

Supporting Information for

**Synthesis, Structure-Activity Relationship and Antiviral Activity of
Indole-Containing Inhibitors of Flavivirus NS2B-NS3 protease**

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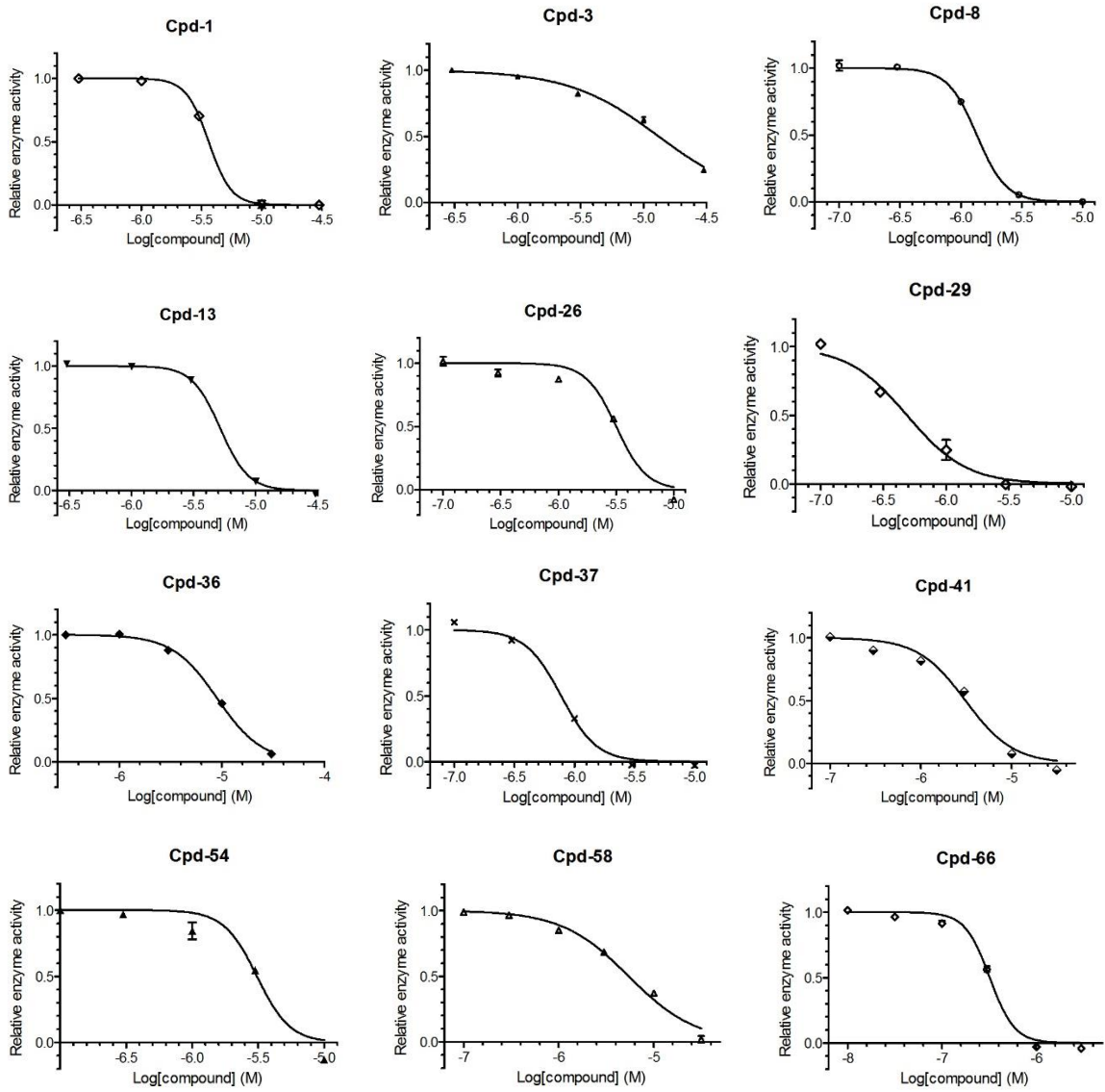
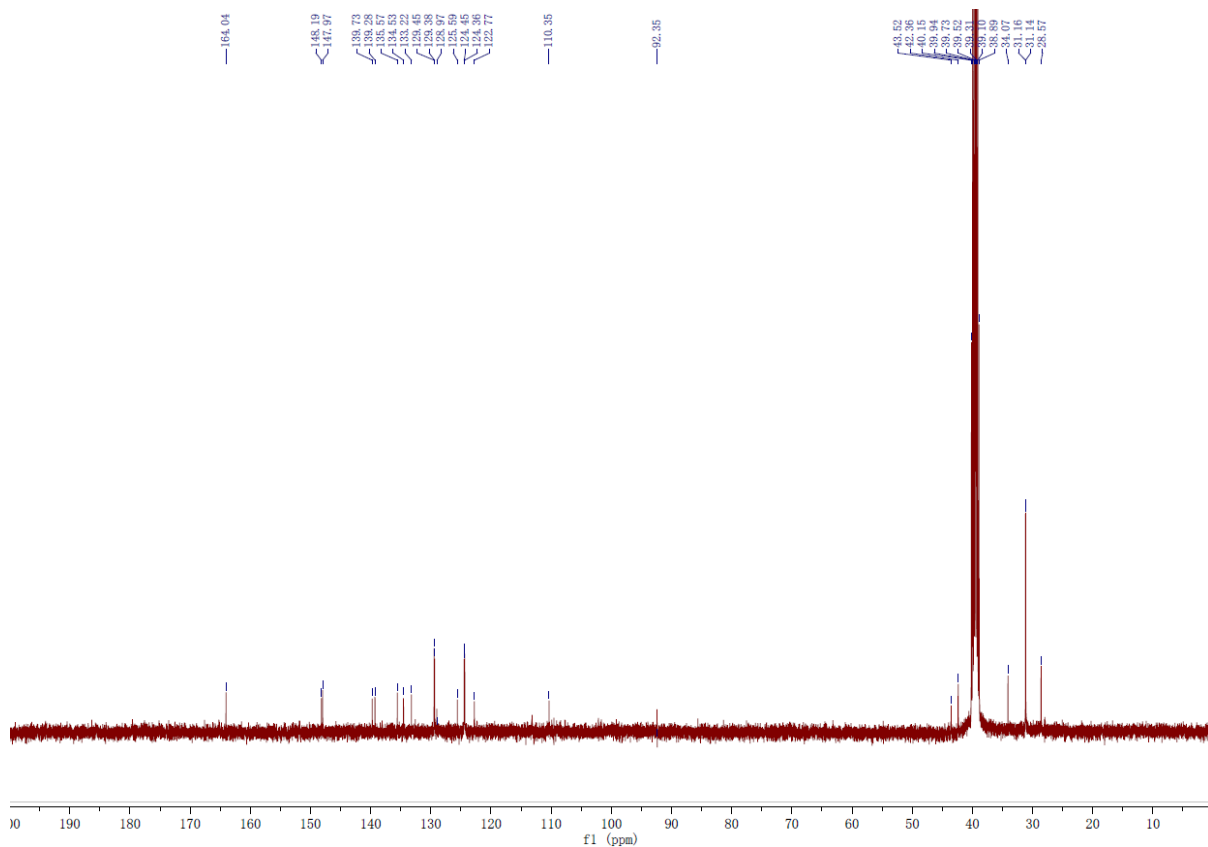
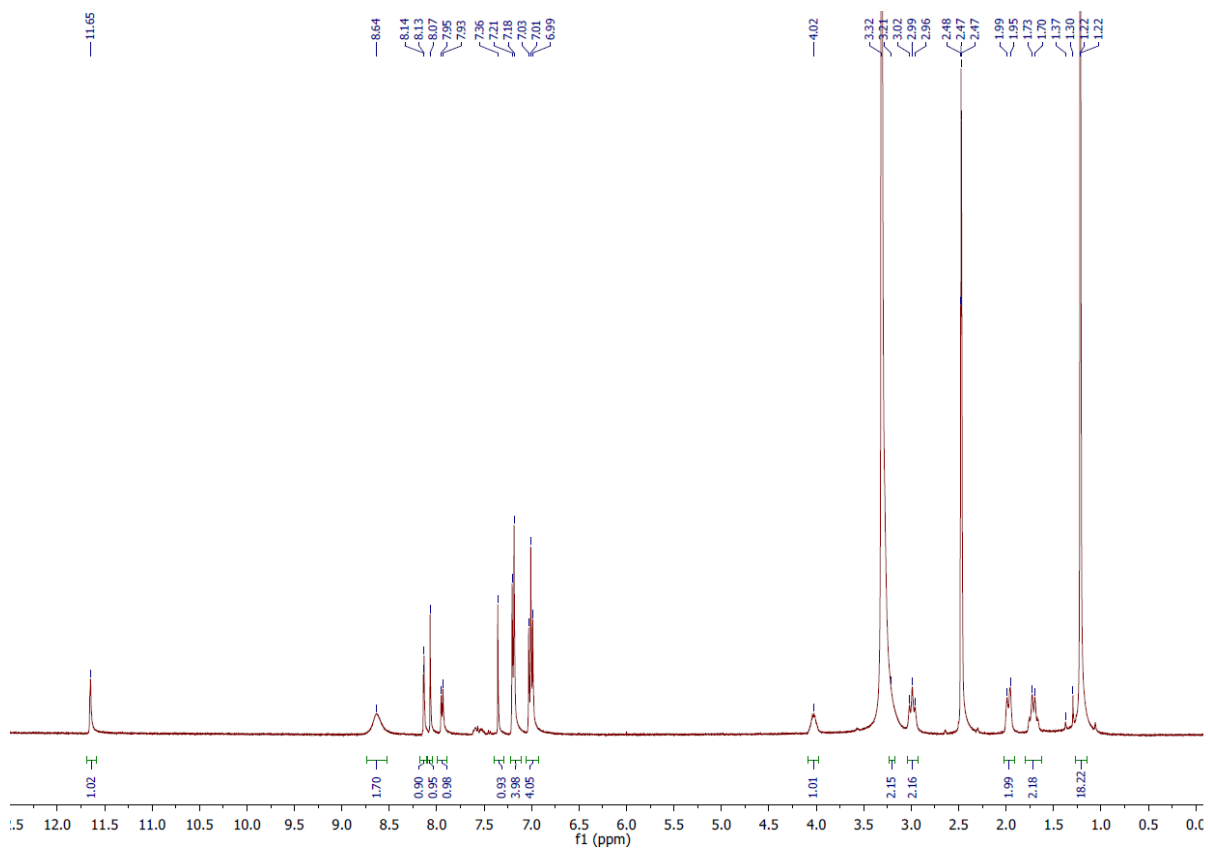


Figure S1. Dose-responsive curves for representative inhibitors of ZVpro.

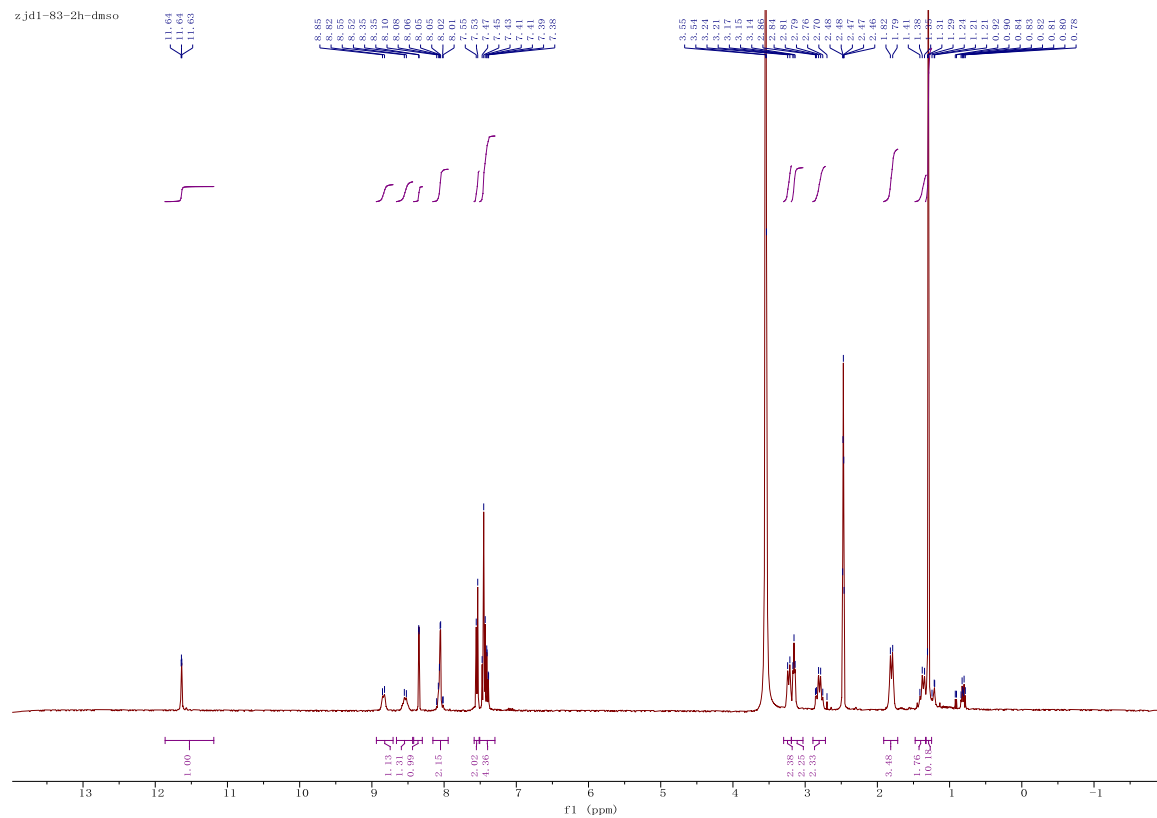
NMR spectra for compounds 1-73.

1. 5,6-Bis(4-(tert-butyl)phenyl)-N-(piperidin-4-yl)-1H-indole-3-carboxamide Hydrochloride (1).

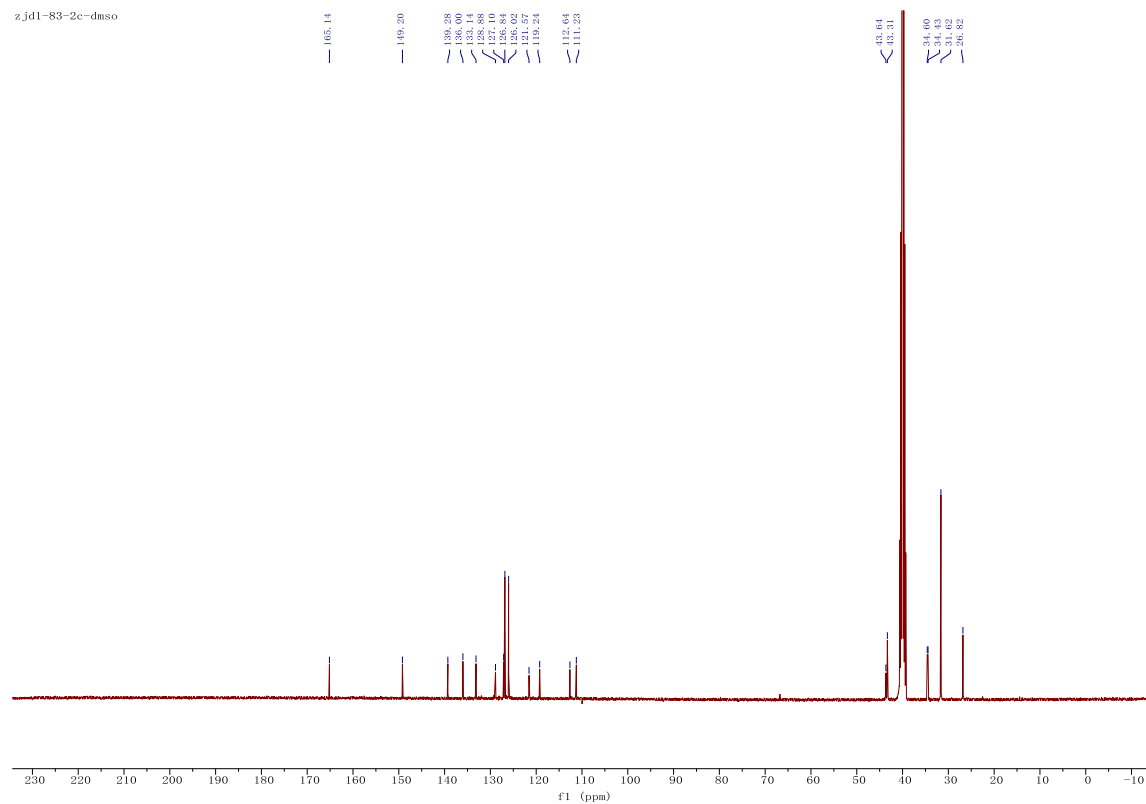


2. 5-(4-(Tert-butyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide (2).

zjd1-83-2h-dmso

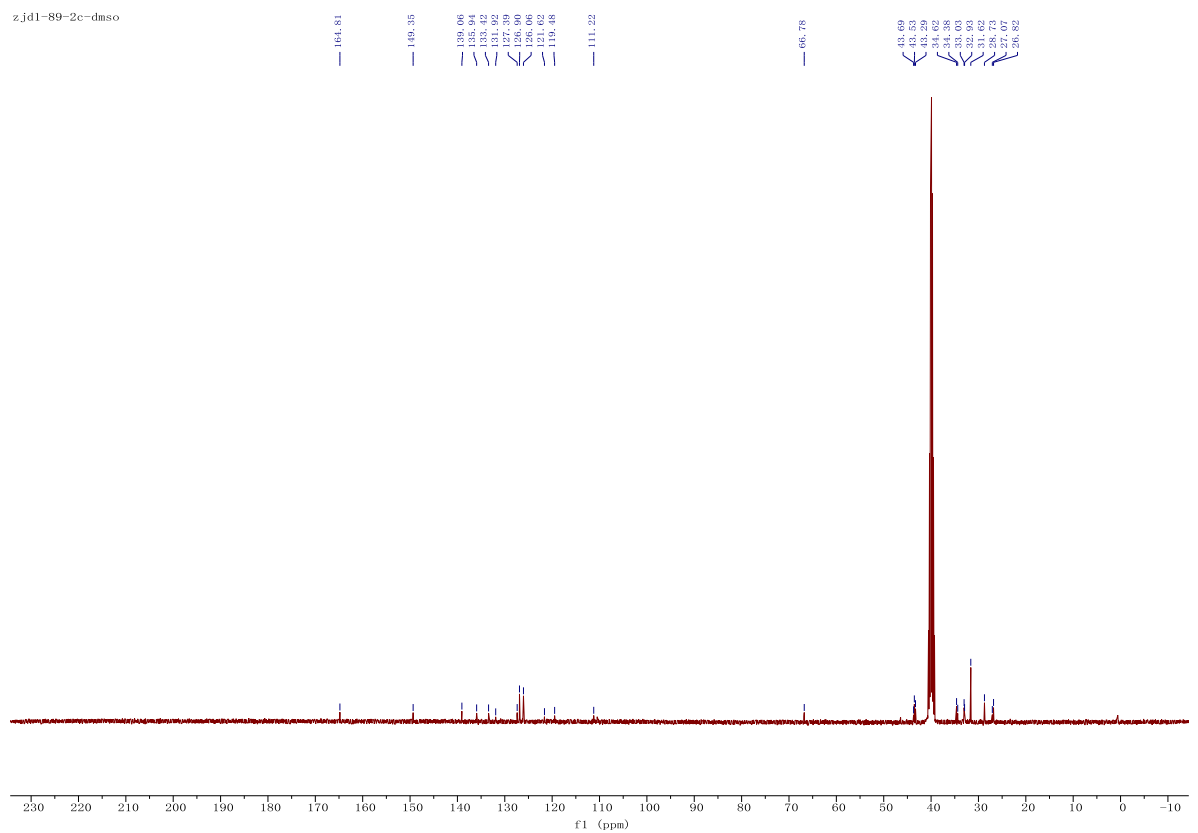
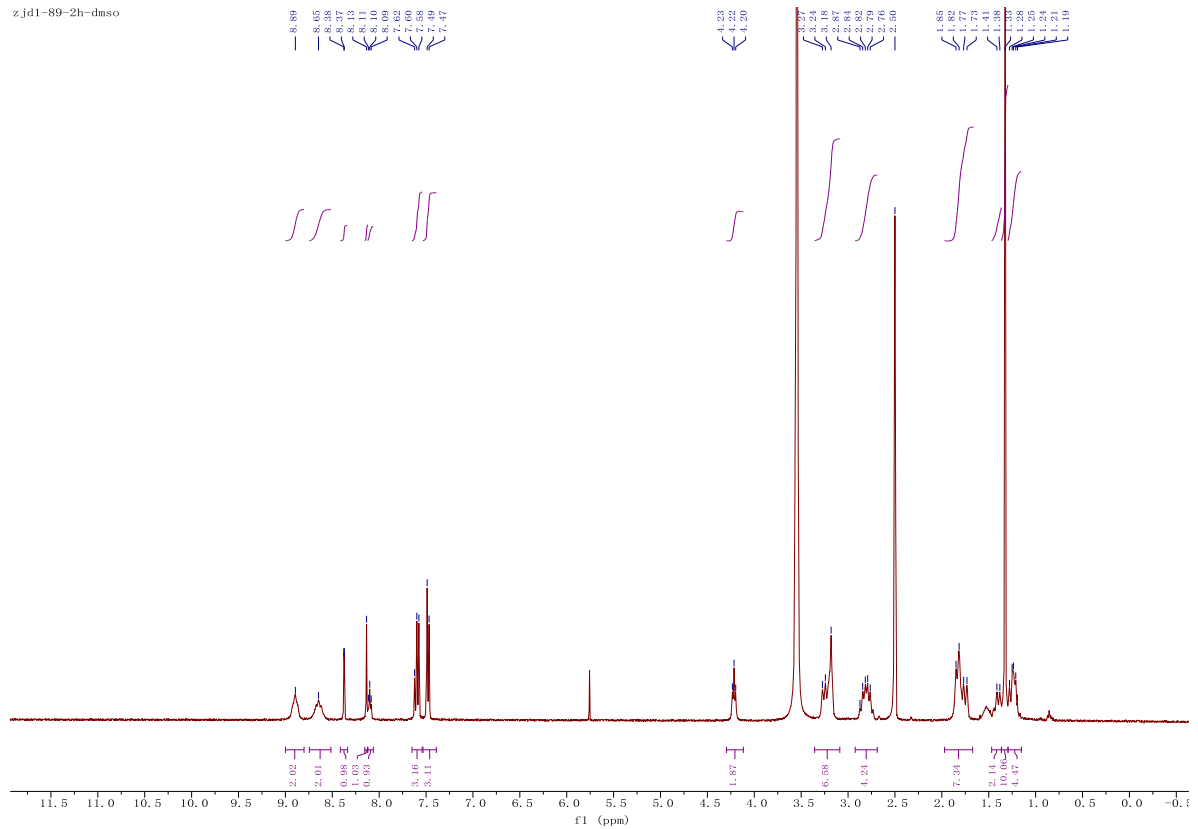


zjd1-83-2c-dmso

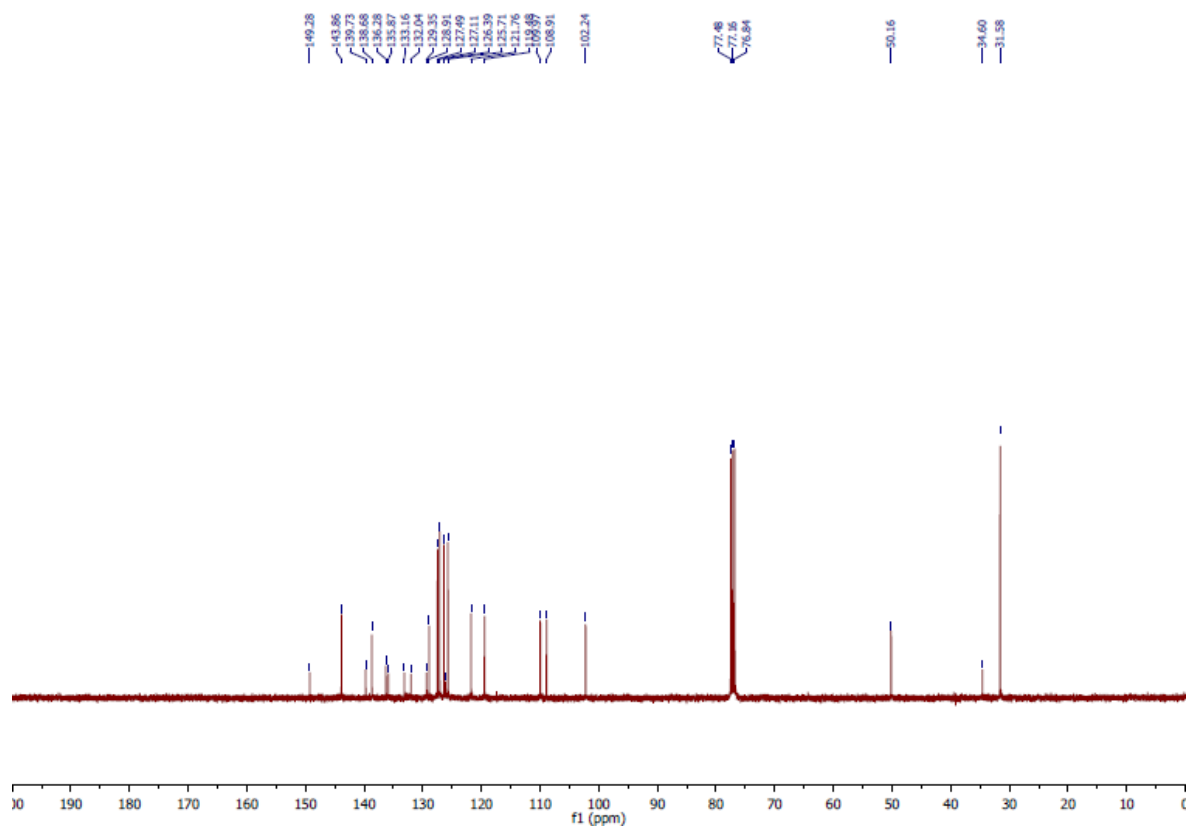
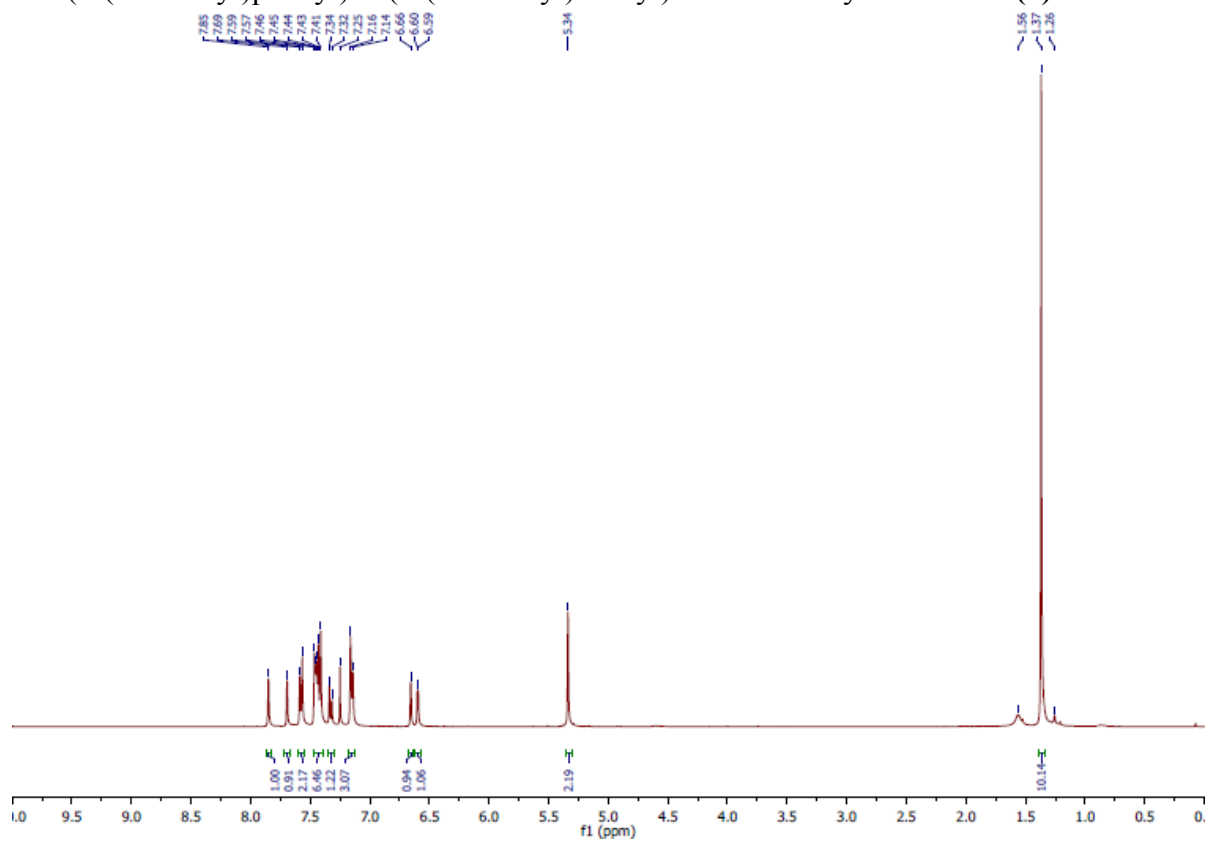


3. 5-(4-(Tert-butyl)phenyl)-1-(3-(piperidin-4-yl)propyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride

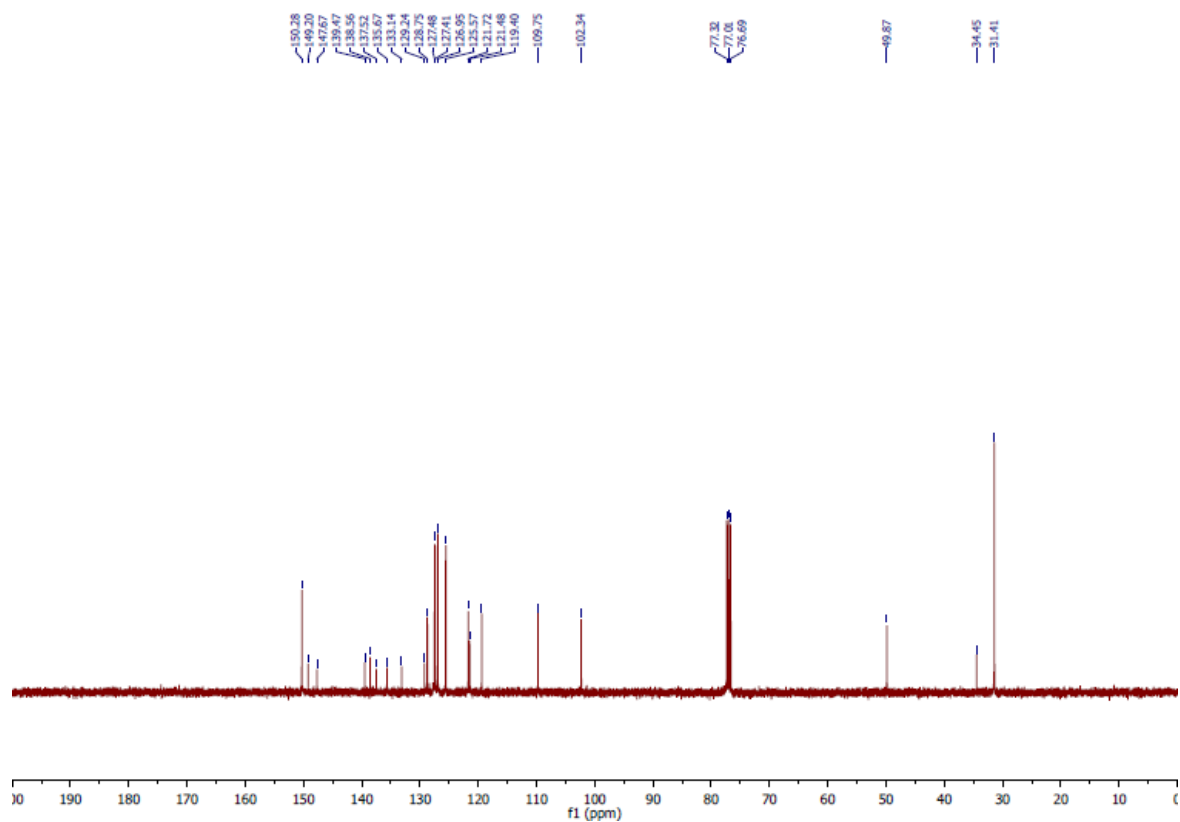
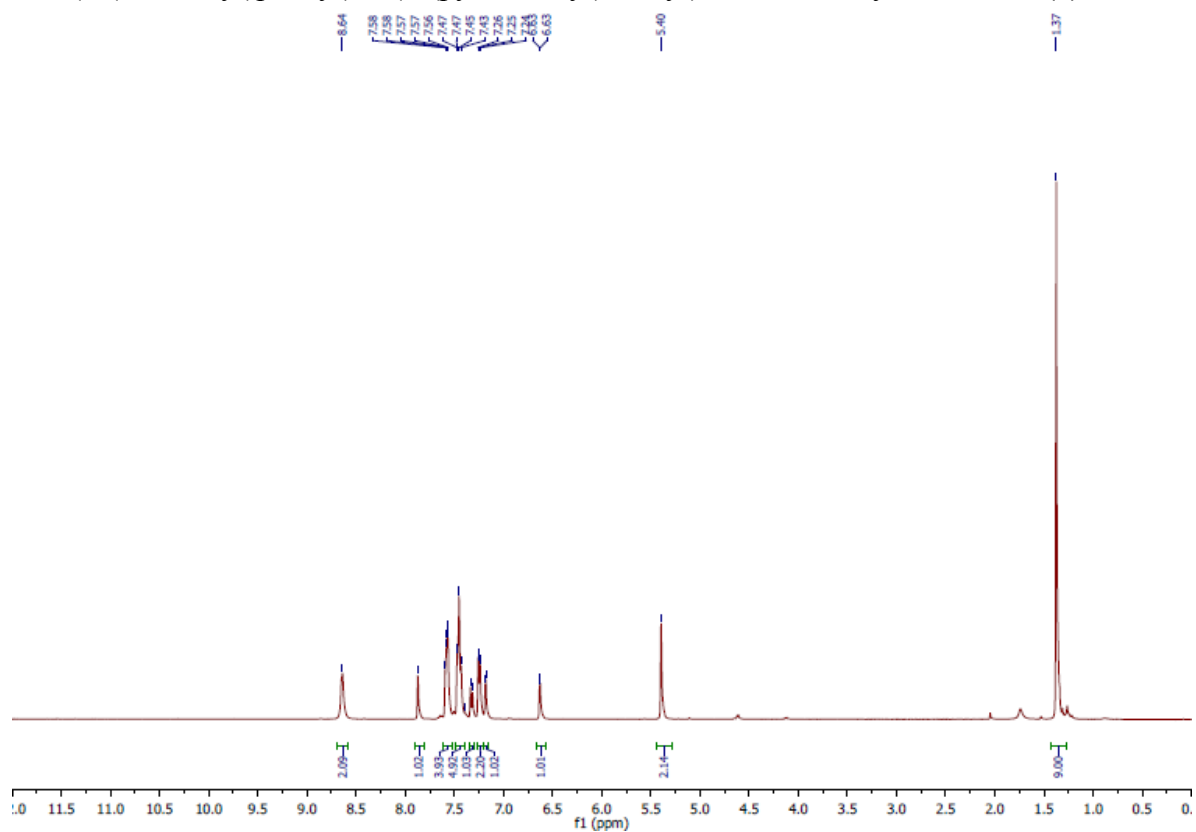
(3).



4. 5-(4-(Tert-butyl)phenyl)-1-(4-(furan-3-yl)benzyl)-1H-indole Hydrochloride (**4**).

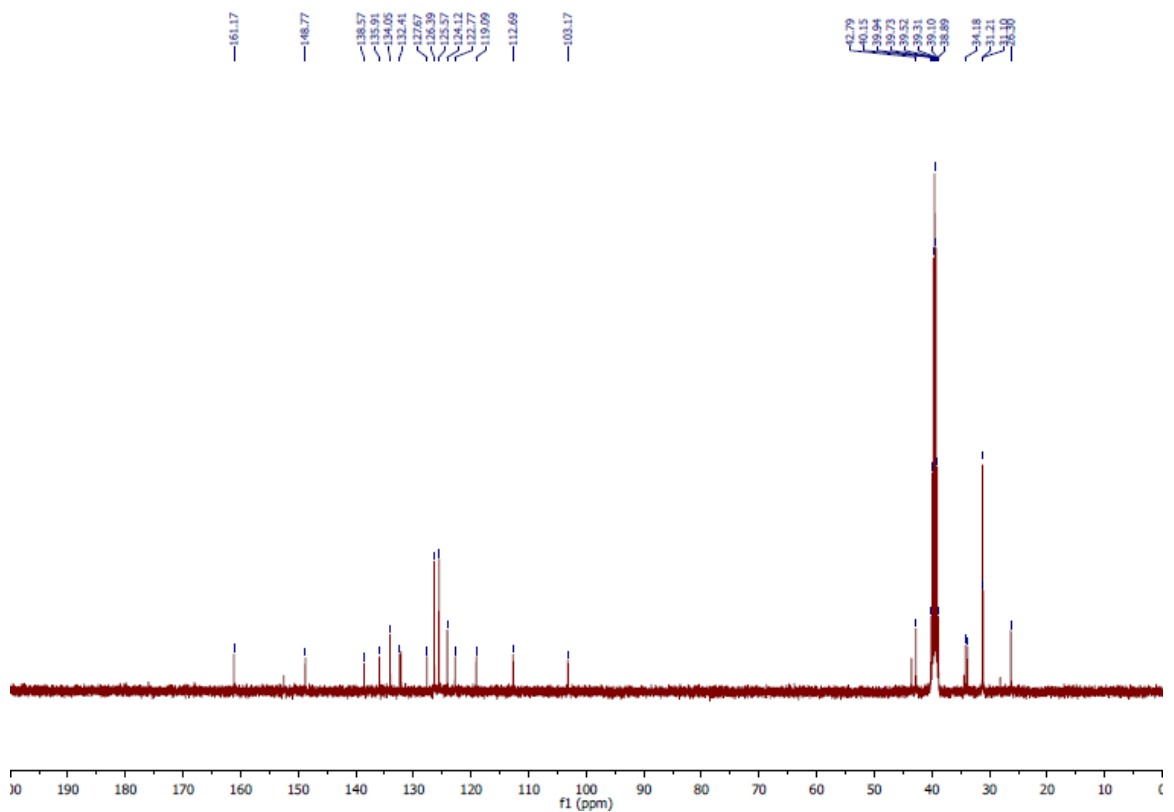
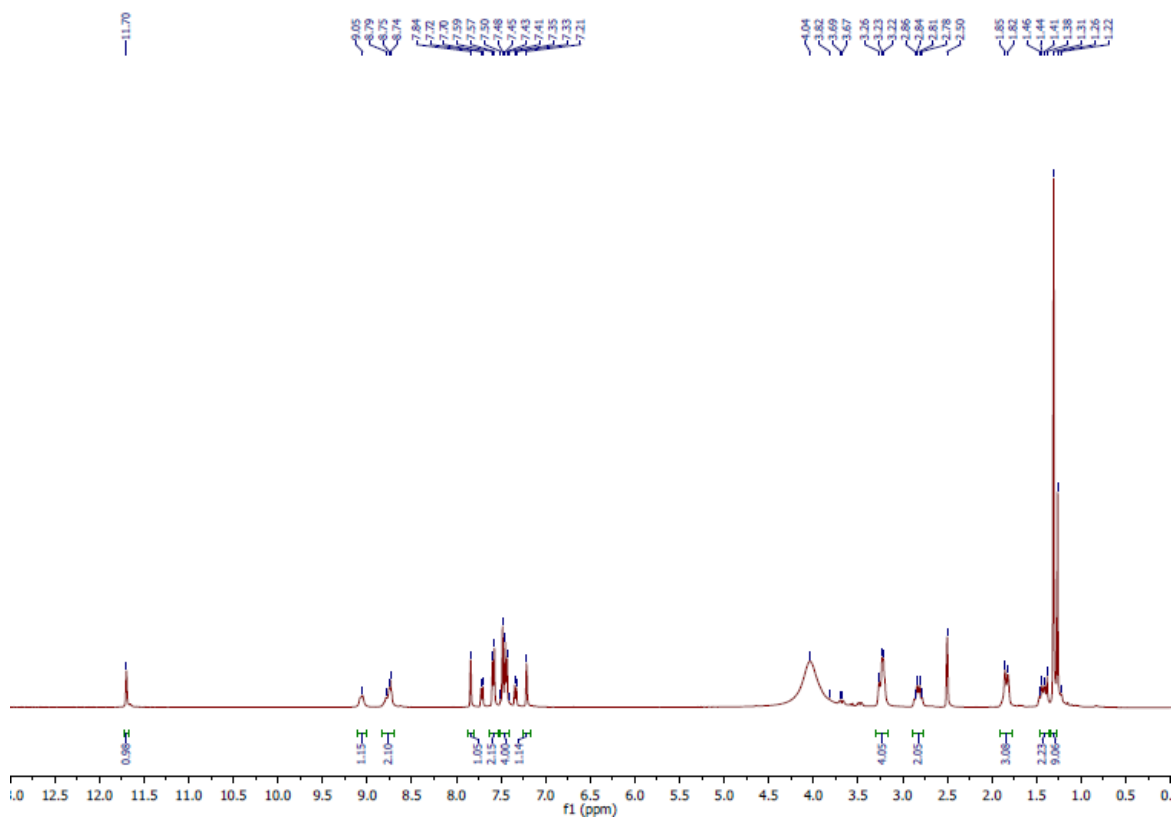


5. 5-(4-(Tert-butyl)phenyl)-1-(4-(pyridin-4-yl)benzyl)-1H-indole Hydrochloride (**5**)



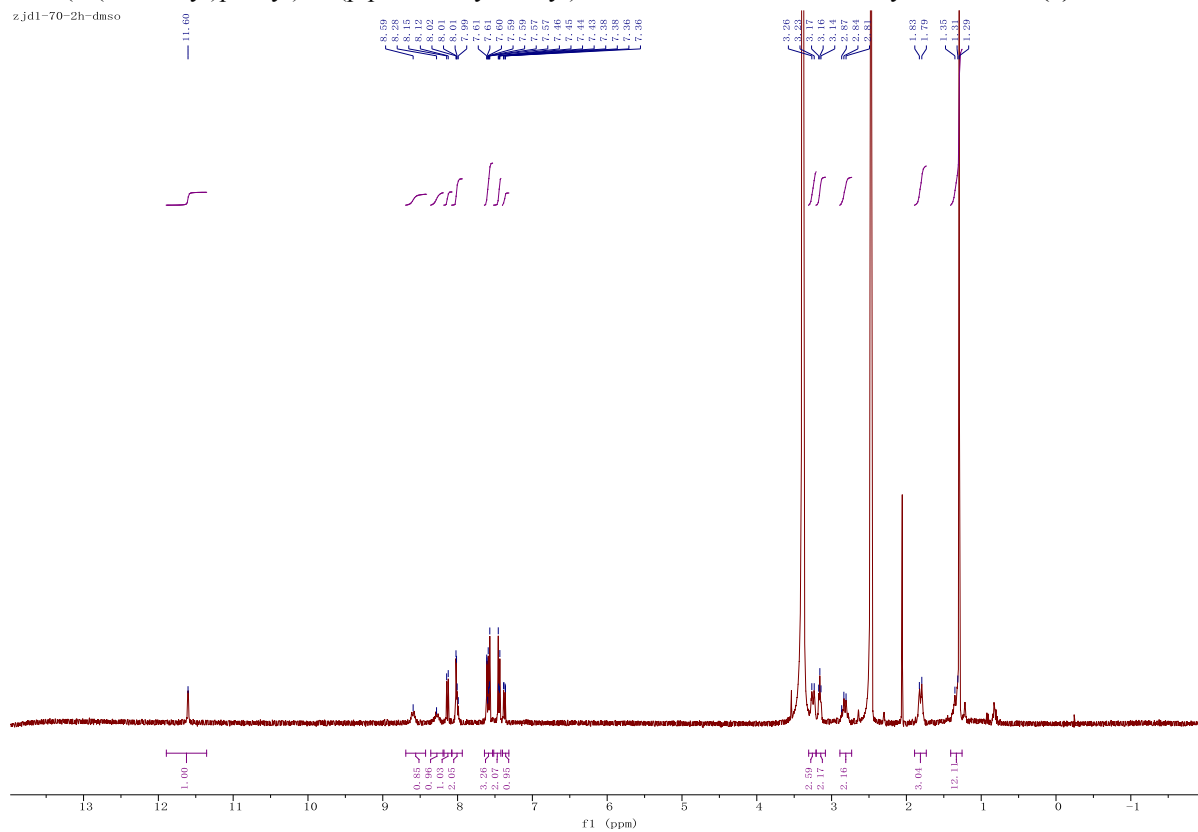
6.

5-(4-(Tert-butyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride
(6).

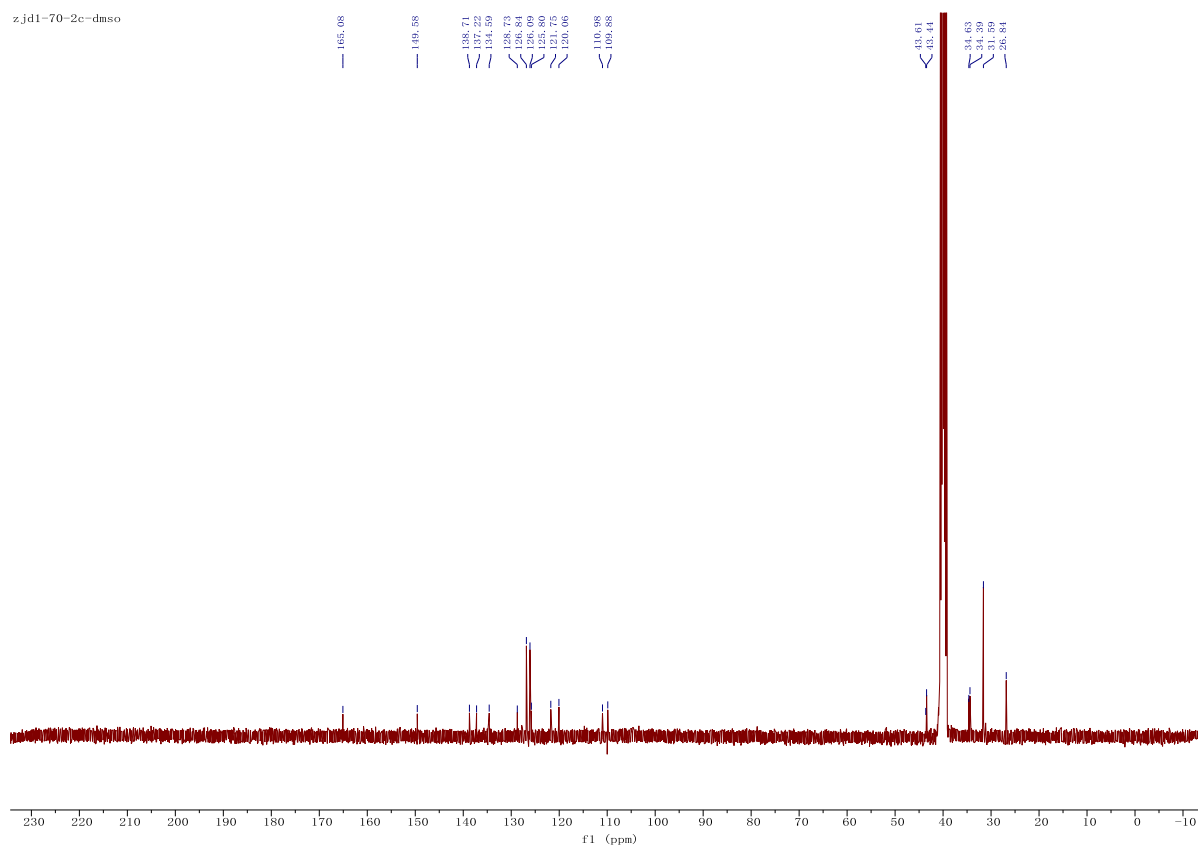


7. 6-(4-(Tert-butyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride. (7).

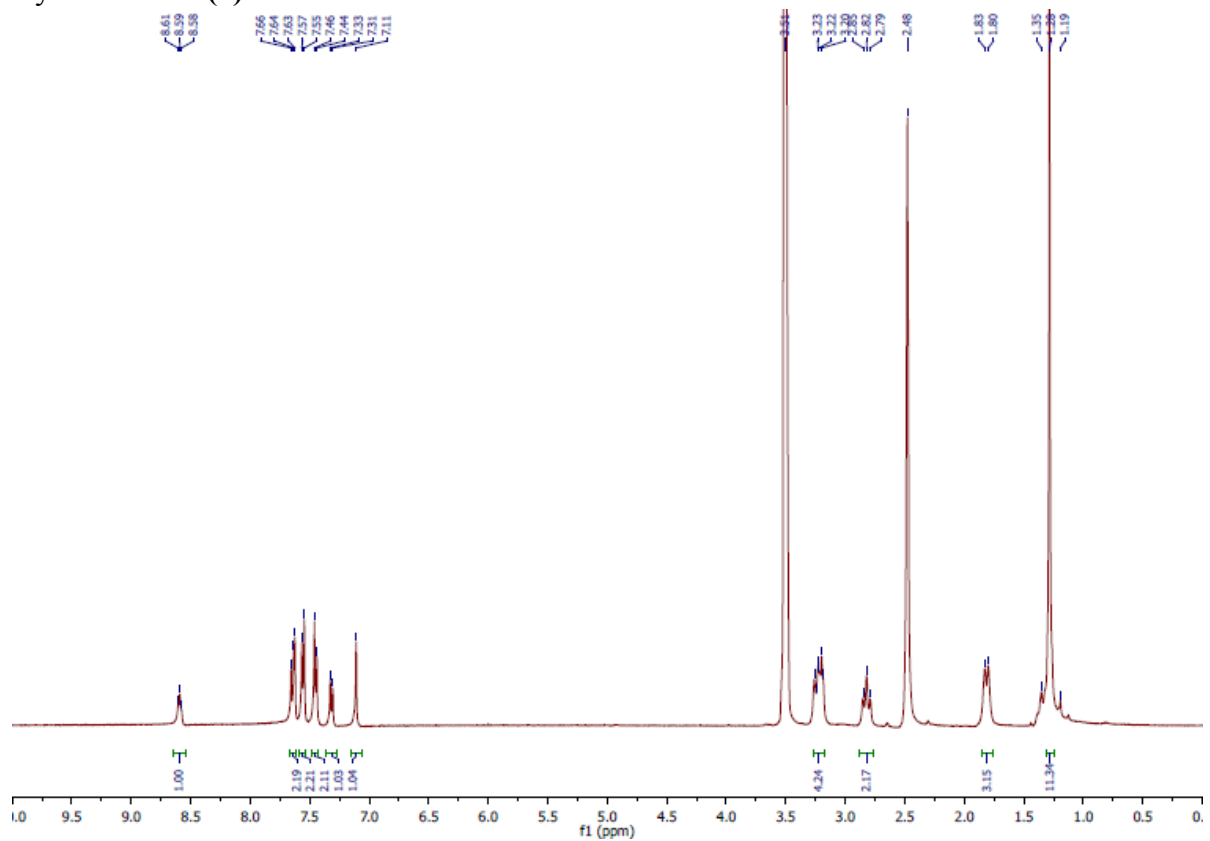
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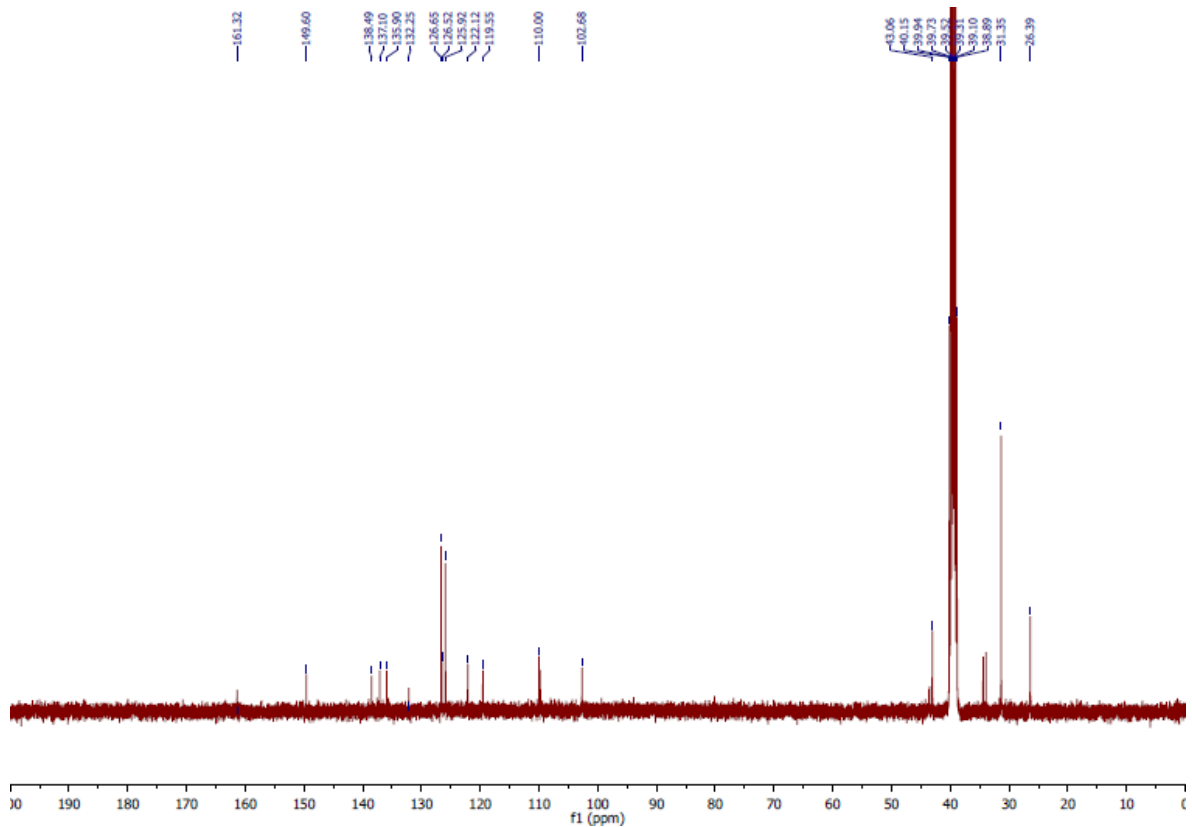


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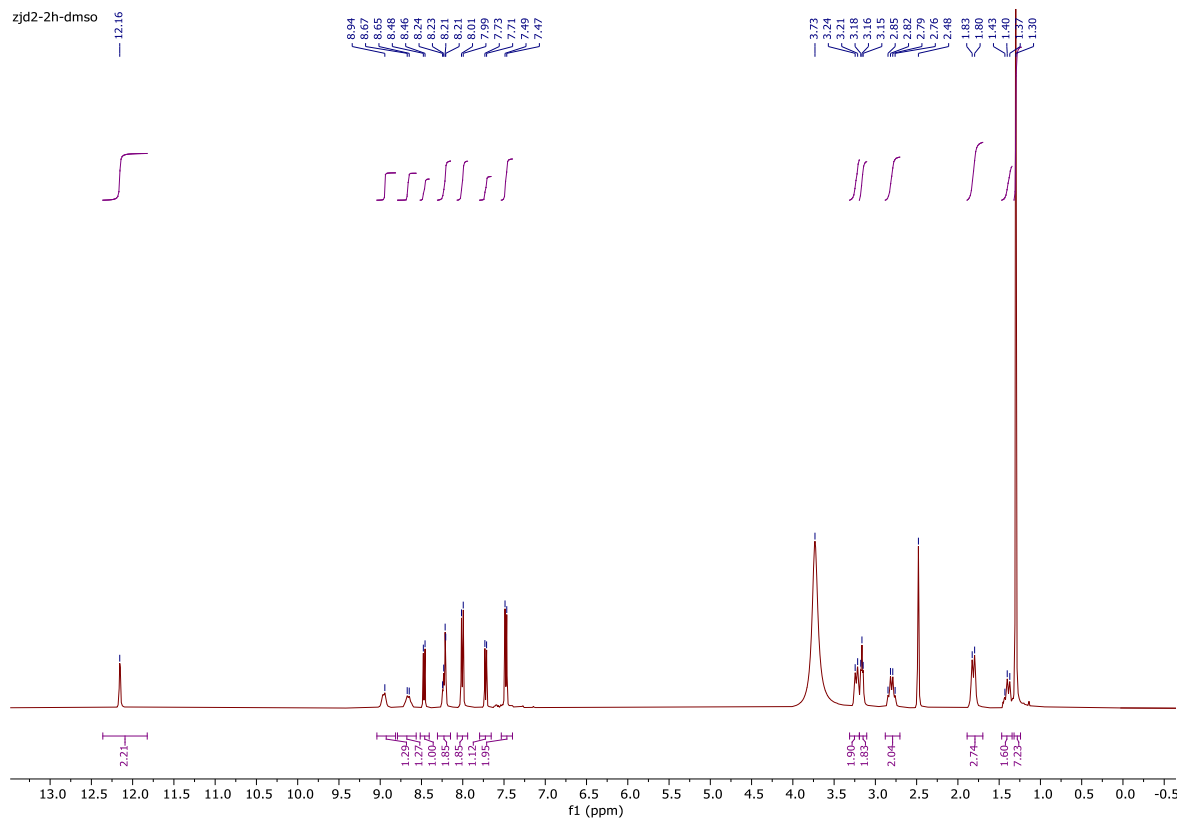


8. 6-(4-(Tert-butyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**8**).

