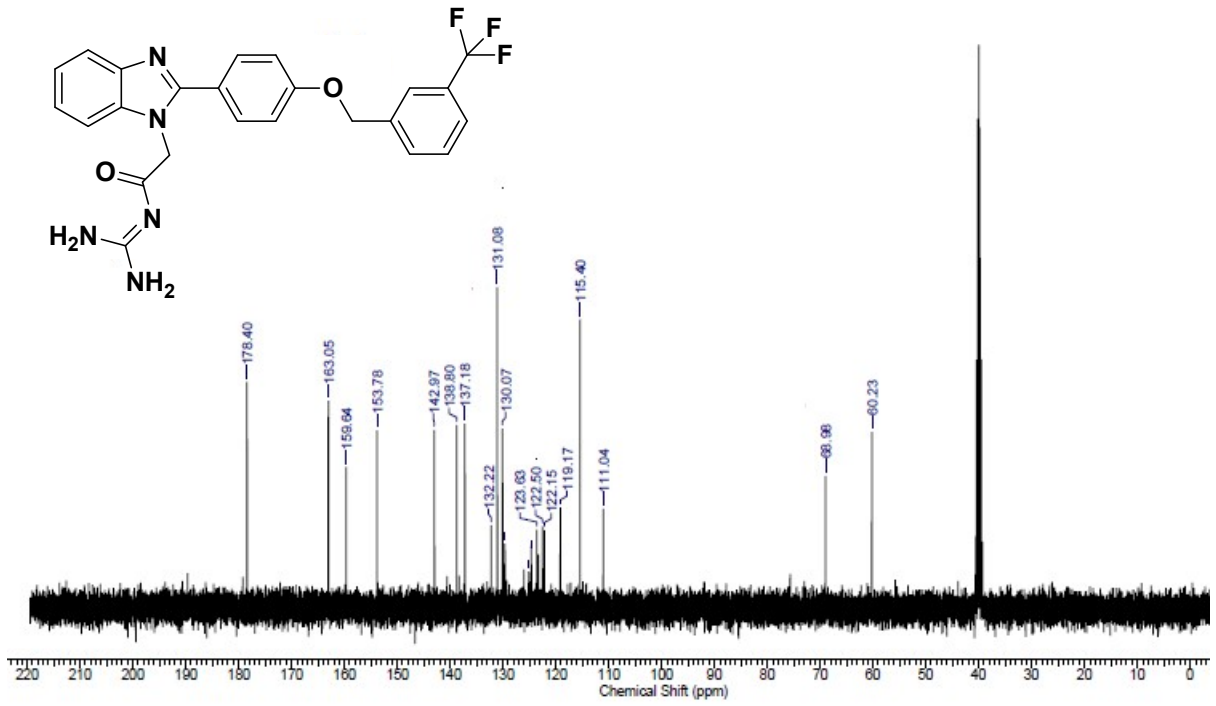


Figure S106. ^{13}C-NMR (101 MHz, DMSO-d_6) spectrum of compound **16h**

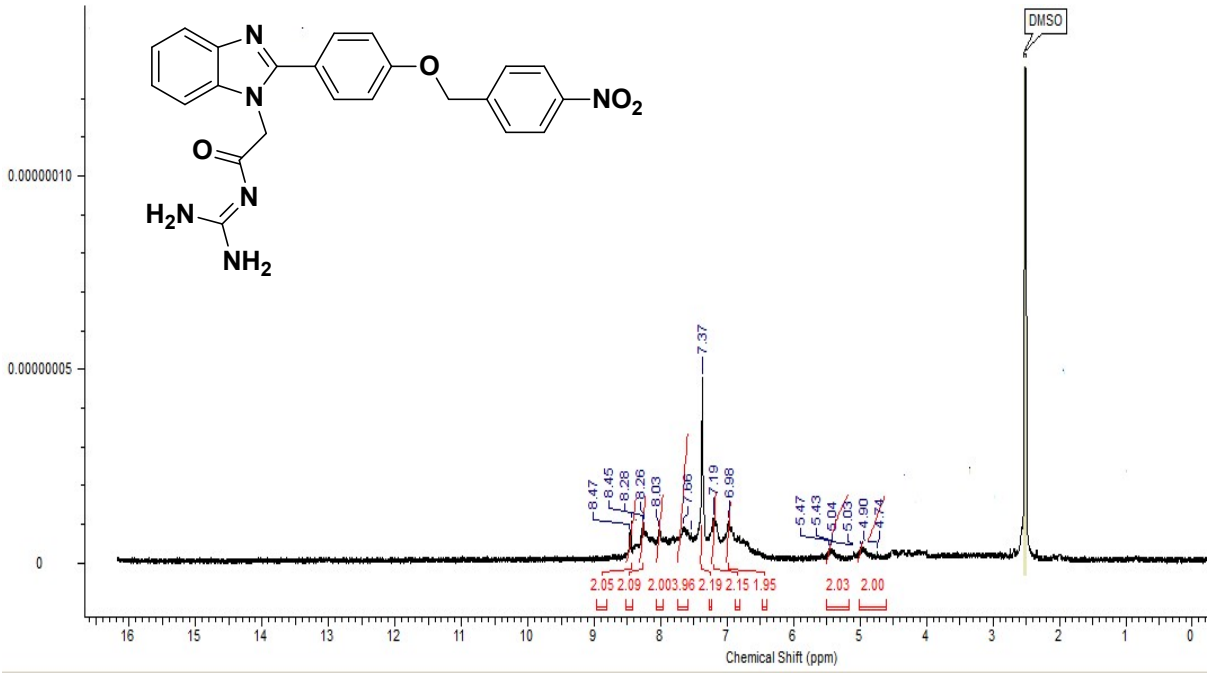


Figure S107. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16i**

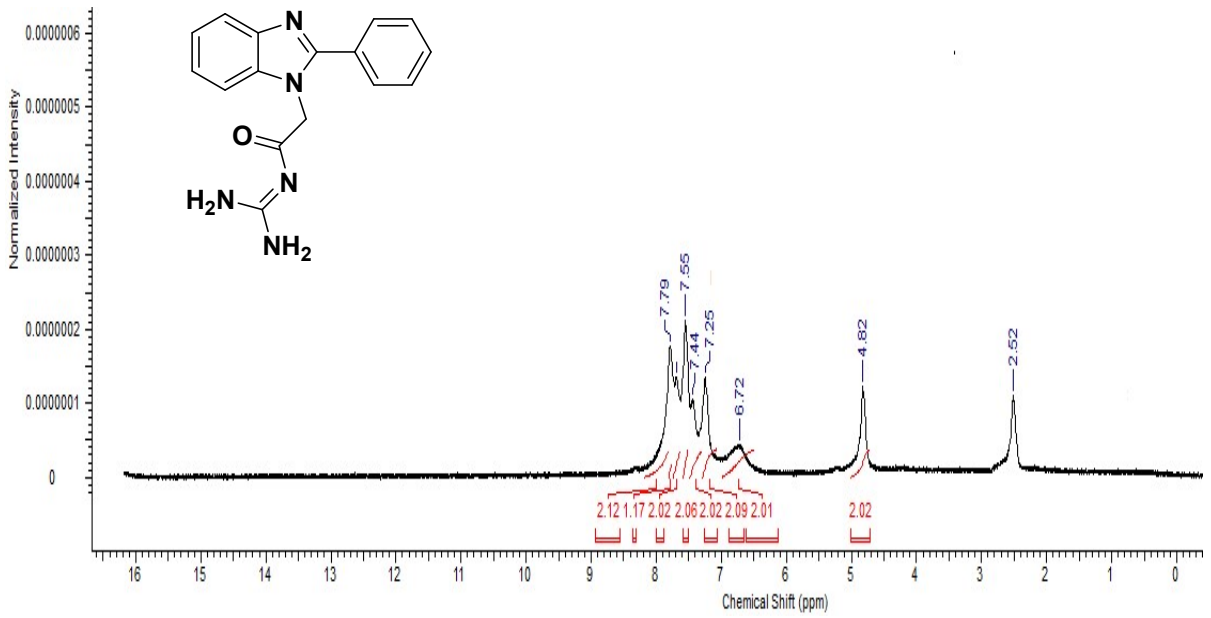


Figure S108. [1]H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16j**

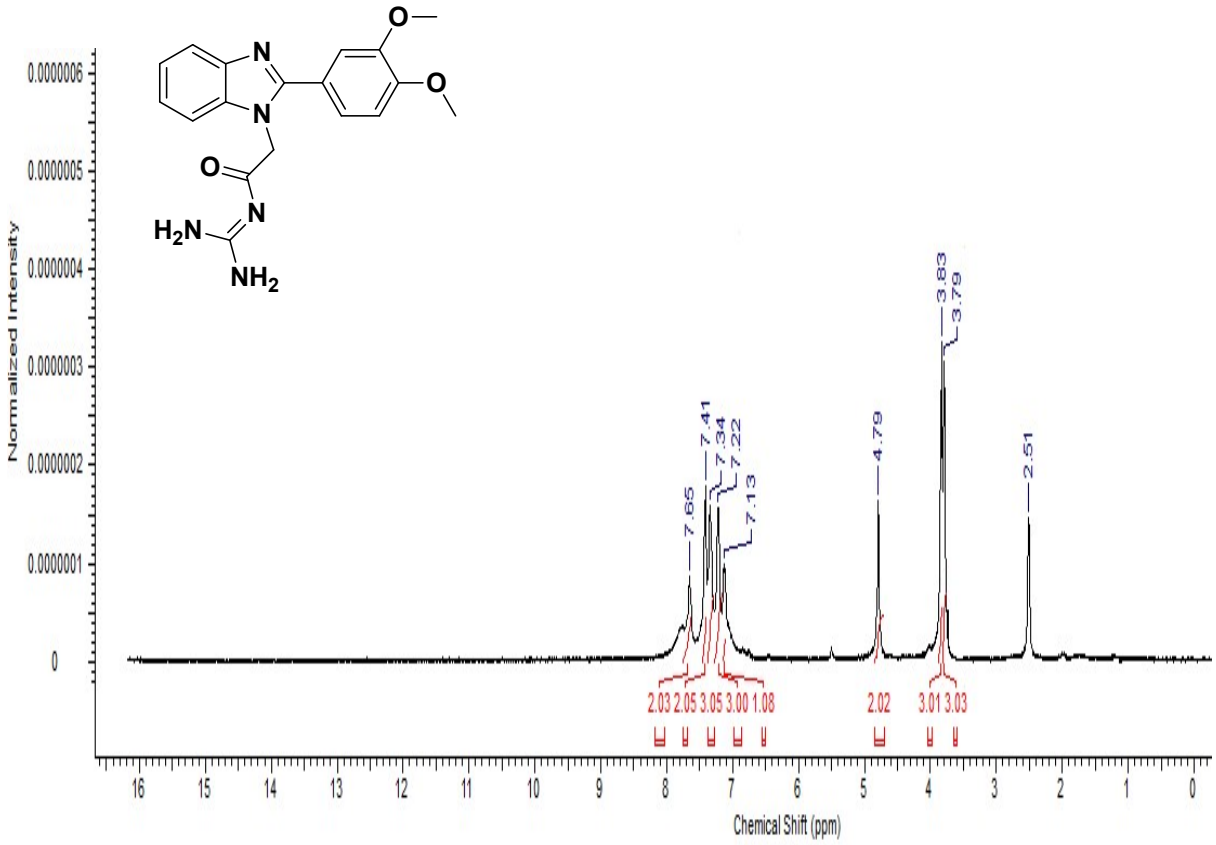
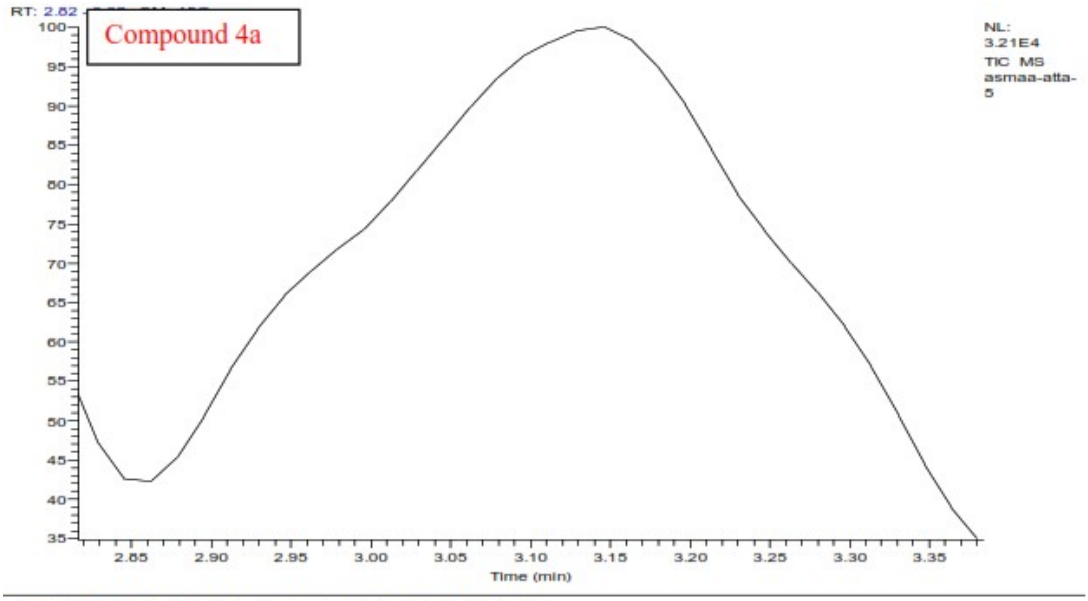
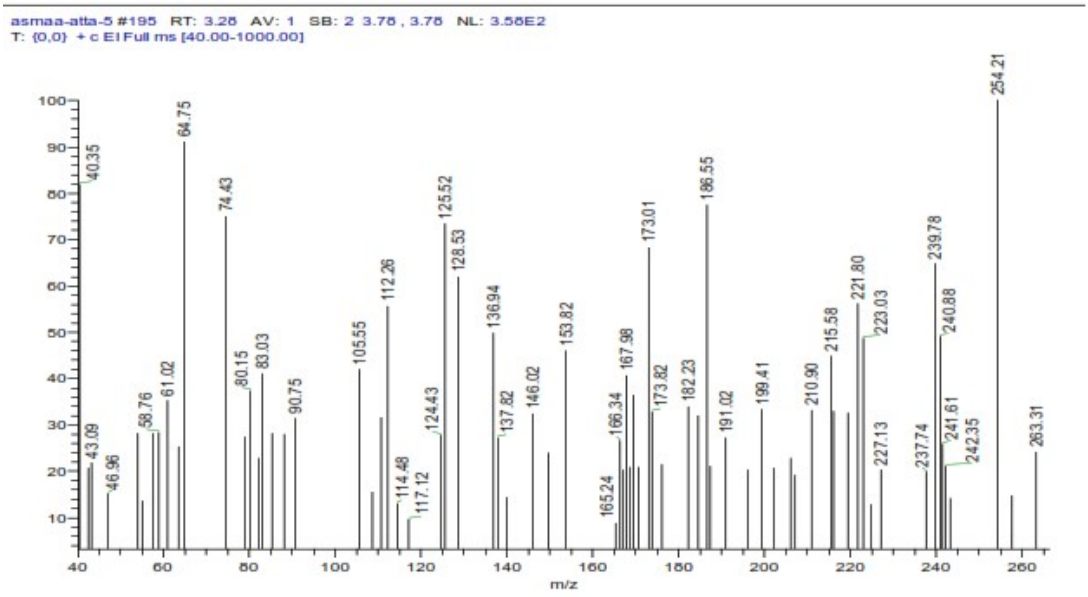
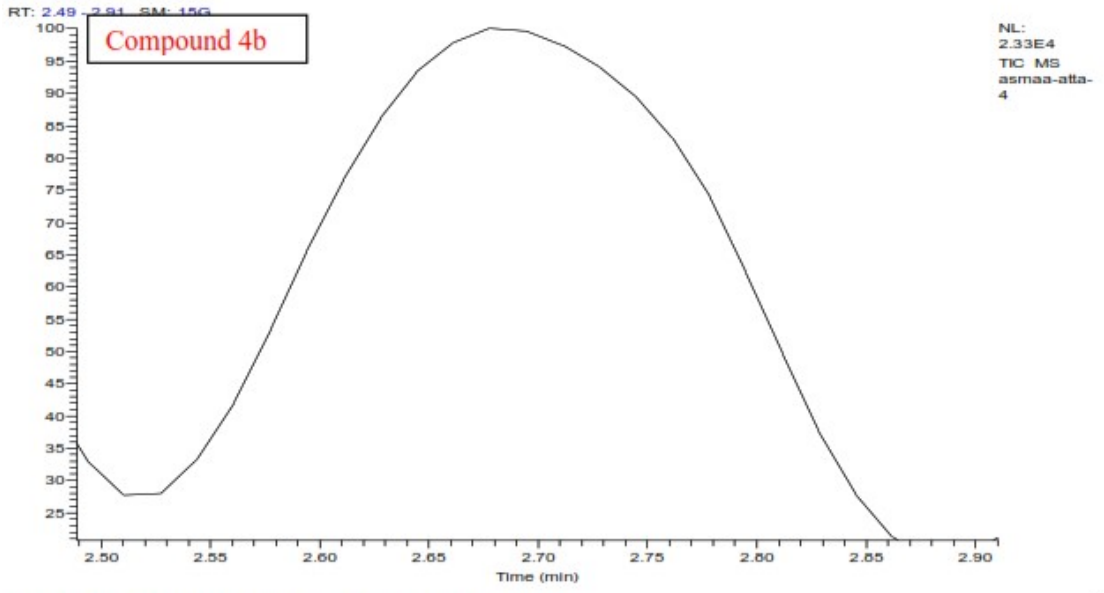
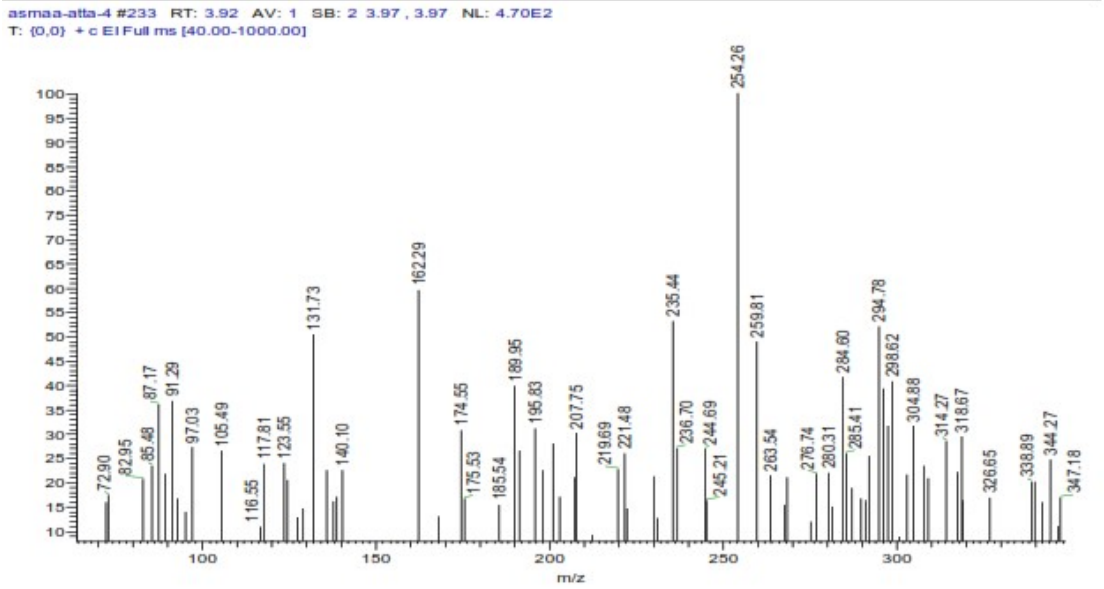


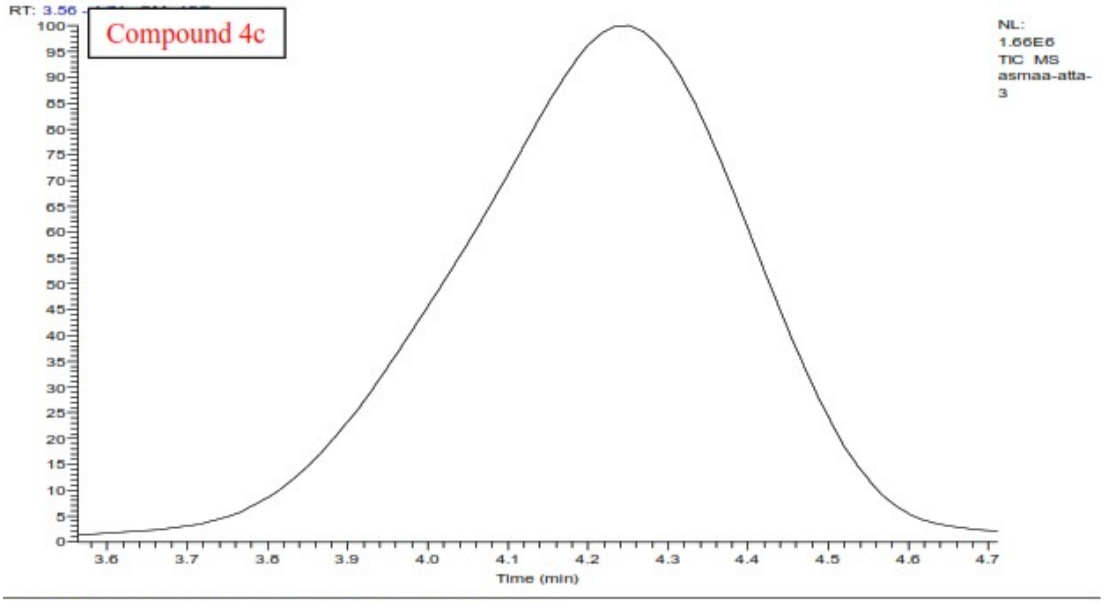
Figure S109. ^{1}H-NMR (400 MHz, DMSO-d_6) spectrum of compound **16k**

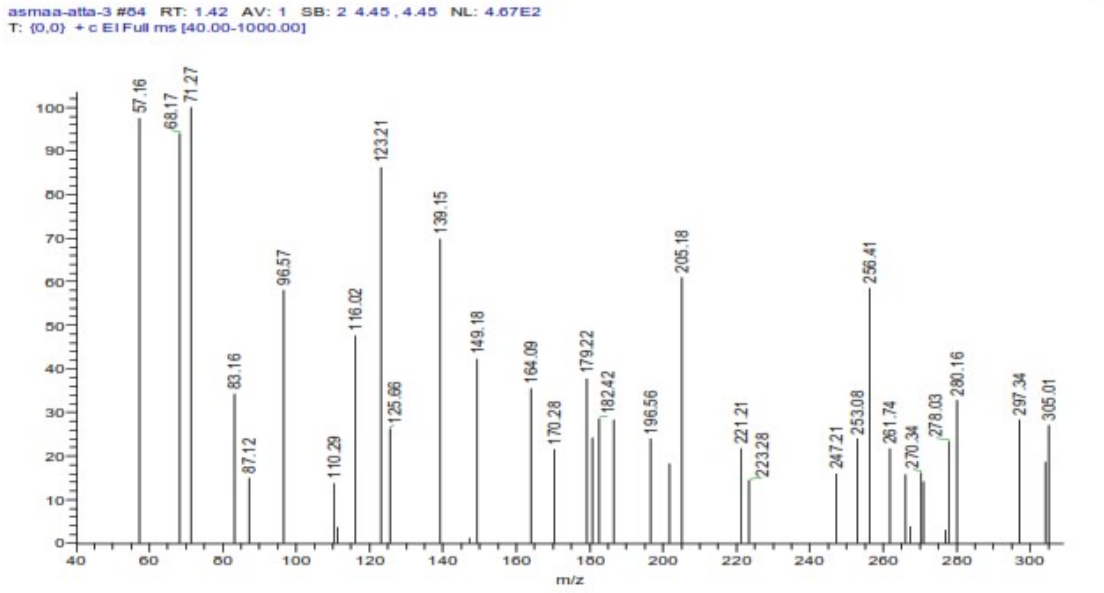

Compound 4a
NL:
3.21E4
TIC MS
asmaa-atta-
5
Time (min)

