

# **Novel quinazoline derivatives as highly effective A<sub>2A</sub> adenosine receptor antagonists**

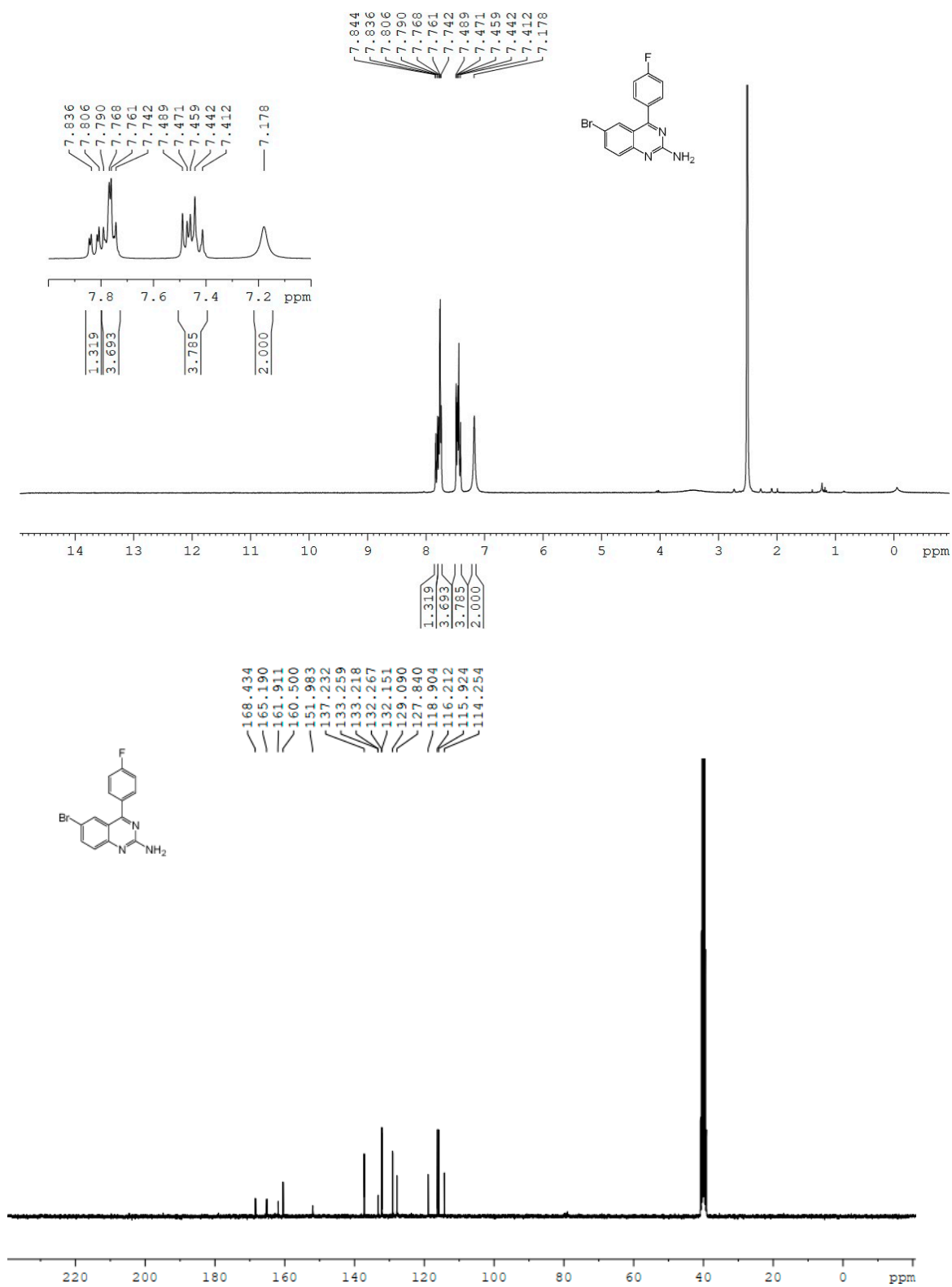
Amélie Laversin, Robin Dufosse<sup>†</sup>, Raphaël Bolteau<sup>†</sup>, Romain Duroux, Séverine Ravez, Sergio Hernandez-Tapia, Martin Fossart, Mathilde Coevoet, Maxime Liberelle, Saïd Yous, Nicolas Lebègue, Patricia Melnyk<sup>\*</sup>

*Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille, France.*

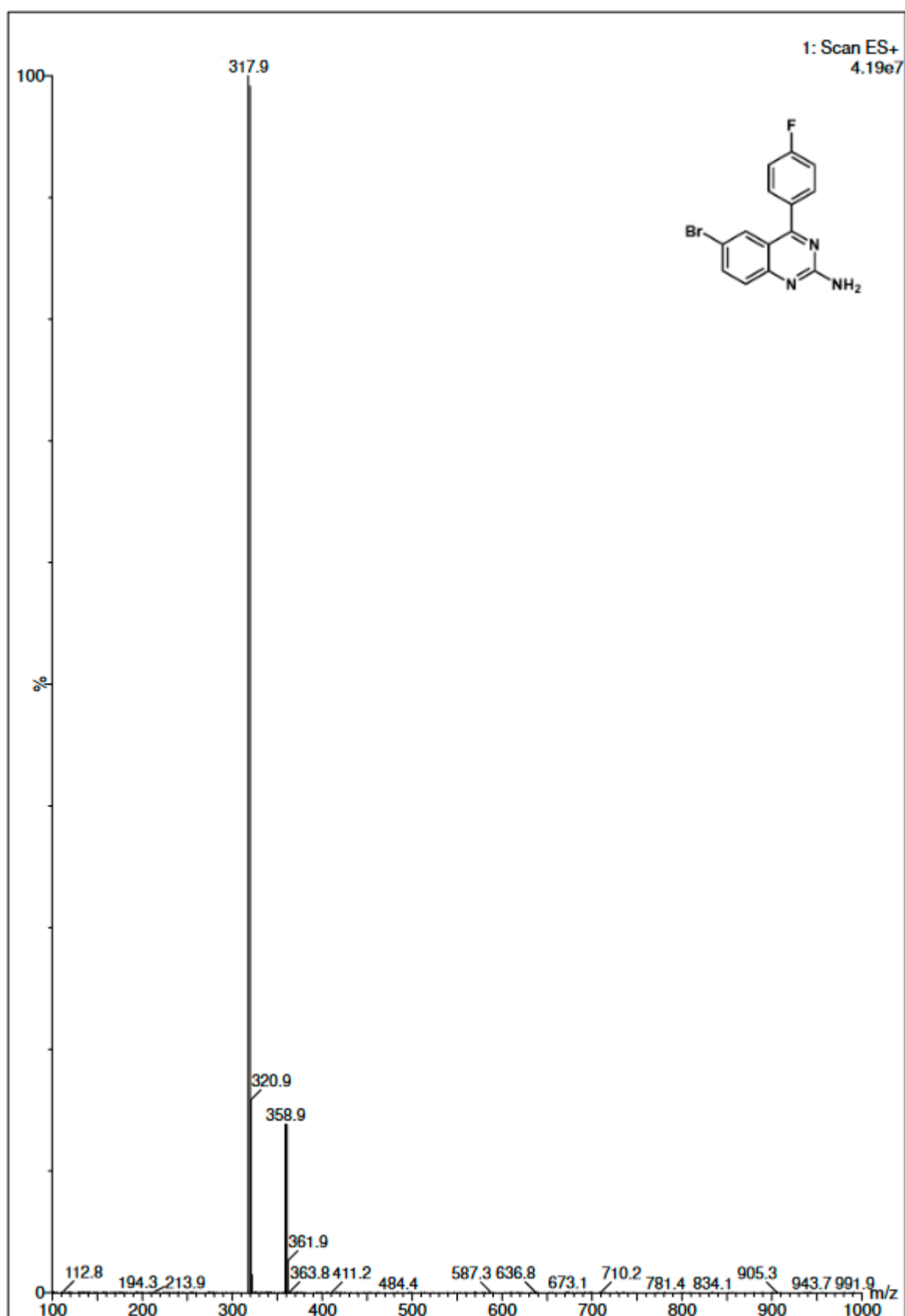
<sup>†</sup>*These authors contributed equally*

**Figure S1.** NMR and LC-MS spectra of final compounds

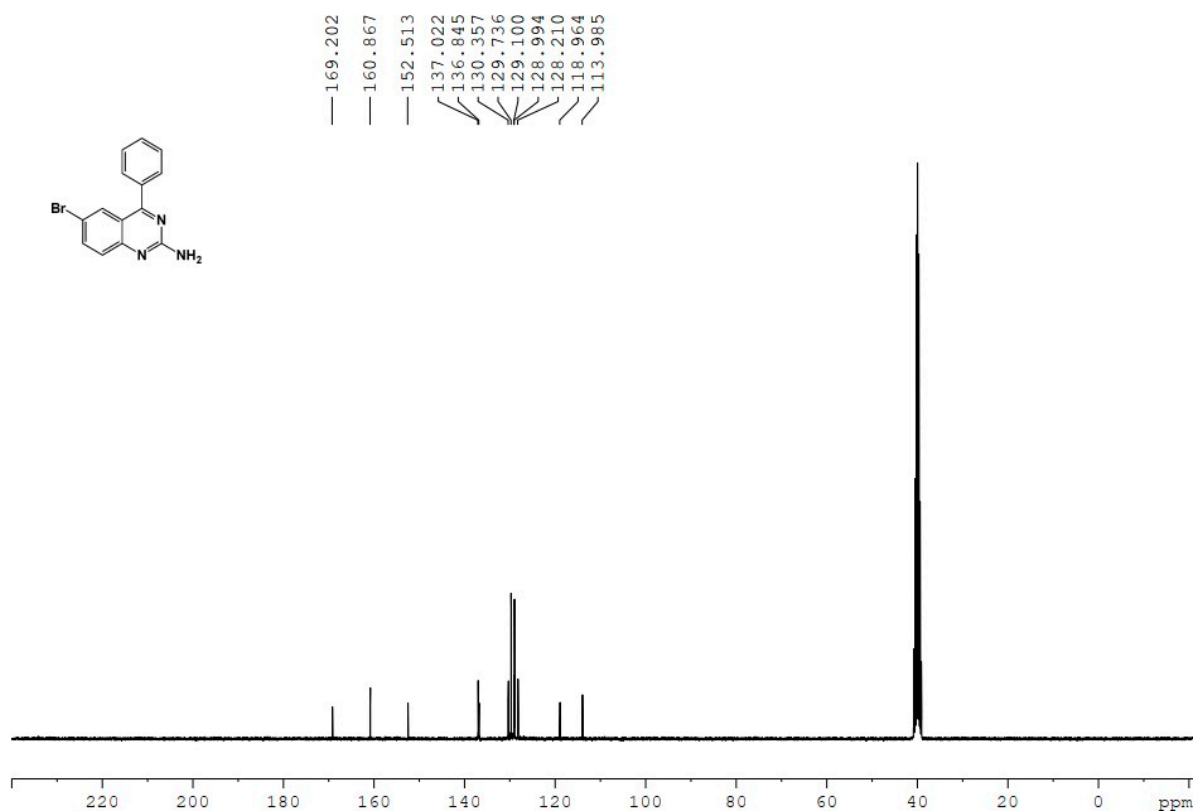
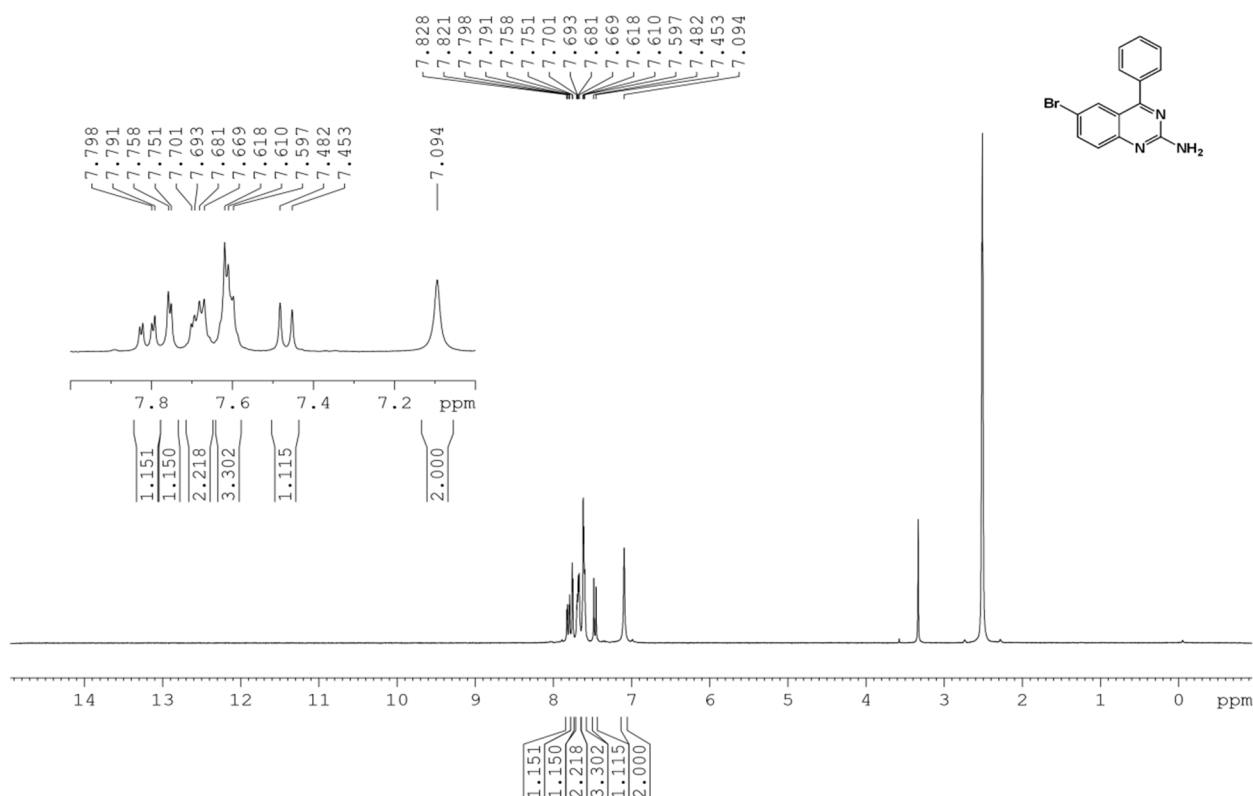
<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5a



LC-MS mass spectrum of compound 5a

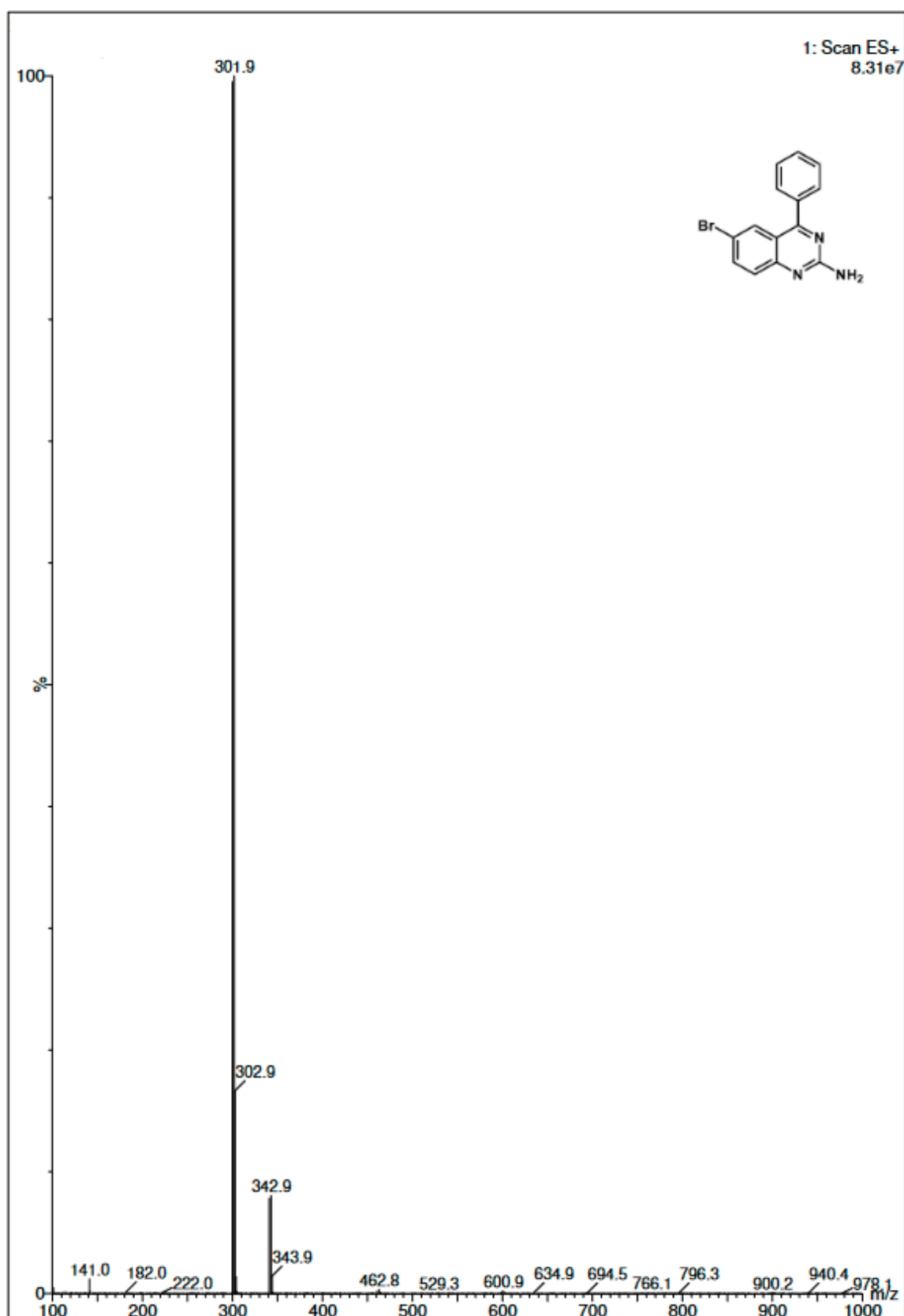


# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5b**

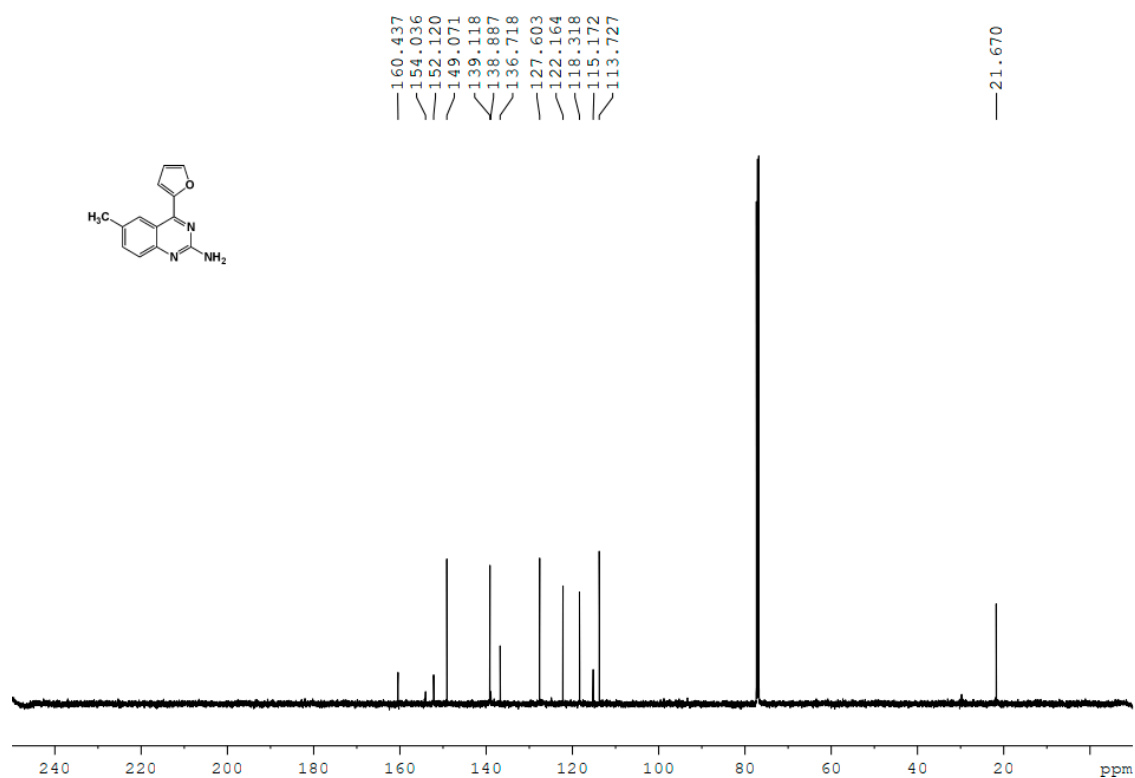
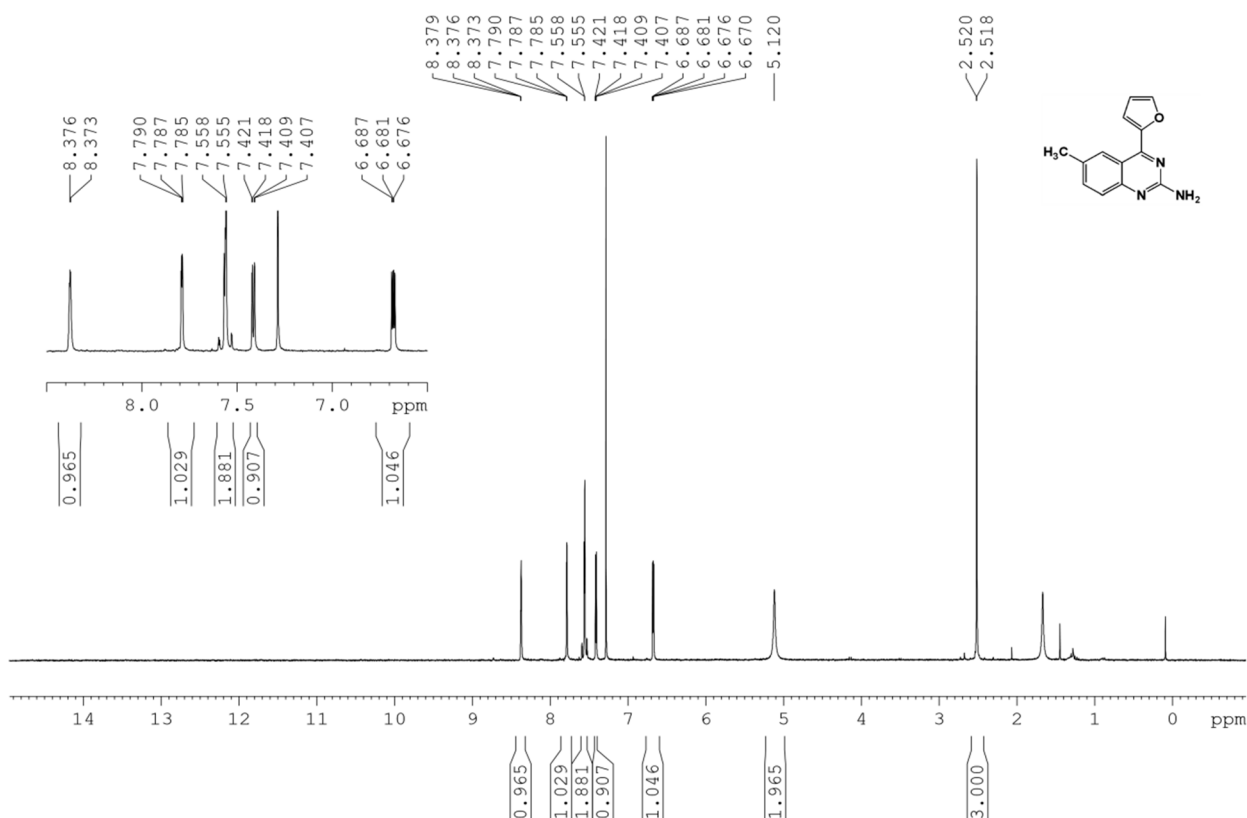




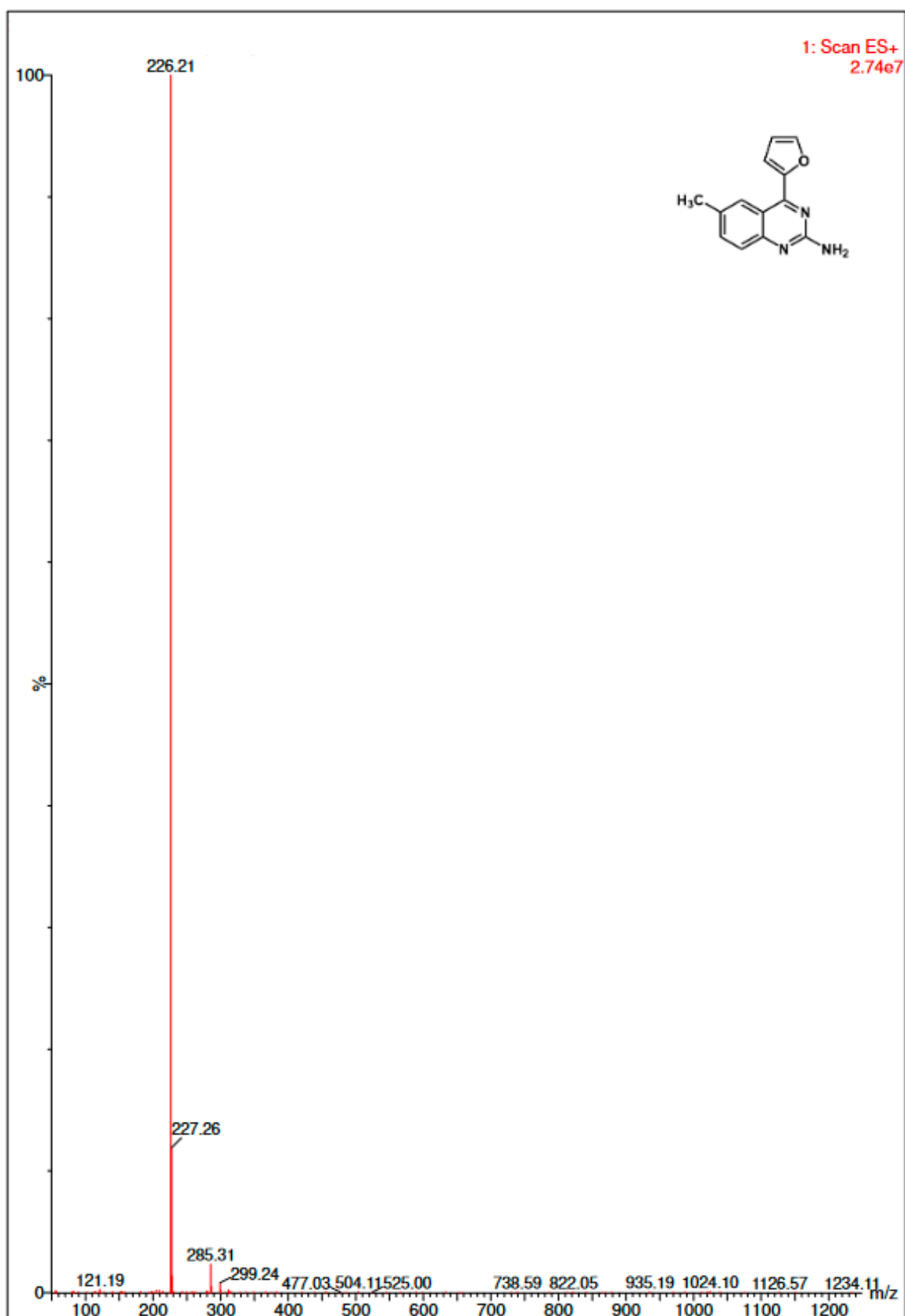
LC-MS mass spectrum of compound 5b



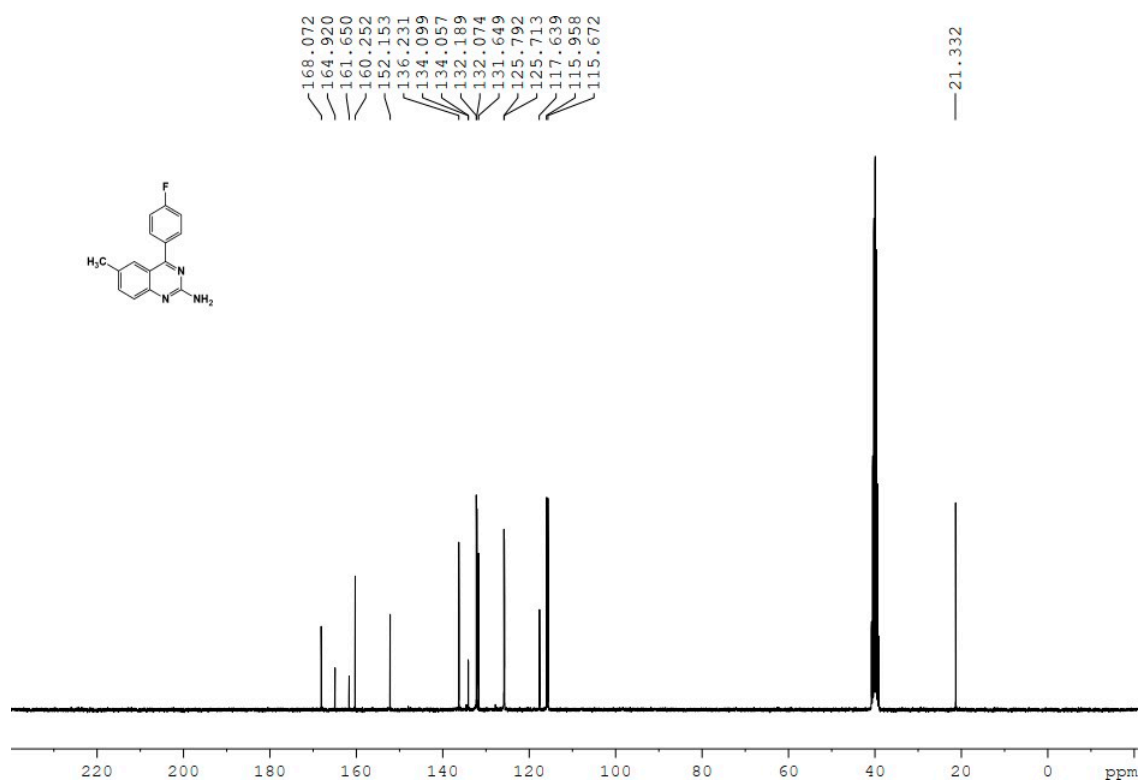
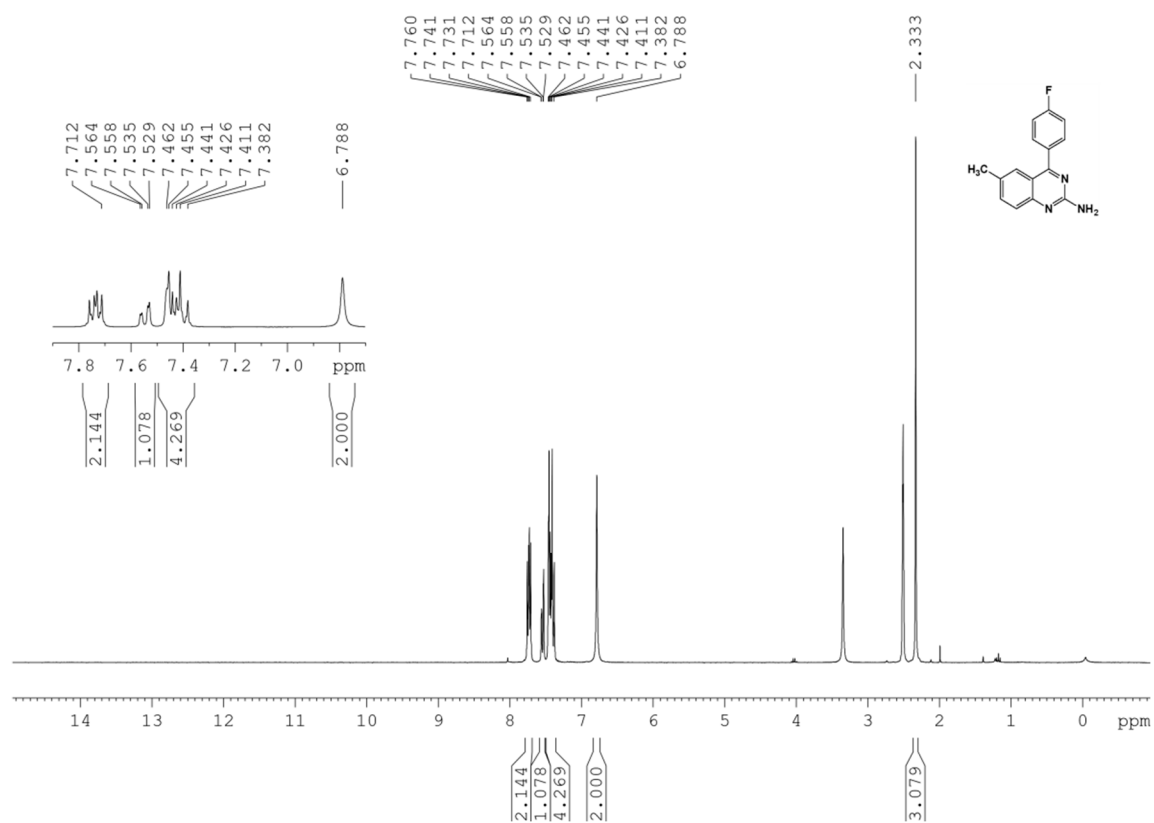
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 5c**