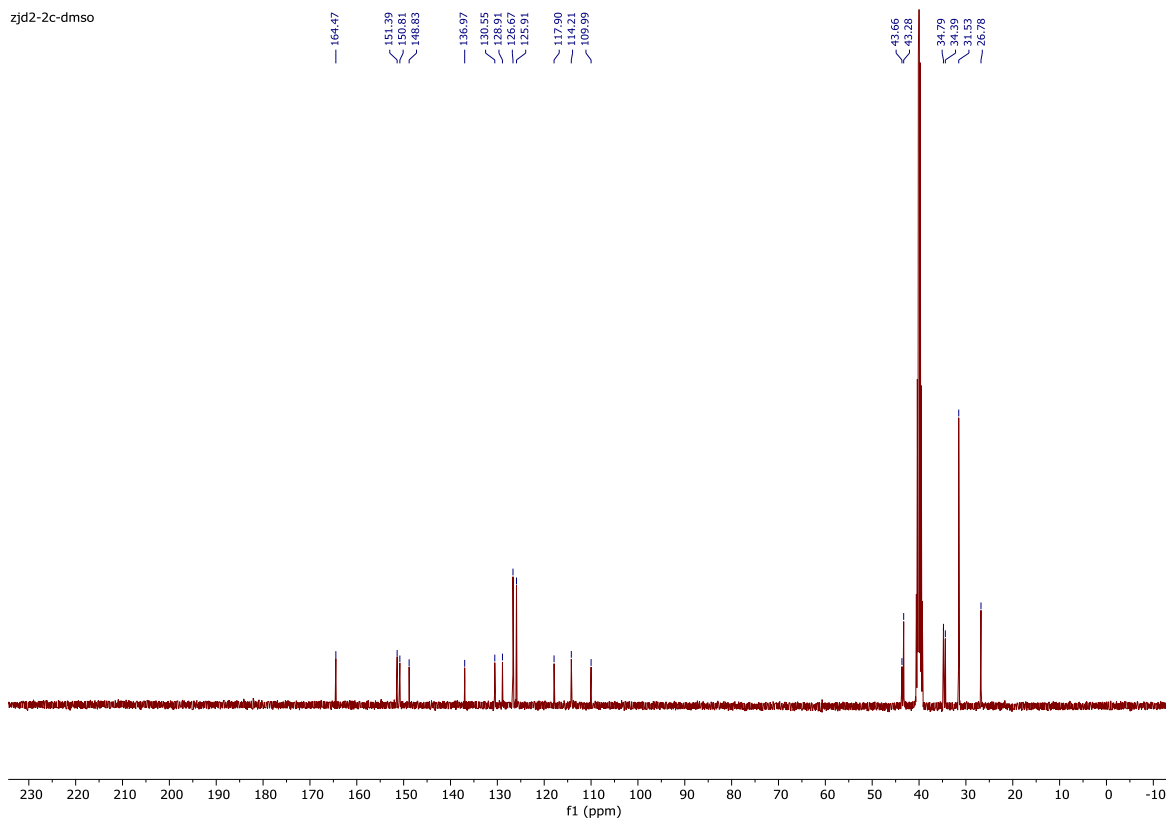




9. 6-(4-(Tert-butyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-pyrrolo[2,3-b]pyridine-3-carboxamide Hydrochloride (9).

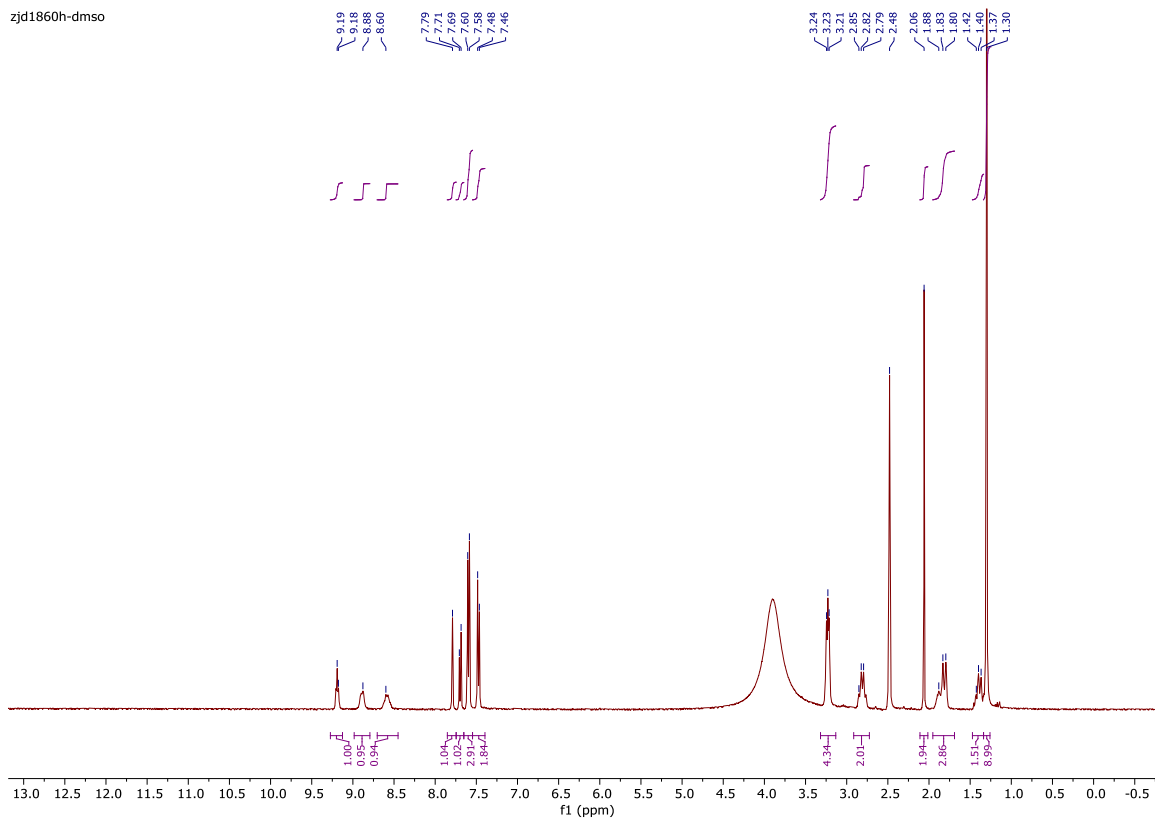


zjd2-2c-dmso

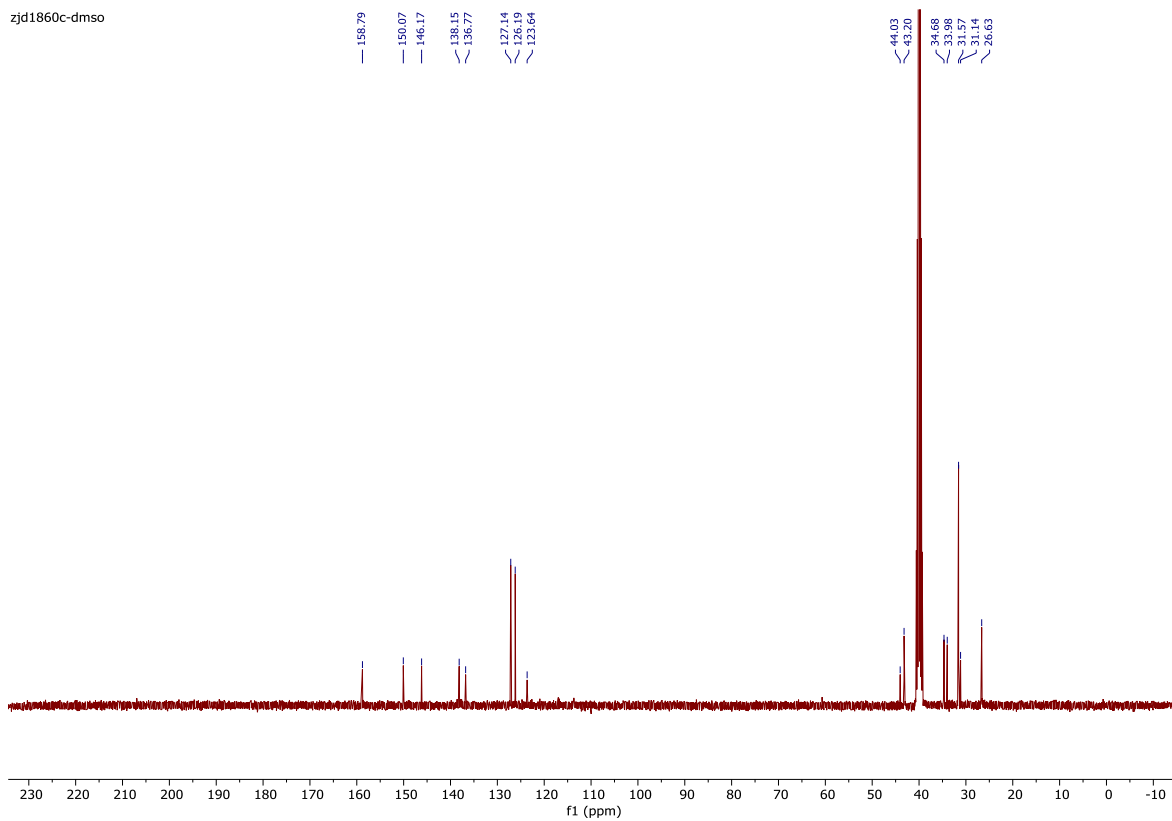


10. 5-(4-(Tert-butyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-benzo[d]imidazole-2 carboxamide Hydrochloride (10).

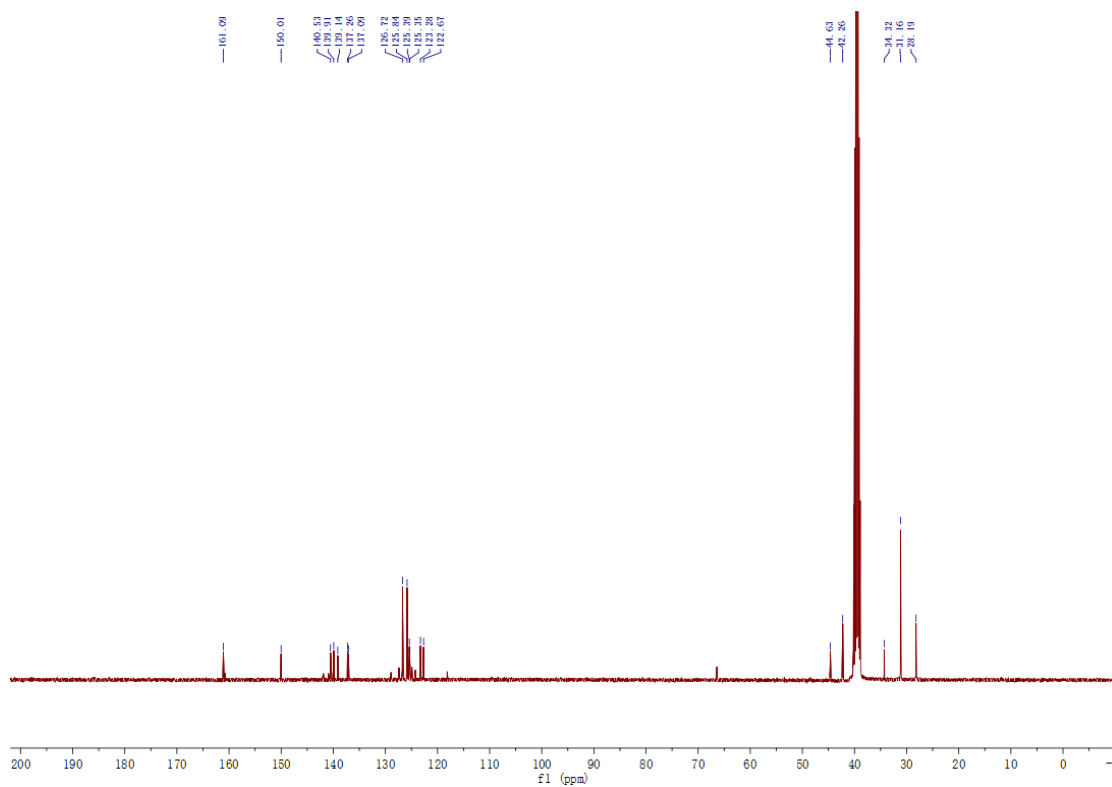
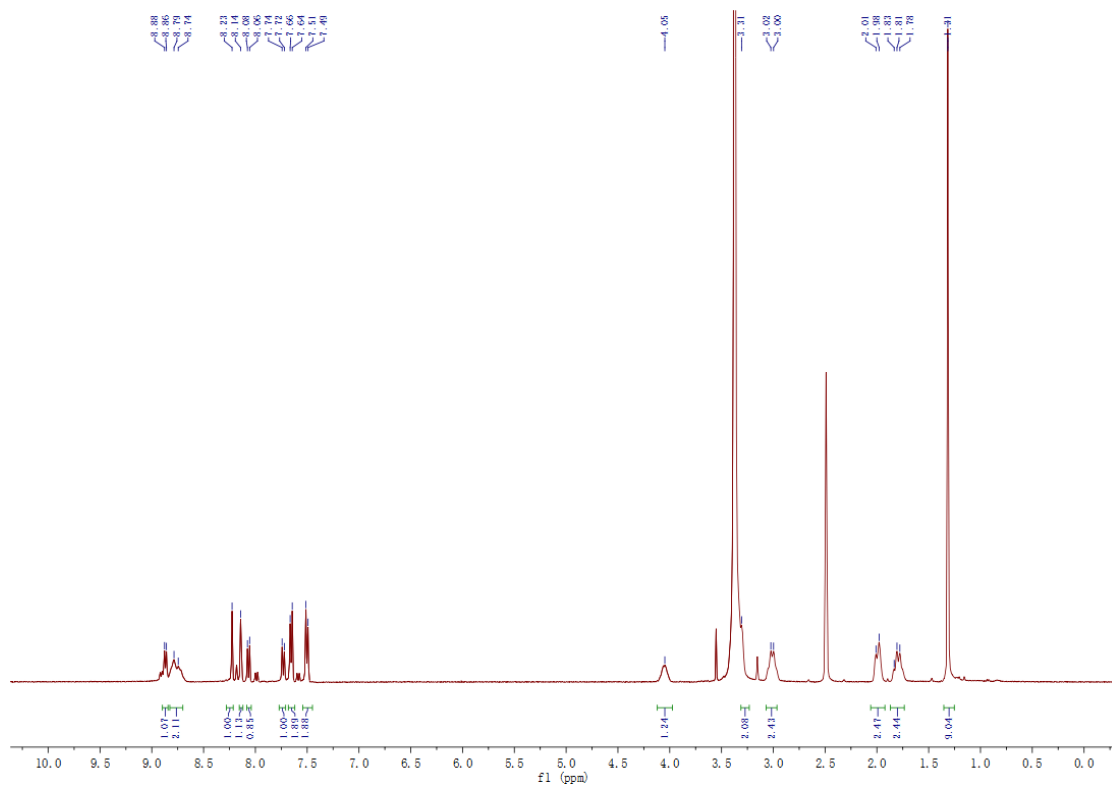
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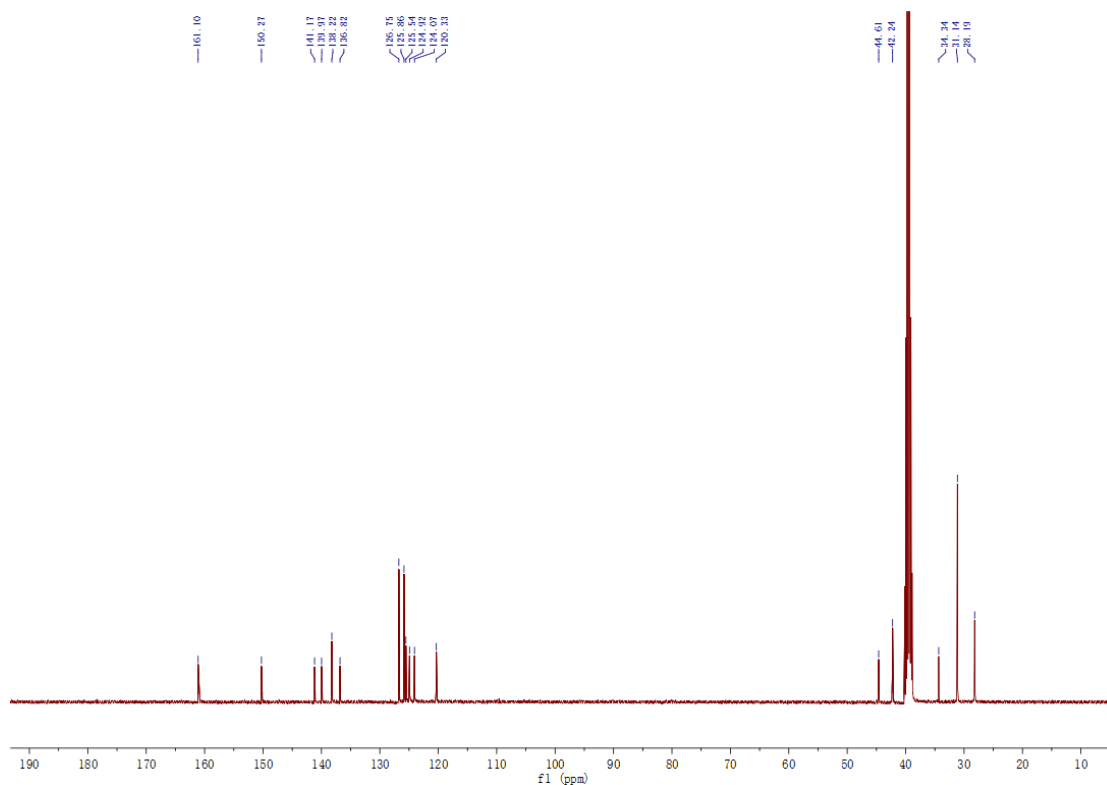
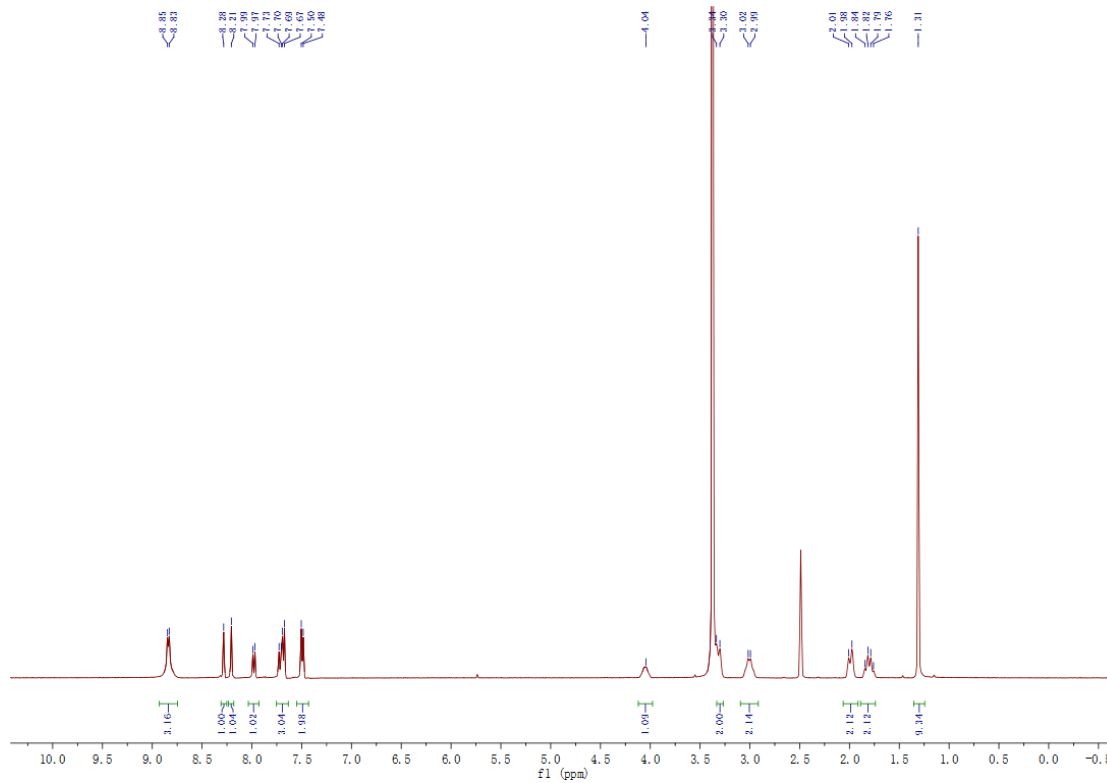
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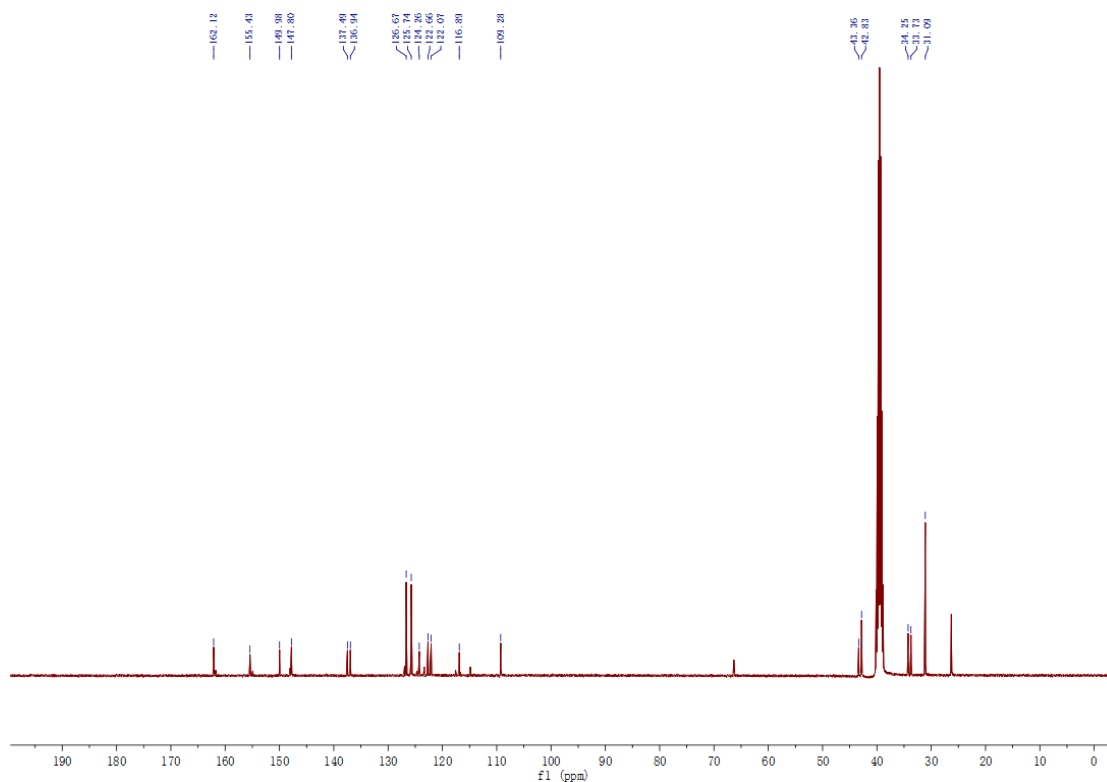
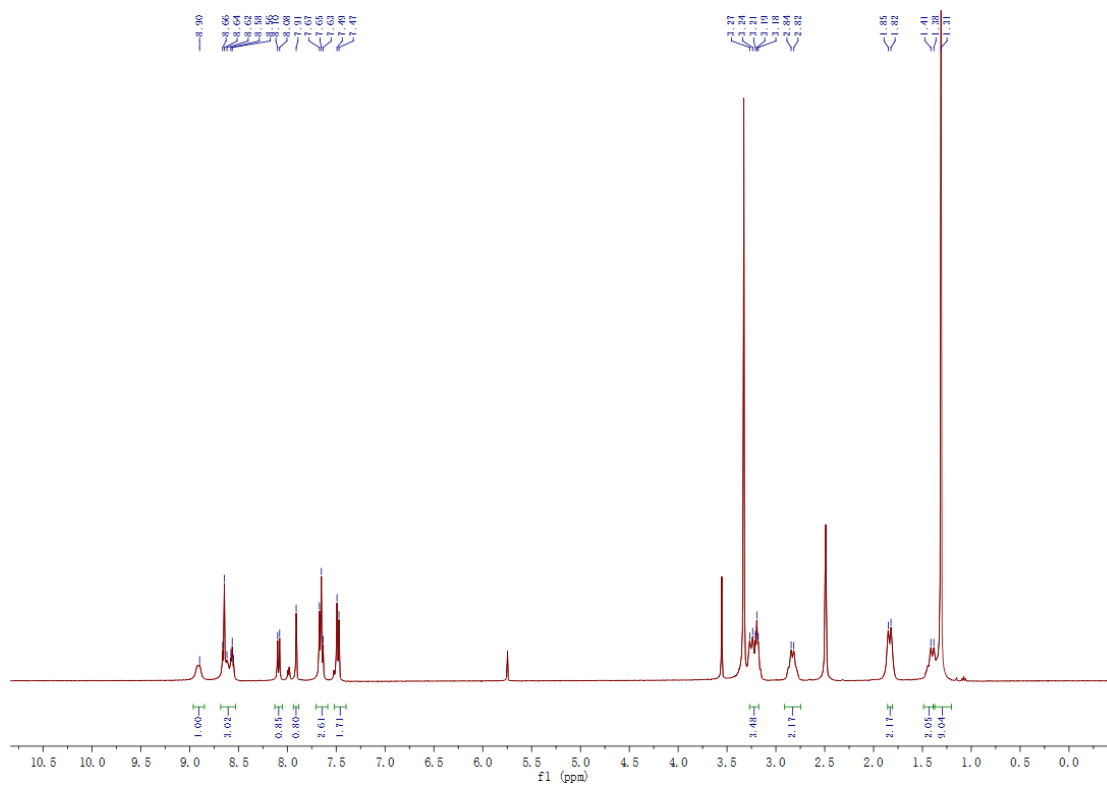
11.5-(4-(tert-butyl)phenyl)-N-(piperidin-4-yl)benzo[b]thiophene-2-carboxamide Hydrochloride (**11**)



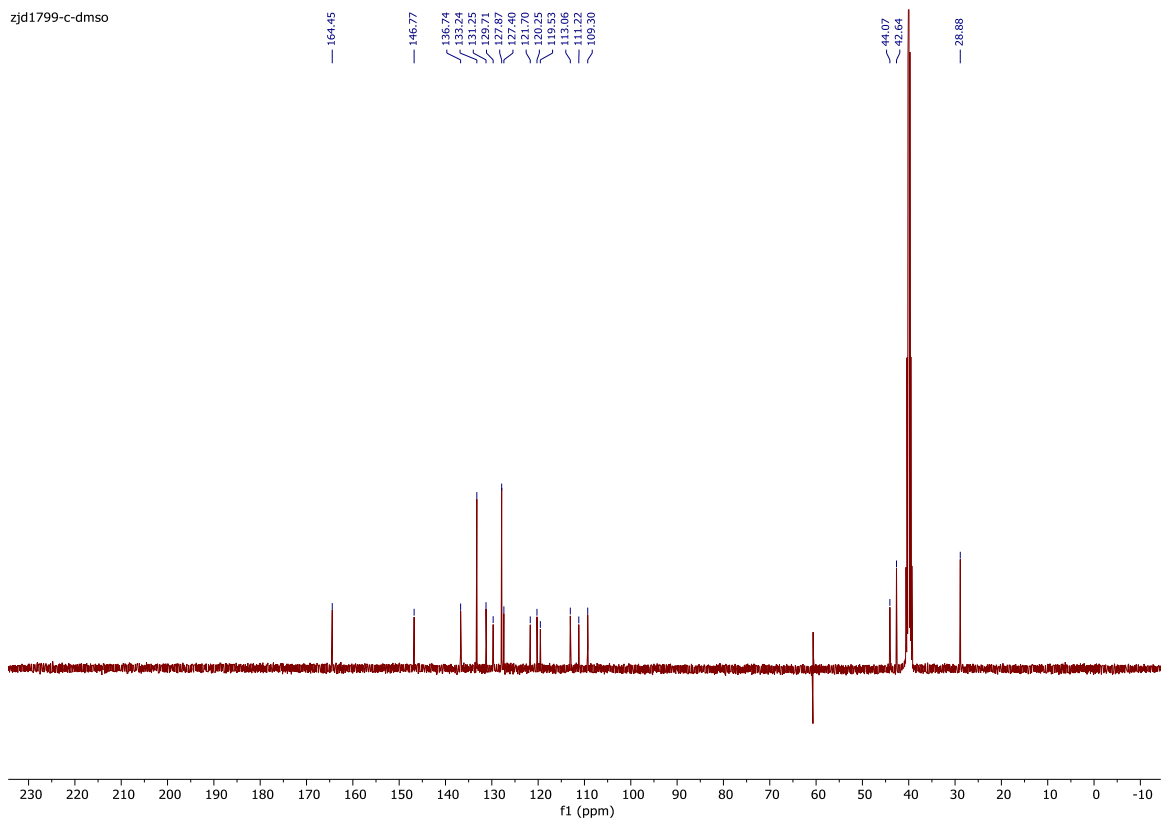
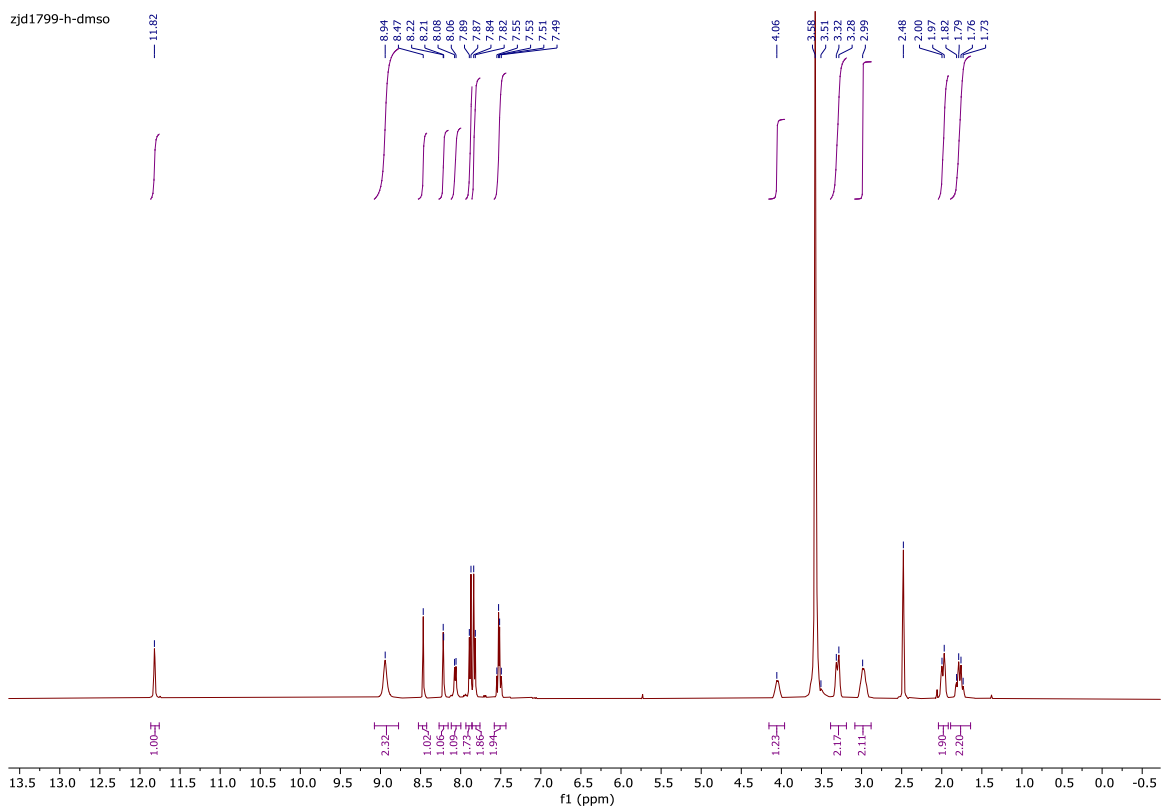
12. 6-(4-(tert-butyl)phenyl)-N-(piperidin-4-yl)benzo[b]thiophene-2-carboxamide Hydrochloride (**12**)



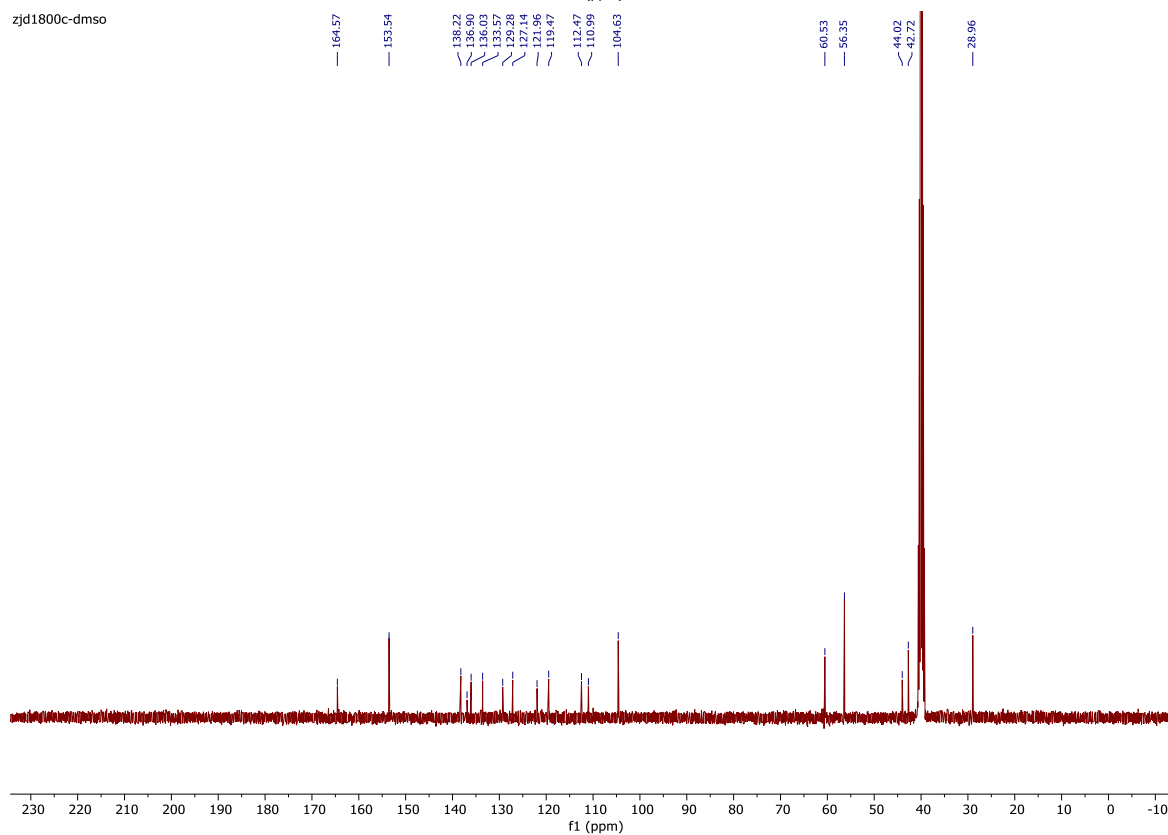
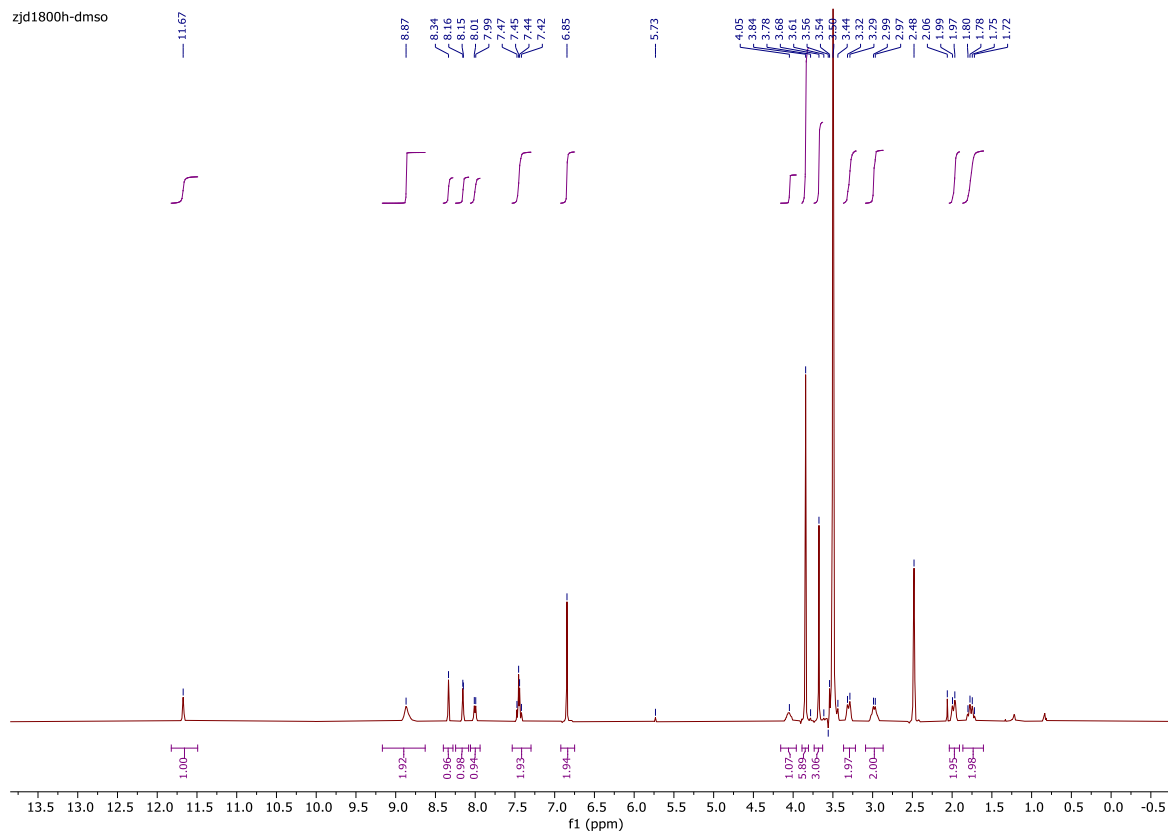
13. 6-(4-(Tert-butyl)phenyl)-N-(piperidin-4-yl)benzofuran-3-carboxamide Hydrochloride (13)



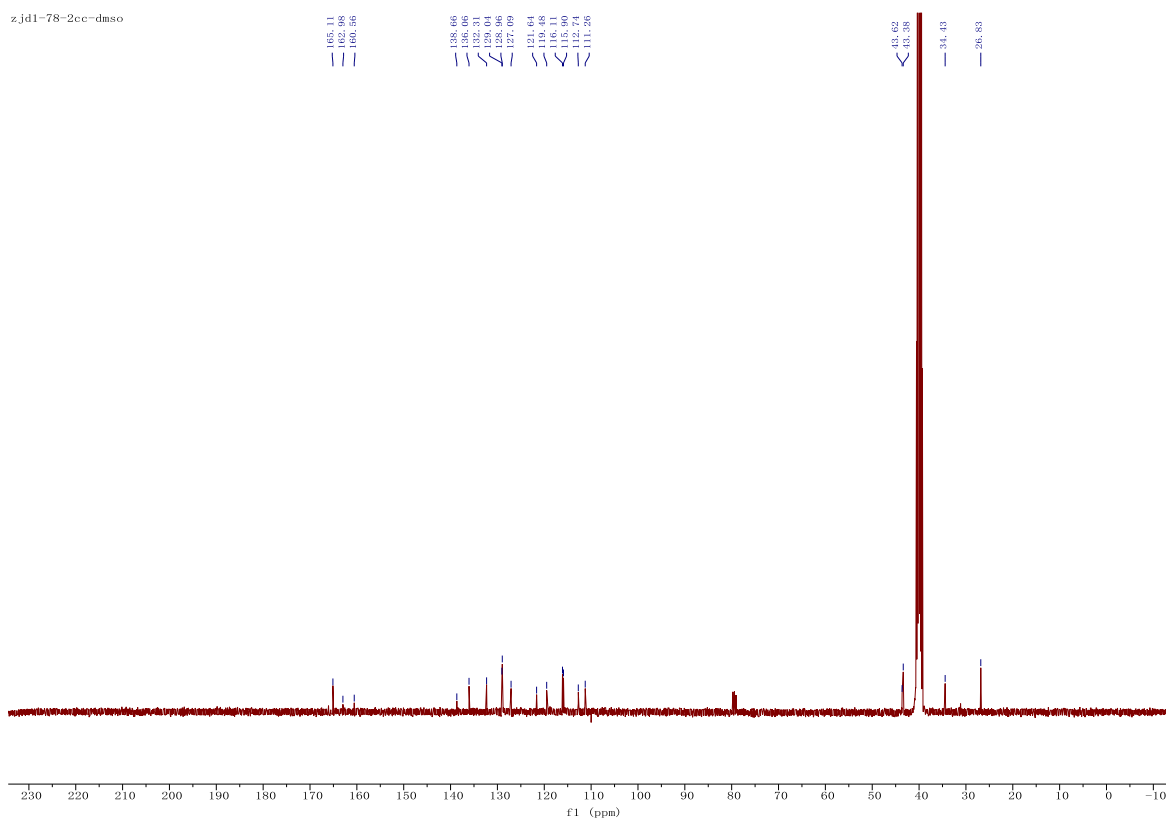
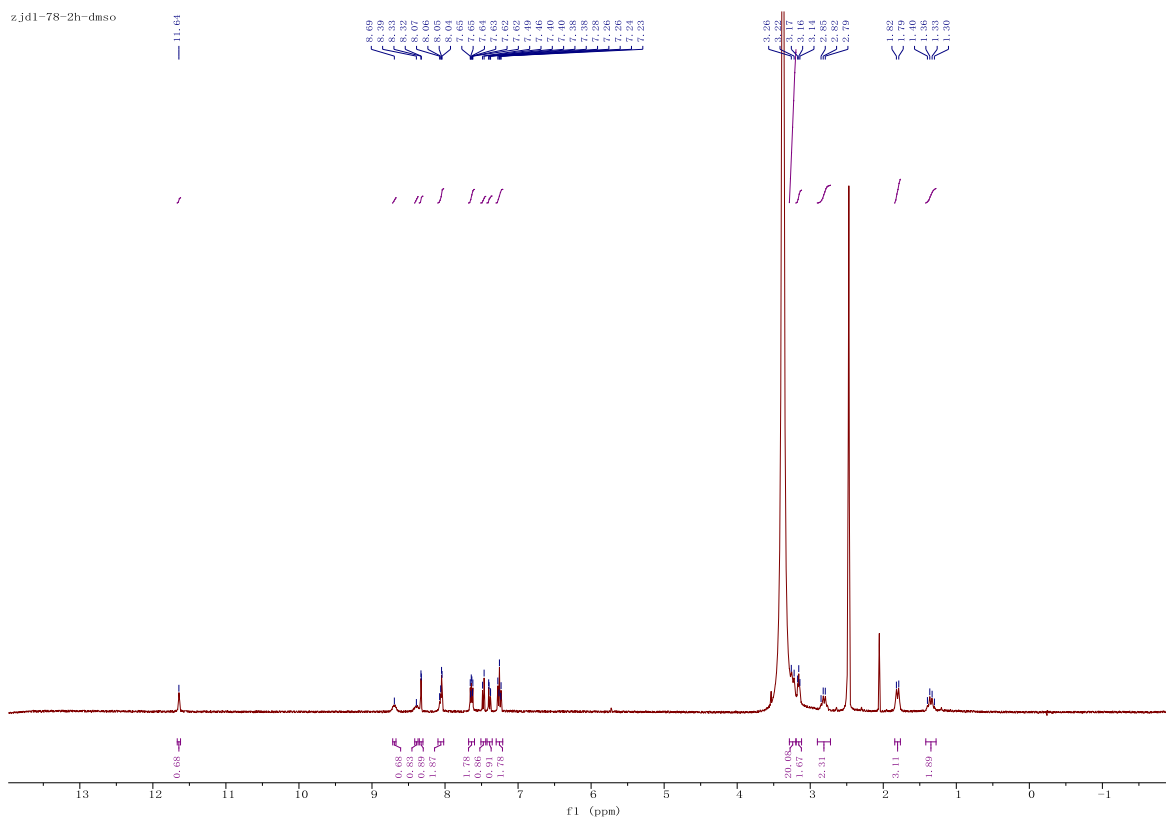
14. 14. 5-(4-Cyanophenyl)-N-(piperidin-4-yl)-1H-indole-3-carboxamide Hydrochloride (14).



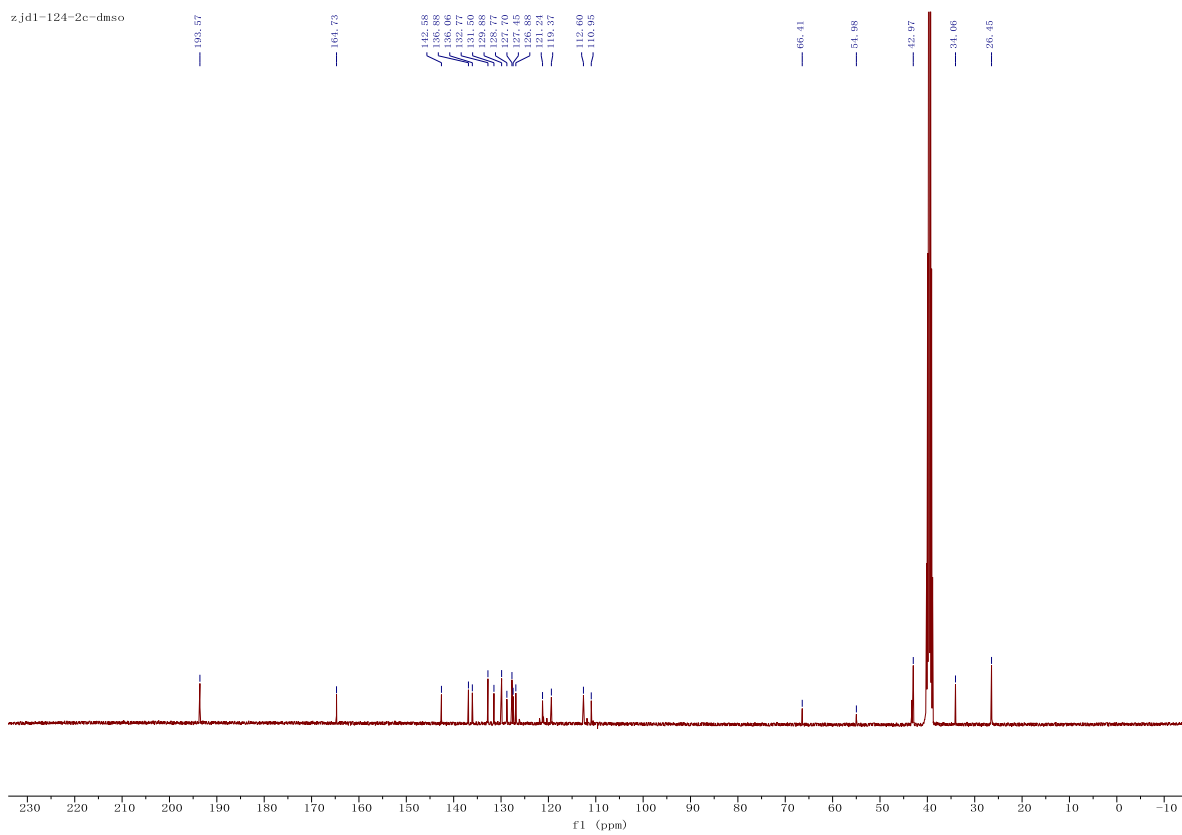
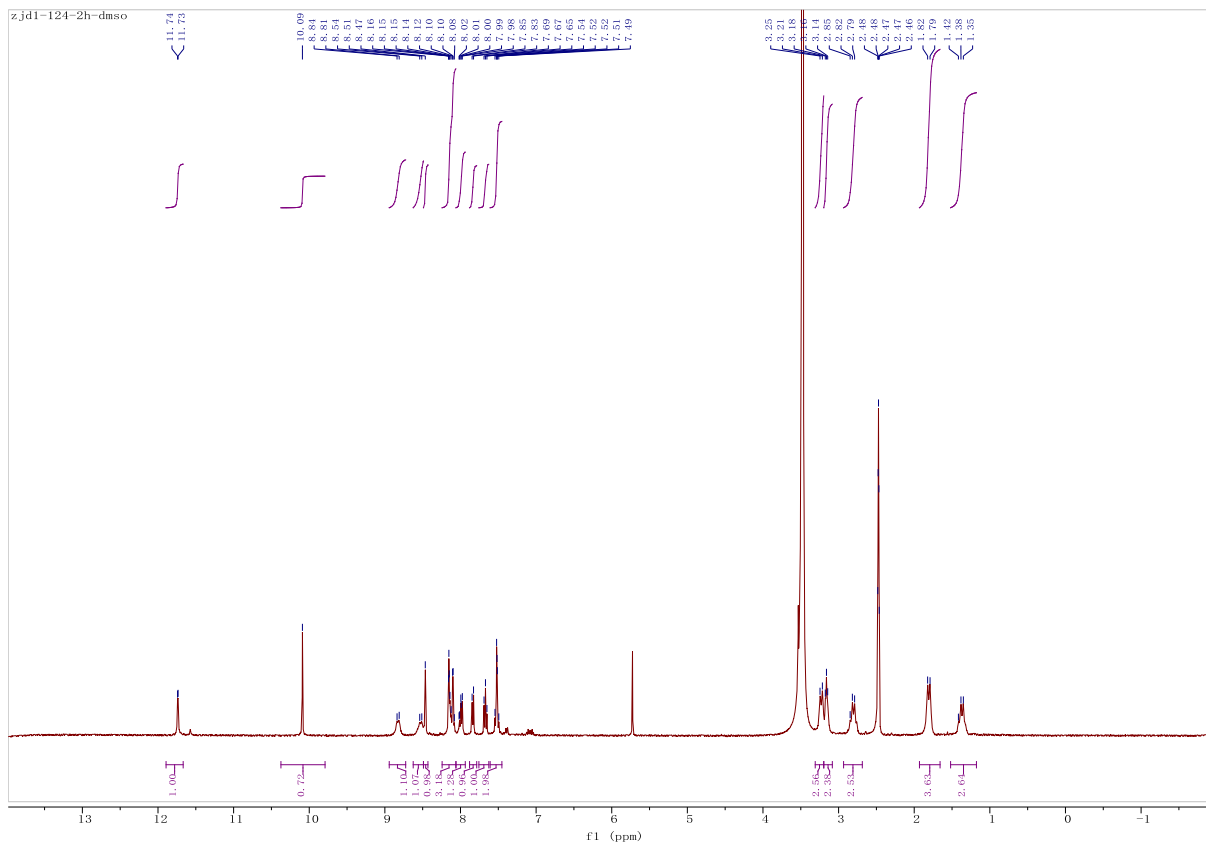
15. N-(Piperidin-4-yl)-5-(3,4,5-trimethoxyphenyl)-1H-indole-3-carboxamide Hydrochloride (15).



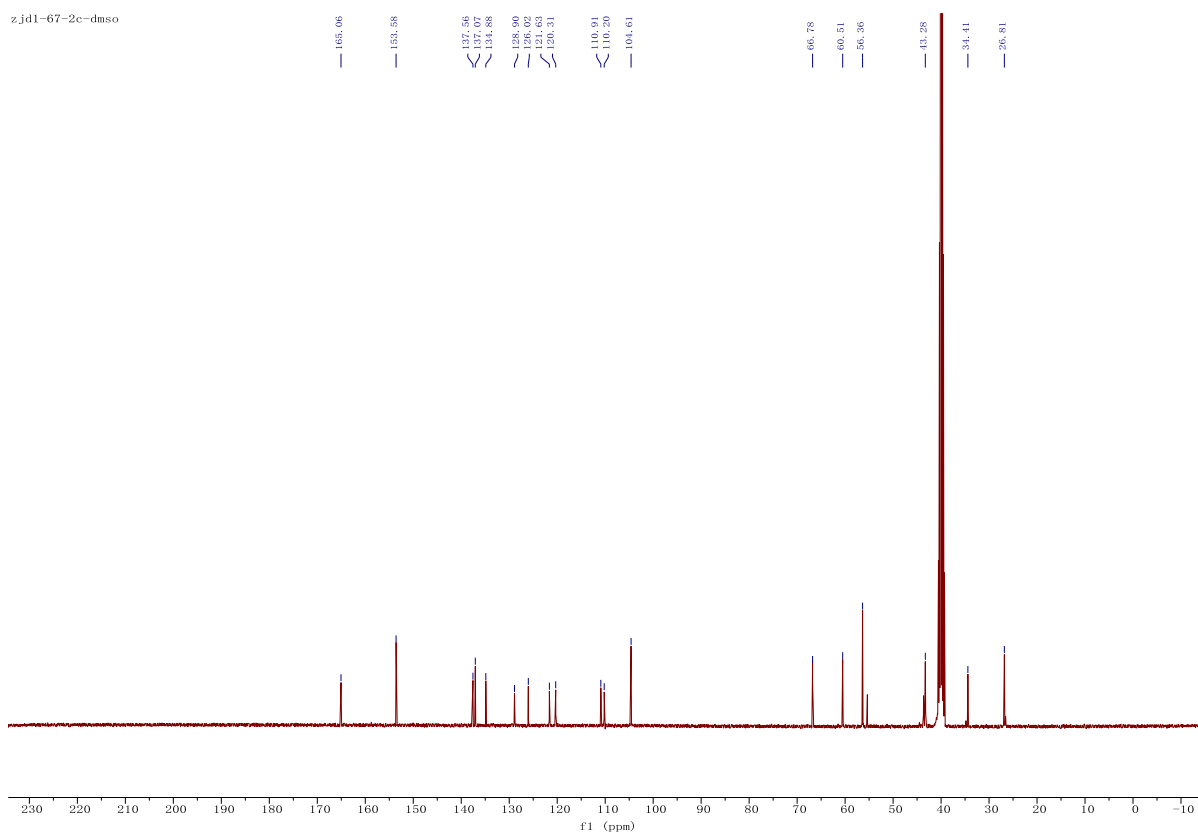
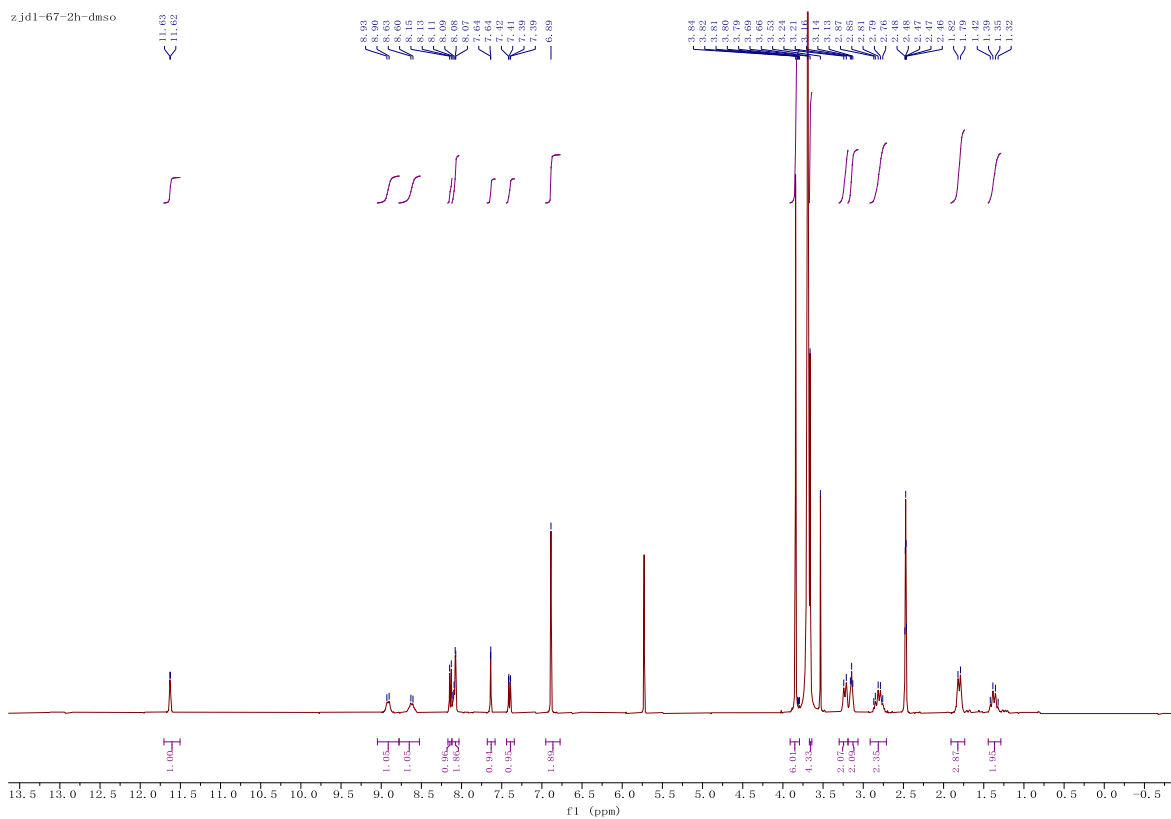
16. 5-(4-Fluorophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (**16**).