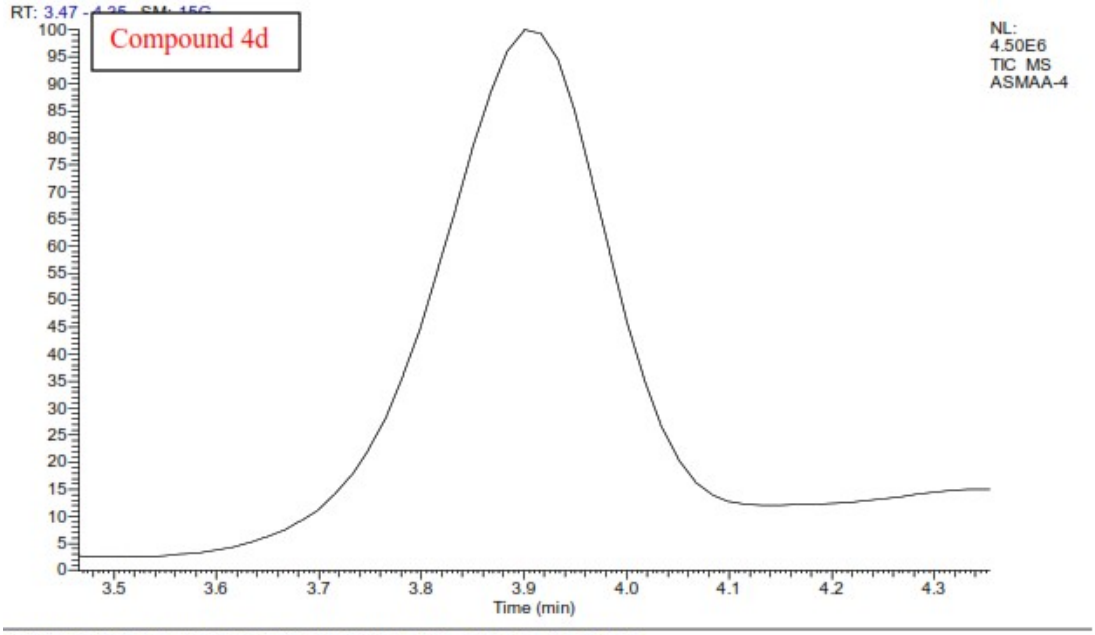

asmaa-atta-5 #195 RT: 3.26 AV: 1 SB: 2 3.76 , 3.76 NL: 3.56E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

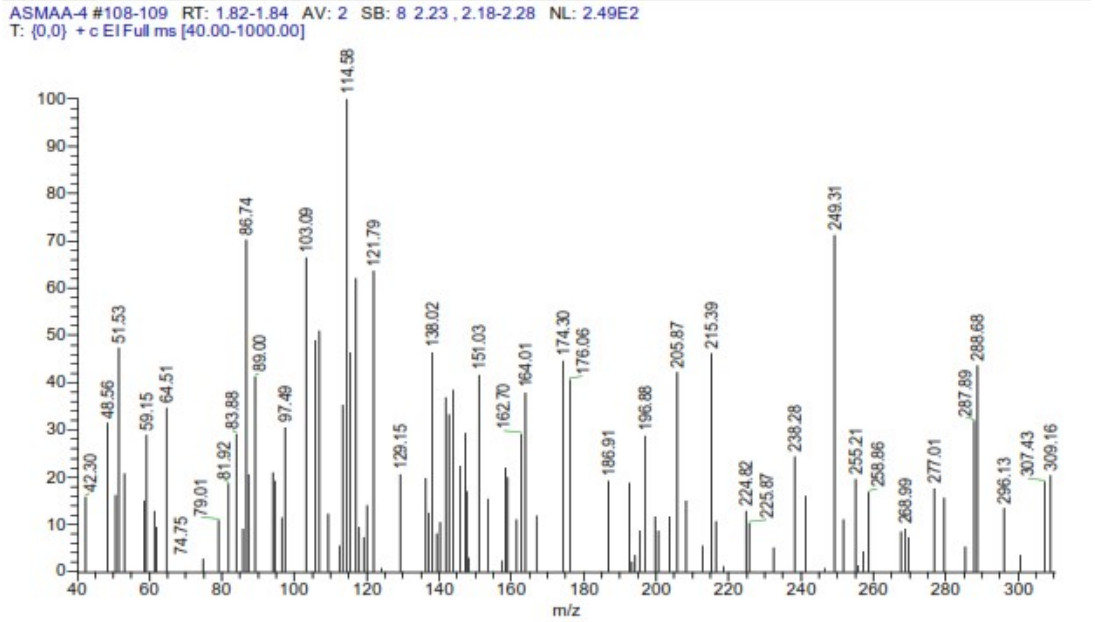

RT: 2.49 - 2.91 SM: 15G
Compound 4b
NL:
2.33E4
TIC MS
asmaa-atta-4
Time (min)

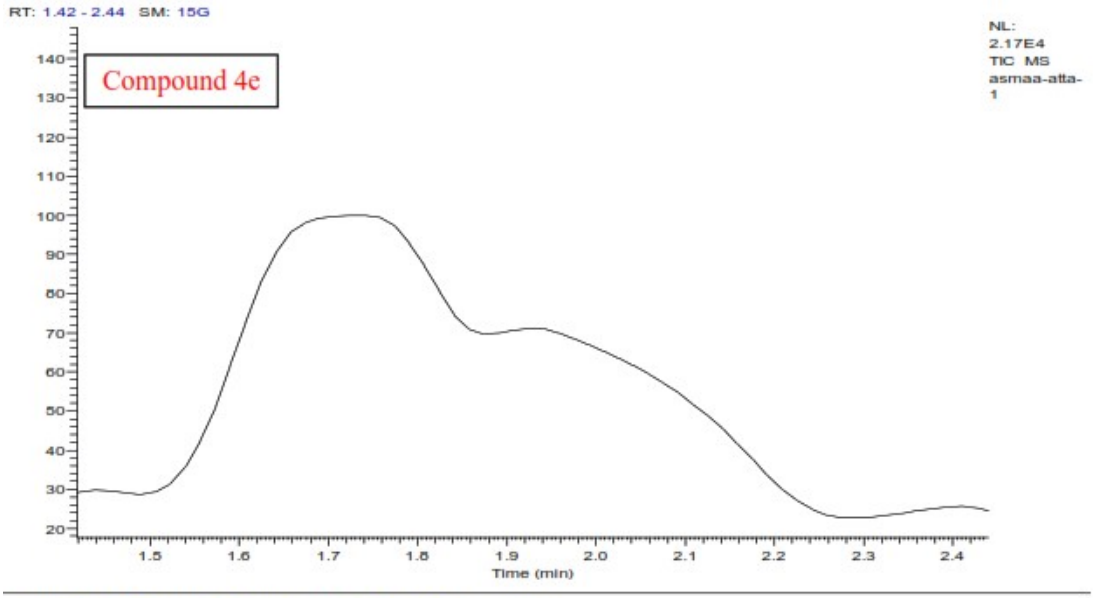

asmaa-atta-4 #233 RT: 3.92 AV: 1 SB: 2 3.97 , 3.97 NL: 4.70E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

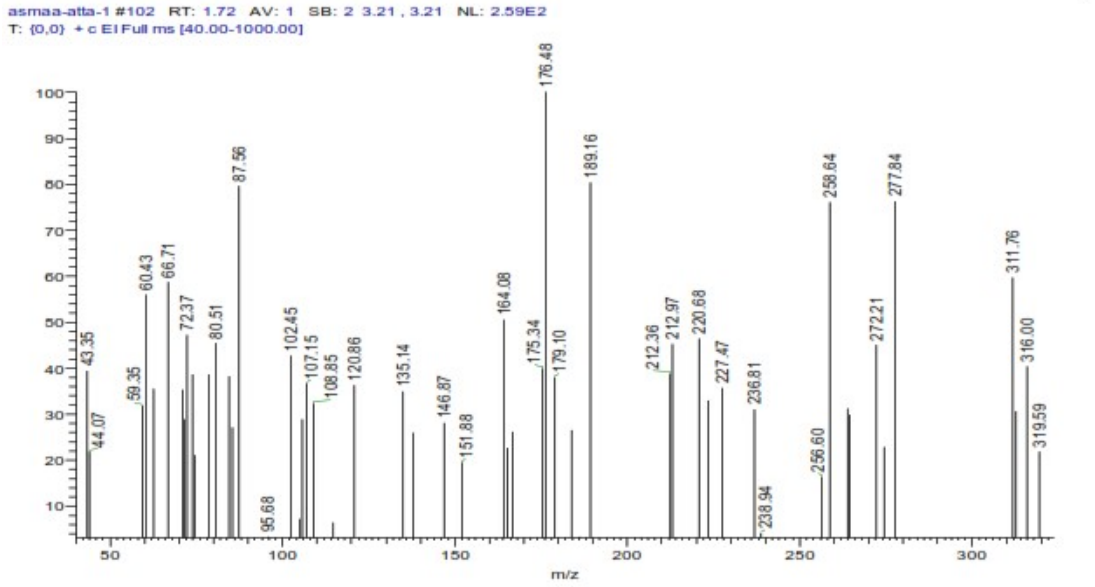

RT: 3.56
Compound 4c
NL:
1.66E6
TIC MS
asmaa-atta-3
Time (min)

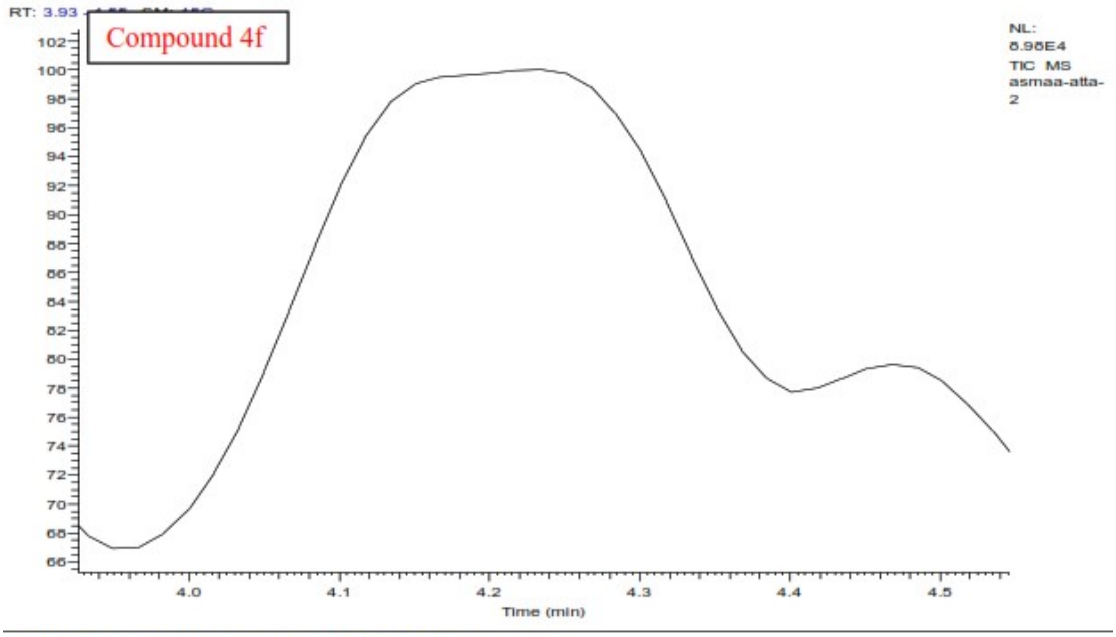

asmaa-atta-3 #84 RT: 1.42 AV: 1 SB: 2 4.45 , 4.45 NL: 4.67E2
T: {0,0} + c EI Full ms [40.00-1000.00]
57.16
68.17
71.27
83.16
87.12
96.57
110.29
116.02
123.21
125.66
139.15
149.18
164.09
170.28
179.22
182.42
196.56
205.18
221.21
223.28
247.21
253.08
256.41
261.74
270.34
278.03
280.16
297.34
305.01
m/z

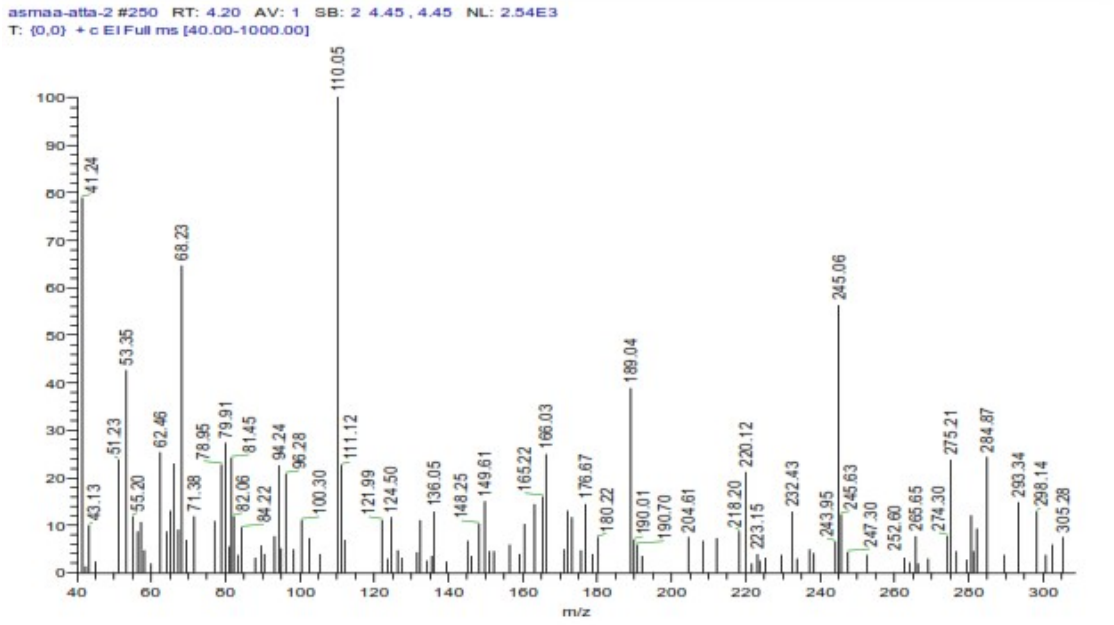

Compound 4d
NL:
4.50E6
TIC MS
ASMAA-4
Time (min)

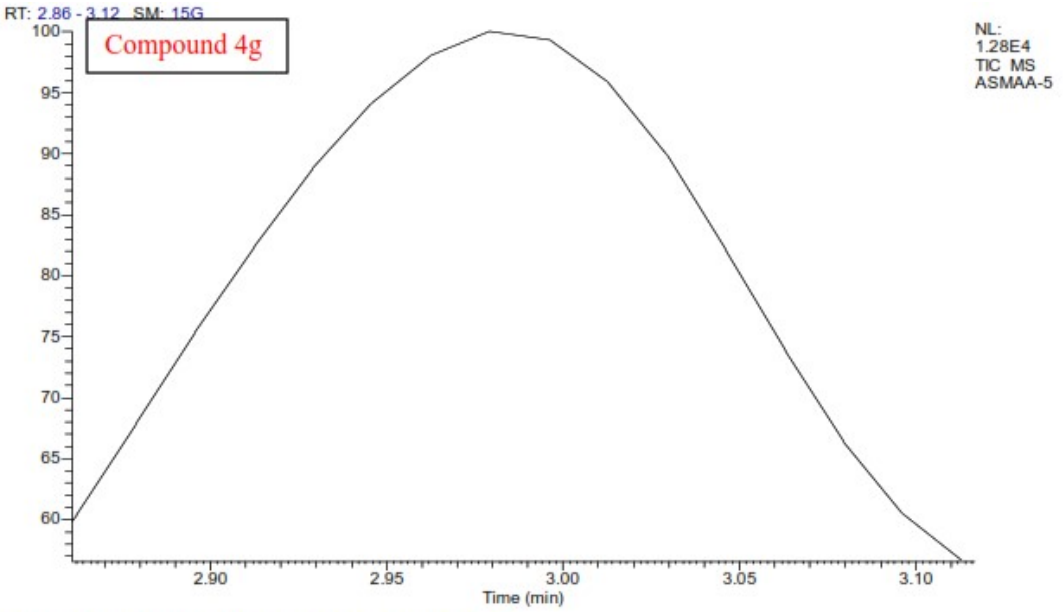

ASMAA-4 #108-109 RT: 1.82-1.84 AV: 2 SB: 8 2.23 , 2.18-2.28 NL: 2.49E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

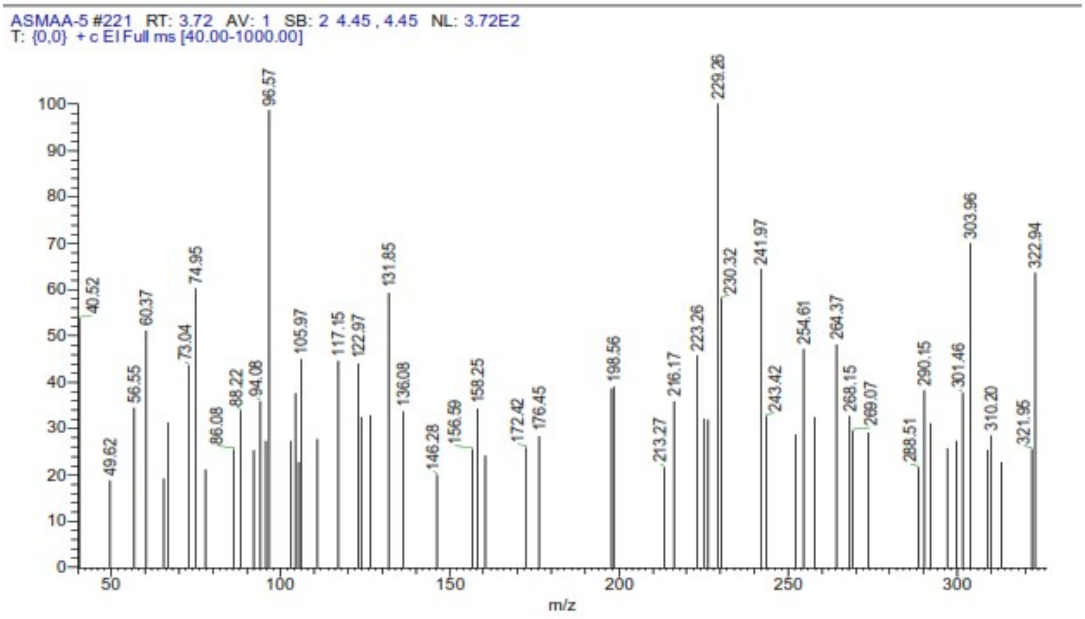

RT: 1.42 - 2.44 SM: 15G
Compound 4e
NL:
2.17E4
TIC MS
asmaa-atta-
1
Time (min)

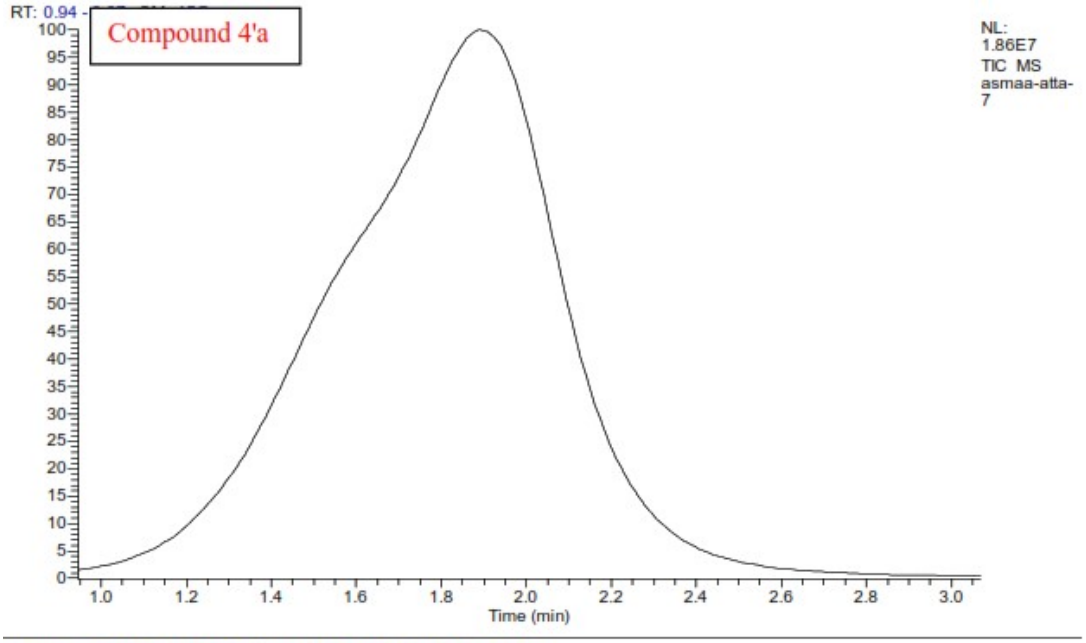

asmaa-atta-1 #102 RT: 1.72 AV: 1 SB: 2 3.21 , 3.21 NL: 2.59E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

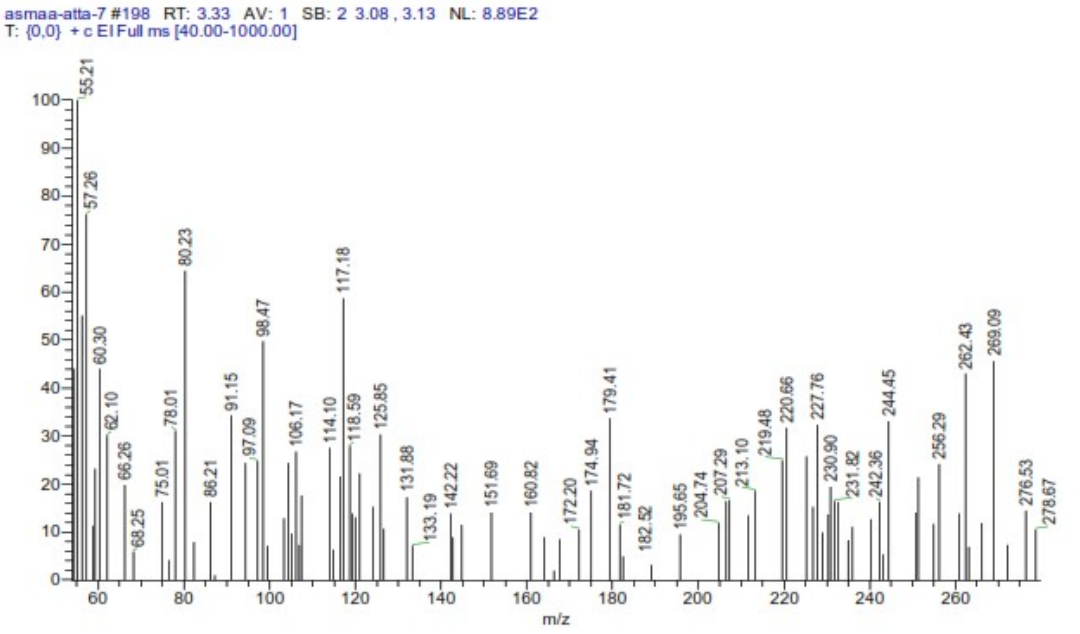

RT: 3.93
Compound 4f
NL:
8.98E4
TIC MS
asmaa-atta-2
Time (min)

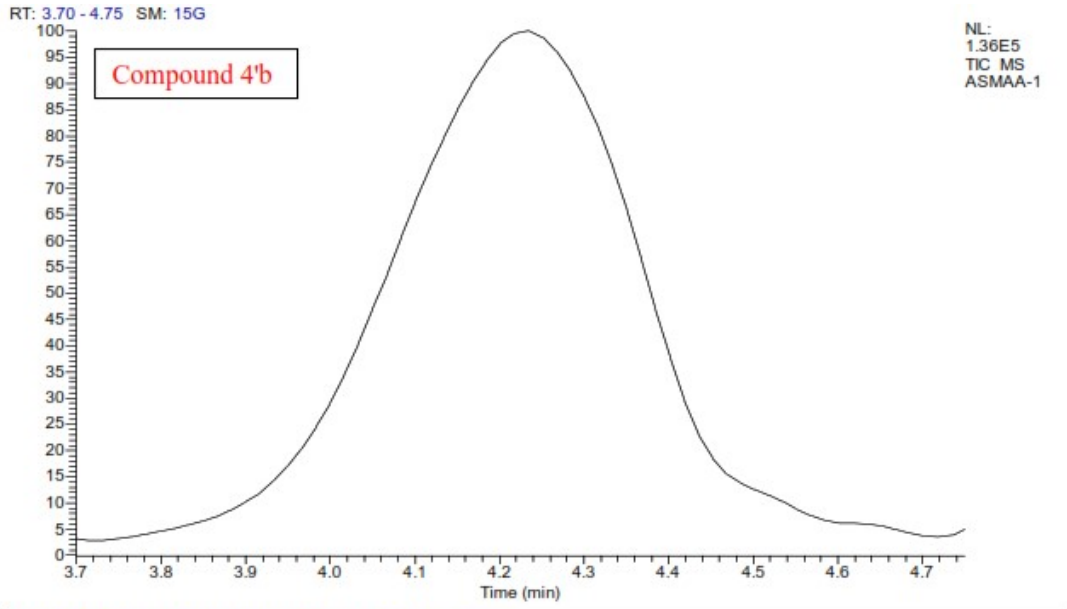

asmaa-atta-2 #250 RT: 4.20 AV: 1 SB: 2 4.45 , 4.45 NL: 2.54E3
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