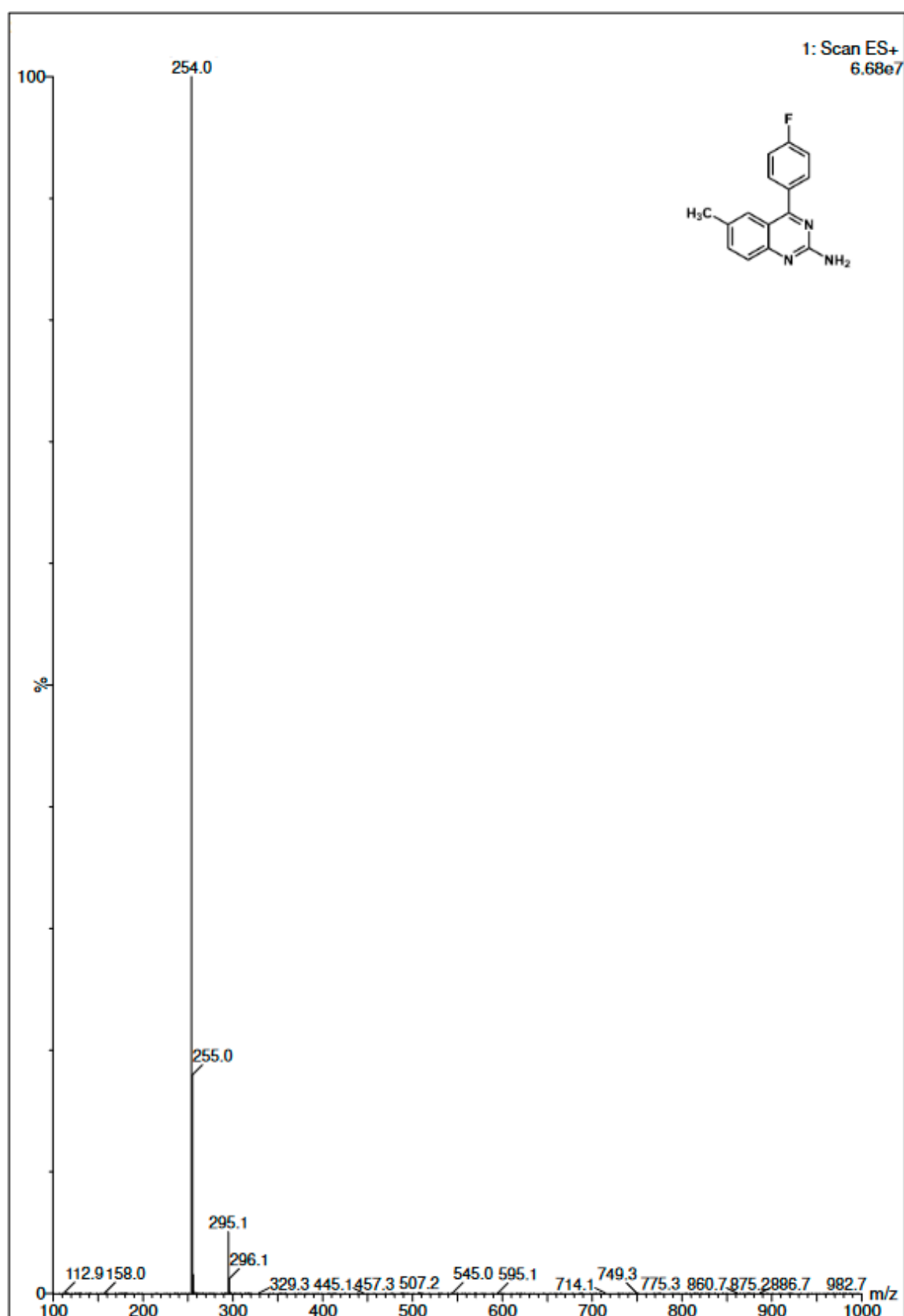
LC-MS mass spectrum of compound 5c



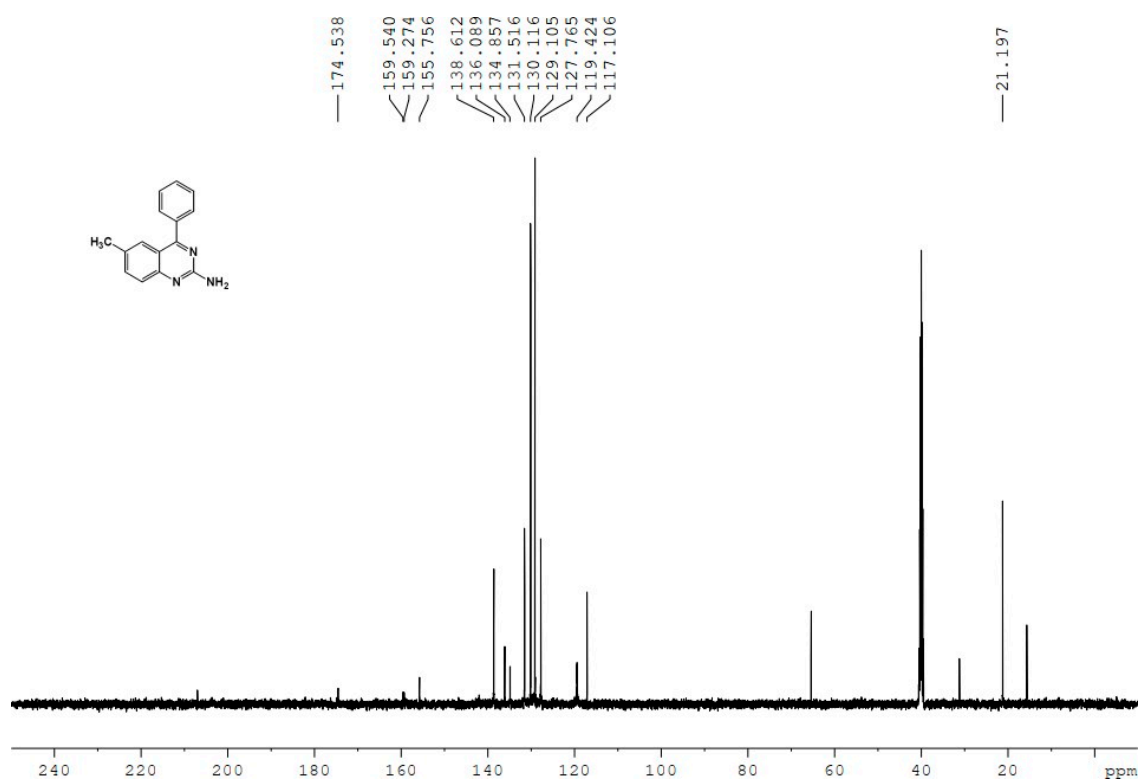
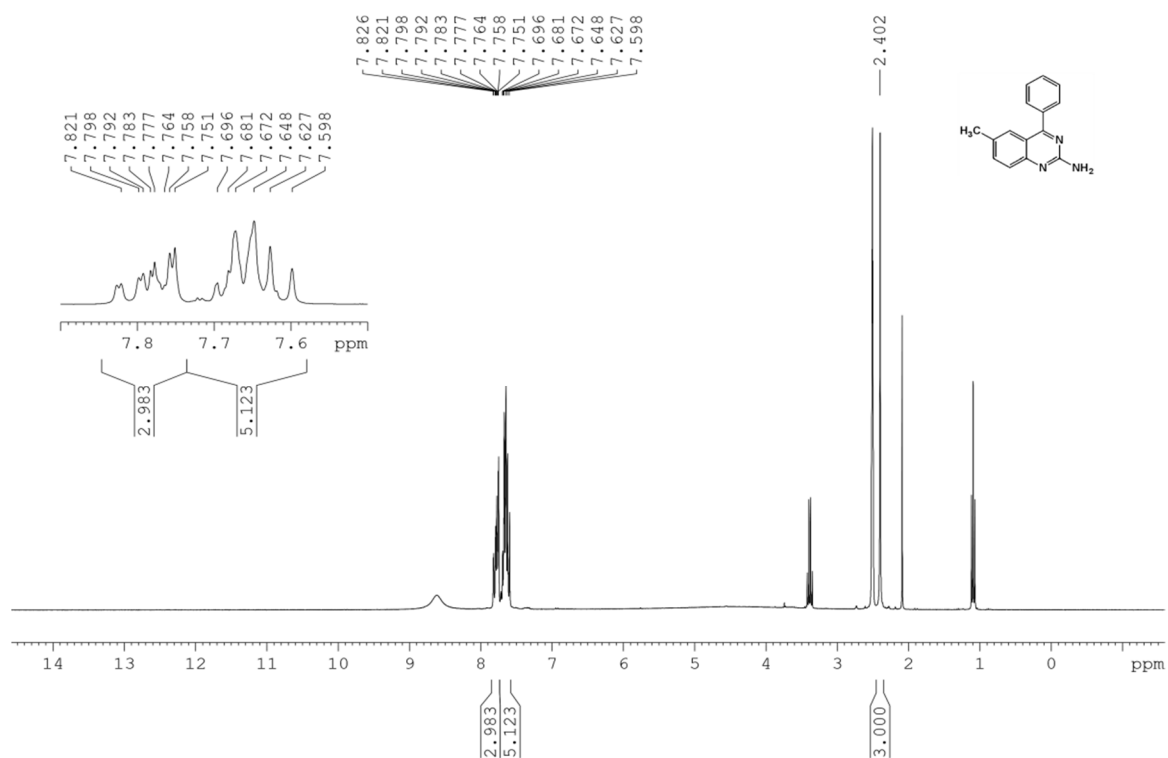
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5d**



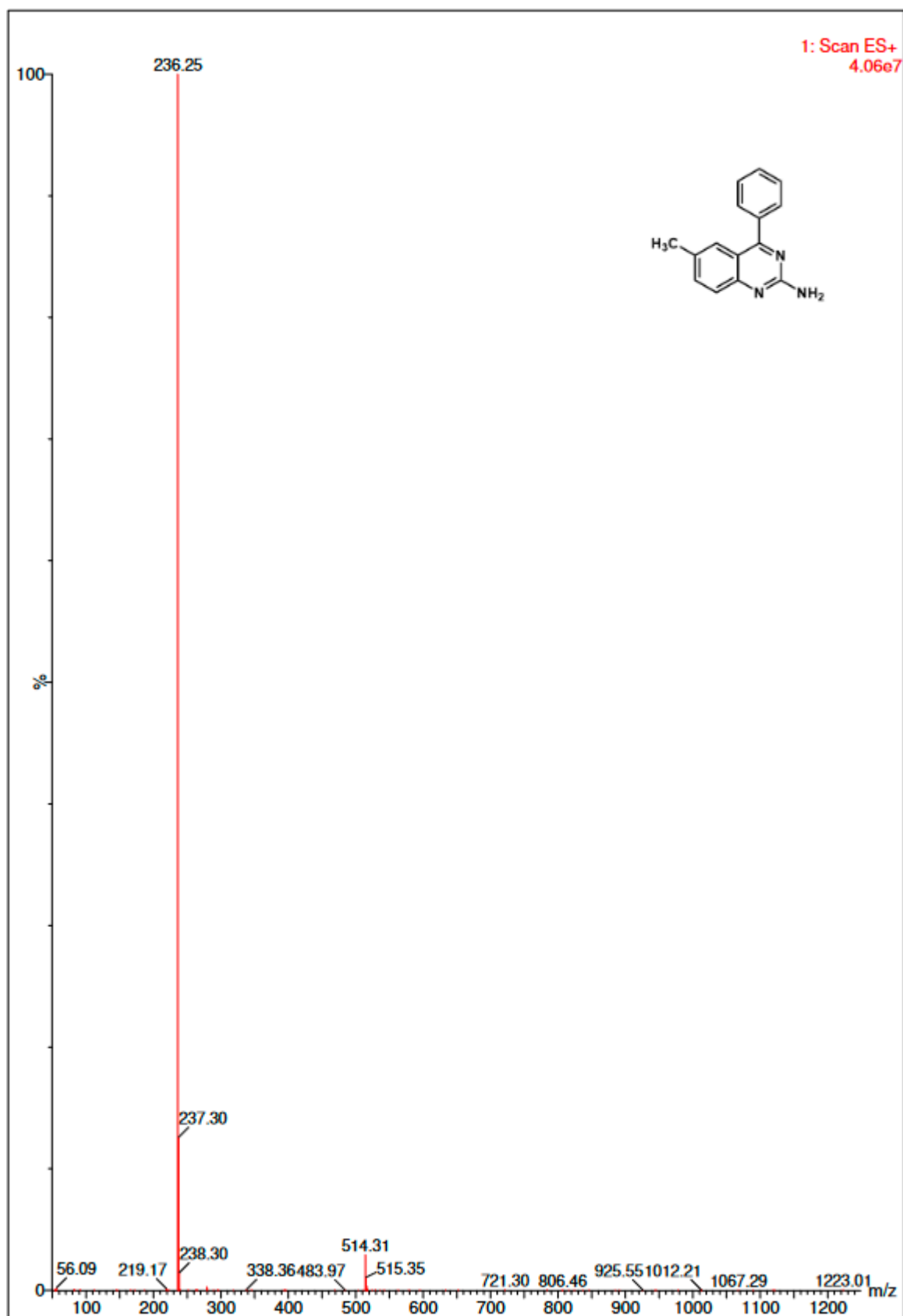
LC-MS mass spectrum of compound 5d



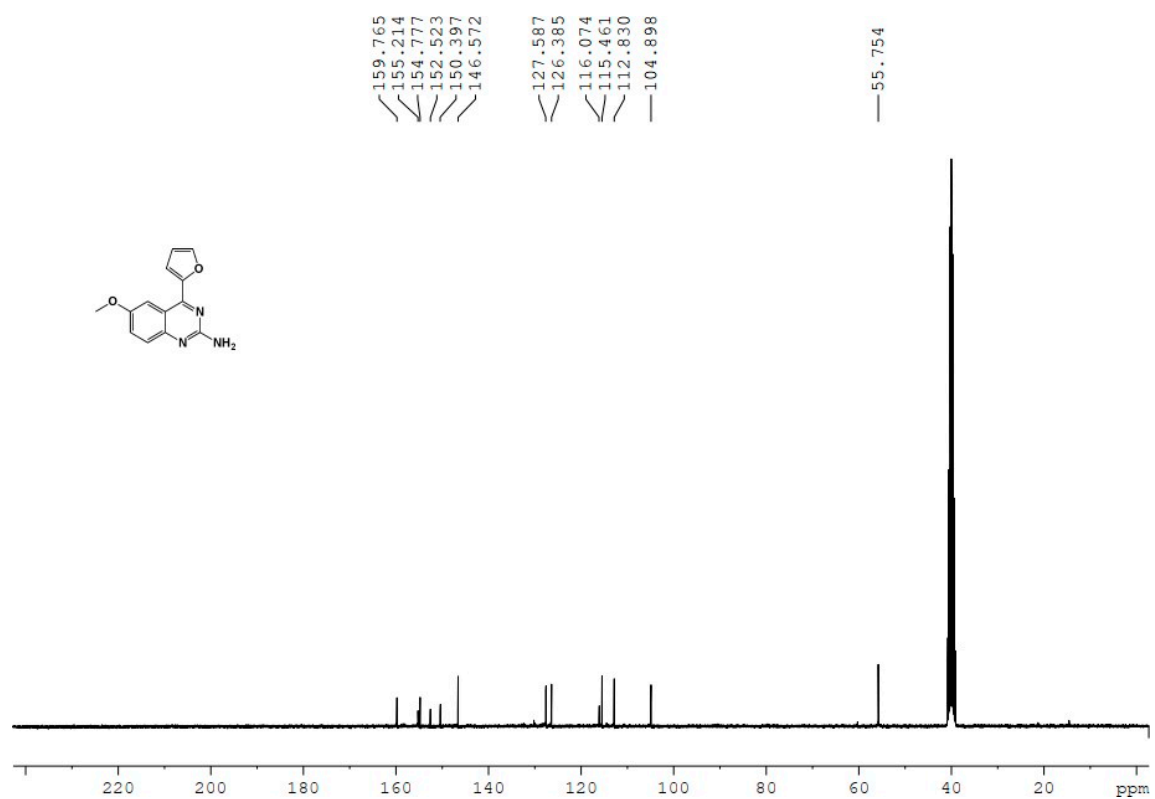
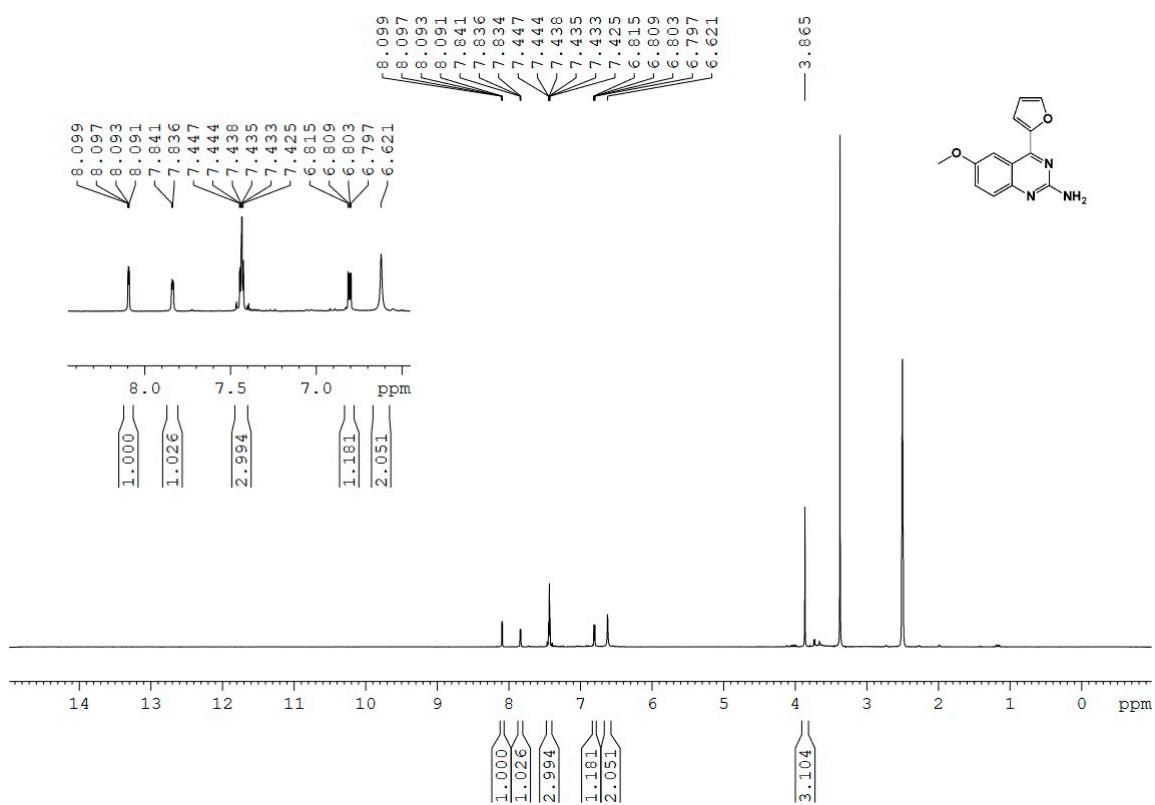
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5e**



LC-MS mass spectrum of compound 5e

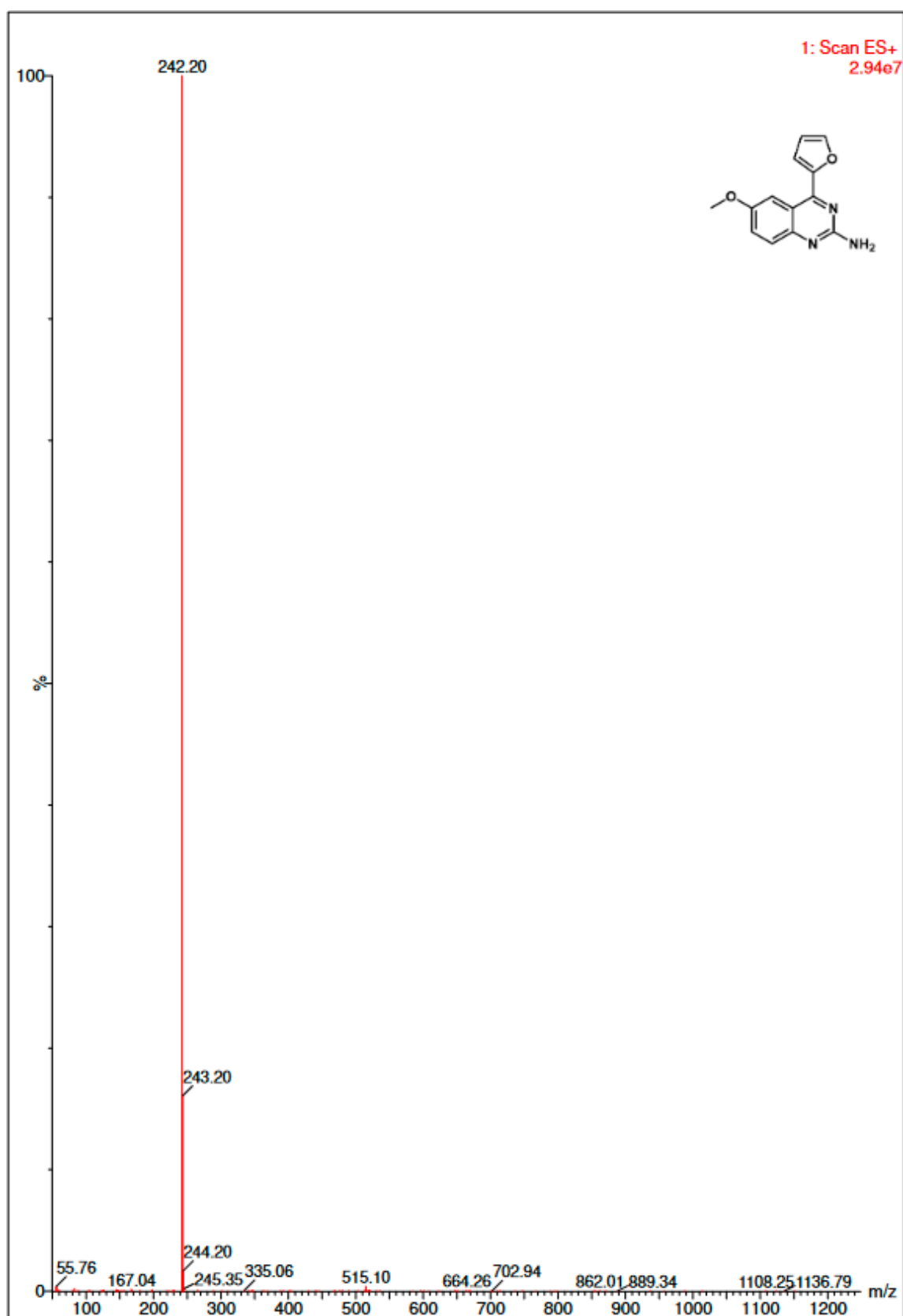


# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5f**

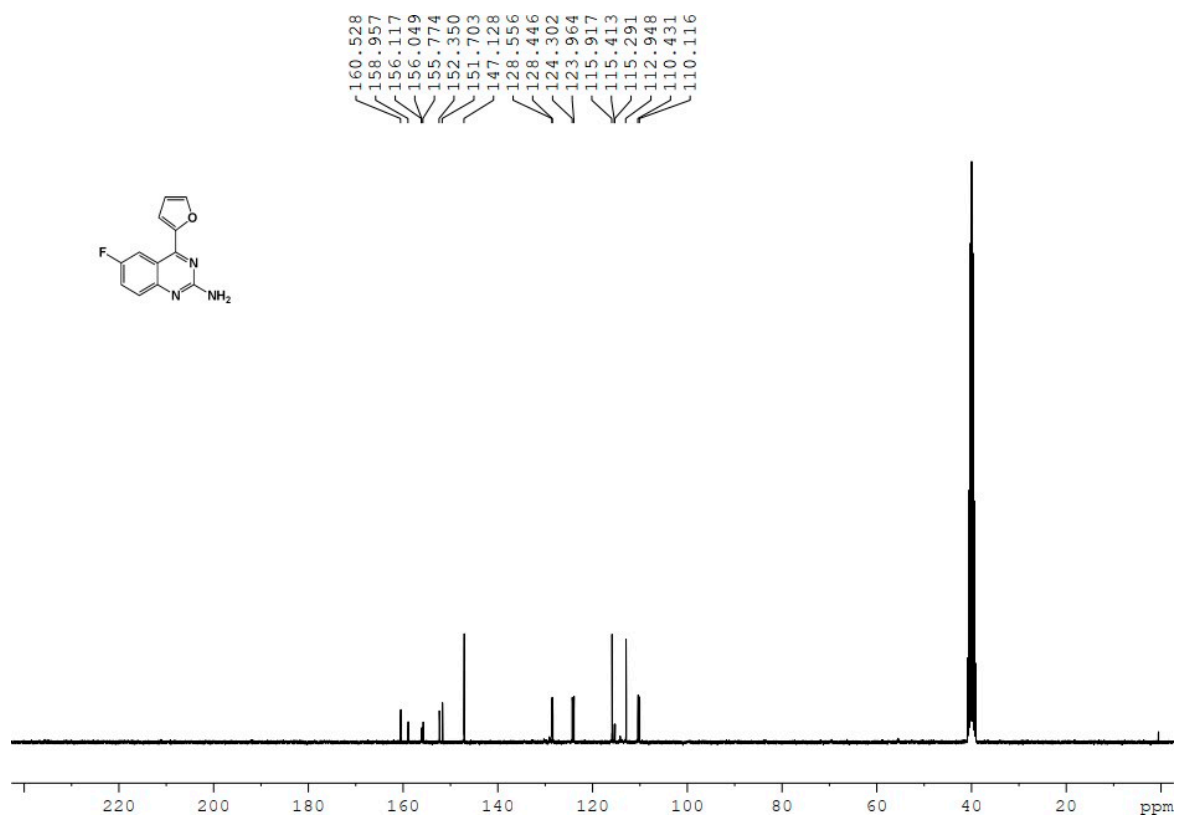
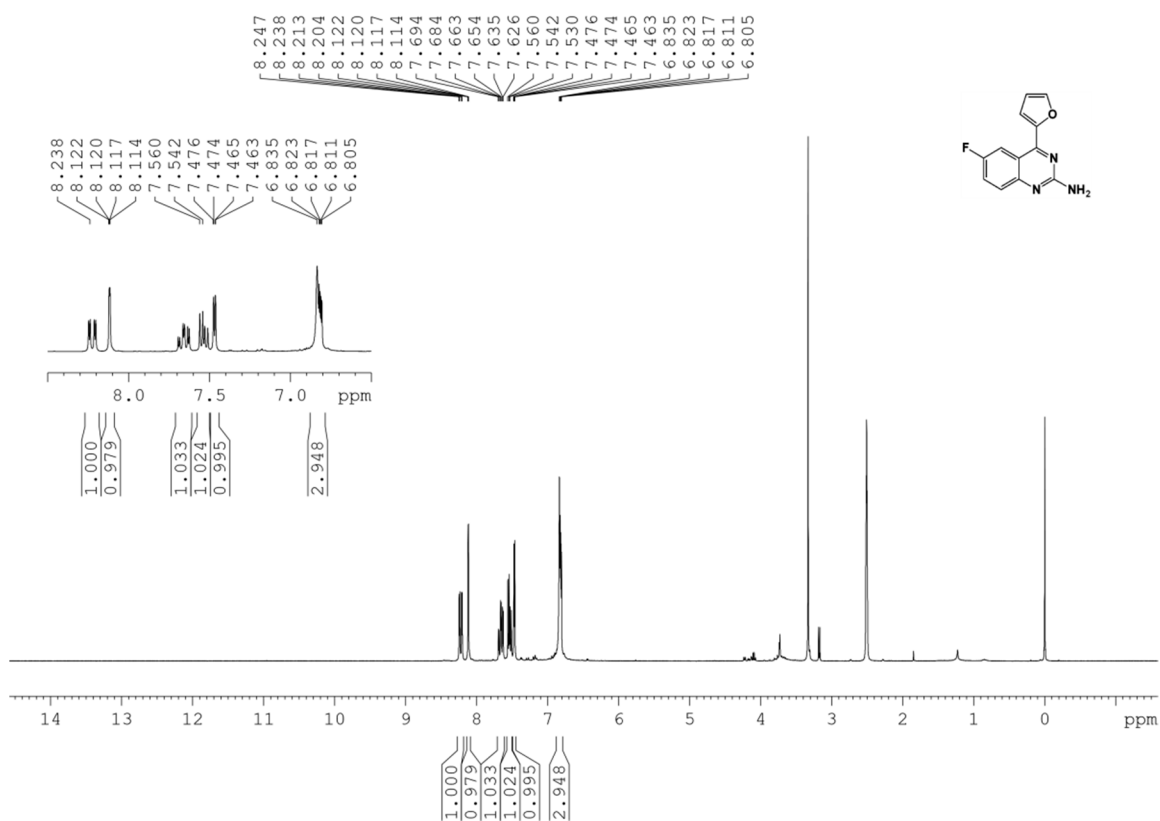