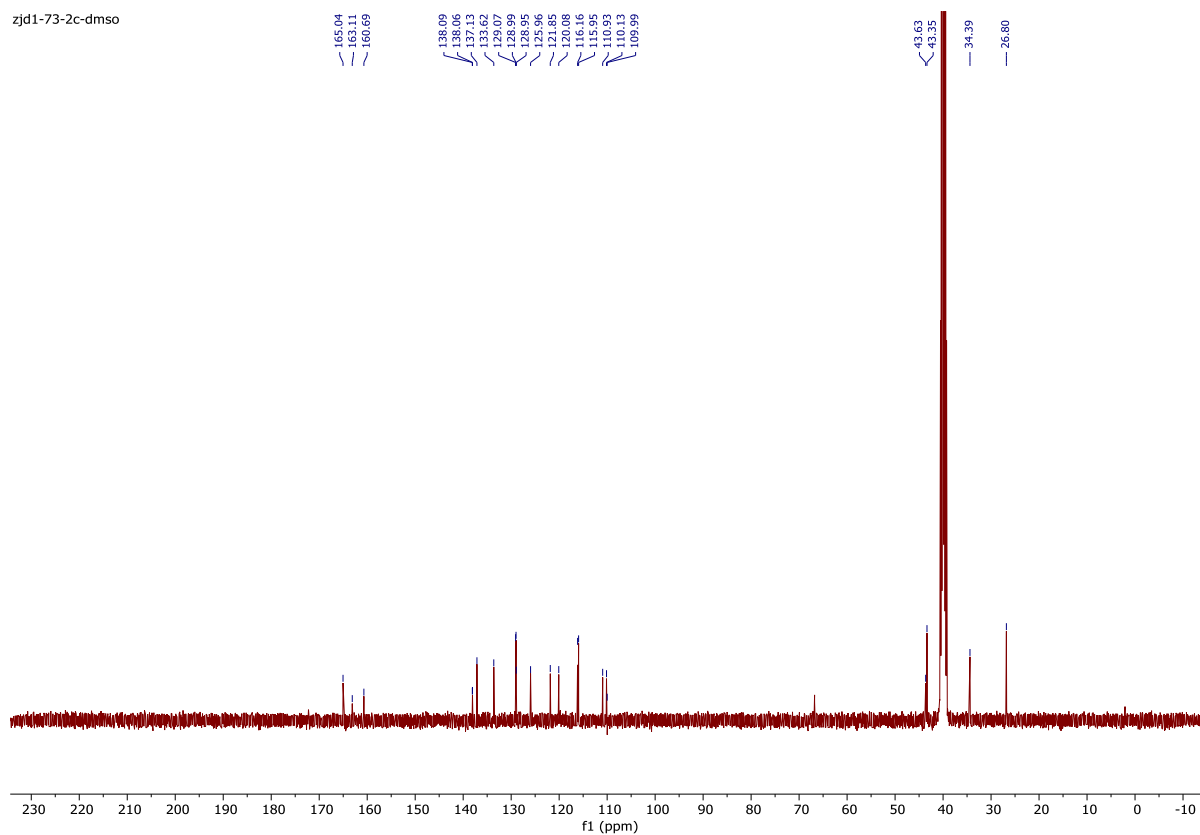
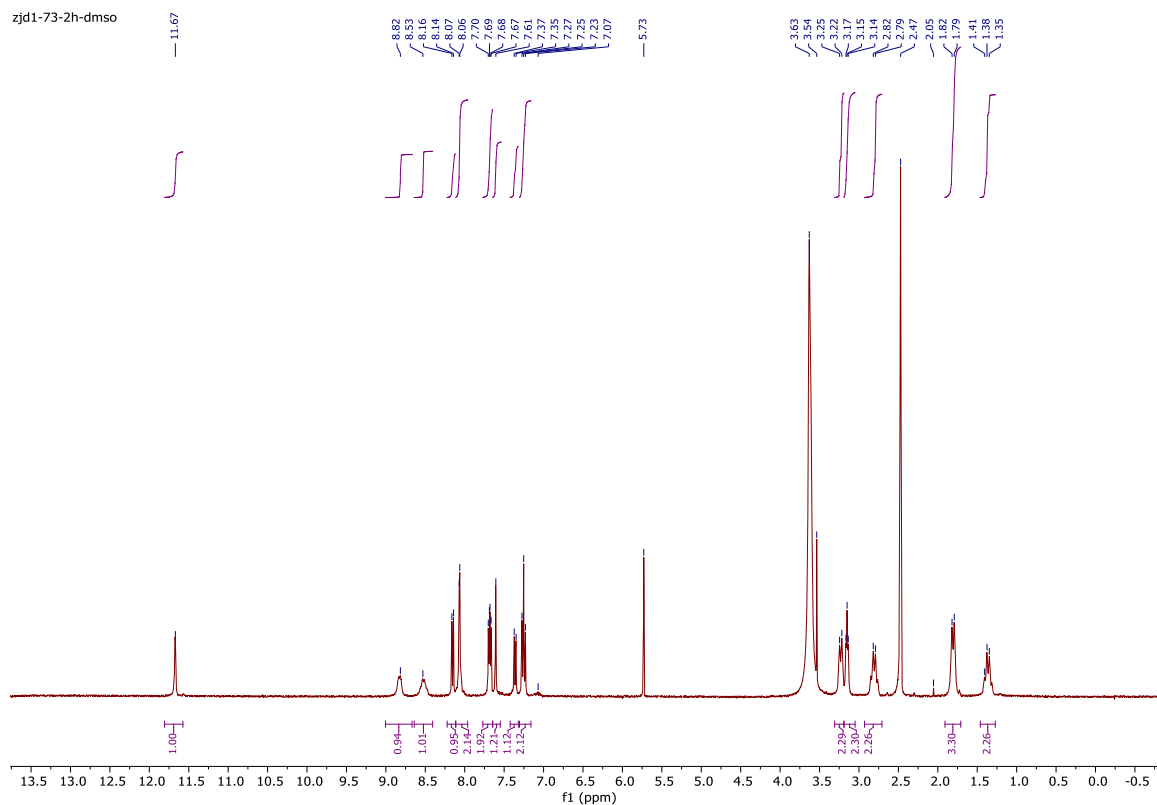
17. 5-(2,4-Difluorophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (17).



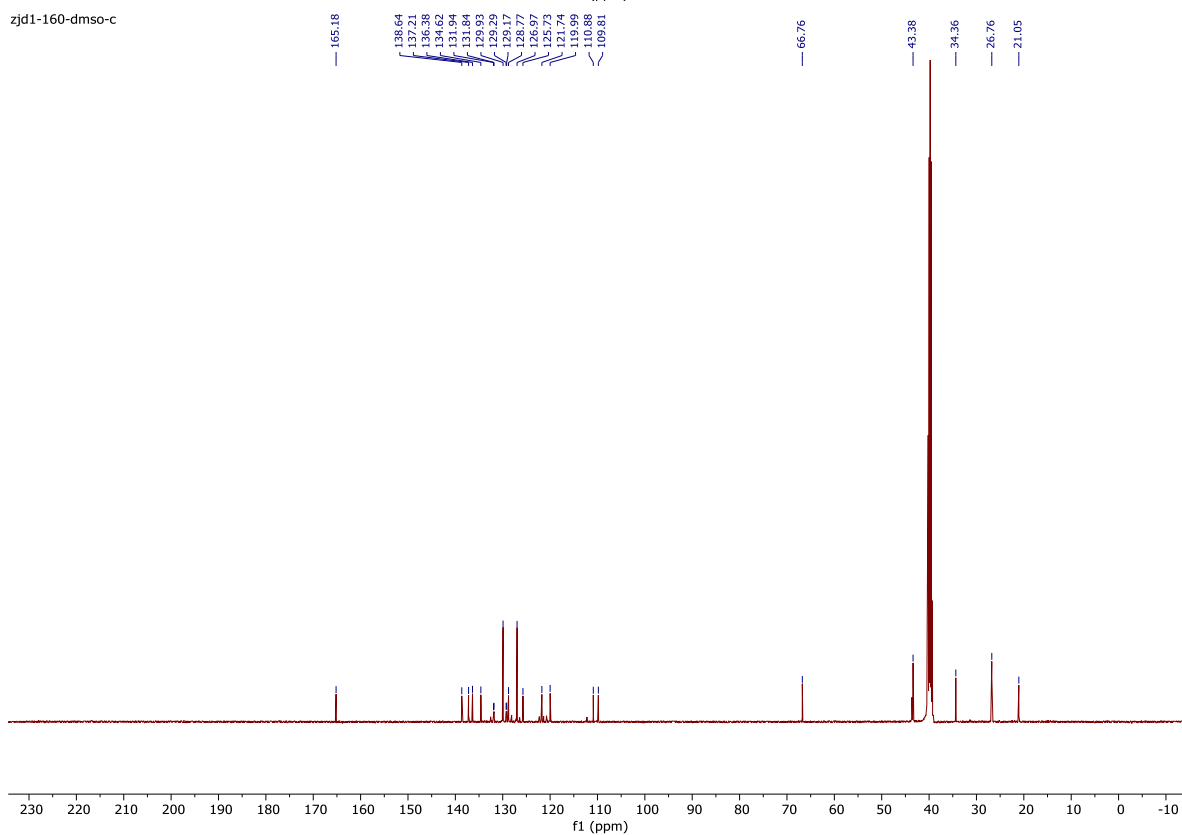
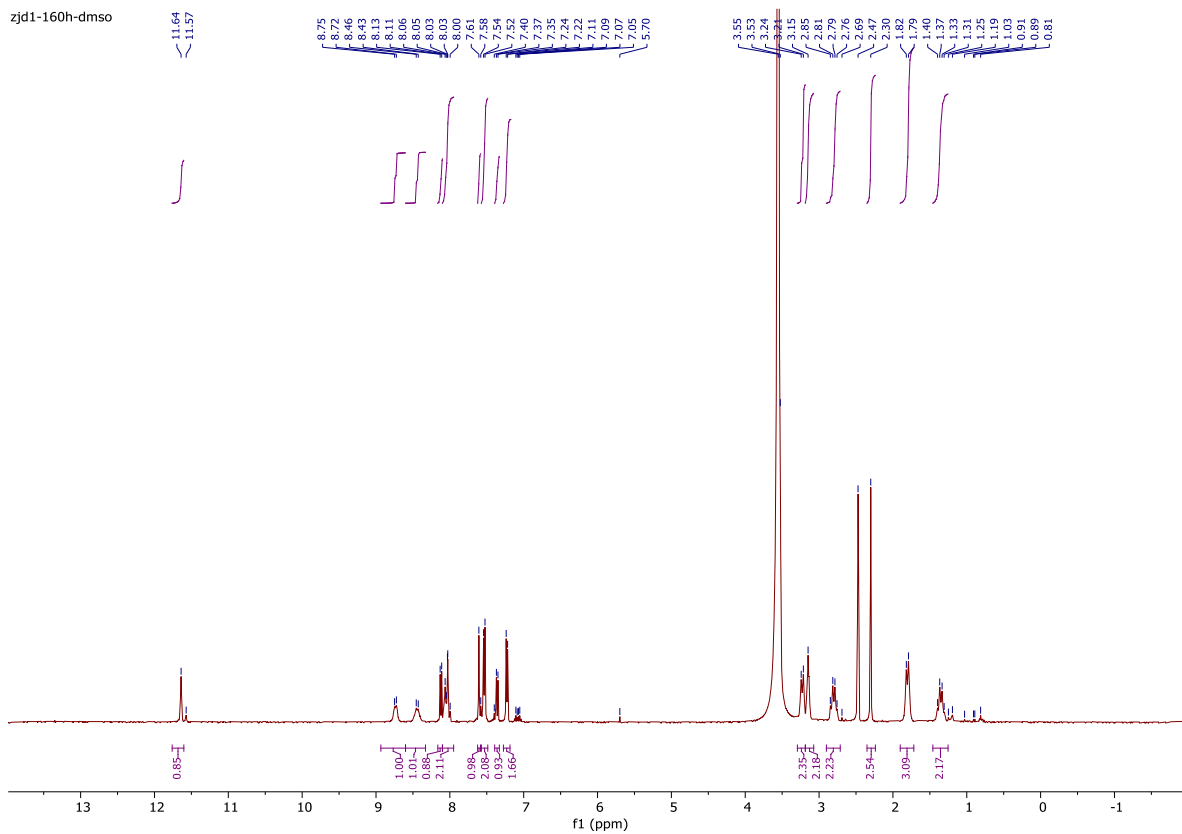
19. N-(Piperidin-4-ylmethyl)-6-(3,4,5-trimethoxyphenyl)-1H-indole-3-carboxamide Hydrochloride (19).



20. 6-(4-Fluorophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (20).

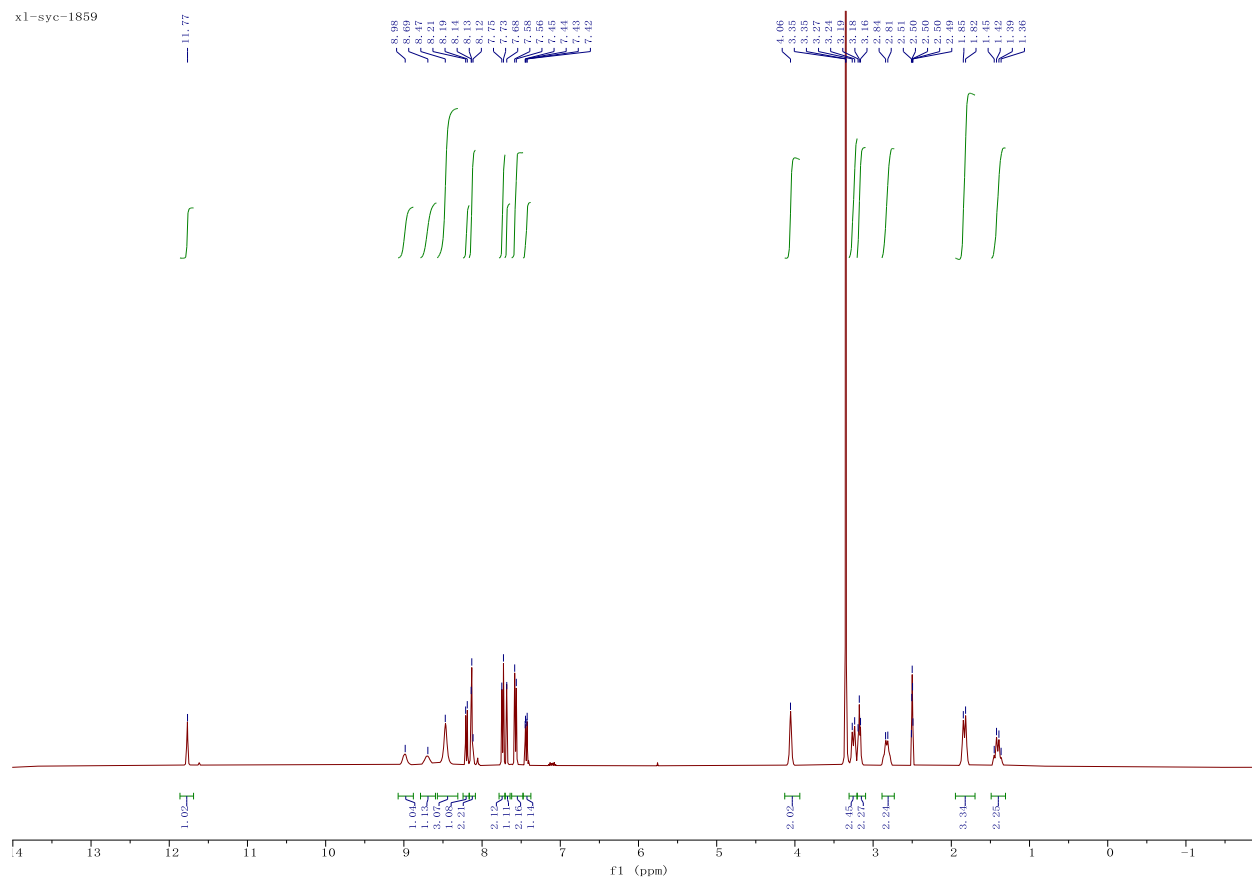


21. 6-(2-Fluorophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (21).

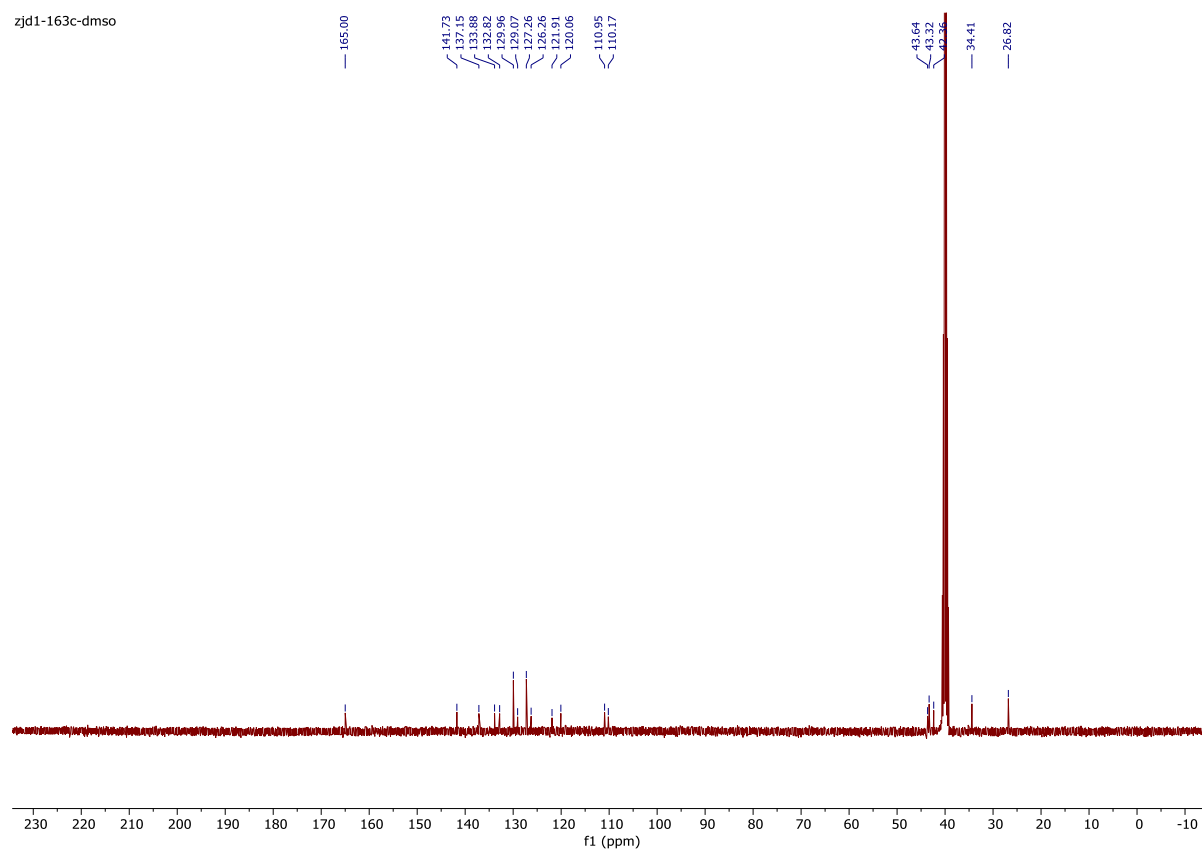


23. 6-(4-(Aminomethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (**23**).

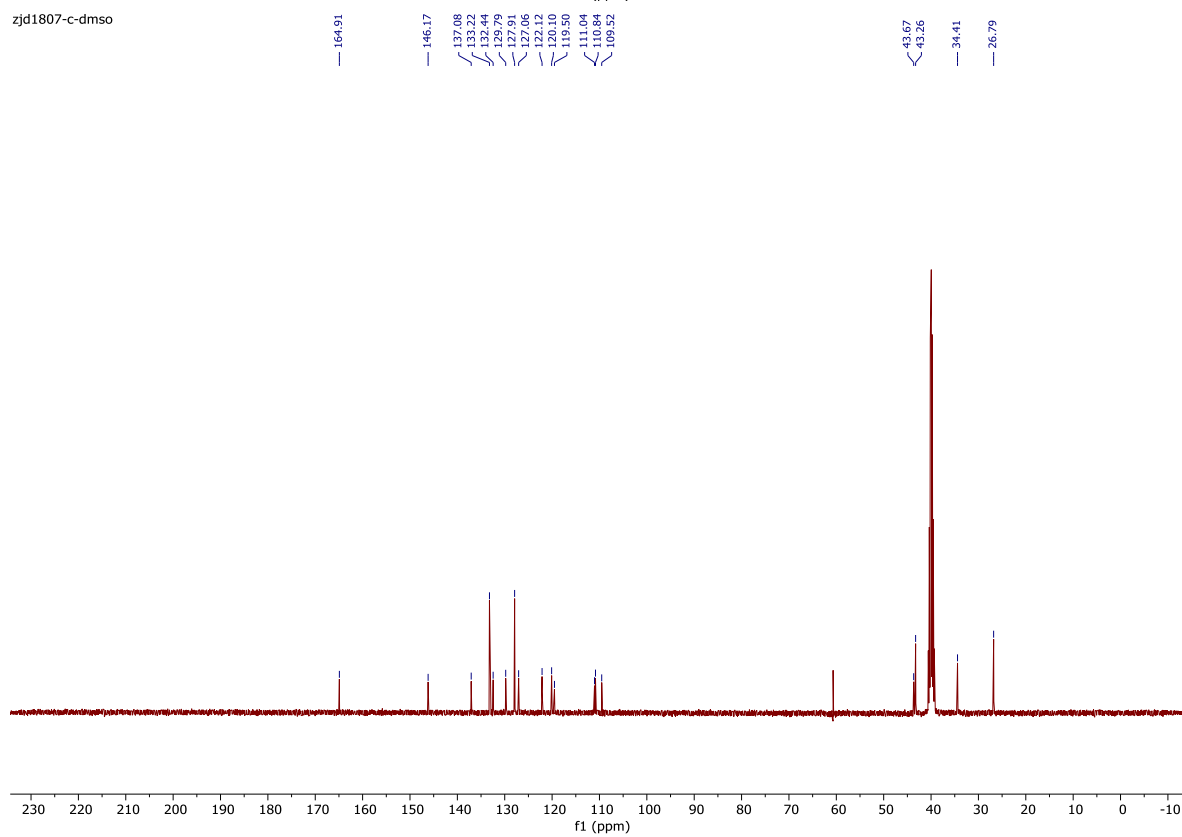
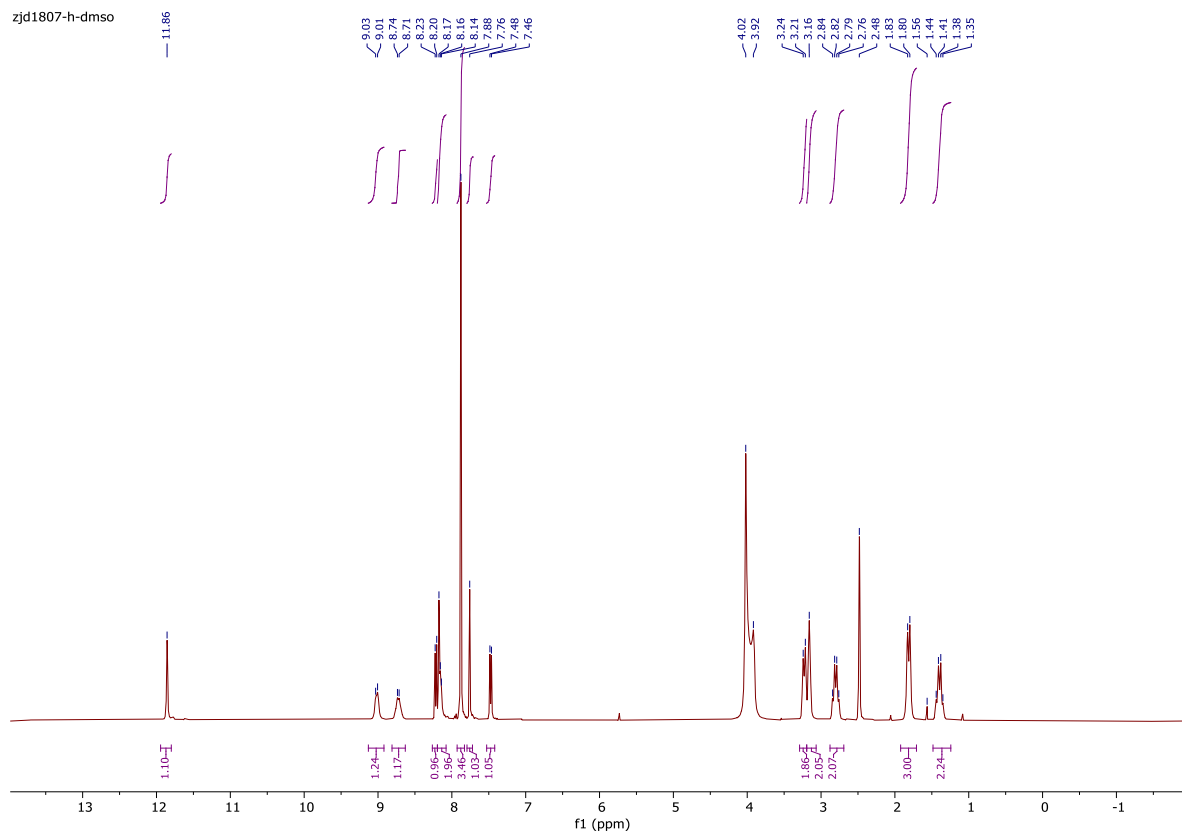
x1-syc-1859



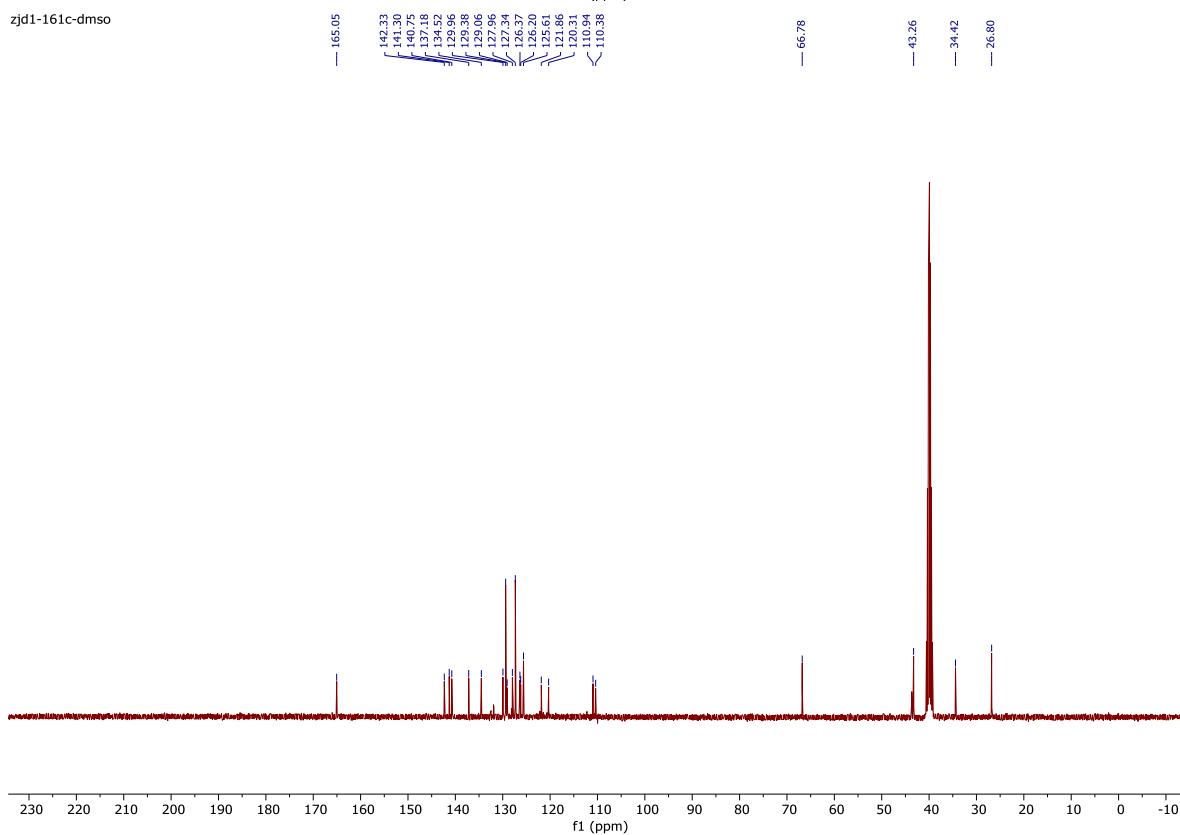
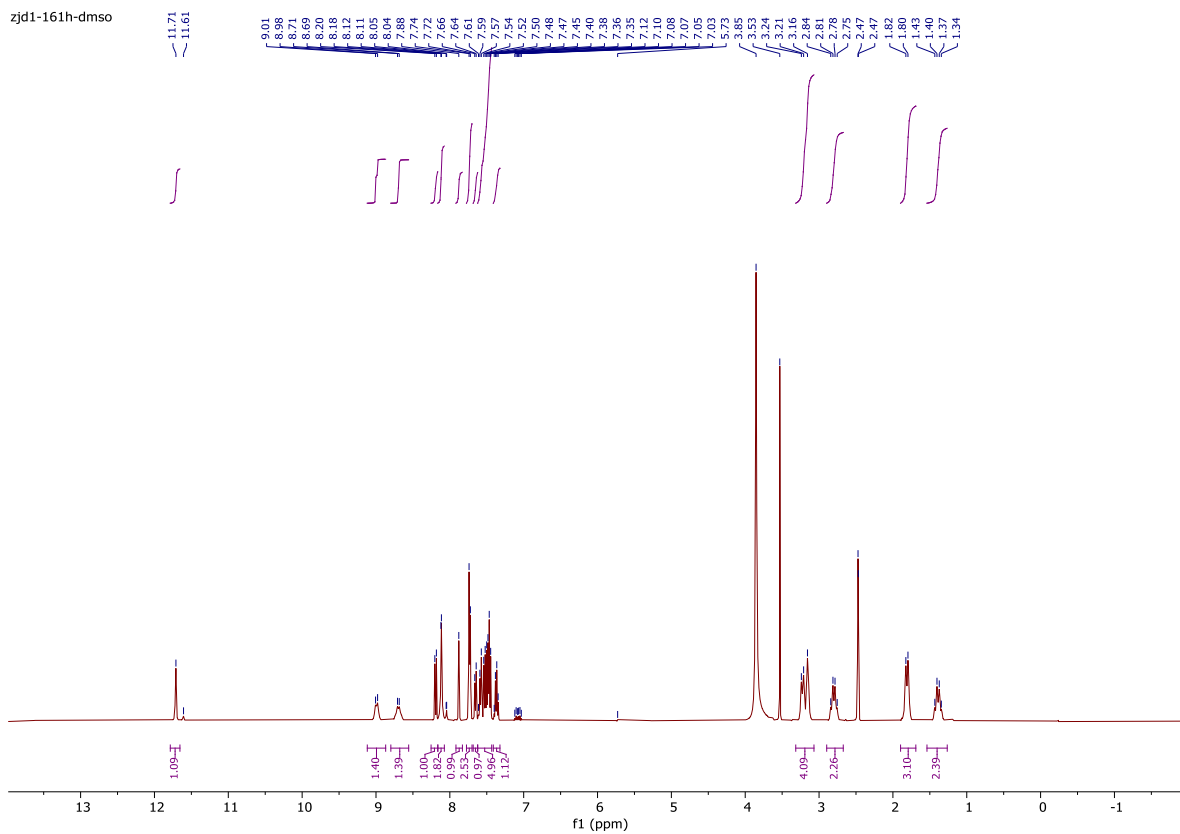
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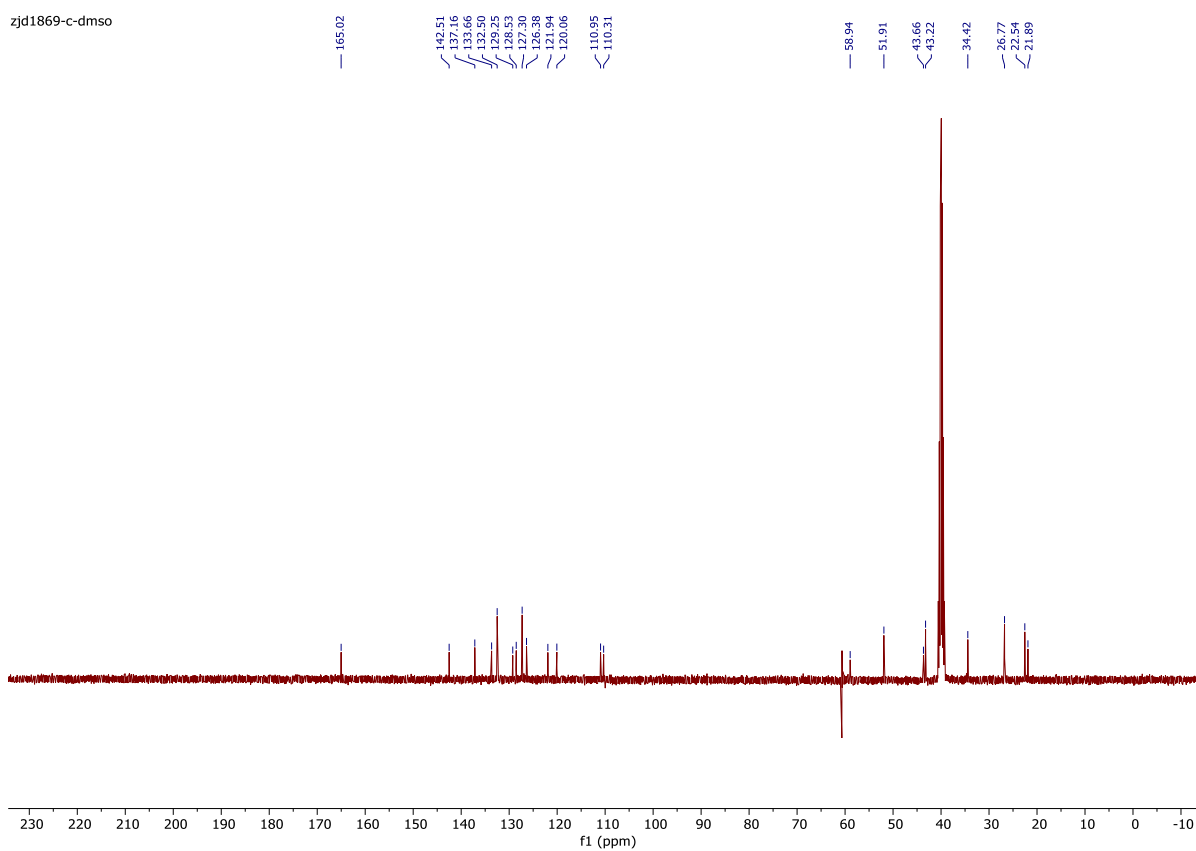
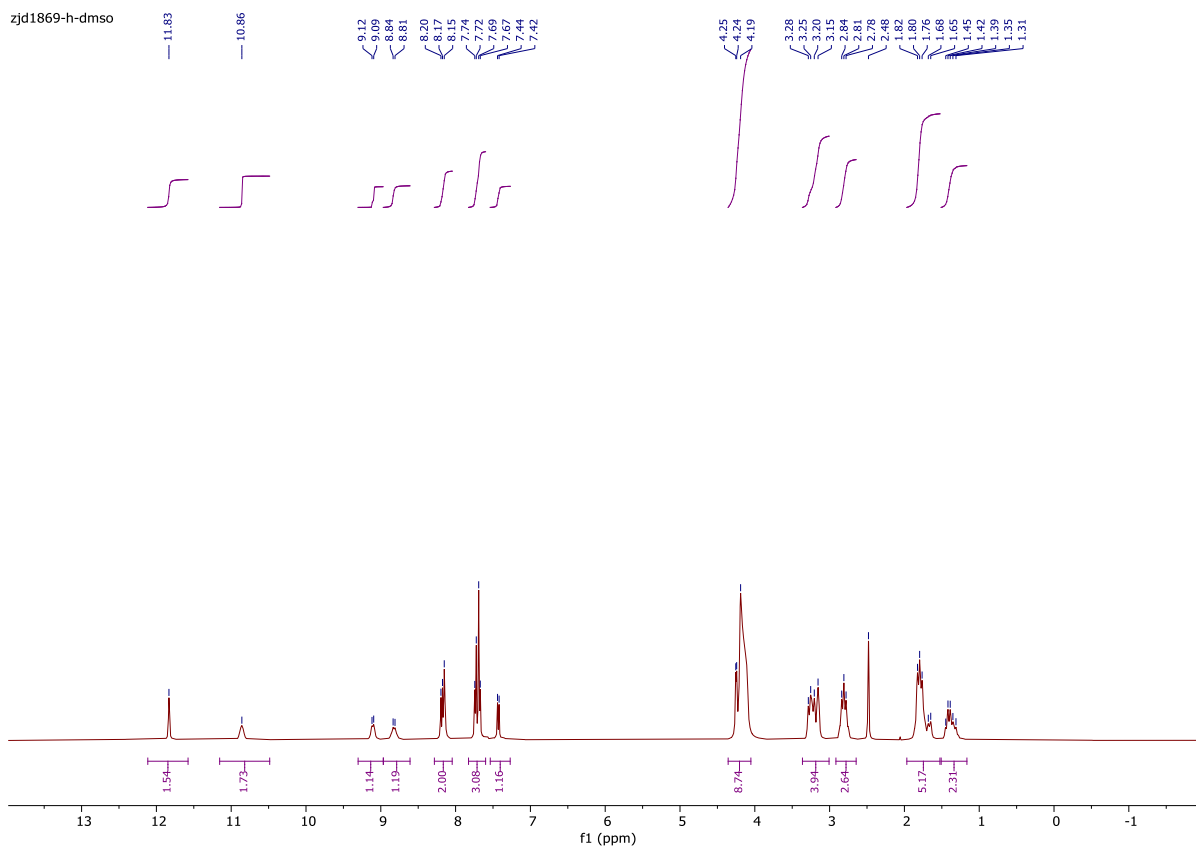
24. 6-(4-Cyanophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (24).



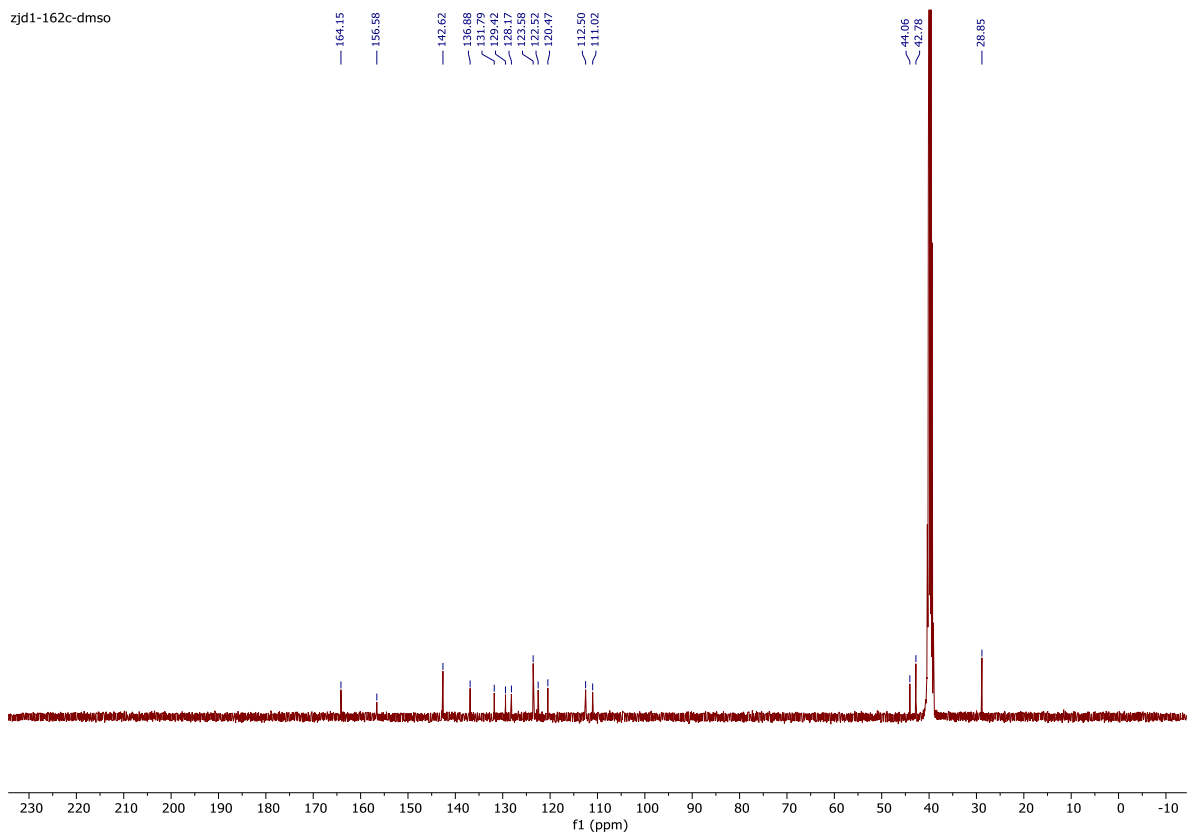
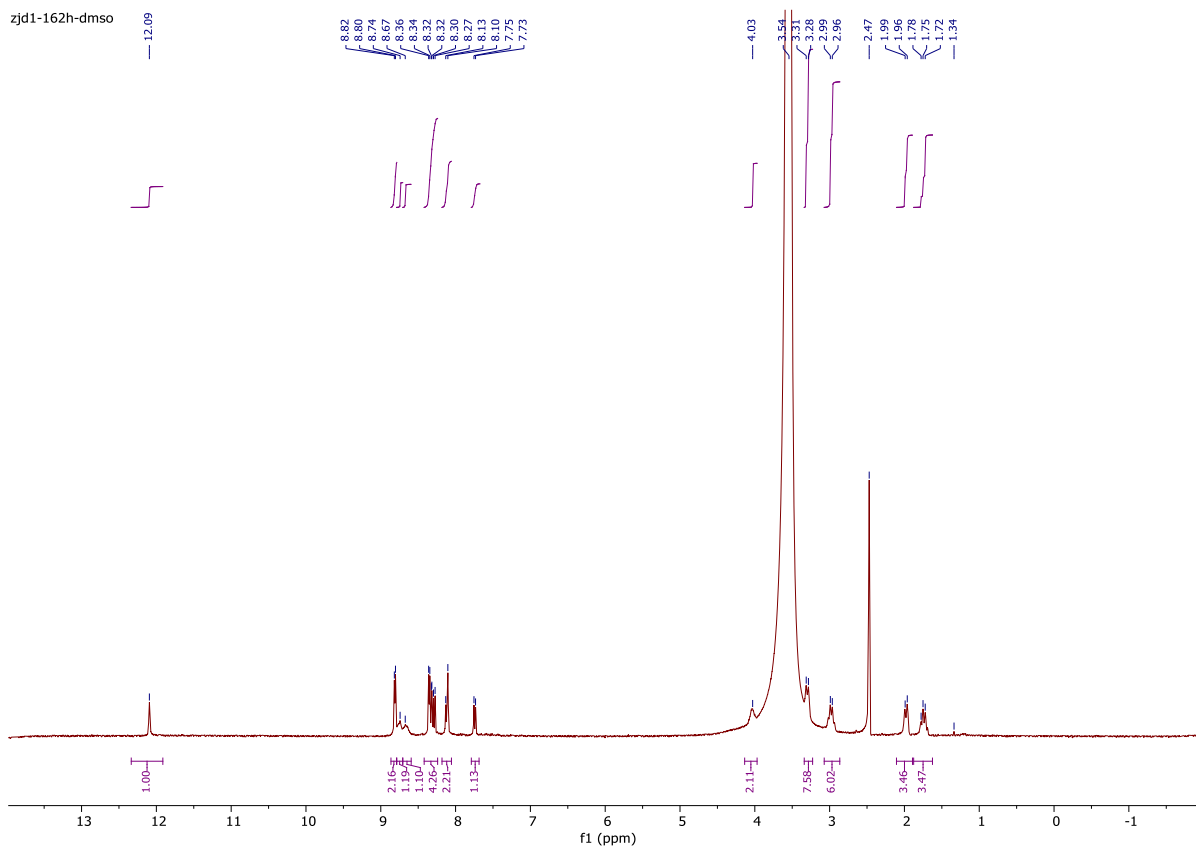
25. 6-([1,1'-Biphenyl]-4-yl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (25).



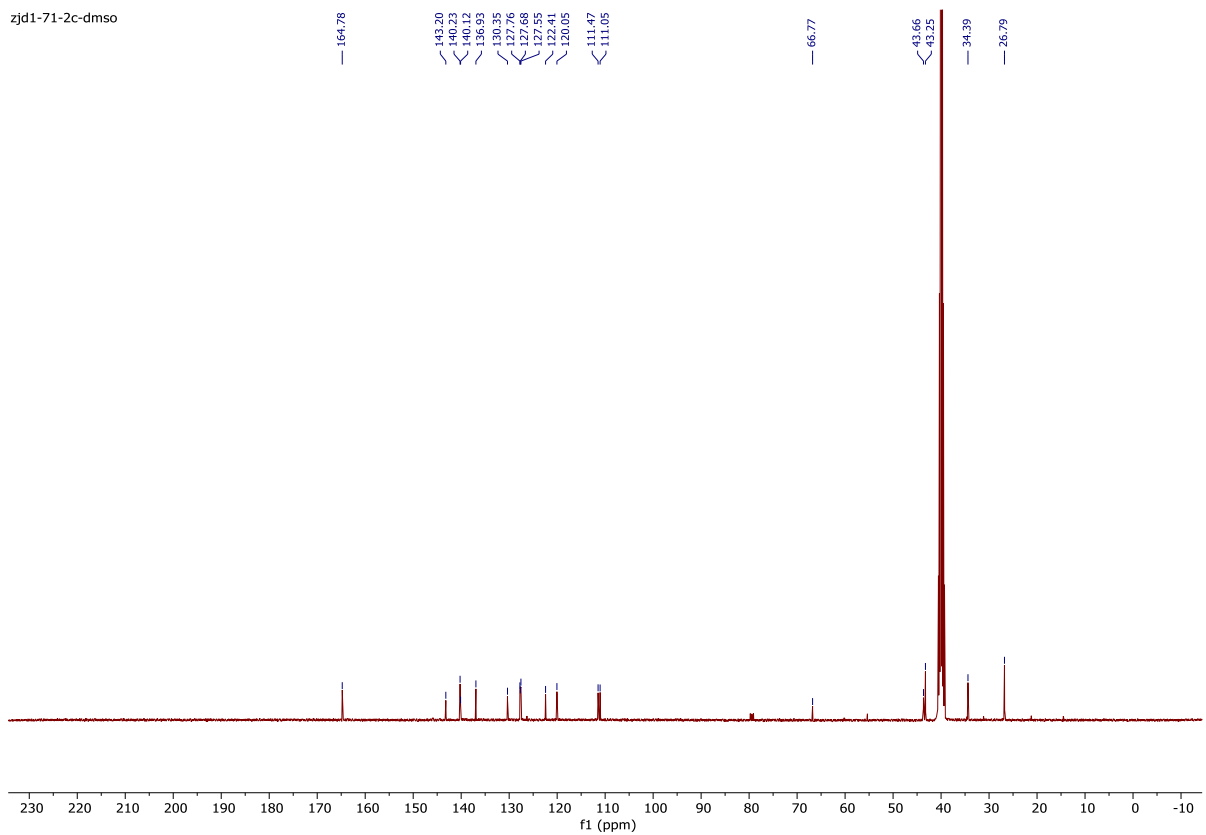
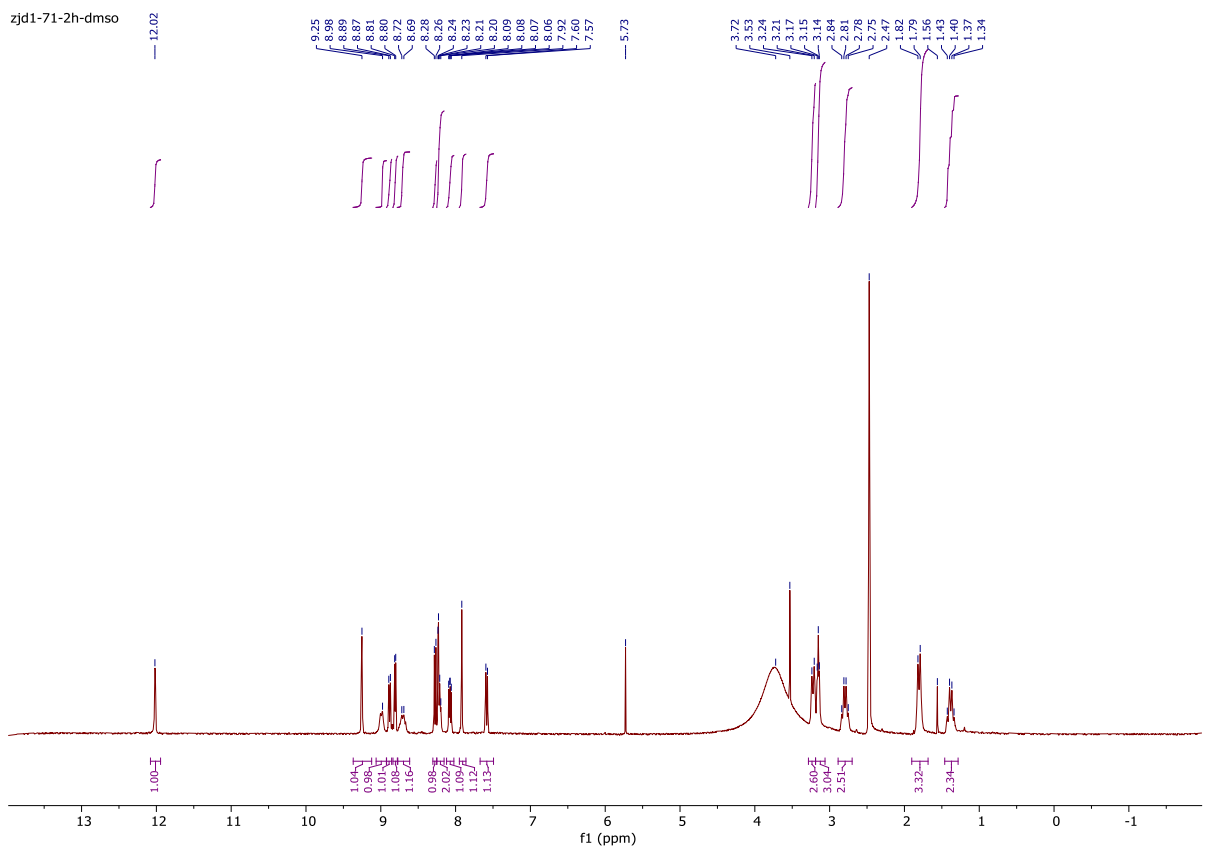
26. 6-(4-(Piperidin-1-ylmethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (**26**).