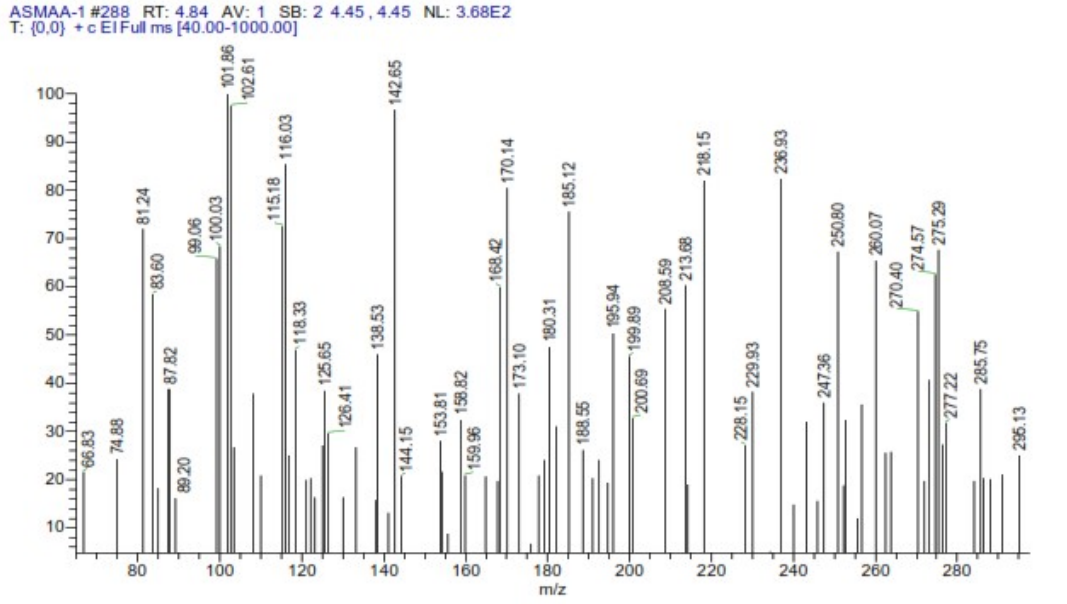

RT: 2.86 - 3.12 SM: 15G
Compound 4g
NL:
1.28E4
TIC MS
ASMAA-5
Time (min)

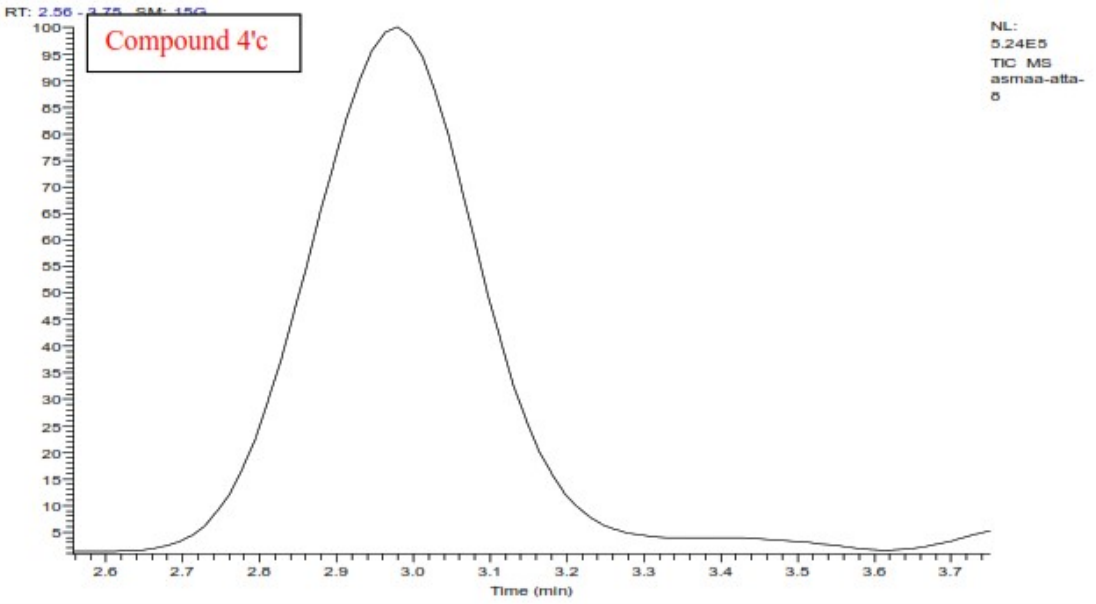

ASMAA-5 #221 RT: 3.72 AV: 1 SB: 2 4.45 , 4.45 NL: 3.72E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

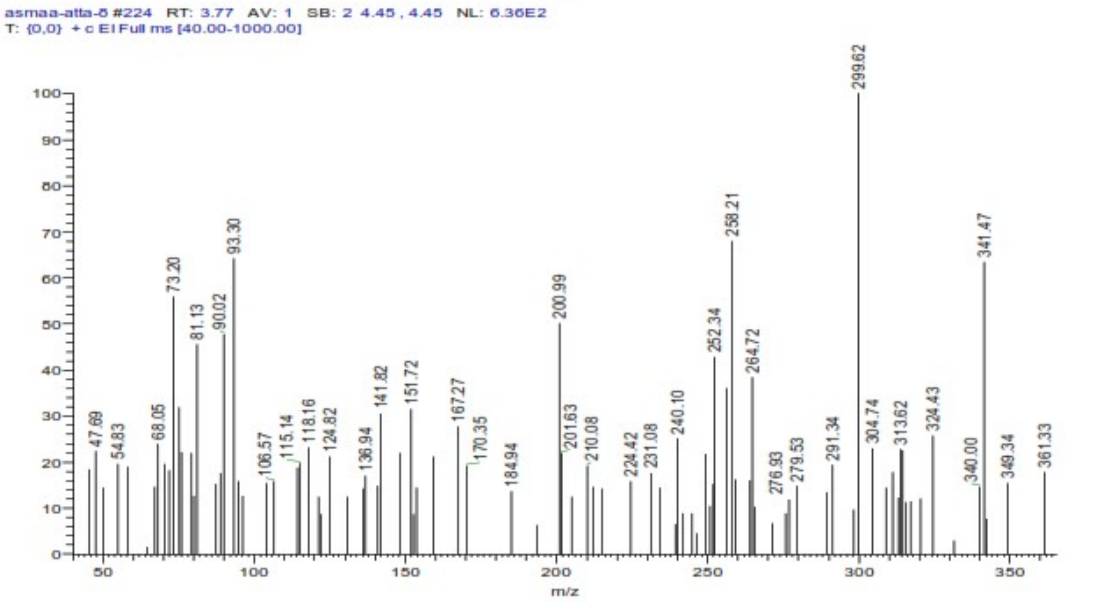

RT: 0.94 -
Compound 4'a
NL:
1.86E7
TIC MS
asmaa-atta-
7
Time (min)

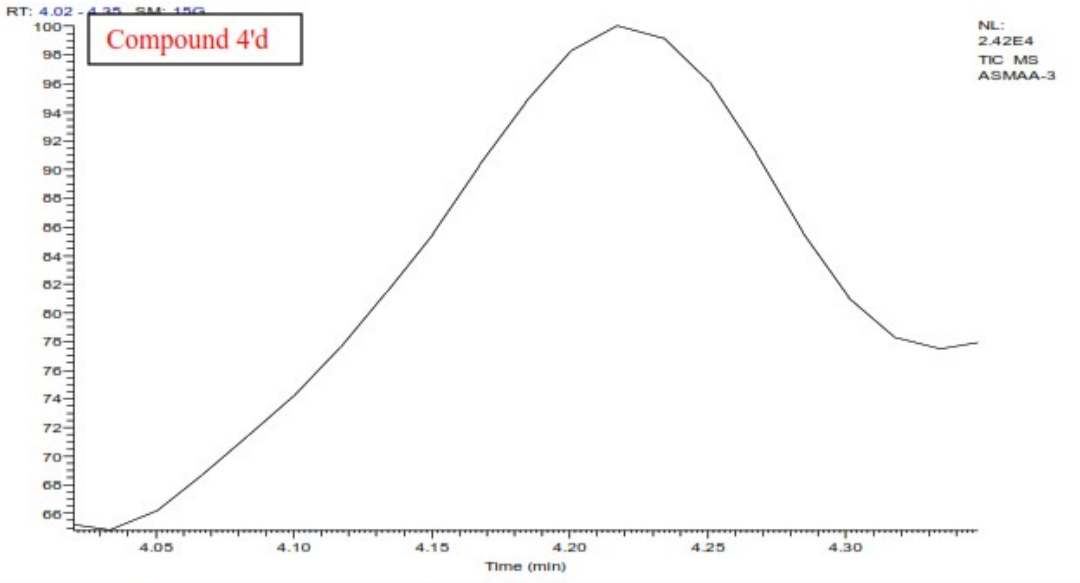

asmaa-atta-7 #198 RT: 3.33 AV: 1 SB: 2 3.08 , 3.13 NL: 8.89E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

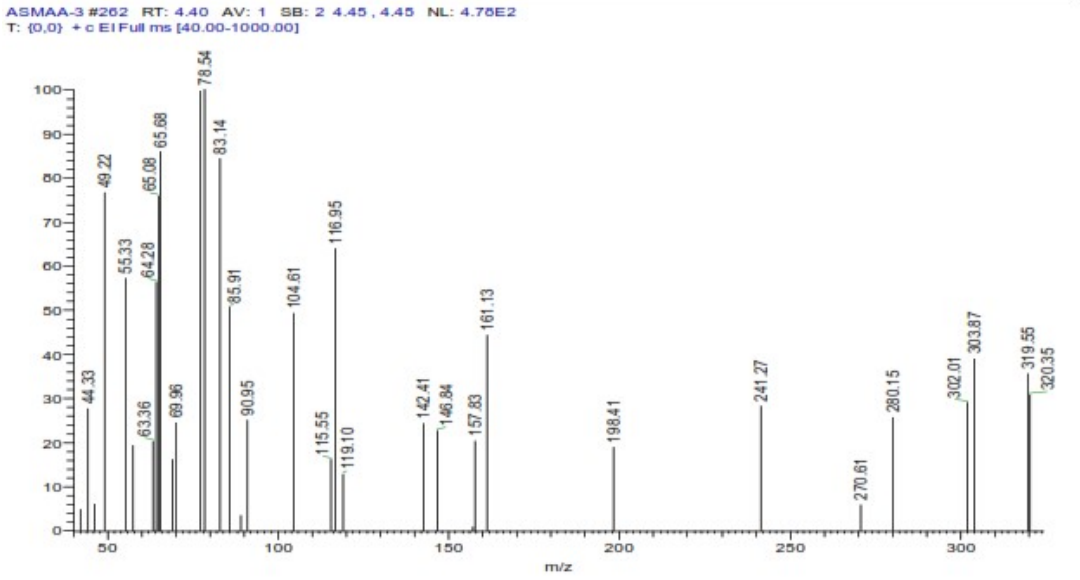

RT: 3.70 - 4.75 SM: 15G
Compound 4'b
NL:
1.36E5
TIC MS
ASMAA-1
Time (min)

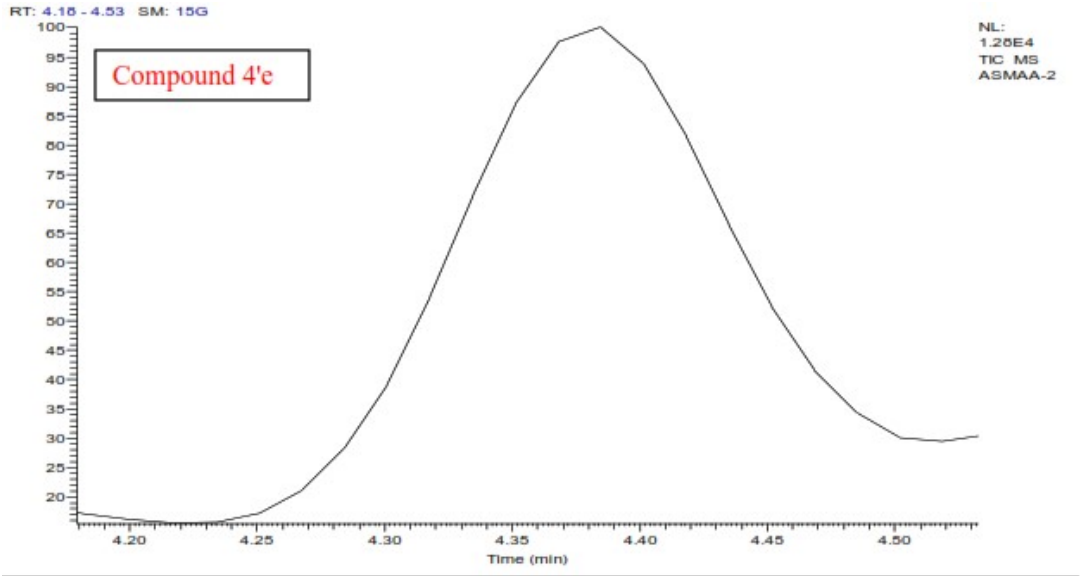

ASMAA-1 #288 RT: 4.84 AV: 1 SB: 2 4.45 , 4.45 NL: 3.68E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

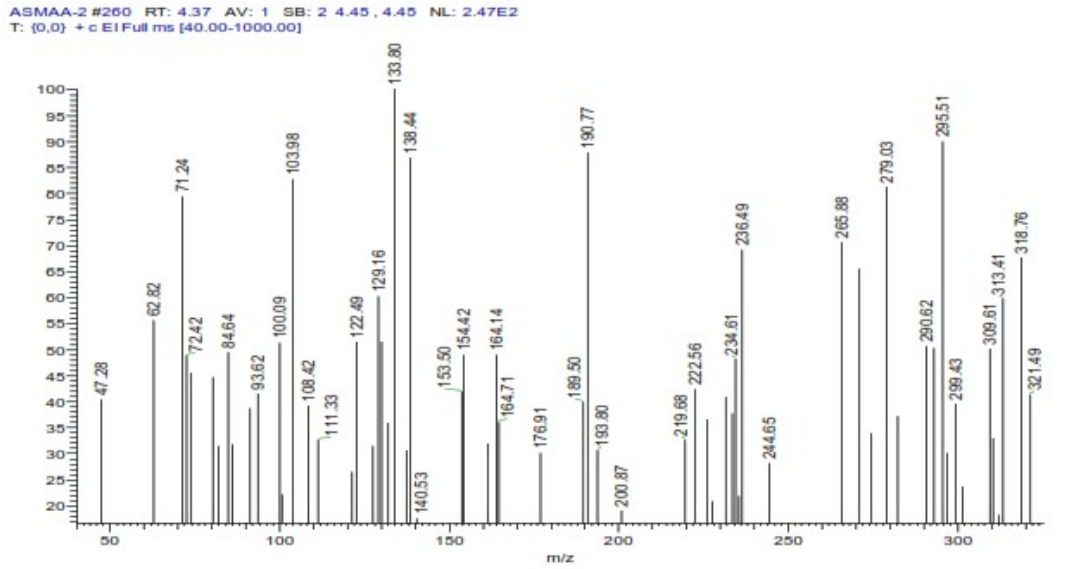

Compound 4'c
NL:
5.24E5
TIC MS
asmaa-atta-
δ
Time (min)

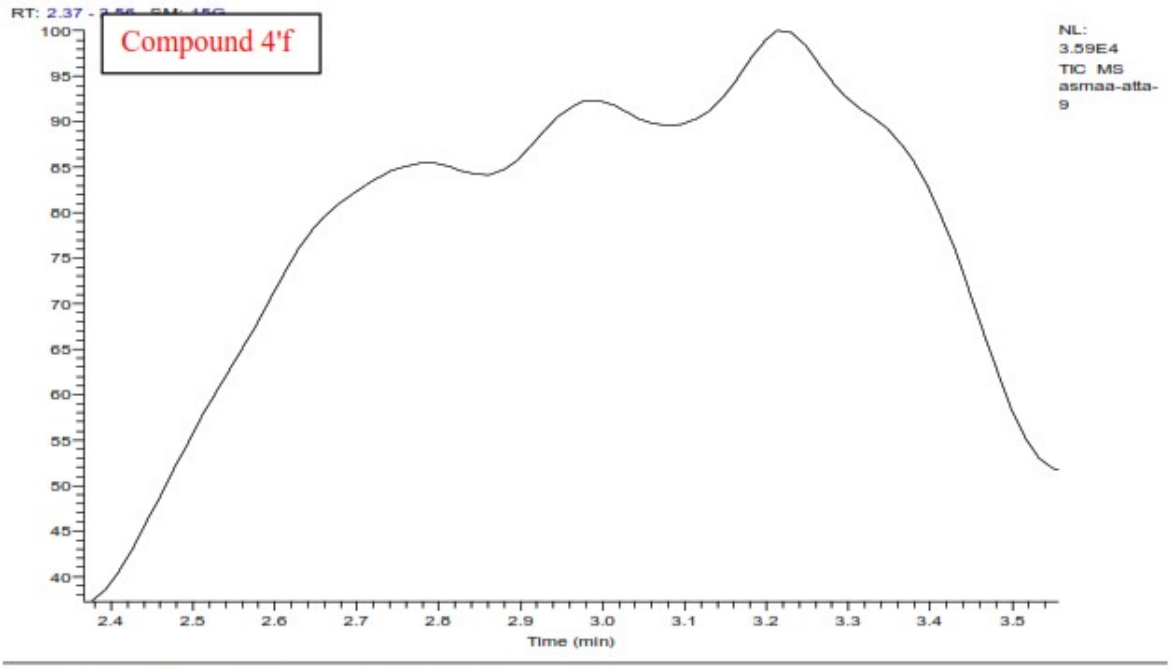

asmaa-atta-δ #224 RT: 3.77 AV: 1 SB: 2 4.45 , 4.45 NL: 6.36E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

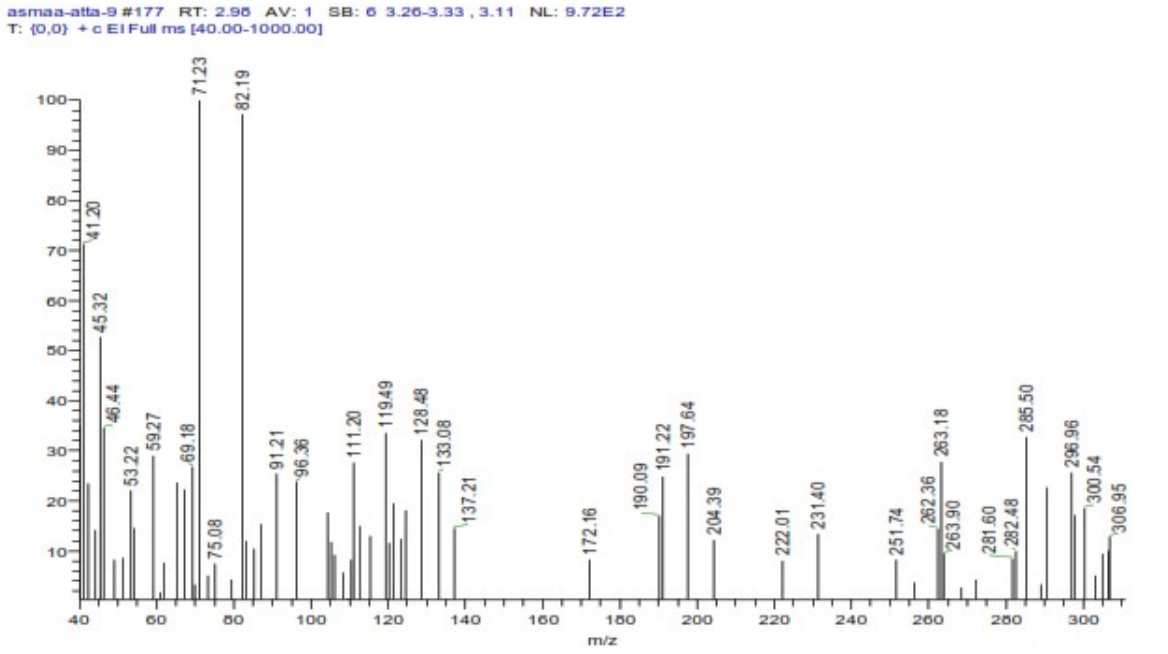

RT: 4.02 - 4.35 SM: 15G
Compound 4'd
NL:
2.42E4
TIC MS
ASMAA-3
Time (min)

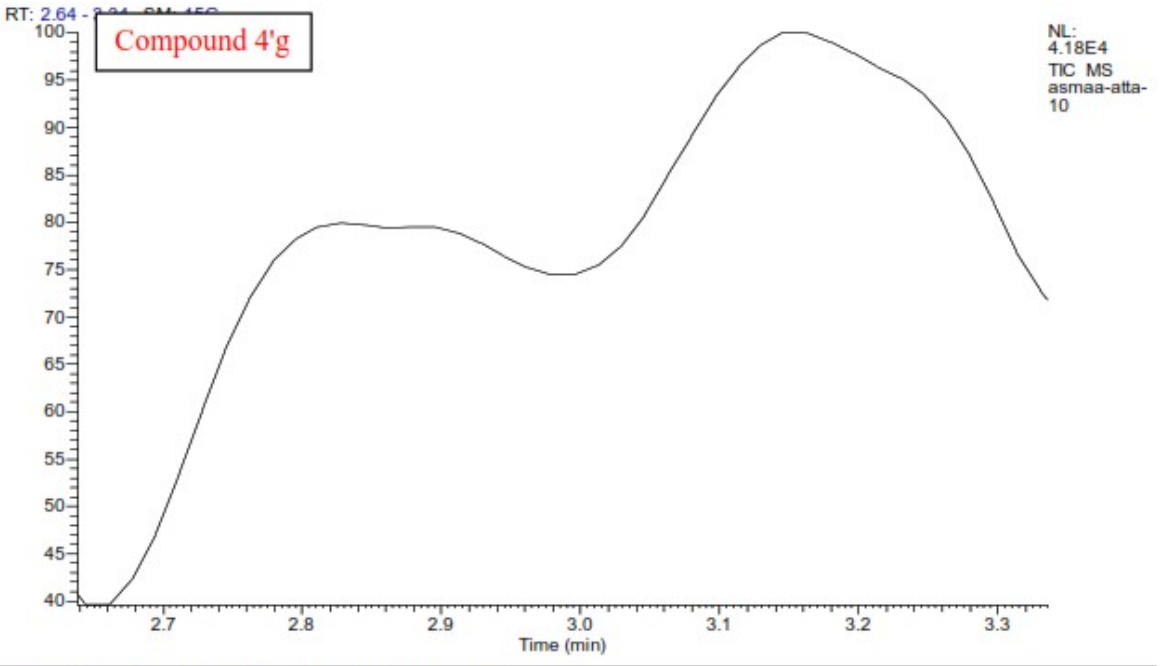

ASMAA-3 #262 RT: 4.40 AV: 1 SB: 2 4.45 , 4.45 NL: 4.76E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

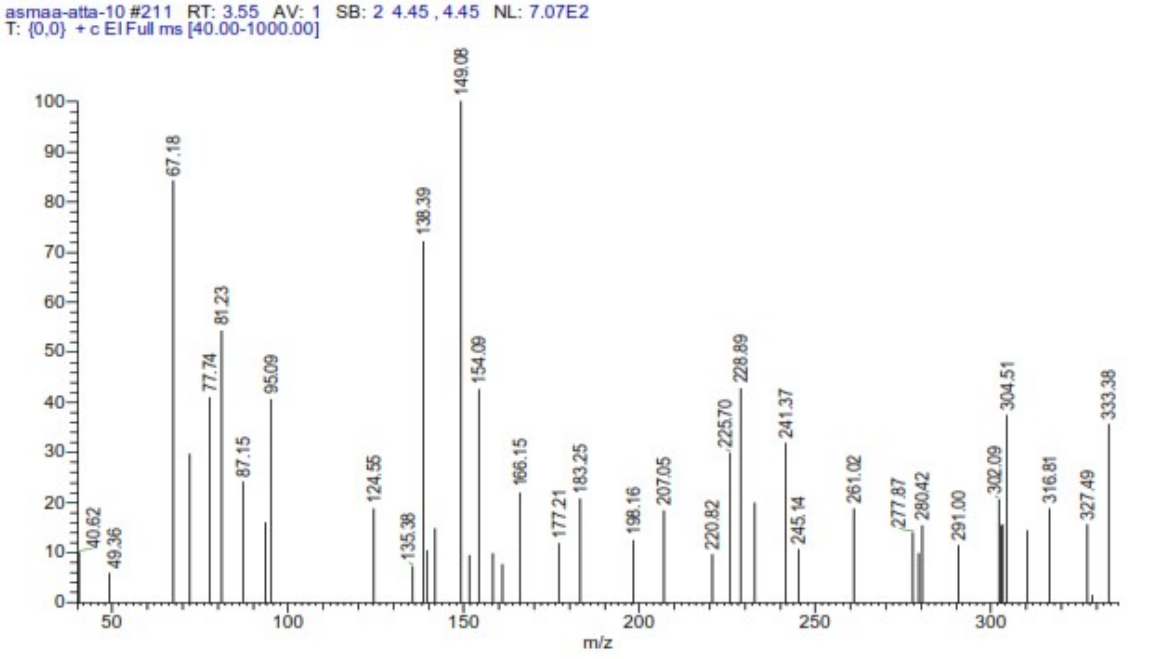

RT: 4.16 - 4.53 SM: 15G
Compound 4'e
NL:
1.28E4
TIC MS
ASMAA-2
Time (min)