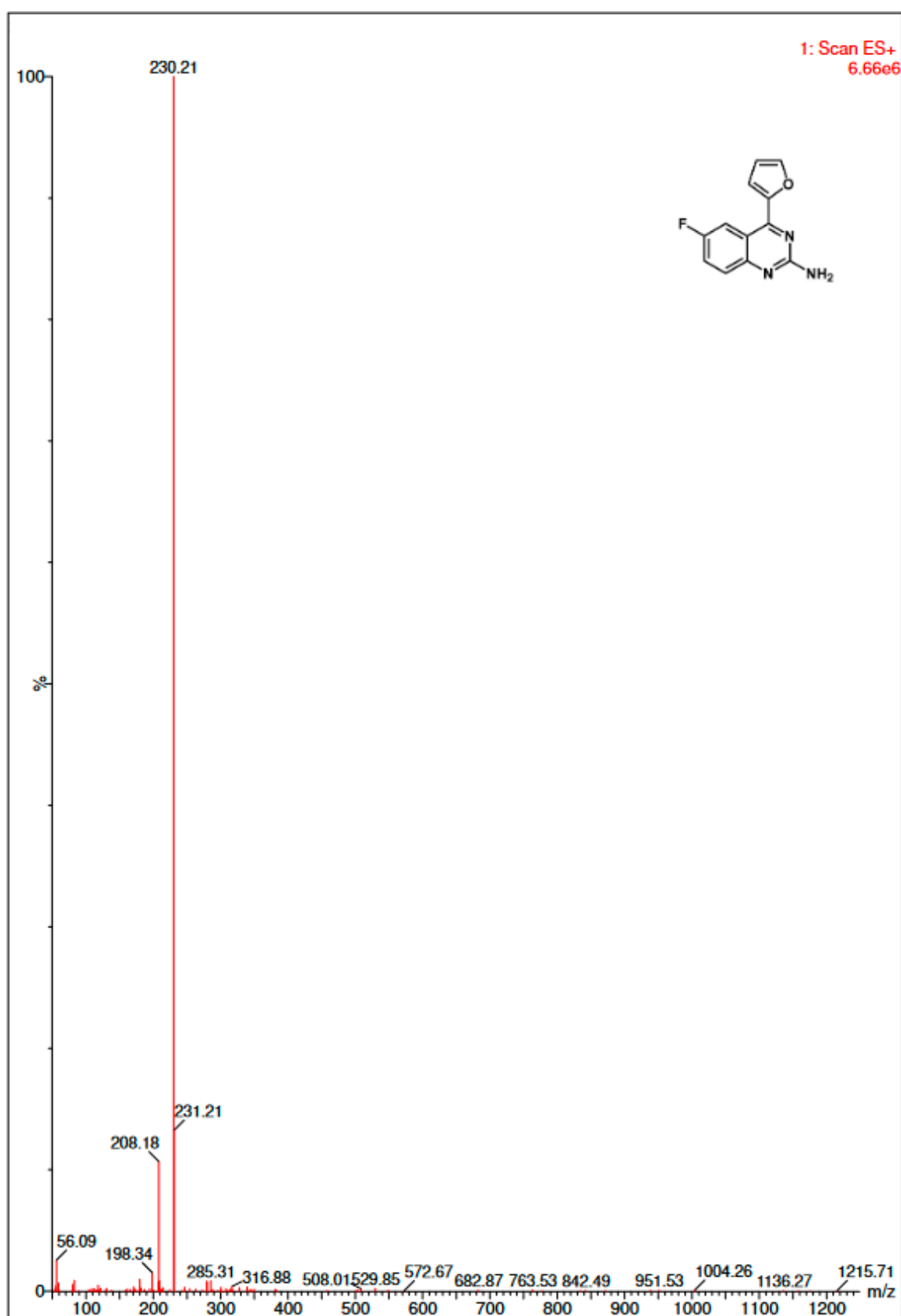
LC-MS mass spectrum of compound 5f



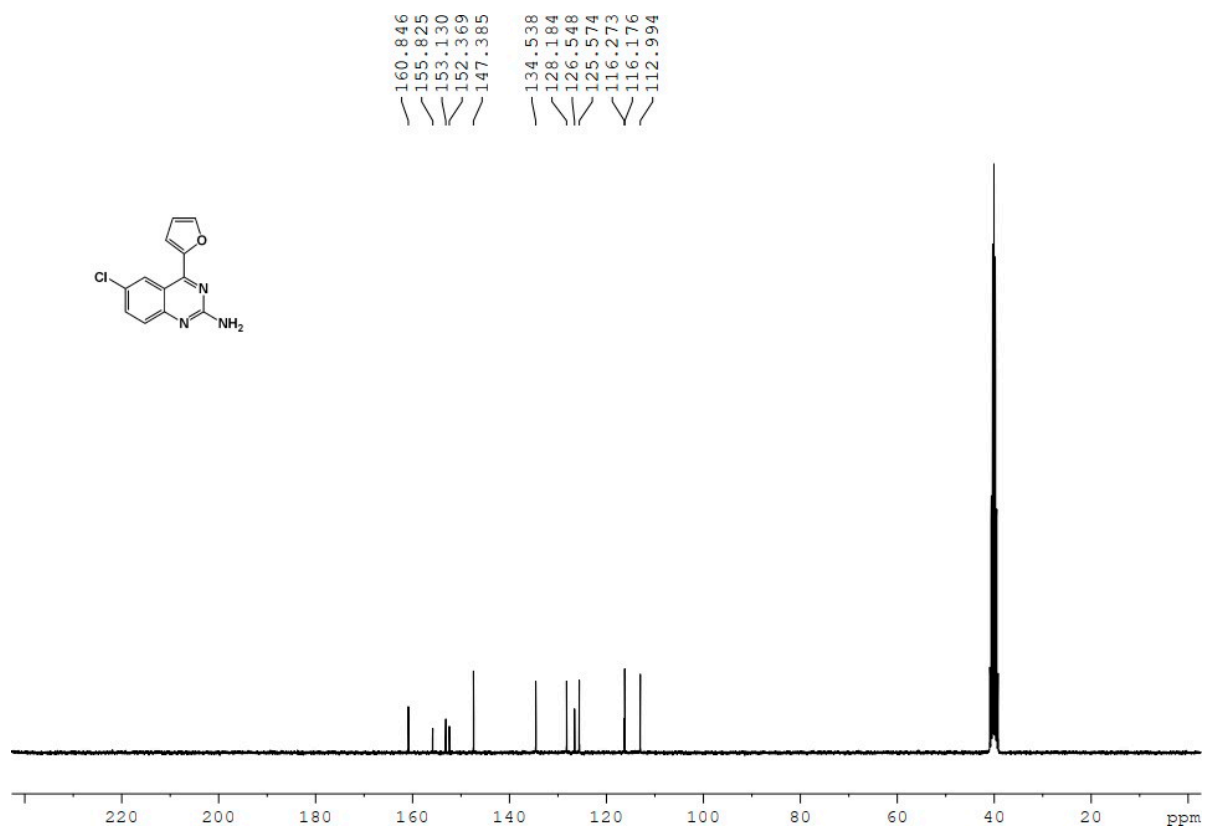
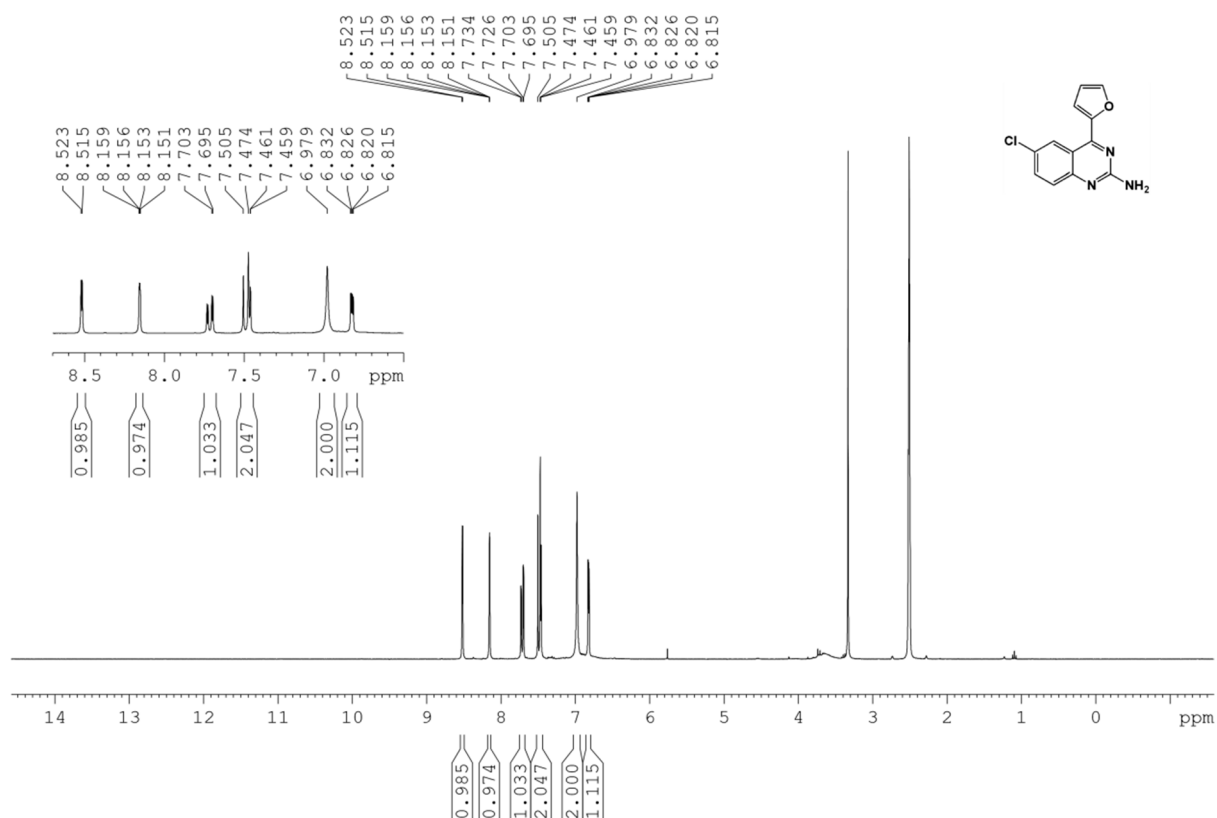
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5g**



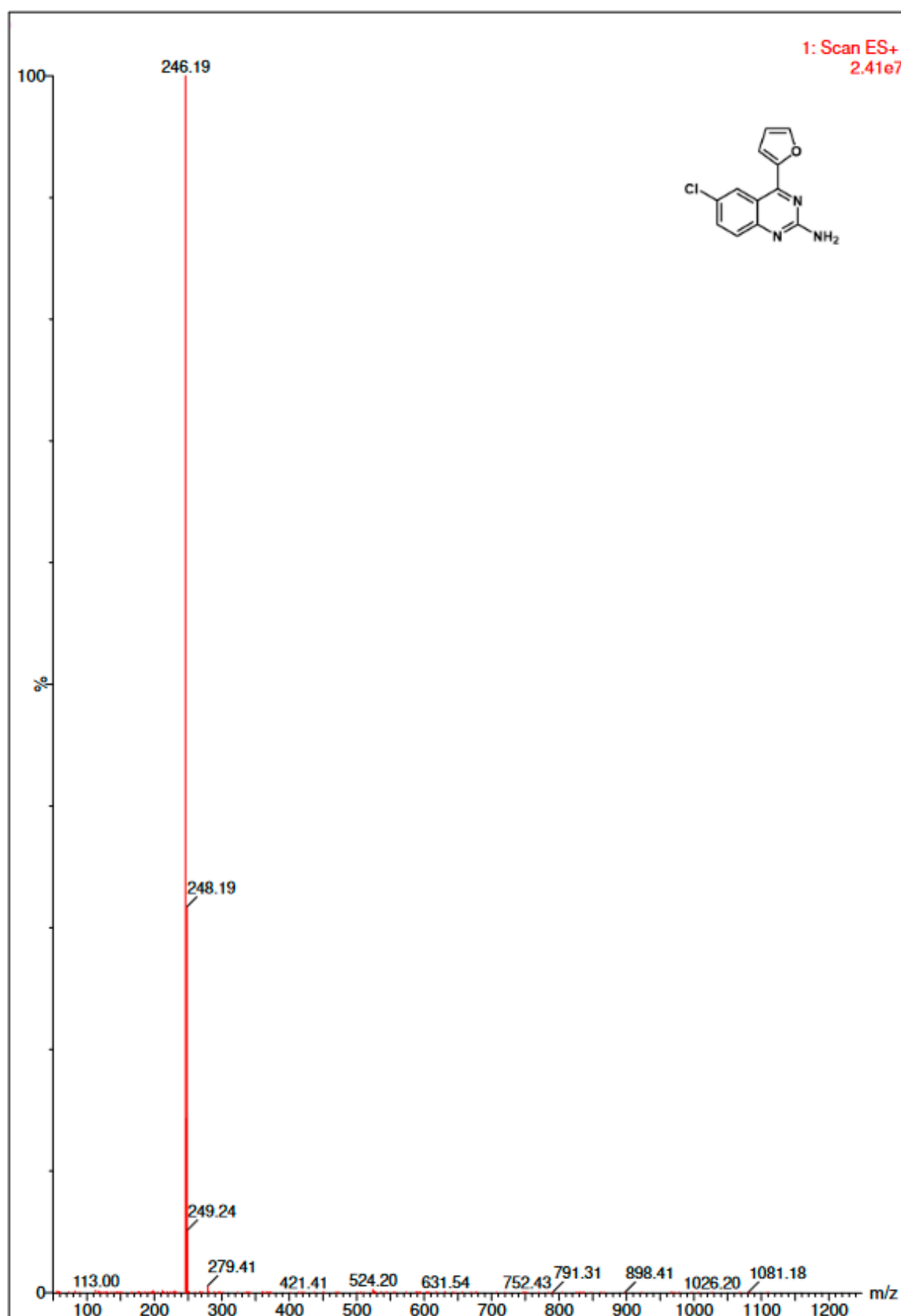
LC-MS mass spectrum of compound 5g



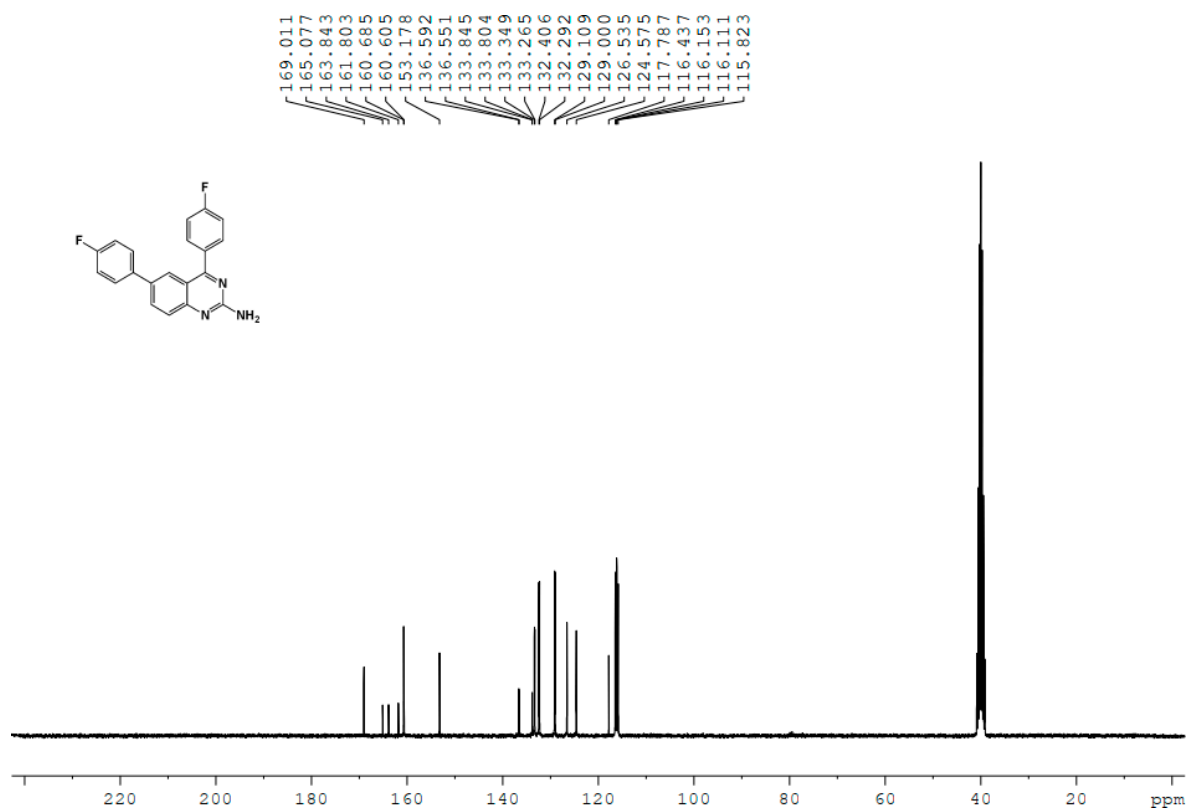
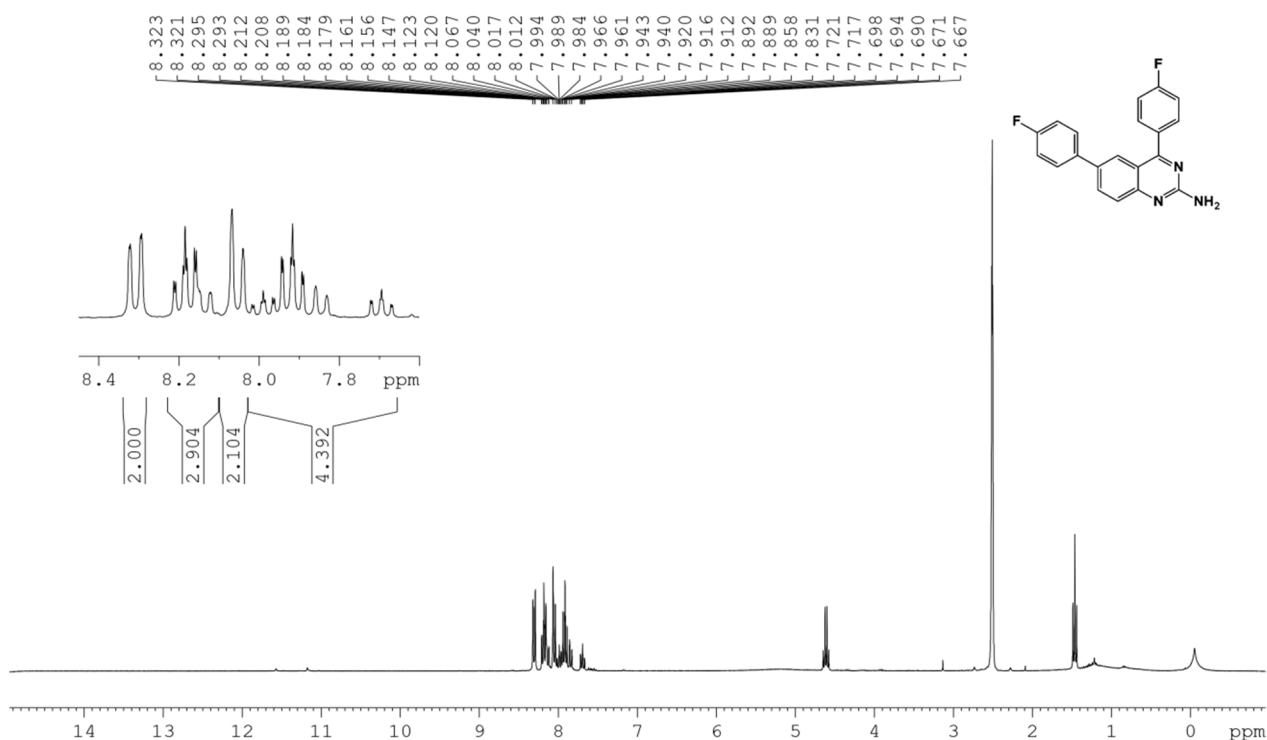
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5h**



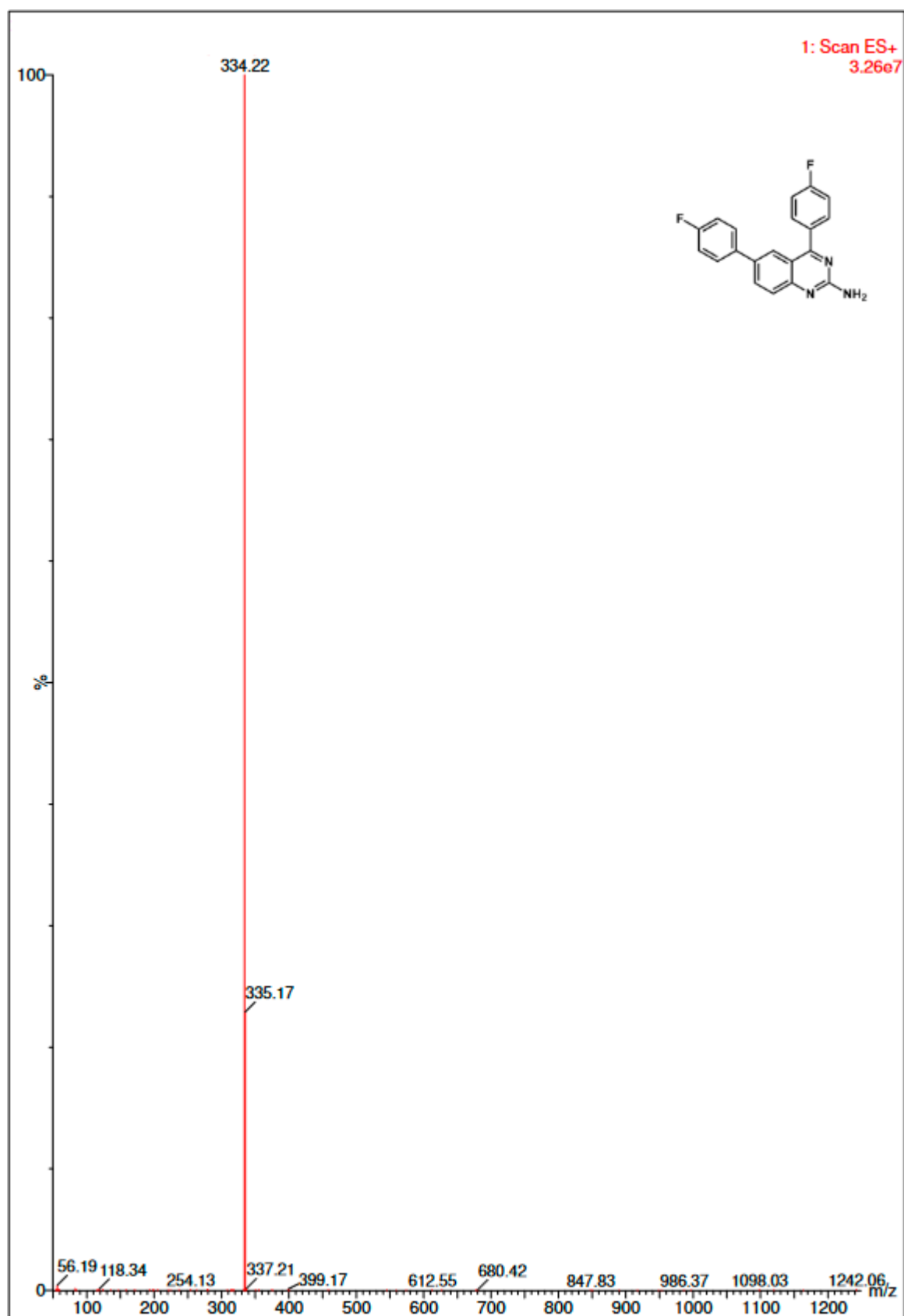
LC-MS mass spectrum of compound 5h



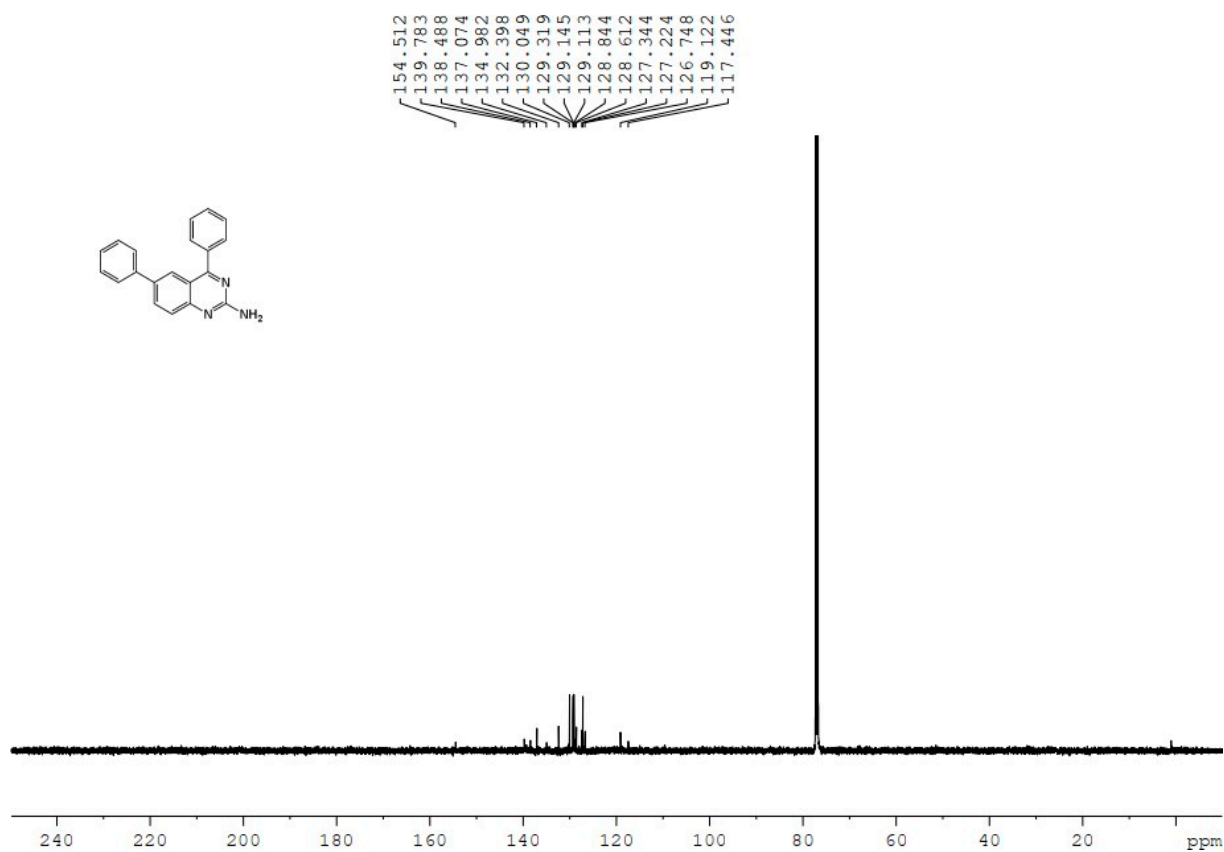
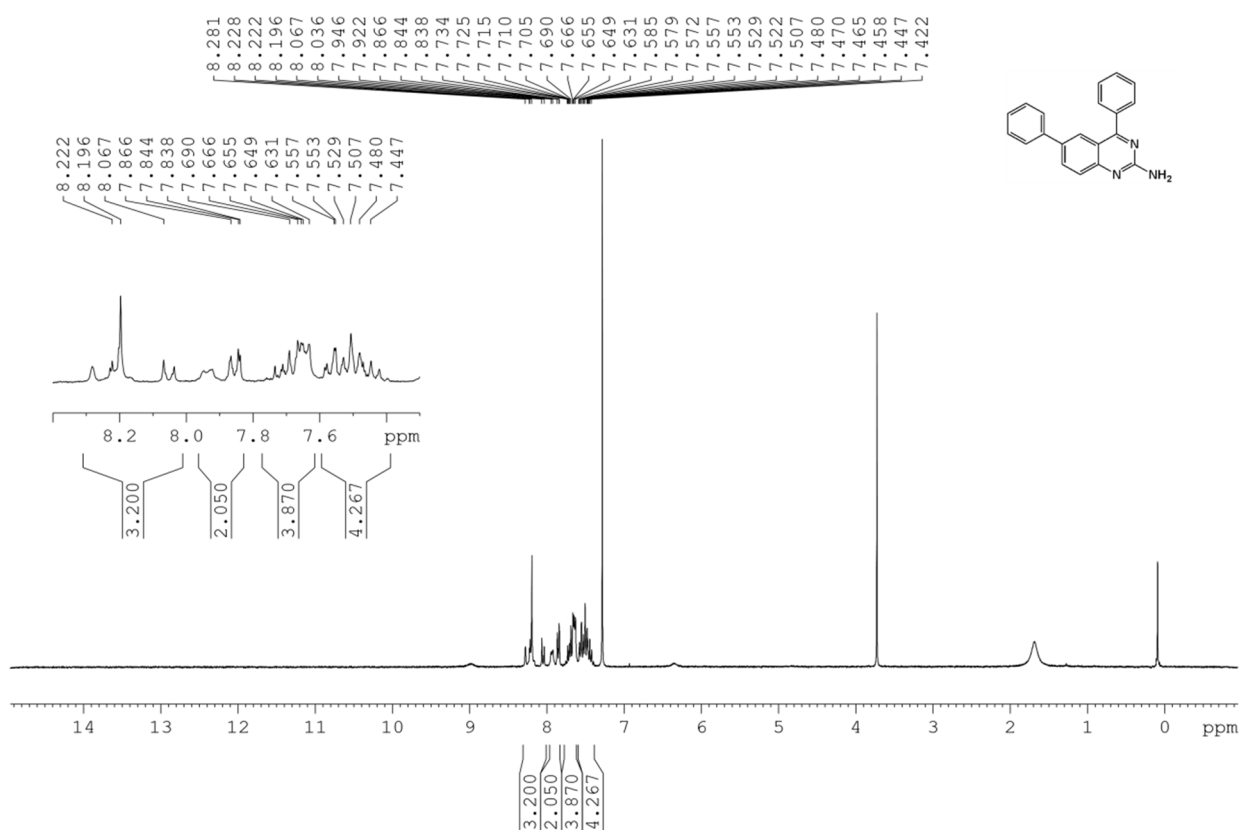
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5i**