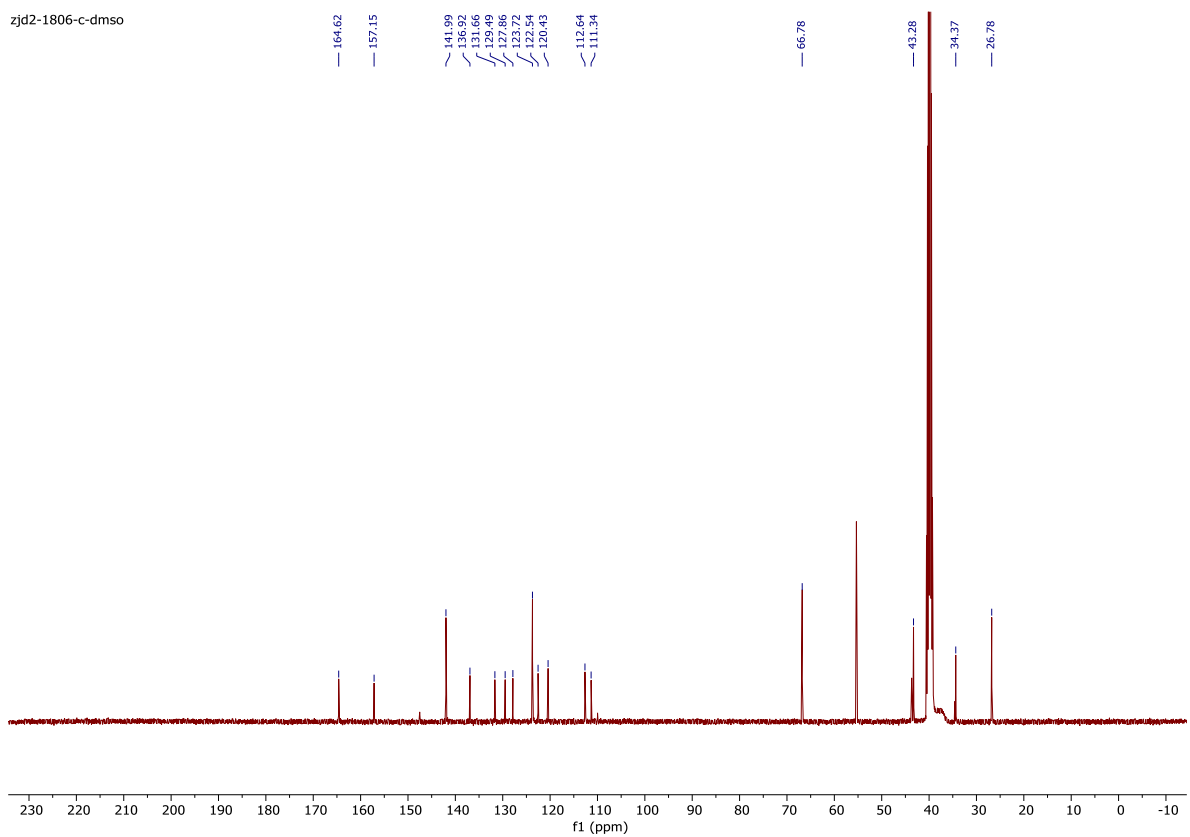
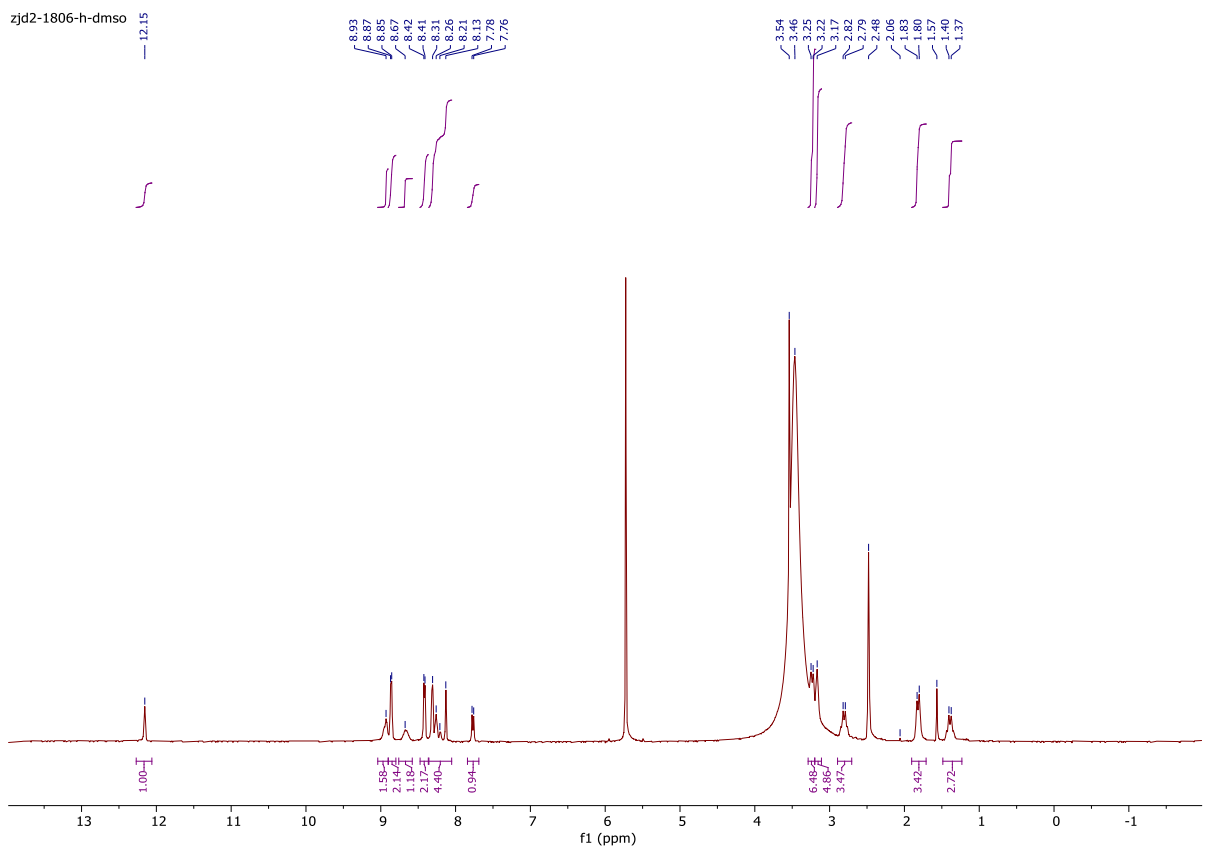
27. 6-(6-Chloropyridin-3-yl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (27).



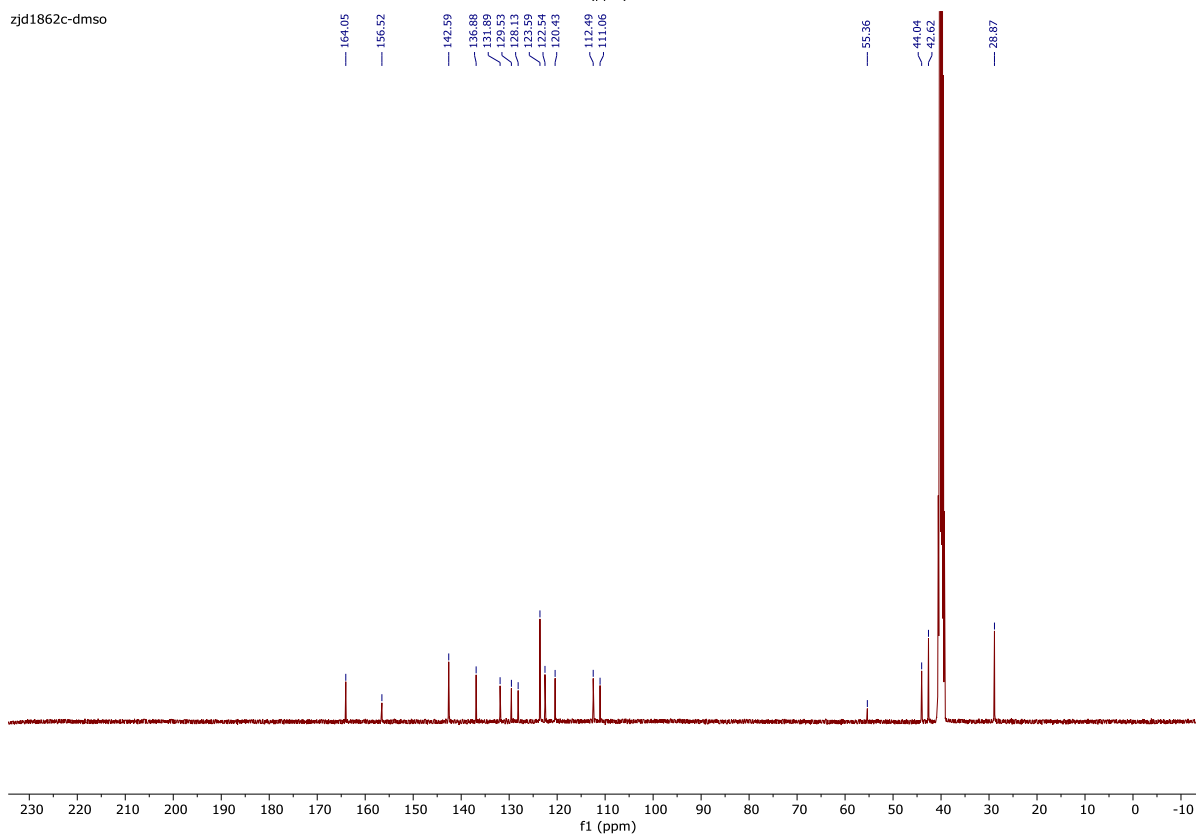
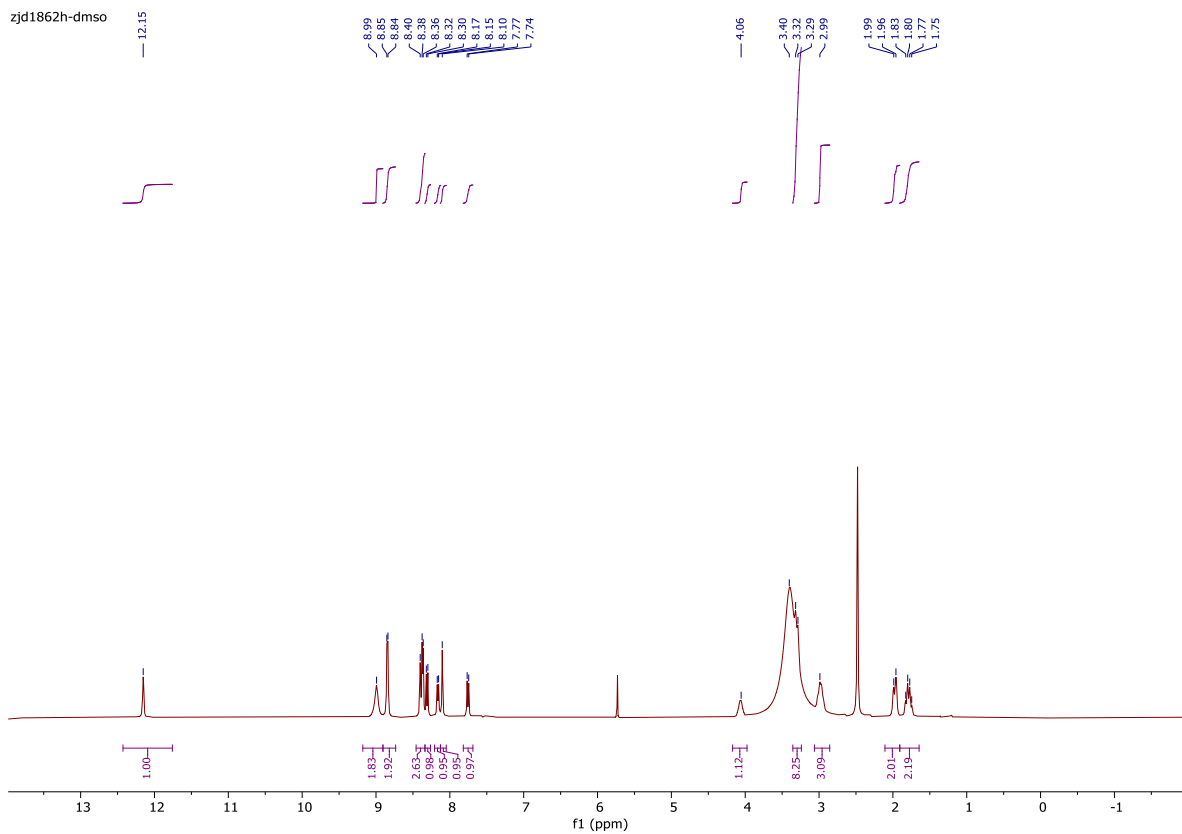
28 . N-(Piperidin-4-ylmethyl)-6-(pyridin-3-yl)-1H-indole-3-carboxamide Hydrochloride (28).



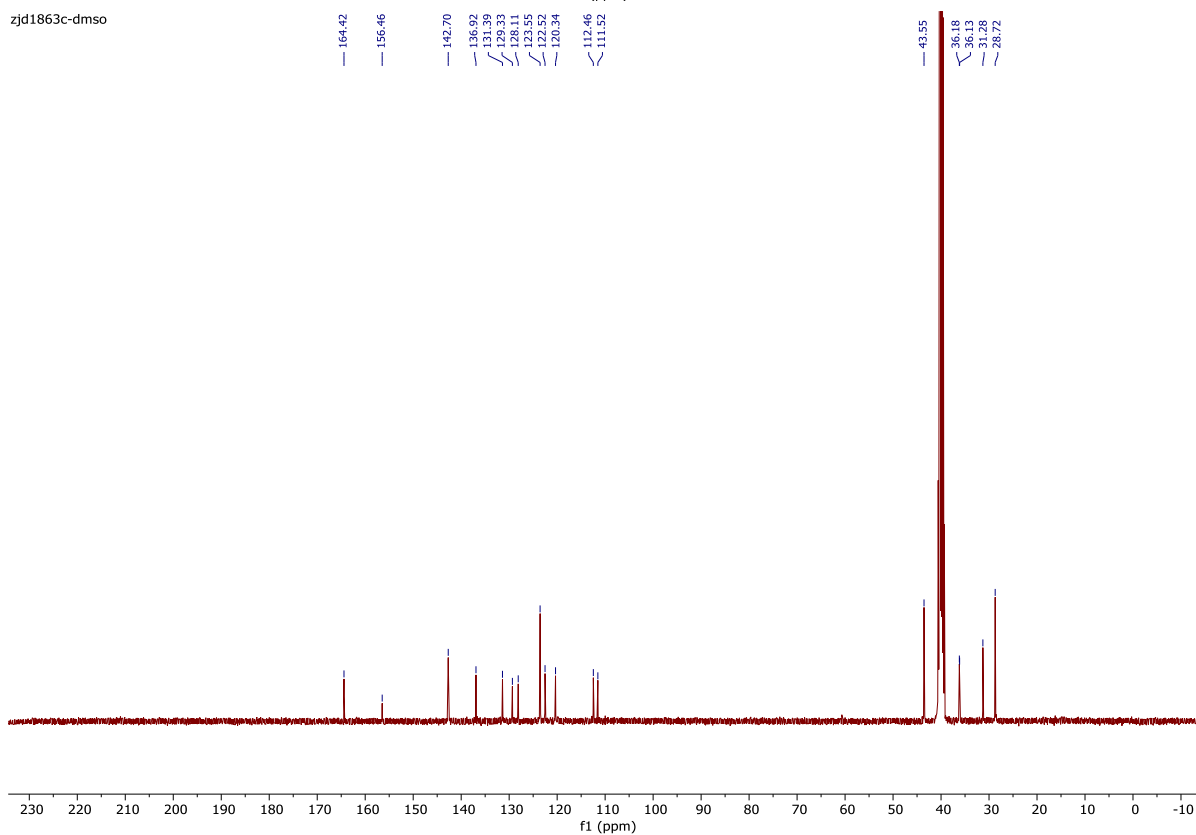
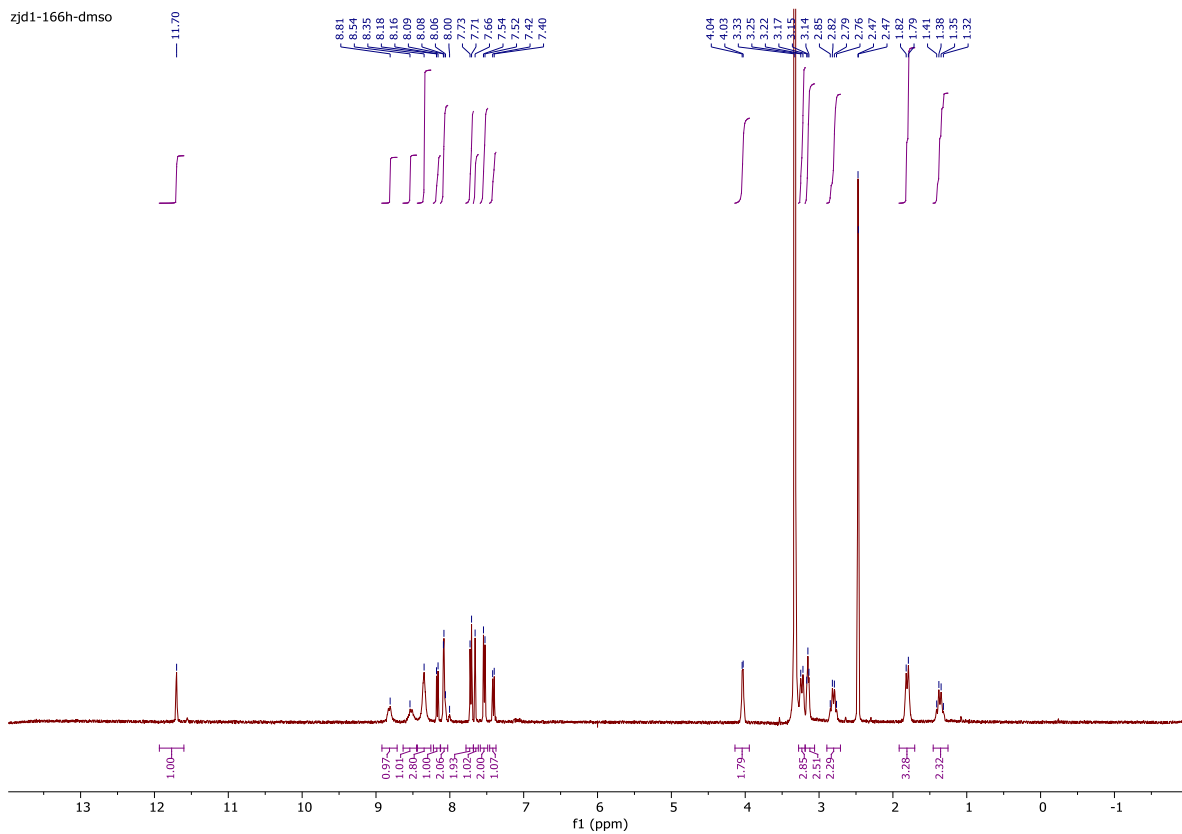
29. N-(Piperidin-4-ylmethyl)-6-(pyridin-4-yl)-1H-indole-3-carboxamide Hydrochloride (29).



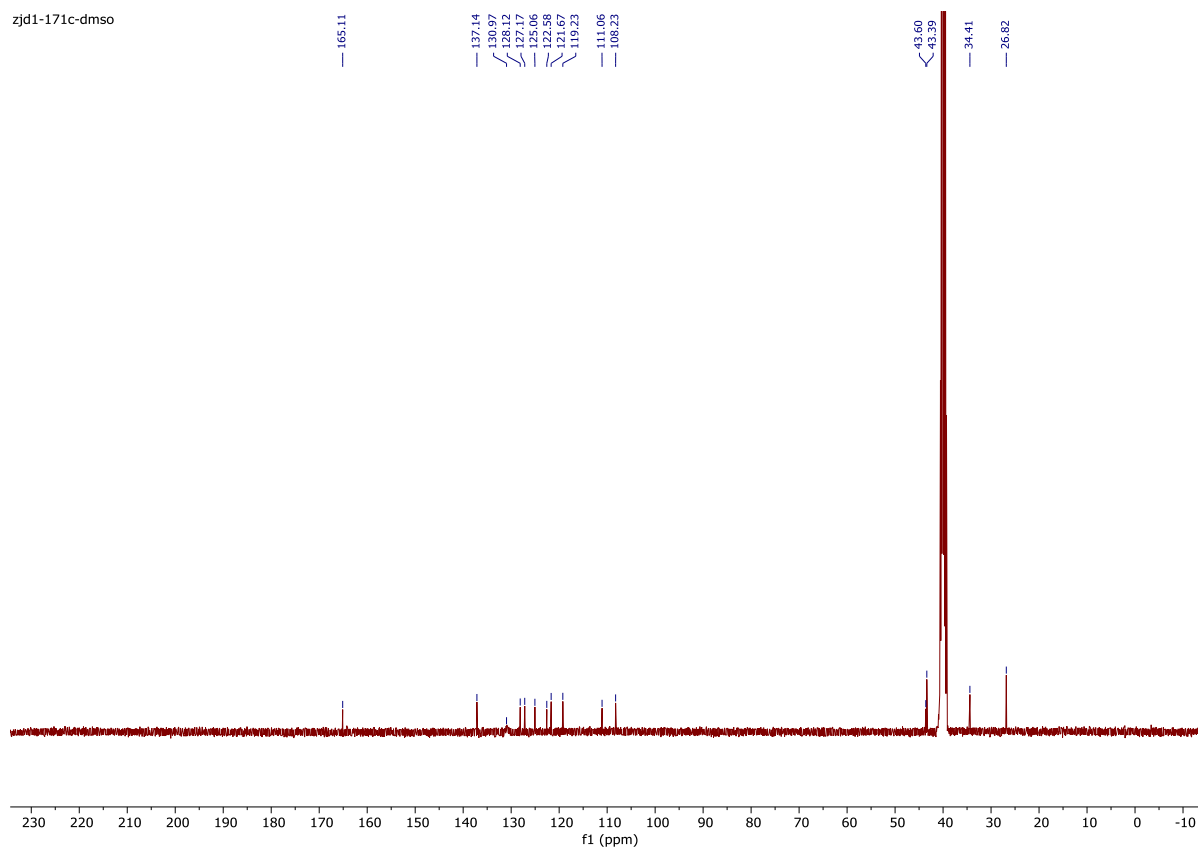
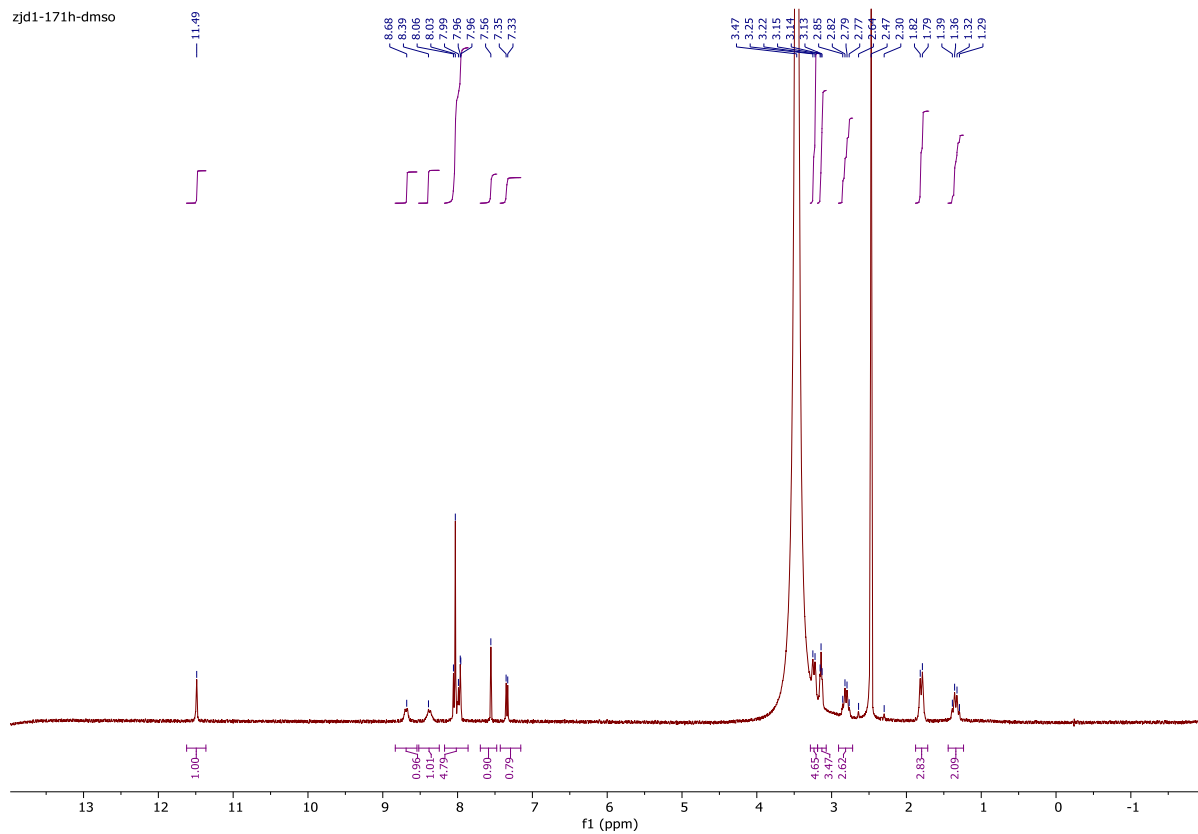
30. N-(Piperidin-4-yl)-6-(pyridin-4-yl)-1H-indole-3-carboxamide Hydrochloride (30).



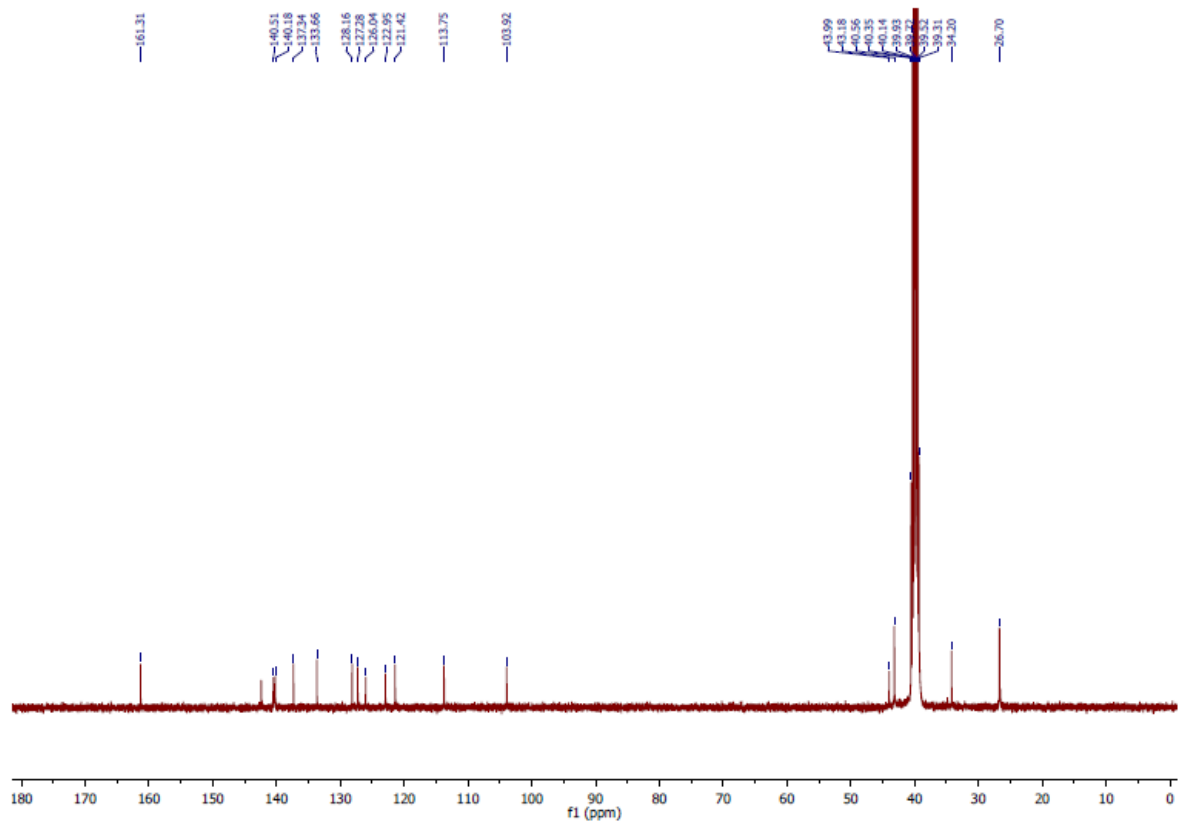
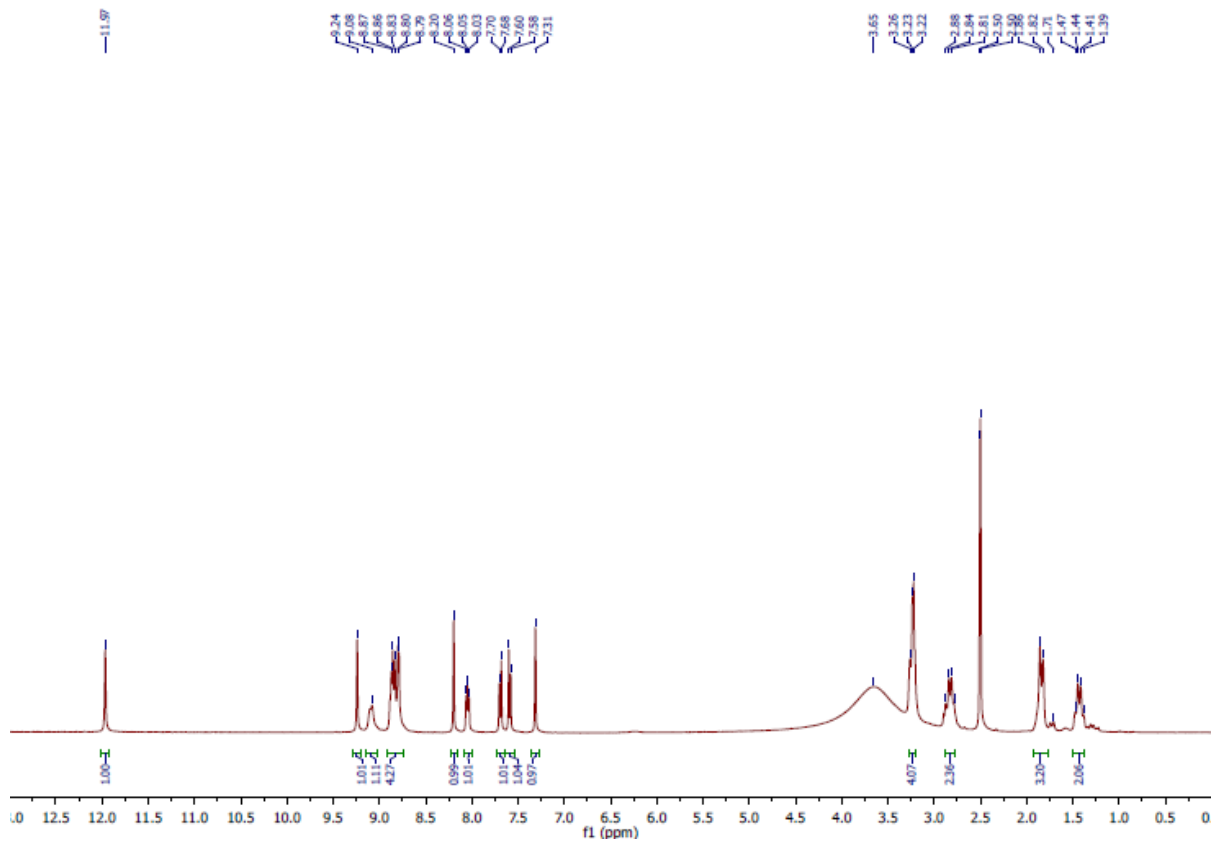
31. N-(2-(Piperidin-4-yl)ethyl)-6-(pyridin-4-yl)-1H-indole-3-carboxamide Hydrochloride (31).



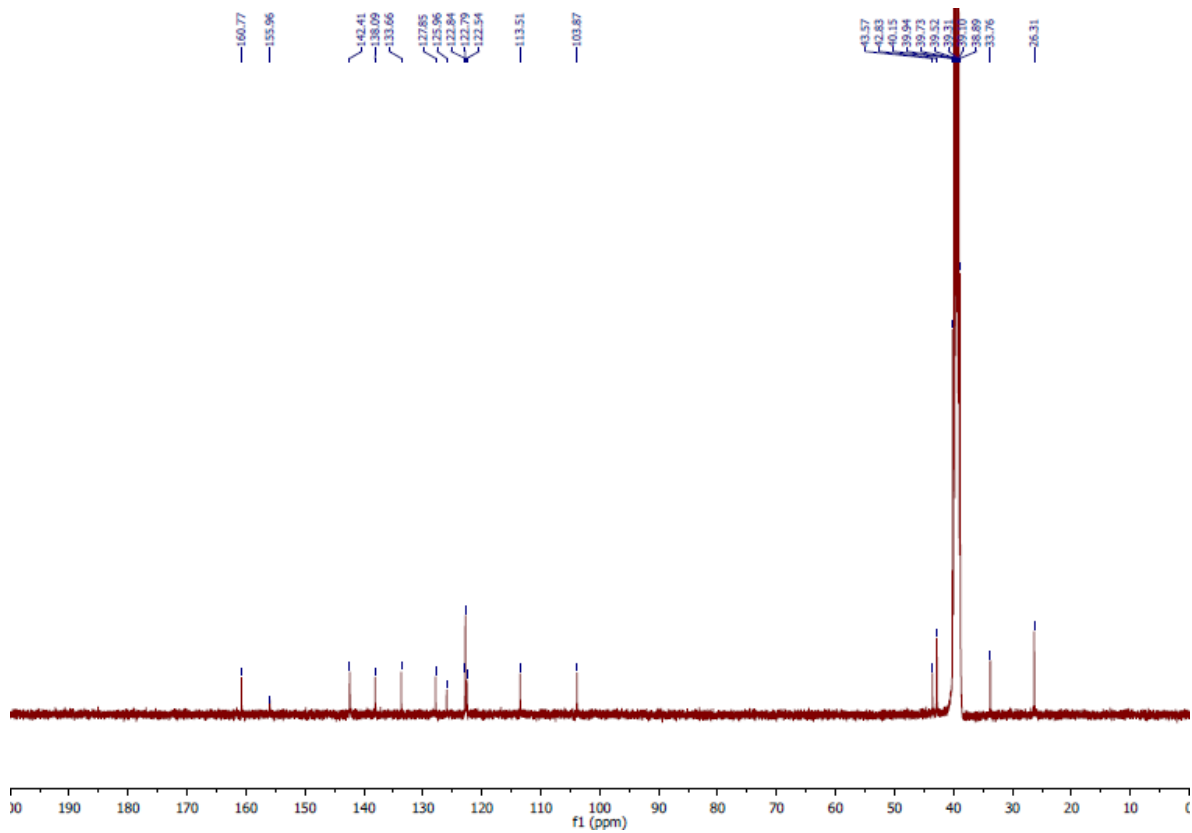
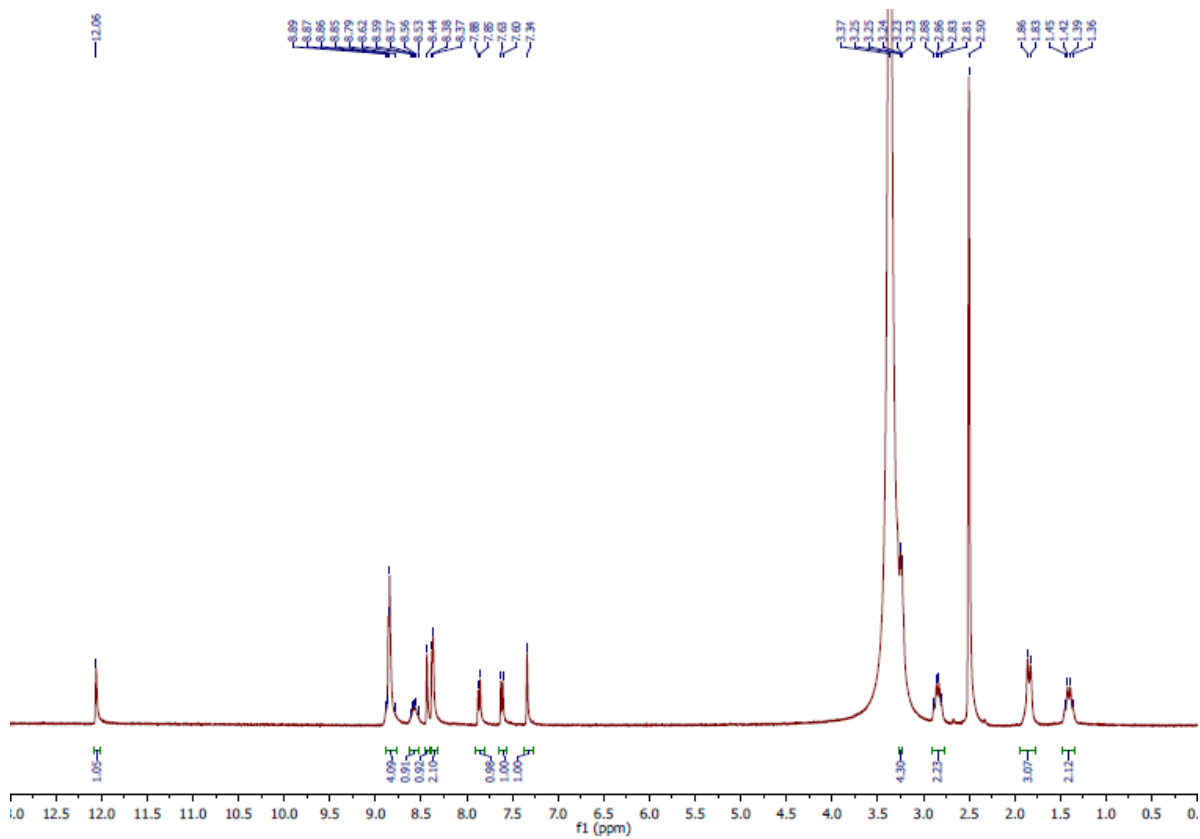
32. N-(Piperidin-4-ylmethyl)-6-(1H-pyrazol-3-yl)-1H-indole-3-carboxamide Hydrochloride (32).



33. N-(Piperidin-4-ylmethyl)-5-(pyridin-3-yl)-1H-indole-2-carboxamide Hydrochloride (**33**).

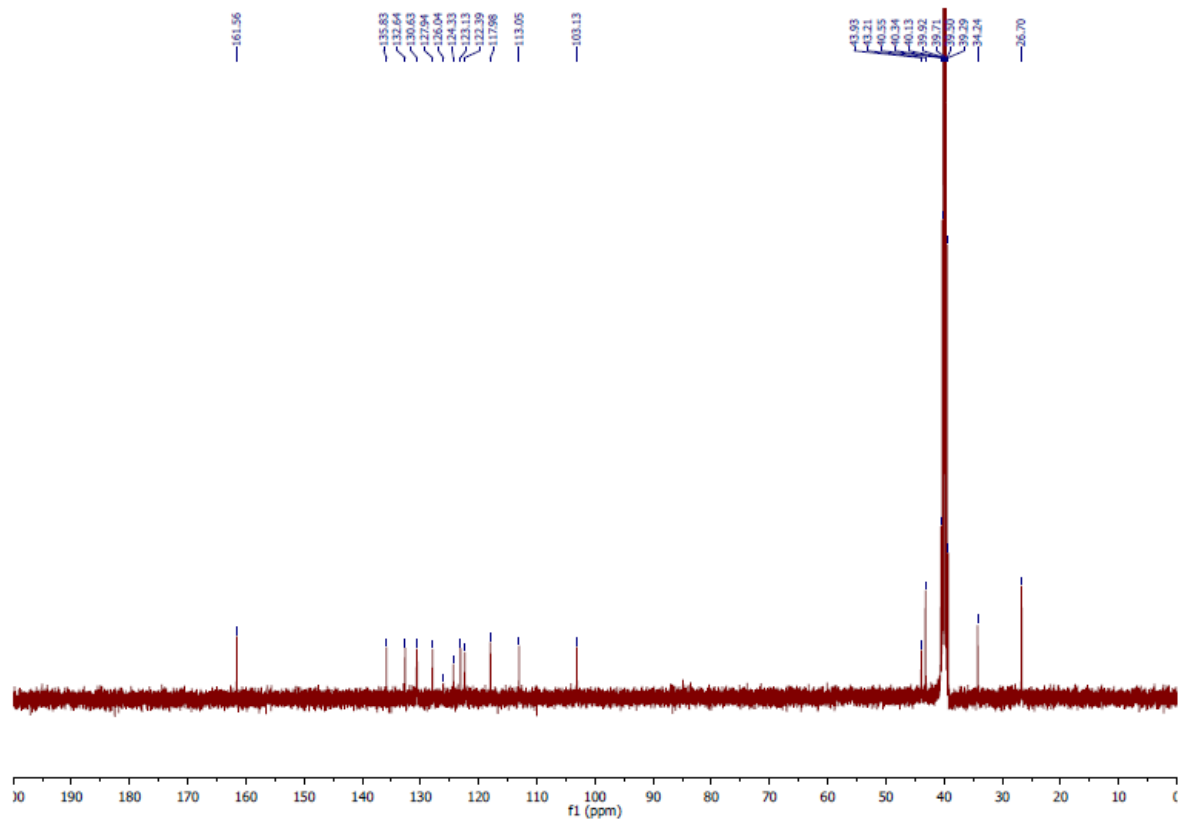
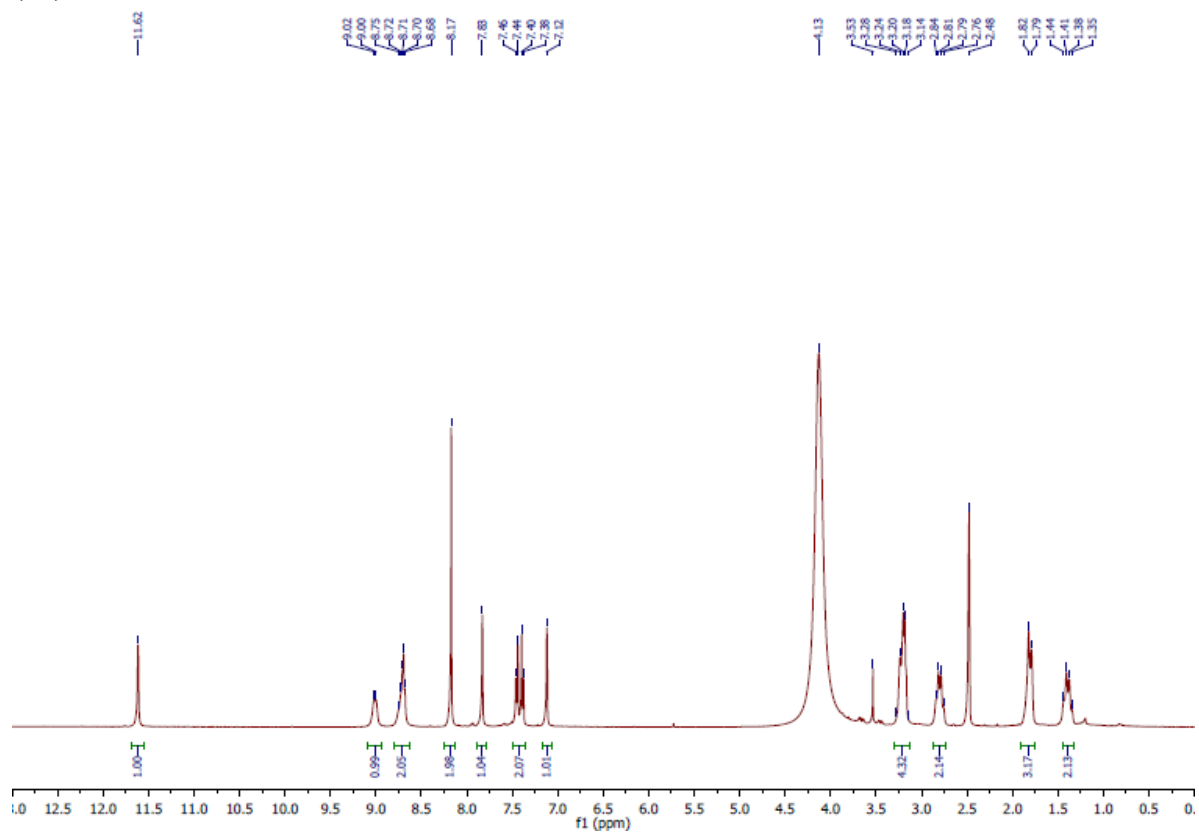


34. N-(Piperidin-4-ylmethyl)-5-(pyridin-4-yl)-1H-indole-2-carboxamide Hydrochloride (**34**).

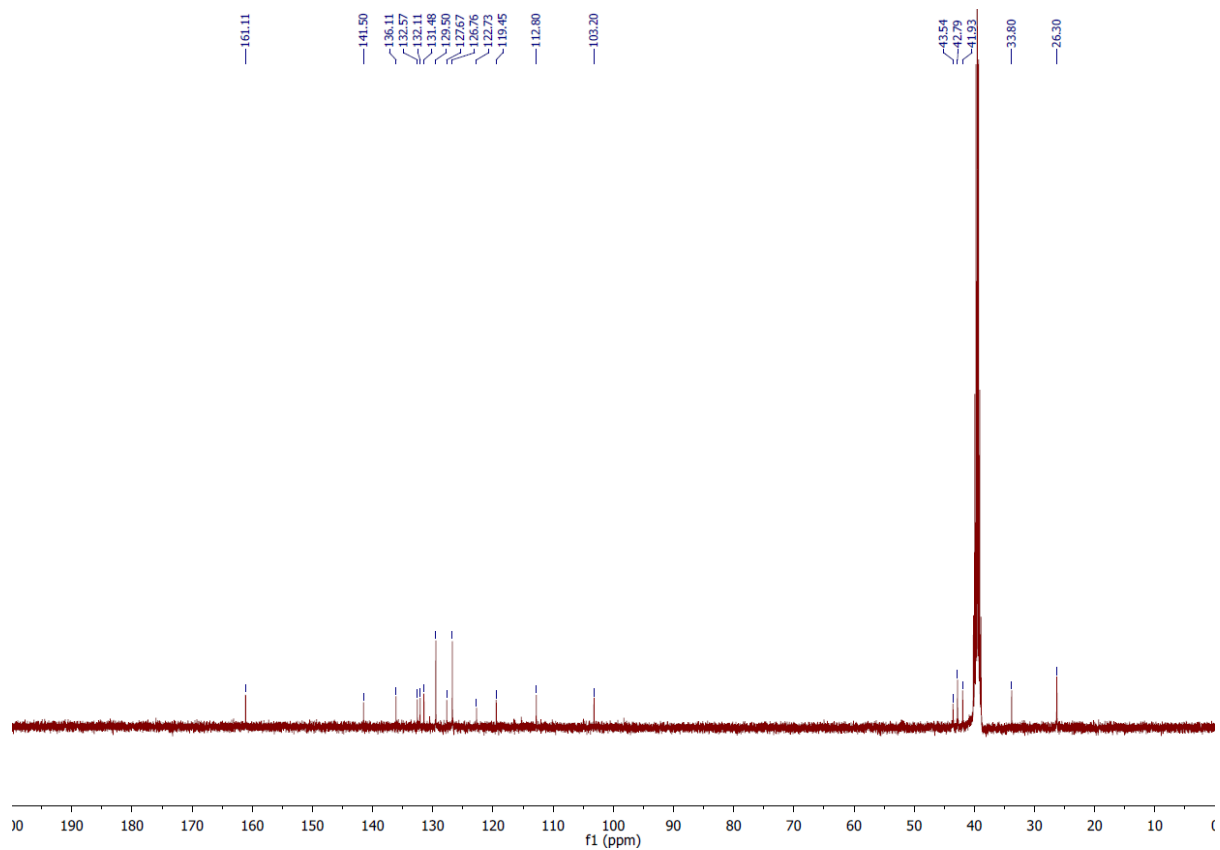
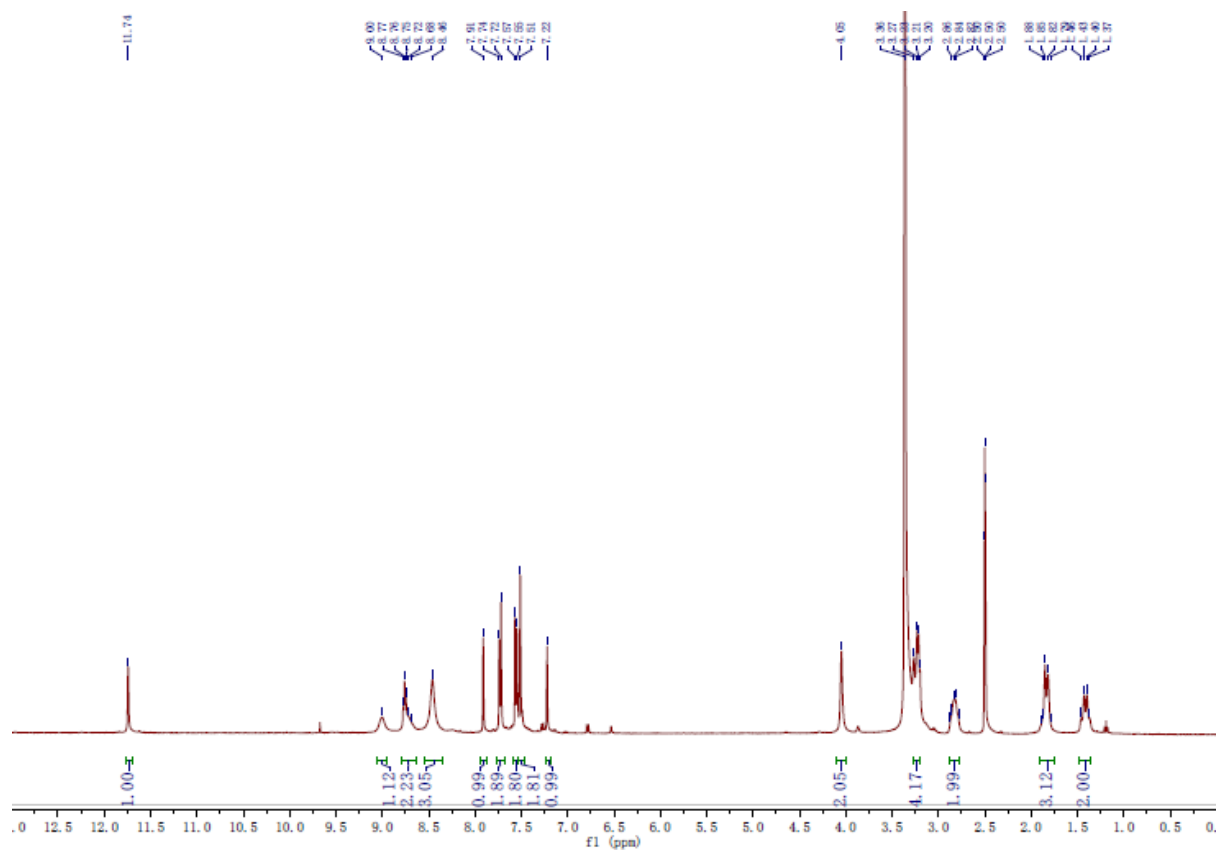


35. N-(Piperidin-4-ylmethyl)-5-(1H-pyrazol-4-yl)-1H-indole-2-carboxamide Hydrochloride

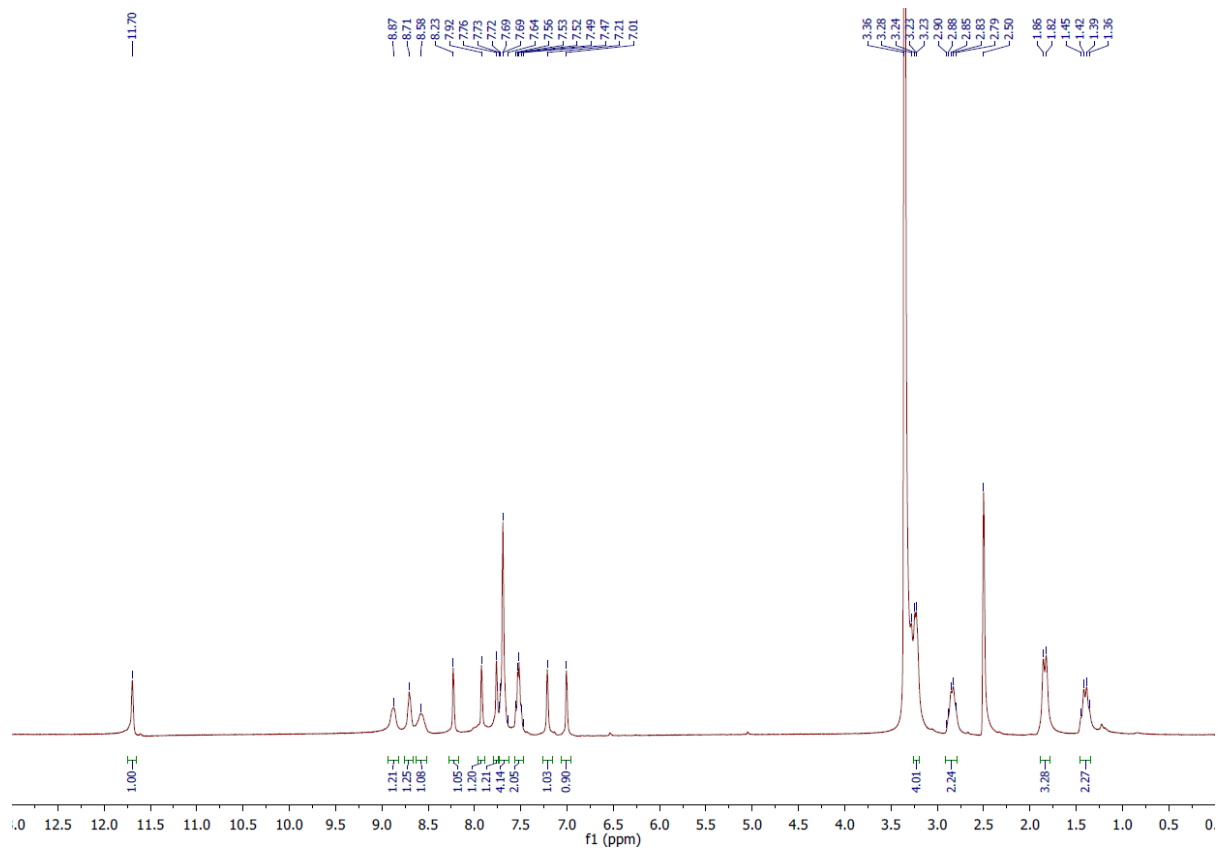
(35).



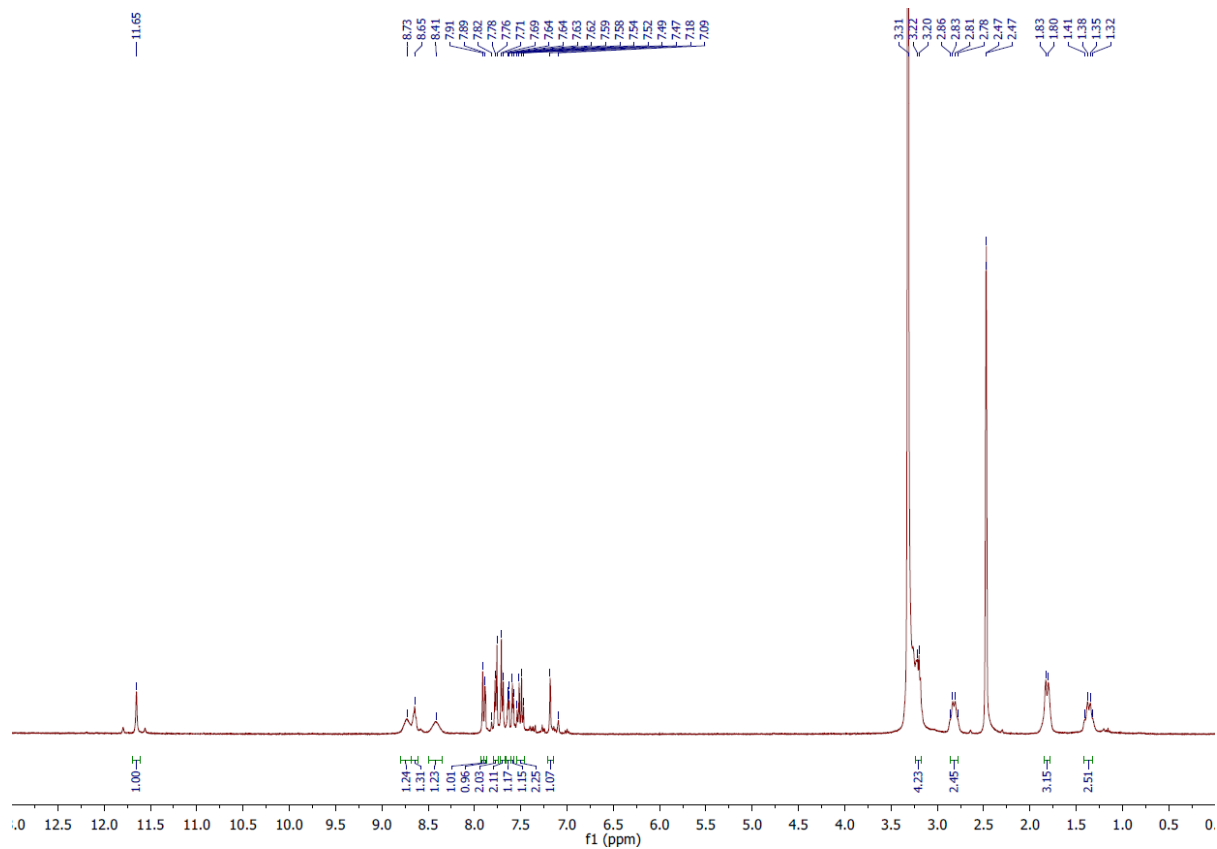
36. 5-(4-(Aminomethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**36**).