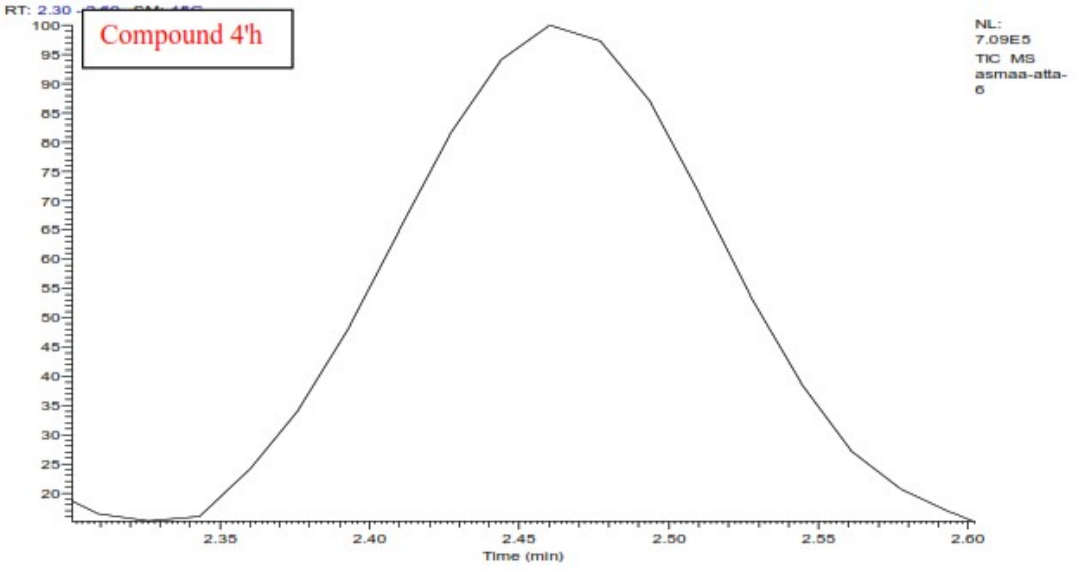

ASMAA-2 #260 RT: 4.37 AV: 1 SB: 2 4.45 , 4.45 NL: 2.47E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

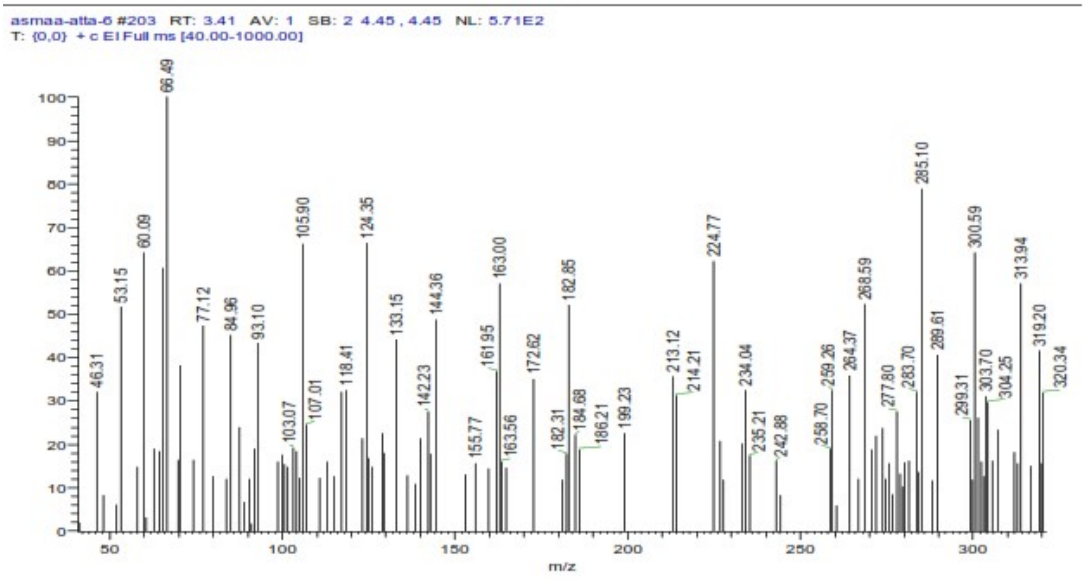

Compound 4'f
NL:
3.59E4
TIC MS
asmaa-atta-
9
Time (min)

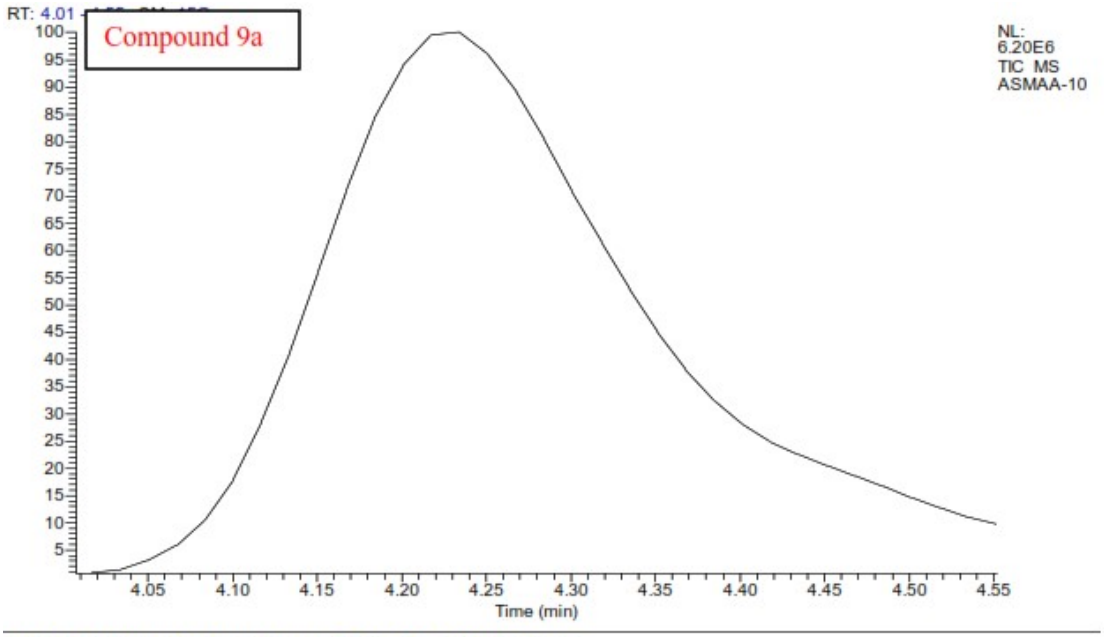

asmaa-atta-9 #177 RT: 2.96 AV: 1 SB: 6 3.26-3.33 , 3.11 NL: 9.72E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

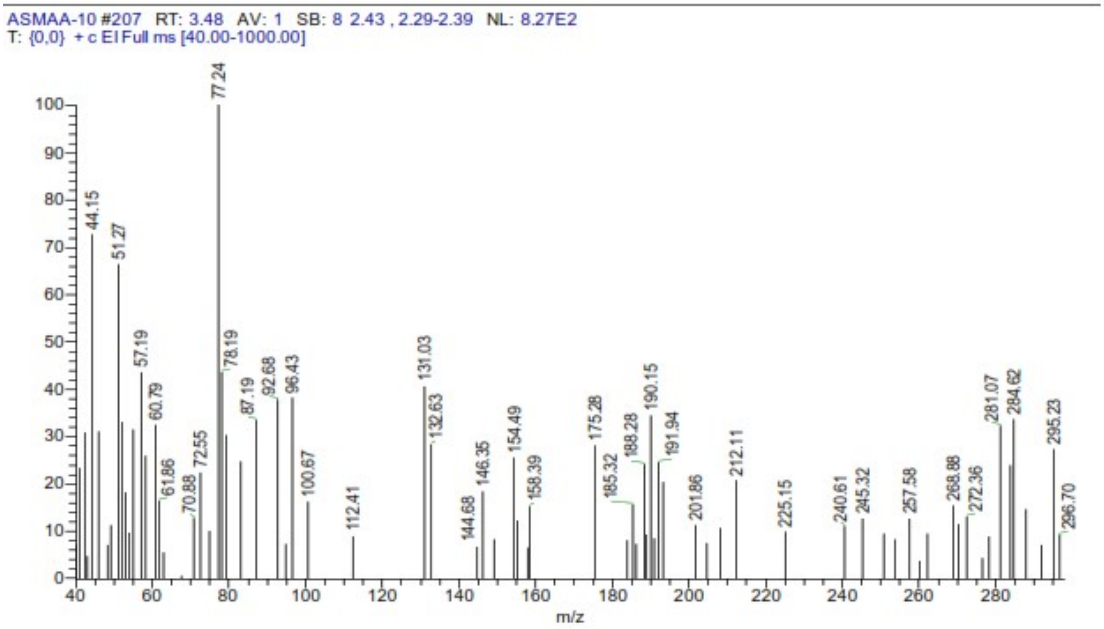

Compound 4'g
NL:
4.18E4
TIC MS
asmaa-atta-
10
Time (min)

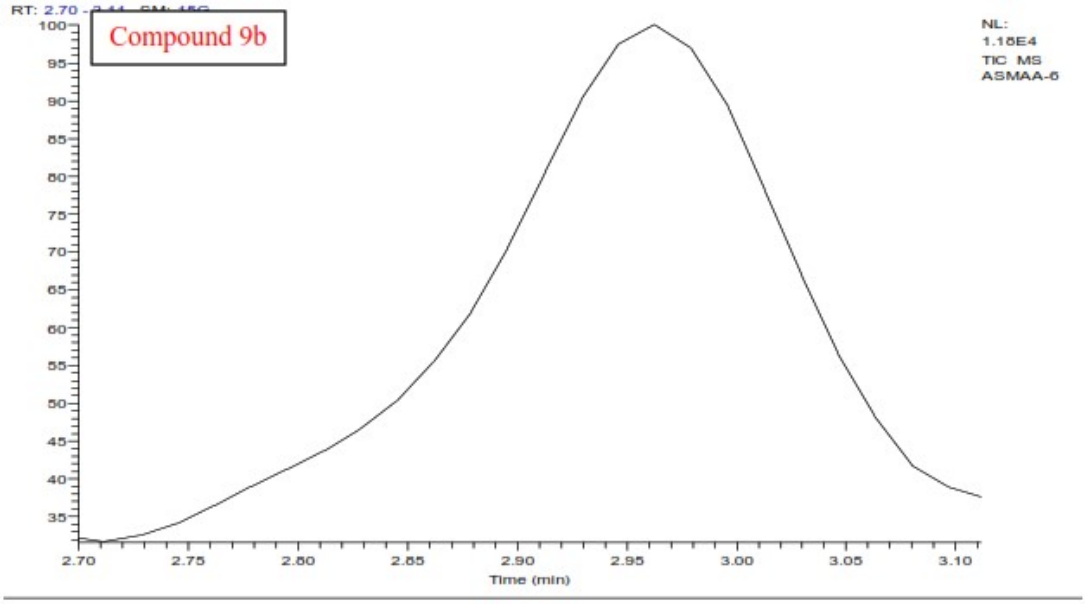

asmaa-atta-10 #211 RT: 3.55 AV: 1 SB: 2 4.45 , 4.45 NL: 7.07E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

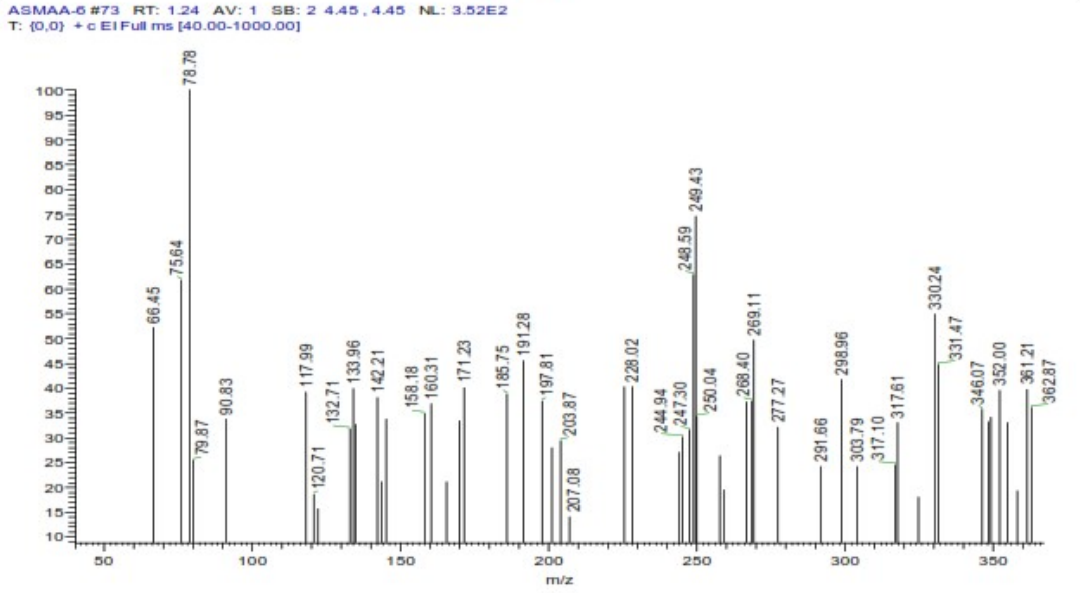

Compound 4'h
NL:
7.09E5
TIC MS
asmaa-atta-6
Time (min)

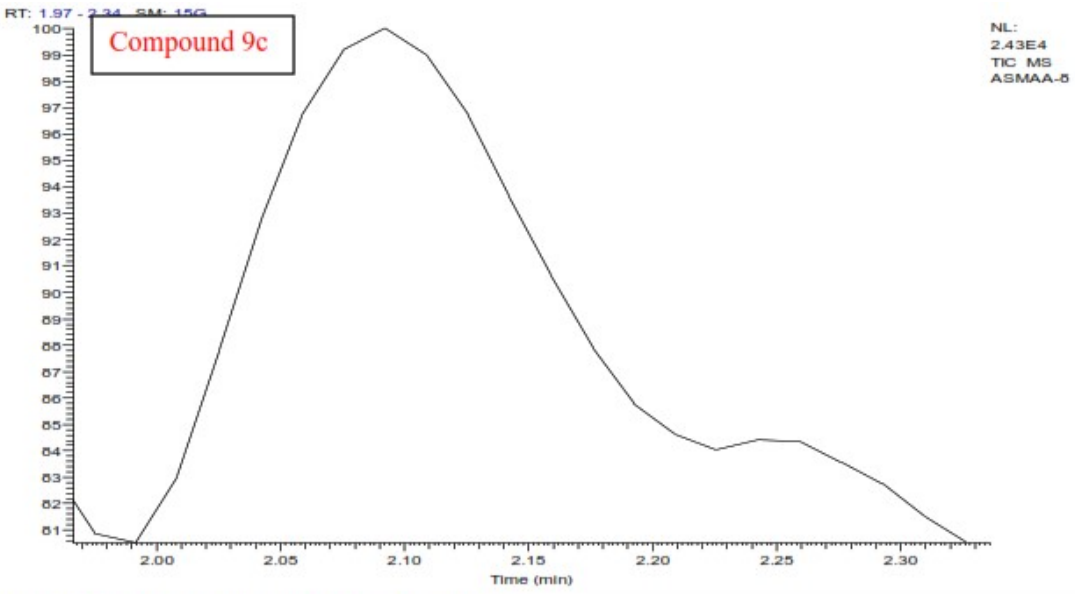

asmaa-atta-6 #203 RT: 3.41 AV: 1 SB: 2 4.45 , 4.45 NL: 5.71E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

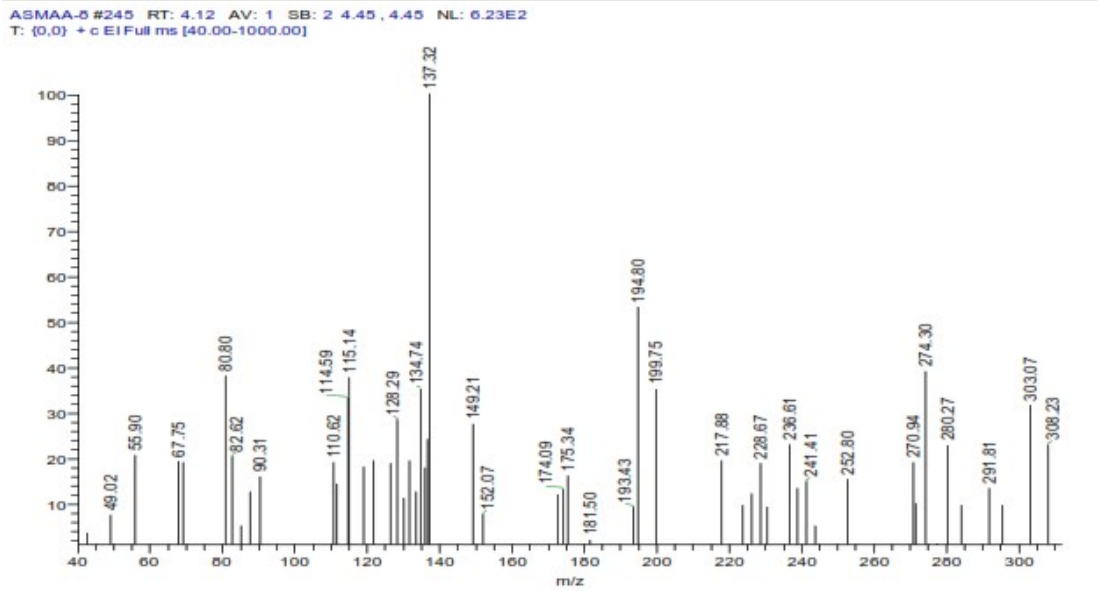

RT: 4.01
Compound 9a
NL:
6.20E6
TIC MS
ASMAA-10
Time (min)

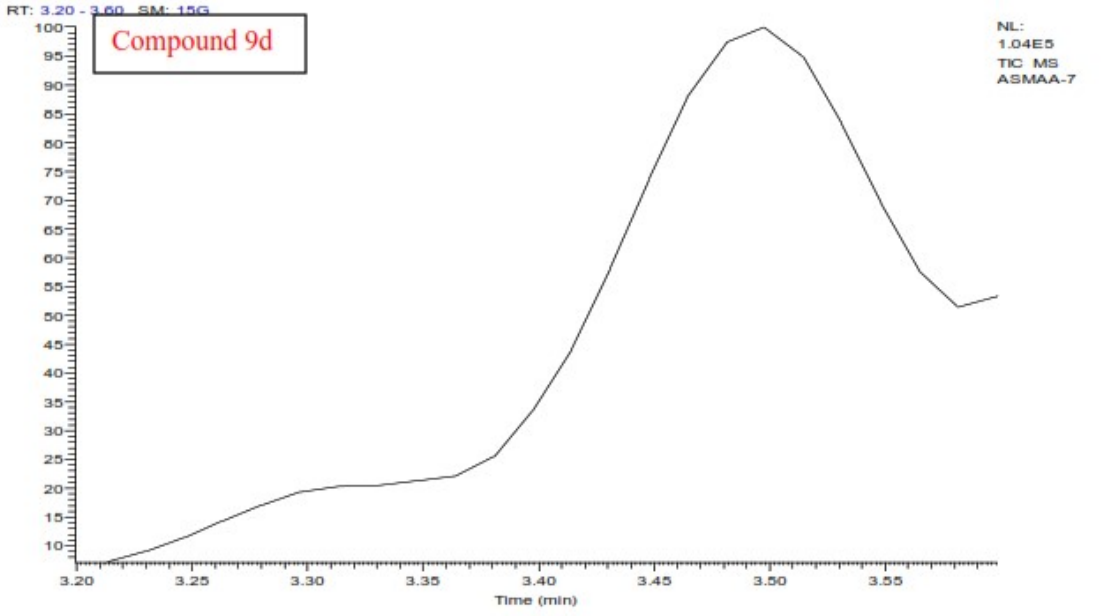

ASMAA-10 #207 RT: 3.48 AV: 1 SB: 8 2.43 , 2.29-2.39 NL: 8.27E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

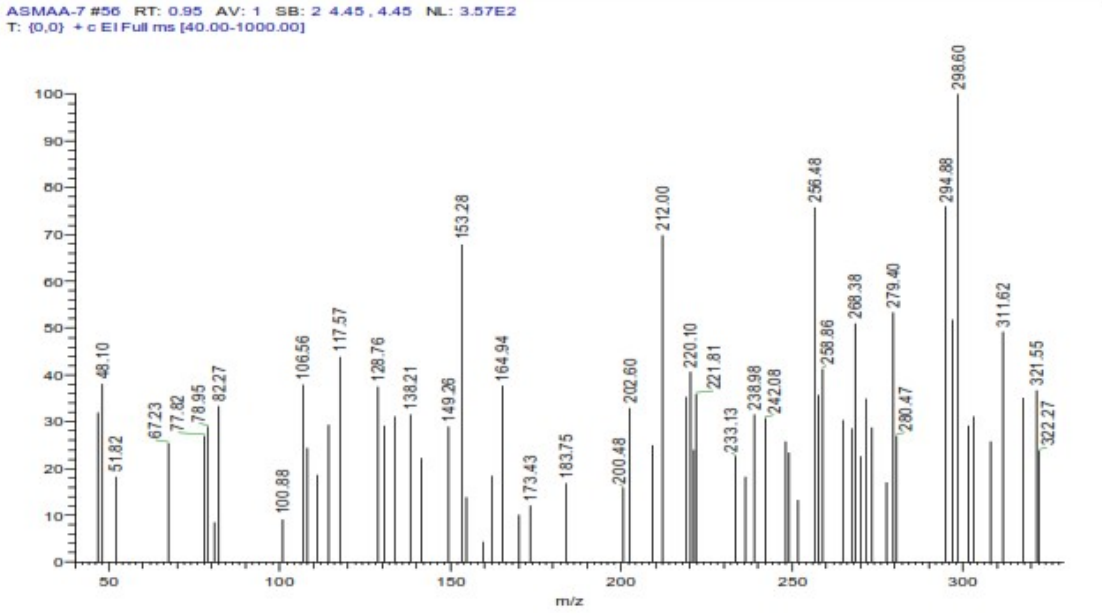

Compound 9b
NL:
1.16E4
TIC MS
ASMAA-6
Time (min)

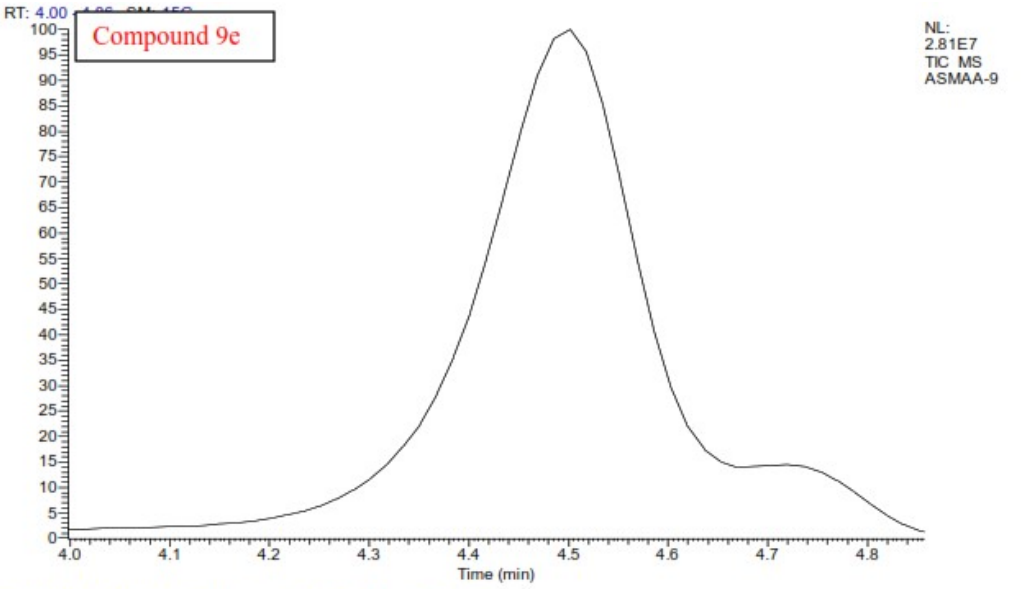

ASMAA-6 #73 RT: 1.24 AV: 1 SB: 2 4.45 , 4.45 NL: 3.52E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