LC-MS mass spectrum of compound 5i

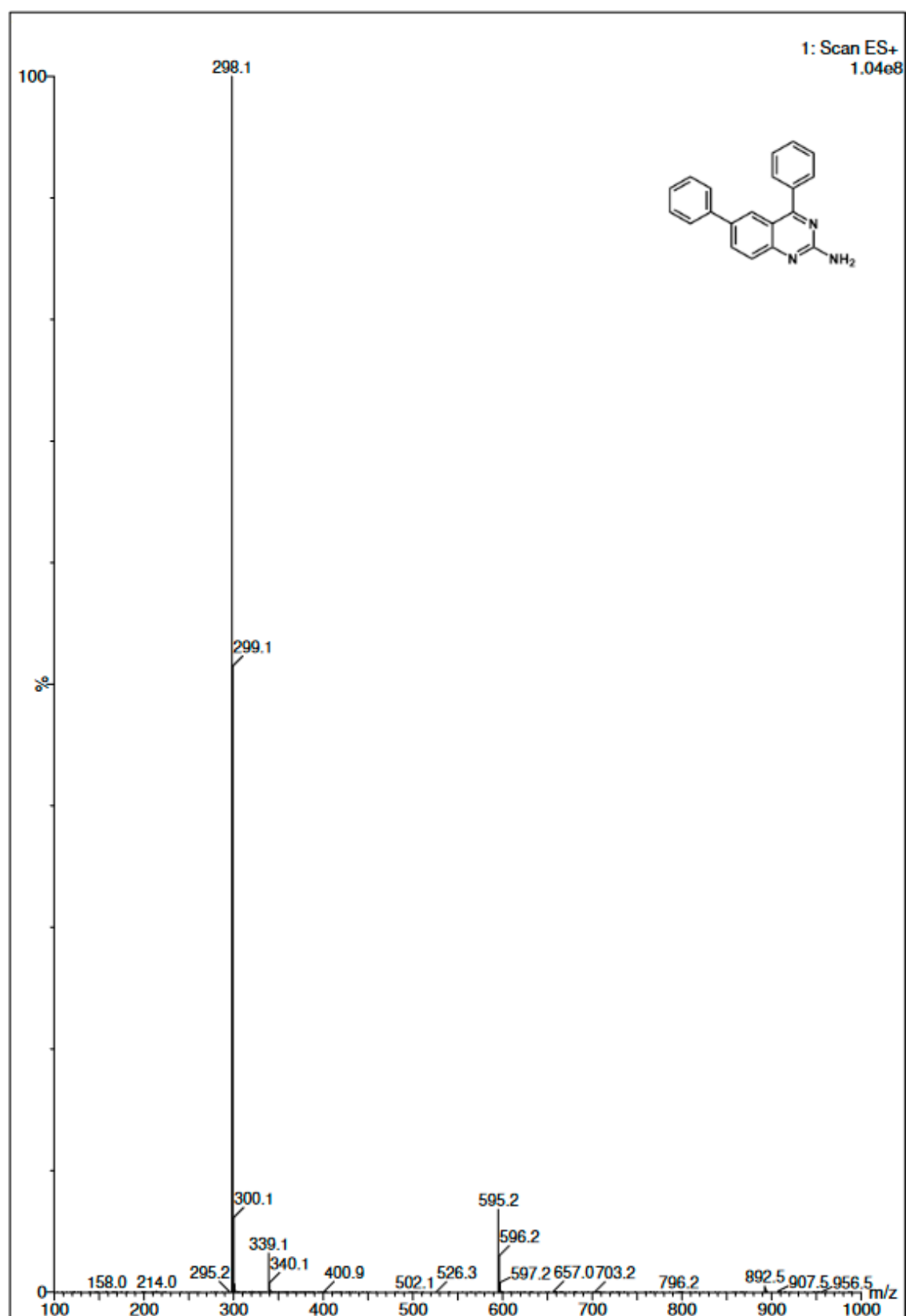


# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 5j

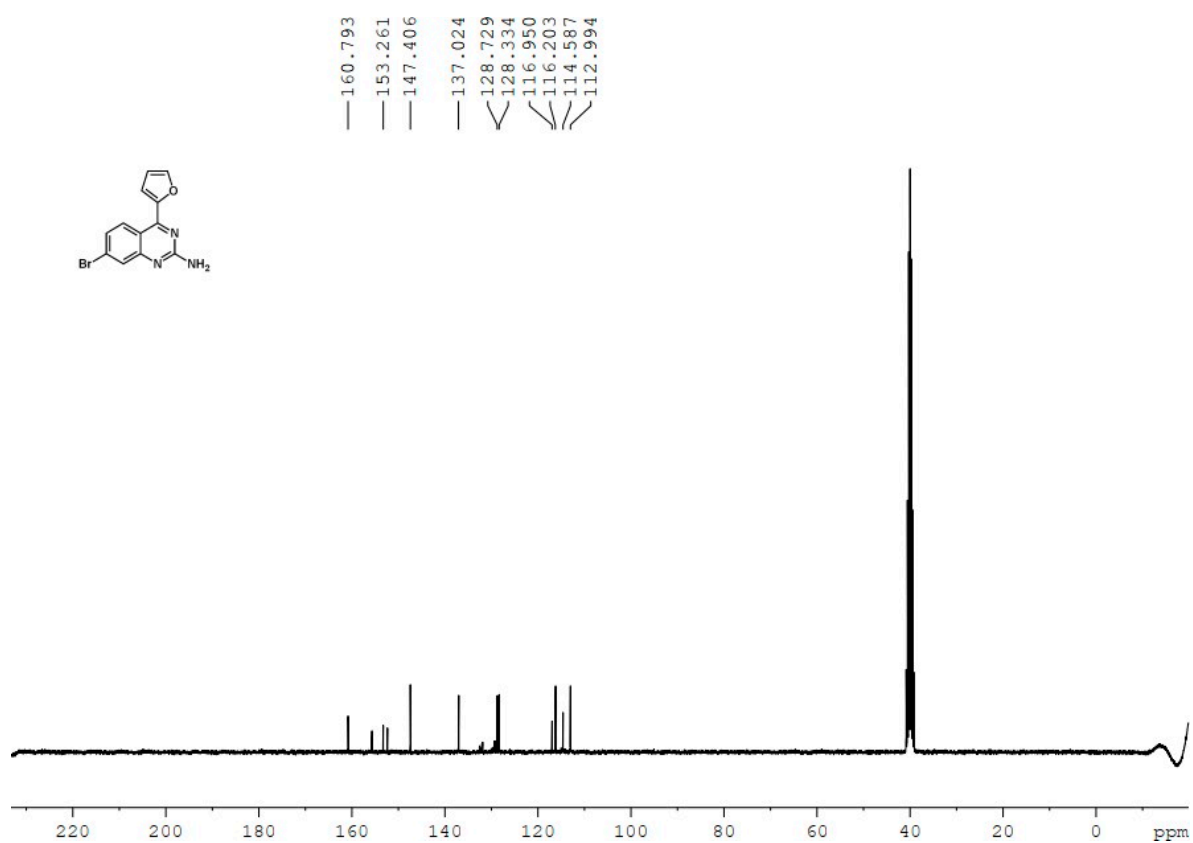
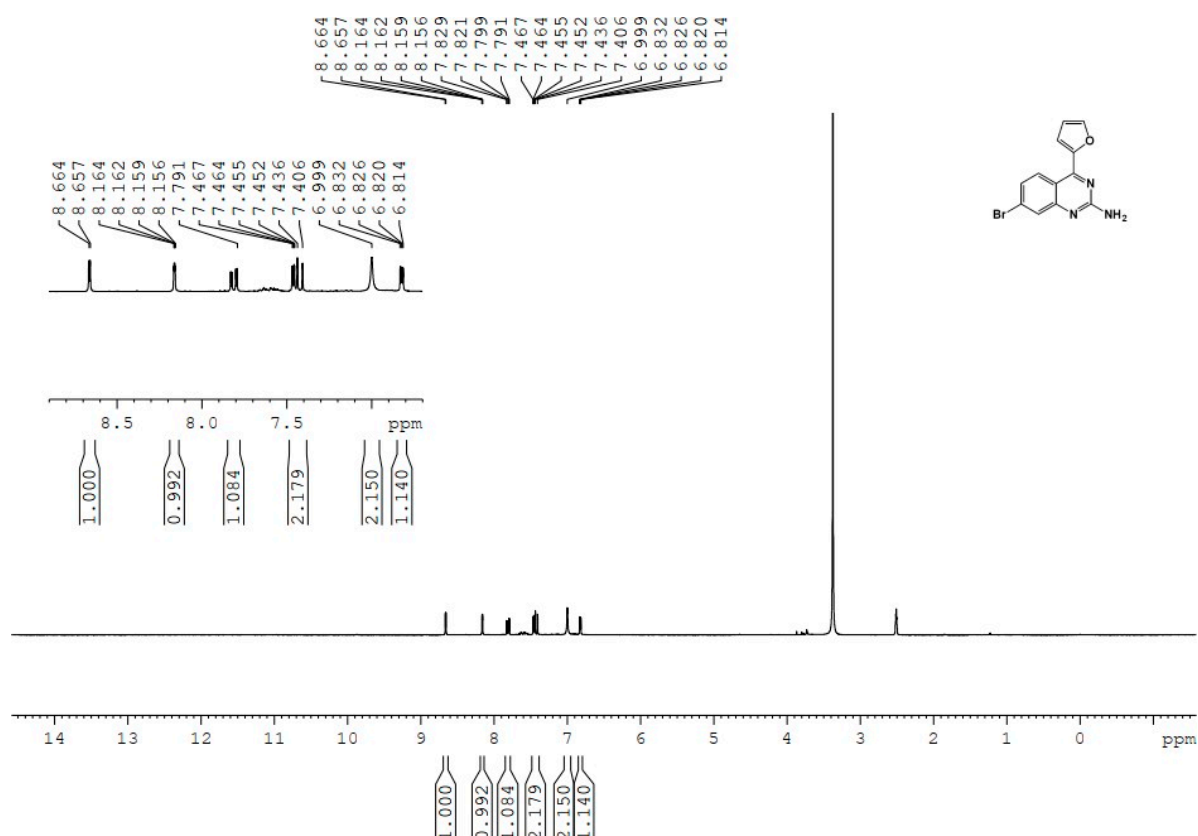




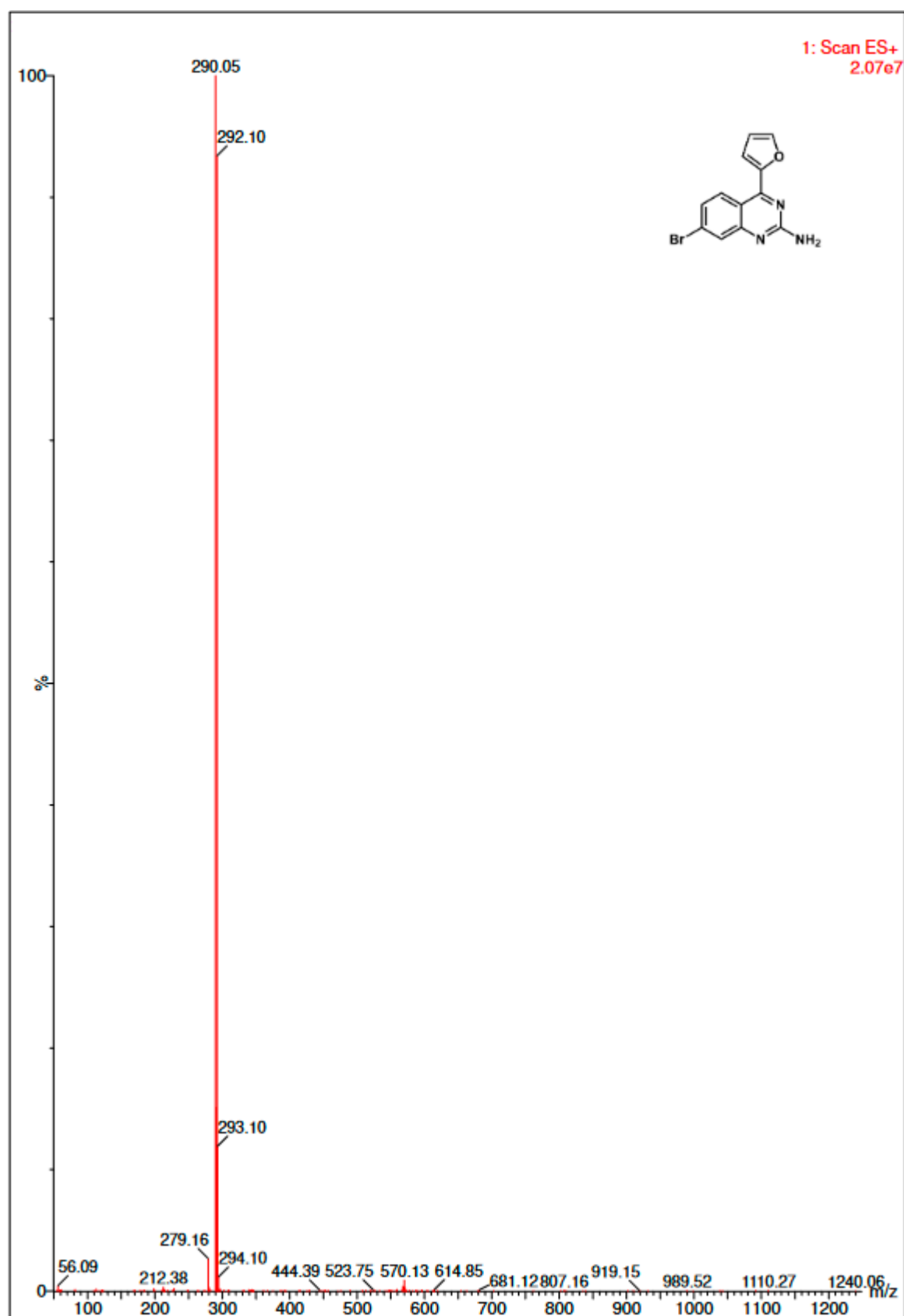
LC-MS mass spectrum of compound 5j



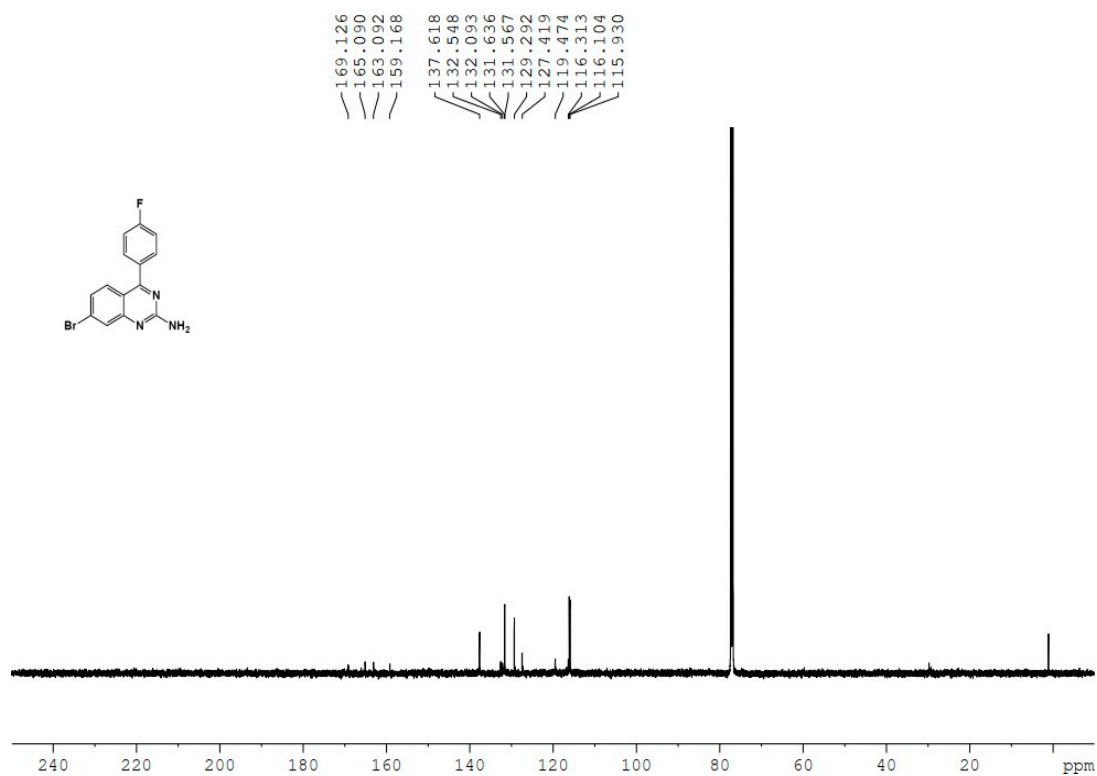
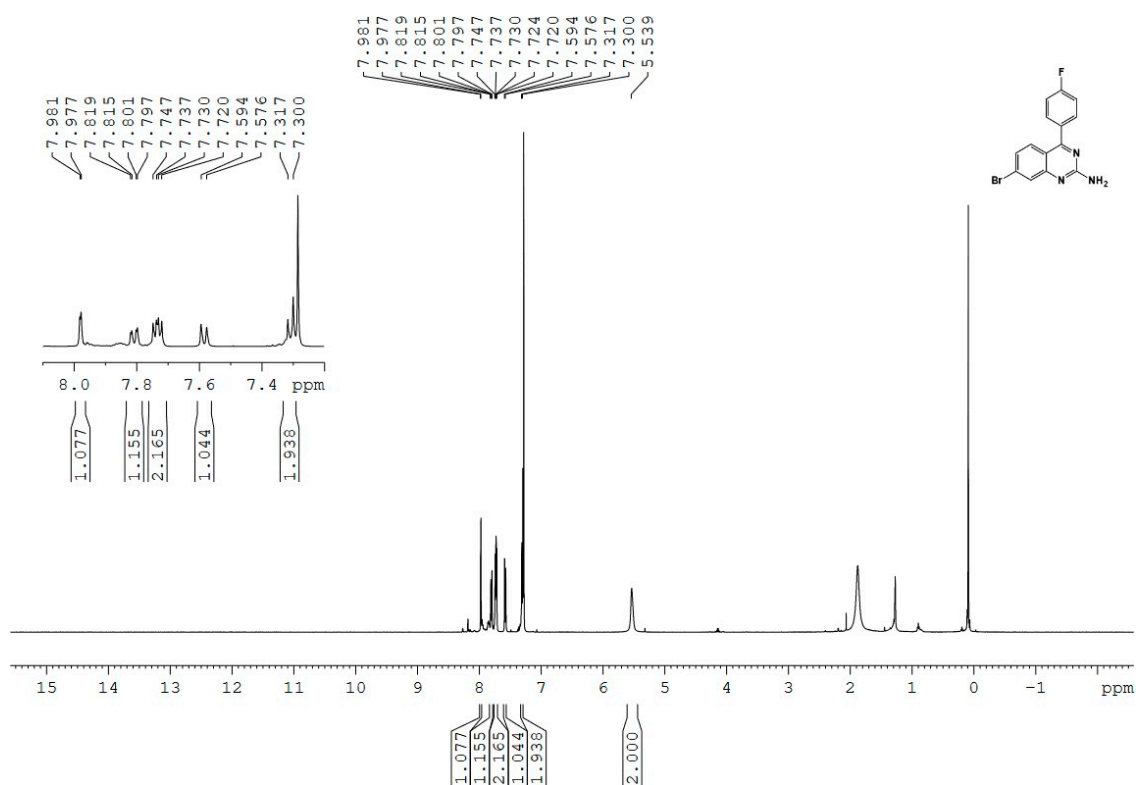
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5k**



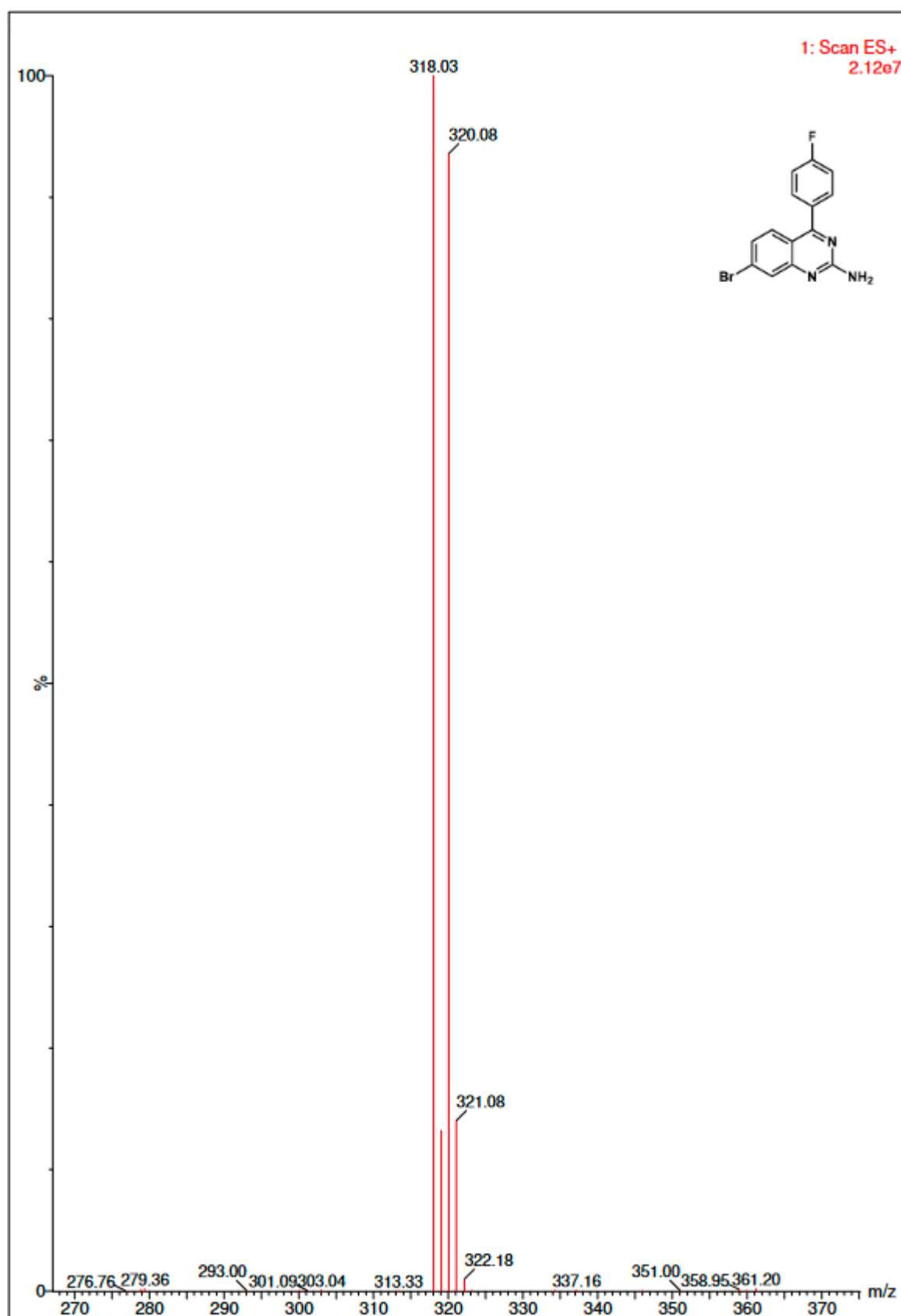
LC-MS mass spectrum of compound 5k



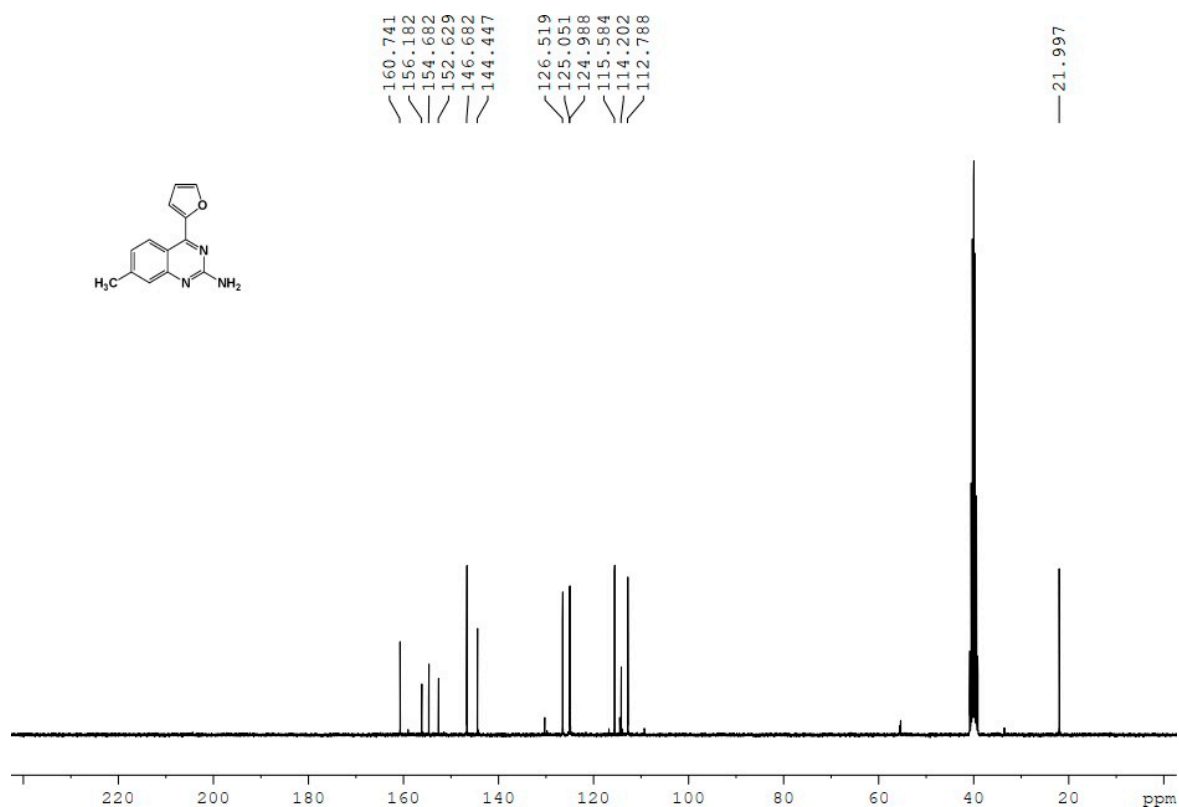
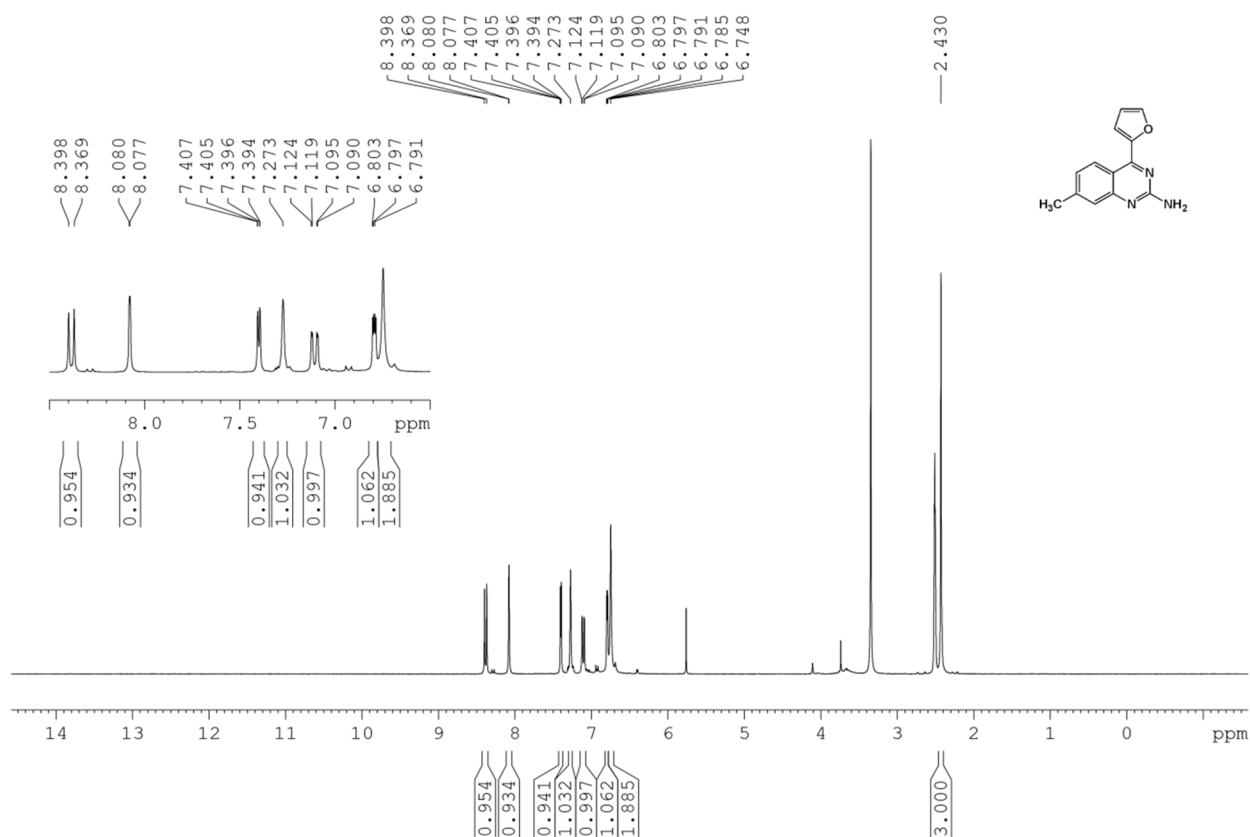
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 5I**