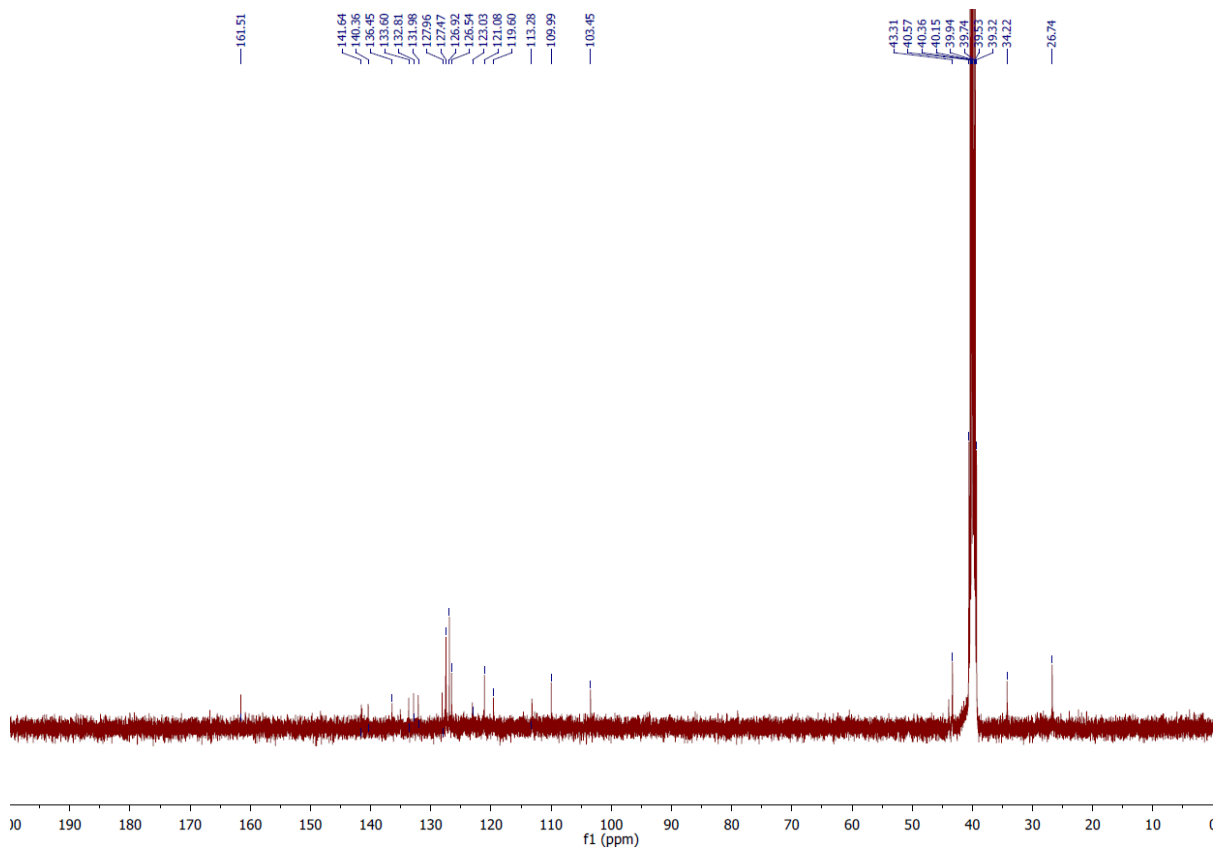


37. 5-(4-(Furan-3-yl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**37**).

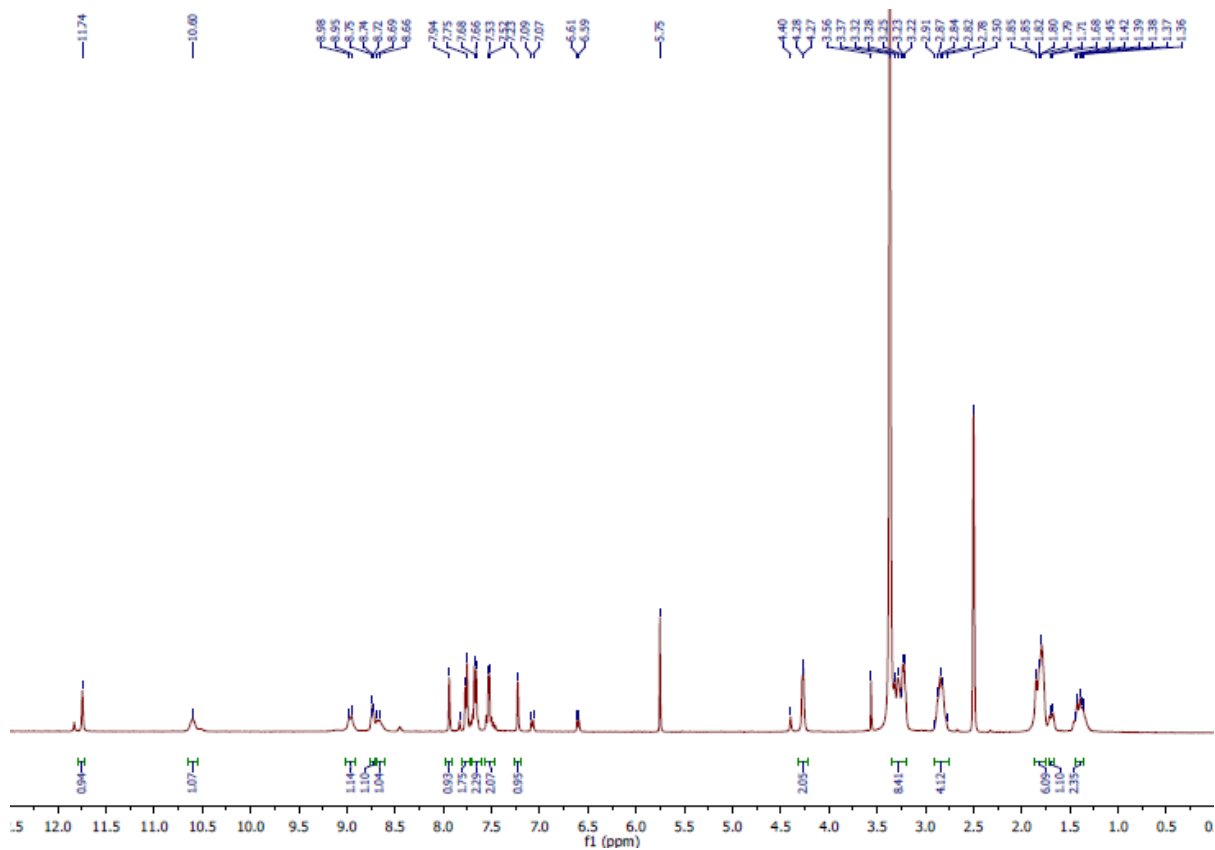


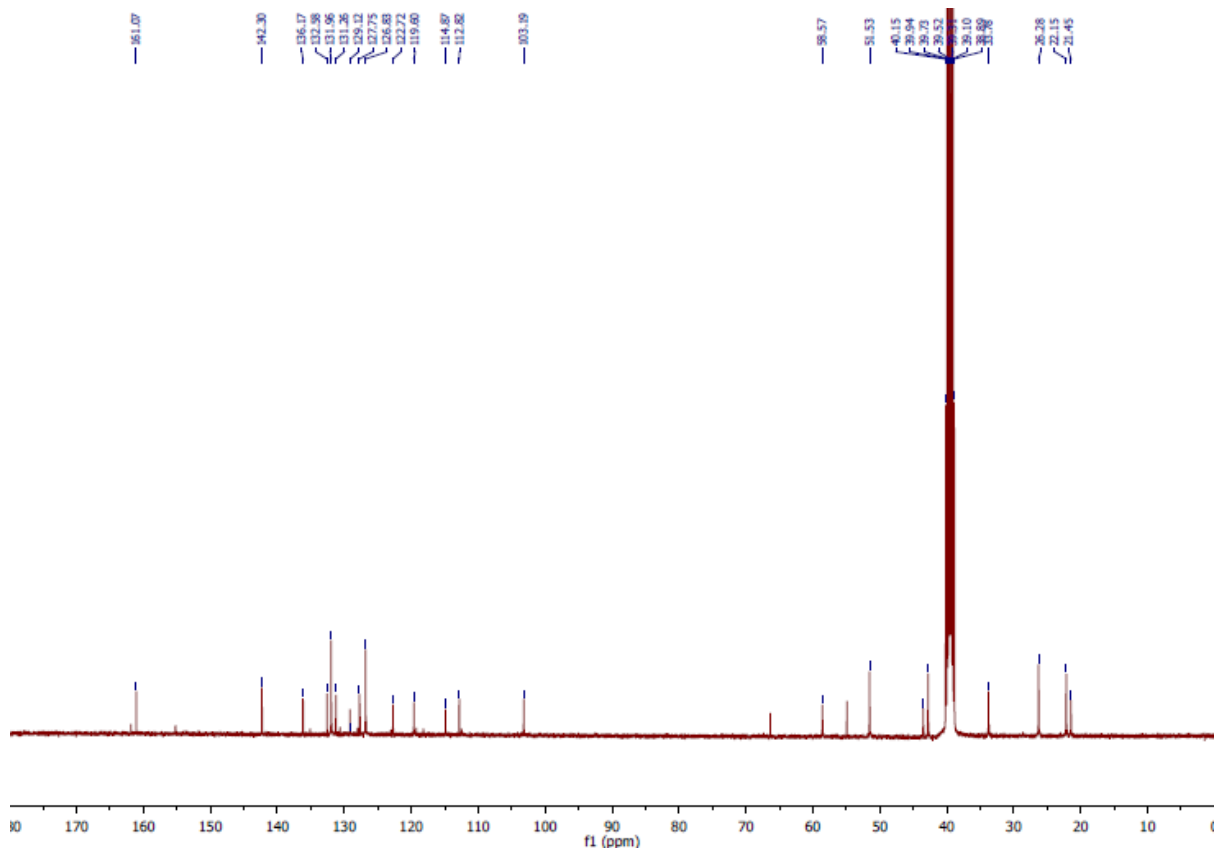
38. N-(Piperidin-4-ylmethyl)-5-(4-(thiophen-3-yl)phenyl)-1H-indole-2-carboxamide Hydrochloride (**38**).



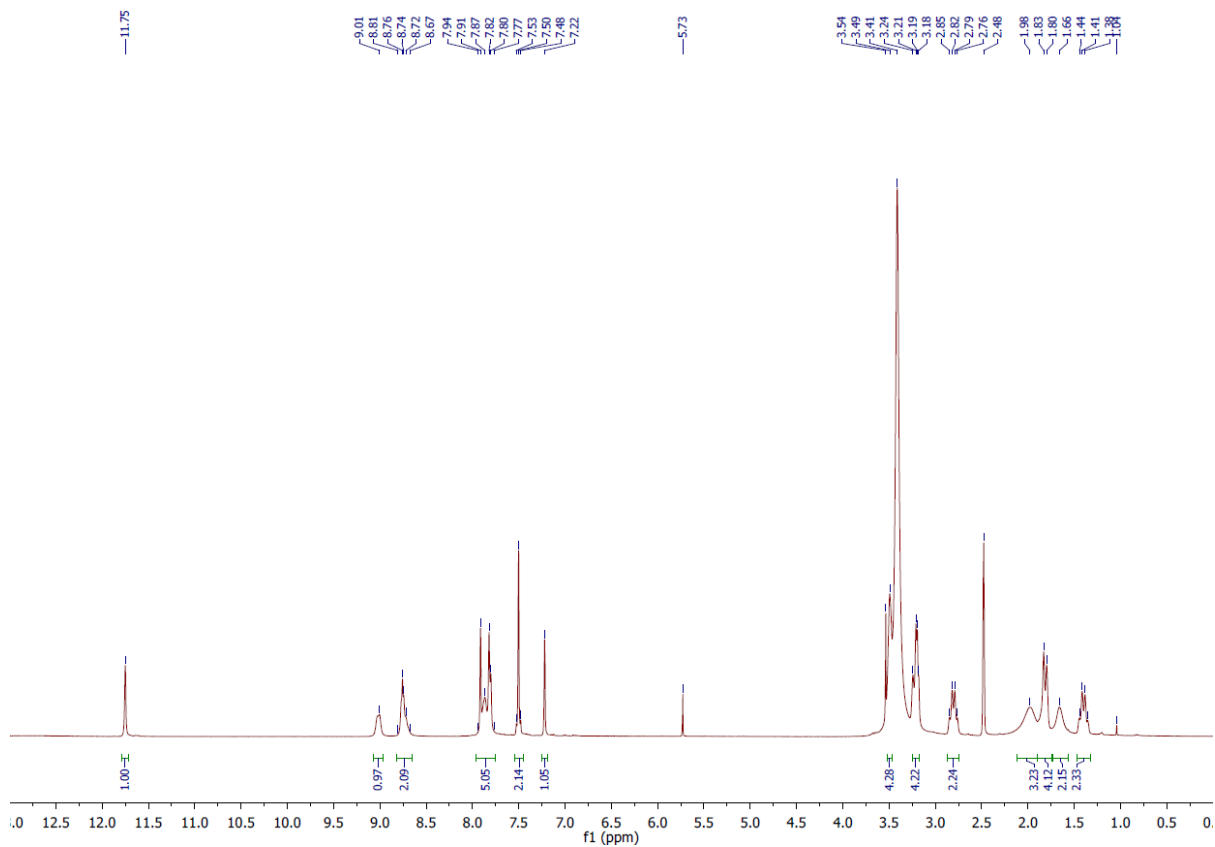


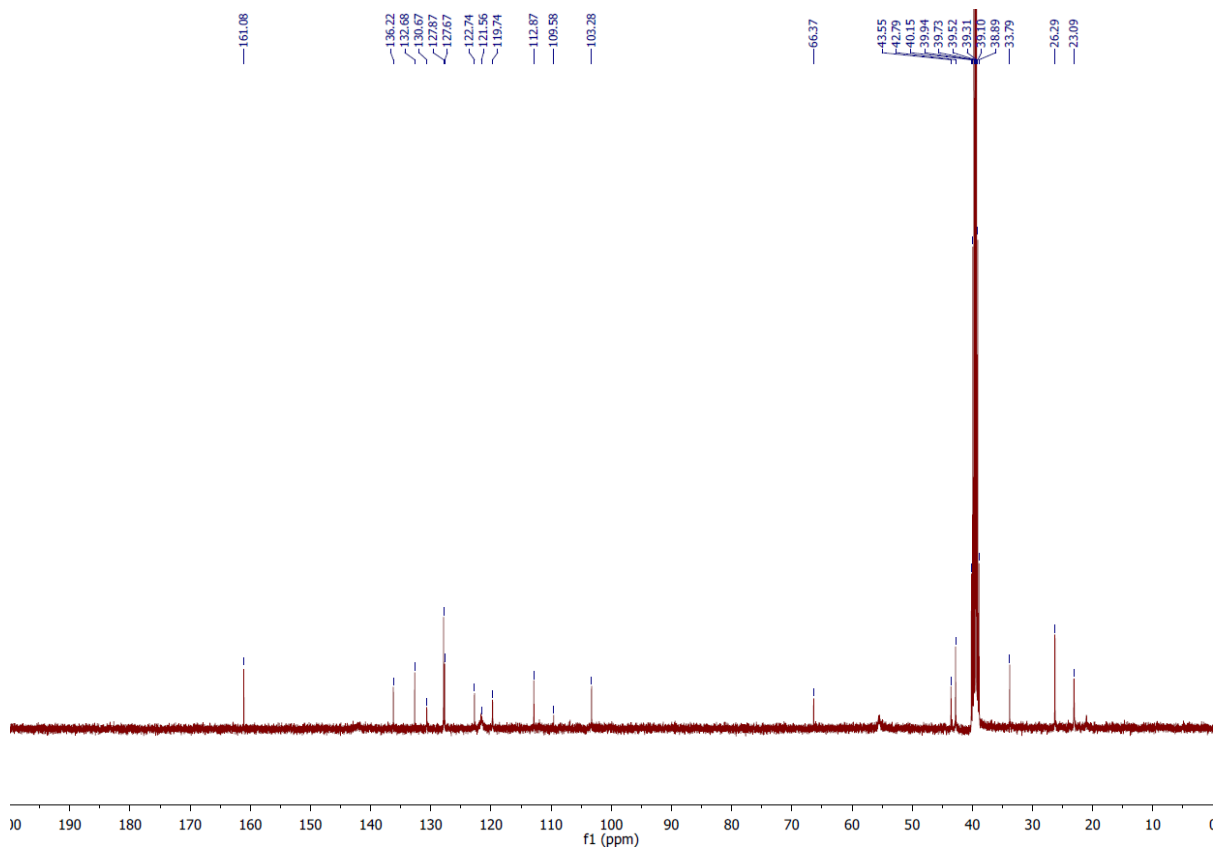
39. 5-(4-(Piperidin-1-ylmethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**39**).



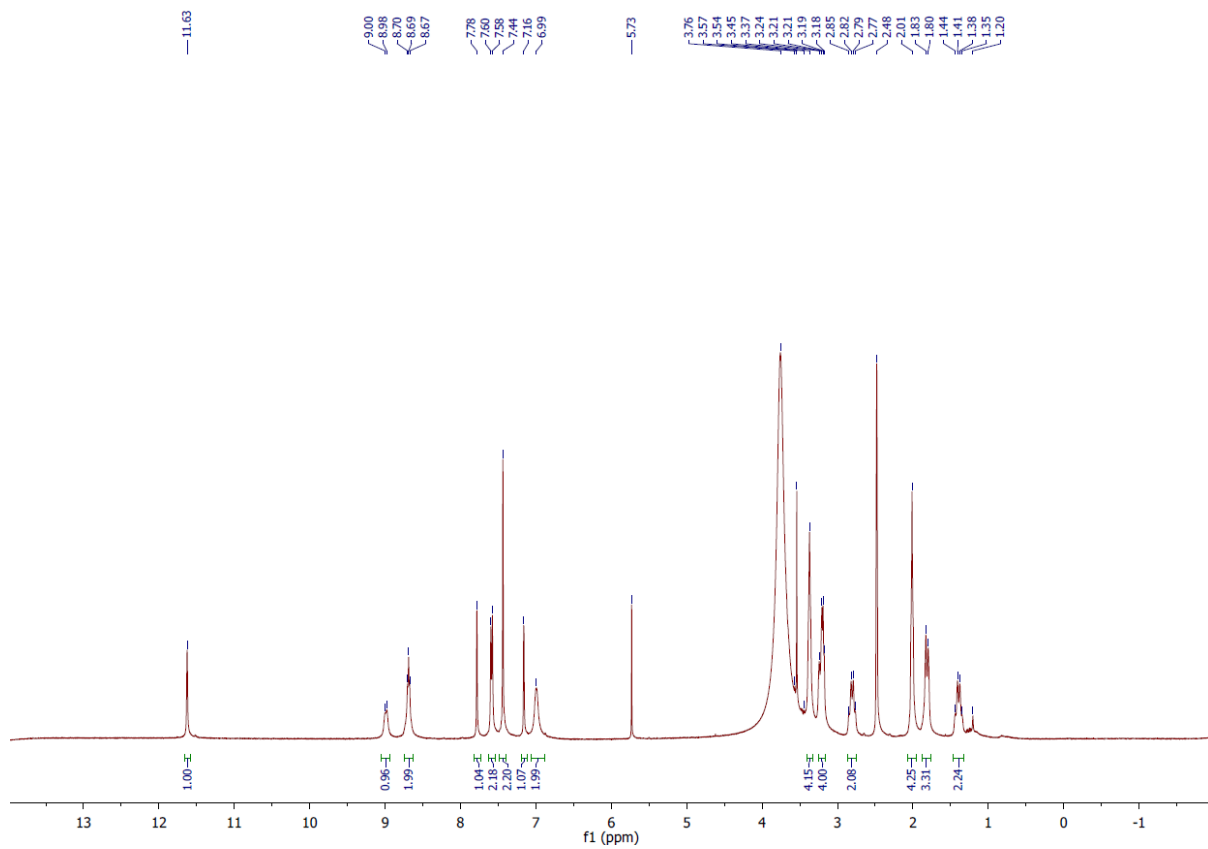


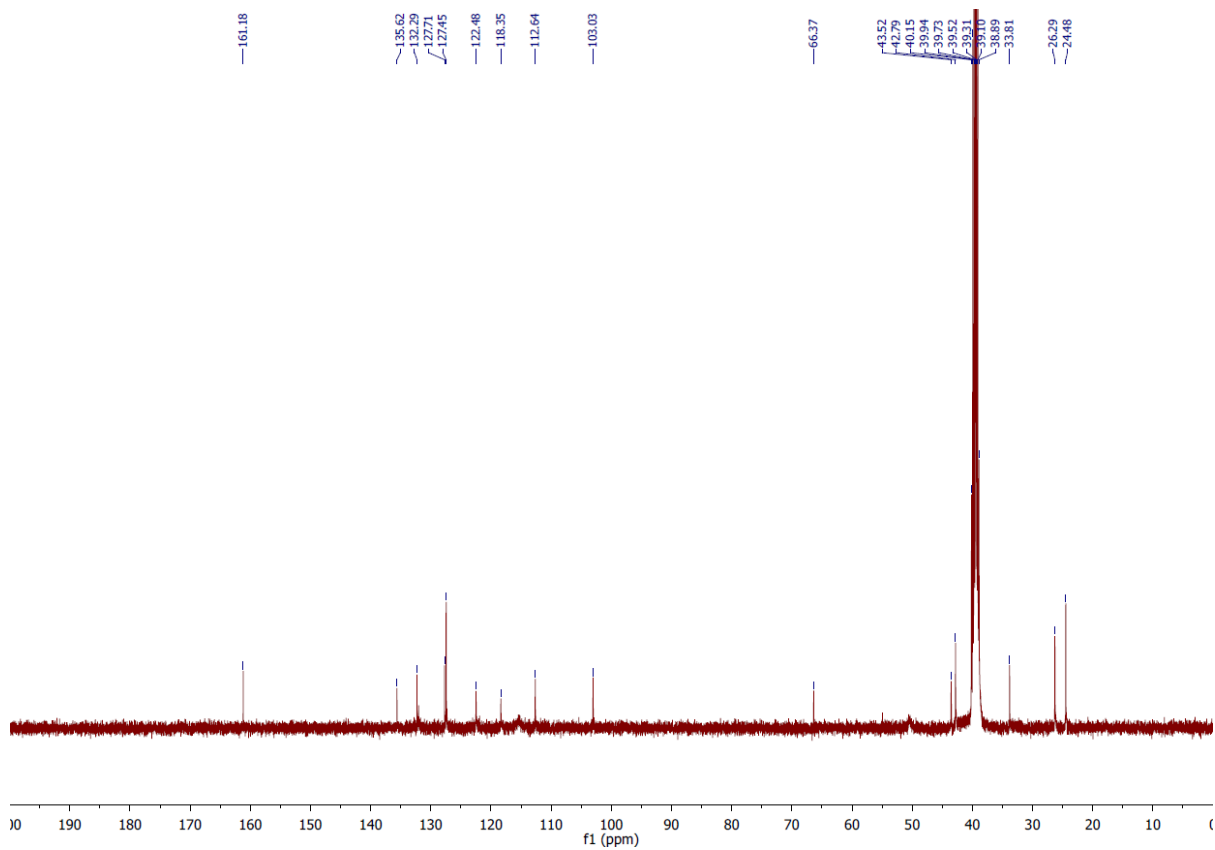
40. 5-(4-(Piperidin-1-yl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**40**).



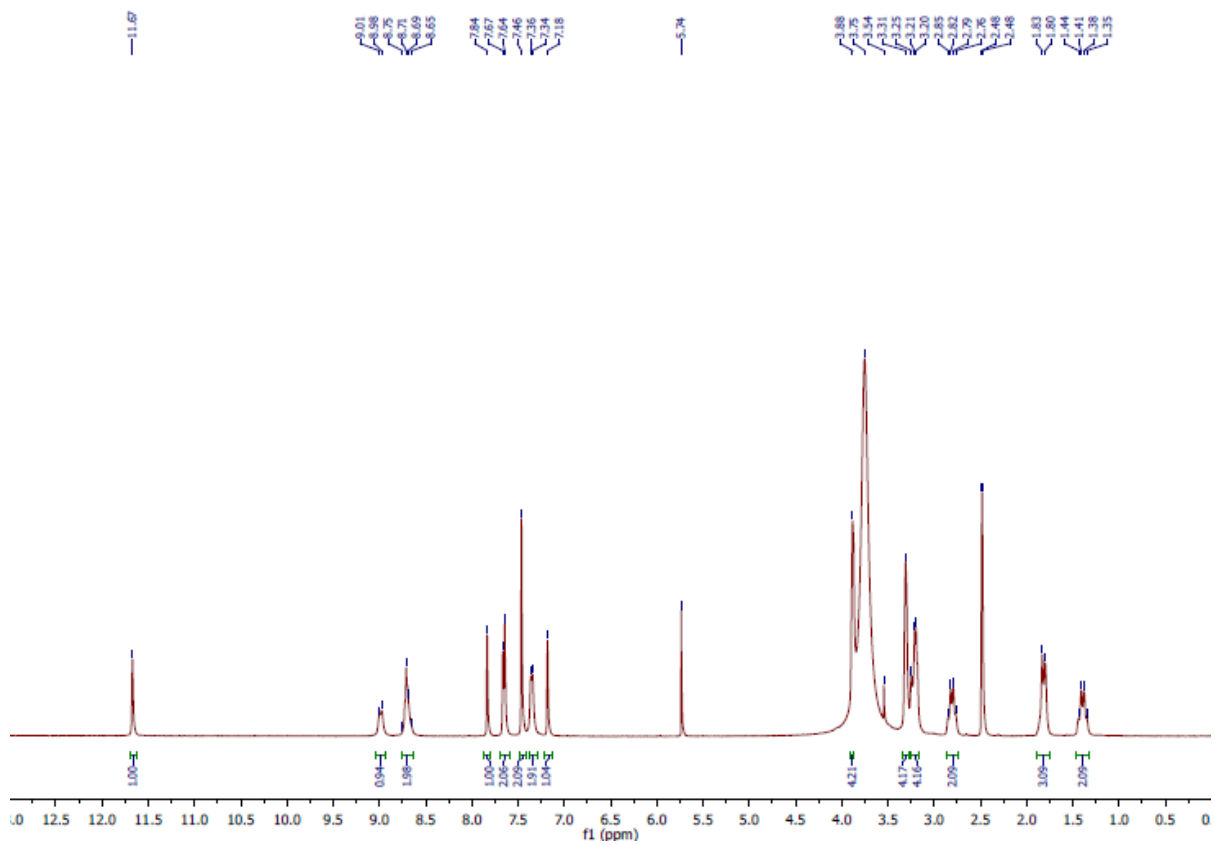


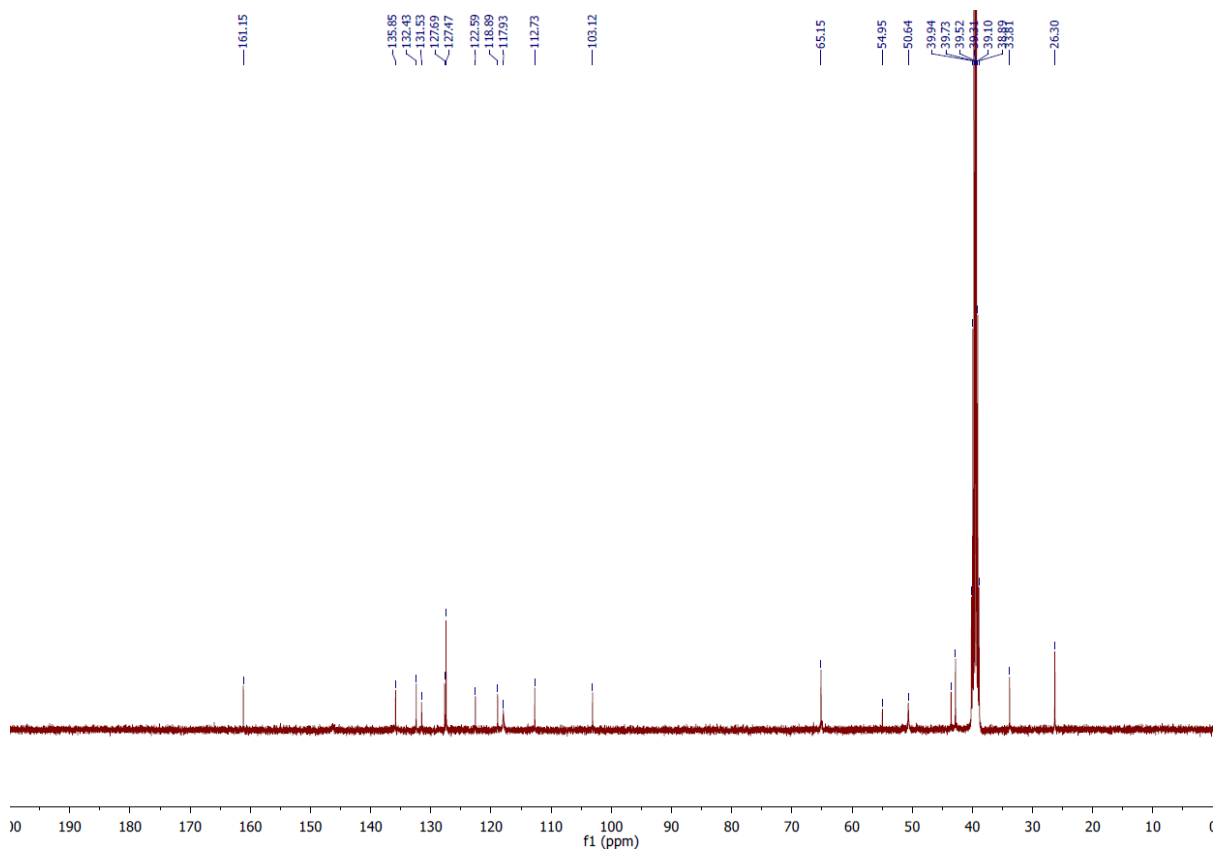
41. N-(Piperidin-4-ylmethyl)-5-(4-(pyrrolidin-1-yl)phenyl)-1H-indole-2-carboxamide Hydrochloride (**41**).



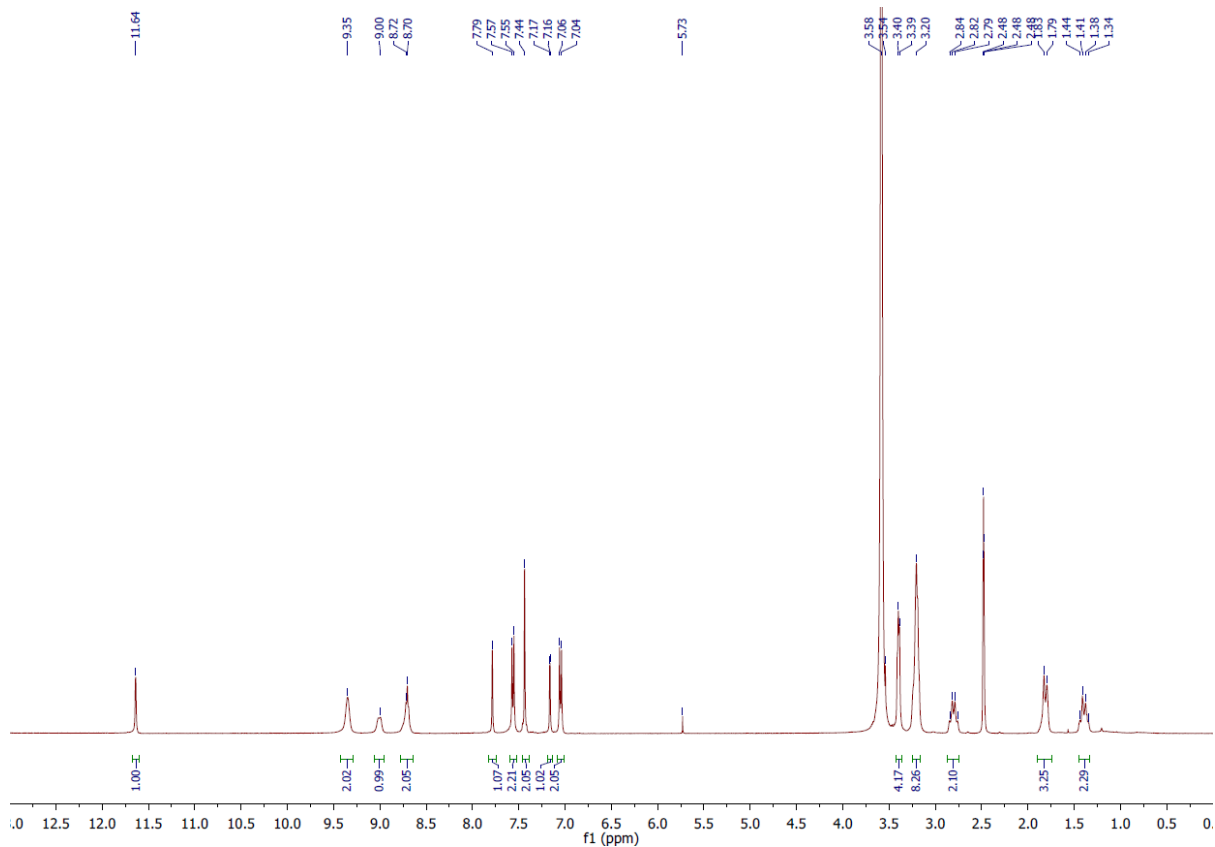


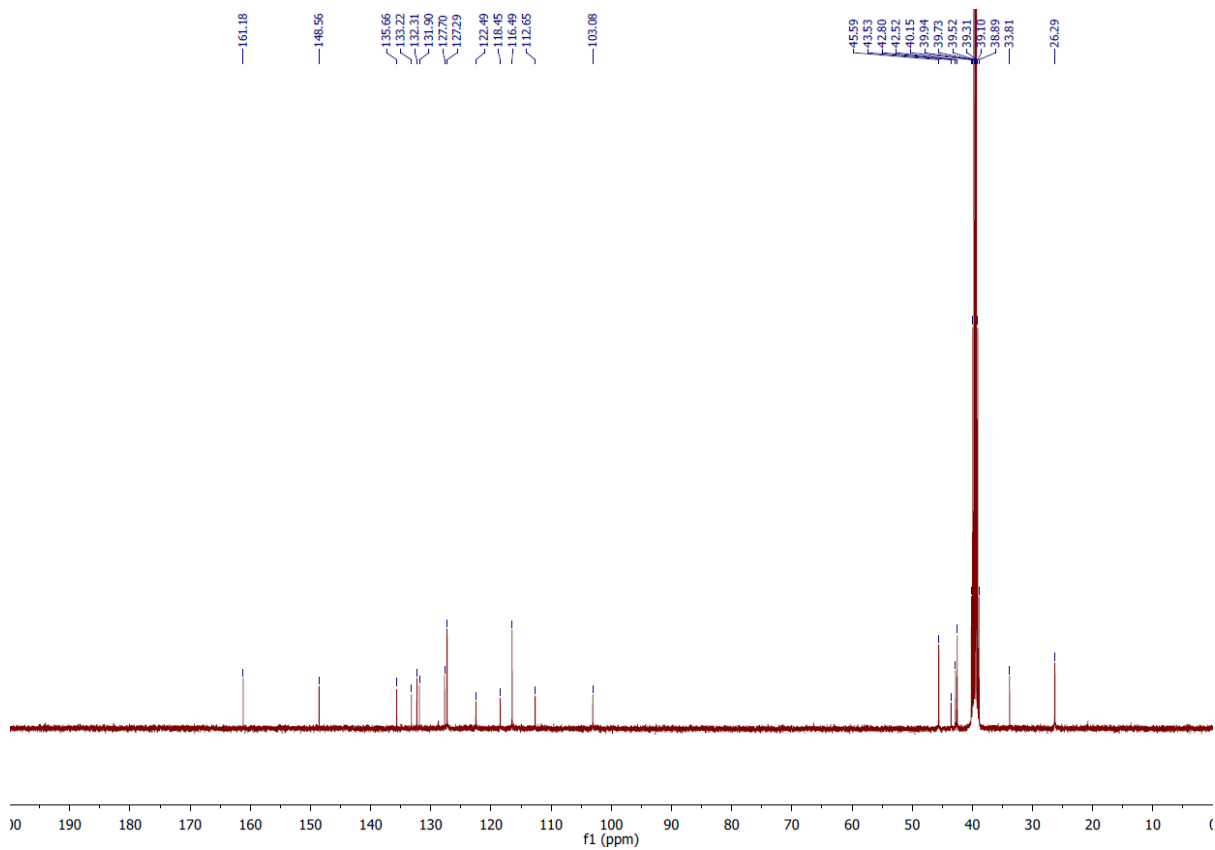
42. 5-(4-Morpholinophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**42**).



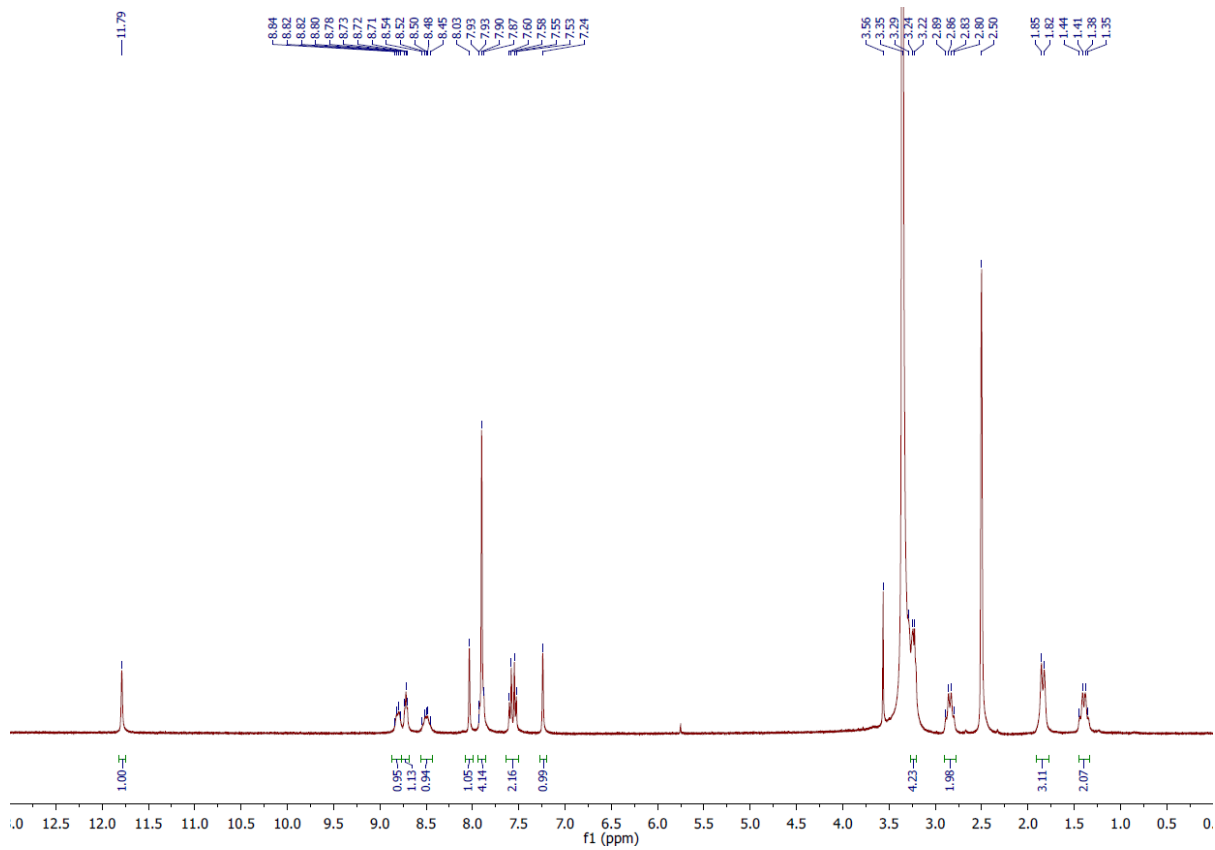


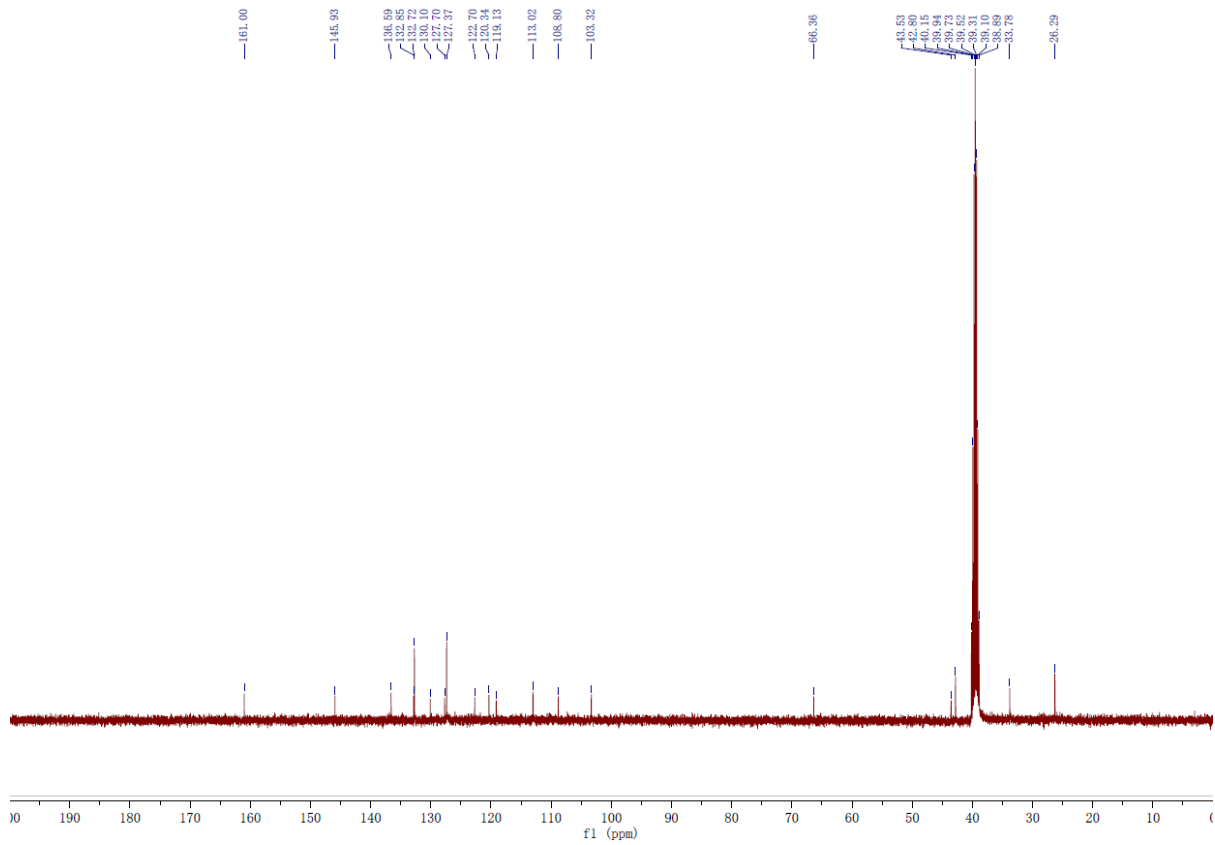
43. 5-(4-(Piperazin-1-yl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**43**).



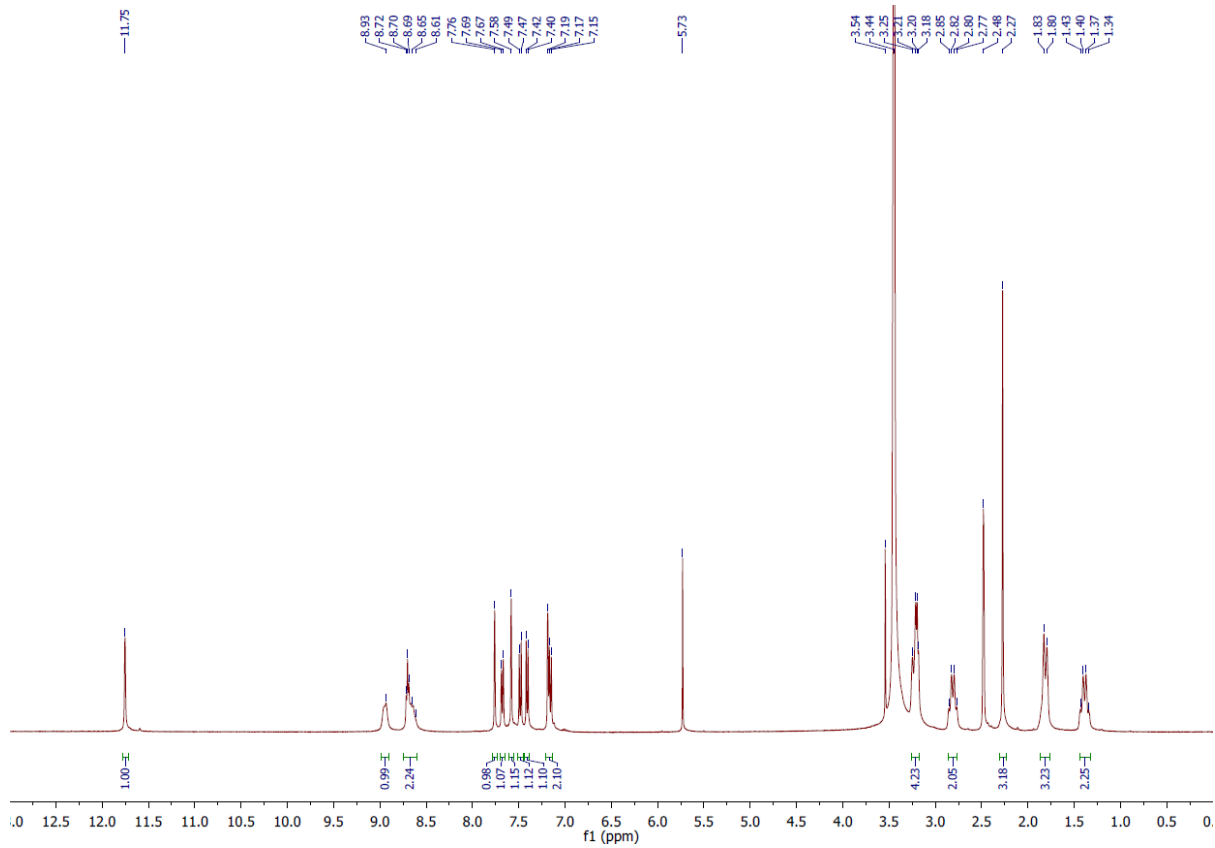


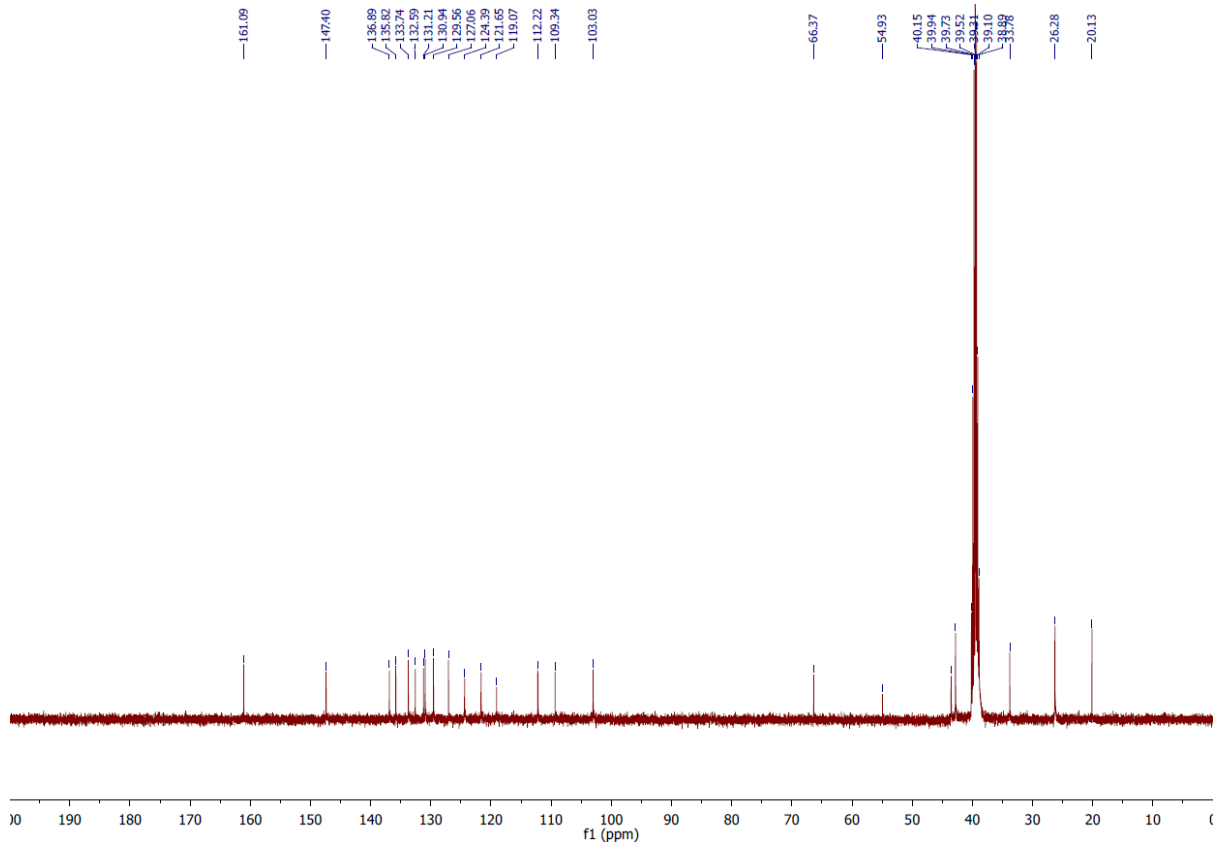
44. 5-(4-Cyanophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (44).



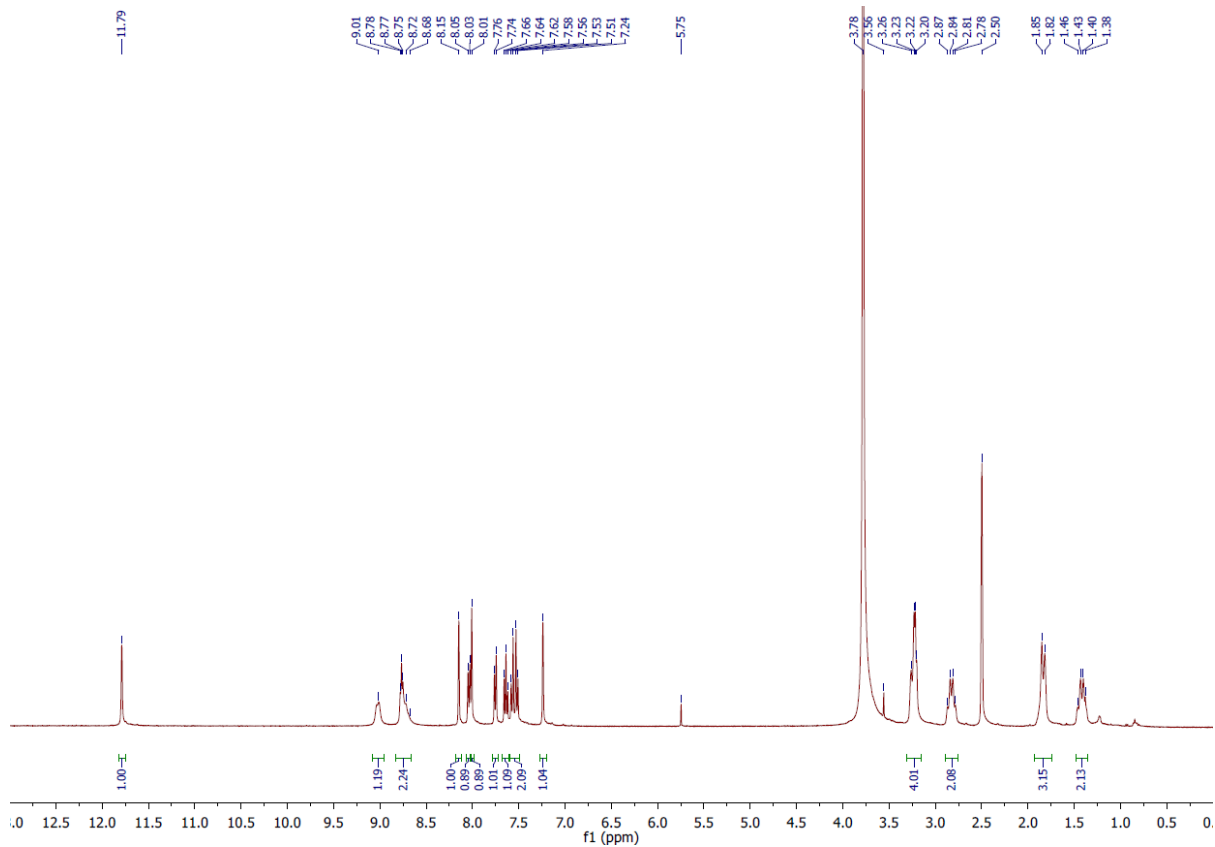


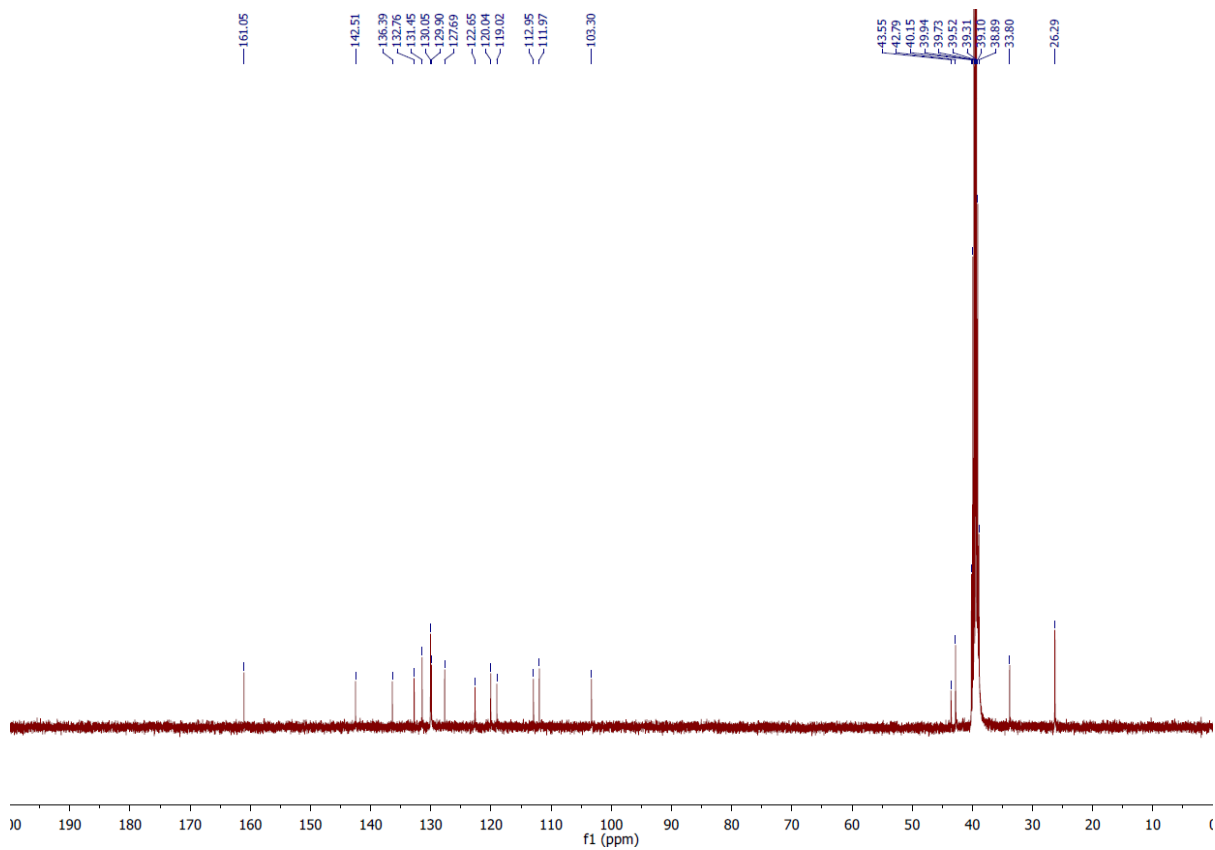
45. 5-(4-Cyano-2-methylphenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**45**).