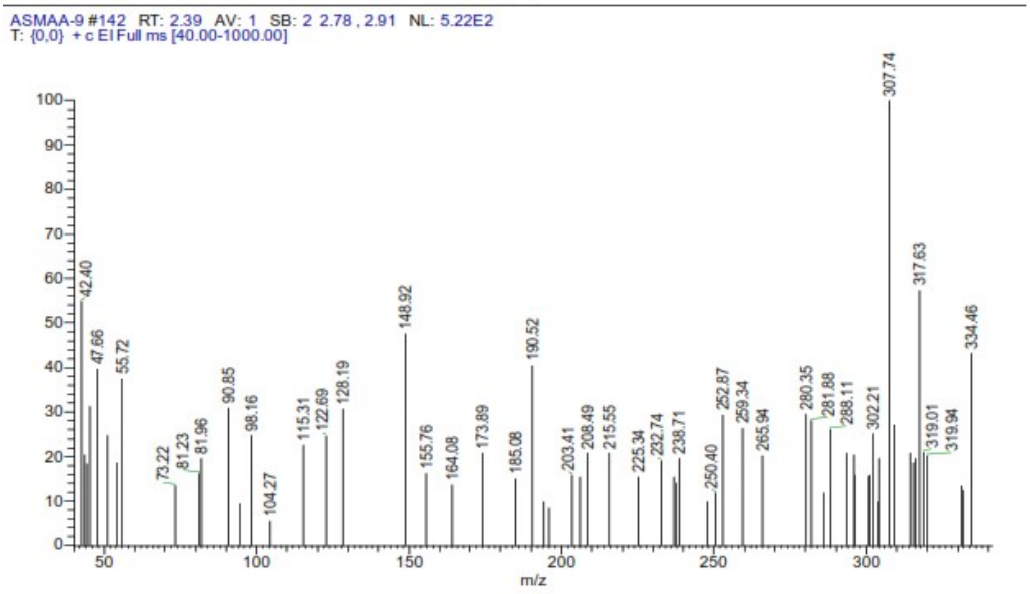

RT: 1.97 - 2.34 SM: 15G
Compound 9c
NL:
2.43E4
TIC MS
ASMAA-δ
Time (min)

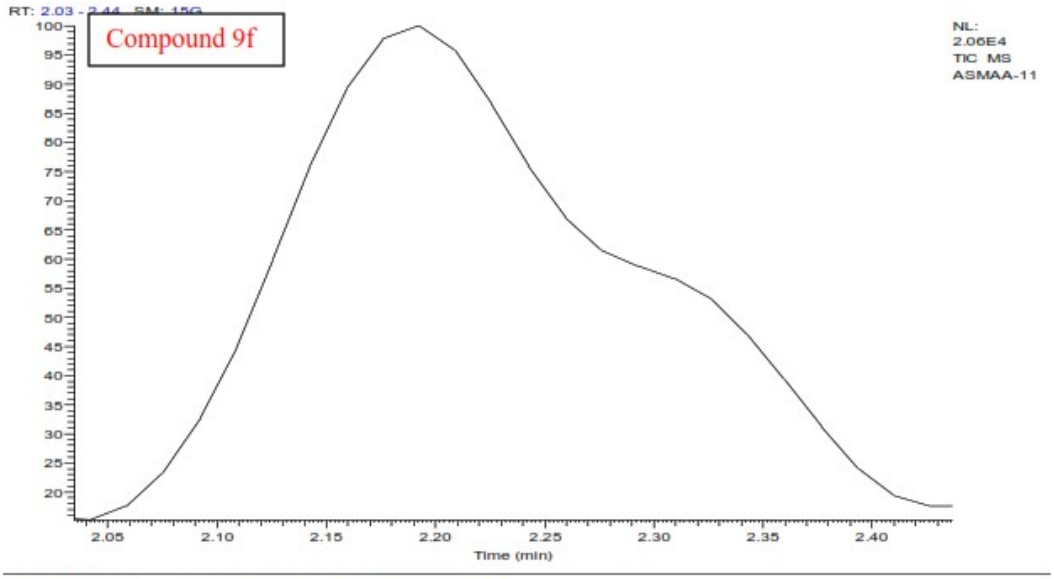

ASMAA-δ #245 RT: 4.12 AV: 1 SB: 2 4.45 , 4.45 NL: 6.23E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

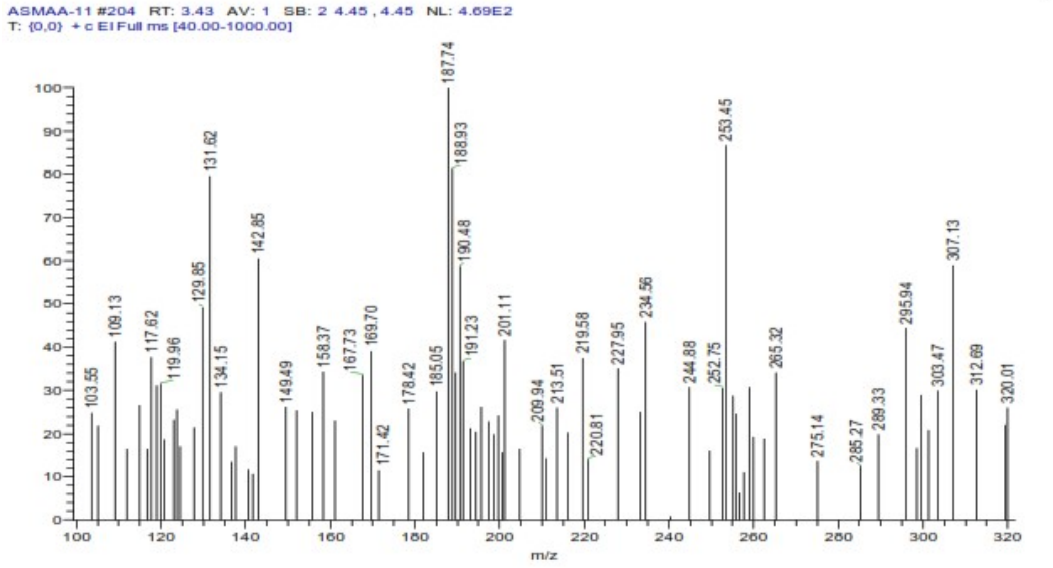

RT: 3.20 - 3.60 SM: 15G
Compound 9d
NL:
1.04E5
TIC MS
ASMAA-7
Time (min)

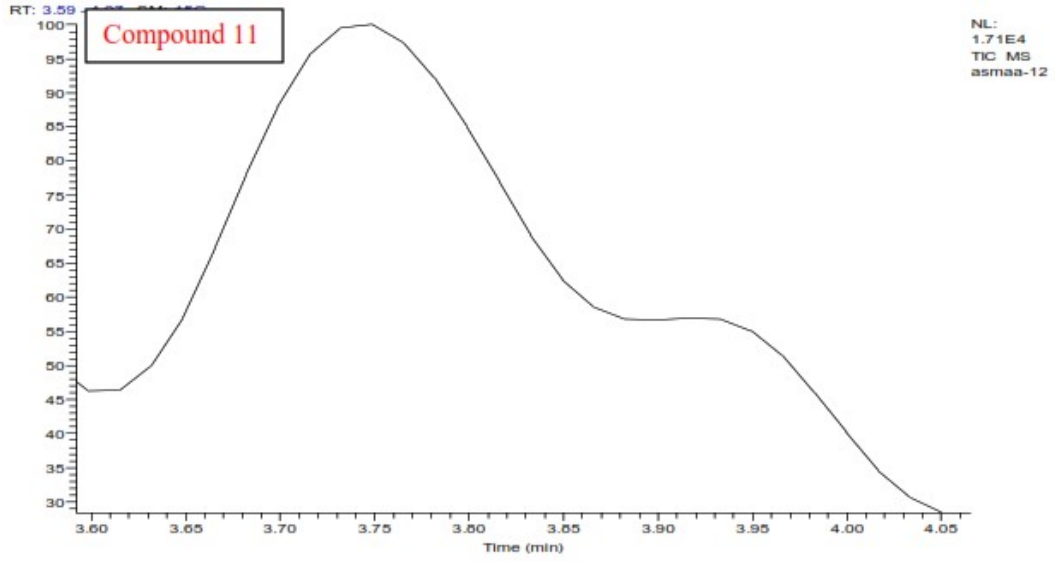

ASMAA-7 #56 RT: 0.95 AV: 1 SB: 2 4.45 , 4.45 NL: 3.57E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

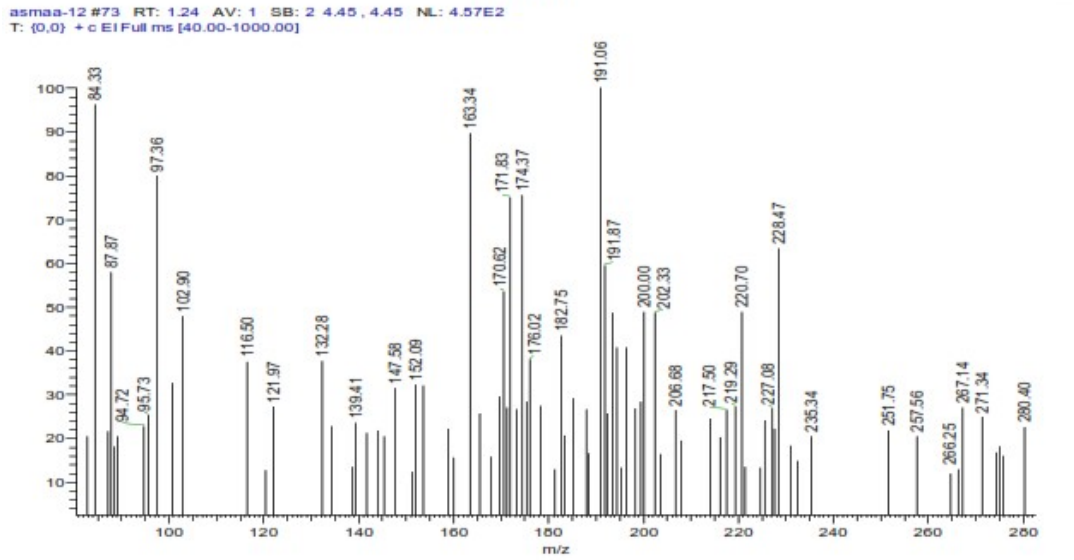

RT: 4.00
Compound 9e
NL:
2.81E7
TIC MS
ASMAA-9
Time (min)

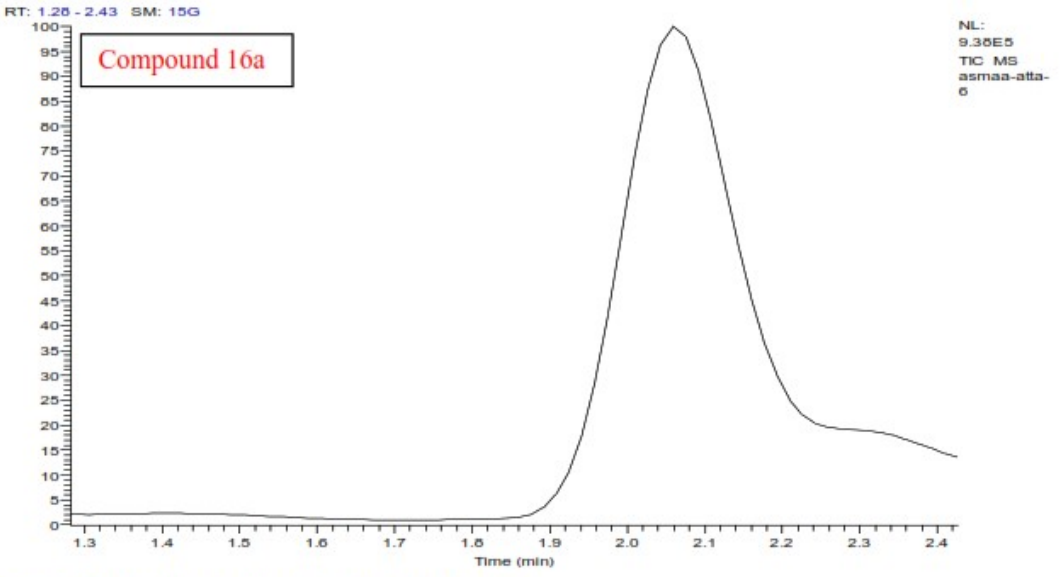

ASMAA-9 #142 RT: 2.39 AV: 1 SB: 2 2.78 , 2.91 NL: 5.22E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

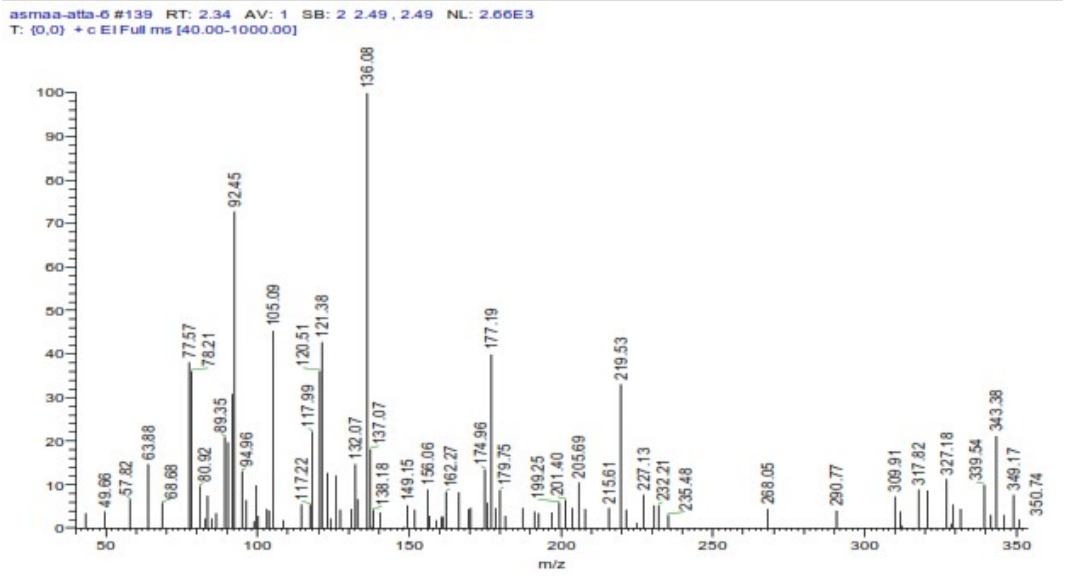

RT: 2.03 - 2.44 SM: 15G
Compound 9f
NL:
2.06E4
TIC MS
ASMAA-11
Time (min)

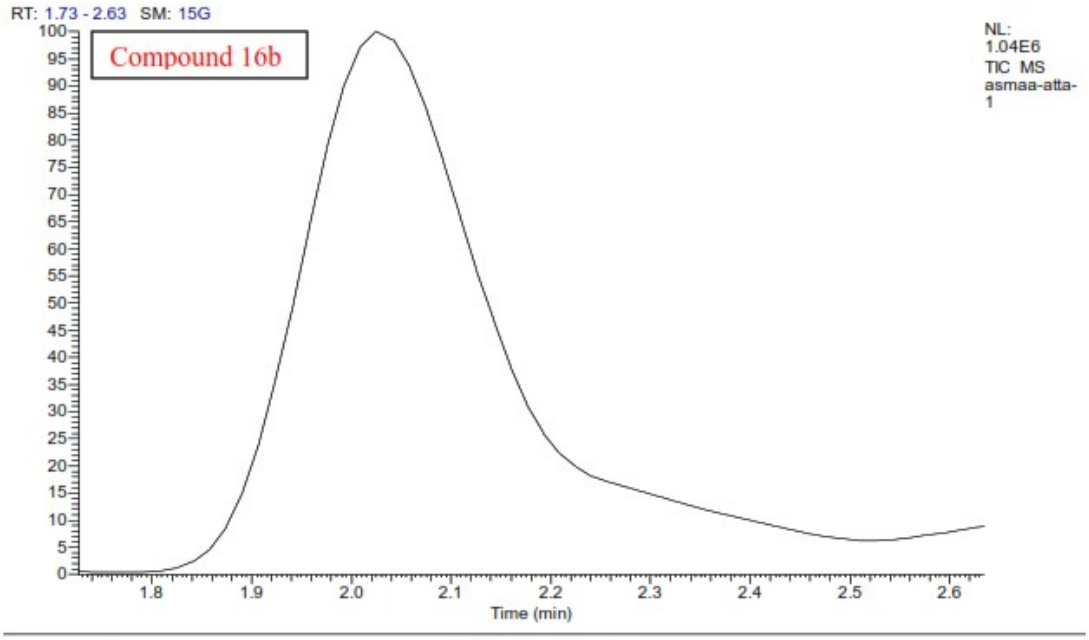

ASMAA-11 #204 RT: 3.43 AV: 1 SB: 2 4.45 , 4.45 NL: 4.69E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

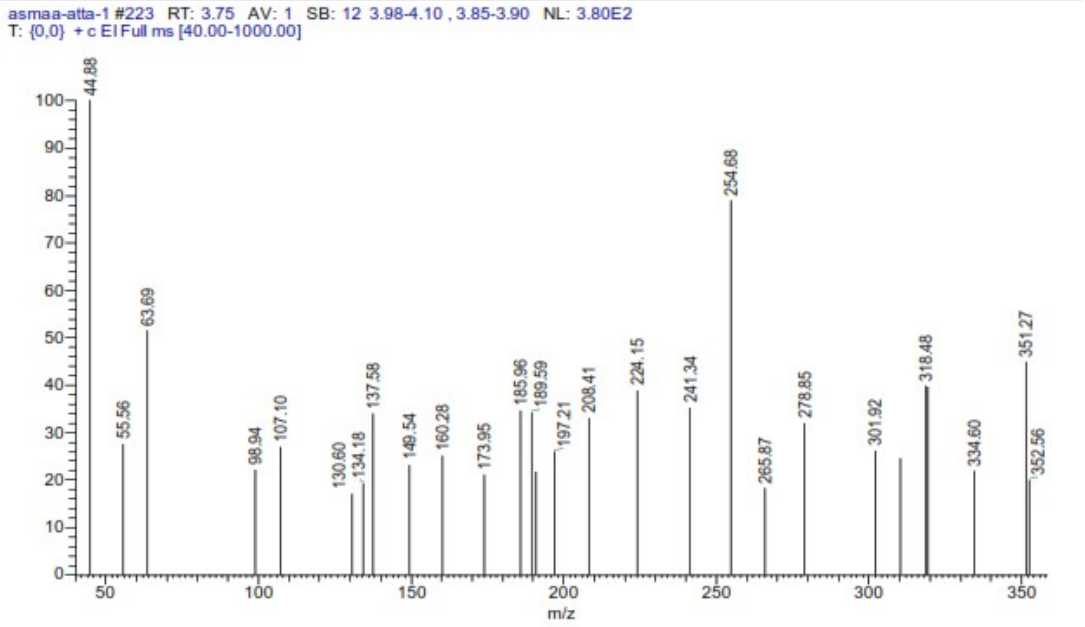

Compound 11
NL:
1.71E4
TIC MS
asmaa-12
Time (min)

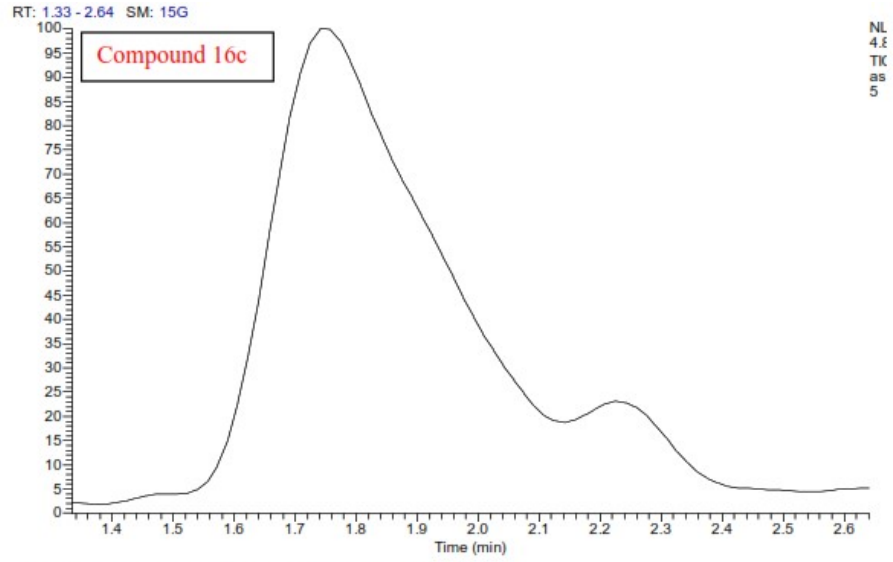

asmaa-12 #73 RT: 1.24 AV: 1 SB: 2 4.45 , 4.45 NL: 4.57E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

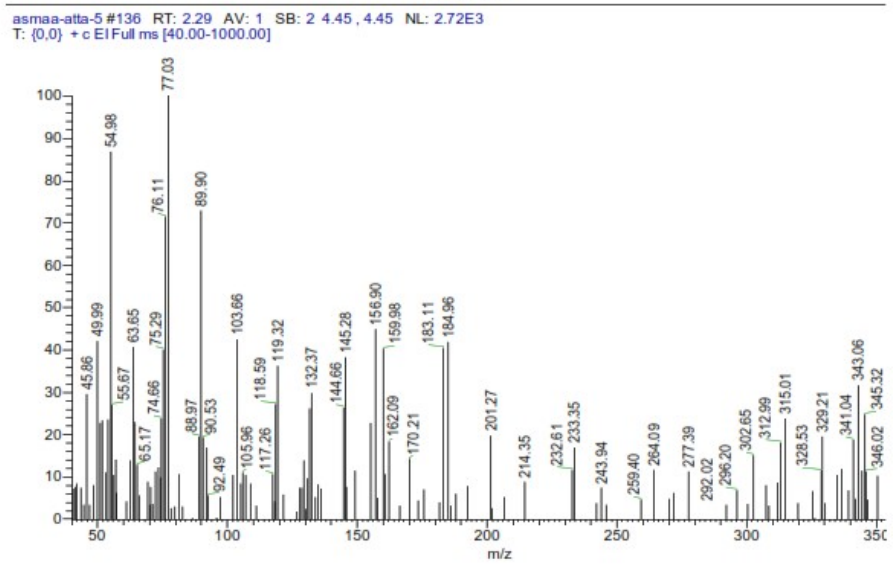

RT: 1.28 - 2.43 SM: 15G
Compound 16a
NL:
9.35E5
TIC MS
asmaa-atta-6
Time (min)

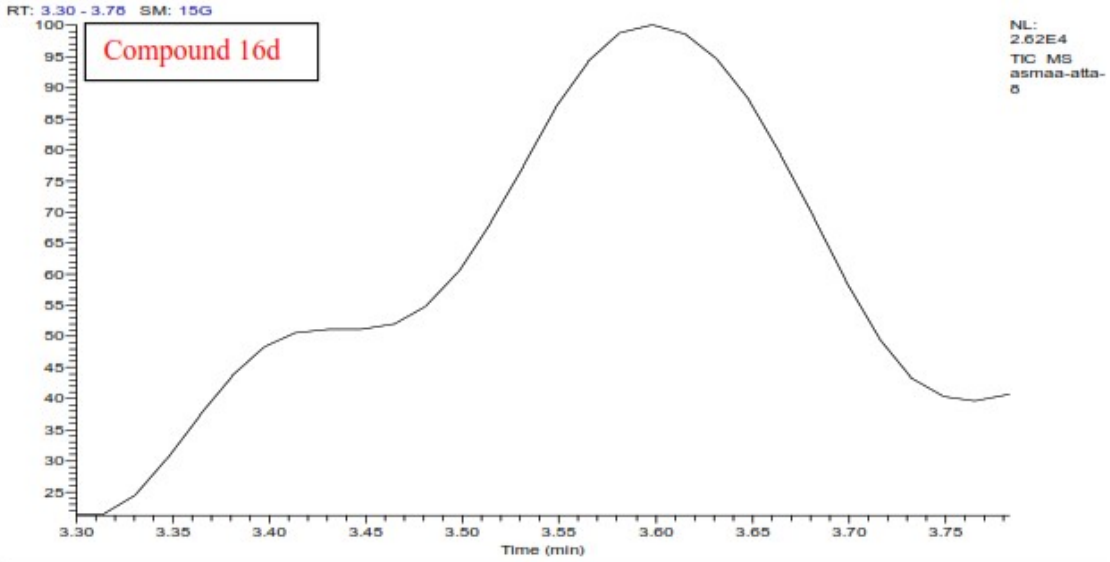

asmaa-atta-6 #139 RT: 2.34 AV: 1 SB: 2 2.49 , 2.49 NL: 2.66E3
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