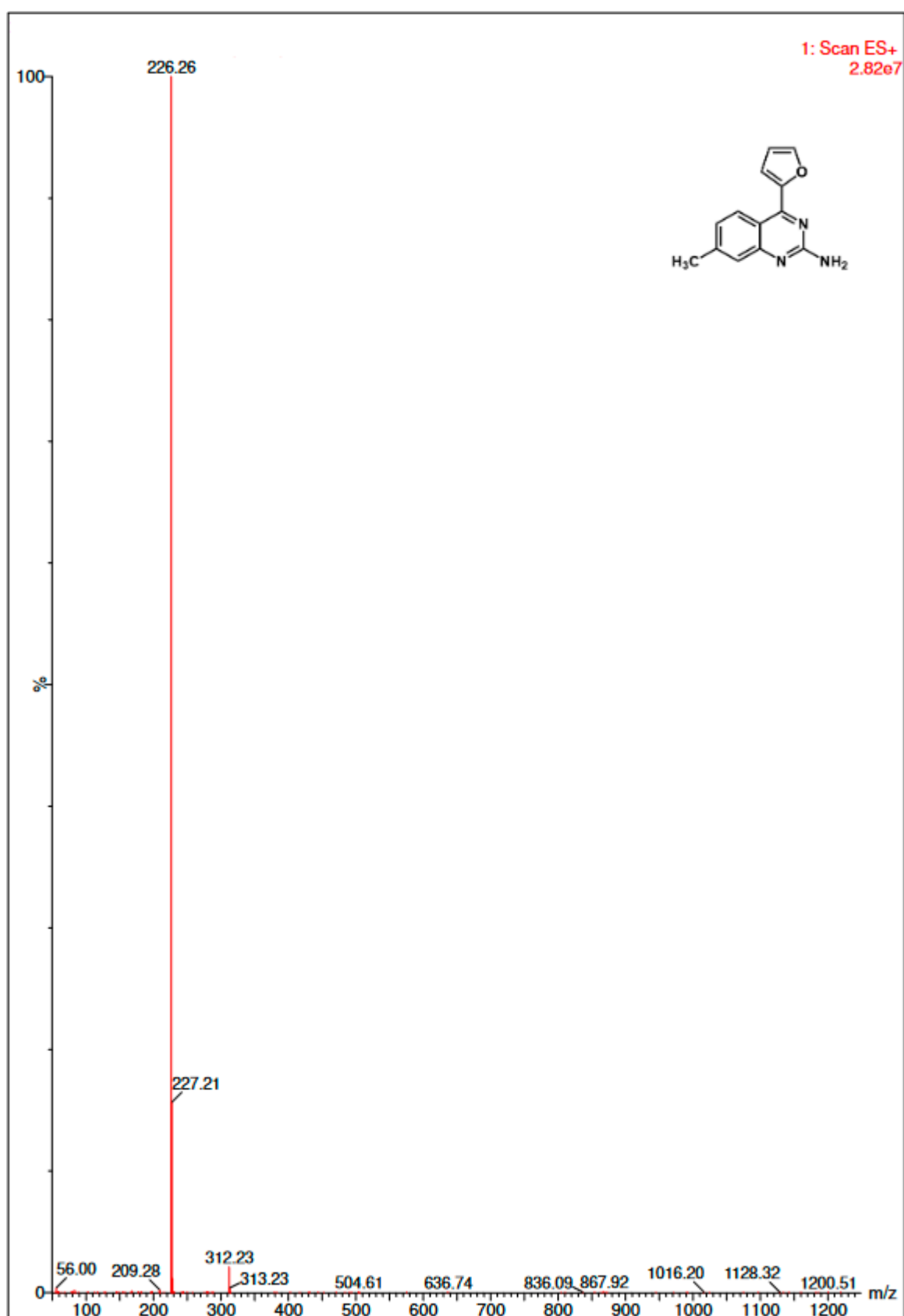
LC-MS mass spectrum of compound 5l



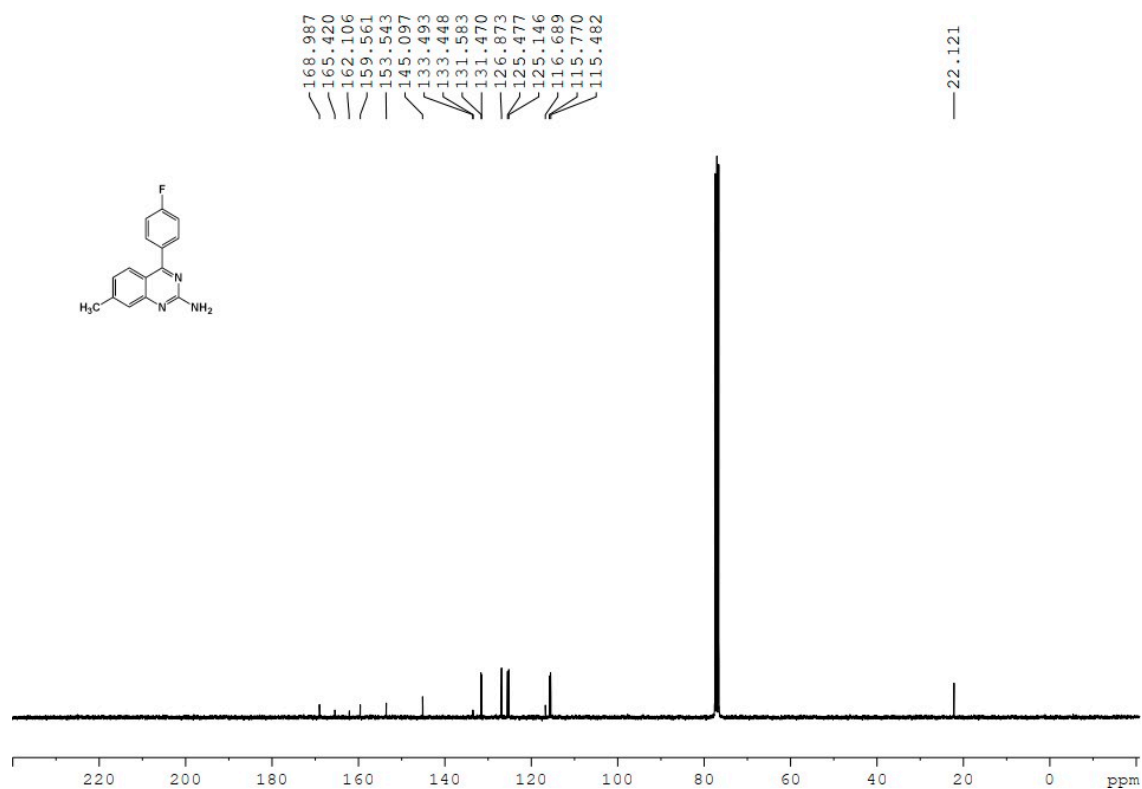
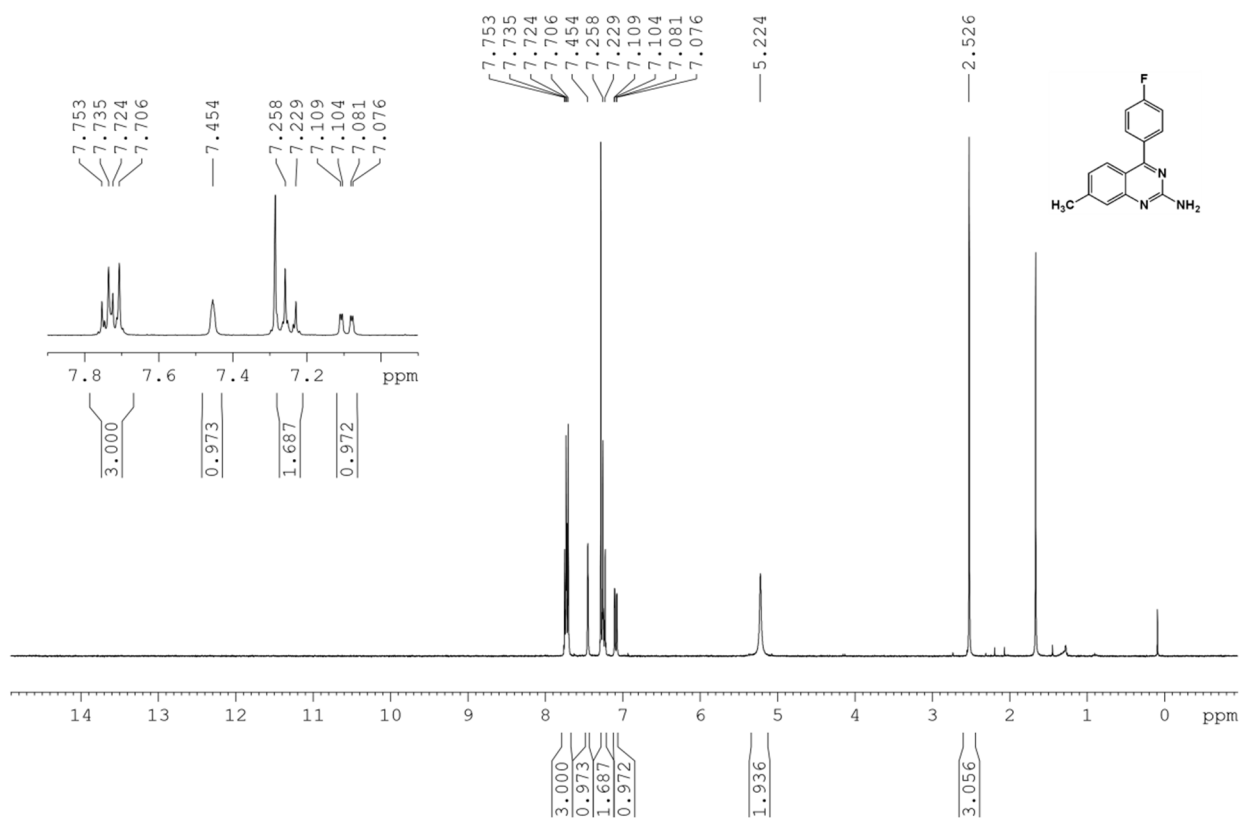
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5m**



LC-MS mass spectrum of compound 5m

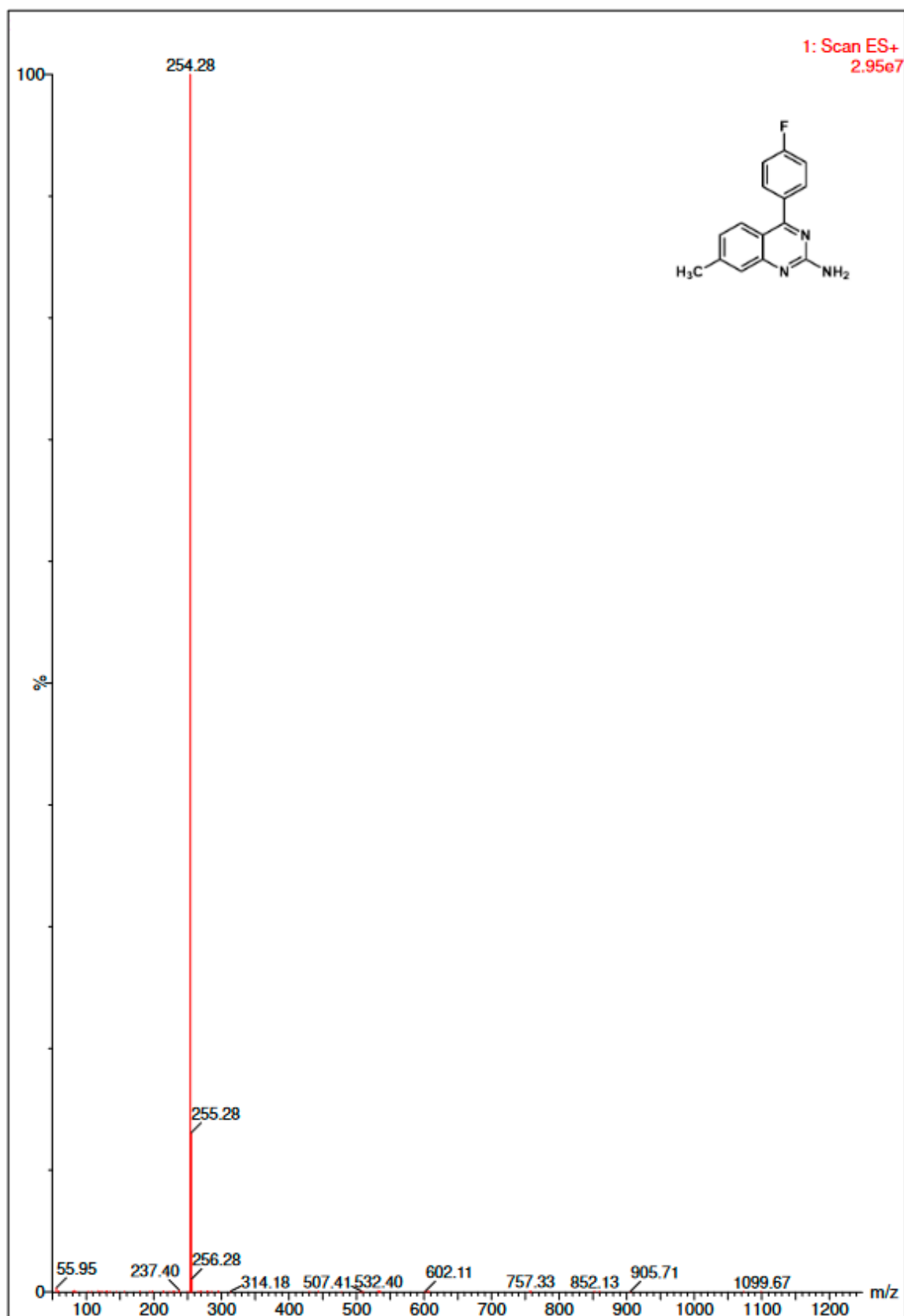


# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 5n**

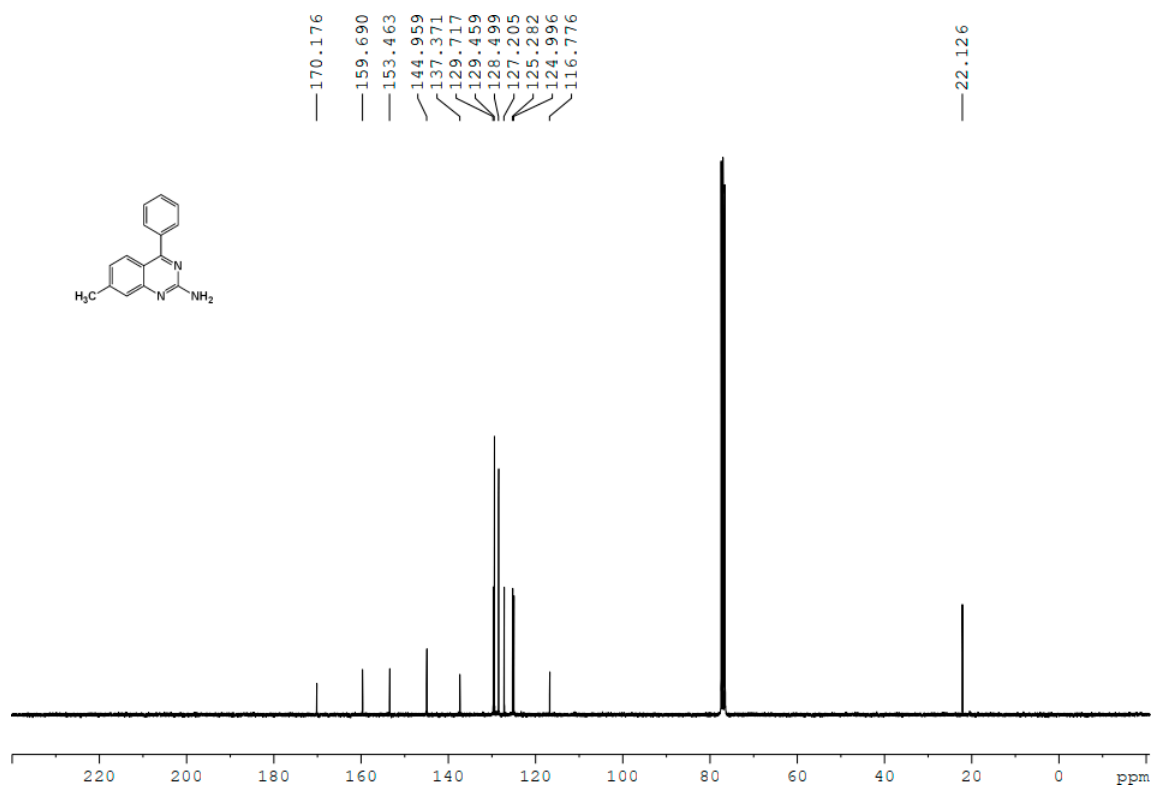
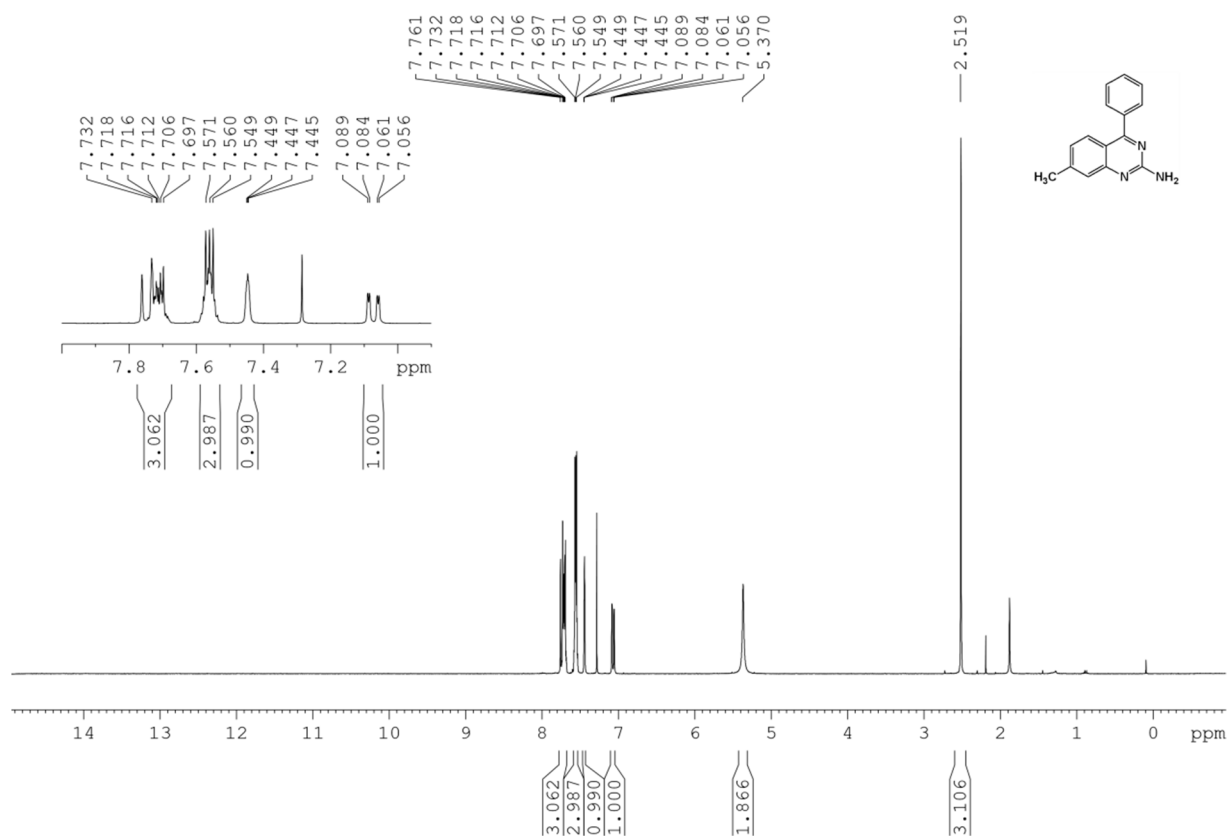




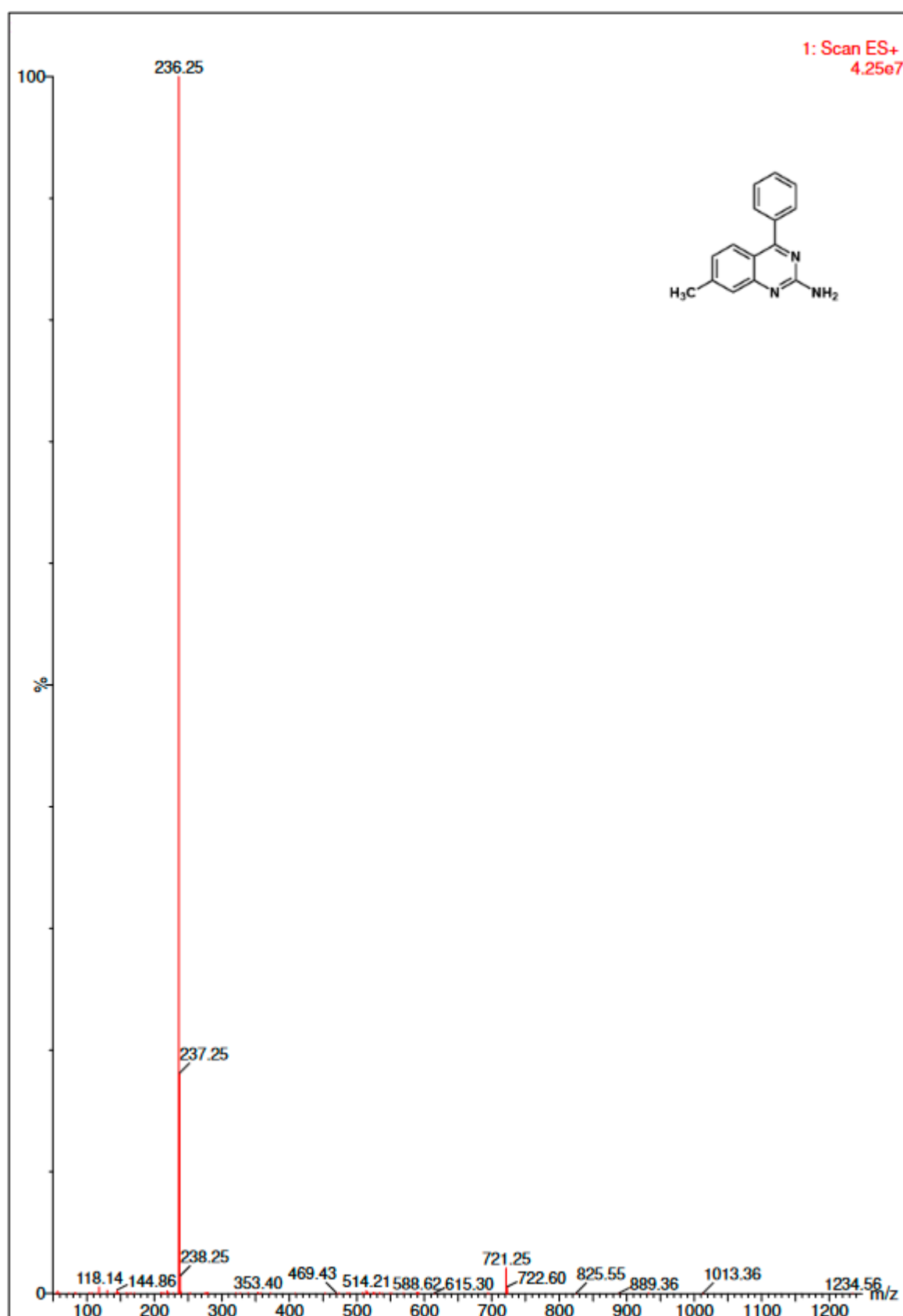
LC-MS mass spectrum of compound 5n



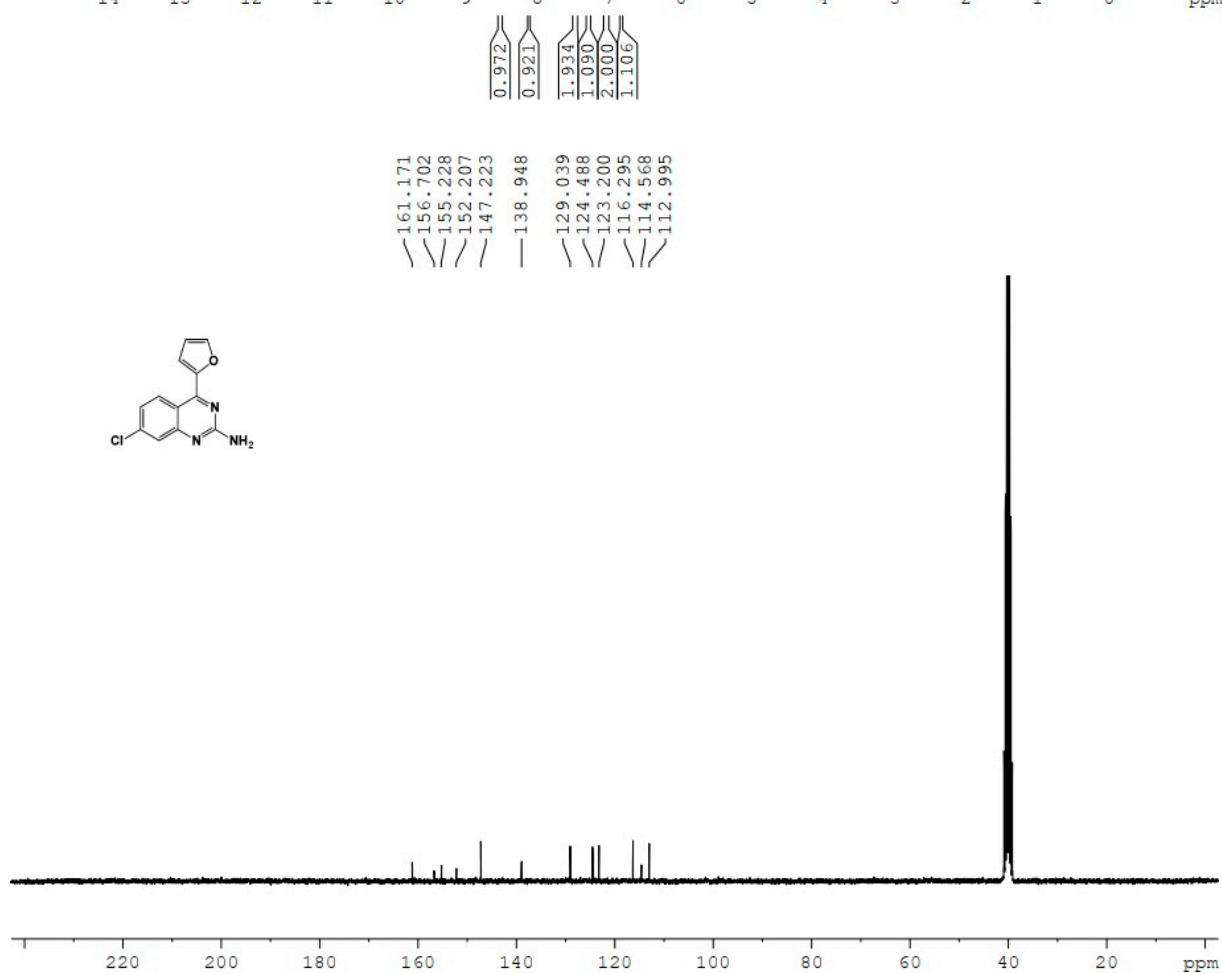
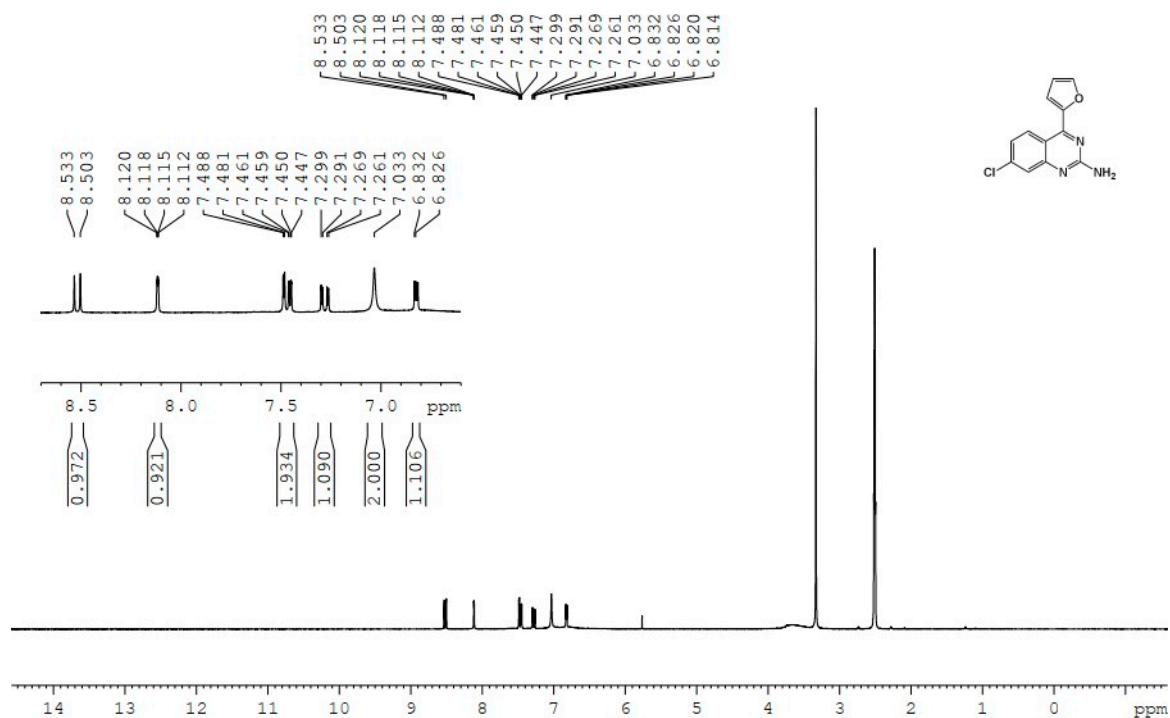
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 5o**



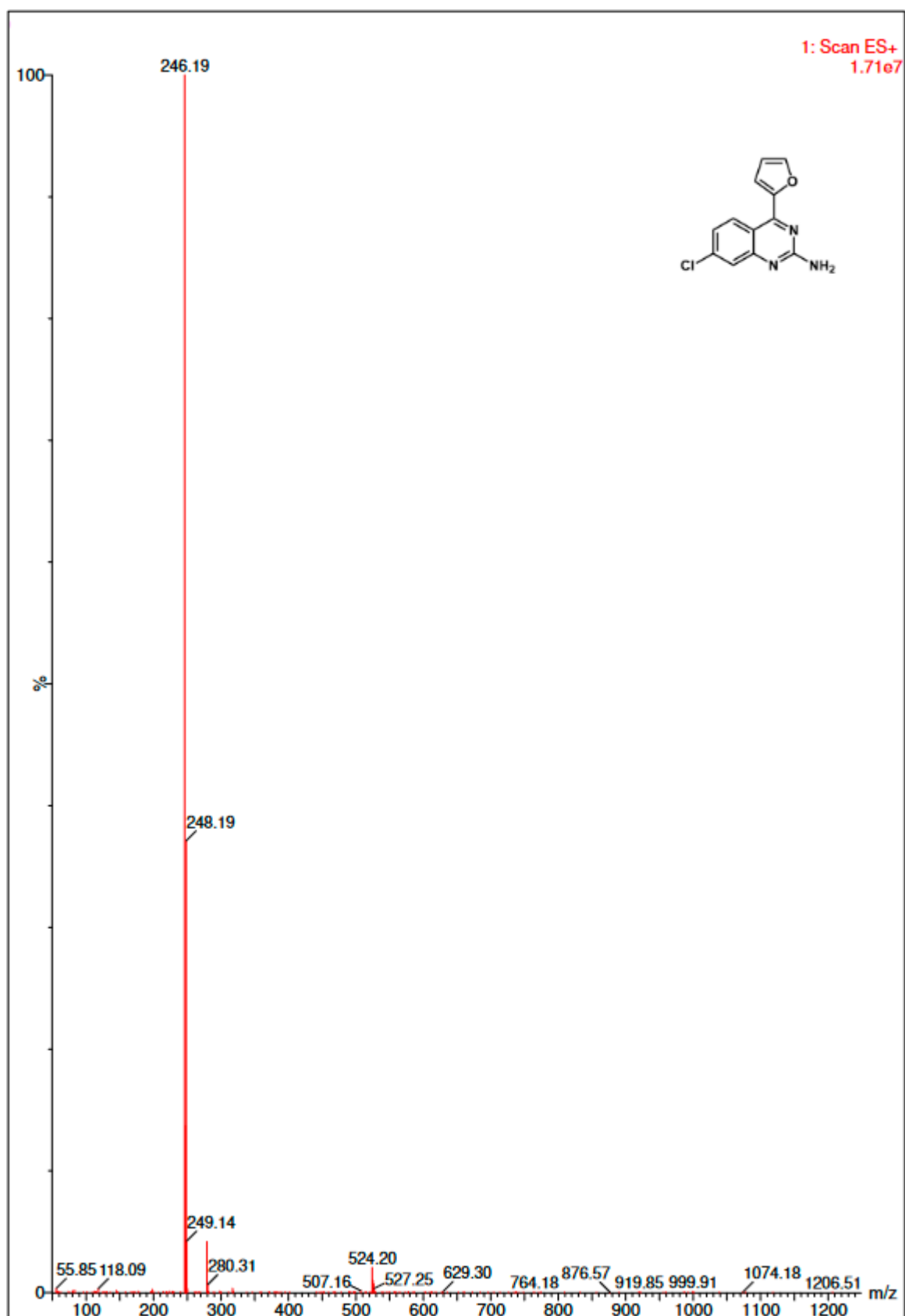
LC-MS mass spectrum of compound 5o



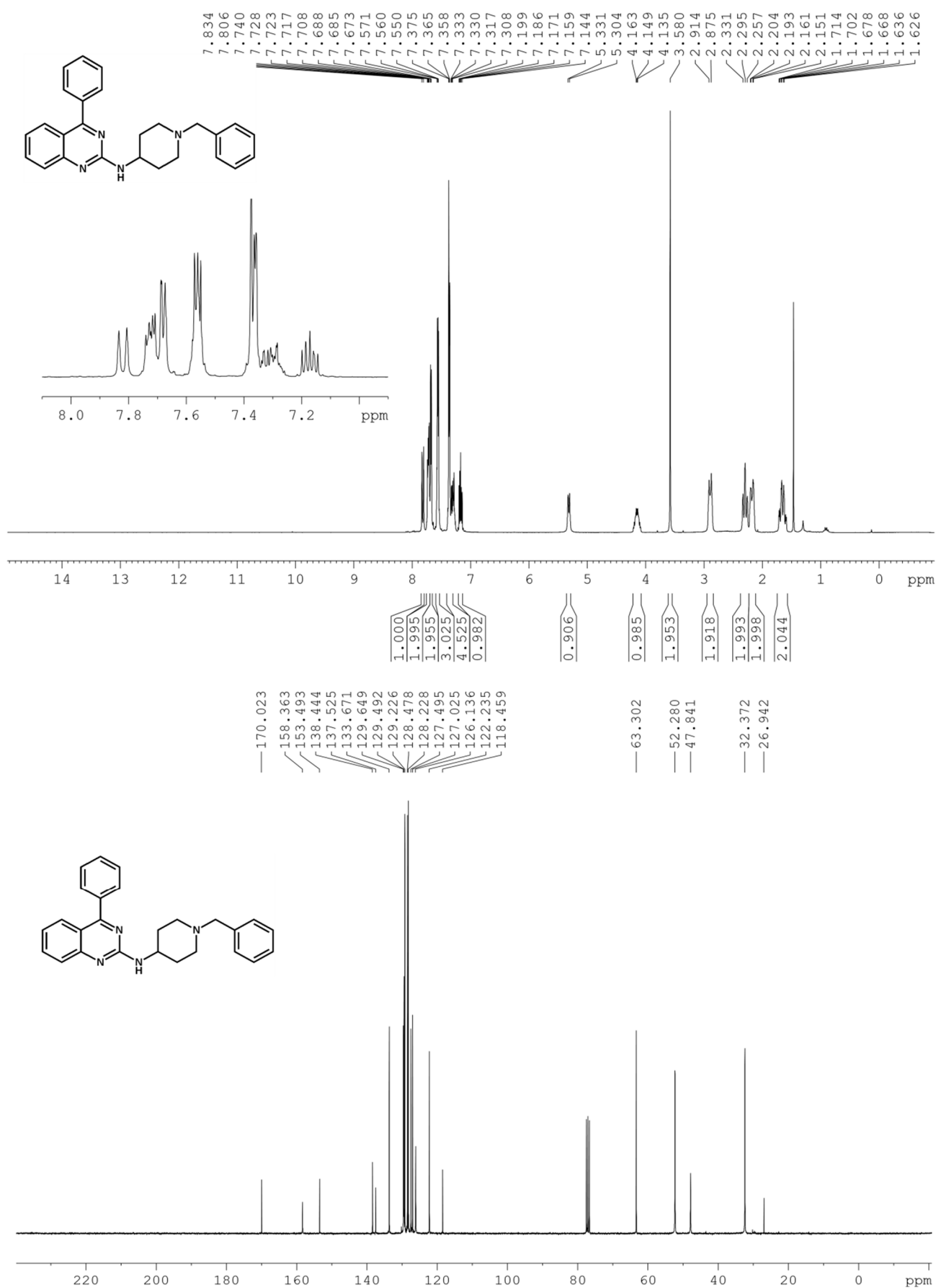
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in DMSO-d<sub>6</sub> of compound 5p**