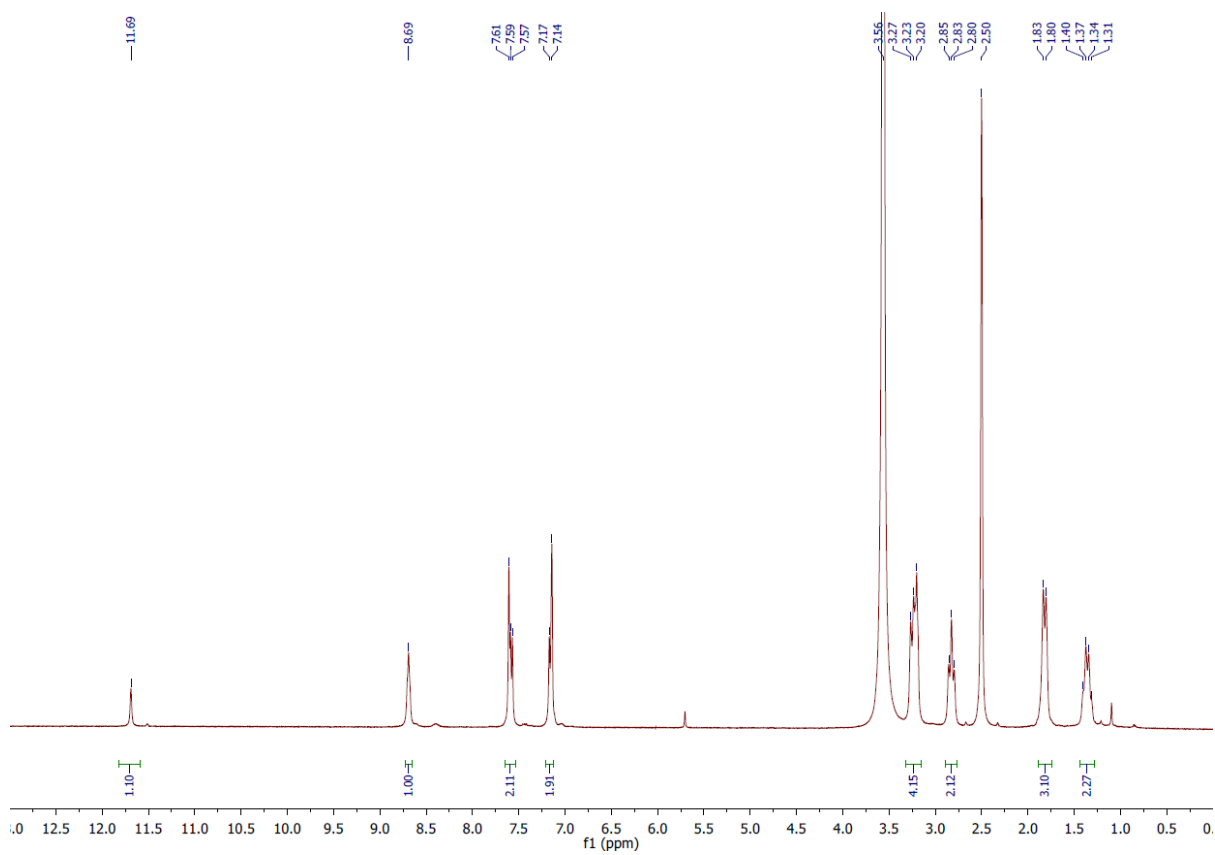


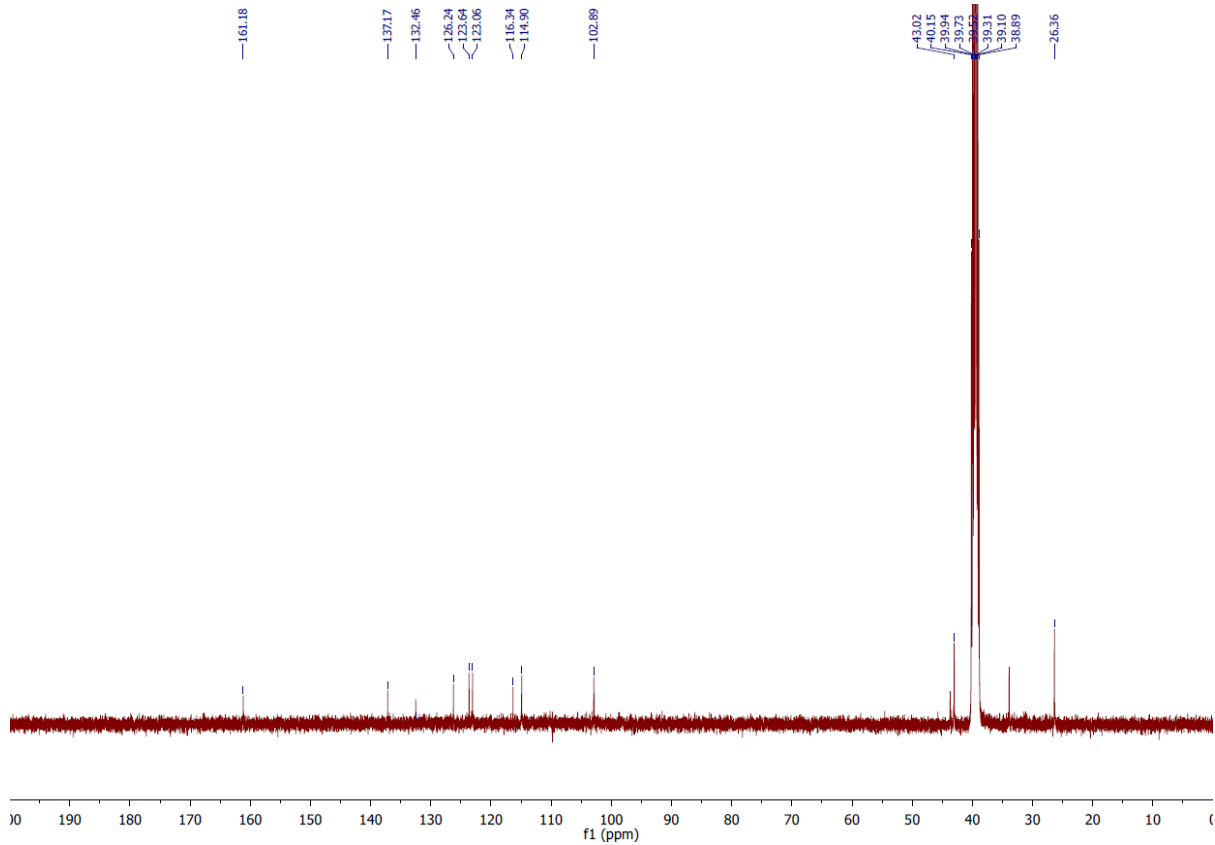
46. 5-(3-Cyanophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (46).



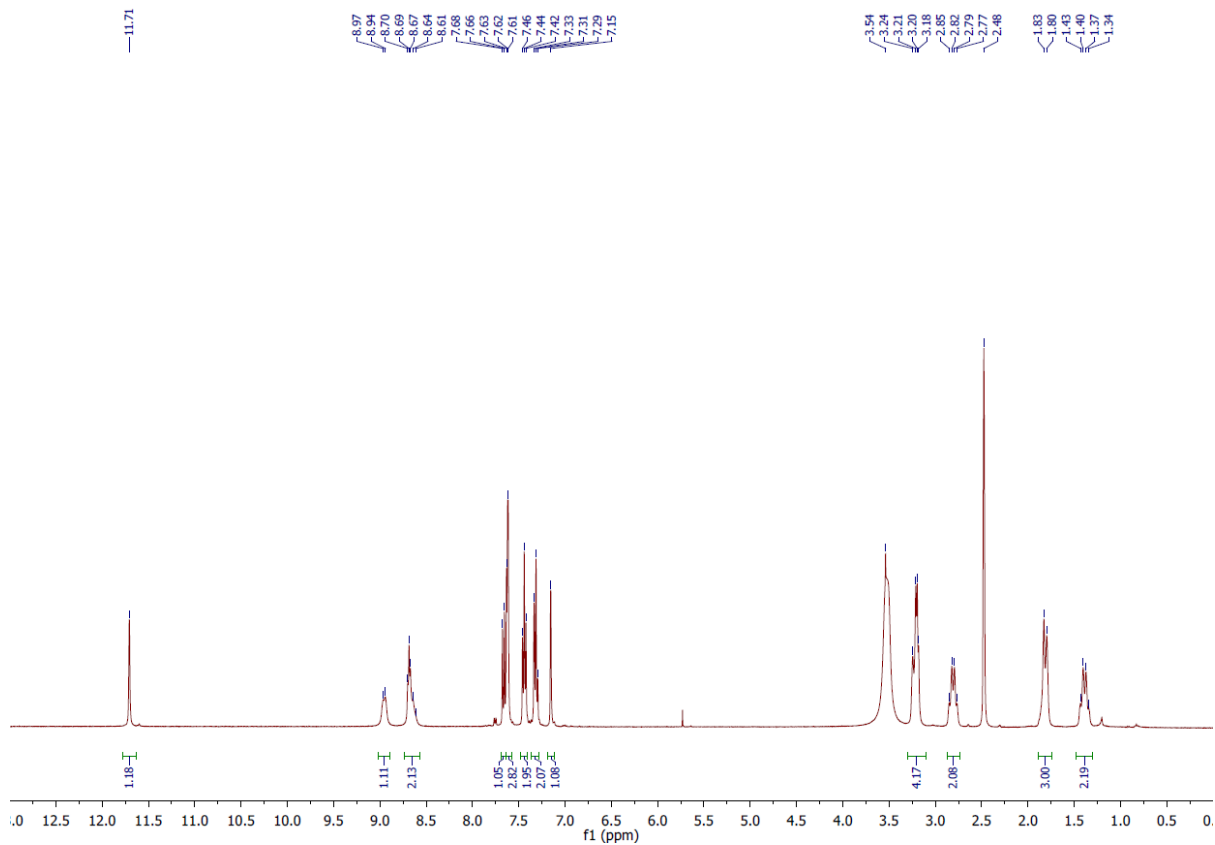


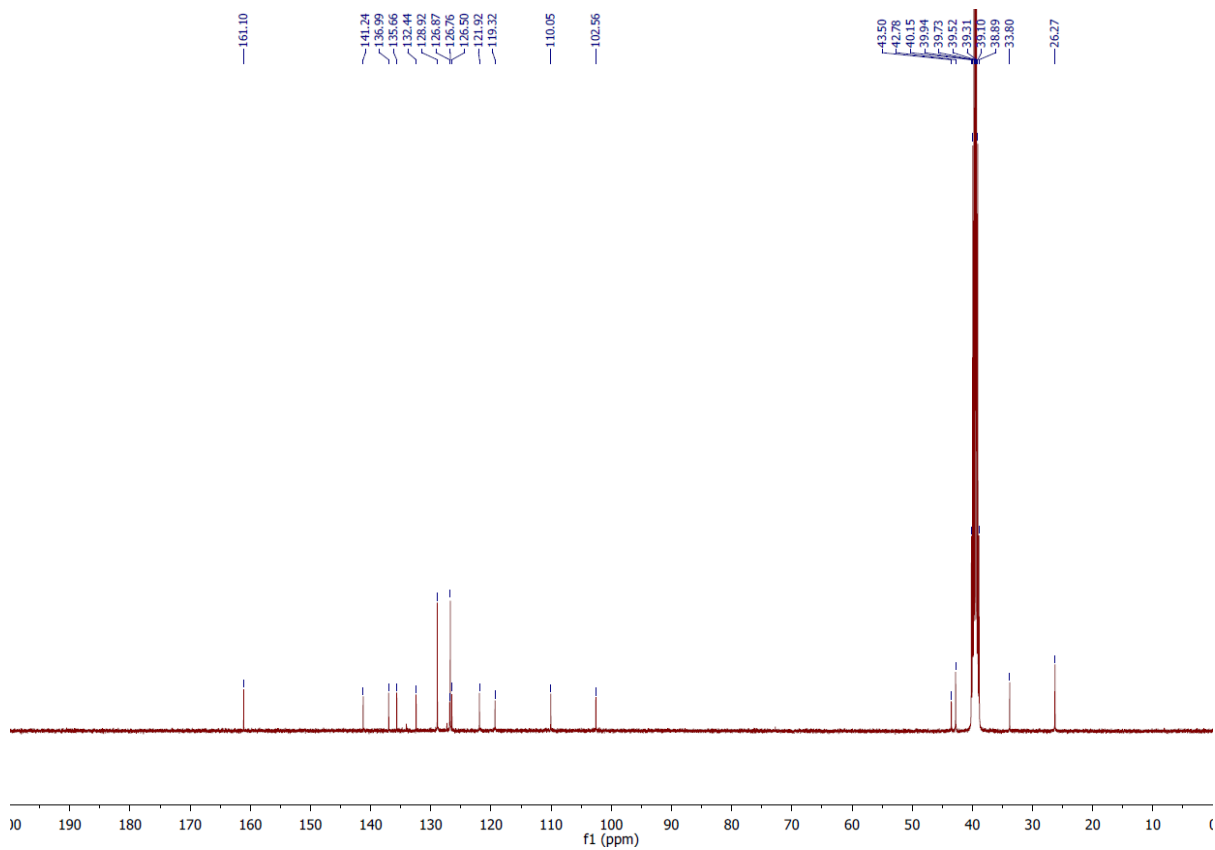
47. N-(Piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (47).



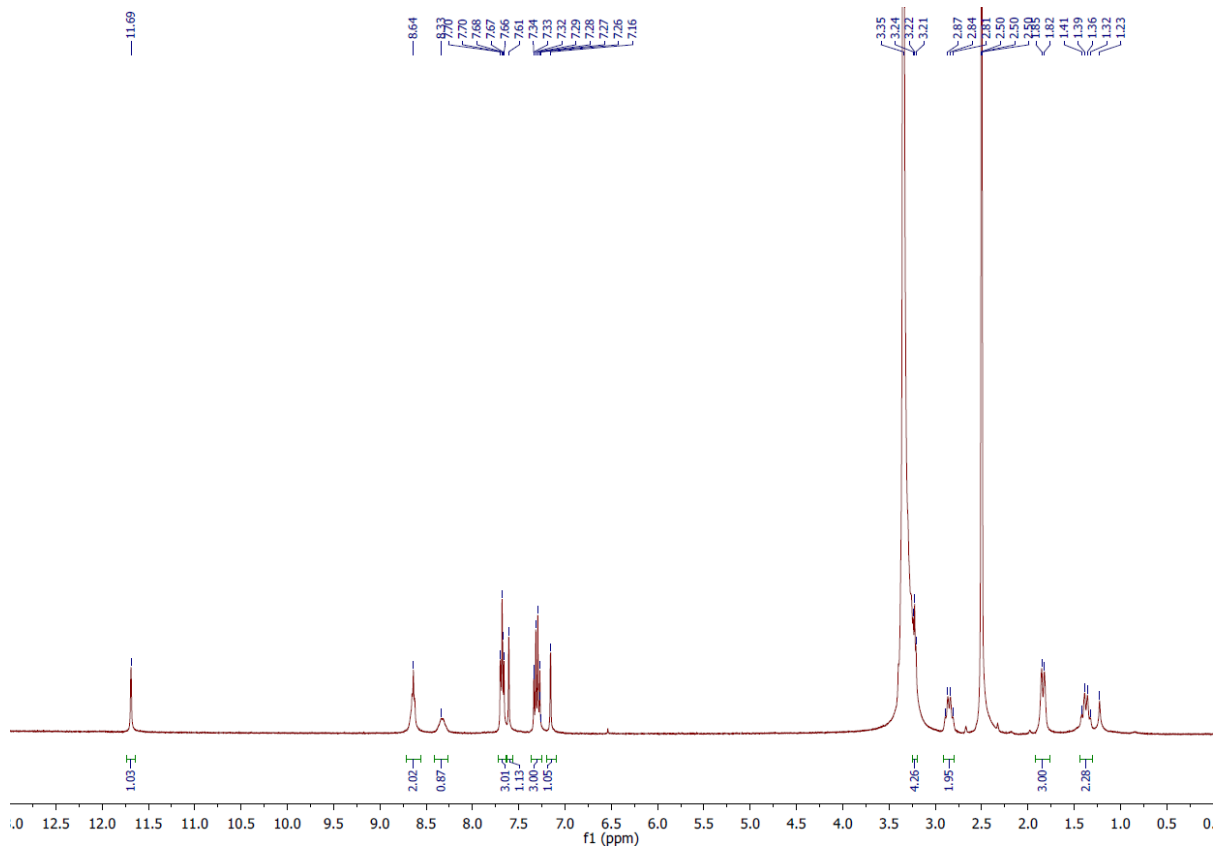


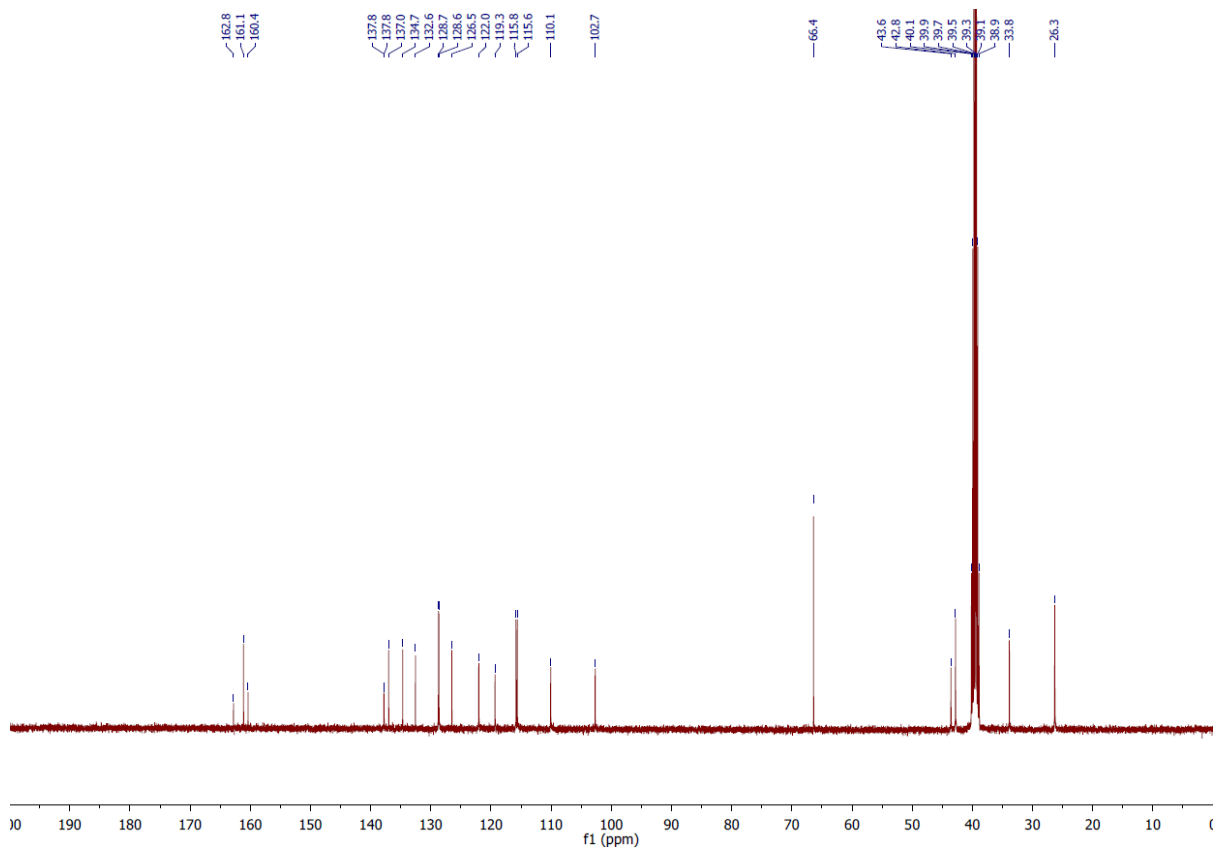
48. 6-Phenyl-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**48**)



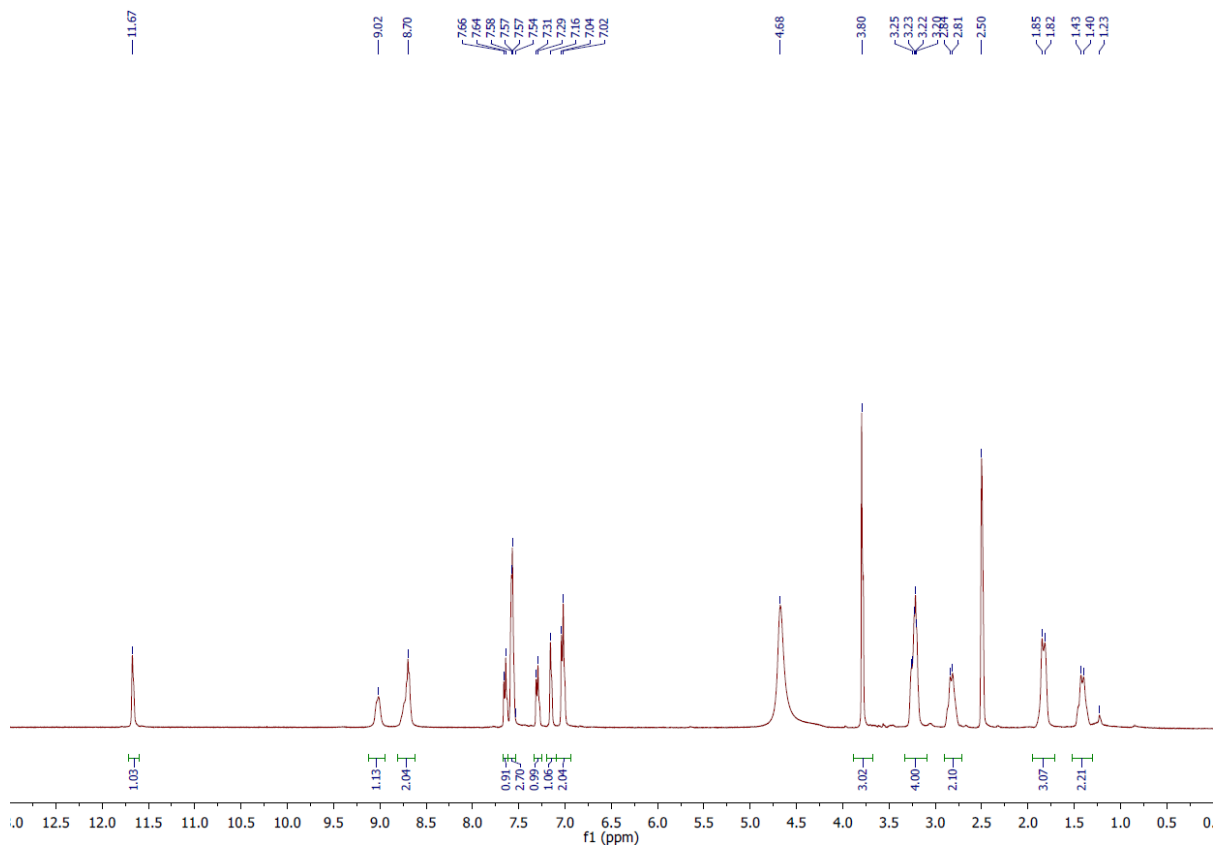


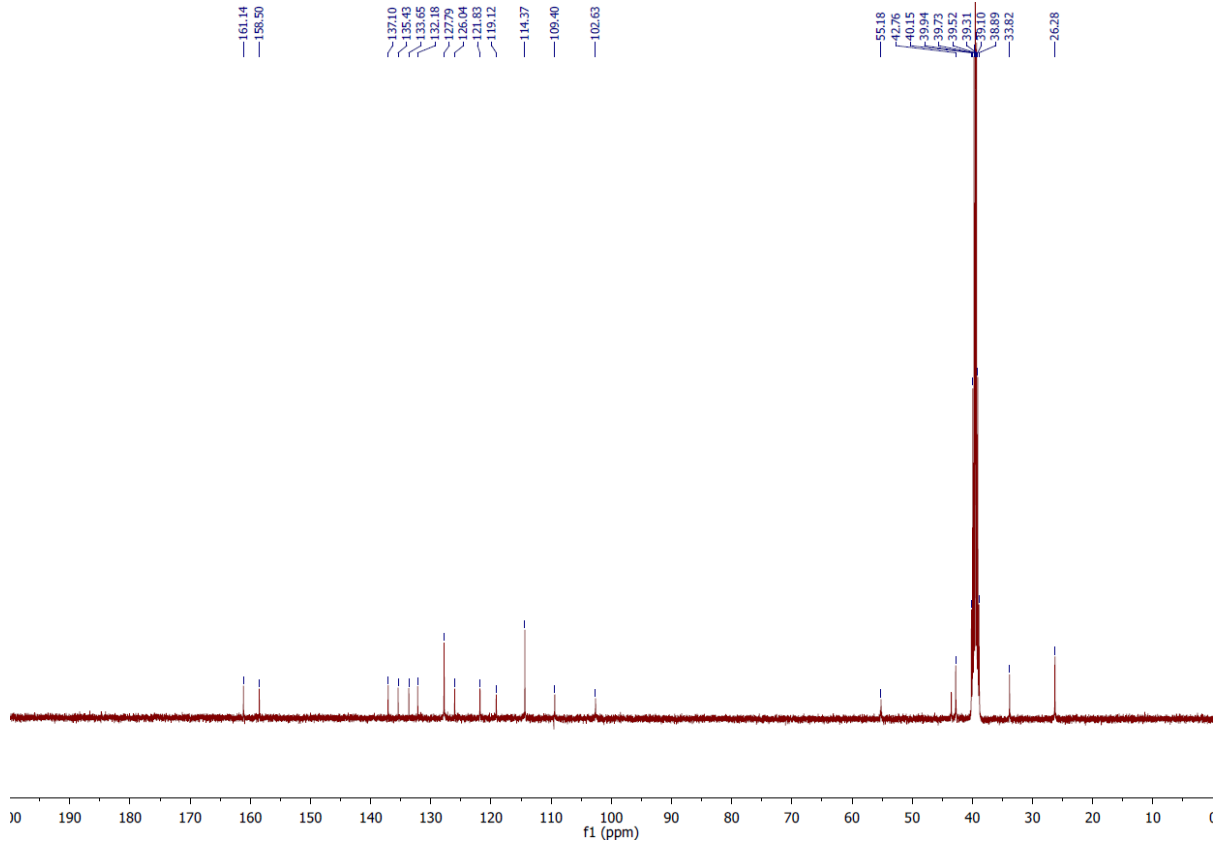
49. 6-(4-Fluorophenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (49).



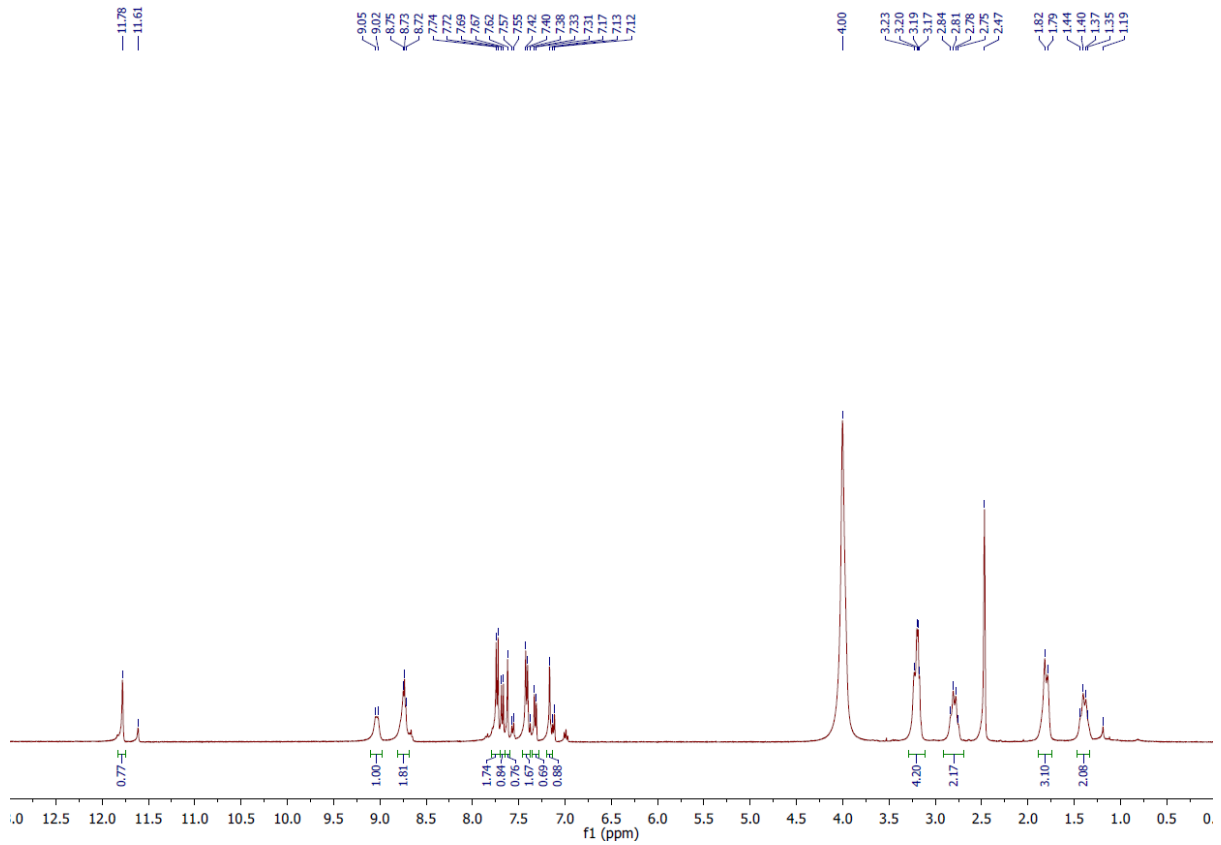


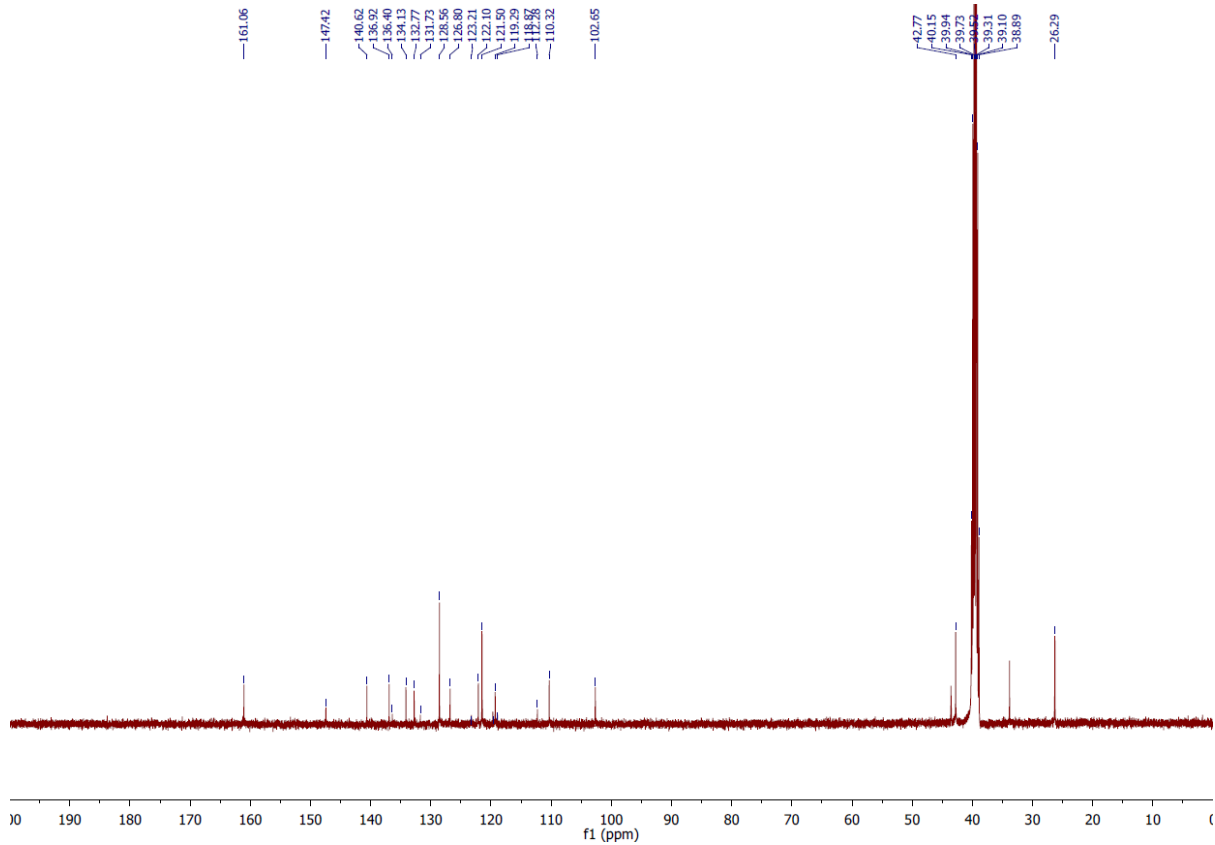
50. 6-(4-Methoxyphenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (50).



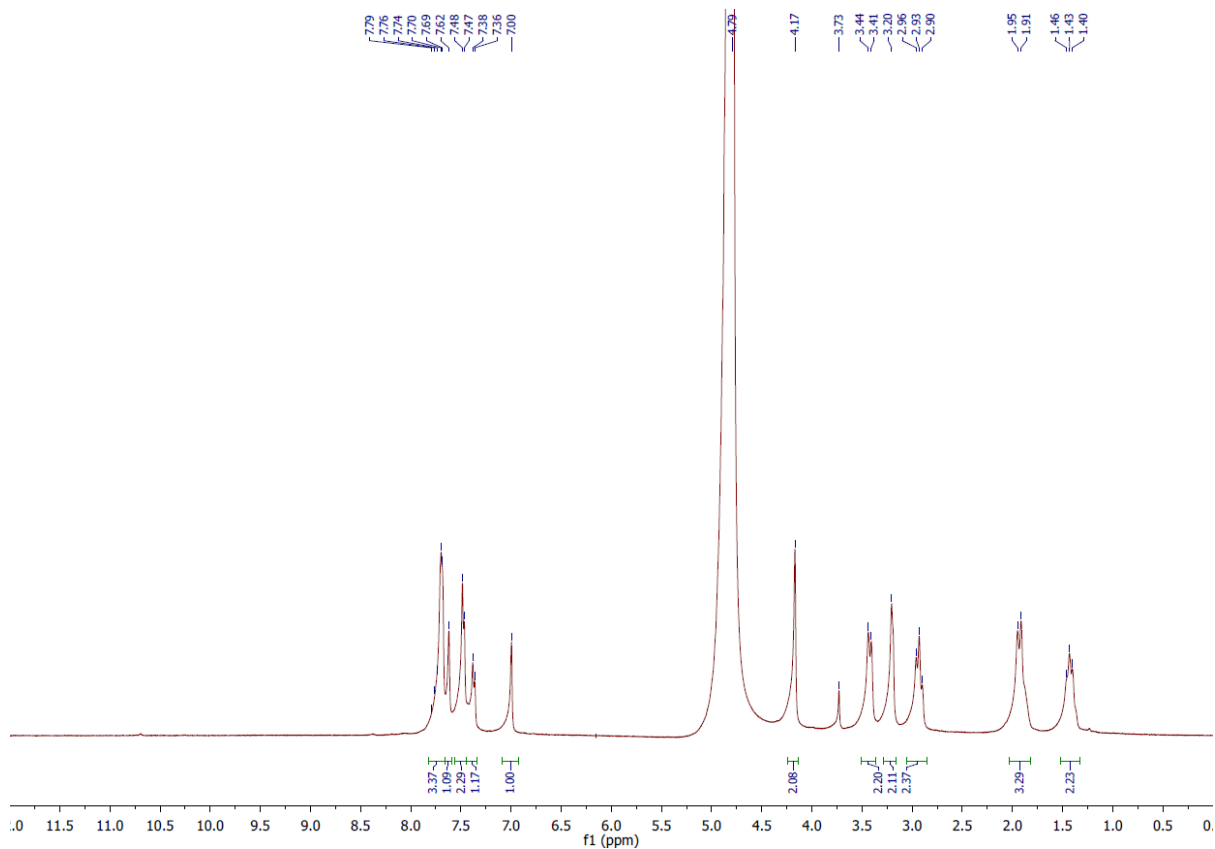


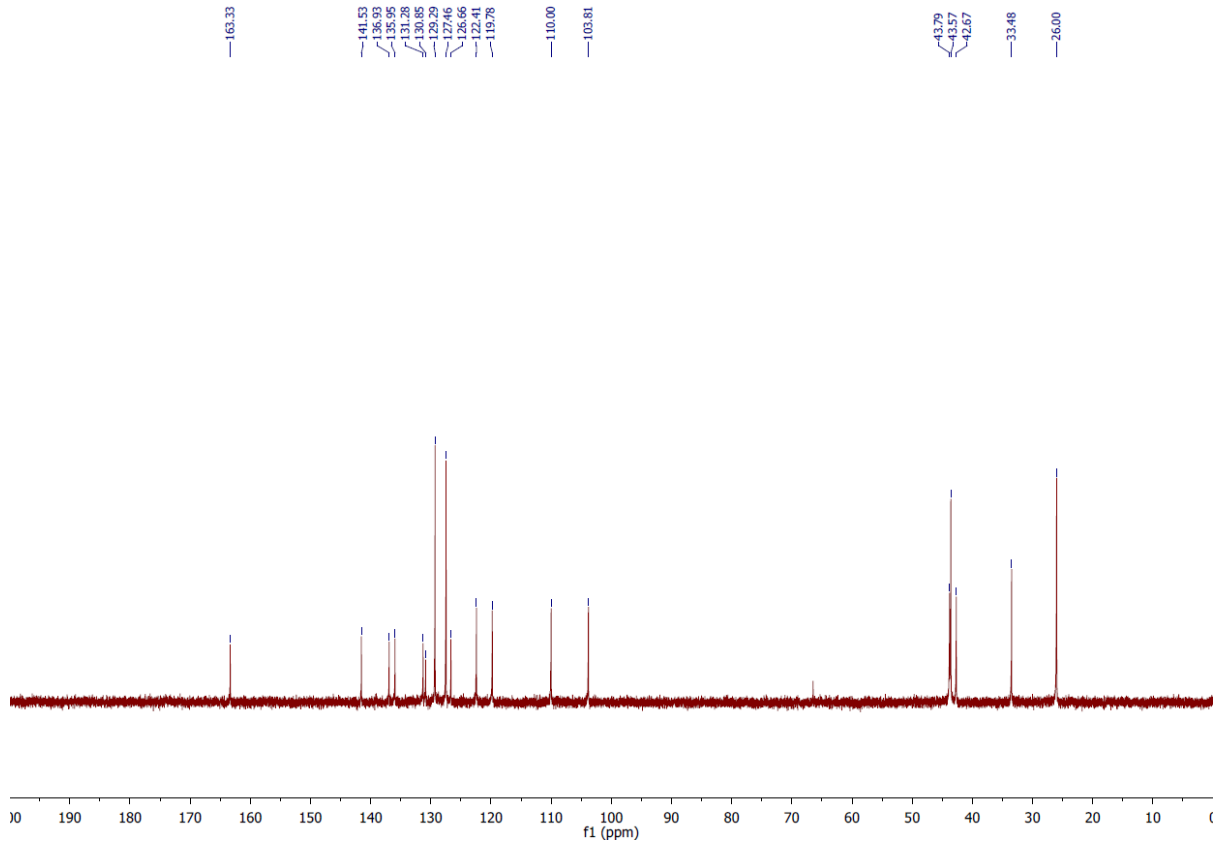
51. N-(Piperidin-4-ylmethyl)-6-(4-(trifluoromethoxy)phenyl)-1H-indole-2-carboxamide Hydrochloride (**51**).



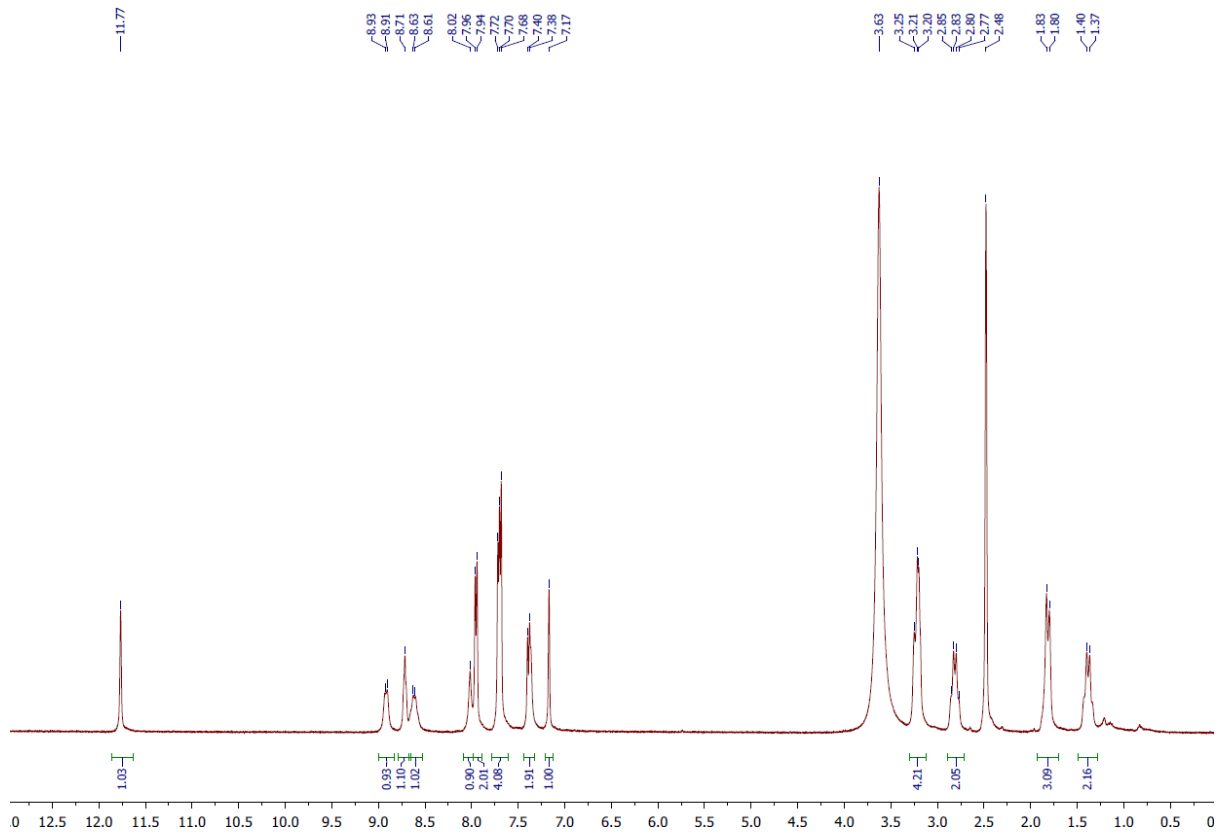


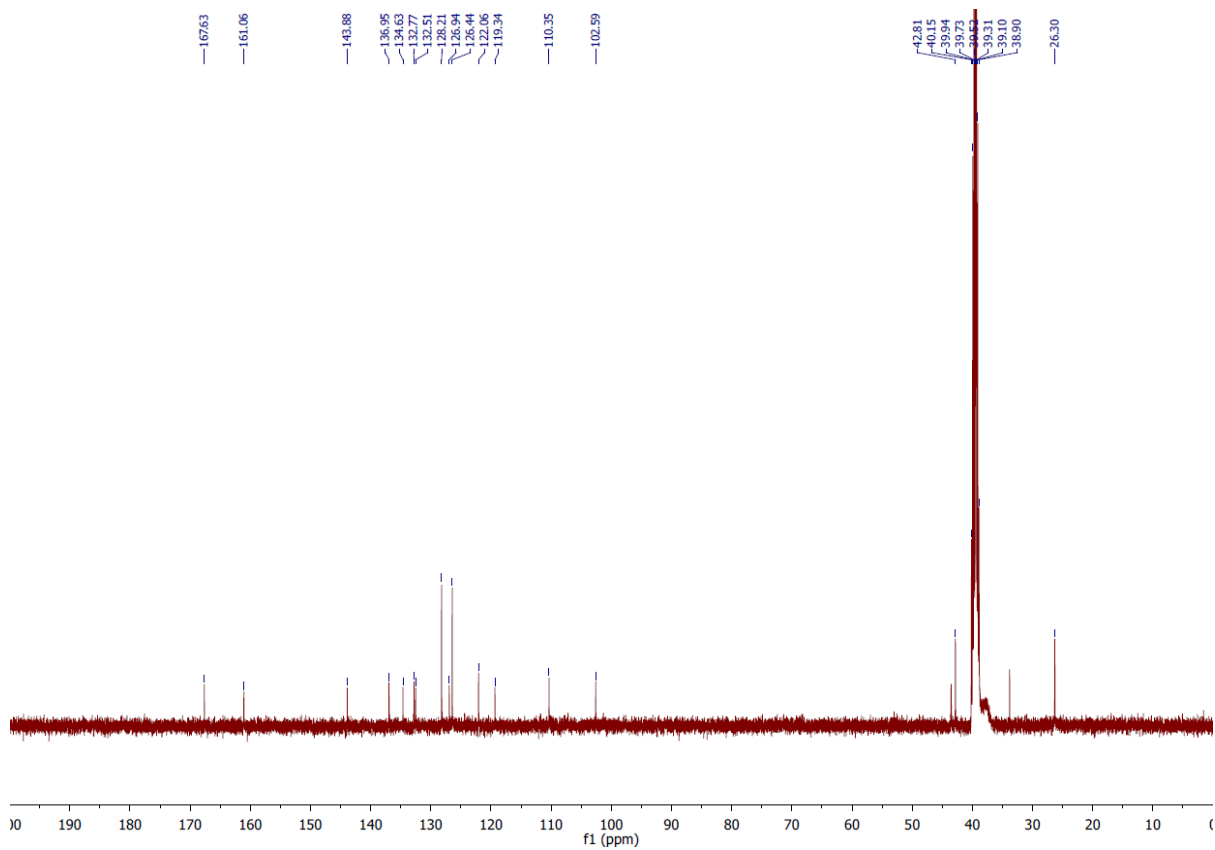
52. 6-(4-(Aminomethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**52**).



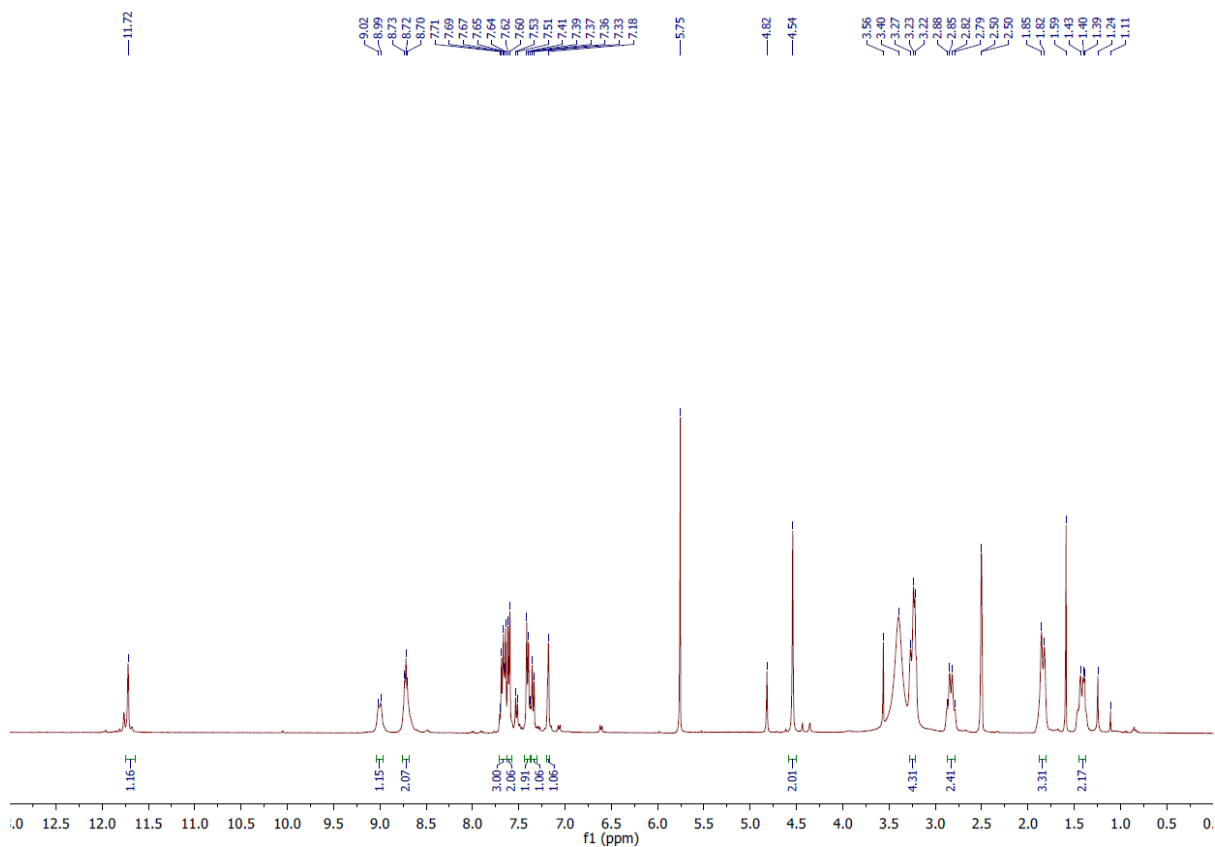


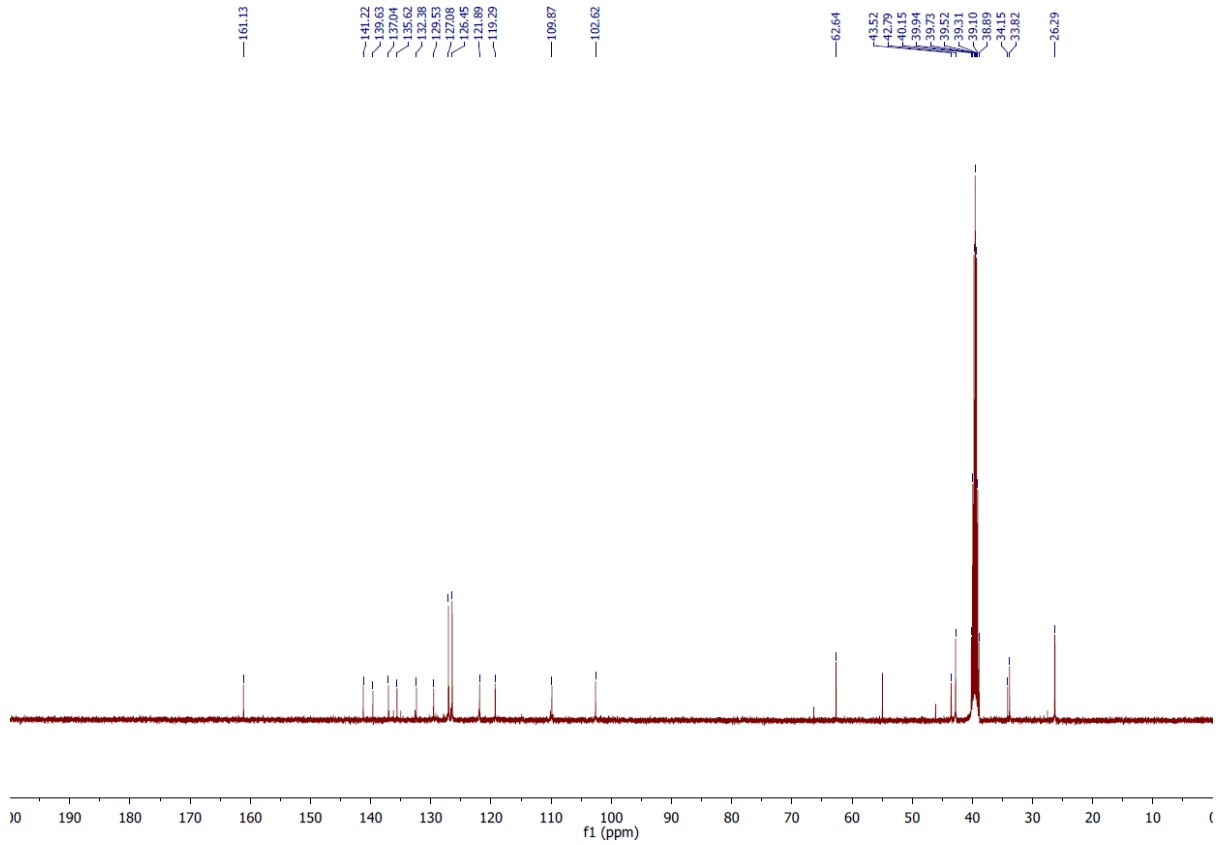
53. 6-(4-Carbamoylphenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**53**).



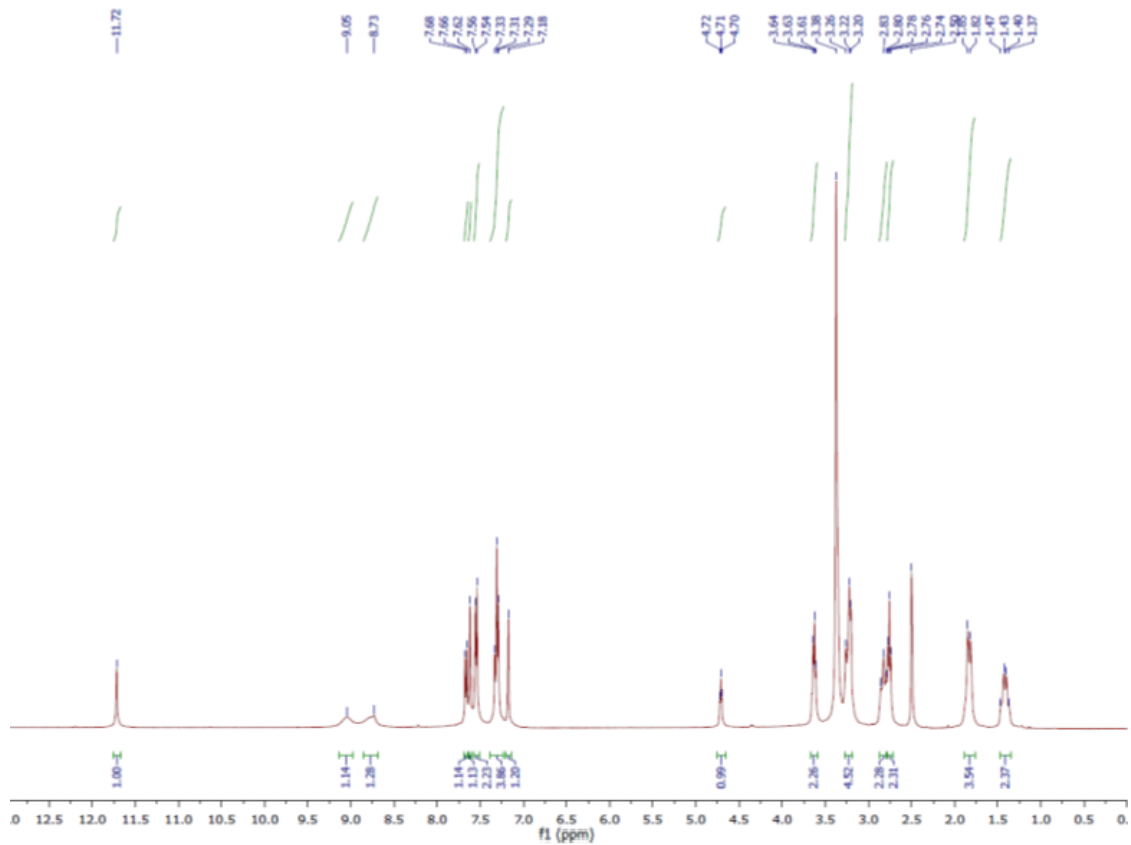


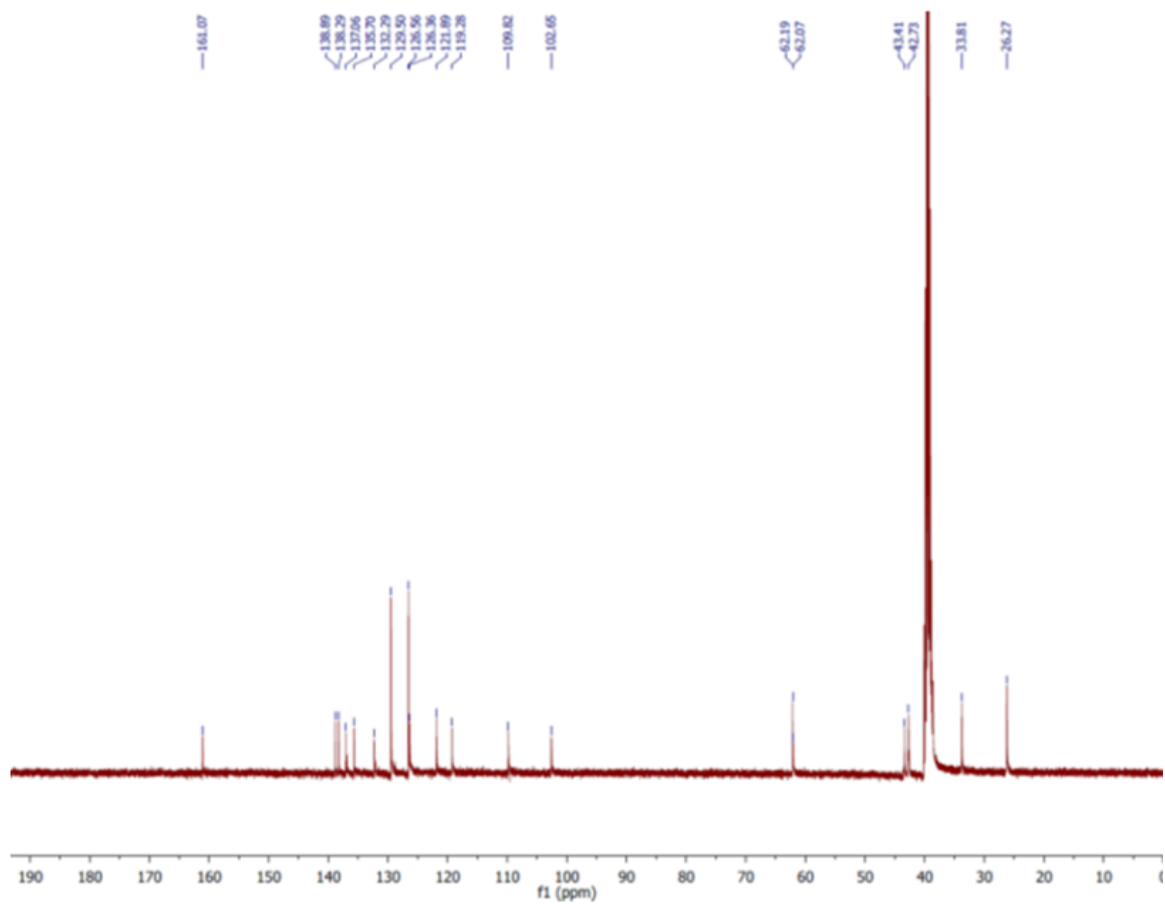
54. 6-(4-(Hydroxymethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**54**).