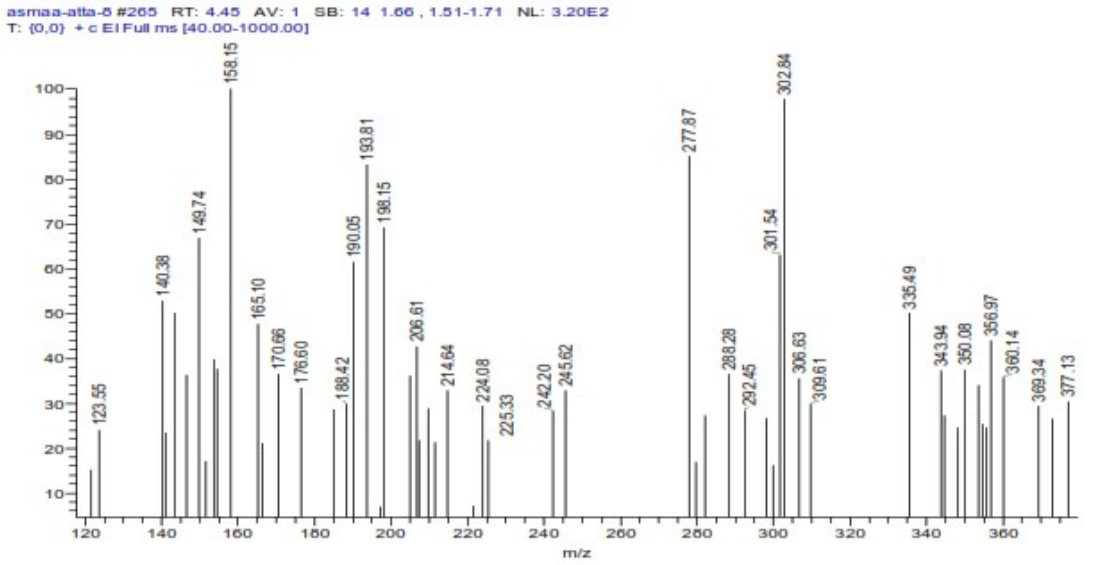

RT: 1.73 - 2.63 SM: 15G
Compound 16b
NL:
1.04E6
TIC MS
asmaa-atta-
1
Time (min)

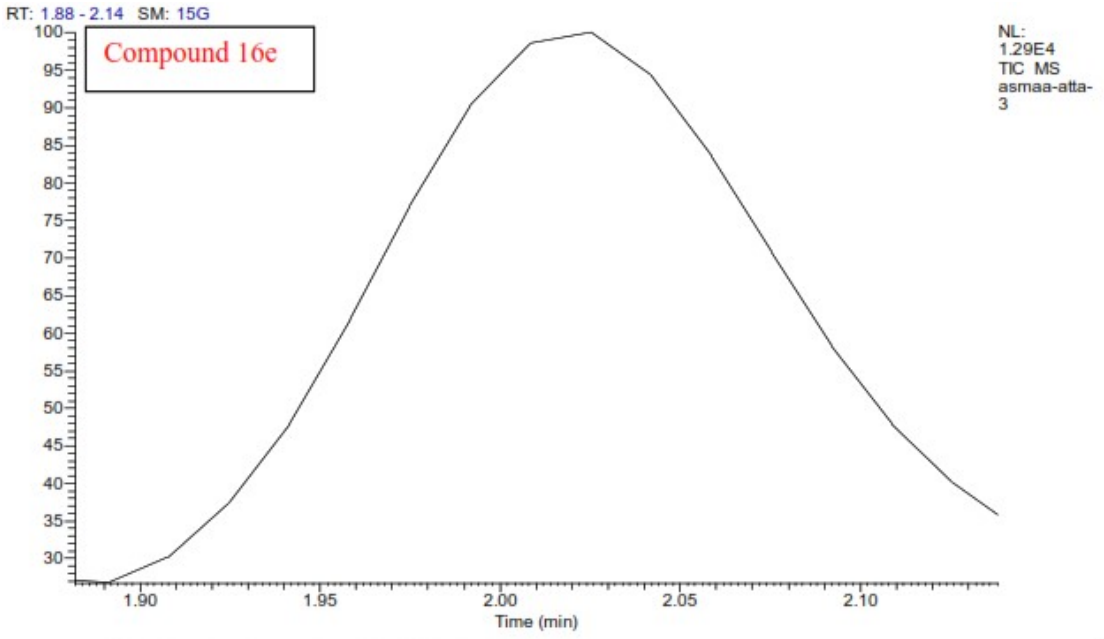

asmaa-atta-1 #223 RT: 3.75 AV: 1 SB: 12 3.98-4.10 , 3.85-3.90 NL: 3.80E2
T: {0,0} + c EI Full ms [40.00-1000.00]
44.88
63.69
55.56
98.94
107.10
130.60
134.18
137.58
149.54
160.28
173.95
185.96
189.59
197.21
208.41
224.15
241.34
254.68
265.87
278.85
301.92
318.48
334.60
351.27
352.56
m/z

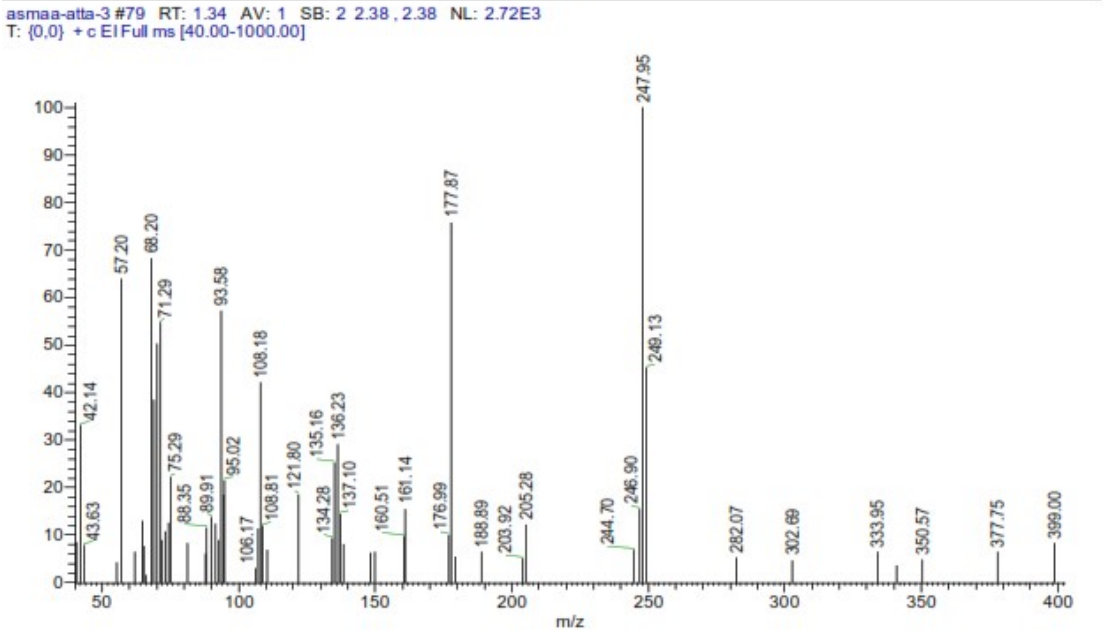

RT: 1.33 - 2.64 SM: 15G
Compound 16c
Time (min)

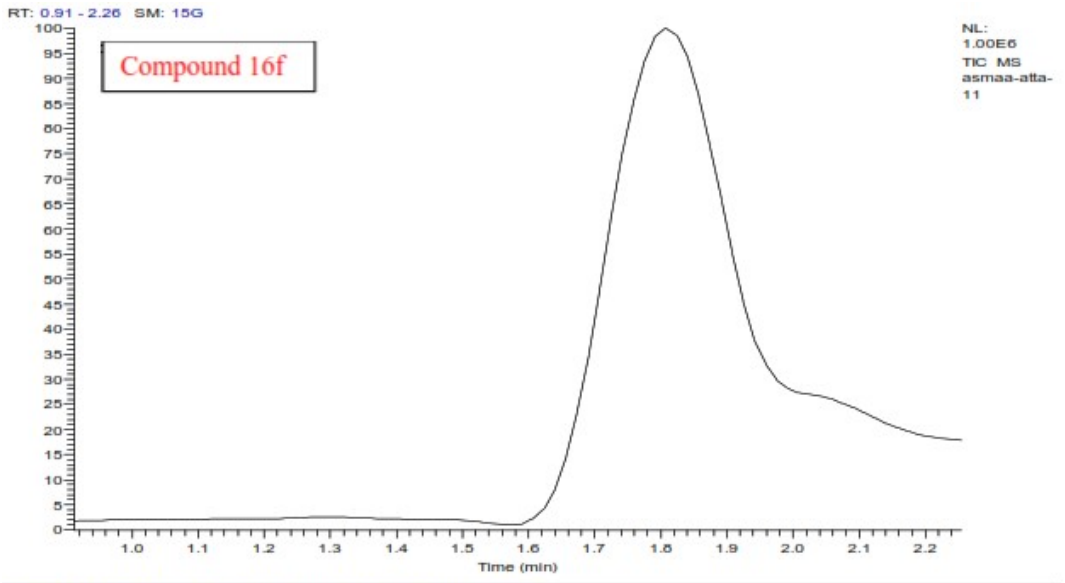

asmaa-atta-5 #136 RT: 2.29 AV: 1 SB: 2 4.45 , 4.45 NL: 2.72E3
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

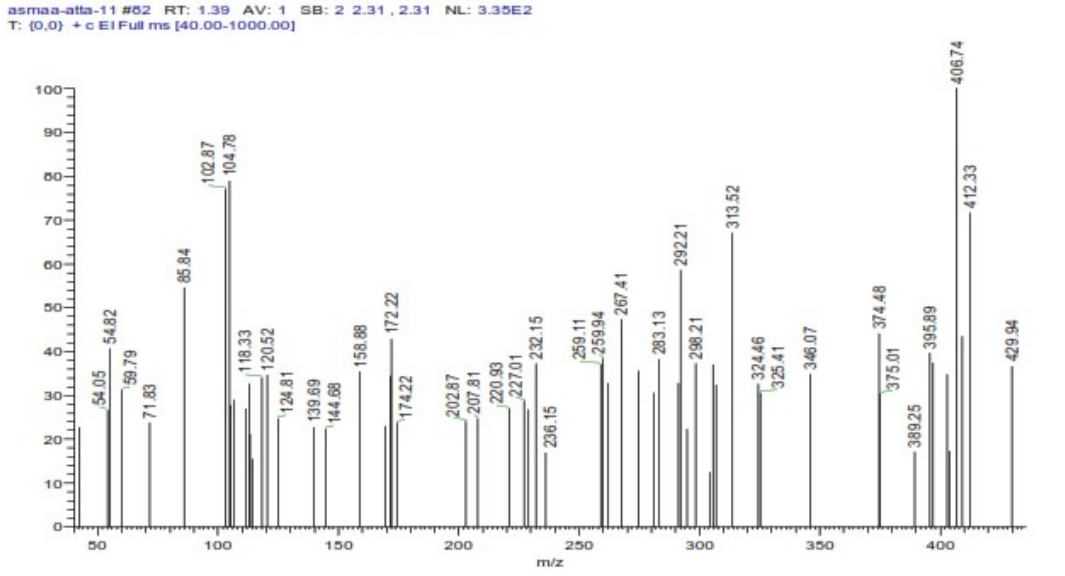

RT: 3.30 - 3.76 SM: 15G
Compound 16d
NL:
2.62E4
TIC MS
asmaa-atta-
δ
Time (min)

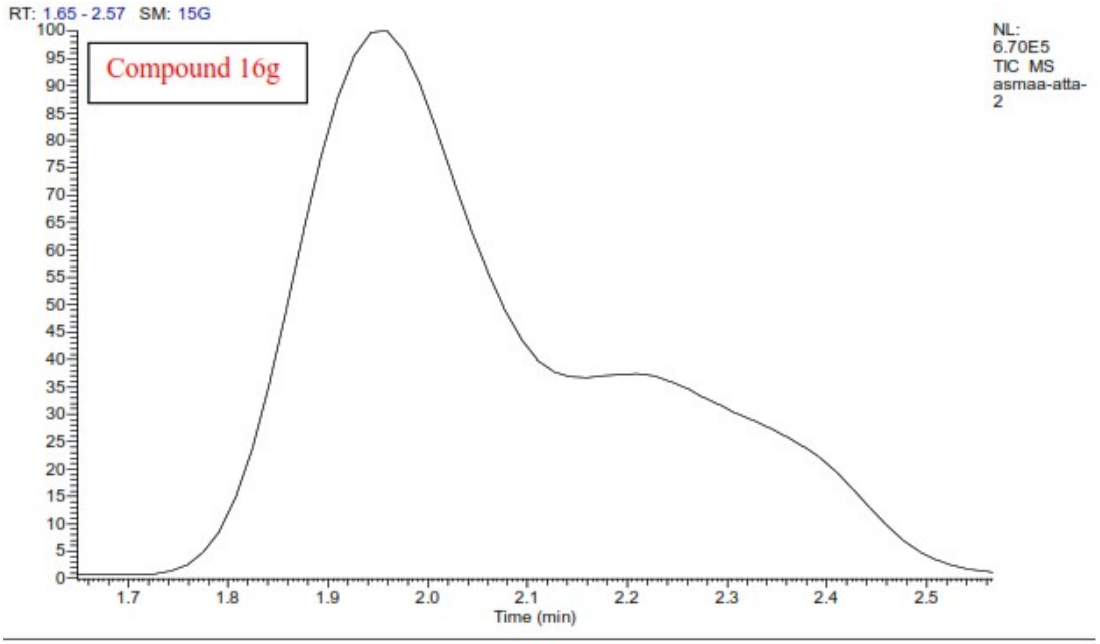

asmaa-atta-δ #265 RT: 4.45 AV: 1 SB: 14 1.66 , 1.51-1.71 NL: 3.20E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

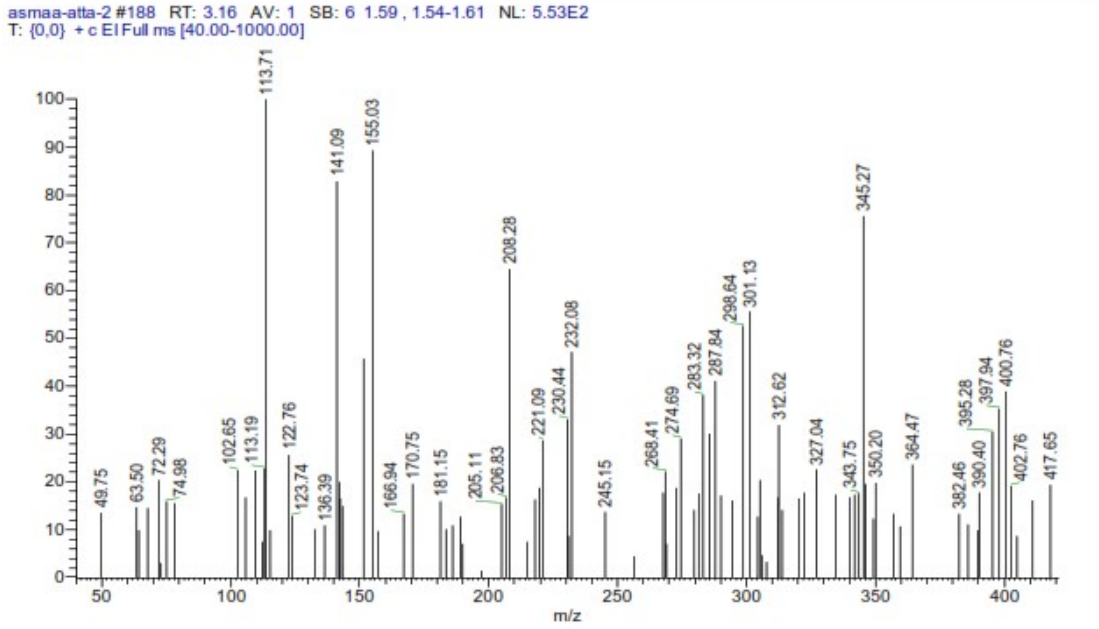

RT: 1.88 - 2.14 SM: 15G
Compound 16e
NL:
1.29E4
TIC MS
asmaa-atta-
3
Time (min)

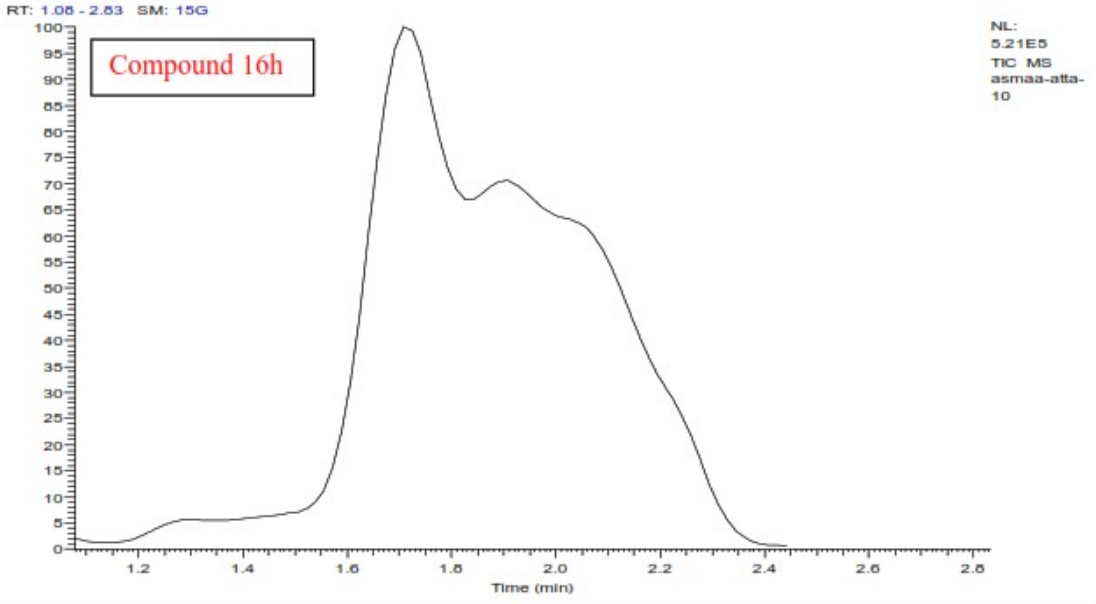

asmaa-atta-3 #79 RT: 1.34 AV: 1 SB: 2 2.38 , 2.38 NL: 2.72E3
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

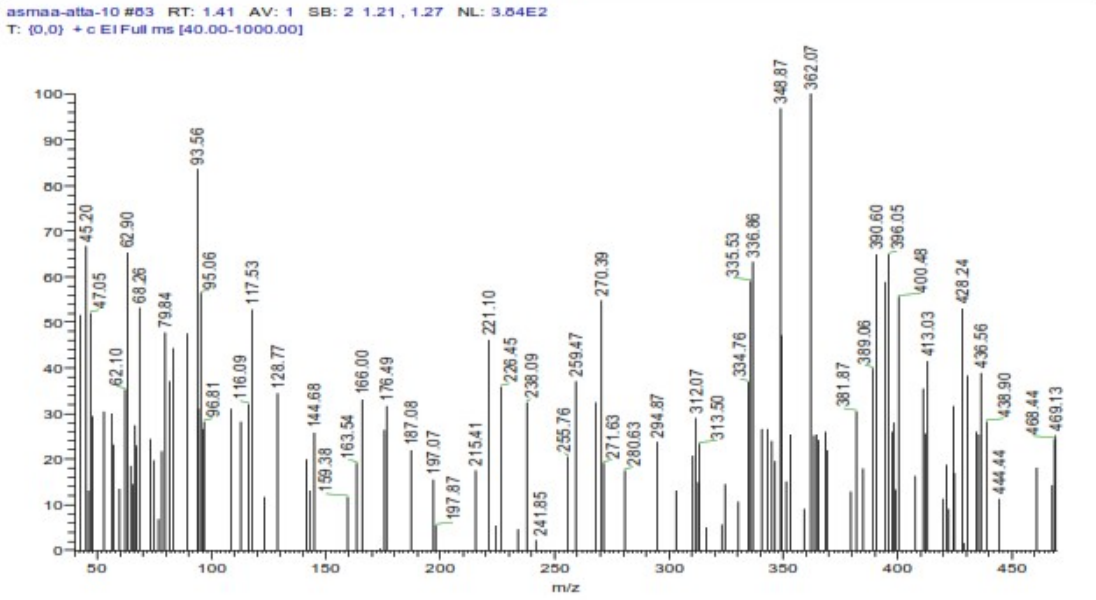

RT: 0.91 - 2.26 SM: 15G
Compound 16f
NL:
1.00E6
TIC MS
asmaa-atta-
11
Time (min)

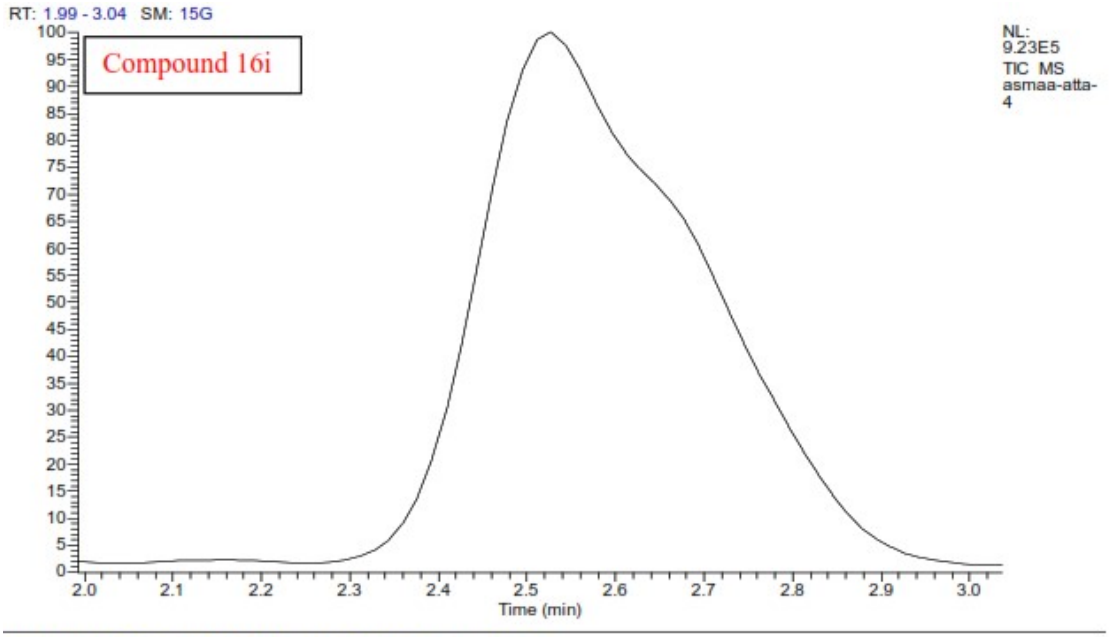

asmaa-atta-11 #62 RT: 1.39 AV: 1 SB: 2 2.31 , 2.31 NL: 3.35E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

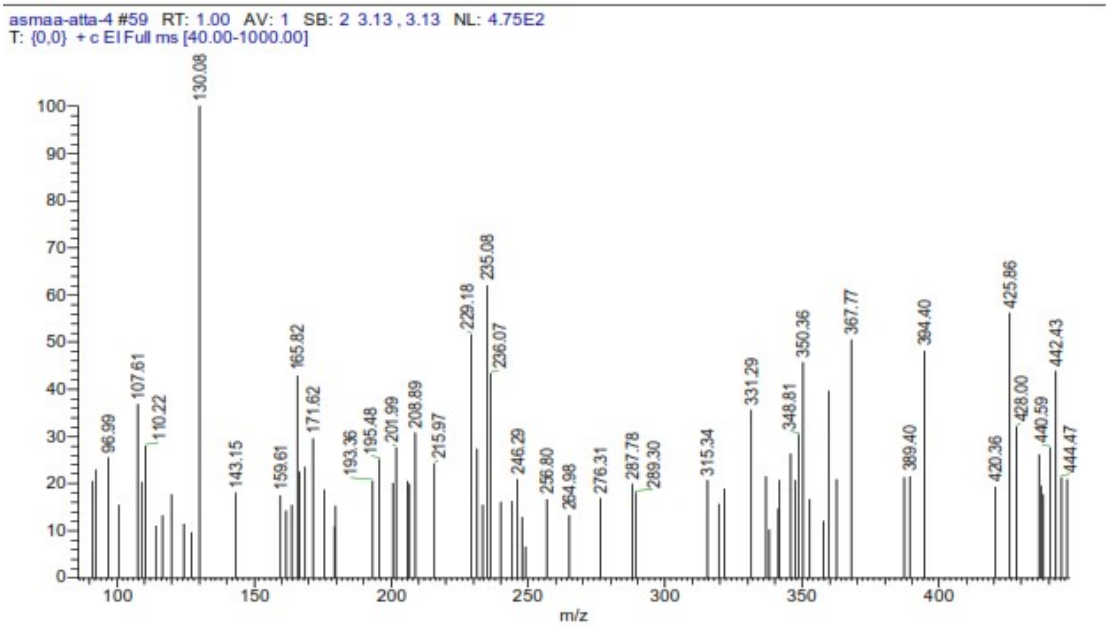

RT: 1.65 - 2.57 SM: 15G
Compound 16g
NL:
6.70E5
TIC MS
asmaa-atta-
2
Time (min)