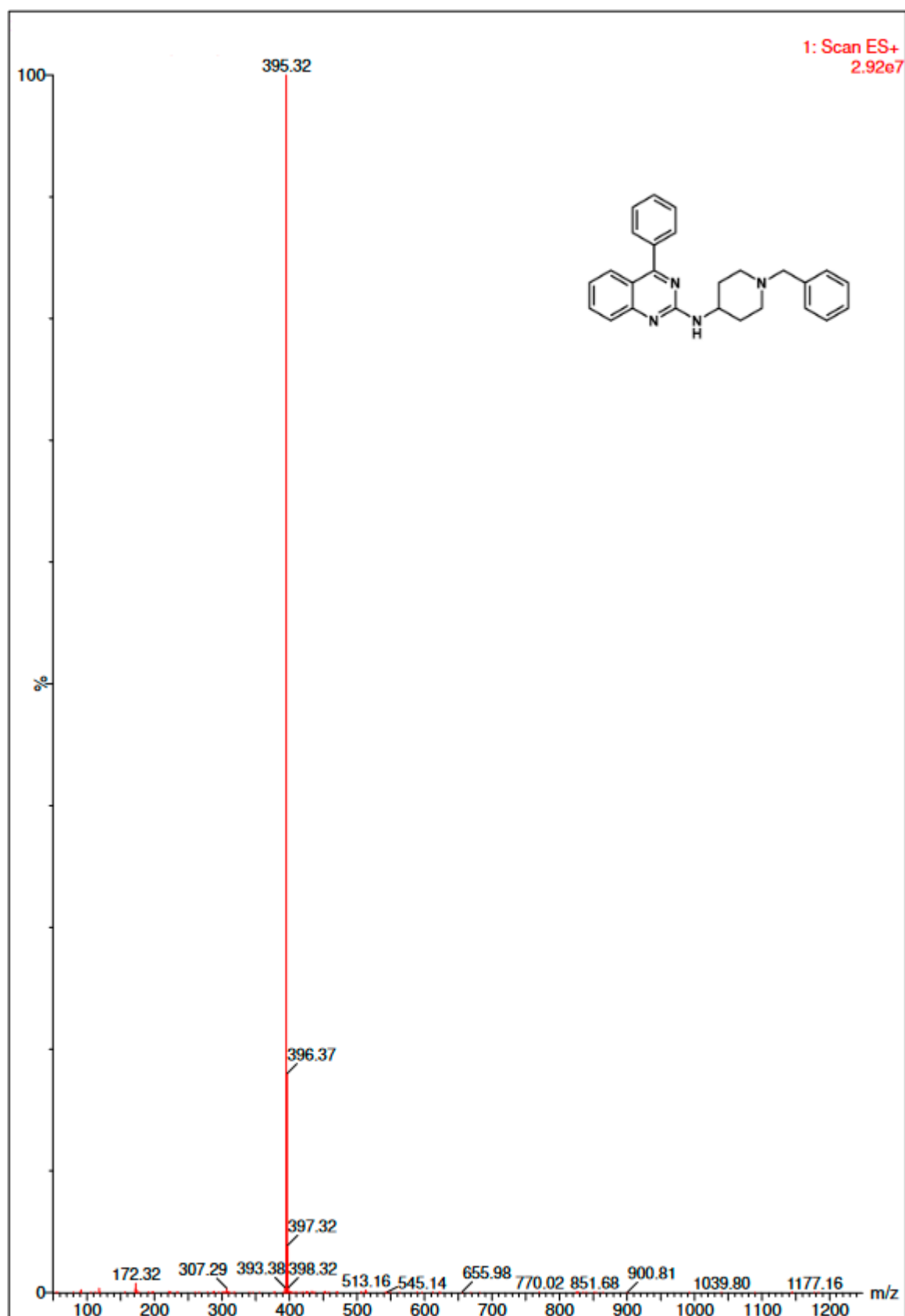
LC-MS mass spectrum of compound 5p



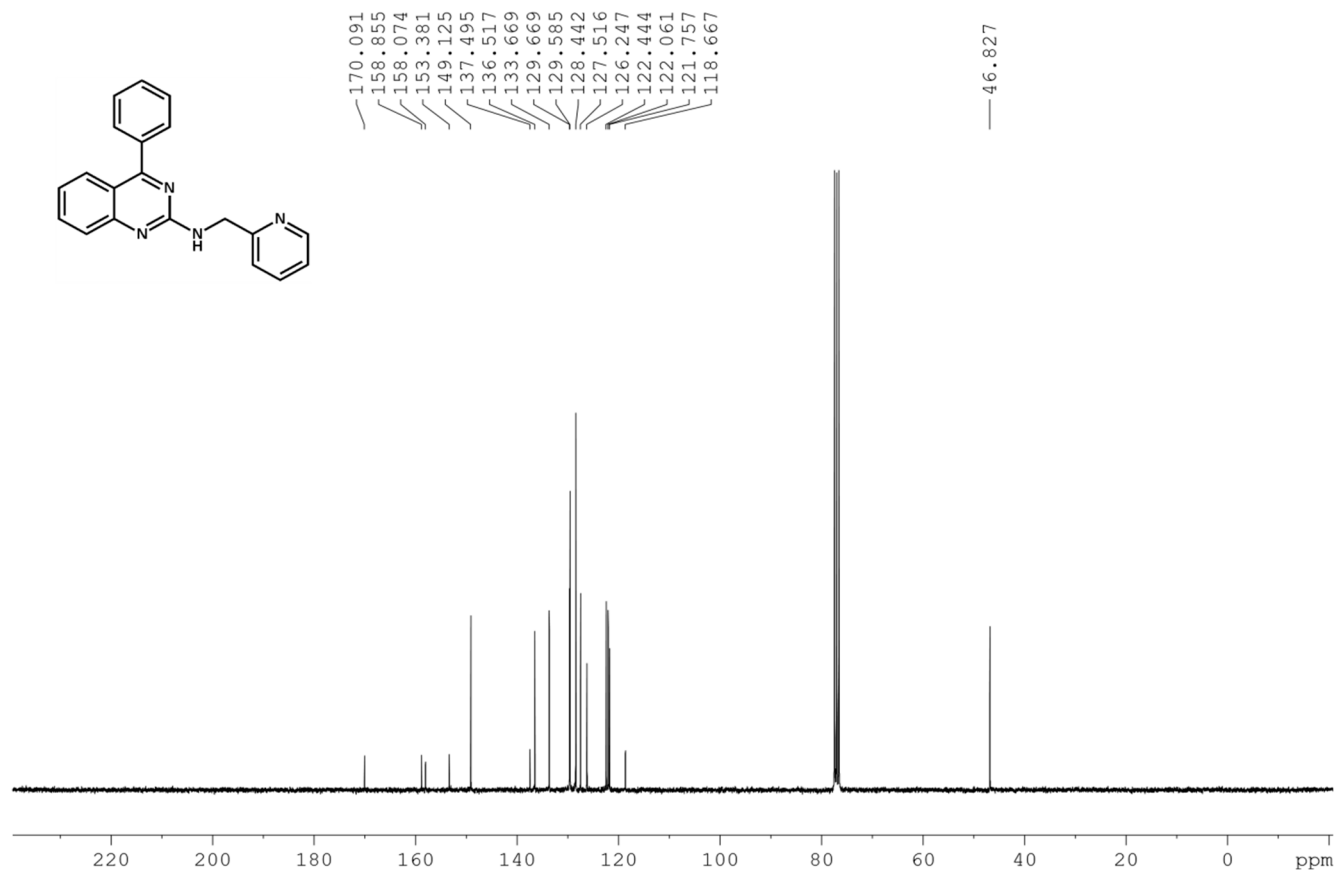
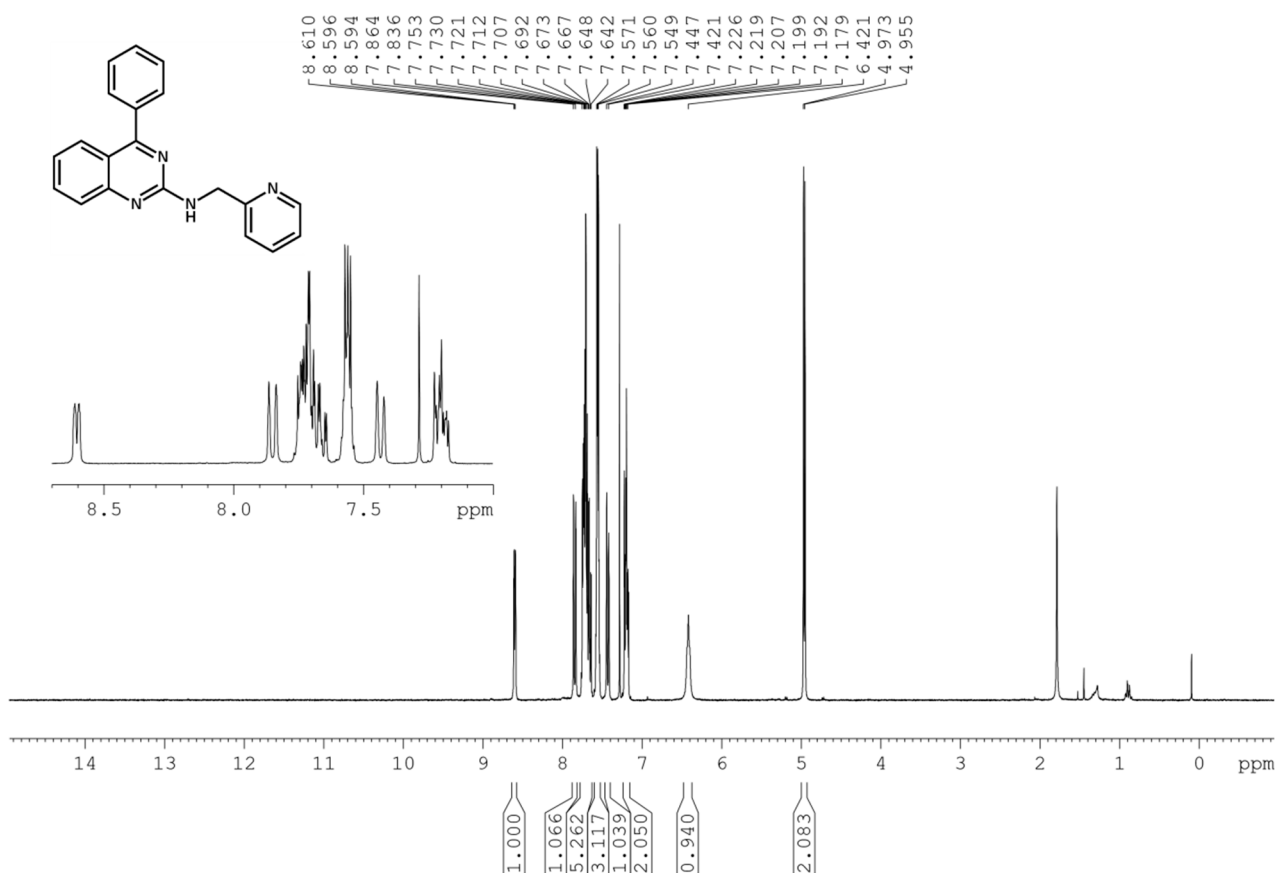
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9a**



LC-MS mass spectrum of compound 9a

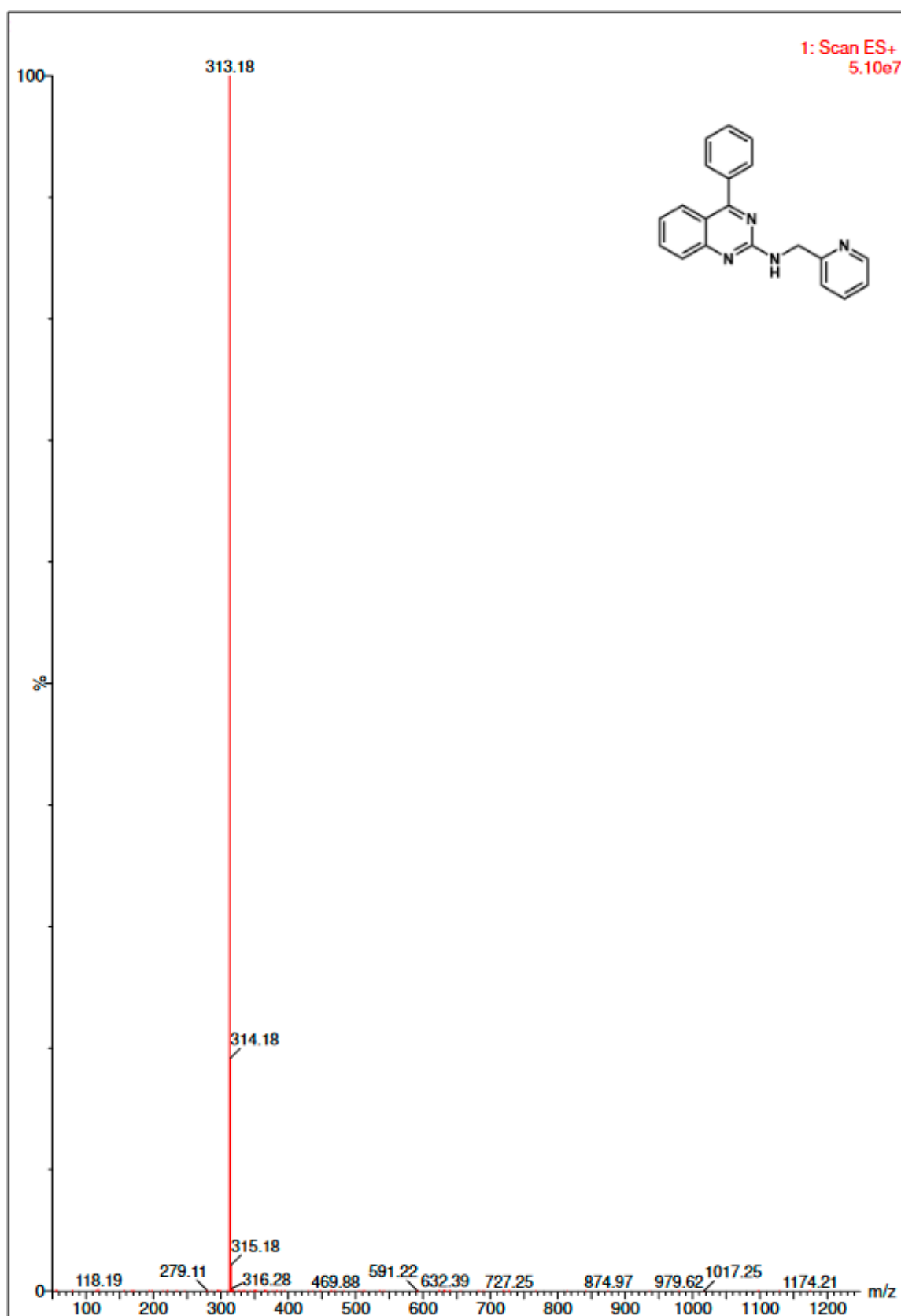


# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9b

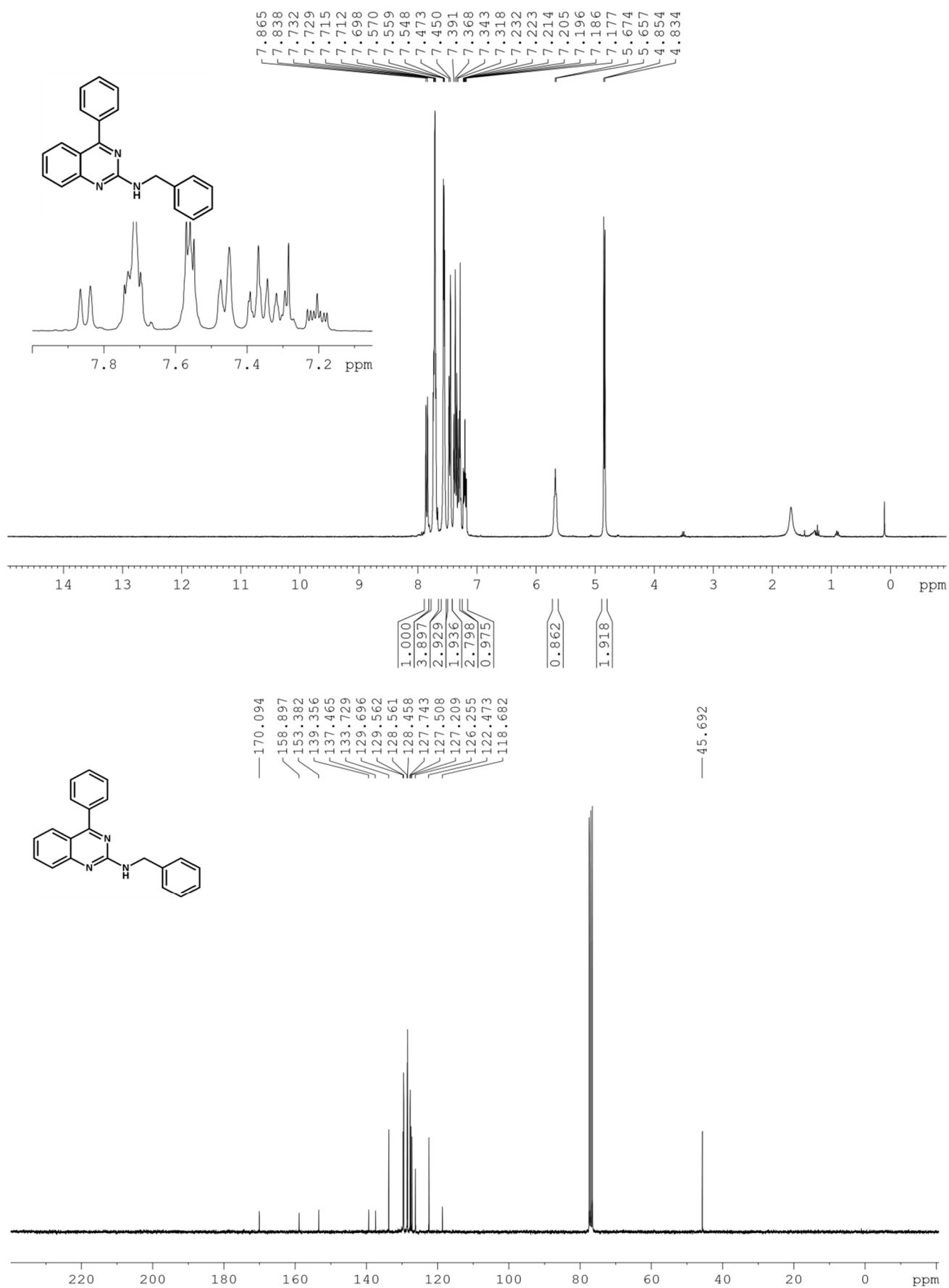




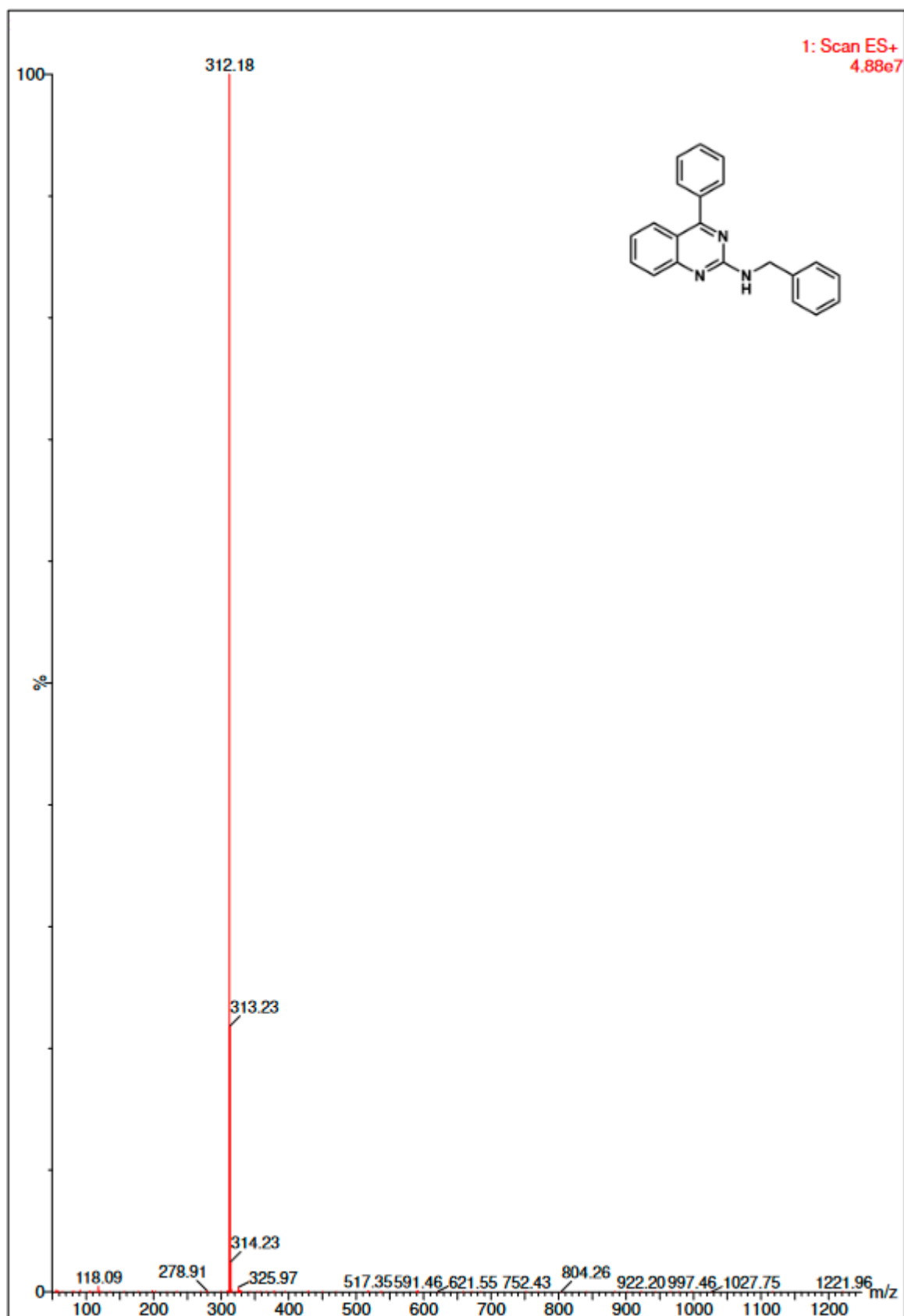
LC-MS mass spectrum of compound 9b



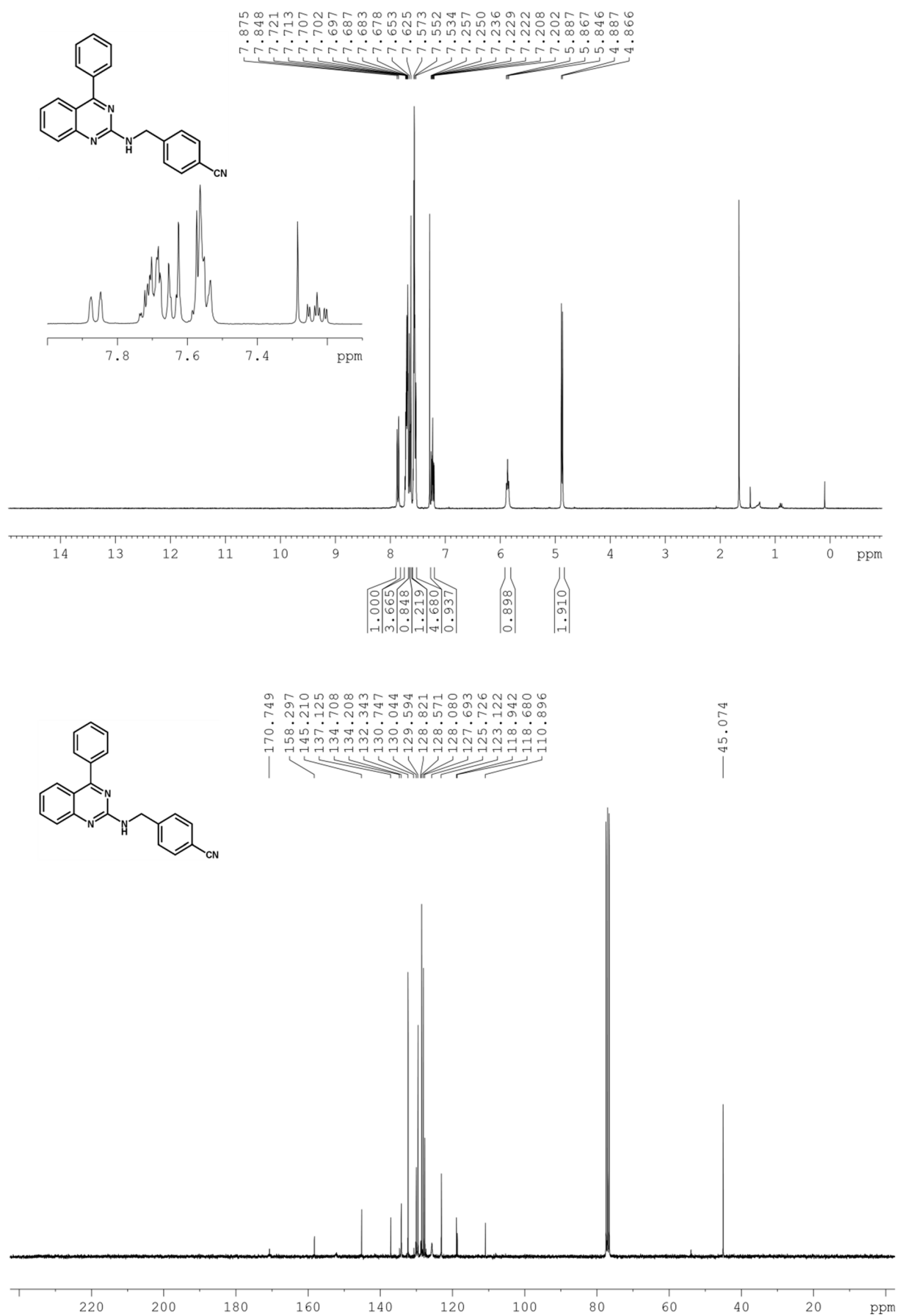
**<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9c**