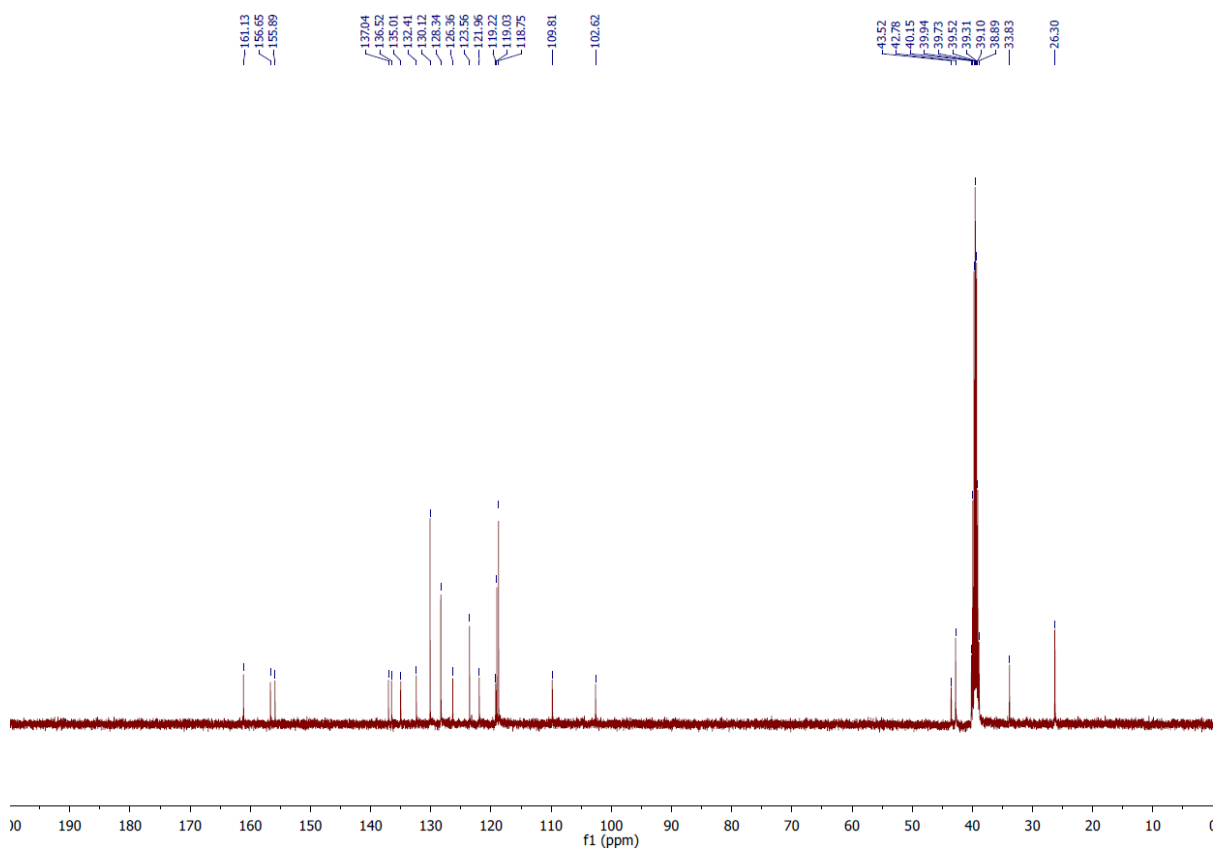
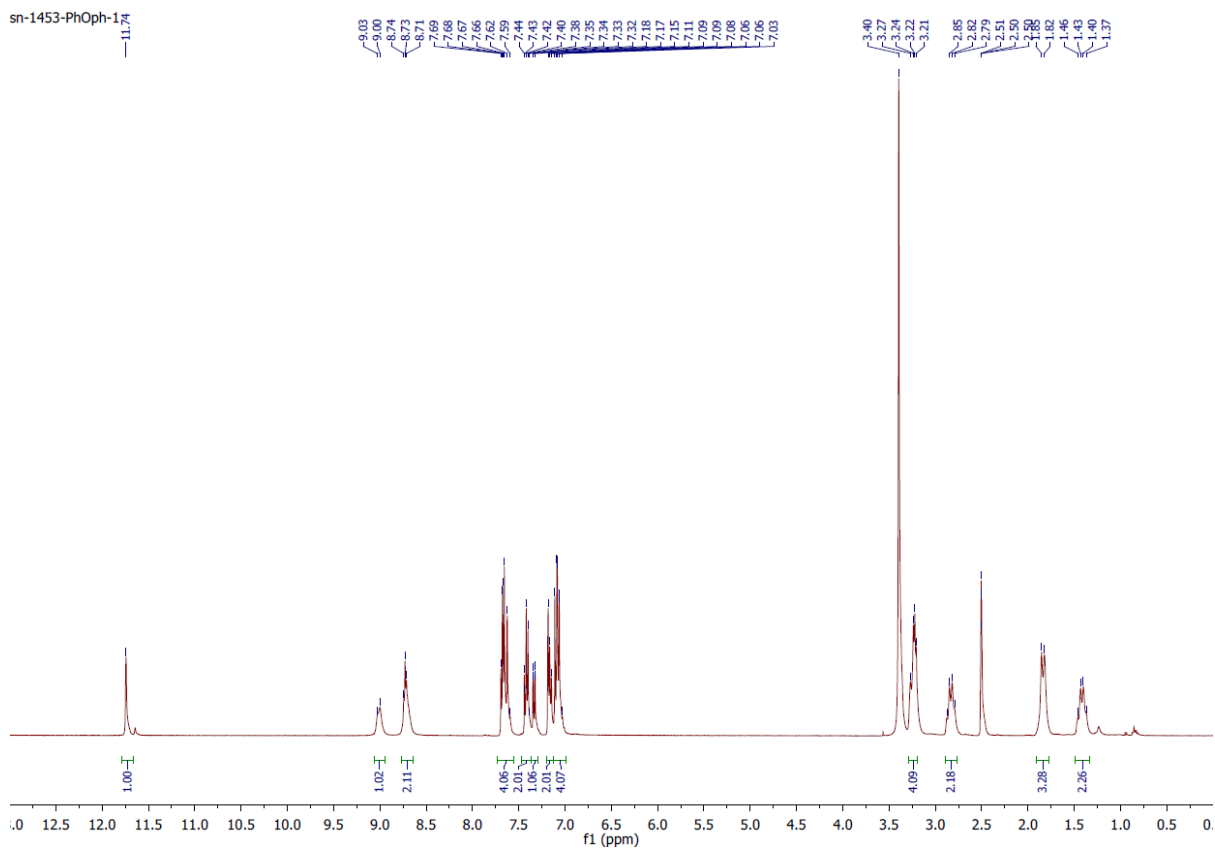


55. 6-(4-(2-Hydroxyethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**55**).

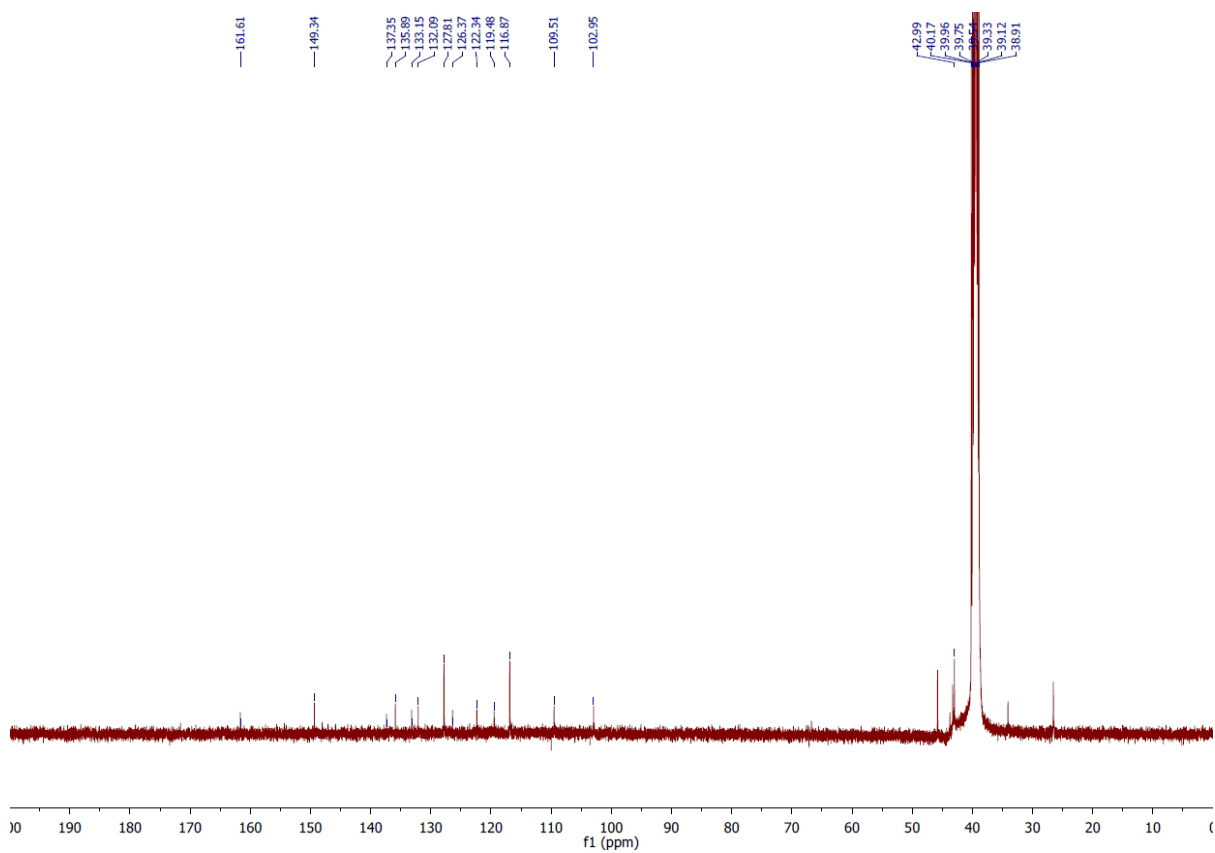
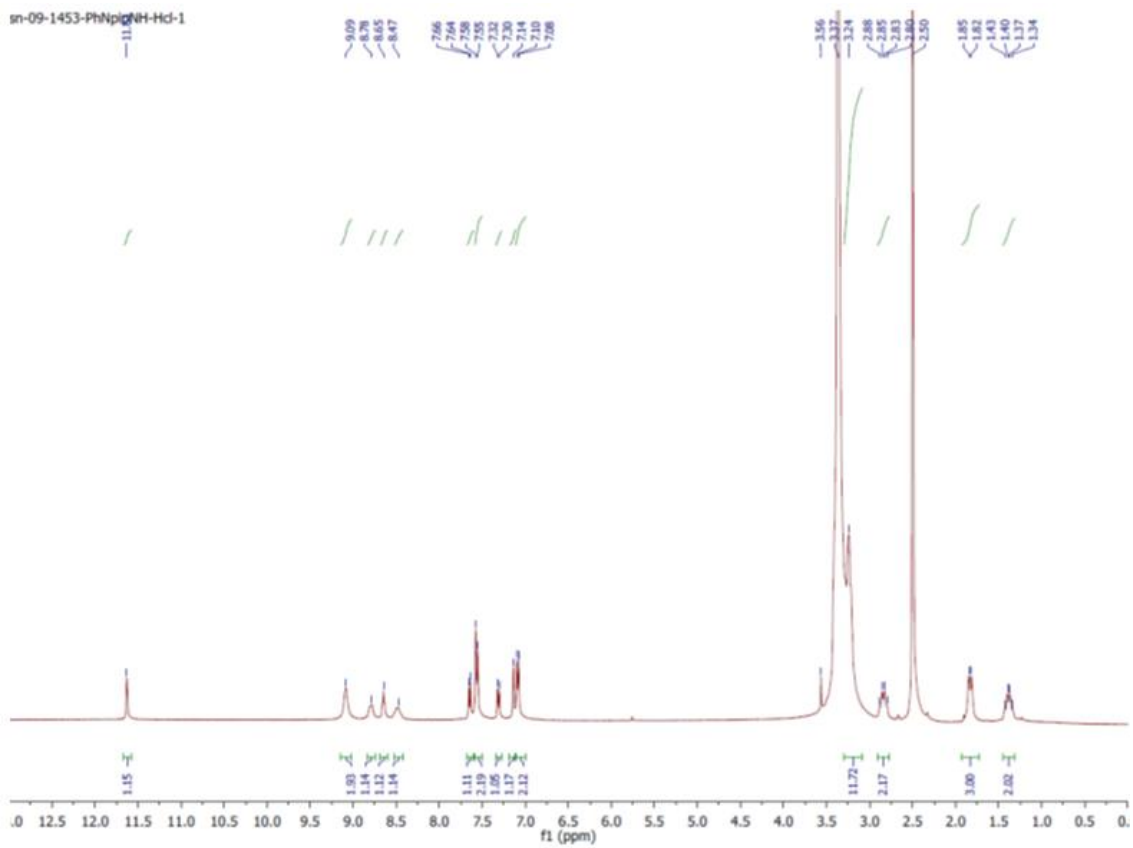




56. 6-(4-Phenoxyphenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**56**).

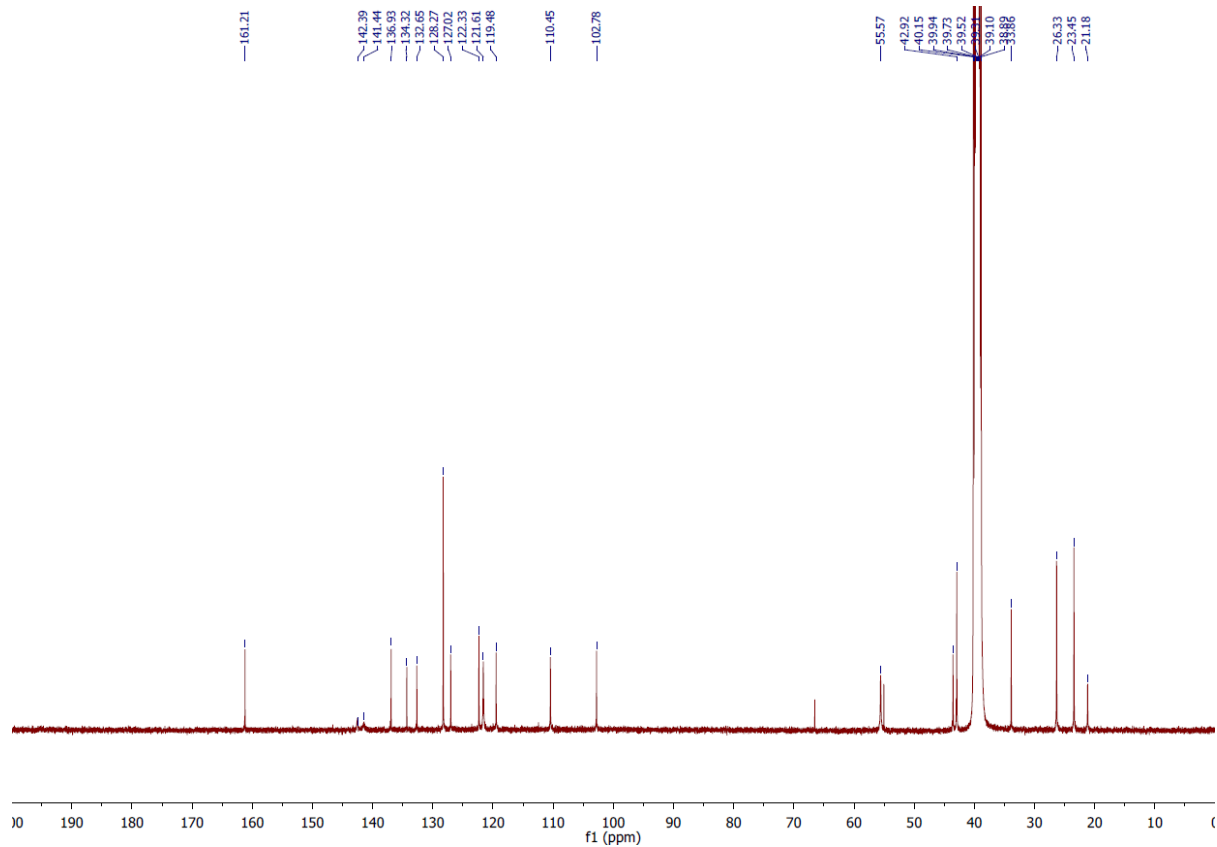
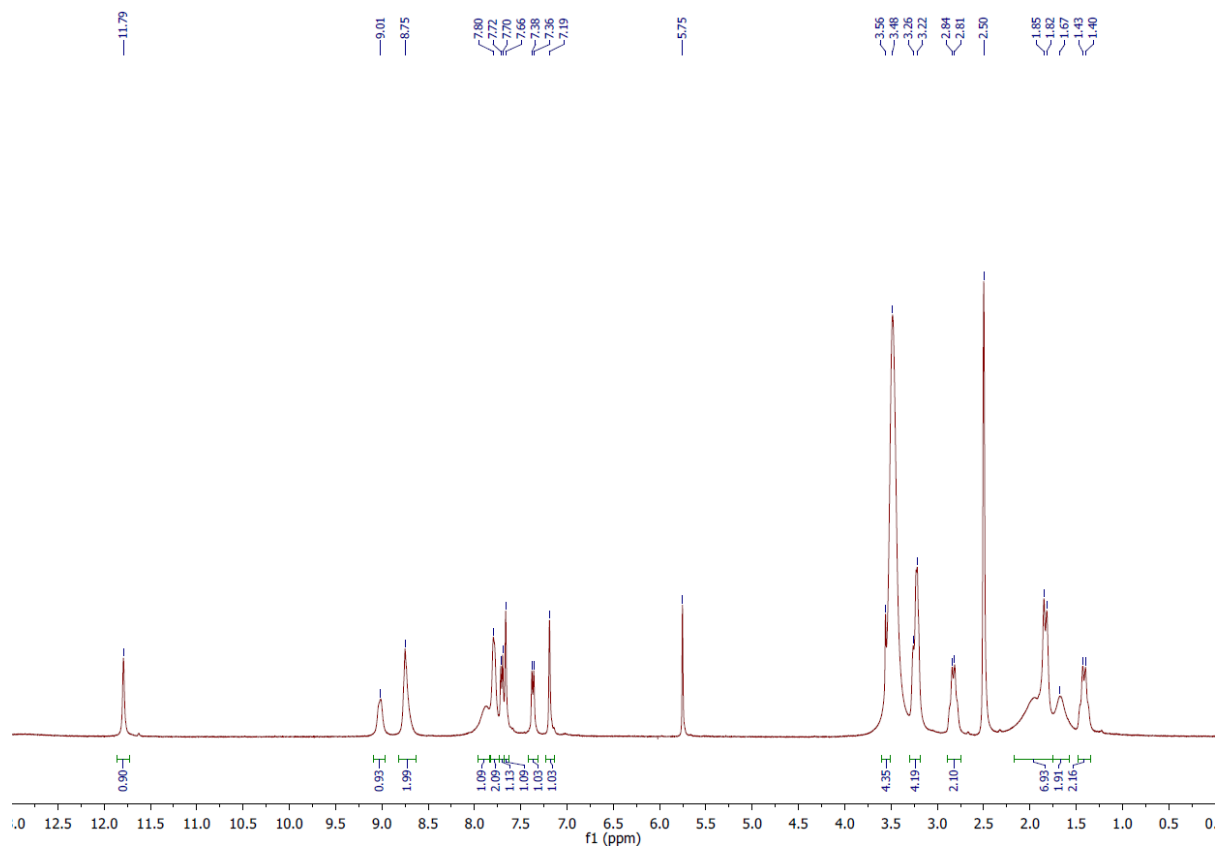


57. 6-(4-(Piperazin-1-yl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**57**).

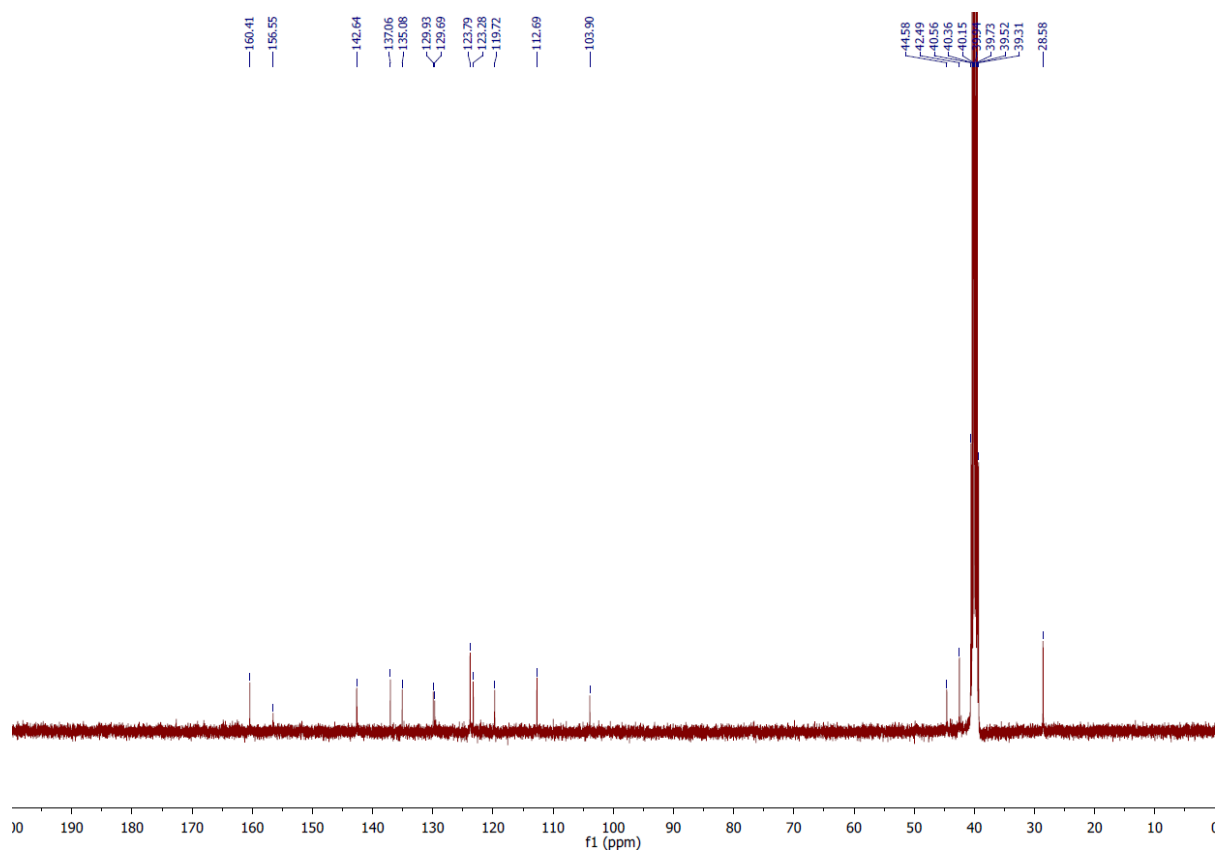
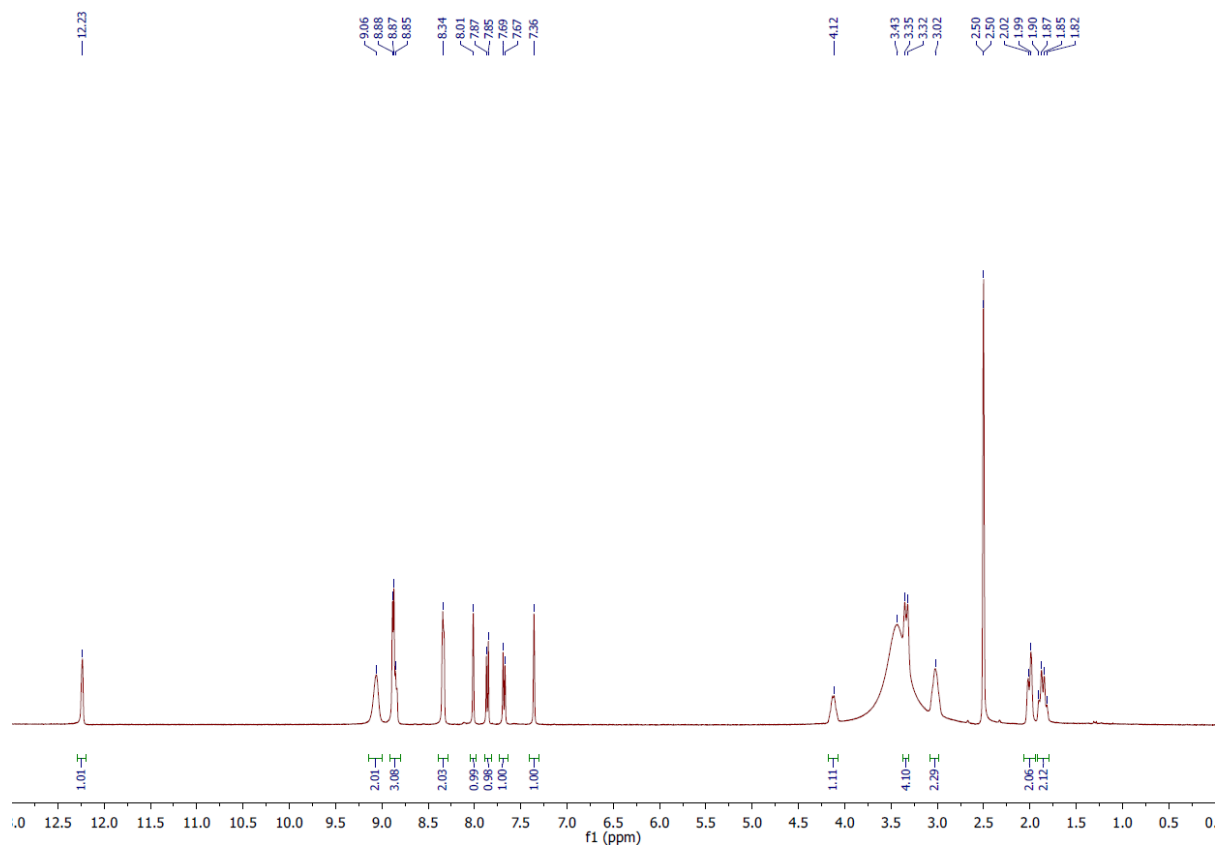


58. 6-(4-(Piperidin-1-yl)phenyl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide

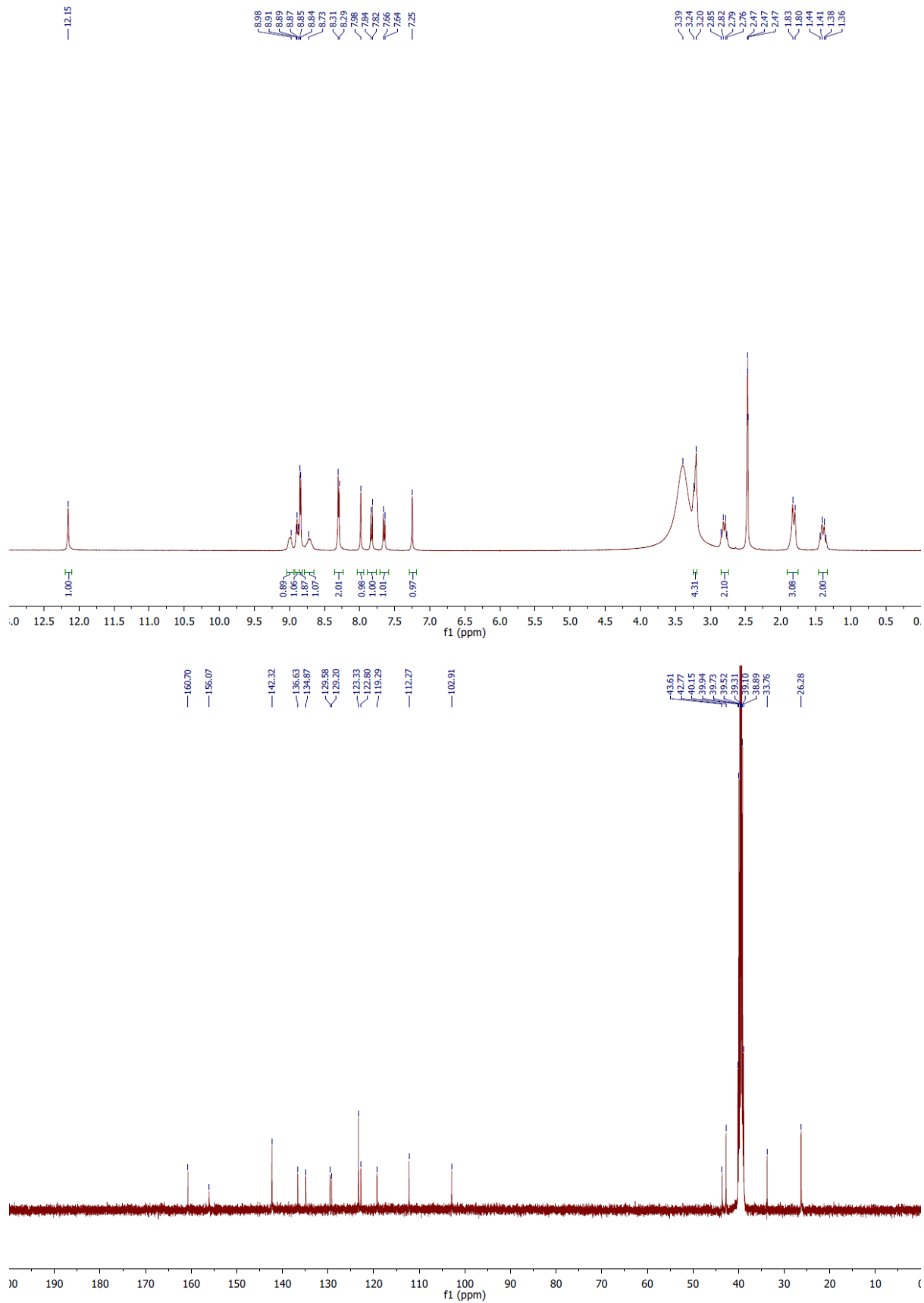
Hydrochloride (58).



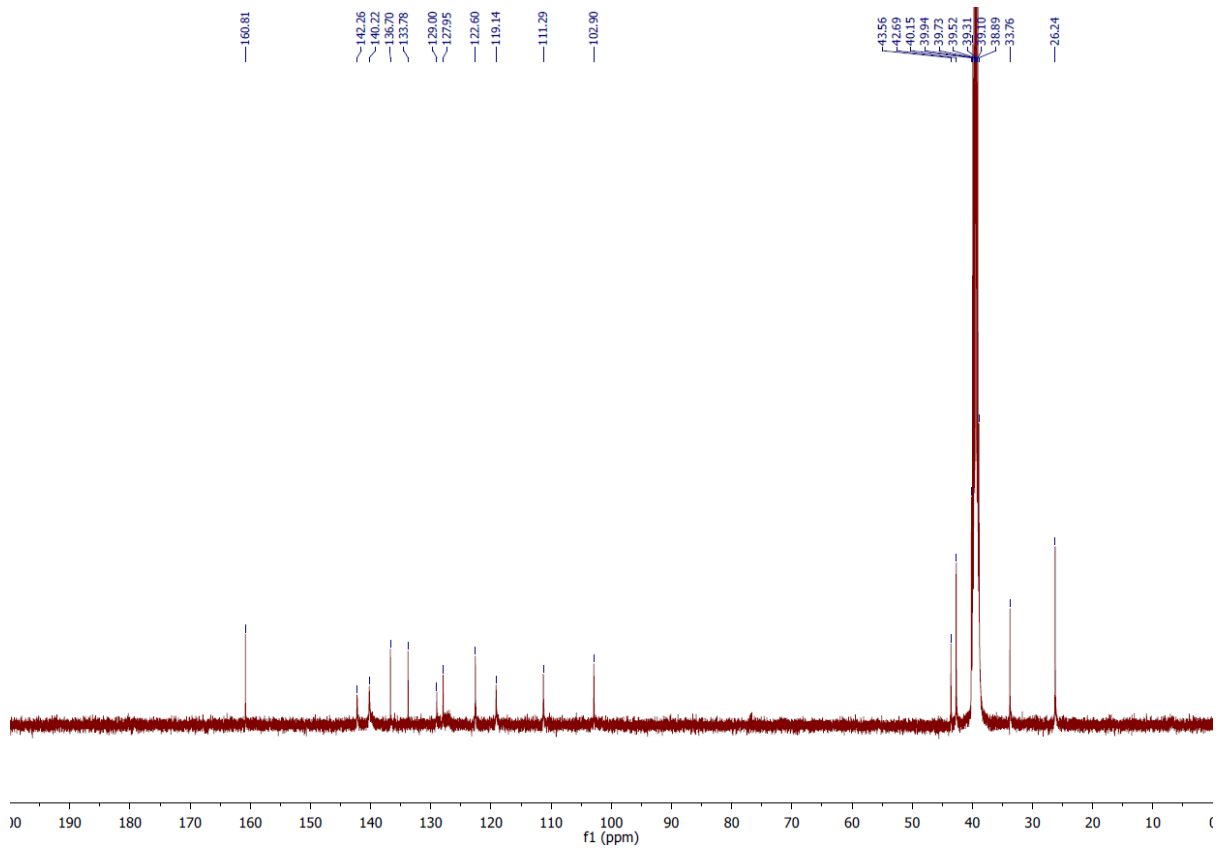
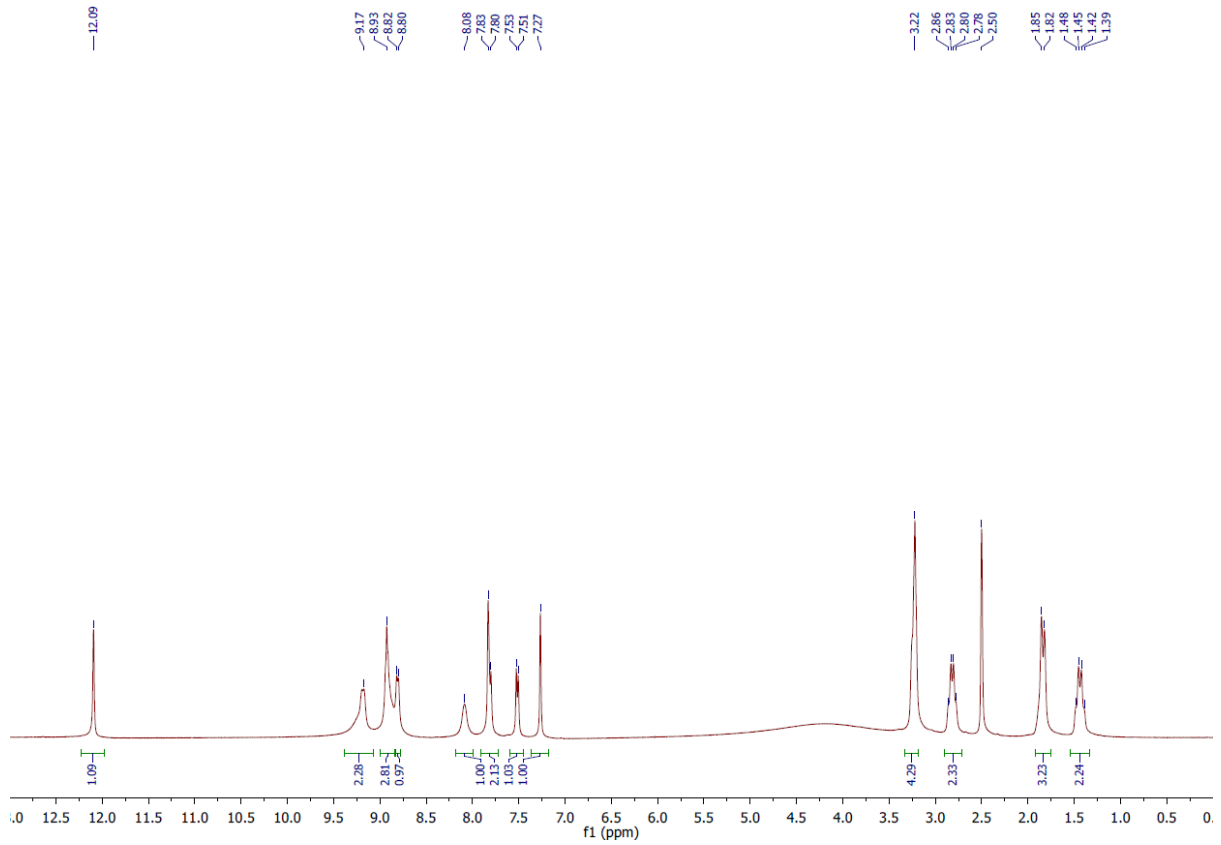
59. N-(Piperidin-4-yl)-6-(pyridin-4-yl)-1H-indole-2-carboxamide Hydrochloride (59)



60. N-(Piperidin-4-ylmethyl)-6-(pyridin-4-yl)-1H-indole-2-carboxamide Hydrochloride (**60**).

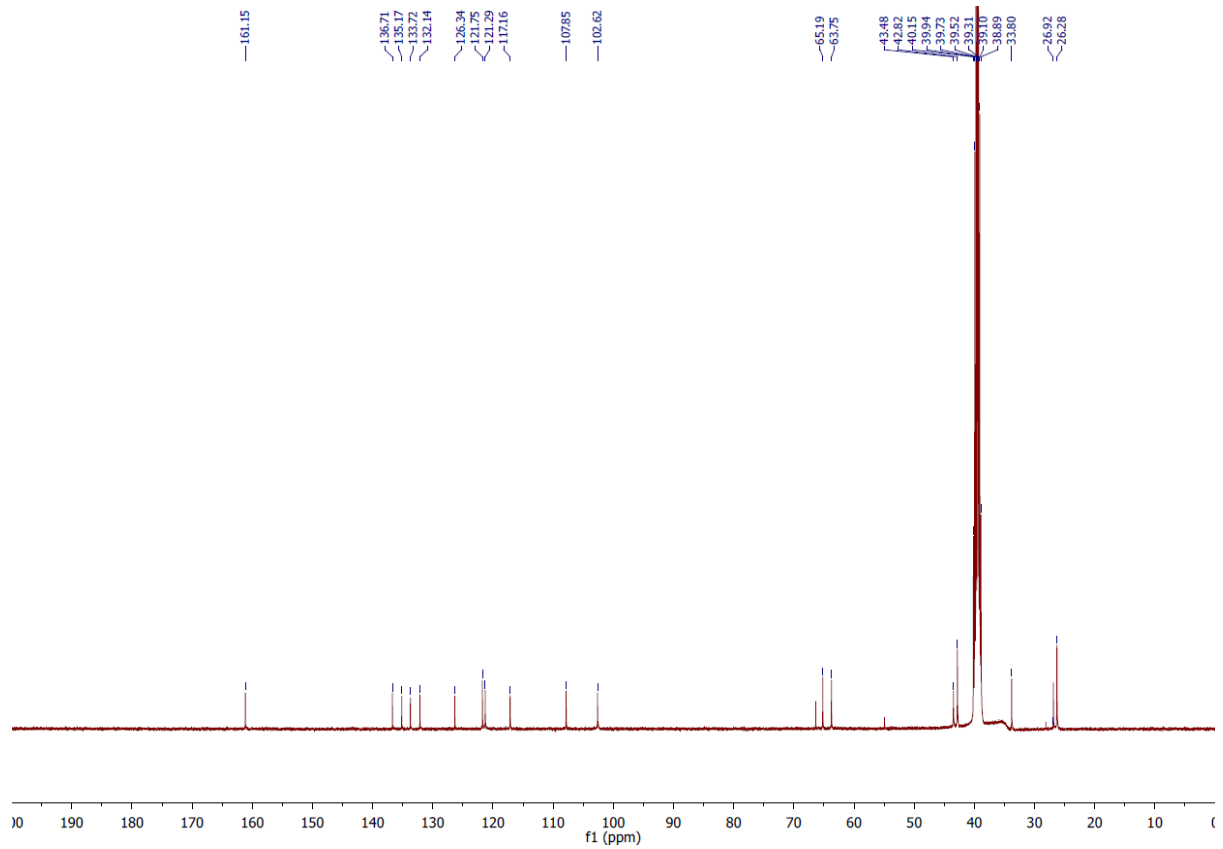
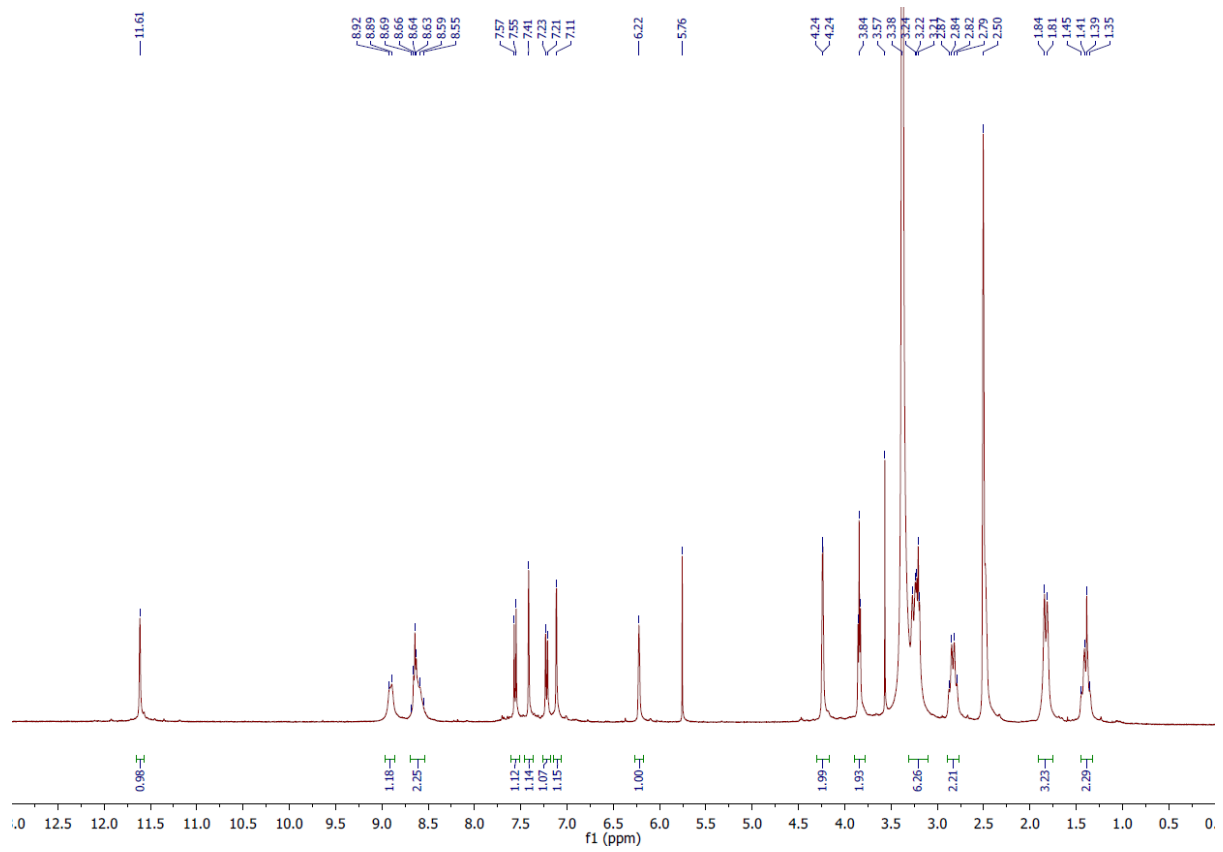


61. N-(Piperidin-4-ylmethyl)-6-(pyridin-3-yl)-1H-indole-2-carboxamide Hydrochloride (**61**).

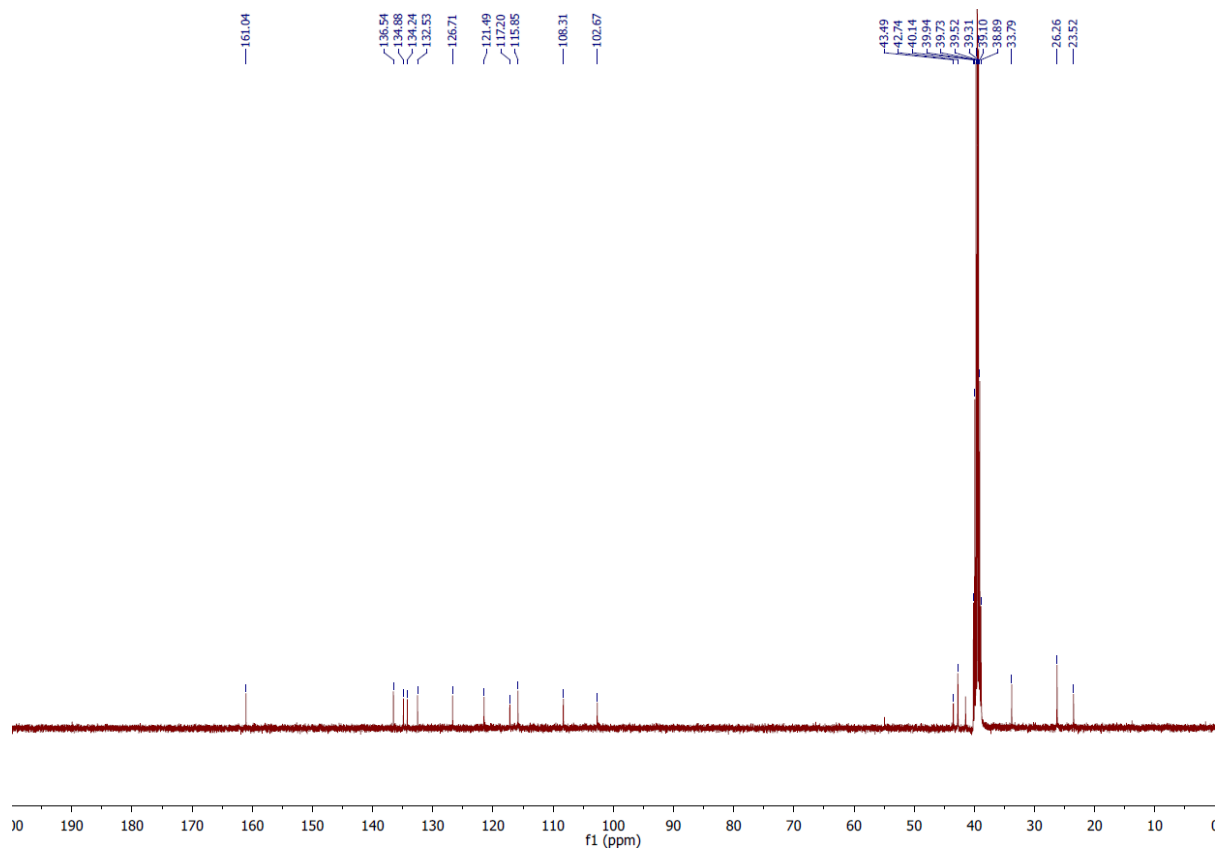
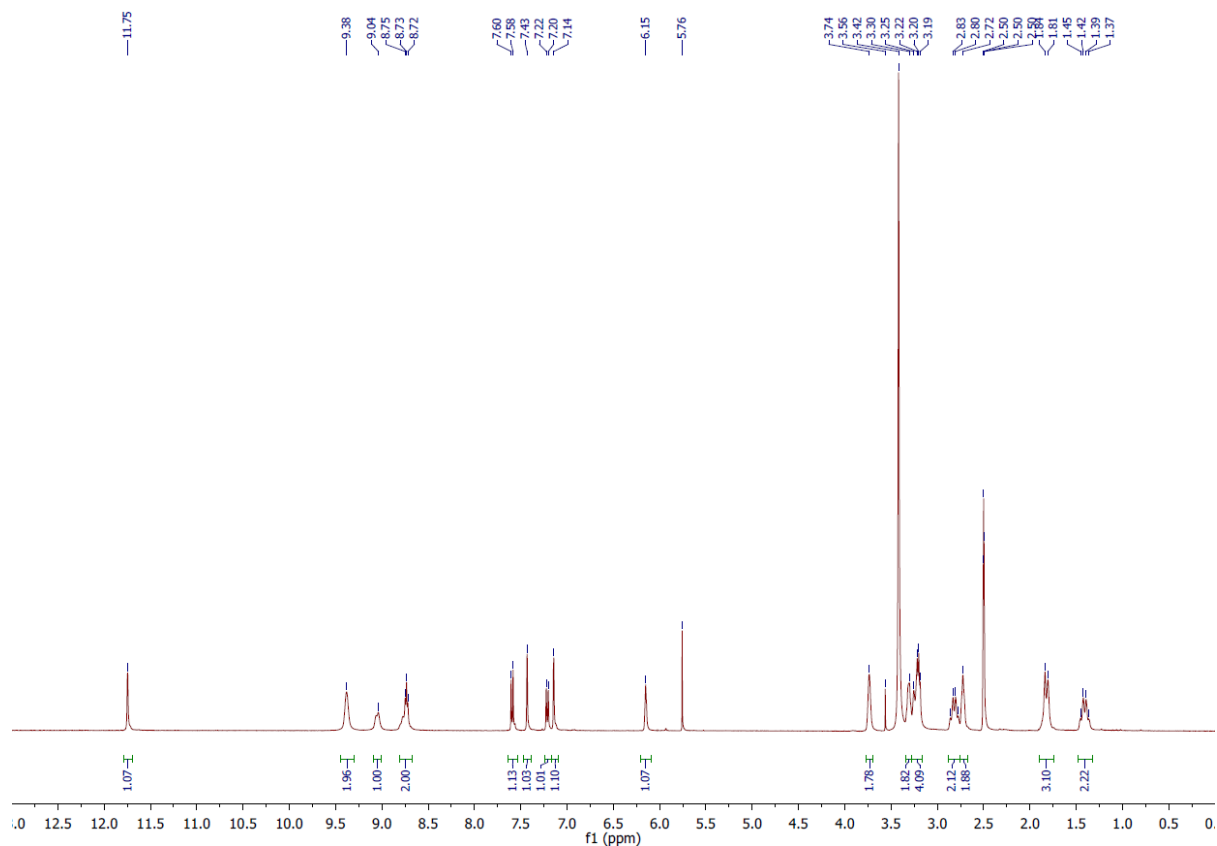


62. 6-(3,6-Dihydro-2H-pyran-4-yl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide

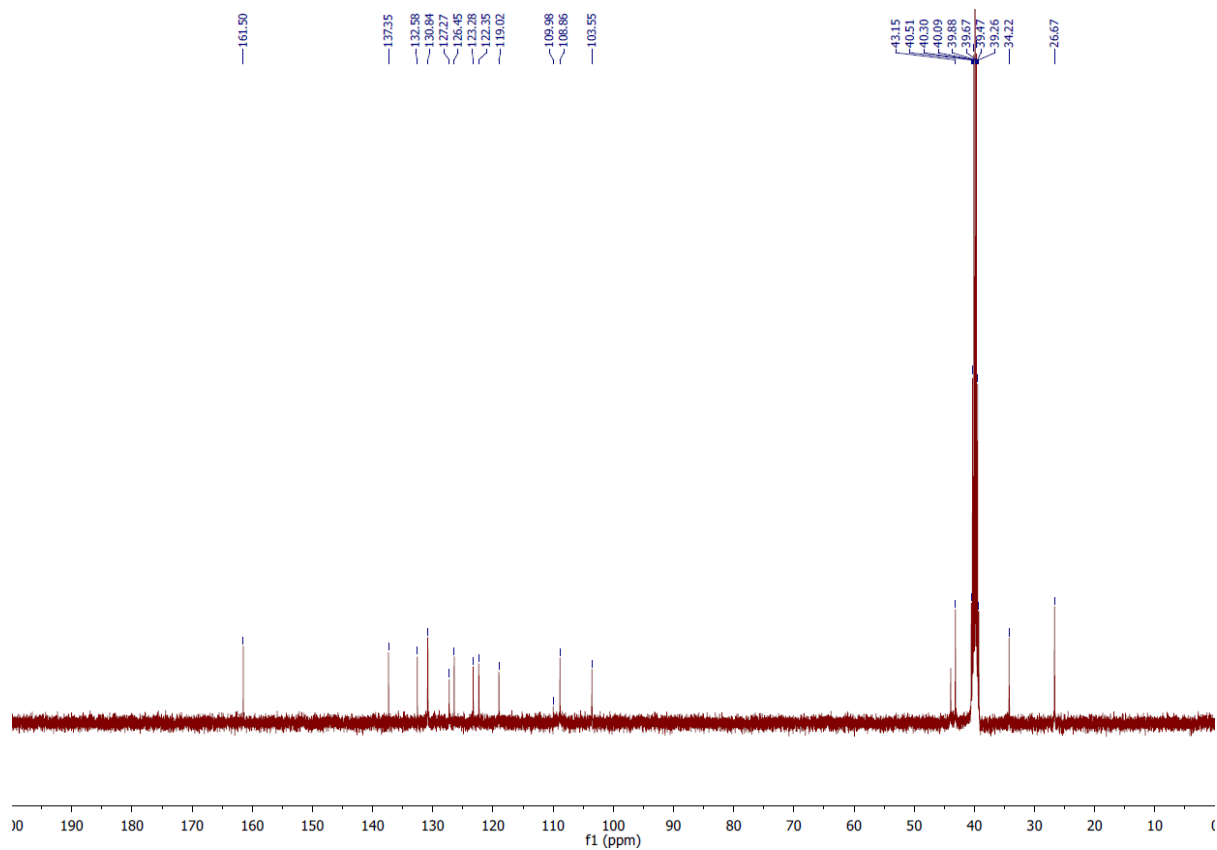
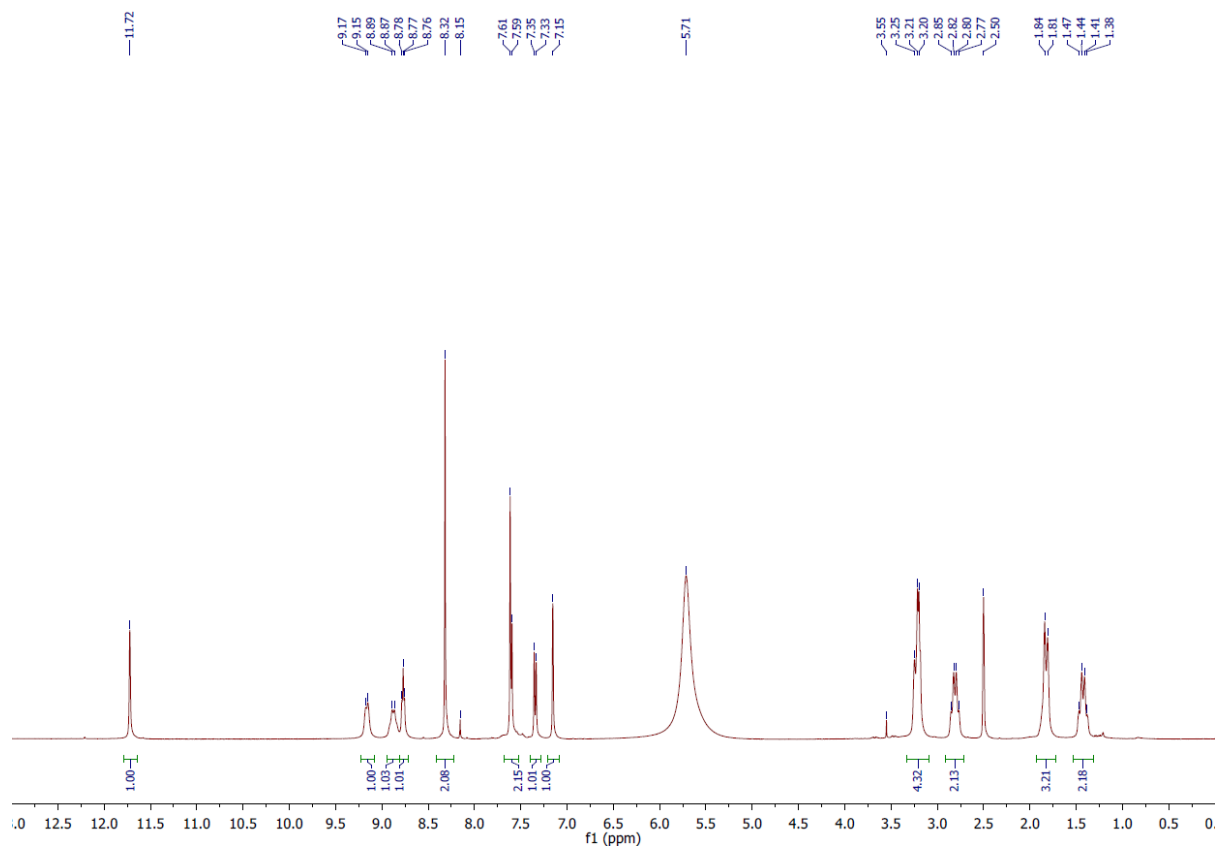
Hydrochloride (62).