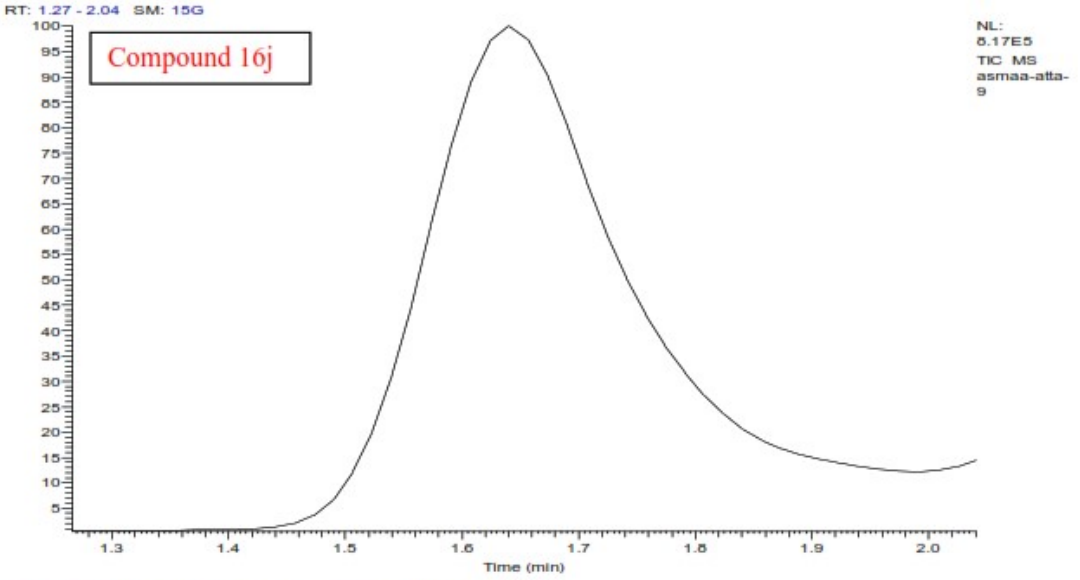

asmaa-atta-2 #188 RT: 3.16 AV: 1 SB: 6 1.59 , 1.54-1.61 NL: 5.53E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

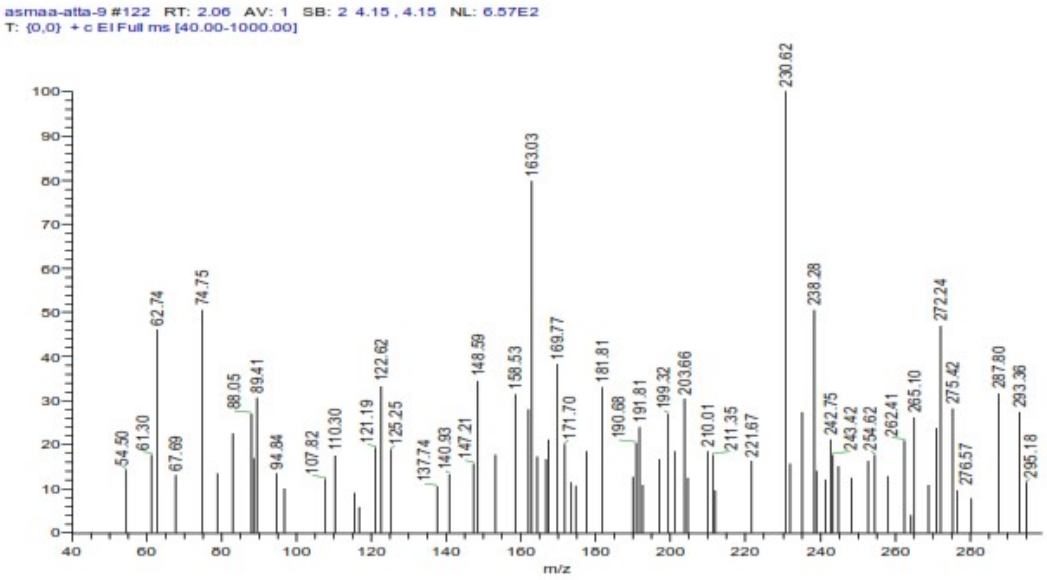

RT: 1.08 - 2.83 SM: 15G
Compound 16h
NL:
5.21E5
TIC MS
asmaa-atta-
10
Time (min)

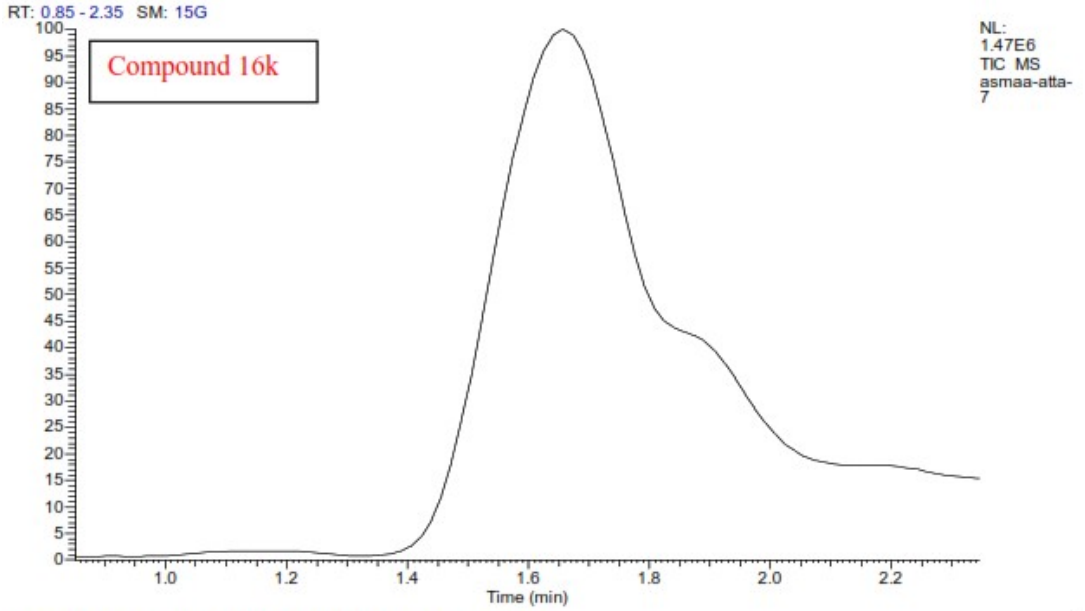

asmaa-atta-10 #83 RT: 1.41 AV: 1 SB: 2 1.21 , 1.27 NL: 3.64E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

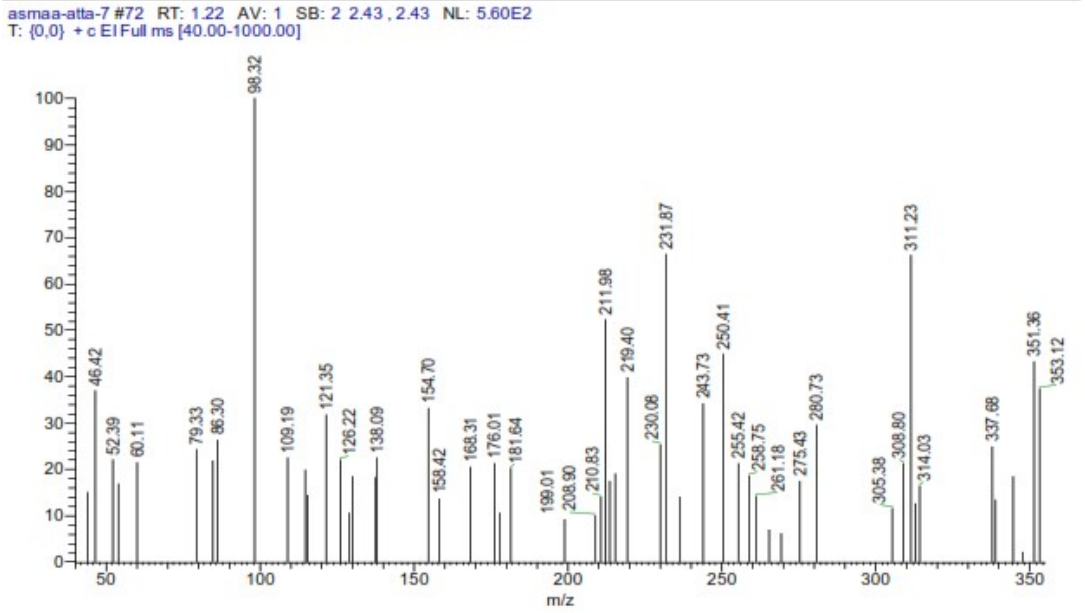

RT: 1.99 - 3.04 SM: 15G
Compound 16i
NL:
9.23E5
TIC MS
asmaa-atta-
4
Time (min)


asmaa-atta-4 #59 RT: 1.00 AV: 1 SB: 2 3.13 , 3.13 NL: 4.75E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z


RT: 1.27 - 2.04 SM: 15G
Compound 16j
NL:
5.17E5
TIC MS
asmaa-atta-9
Time (min)


asmaa-atta-9 #122 RT: 2.06 AV: 1 SB: 2 4.15 , 4.15 NL: 6.57E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z


RT: 0.85 - 2.35 SM: 15G
Compound 16k
NL:
1.47E6
TIC MS
asmaa-atta-
7
Time (min)


asmaa-atta-7 #72 RT: 1.22 AV: 1 SB: 2 2.43 , 2.43 NL: 5.60E2
T: {0,0} + c EI Full ms [40.00-1000.00]
m/z

Name: **Dr/AsmaaAtta**

Analysis Report:

Compound Code	C%	H %	N%
4e	75.29	6.80	13.24
4f	74.65	6.44	14.00
4c	70.79	5.02	13.66
4b	58.69	3.55	12.11
4a	72.86	5.03	15.88
4'h	75.11	6.77	13.15
4'a	73.55	5.39	15.09
4'c	59.77	3.89	11.55
4'f	70.45	5.60	13.69
4'g	75.63	7.02	12.77

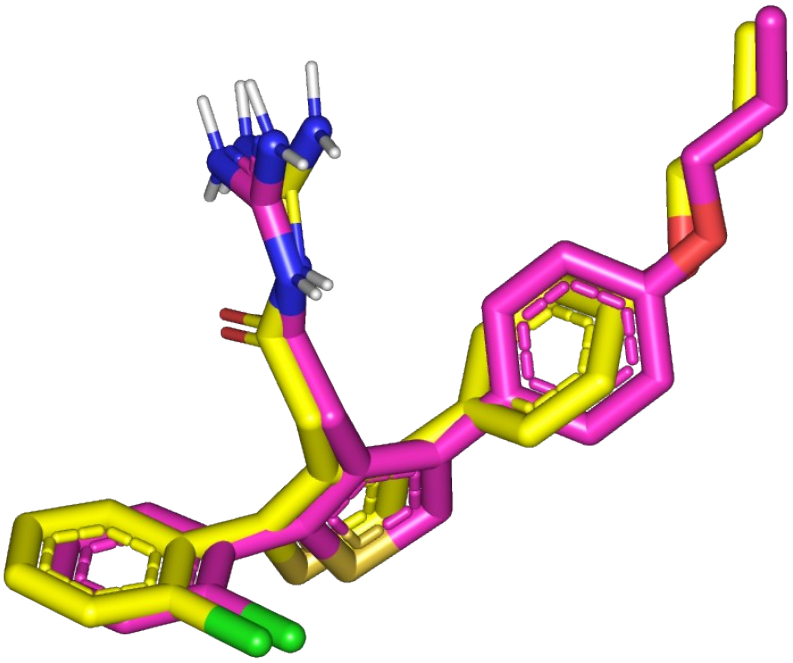
Analysis Report:

Compound Code	C %	H %	N %
4'b	69.11	4.66	14.20
4'e	70.99	5.94	13.11
4'd	71.33	5.35	13.12
4d	70.33	5.56	13.64
4g	66.88	5.28	12.98
9b	56.38	3.65	15.44
9d	66.97	5.66	17.12
9c	66.23	5.19	18.20
9e	71.84	6.65	16.77
9a	64.88	4.44	18.90
9f	71.25	6.28	17.44
11	42.66	3.20	19.89

Name: **Dr/ Asmaa Atta**

Analysis Report:

Compound Code	C %	H %	N %
16b	65.12	6.15	20.21
16g	66.02	5.09	16.89
16e	69.40	5.43	17.81
16i	61.98	4.70	19.14
16c	65.98	6.25	19.42
16a	65.41	5.62	19.87
16k	61.04	5.63	18.98
16d	66.59	6.32	18.70
16j	65.43	5.27	23.71
16h	61.55	4.48	15.16
16f	67.41	5.64	16.59

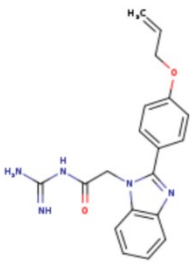


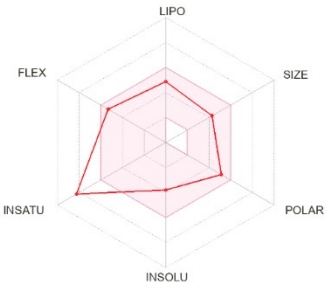
Aligned poses of the BACE1 co-crystallized ligand (magenta) and its redocked conformation (yellow)

SwissADME Profiles

a

Molecule 1





SMILES C=CCOc1ccc(cc1)c1nc2c(n1CC(=O)NC(=N)N)cccc2

Physicochemical Properties	
Formula	C19H19N5O2
Molecular weight	349.39 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	15
Fraction Csp3	0.11
Num. rotatable bonds	8
Num. H-bond acceptors	4
Num. H-bond donors	3
Molar Refractivity	100.98
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.84
Log $P_{o/w}$ (XLOGP3)	3.01
Log $P_{o/w}$ (WLOGP)	2.28
Log $P_{o/w}$ (MLOGP)	1.79
Log $P_{o/w}$ (SILICOS-IT)	2.07
Consensus Log $P_{o/w}$	2.20

Water Solubility	
Log *S* (ESOL)	-3.80
Solubility	5.52e-02 mg/ml ; 1.58e-04 mol/l
Class	Soluble
Log *S* (Ali)	-4.90
Solubility	4.39e-03 mg/ml ; 1.26e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-5.29
Solubility	1.77e-03 mg/ml ; 5.07e-06 mol/l
Class	Moderately soluble

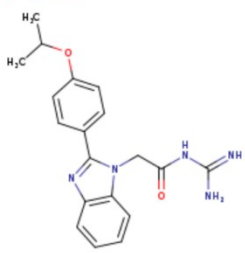
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.29 cm/s

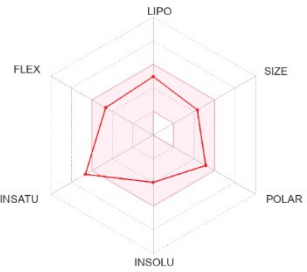
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: imine_1, imine_2, isolated_alkene
Leadlikeness	No; 1 violation: Rotors>7
Synthetic accessibility	2.77

b

Molecule 2





SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccc(cc1)OC(C)C

Physicochemical Properties	
Formula	C19H21N5O2
Molecular weight	351.40 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	15
Fraction Csp3	0.21
Num. rotatable bonds	7
Num. H-bond acceptors	4
Num. H-bond donors	3
Molar Refractivity	101.45
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.59
Log $P_{o/w}$ (XLOGP3)	3.17
Log $P_{o/w}$ (WLOGP)	2.50
Log $P_{o/w}$ (MLOGP)	1.86
Log $P_{o/w}$ (SILICOS-IT)	1.91
Consensus Log $P_{o/w}$	2.21

Water Solubility	
Log *S* (ESOL)	-3.98
Solubility	3.67e-02 mg/ml ; 1.05e-04 mol/l
Class	Soluble
Log *S* (Ali)	-5.07
Solubility	3.01e-03 mg/ml ; 8.57e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-5.26
Solubility	1.91e-03 mg/ml ; 5.43e-06 mol/l
Class	Moderately soluble

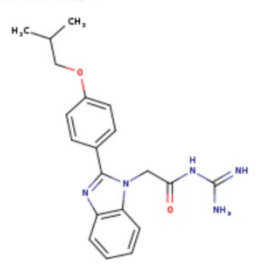
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.19 cm/s

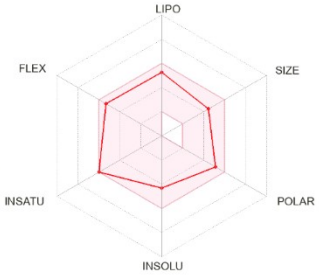
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	2.80

c

Molecule 1





SMILES CC(COc1ccc(cc1)c1nc2c(n1CC(=O)NC(=N)N)cccc2)C

Physicochemical Properties	
Formula	C20H23N5O2
Molecular weight	365.43 g/mol
Num. heavy atoms	27
Num. arom. heavy atoms	15
Fraction Csp3	0.25
Num. rotatable bonds	8
Num. H-bond acceptors	4
Num. H-bond donors	3
Molar Refractivity	106.26
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.84
Log $P_{o/w}$ (XLOGP3)	3.70
Log $P_{o/w}$ (WLOGP)	2.75
Log $P_{o/w}$ (MLOGP)	2.09
Log $P_{o/w}$ (SILICOS-IT)	2.30
Consensus Log $P_{o/w}$	2.54

Water Solubility	
Log *S* (ESOL)	-4.32
Solubility	1.75e-02 mg/ml ; 4.79e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.62
Solubility	8.82e-04 mg/ml ; 2.41e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-5.66
Solubility	7.99e-04 mg/ml ; 2.19e-06 mol/l
Class	Moderately soluble

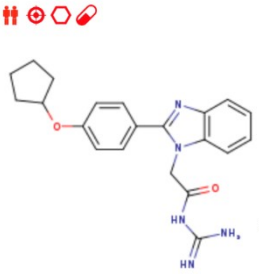
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.90 cm/s

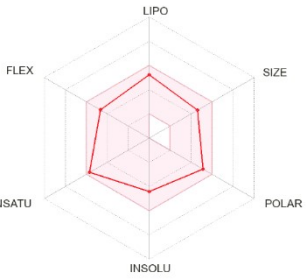
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	2.92

d

Molecule 1





SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccc(cc1)OC1CCCC1

Physicochemical Properties	
Formula	C21H23N5O2
Molecular weight	377.44 g/mol
Num. heavy atoms	28
Num. arom. heavy atoms	15
Fraction Csp3	0.29
Num. rotatable bonds	7
Num. H-bond acceptors	4
Num. H-bond donors	3
Molar Refractivity	108.95
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.01
Log $P_{o/w}$ (XLOGP3)	3.64
Log $P_{o/w}$ (WLOGP)	3.03
Log $P_{o/w}$ (MLOGP)	2.31
Log $P_{o/w}$ (SILICOS-IT)	2.23
Consensus Log $P_{o/w}$	2.65

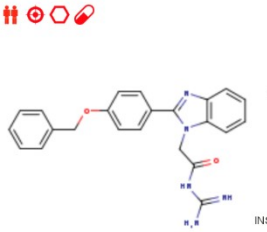
Water Solubility	
Log *S* (ESOL)	-4.41
Solubility	1.48e-02 mg/ml ; 3.91e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.55
Solubility	1.05e-03 mg/ml ; 2.79e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-5.58
Solubility	9.90e-04 mg/ml ; 2.62e-06 mol/l
Class	Moderately soluble

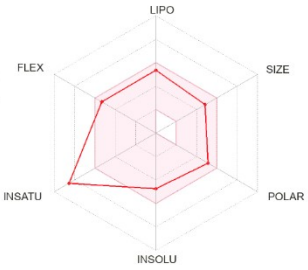
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.02 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 2 violations: MW>350, XLOGP3>3.5
Synthetic accessibility	3.01

e





SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccc(cc1)OCc1ccccc1

Physicochemical Properties	
Formula	C23H21N5O2
Molecular weight	399.45 g/mol
Num. heavy atoms	30
Num. arom. heavy atoms	21
Fraction Csp3	0.09
Num. rotatable bonds	8
Num. H-bond acceptors	4
Num. H-bond donors	3
Molar Refractivity	116.32
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.98
Log $P_{o/w}$ (XLOGP3)	3.86
Log $P_{o/w}$ (WLOGP)	3.14
Log $P_{o/w}$ (MLOGP)	2.53
Log $P_{o/w}$ (SILICOS-IT)	2.76
Consensus Log $P_{o/w}$	2.86

Water Solubility	
Log *S* (ESOL)	-4.74
Solubility	7.30e-03 mg/ml ; 1.83e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.78
Solubility	6.58e-04 mg/ml ; 1.65e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-7.33
Solubility	1.88e-05 mg/ml ; 4.71e-08 mol/l
Class	Poorly soluble

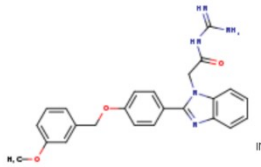
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.00 cm/s

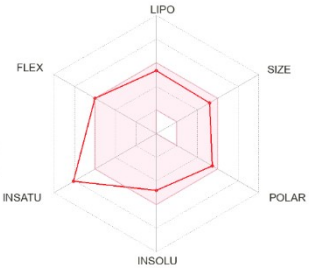
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	3.01

f

Molecule 1





SMILES COc1cccc(c1)COc1ccc(cc1)c1nc2c(n1CC(=O)NC(=N)N)cccc2

Physicochemical Properties	
Formula	C24H23N5O3
Molecular weight	429.47 g/mol
Num. heavy atoms	32
Num. arom. heavy atoms	21
Fraction Csp3	0.12
Num. rotatable bonds	9
Num. H-bond acceptors	5
Num. H-bond donors	3
Molar Refractivity	122.82
TPSA	115.25 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.78
Log $P_{o/w}$ (XLOGP3)	3.83
Log $P_{o/w}$ (WLOGP)	3.15
Log $P_{o/w}$ (MLOGP)	2.22
Log $P_{o/w}$ (SILICOS-IT)	2.83
Consensus Log $P_{o/w}$	2.96

Water Solubility	
Log *S* (ESOL)	-4.81
Solubility	6.69e-03 mg/ml ; 1.56e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.95
Solubility	4.87e-04 mg/ml ; 1.13e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-7.43
Solubility	1.61e-05 mg/ml ; 3.74e-08 mol/l
Class	Poorly soluble

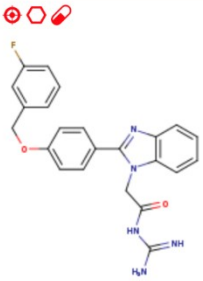
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	Yes
Log K_p (skin permeation)	-6.20 cm/s

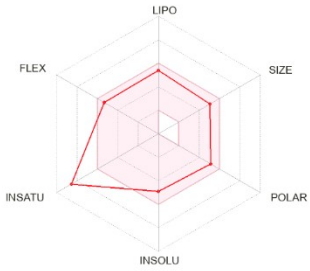
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	3.24

g

Molecule 1





SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccc(cc1)OCc1cccc(c1)F

Physicochemical Properties	
Formula	C23H20FN5O2
Molecular weight	417.44 g/mol
Num. heavy atoms	31
Num. arom. heavy atoms	21
Fraction Csp3	0.09
Num. rotatable bonds	8
Num. H-bond acceptors	5
Num. H-bond donors	3
Molar Refractivity	116.28
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.22
Log $P_{o/w}$ (XLOGP3)	3.96
Log $P_{o/w}$ (WLOGP)	3.70
Log $P_{o/w}$ (MLOGP)	2.91
Log $P_{o/w}$ (SILICOS-IT)	3.19
Consensus Log $P_{o/w}$	3.20

Water Solubility	
Log *S* (ESOL)	-4.90
Solubility	5.30e-03 mg/ml ; 1.27e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-5.89
Solubility	5.42e-04 mg/ml ; 1.30e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-7.59
Solubility	1.07e-05 mg/ml ; 2.57e-08 mol/l
Class	Poorly soluble

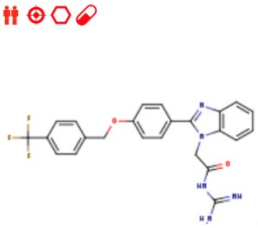
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.03 cm/s

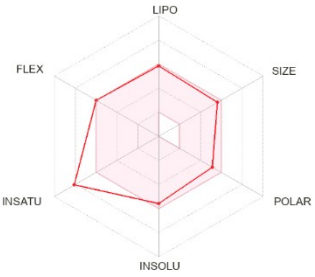
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	3.08

h

Molecule 1





SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccc(cc1)OCc1ccc(cc1)C(F)(F)F