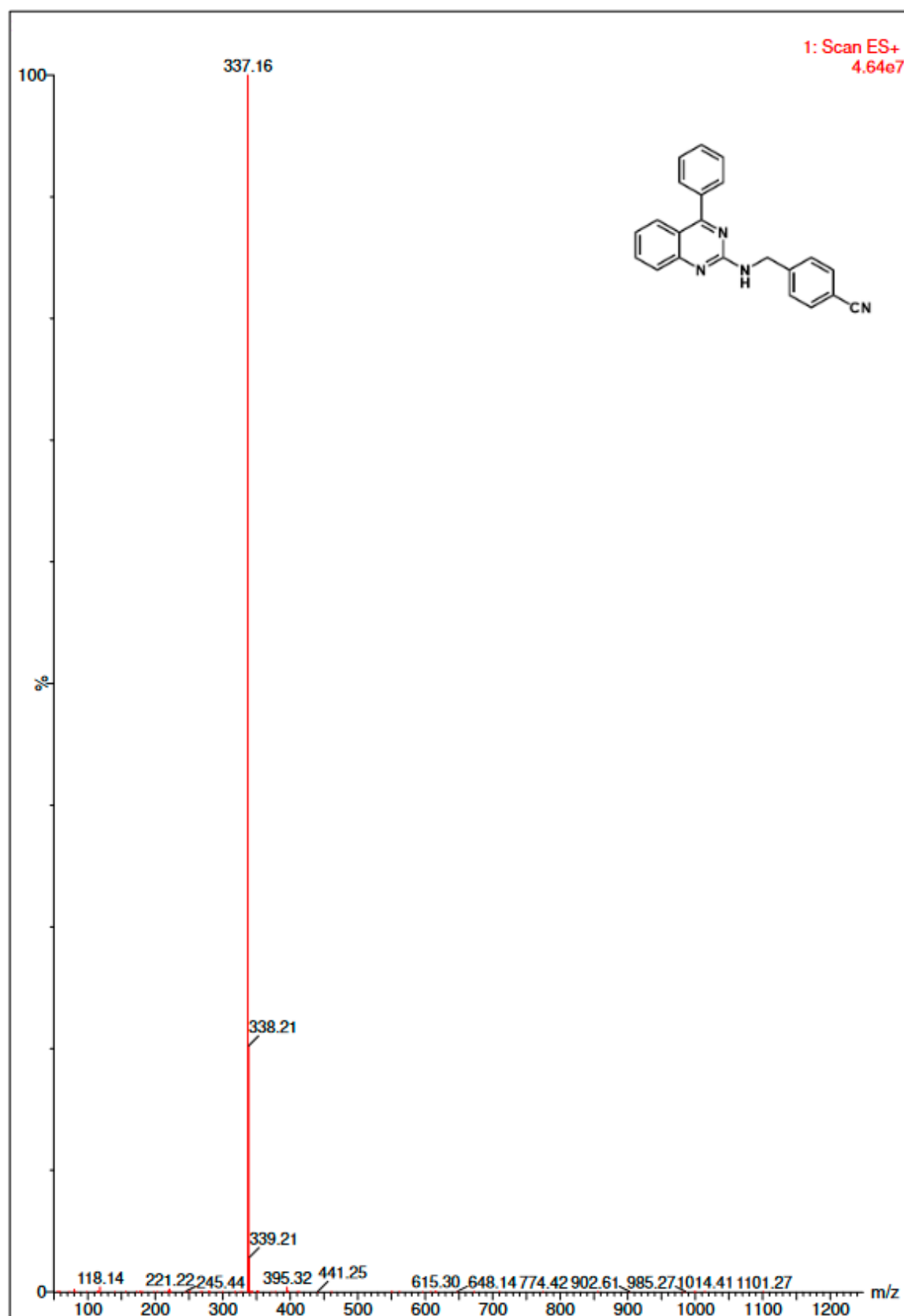
LC-MS mass spectrum of compound 9c



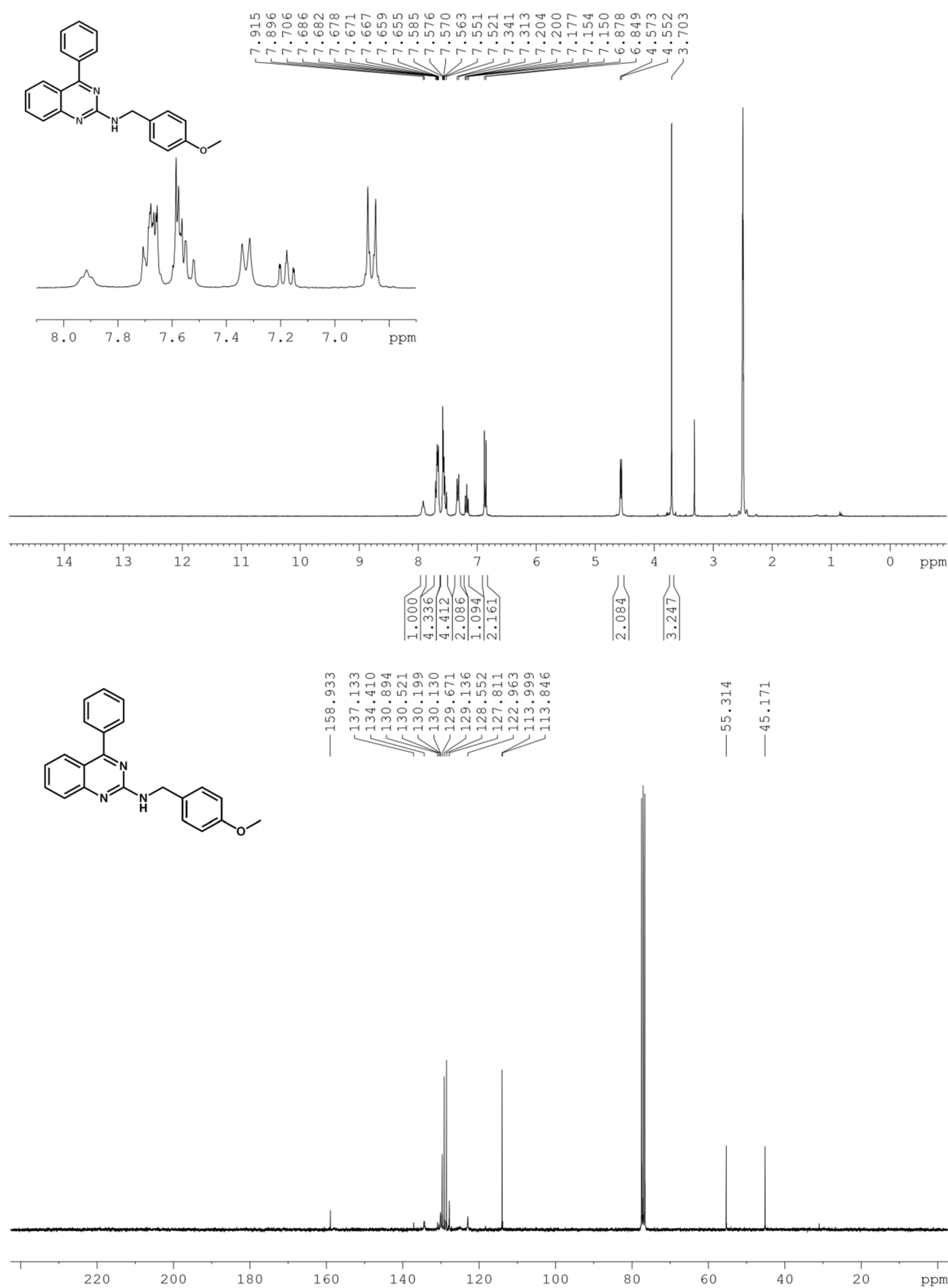
# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9d



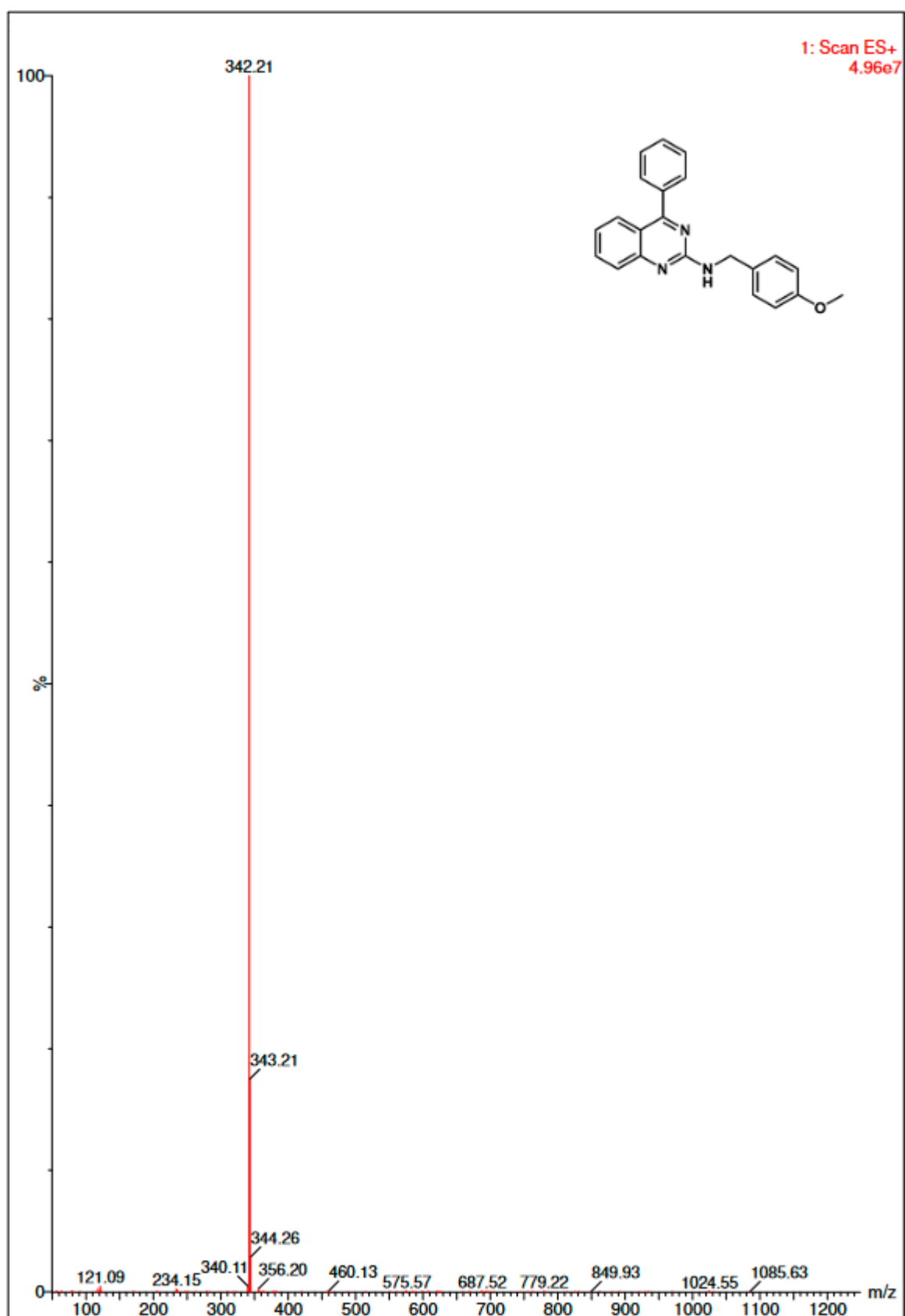
LC-MS mass spectrum of compound 9d



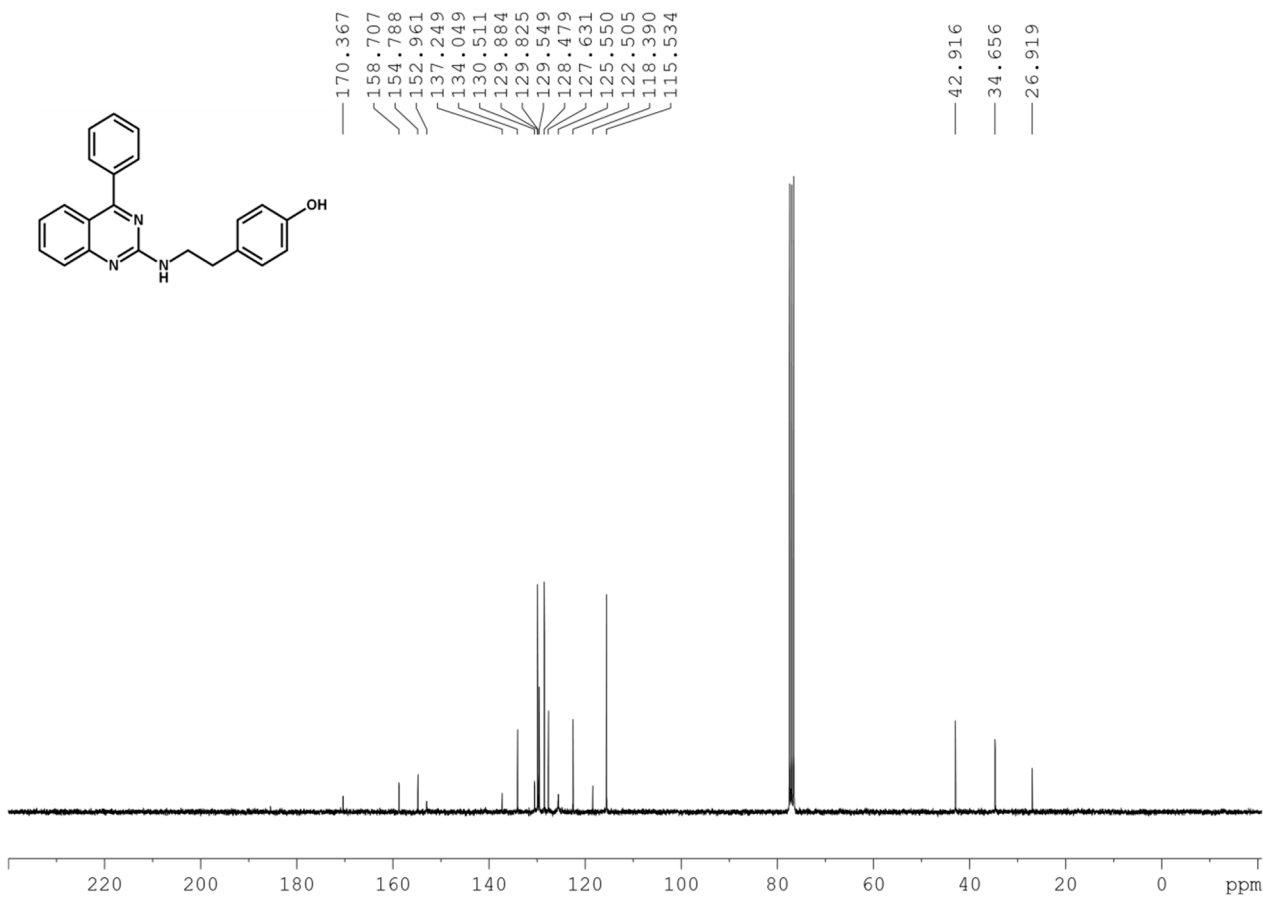
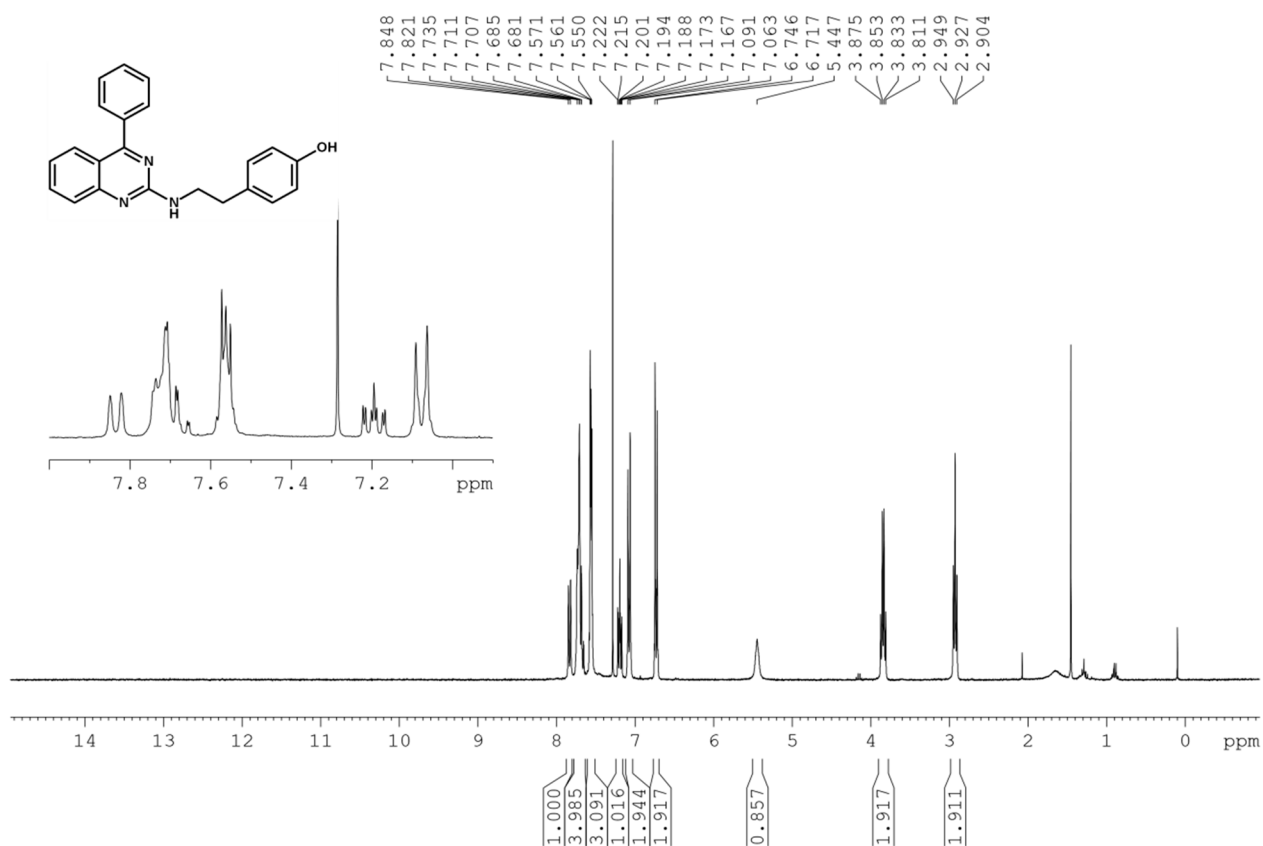
**<sup>1</sup>H-NMR Spectra in DMSO-d<sub>6</sub> and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9e**



LC-MS mass spectrum of compound 9e

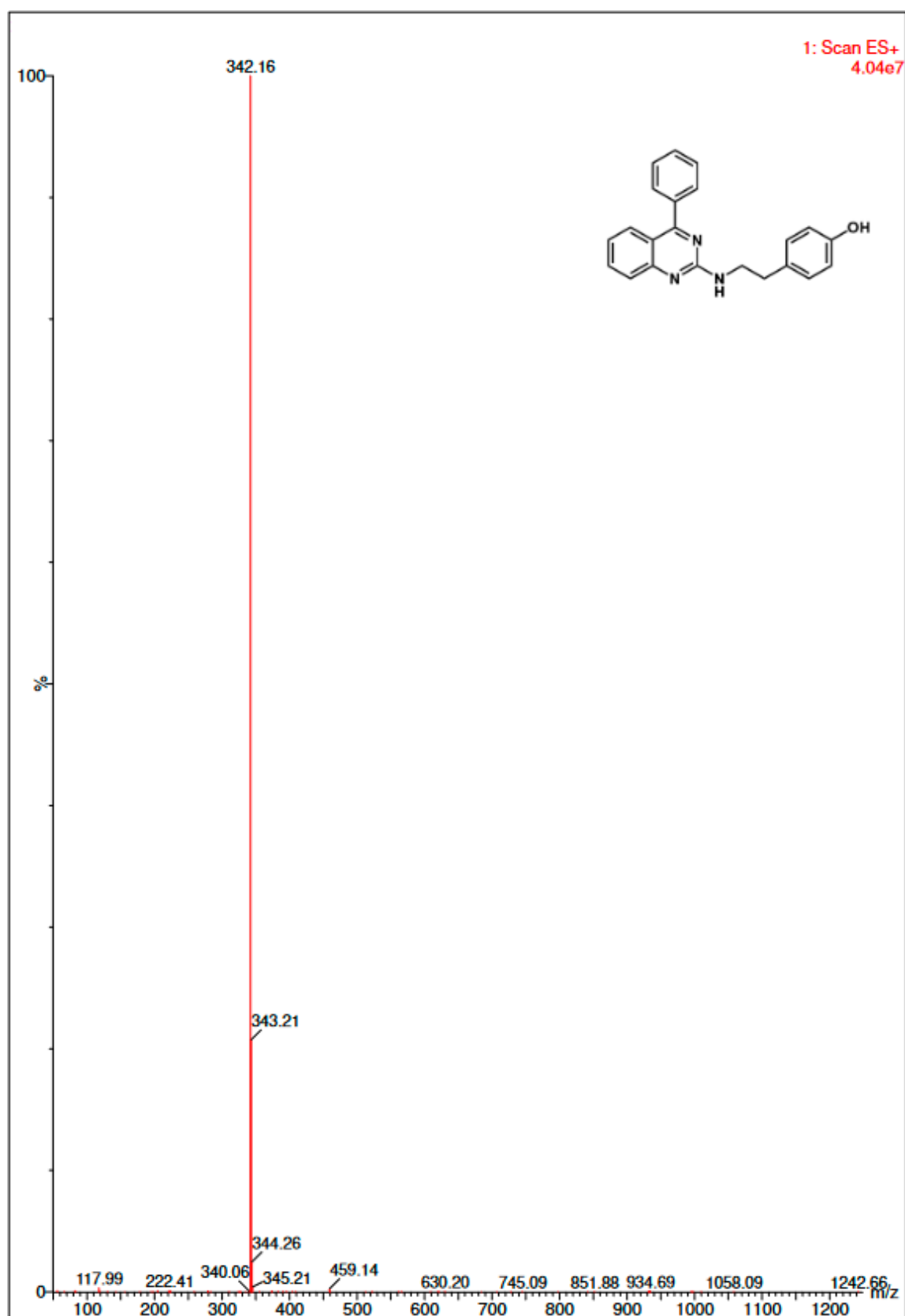


# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9f

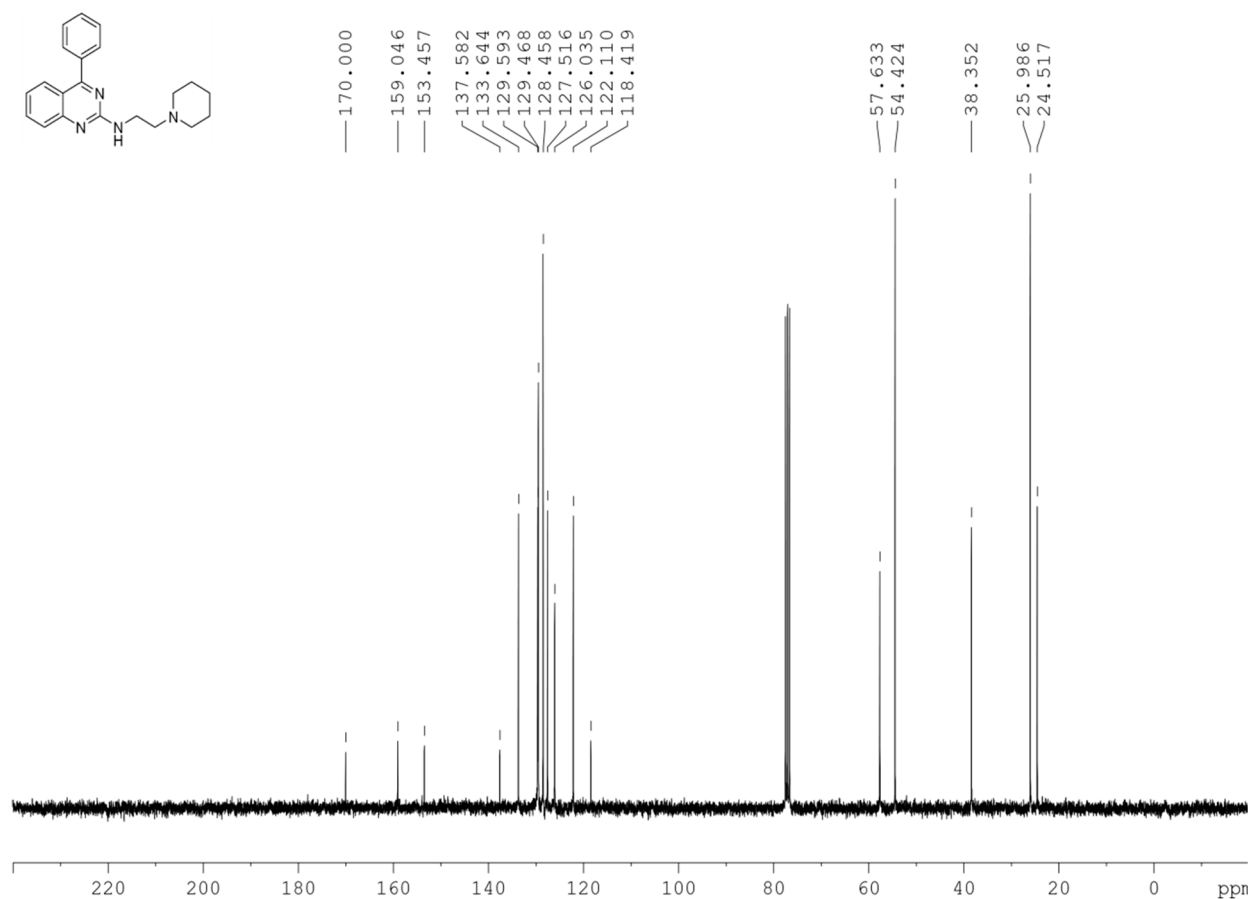
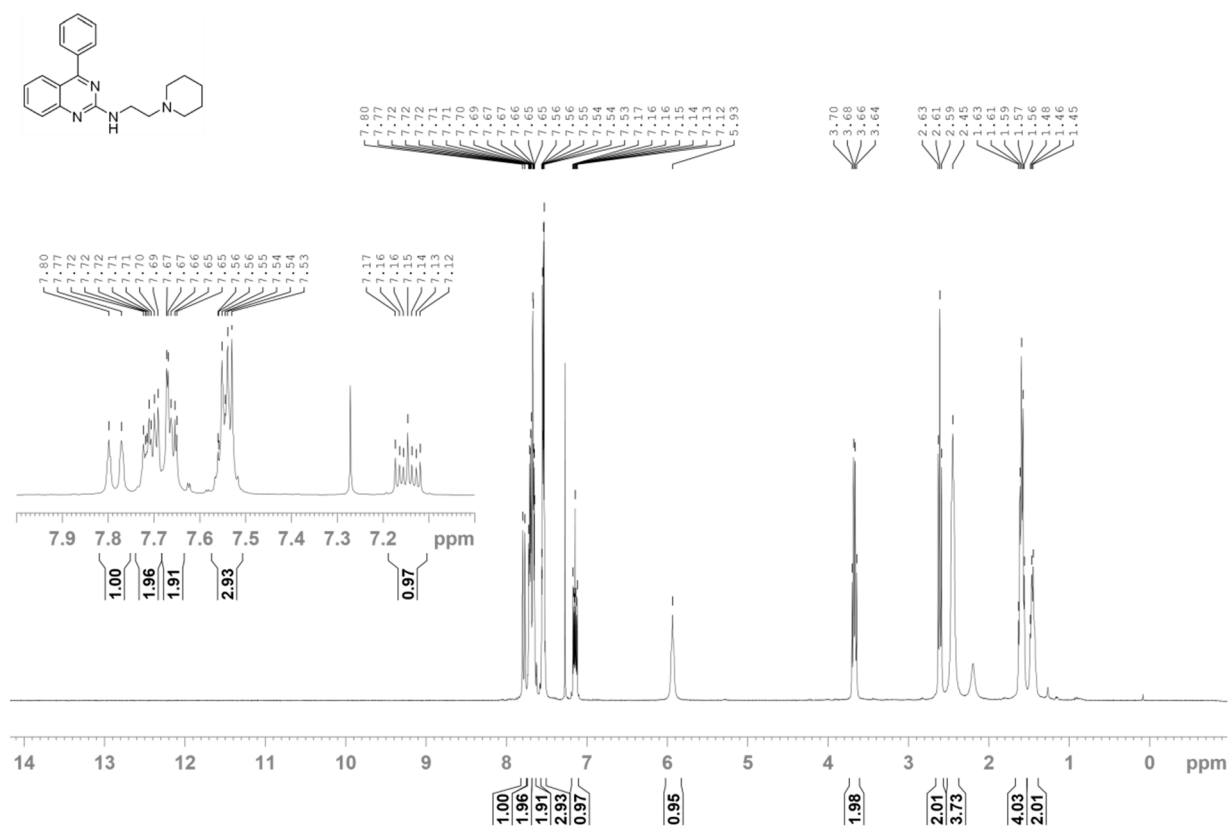