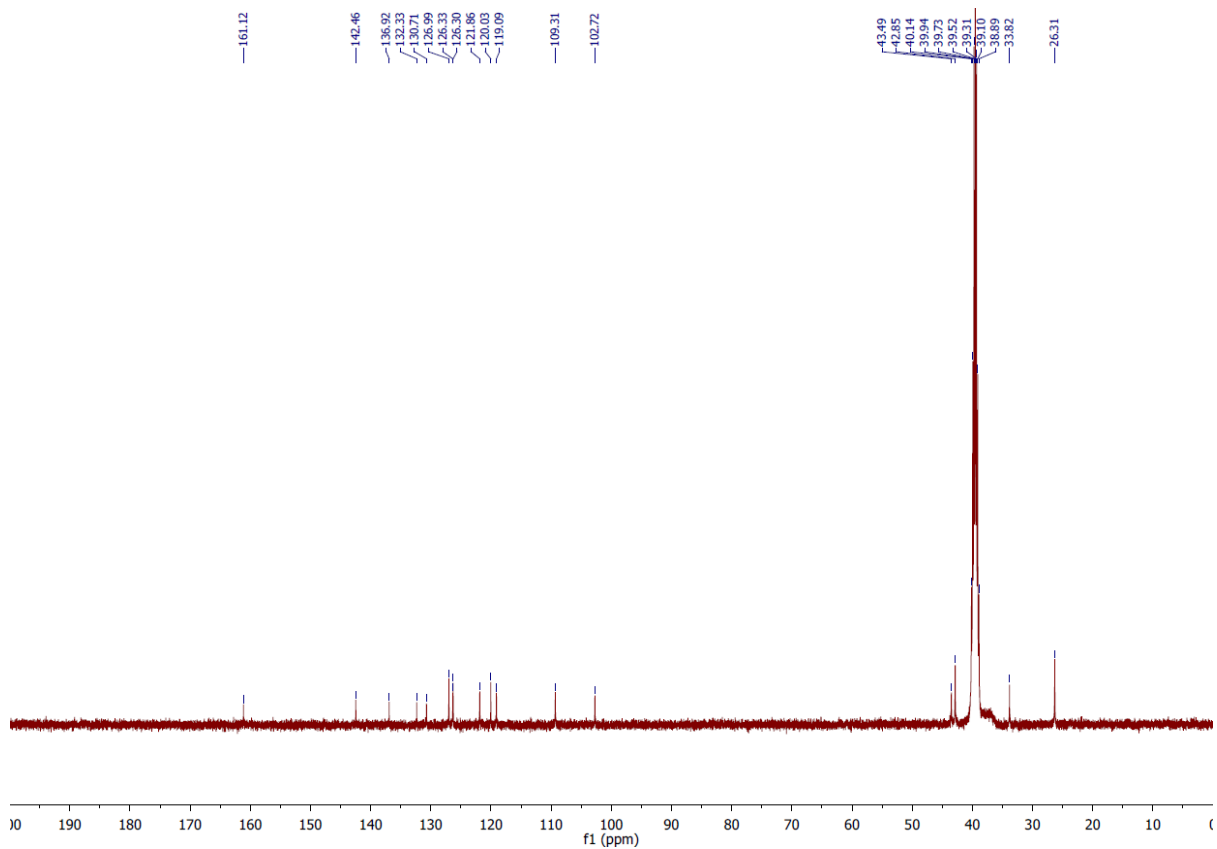
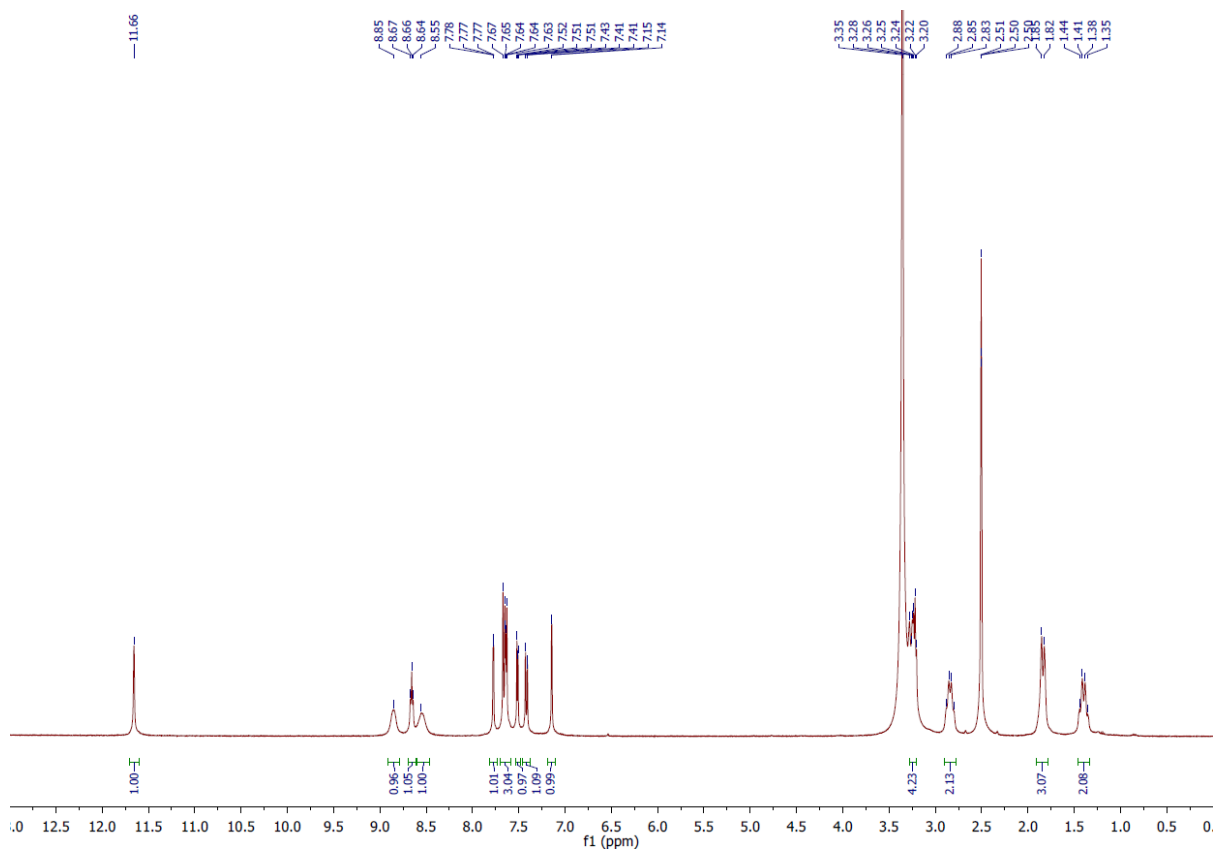
63. N-(Piperidin-4-ylmethyl)-6-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indole-2-carboxamide Hydrochloride (**63**).



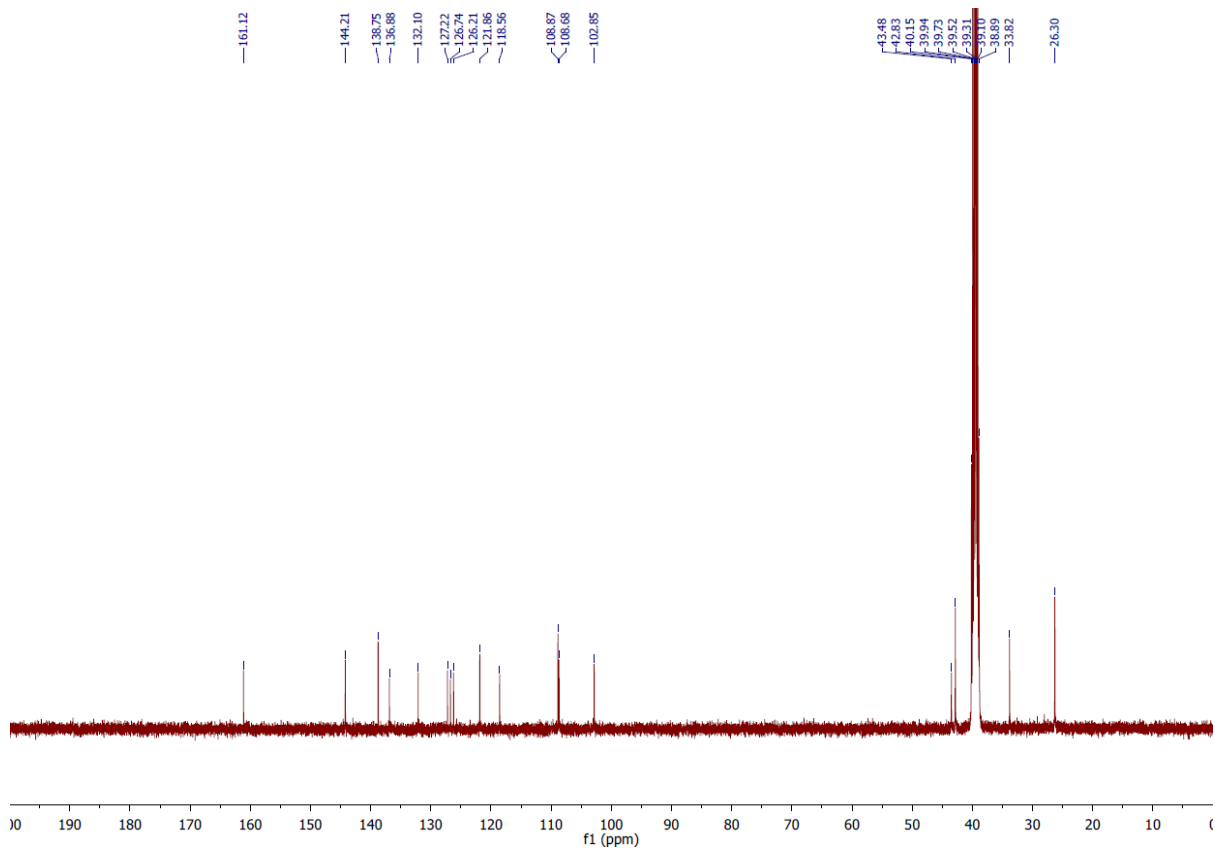
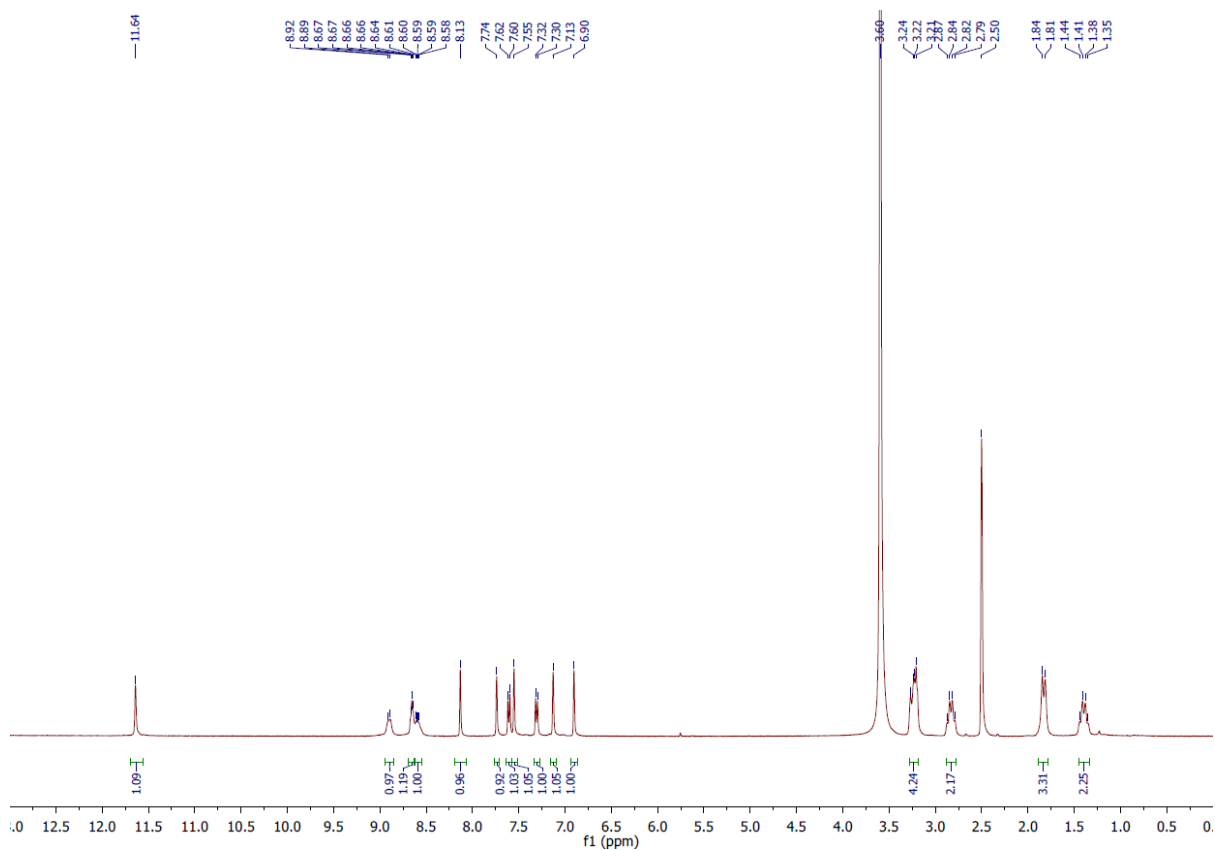
64. N-(Piperidin-4-ylmethyl)-6-(1H-pyrazol-4-yl)-1H-indole-2-carboxamide Hydrochloride (64).



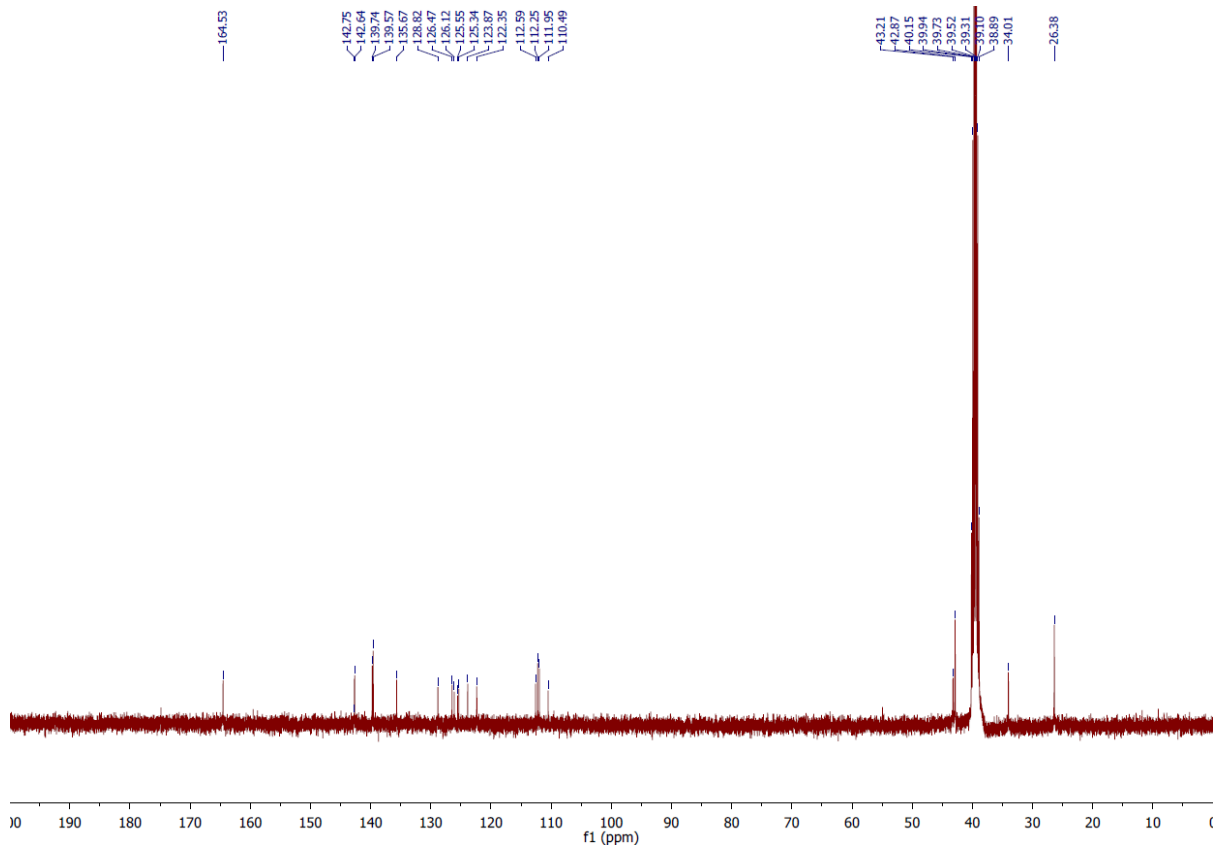
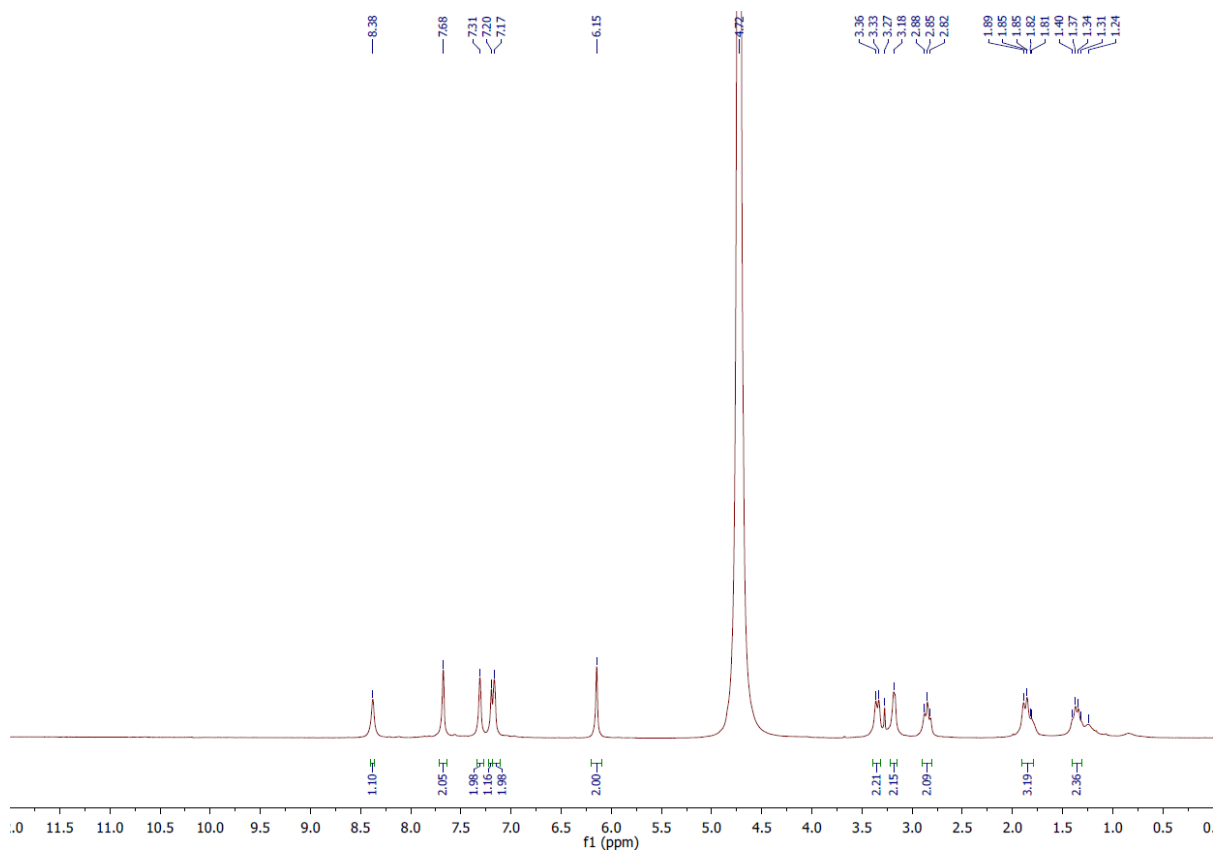
65. N-(Piperidin-4-ylmethyl)-6-(thiophen-3-yl)-1H-indole-2-carboxamide Hydrochloride (**65**).



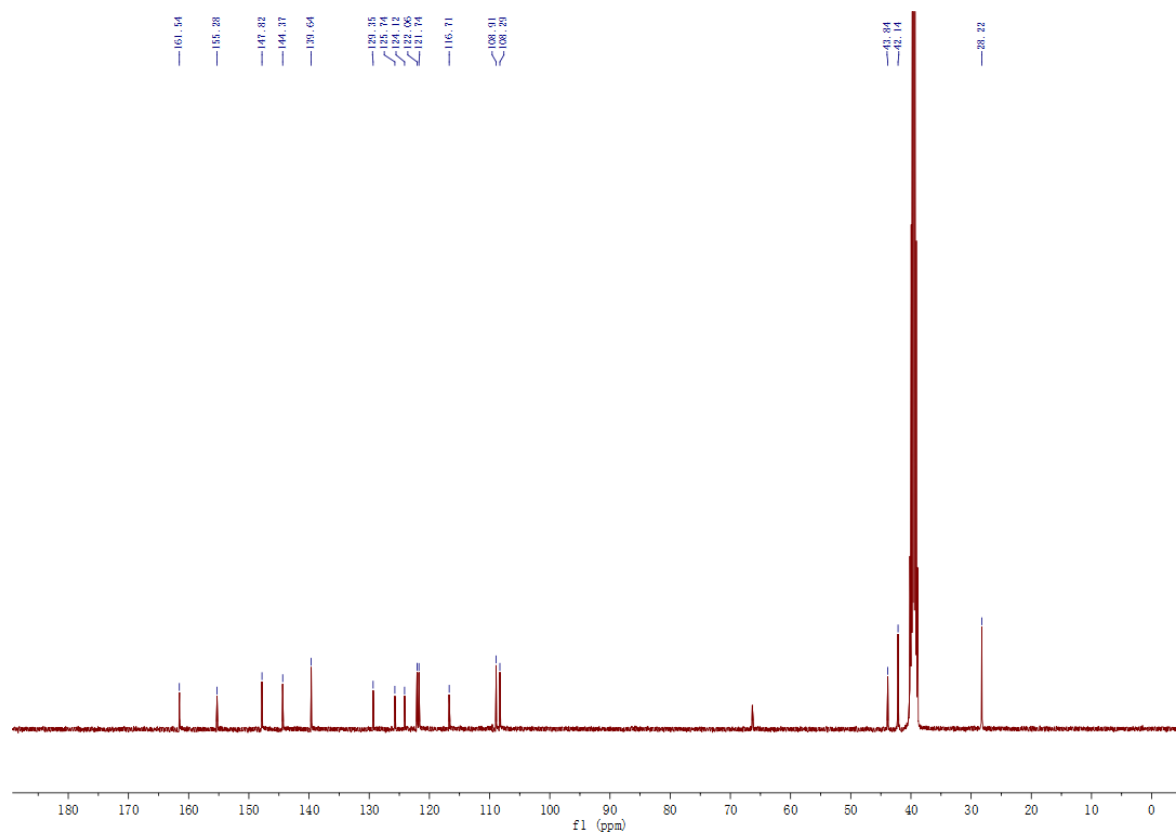
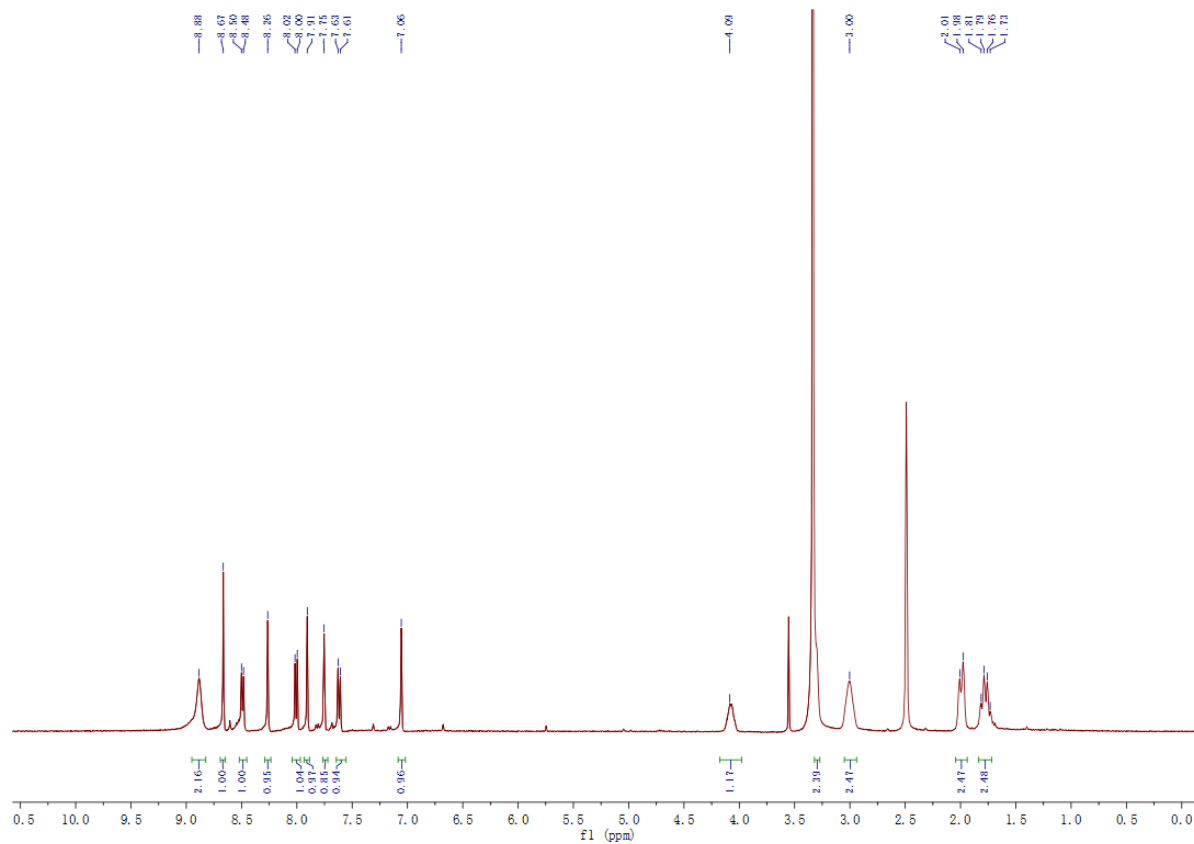
66. 6-(Furan-3-yl)-N-(piperidin-4-ylmethyl)-1H-indole-2-carboxamide Hydrochloride (**66**)



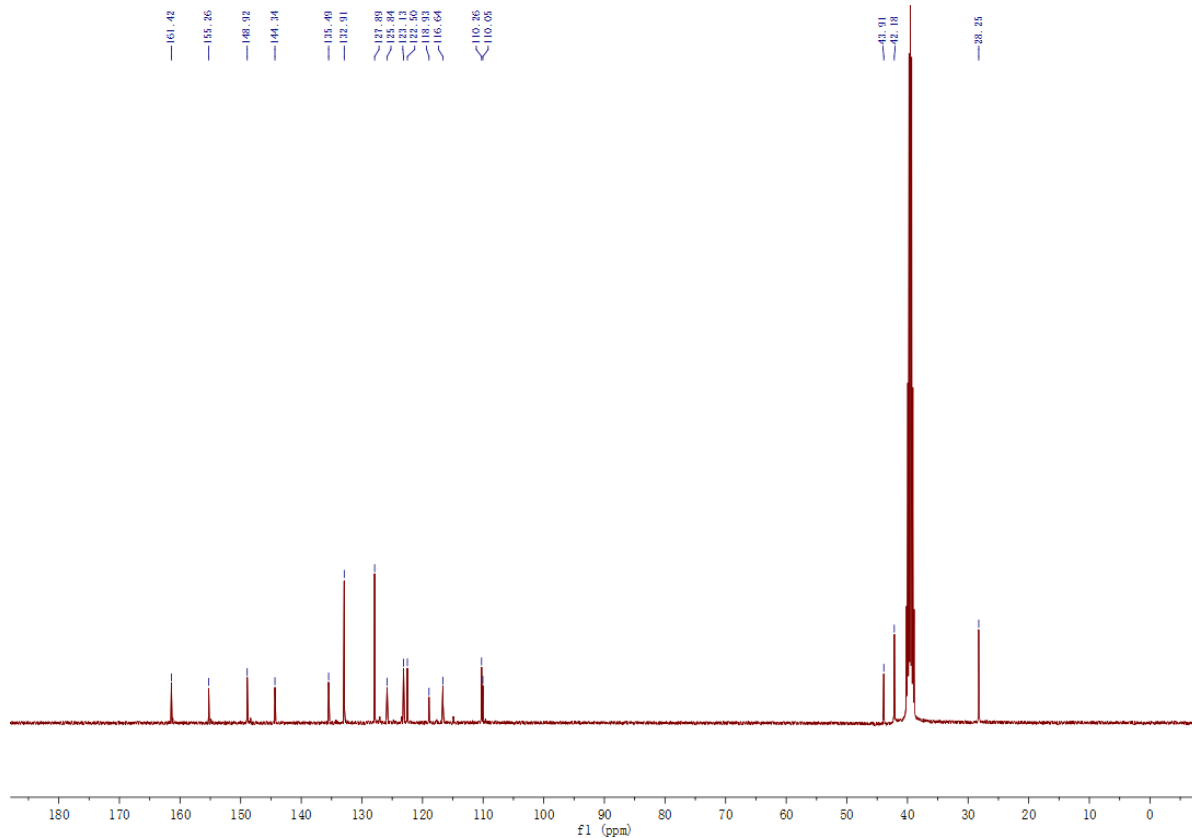
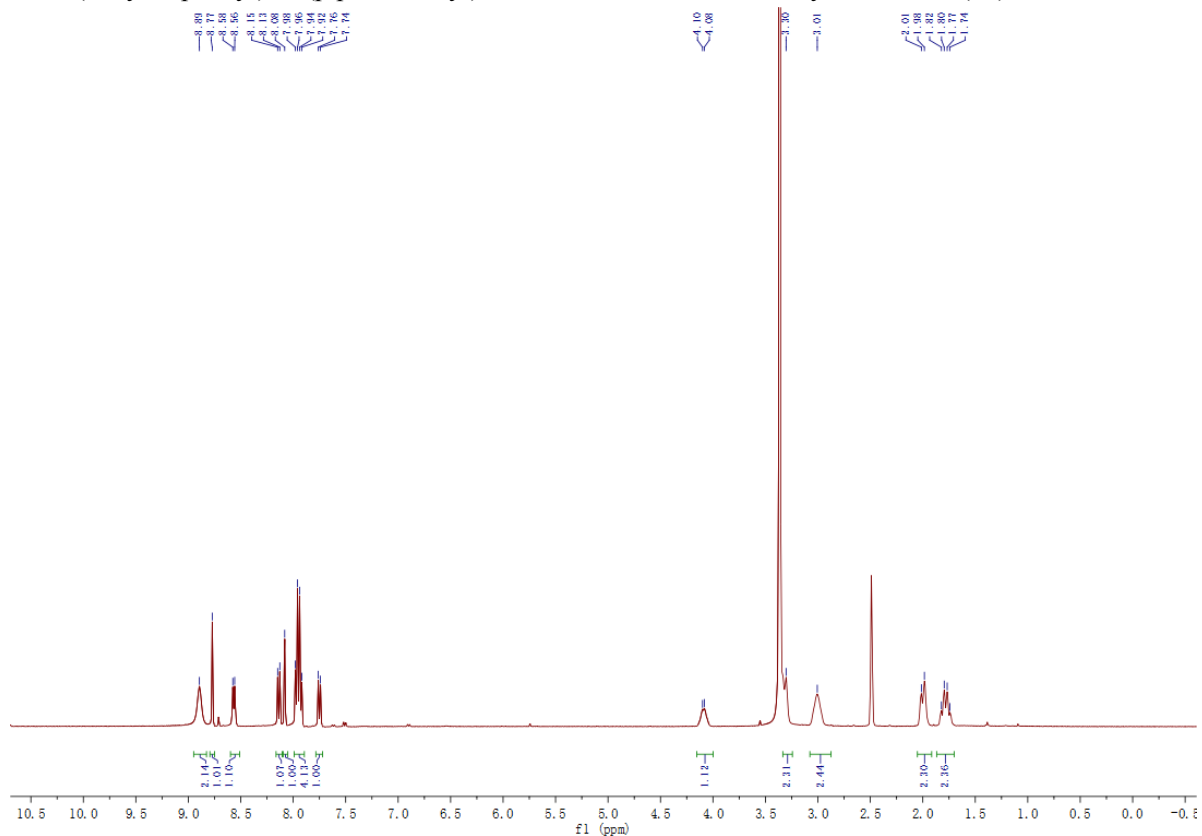
67. 5,6-Di(furan-3-yl)-N-(piperidin-4-ylmethyl)-1H-indole-3-carboxamide Hydrochloride (**67**).



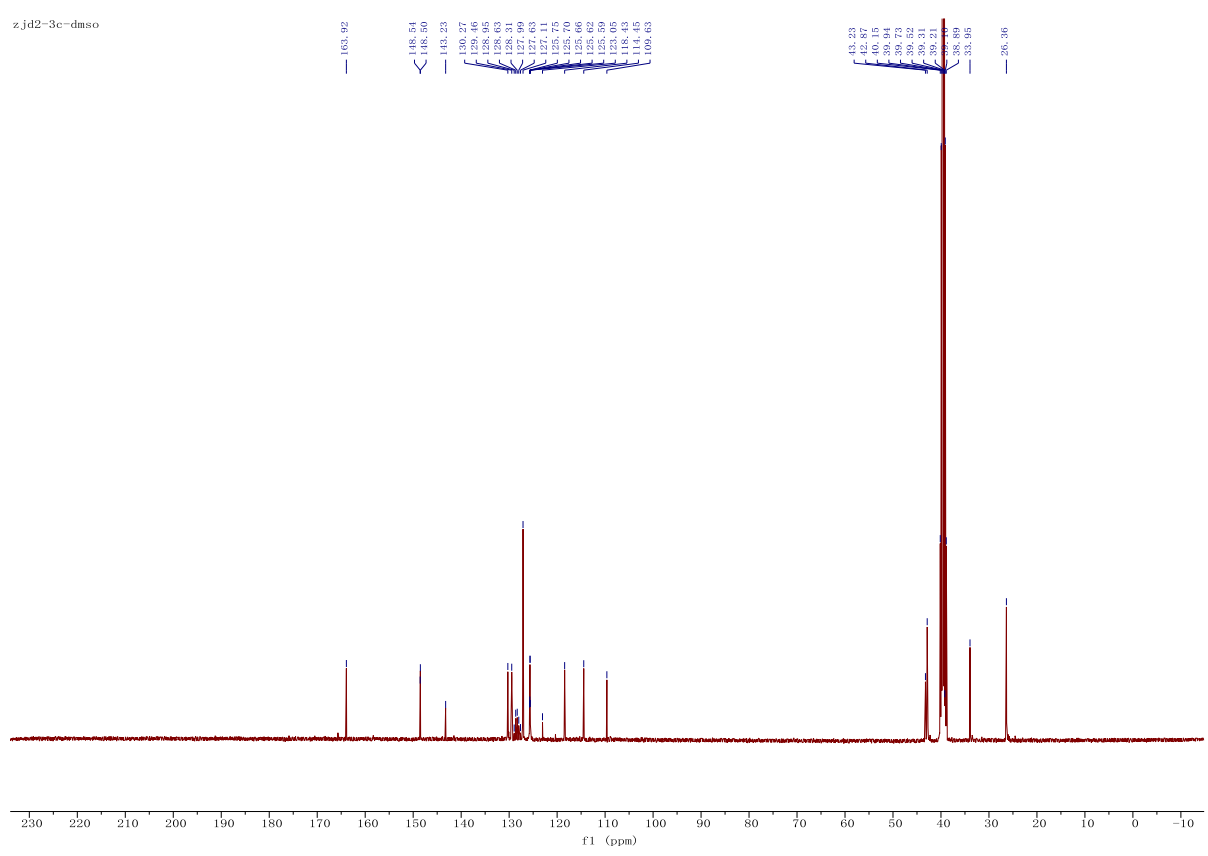
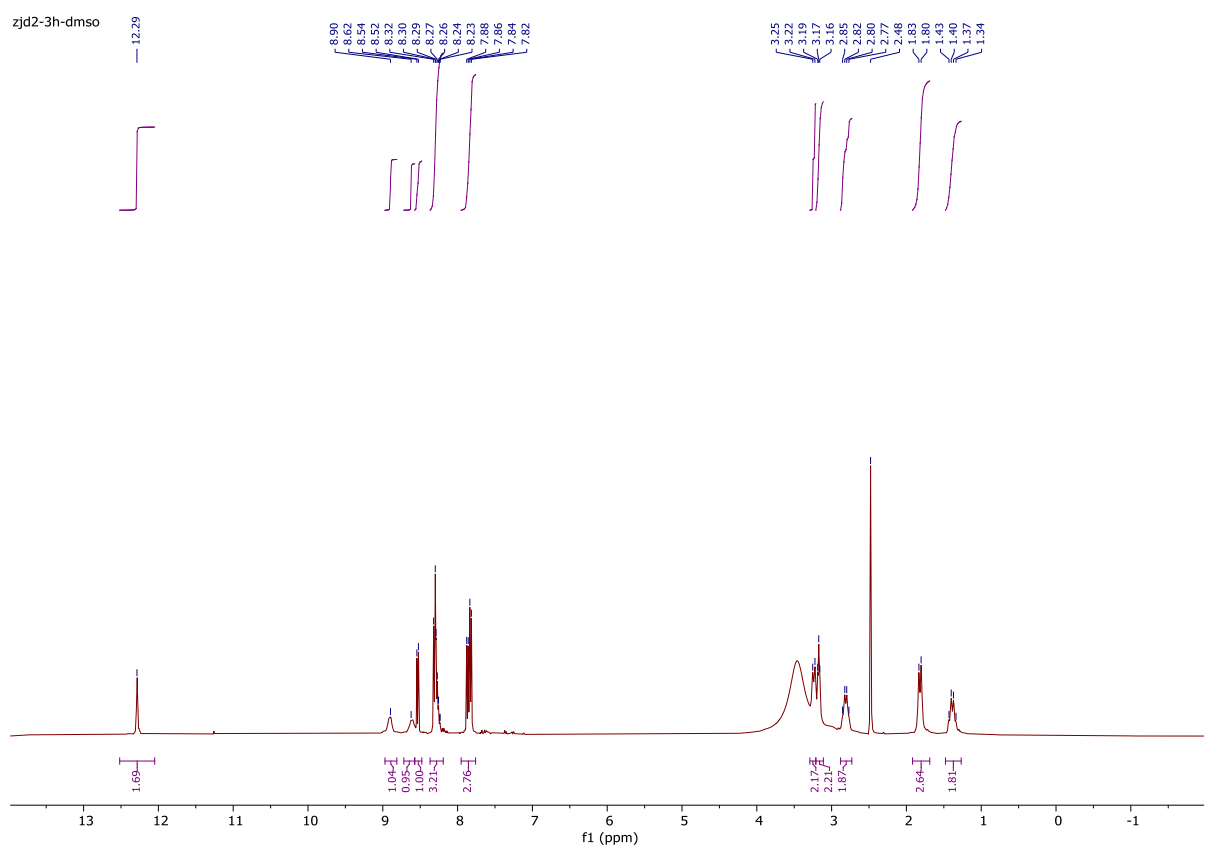
68. 6-(Furan-3-yl)-N-(piperidin-4-yl)benzofuran-3-carboxamide Hydrochloride (**68**).



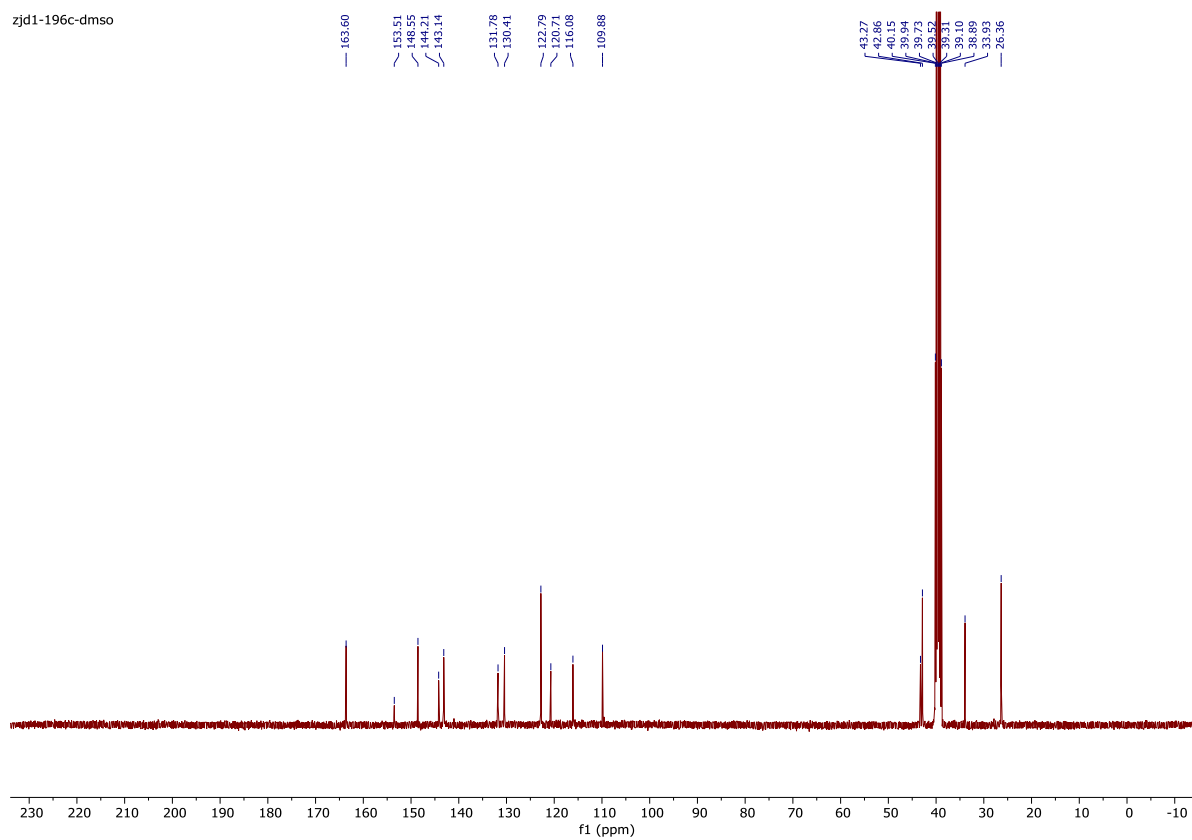
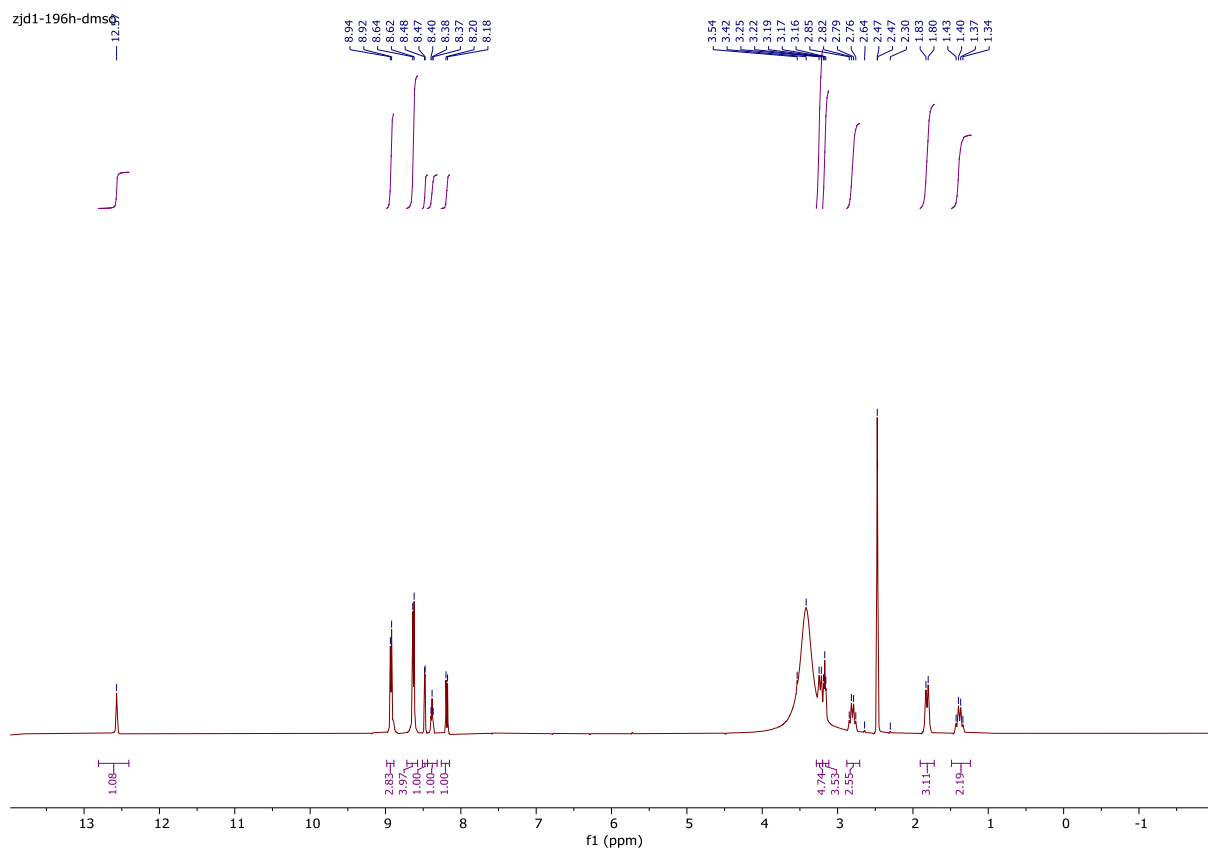
69. 6-(4-Cyanophenyl)-N-(piperidin-4-yl)benzofuran-3-carboxamide Hydrochloride (69)



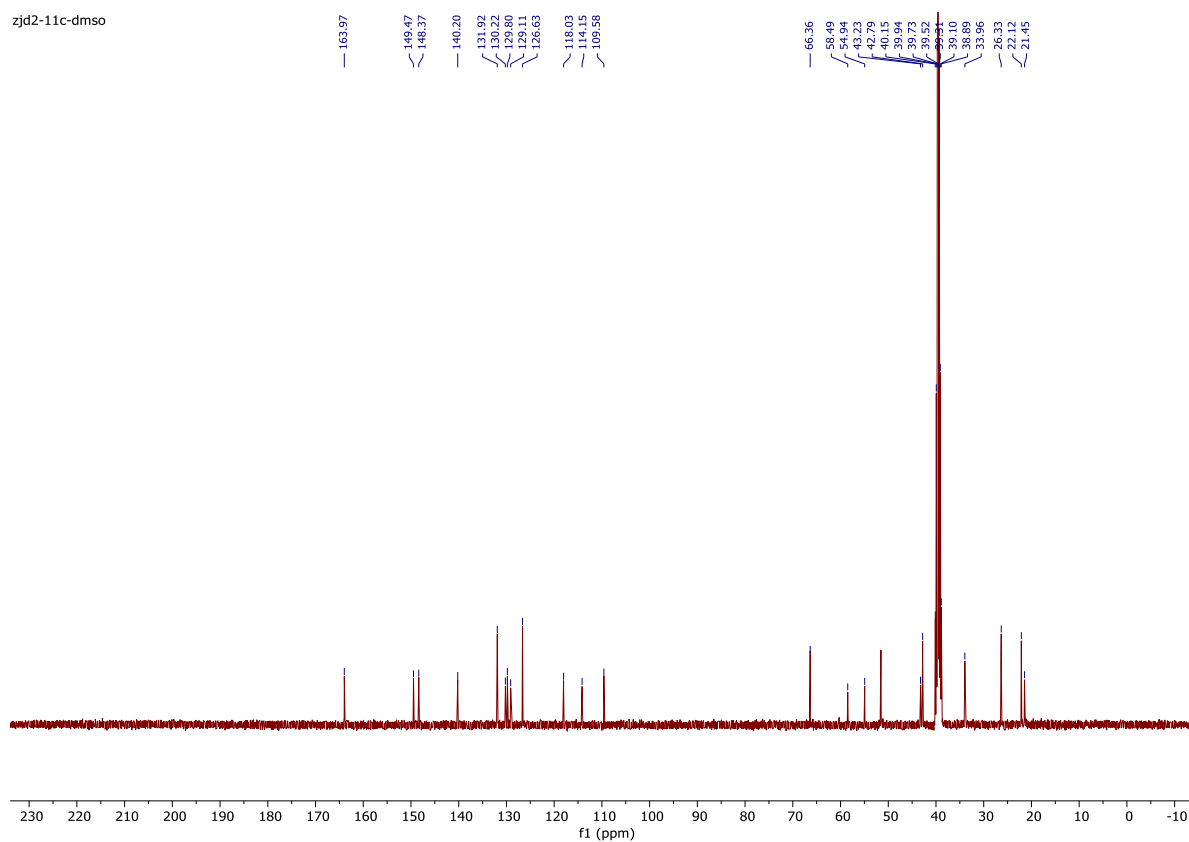
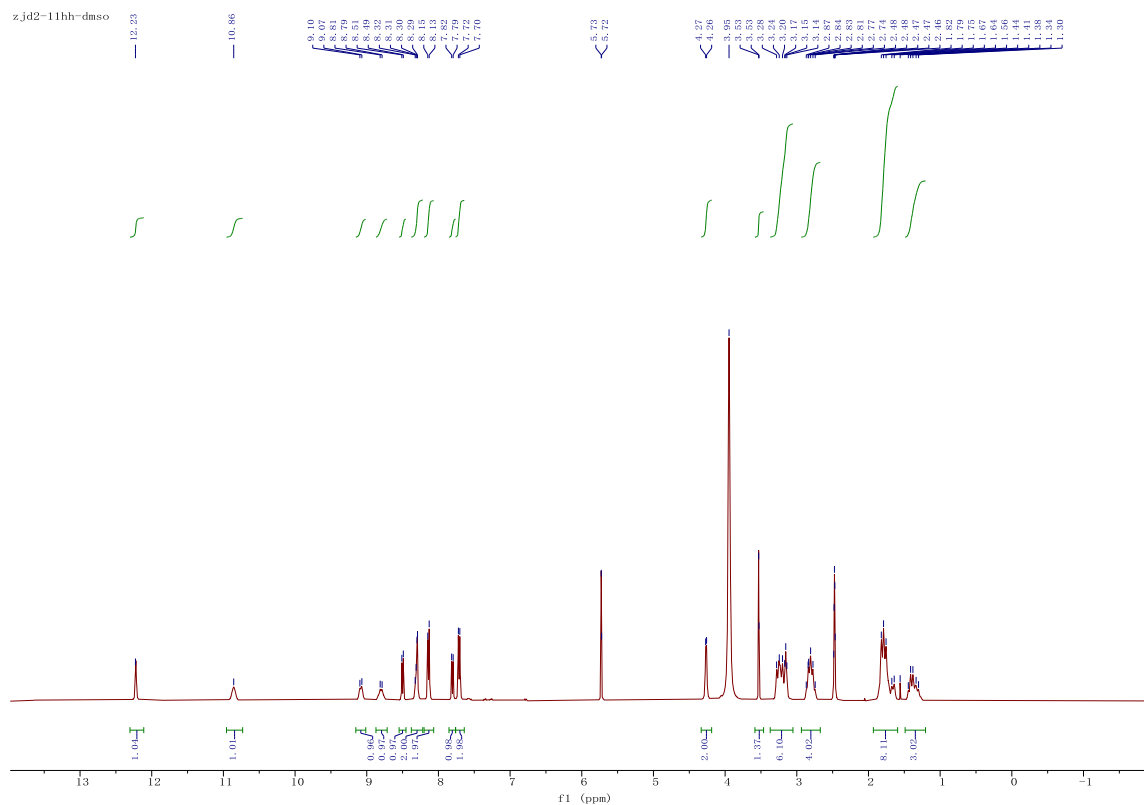
70. N-(Piperidin-4-ylmethyl)-6-(4-(trifluoromethyl)phenyl)-1H-pyrrolo[2,3-b]pyridine-3-carboxamide Hydrochloride (70).



71.N-(Piperidin-4-ylmethyl)-6-(pyridin-4-yl)-1H-pyrrolo[2,3-b]pyridine-3-carboxamide Hydrochloride (71).



72. 6-(4-(Piperidin-1-ylmethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-pyrrolo[2,3-b]pyridine-3-carboxamide Hydrochloride (72).



73. 6-(4-(Morpholinomethyl)phenyl)-N-(piperidin-4-ylmethyl)-1H-pyrrolo[2,3-b]pyridine-3-carboxamide Hydrochloride

(73).