Physicochemical Properties	
Formula	C24H20F3N5O2
Molecular weight	467.44 g/mol
Num. heavy atoms	34
Num. arom. heavy atoms	21
Fraction Csp3	0.12
Num. rotatable bonds	9
Num. H-bond acceptors	7
Num. H-bond donors	3
Molar Refractivity	121.33
TPSA	106.02 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	2.40
Log $P_{o/w}$ (XLOGP3)	4.75
Log $P_{o/w}$ (WLOGP)	5.31
Log $P_{o/w}$ (MLOGP)	3.05
Log $P_{o/w}$ (SILICOS-IT)	3.86
Consensus Log $P_{o/w}$	3.87

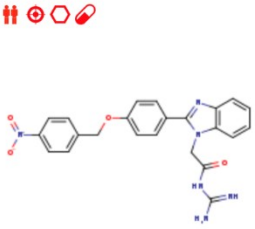
Water Solubility	
Log *S* (ESOL)	-5.59
Solubility	1.19e-03 mg/ml ; 2.55e-06 mol/l
Class	Moderately soluble
Log *S* (Ali)	-6.71
Solubility	9.18e-05 mg/ml ; 1.96e-07 mol/l
Class	Poorly soluble
Log *S* (SILICOS-IT)	-8.15
Solubility	3.32e-06 mg/ml ; 7.11e-09 mol/l
Class	Poorly soluble

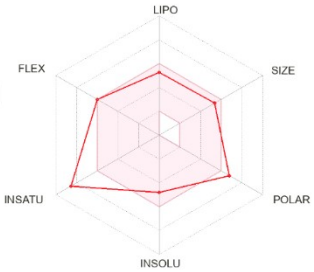
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-5.78 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	3.19

i





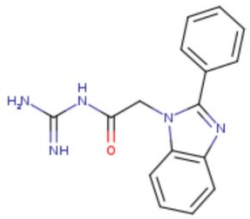
SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccc(cc1)OCc1ccc(cc1)[N+](=O)[O-]

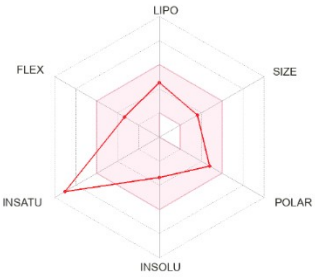
Physicochemical Properties	
Formula	C23H20N6O4
Molecular weight	444.44 g/mol
Num. heavy atoms	33
Num. arom. heavy atoms	21
Fraction Csp3	0.09
Num. rotatable bonds	9
Num. H-bond acceptors	6
Num. H-bond donors	3
Molar Refractivity	125.15
TPSA	151.84 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.73
Log $P_{o/w}$ (XLOGP3)	3.69
Log $P_{o/w}$ (WLOGP)	3.05
Log $P_{o/w}$ (MLOGP)	1.68
Log $P_{o/w}$ (SILICOS-IT)	0.61
Consensus Log $P_{o/w}$	2.15

Water Solubility	
Log *S* (ESOL)	-4.80
Solubility	7.09e-03 mg/ml ; 1.60e-05 mol/l
Class	Moderately soluble
Log *S* (Ali)	-6.57
Solubility	1.20e-04 mg/ml ; 2.70e-07 mol/l
Class	Poorly soluble
Log *S* (SILICOS-IT)	-6.67
Solubility	9.61e-05 mg/ml ; 2.16e-07 mol/l
Class	Poorly soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	Yes
Log K_p (skin permeation)	-6.39 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	No; 1 violation: TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 1 violation: TPSA>150
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	0 alert
Brenk	4 alerts: imine_1, imine_2, nitro_group, oxygen-nitrogen_single_bond
Leadlikeness	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
Synthetic accessibility	3.22

j

Molecule 1





SMILES NC(=N)NC(=O)Cn1c(nc2c1cccc2)c1ccccc1

Physicochemical Properties	
Formula	C16H15N5O
Molecular weight	293.32 g/mol
Num. heavy atoms	22
Num. arom. heavy atoms	15
Fraction Csp3	0.06
Num. rotatable bonds	5
Num. H-bond acceptors	3
Num. H-bond donors	3
Molar Refractivity	85.34
TPSA	96.79 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.93
Log $P_{o/w}$ (XLOGP3)	2.40
Log $P_{o/w}$ (WLOGP)	1.71
Log $P_{o/w}$ (MLOGP)	1.68
Log $P_{o/w}$ (SILICOS-IT)	1.25
Consensus Log $P_{o/w}$	1.59

Water Solubility	
Log *S* (ESOL)	-3.35
Solubility	1.32e-01 mg/ml ; 4.52e-04 mol/l
Class	Soluble
Log *S* (Ali)	-4.07
Solubility	2.47e-02 mg/ml ; 8.43e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-4.73
Solubility	5.41e-03 mg/ml ; 1.85e-05 mol/l
Class	Moderately soluble

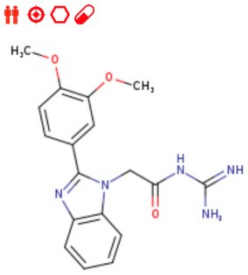
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.39 cm/s

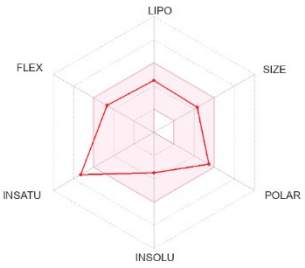
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	Yes
Synthetic accessibility	2.50

k

Molecule 1





SMILES COc1cc(ccc1OC)c1nc2c(n1CC(=O)NC(=N)N)cccc2

Physicochemical Properties	
Formula	C18H19N5O3
Molecular weight	353.38 g/mol
Num. heavy atoms	26
Num. arom. heavy atoms	15
Fraction Csp3	0.17
Num. rotatable bonds	7
Num. H-bond acceptors	5
Num. H-bond donors	3
Molar Refractivity	98.33
TPSA	115.25 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.61
Log $P_{o/w}$ (XLOGP3)	2.34
Log $P_{o/w}$ (WLOGP)	1.73
Log $P_{o/w}$ (MLOGP)	1.11
Log $P_{o/w}$ (SILICOS-IT)	1.36
Consensus Log $P_{o/w}$	1.63

Water Solubility	
Log *S* (ESOL)	-3.47
Solubility	1.20e-01 mg/ml ; 3.39e-04 mol/l
Class	Soluble
Log *S* (Ali)	-4.40
Solubility	1.41e-02 mg/ml ; 3.98e-05 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-4.96
Solubility	3.91e-03 mg/ml ; 1.11e-05 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.79 cm/s

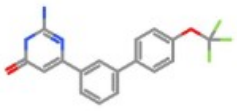
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: imine_1, imine_2
Leadlikeness	No; 1 violation: MW>350
Synthetic accessibility	2.80

Pro-Tox 3.0 Toxicity Analysis Webserver

ProTox-3.0 - Prediction of TOXicity of chemicals

Oral toxicity prediction results for input compound



4b

Predicted LD50: 1000mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

Average similarity: 45.47%

Prediction accuracy: 54.26%

Name	O=C1NC(N)=NC(C2=CC(F)(F)C=C3)=CC=C2)=C1
Molweight	347.29
Number of hydrogen bond acceptors	4
Number of hydrogen bond donors	2
Number of atoms	25
Number of bonds	27
Number of rotable bonds	4
Molecular refractivity	86.82
Topological Polar Surface Area	81
octanol/water partition coefficient(logP)	4.17

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.56
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.89
Toxicity end points	Immunotoxicity	immuno	Inactive	0.98
Toxicity end points	Mutagenicity	mutagen	Inactive	0.65
Toxicity end points	Cytotoxicity	cyto	Inactive	0.71
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.76
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.54
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.99
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.93
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.85
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.97
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.96
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.96
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.96
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.63
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.79
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.86
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.88
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.86
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.52
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.97
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.86
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.95
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.99
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	1.0
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.92
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.98
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.62
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.98
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.90
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.74
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.82
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.71

ProTox-3.0 - Prediction of TOXicity of chemicals

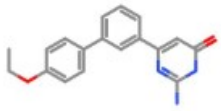
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.68
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.81
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	1.0

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



4d

Predicted LD50: 1000mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

Average similarity: 48.19%

Prediction accuracy: 54.26%

Name	O=C1NC(N)=NC(C2=CC
Molweight	307.35
Number of hydrogen bond acceptors	4
Number of hydrogen bond donors	2
Number of atoms	23
Number of bonds	25
Number of rotable bonds	4
Molecular refractivity	91.43
Topological Polar Surface Area	81
octanol/water partition coefficient(logP)	3.67

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.86
Toxicity end points	Immunotoxicity	immuno	Inactive	0.98
Toxicity end points	Mutagenicity	mutagen	Inactive	0.56
Toxicity end points	Cytotoxicity	cyto	Inactive	0.77
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.74
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.56
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.90
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.97
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.91
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.82
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.96
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.96
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.96
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.67
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.87
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.86
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.88
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.83
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.57
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.96
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.82
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.96
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.99
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	1.0
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.92
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.98
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.90
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.96
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.79
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.77
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.81
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.71
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.59
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.69

ProTox-3.0 - Prediction of TOXicity of chemicals

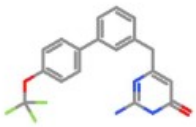
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	0.99

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



4'c

Predicted LD50: 350mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

Average similarity: 43.05%

Prediction accuracy: 54.26%

Name	O=C1NC(N)=NC(CC2=C(F)F)C=C3)=CC=C2)=C1
Molweight	361.32
Number of hydrogen bond acceptors	4
Number of hydrogen bond donors	2
Number of atoms	26
Number of bonds	28
Number of rotable bonds	5
Molecular refractivity	90.83
Topological Polar Surface Area	81
octanol/water partition coefficient(logP)	4.09

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.53
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.84
Toxicity end points	Immunotoxicity	immuno	Inactive	0.97
Toxicity end points	Mutagenicity	mutagen	Inactive	0.66
Toxicity end points	Cytotoxicity	cyto	Inactive	0.70
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.75
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.61
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.92
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.82
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.95
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.95
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.95
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.71
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.83
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.92
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.88
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.84
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.62
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.95
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.79
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.94
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.99
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	1.0
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.85
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.98
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.67
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.97
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.88
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.79
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.76
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.66

ProTox-3.0 - Prediction of TOXicity of chemicals

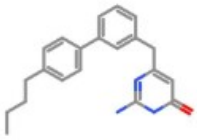
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.63
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.72
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	1.0

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



4'g

Predicted LD50: 300mg/kg

Predicted Toxicity Class: 3

1 2 3 4 5 6

Average similarity: 46.06%

Prediction accuracy: 54.26%

Name	O=C1NC(N)=NC(CC2=C
Molweight	333.43
Number of hydrogen bond acceptors	3
Number of hydrogen bond donors	2
Number of atoms	25
Number of bonds	27
Number of rotable bonds	6
Molecular refractivity	103.54
Topological Polar Surface Area	71.77
octanol/water partition coefficient(logP)	4.53

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.55
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.65
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.89
Toxicity end points	Carcinogenicity	carcino	Inactive	0.52
Toxicity end points	Immunotoxicity	immuno	Inactive	0.95
Toxicity end points	Mutagenicity	mutagen	Inactive	0.68
Toxicity end points	Cytotoxicity	cyto	Inactive	0.77
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.72
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.64
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.92
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.91
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.83
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.97
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.95
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.95
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.83
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.91
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.93
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.91
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.85
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.70
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.92
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.69
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.91
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.99
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	1.0
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.80
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.98
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.87
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.91
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.86
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.82
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.82

ProTox-3.0 - Prediction of TOXicity of chemicals

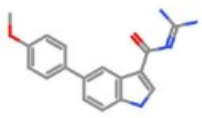
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.71
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.63
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.78
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	0.99

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



9c

Predicted LD50: 200mg/kg

Predicted Toxicity Class: 3

1 2 3 4 5 6

Average similarity: 49.45%

Prediction accuracy: 54.26%

Name	O=C(C1=CNC2=C1C=C(
Molweight	308.34
Number of hydrogen bond acceptors	5
Number of hydrogen bond donors	3
Number of atoms	23
Number of bonds	25
Number of rotable bonds	4
Molecular refractivity	89.52
Topological Polar Surface Area	106.49
octanol/water partition coefficient(logP)	3.66

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.55
Organ toxicity	Respiratory toxicity	respi	Inactive	0.64
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.80
Toxicity end points	Immunotoxicity	immuno	Inactive	0.96
Toxicity end points	Mutagenicity	mutagen	Inactive	0.53
Toxicity end points	Cytotoxicity	cyto	Inactive	0.65
Toxicity end points	Clinical toxicity	clinical	Inactive	0.50
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.59
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.50
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.87
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.95
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.91
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.84
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.94
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.94
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.94
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.56
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.74
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.78
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.93
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.89
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.52
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.96
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.82
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.97
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.99
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	1.0
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.81
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.88
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.86
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.96
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.89
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.50
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.78

ProTox-3.0 - Prediction of TOXicity of chemicals

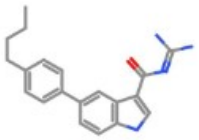
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.63
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.68
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.72
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	0.99

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



9e

Predicted LD50: 200mg/kg

Predicted Toxicity Class: 3

1 2 3 4 5 6

Average similarity: 44.47%

Prediction accuracy: 54.26%

Name	O=C(C1=CNC2=C1C=C(
Molweight	334.42
Number of hydrogen bond acceptors	4
Number of hydrogen bond donors	3
Number of atoms	25
Number of bonds	27
Number of rotable bonds	6
Molecular refractivity	102.42
Topological Polar Surface Area	97.26
octanol/water partition coefficient(logP)	4.99

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.52
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.61
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.81
Toxicity end points	Carcinogenicity	carcino	Inactive	0.57
Toxicity end points	Immunotoxicity	immuno	Inactive	0.95
Toxicity end points	Mutagenicity	mutagen	Inactive	0.62
Toxicity end points	Cytotoxicity	cyto	Inactive	0.72
Toxicity end points	Clinical toxicity	clinical	Inactive	0.56
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.57
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.61
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.84
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.93
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.85
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.81
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.92
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.90
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.90
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.66
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.80
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.83
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.94
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.91
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.67
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.94
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.61
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.97
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.99
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	0.99
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.78
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.97
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.84
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.94
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.87
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.58

ProTox-3.0 - Prediction of TOXicity of chemicals

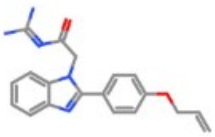
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.72
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.62
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.59
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.72
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	0.99

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



16a

Predicted LD50: 800mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

Average similarity: 52.33%

Prediction accuracy: 67.38%

Name	O=C(/N=C(N)/N)CN1C(C
Molweight	349.39
Number of hydrogen bond acceptors	6
Number of hydrogen bond donors	2
Number of atoms	26
Number of bonds	28
Number of rotable bonds	7
Molecular refractivity	100.98
Topological Polar Surface Area	108.52
octanol/water partition coefficient(logP)	3.47

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.70
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.52
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.77
Toxicity end points	Carcinogenicity	carcino	Inactive	0.51
Toxicity end points	Immunotoxicity	immuno	Inactive	0.99
Toxicity end points	Mutagenicity	mutagen	Inactive	0.61
Toxicity end points	Cytotoxicity	cyto	Inactive	0.61
Toxicity end points	Ecotoxicity	eco	Inactive	0.55
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.54
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.71
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.96
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.91
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.85
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.92
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.89
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.90
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.90
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.80
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.86
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.89
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.89
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.81
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.80
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.90
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.62
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.95
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.95
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	0.99
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.81
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.99
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.75
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.97
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.75
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.73

ProTox-3.0 - Prediction of TOXicity of chemicals

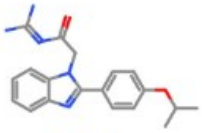
Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.71
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.61
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.70
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.59
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	0.99

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

Oral toxicity prediction results for input compound



16b

Predicted LD50: 700mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

Average similarity: 54.73%

Prediction accuracy: 67.38%

Name	O=C(/N=C(N)/N)CN1C(C
Molweight	351.4
Number of hydrogen bond acceptors	6
Number of hydrogen bond donors	2
Number of atoms	26
Number of bonds	28
Number of rotable bonds	6
Molecular refractivity	101.45
Topological Polar Surface Area	108.52
octanol/water partition coefficient(logP)	3.69

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.70
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.60
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.78
Toxicity end points	Carcinogenicity	carcino	Inactive	0.55
Toxicity end points	Immunotoxicity	immuno	Inactive	0.98
Toxicity end points	Mutagenicity	mutagen	Inactive	0.61
Toxicity end points	Cytotoxicity	cyto	Inactive	0.62
Toxicity end points	Ecotoxicity	eco	Inactive	0.53
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.53
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.66
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.97
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.99
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.90
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.90
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.90
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.96
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.96
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.79
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.87
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.89
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.85
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.78
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.82
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.91
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.61
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.97
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.98
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	0.99
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.83
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.99
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.75
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.98
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.89
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.69

ProTox-3.0 - Prediction of TOXicity of chemicals

Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.77
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.59
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.74
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.59
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	1.0

Toxicity targets

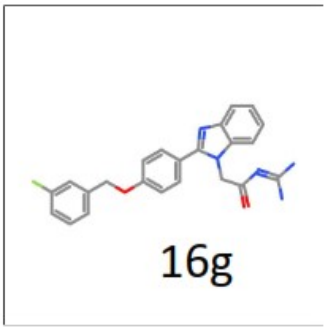
Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

ProTox-3.0 - Prediction of TOXicity of chemicals

Toxicity Model Computation
If you want to close this window, you can get your results later with this link :
Access results (please copy link location)
Model computation is complete. You can view the toxicity radar chart here (opens a new tab) **Toxicity Radar Chart** and the network chart here **Network Chart**

Oral toxicity prediction results for input compound



Predicted LD50: 700mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

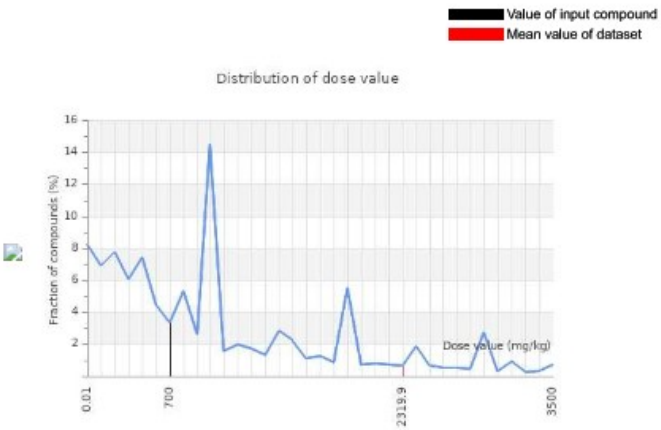
Average similarity: 49.6%

Prediction accuracy: 54.26%

Print Toxicity Report

Name	O=C(/N=C(N)/N)CN1C(C
Molweight	417.44
Number of hydrogen bond acceptors	6
Number of hydrogen bond donors	2
Number of atoms	31
Number of bonds	34
Number of rotable bonds	7
Molecular refractivity	116.28
Topological Polar Surface Area	108.52
octanol/water partition coefficient(logP)	4.62

Comparison of input compound with dataset compounds



+ Similar compounds

Toxicity Model Report

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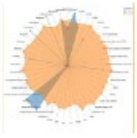
Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.73
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.51
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.79
Toxicity end points	Carcinogenicity	carcino	Inactive	0.57
Toxicity end points	Immunotoxicity	immuno	Inactive	0.96

ProTox-3.0 - Prediction of TOXicity of chemicals

Classification	Target	Shorthand	Prediction	Probability
Toxicity end points	Mutagenicity	mutagen	Inactive	0.65
Toxicity end points	Cytotoxicity	cyto	Inactive	0.57
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.54
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.68
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.90
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.87
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.95
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.92
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.92
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.92
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.76
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.85
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.91
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.88
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.80
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.81
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.90
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.66
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.95
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.95
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	0.99
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.82
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.99
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.70
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.98
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.81
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.74
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.75
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.55
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.68
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.64
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	1.0



The toxicity radar chart is intended to quickly illustrate the confidence of positive toxicity results compared to the average of its class.
Click the thumbnail to access the plot once it has finished loading.

The network chart is intended to quickly illustrate the connection between the selected compound and predicted activities.
Click the thumbnail to access the plot once it has finished loading.

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

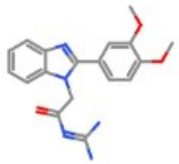
AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

ProTox-3.0 - Prediction of TOXicity of chemicals

[redacted]

Last updated: May 2024

Oral toxicity prediction results for input compound



16k

Predicted LD50: 1200mg/kg

Predicted Toxicity Class: 4

1 2 3 4 5 6

Average similarity: 52.41%

Prediction accuracy: 67.38%

Name	O=C(/N=C(N)/N)CN1C(C
Molweight	353.38
Number of hydrogen bond acceptors	7
Number of hydrogen bond donors	2
Number of atoms	26
Number of bonds	28
Number of rotable bonds	6
Molecular refractivity	98.33
Topological Polar Surface Area	117.75
octanol/water partition coefficient(logP)	2.92

Toxicity Model Report

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Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.69
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.57
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.77
Toxicity end points	Carcinogenicity	carcino	Inactive	0.52
Toxicity end points	Immunotoxicity	immuno	Inactive	0.92
Toxicity end points	Mutagenicity	mutagen	Inactive	0.58
Toxicity end points	Cytotoxicity	cyto	Inactive	0.54
Toxicity end points	Ecotoxicity	eco	Inactive	0.57
Toxicity end points	Nutritional toxicity	nutri	Inactive	0.55
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive	0.67
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive	0.99
Tox21-Nuclear receptor signalling pathways	Aromatase	nr_aromatase	Inactive	0.89
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	nr_er	Inactive	0.89
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	nr_er_lbd	Inactive	0.98
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	nr_ppar_gamma	Inactive	0.91
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	sr_are	Inactive	0.96
Tox21-Stress response pathways	Heat shock factor response element (HSE)	sr_hse	Inactive	0.96
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	sr_mmp	Inactive	0.82
Tox21-Stress response pathways	Phosphoprotein (Tumor Supressor) p53	sr_p53	Inactive	0.84
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	sr_atad5	Inactive	0.90
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	mie_thr_alpha	Inactive	0.87
Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	mie_thr_beta	Inactive	0.79
Molecular Initiating Events	Transtyretrin (TTR)	mie_ttr	Inactive	0.81
Molecular Initiating Events	Ryanodine receptor (RYR)	mie_ryr	Inactive	0.89
Molecular Initiating Events	GABA receptor (GABAR)	mie_gabar	Inactive	0.61
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	mie_nmdar	Inactive	0.97
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	mie_ampar	Inactive	0.97
Molecular Initiating Events	Kainate receptor (KAR)	mie_kar	Inactive	0.99
Molecular Initiating Events	Achetylcholinesterase (AChE)	mie_ache	Inactive	0.76
Molecular Initiating Events	Constitutive androstane receptor (CAR)	mie_car	Inactive	0.99
Molecular Initiating Events	Pregnane X receptor (PXR)	mie_pxr	Inactive	0.77
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	mie_nadhox	Inactive	0.97
Molecular Initiating Events	Na+/I- symporter (NIS)	mie_nis	Inactive	0.87
Metabolism	Cytochrome CYP1A2	CYP1A2	Inactive	0.74

ProTox-3.0 - Prediction of TOXicity of chemicals

Classification	Target	Shorthand	Prediction	Probability
Metabolism	Cytochrome CYP2C19	CYP2C19	Inactive	0.80
Metabolism	Cytochrome CYP2C9	CYP2C9	Inactive	0.60
Metabolism	Cytochrome CYP2D6	CYP2D6	Inactive	0.77
Metabolism	Cytochrome CYP3A4	CYP3A4	Inactive	0.55
Metabolism	Cytochrome CYP2E1	CYP2E1	Inactive	0.99

Toxicity targets

Possible binding to toxicity targets is shown below. For more information on the targets, please click on the individual abbreviations.

AA2AR	ADRB2	ANDR	AOFA	CRFR1	DRD3	ESR1	ESR2	GCR	HRH1	NR1I2	OPRK	OPRM	PDE4D	PGH1	PRGR

*** Toxicity-related biotargets tested include;** Adenosine receptor A2a (AA2AR), Beta-2 adrenergic receptor (ADRB2), Androgen receptor (ANDR), Amine oxidase flavin A (AOFA), Corticotropin-releasing factor receptor 1 (CRFR1), D3 dopaminergic receptor (DRD3), Estrogen receptor alpha (ESR1), Estrogen receptor beta (ESR2), Glucocorticoid receptor (GCR), Histamine H1 receptor (HRH1), Nuclear receptor subfamily 1 group I member 2 (NR1I2), Kappa-type opioid receptor (OPRK), Mu-type opioid receptor (OPRM), 3',5'-cyclic-AMP phosphodiesterase 4D (PDE4D), Prostaglandin G/H synthase 1 (PGH1), and Progesterone receptor (PRGR).