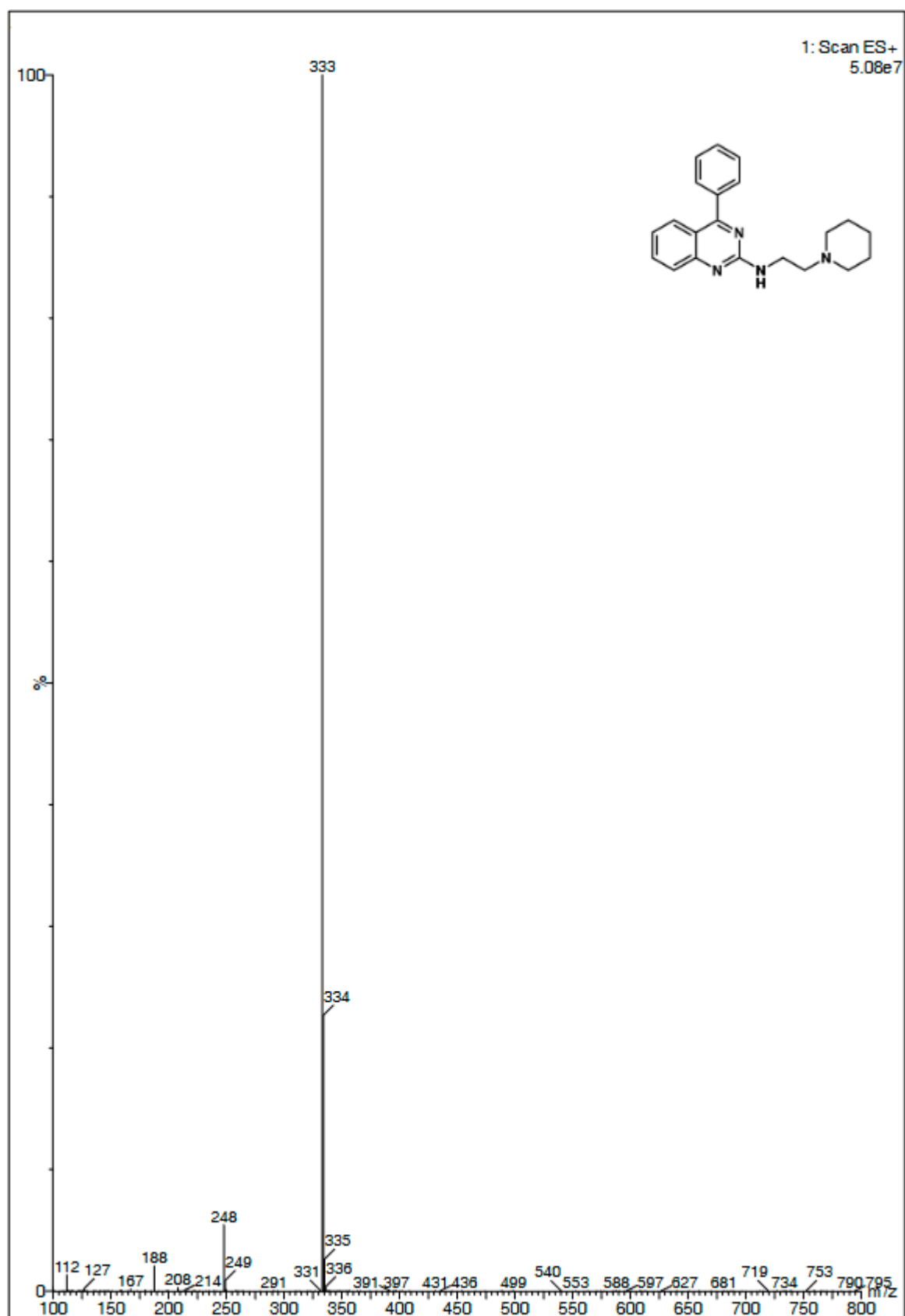
LC-MS mass spectrum of compound 9f



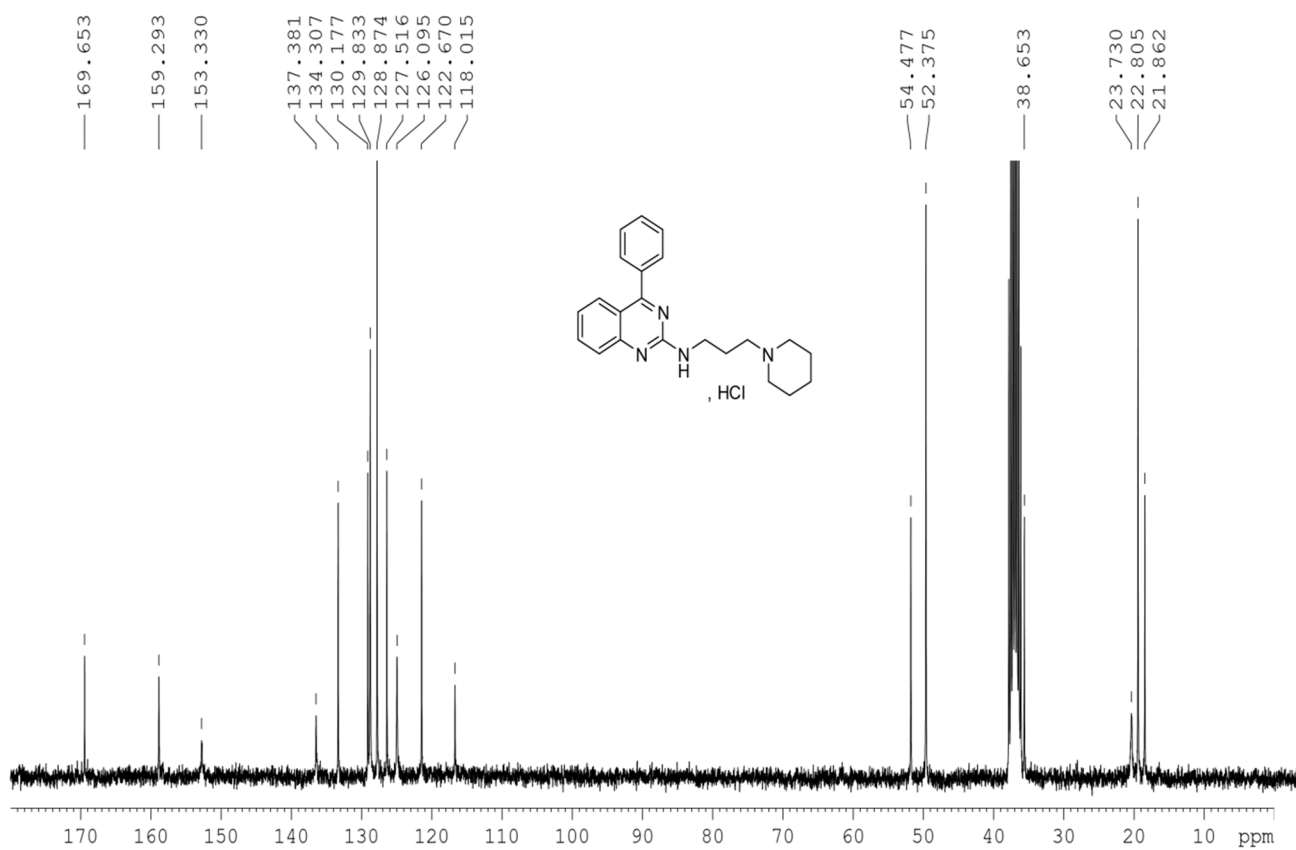
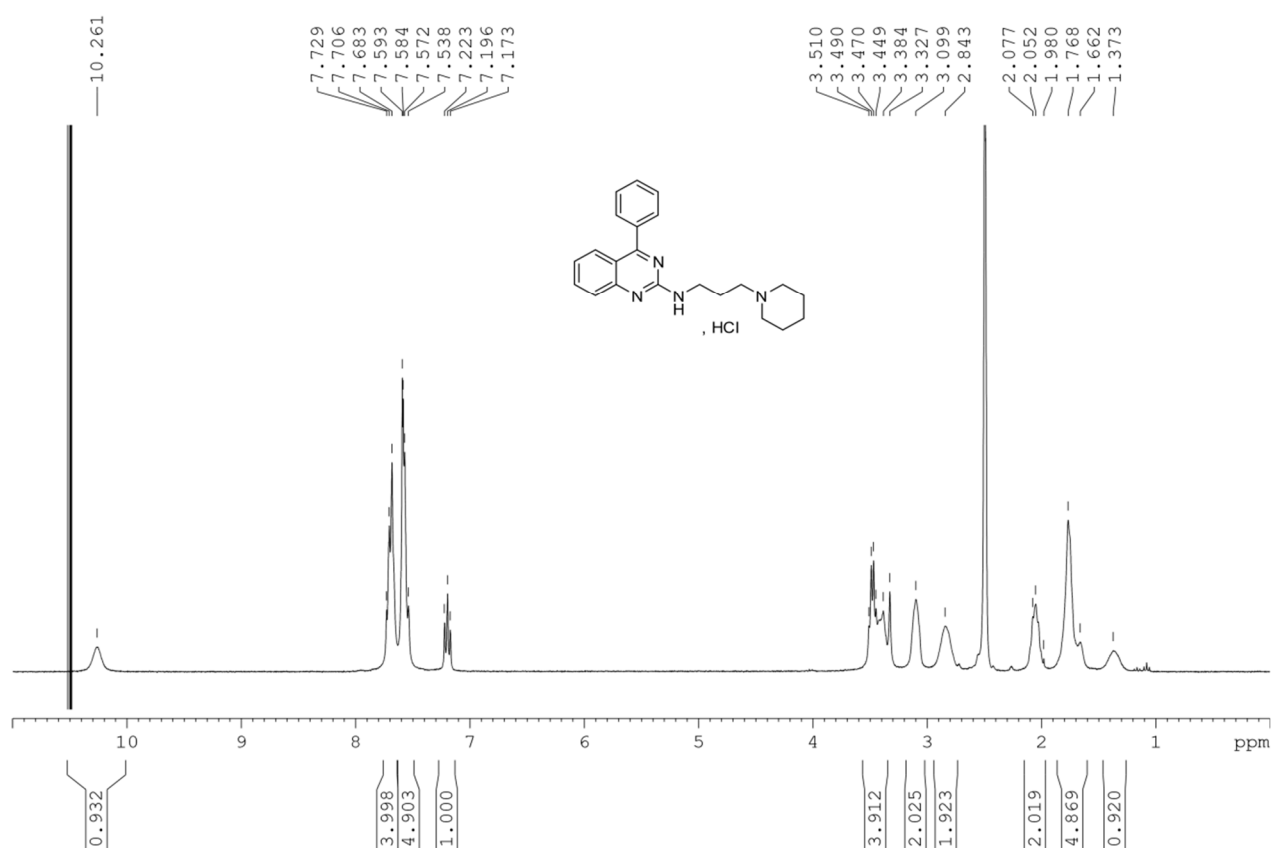
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9g**



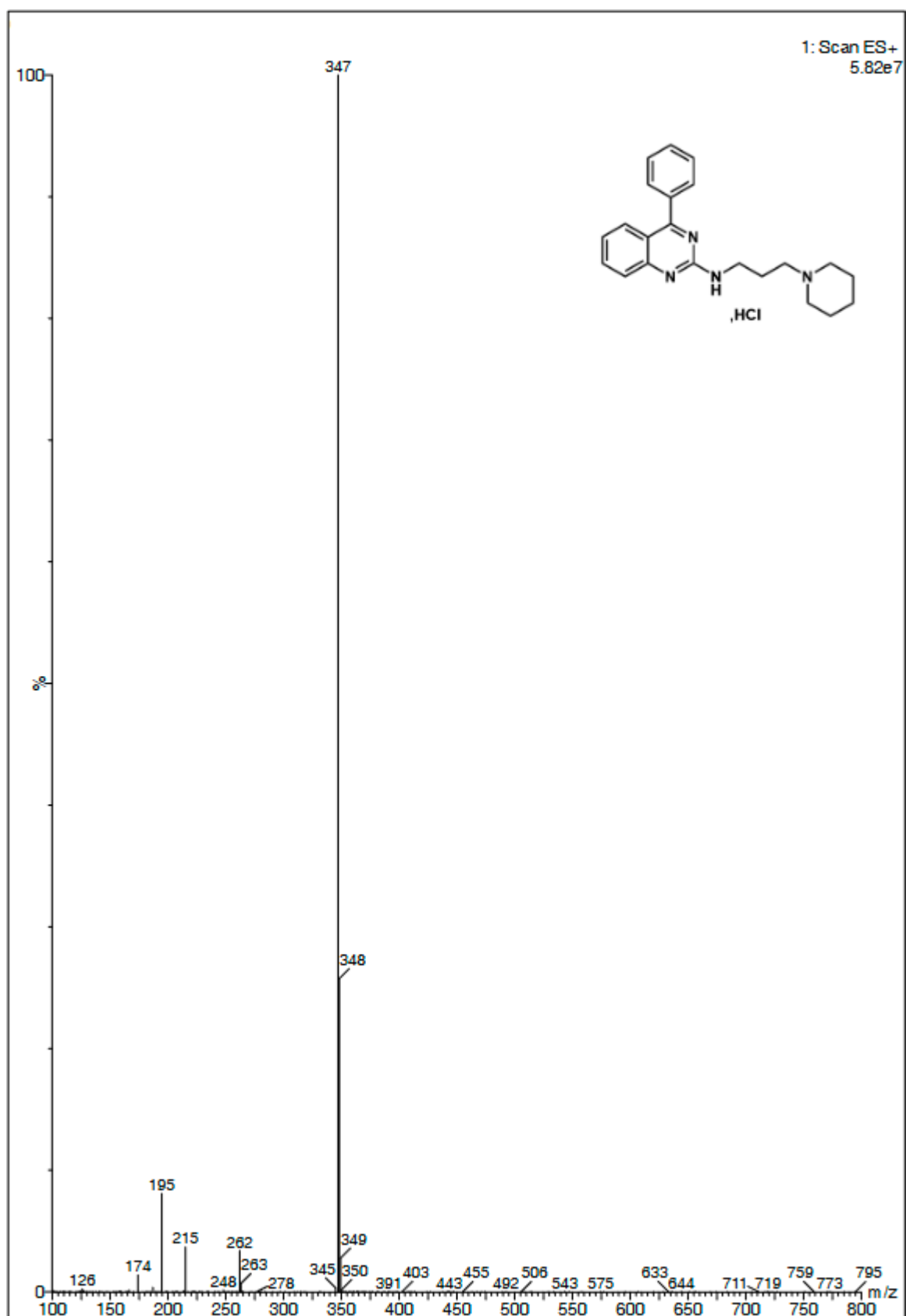
LC-MS mass spectrum of compound 9g



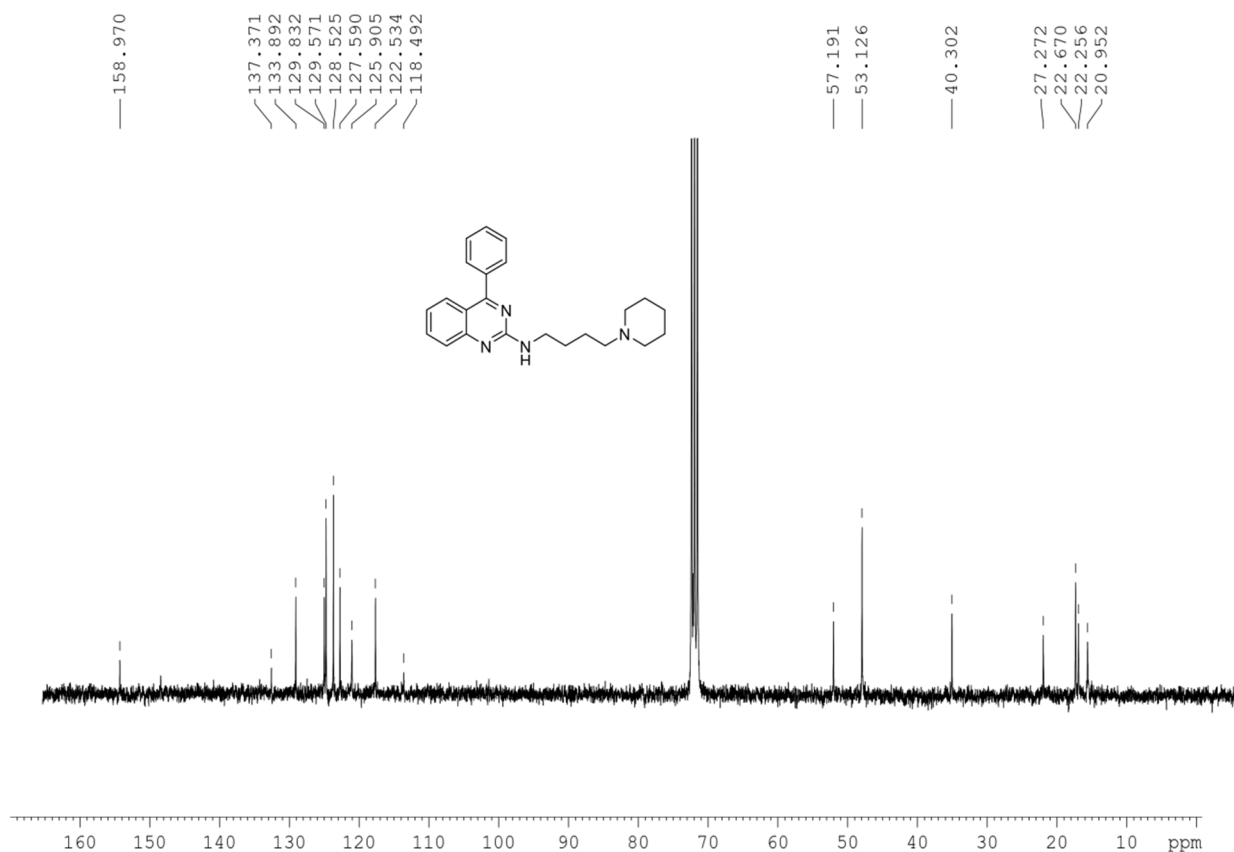
# 1H- and 13C-NMR Spectra in DMSO-d6 of compound 9h



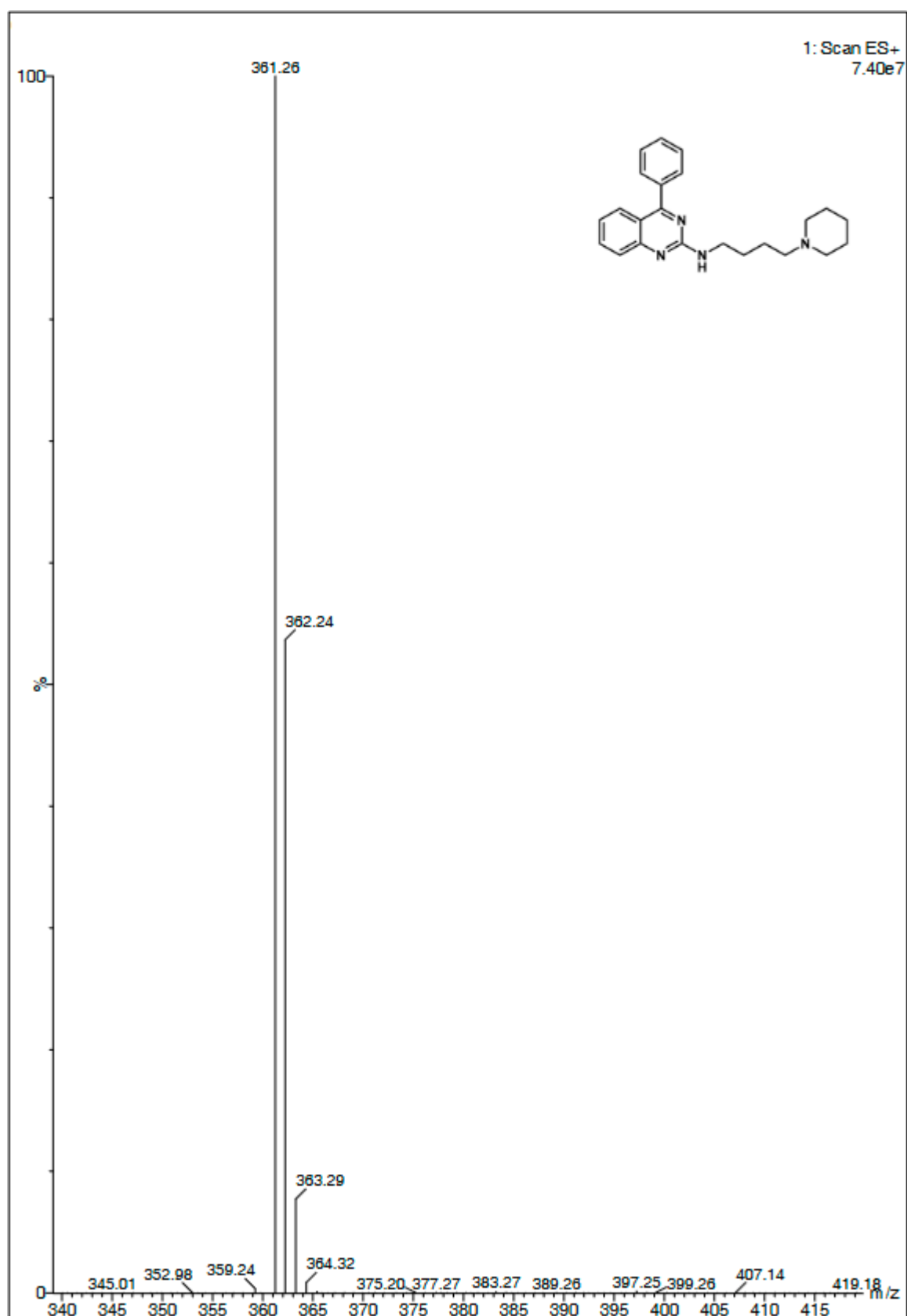
LC-MS mass spectrum of compound 9h



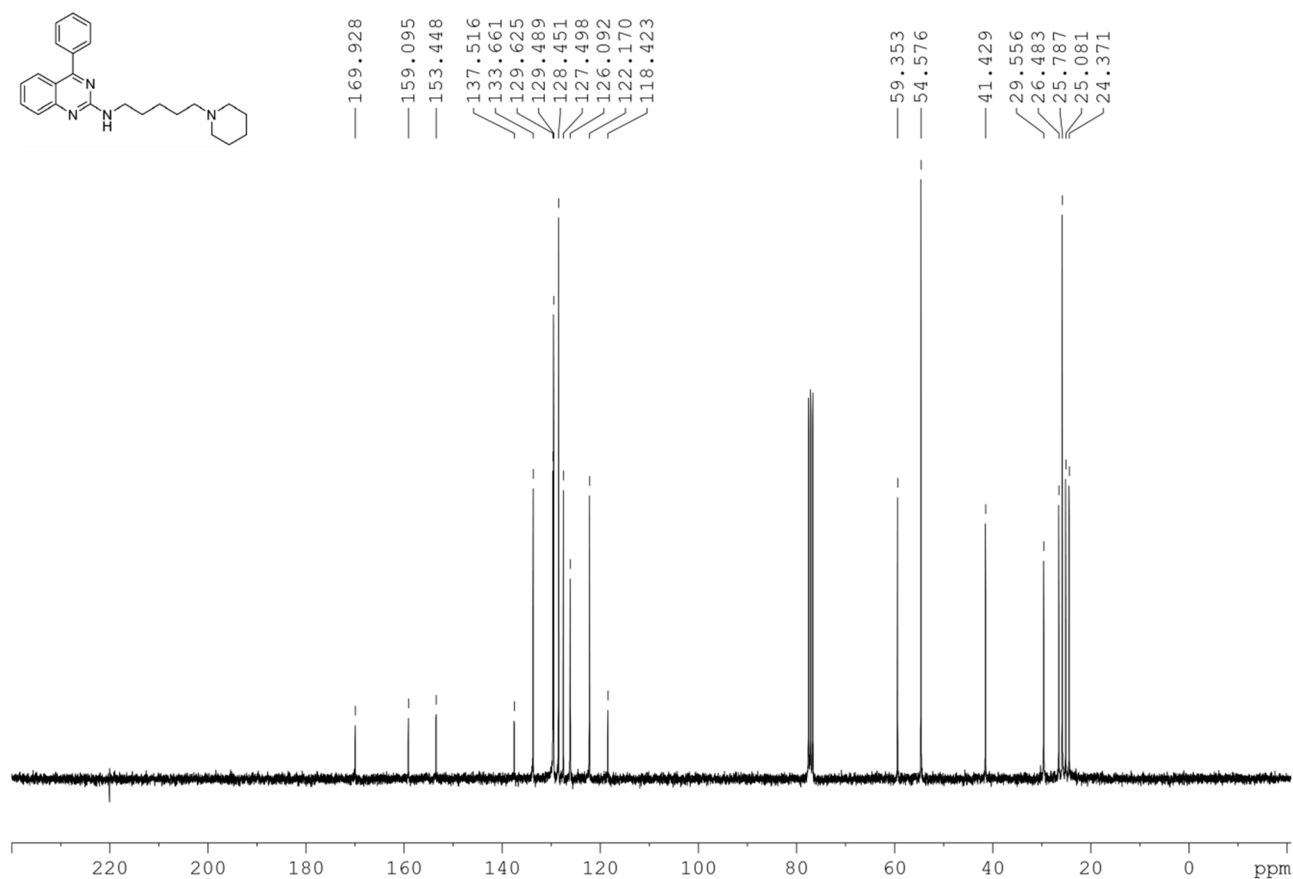
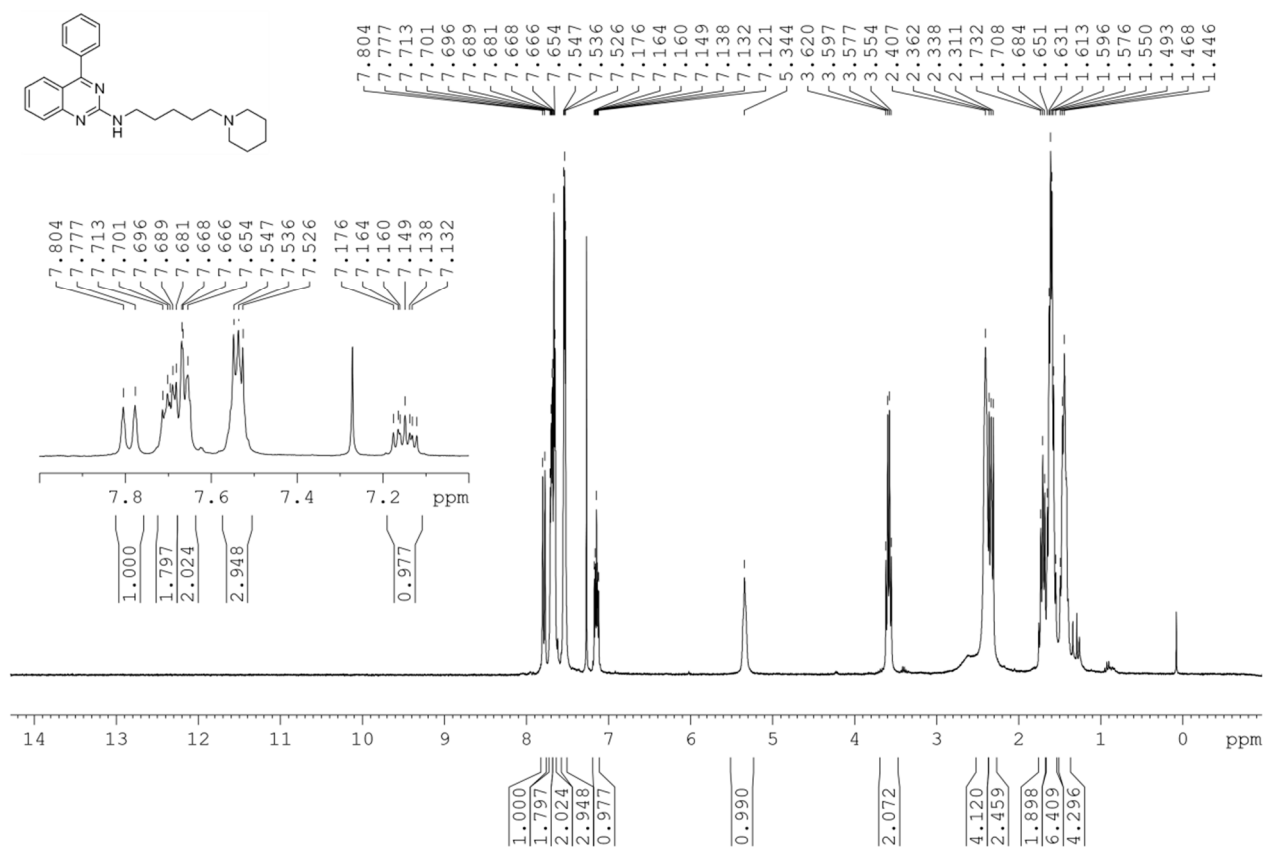
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9i**



LC-MS mass spectrum of compound 9i

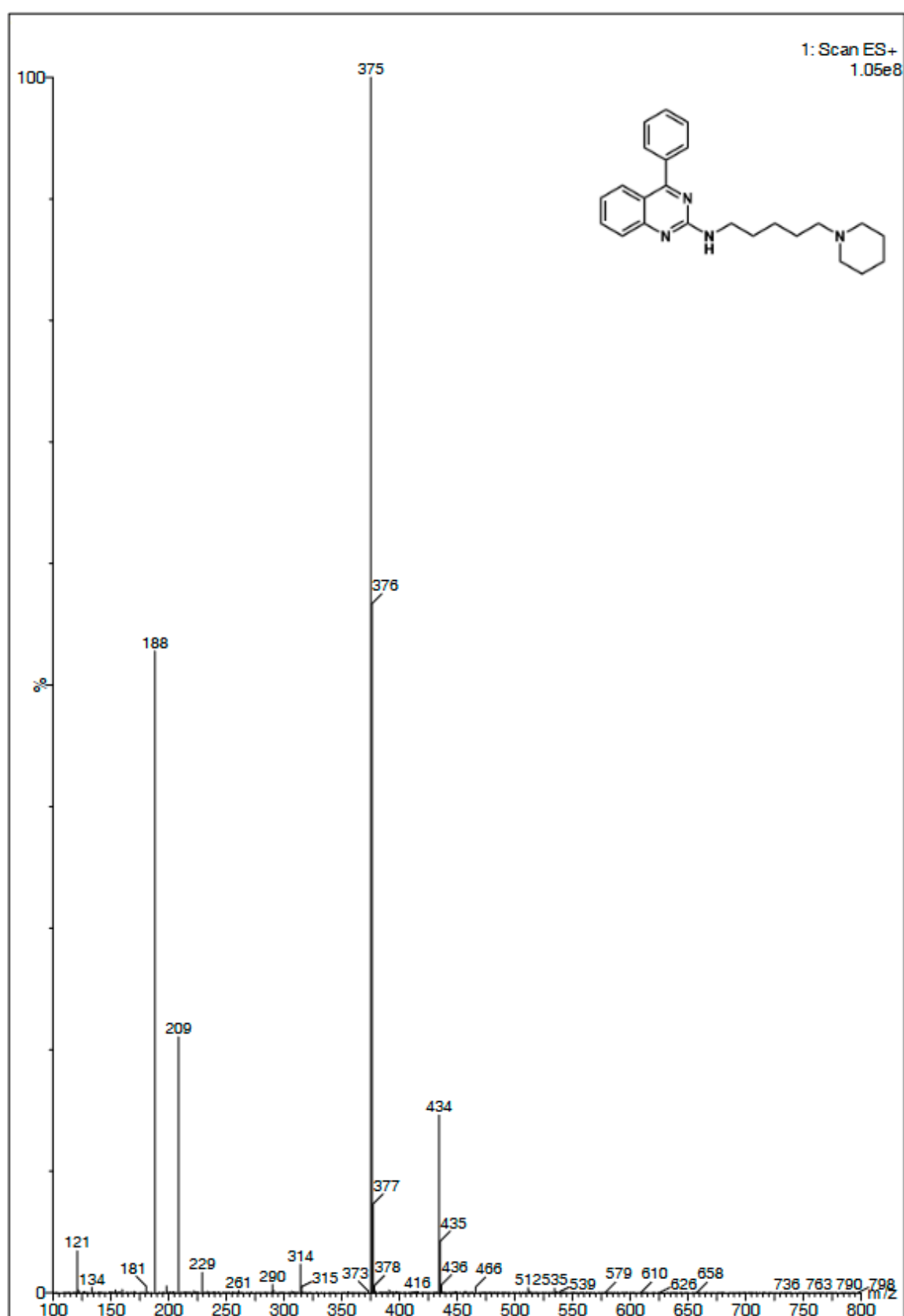


# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9j**

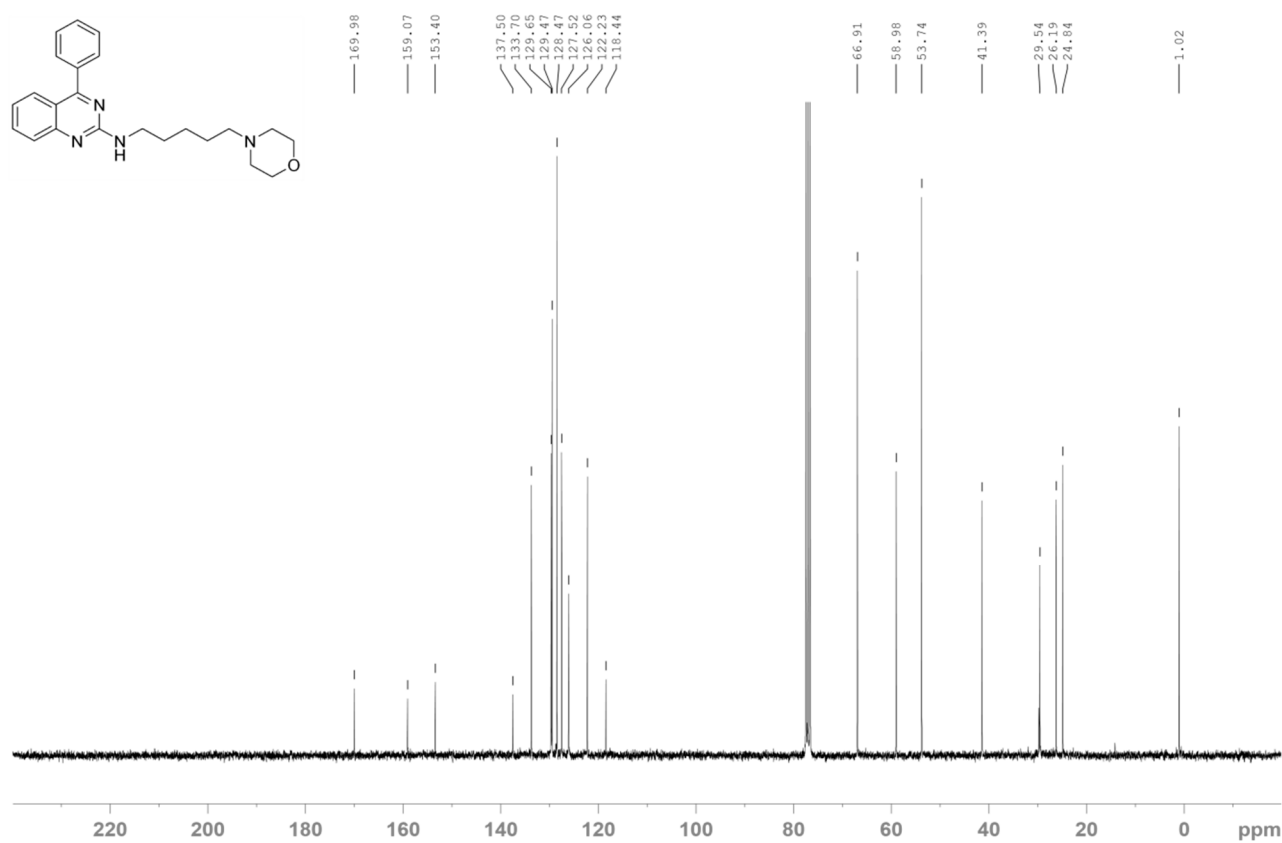
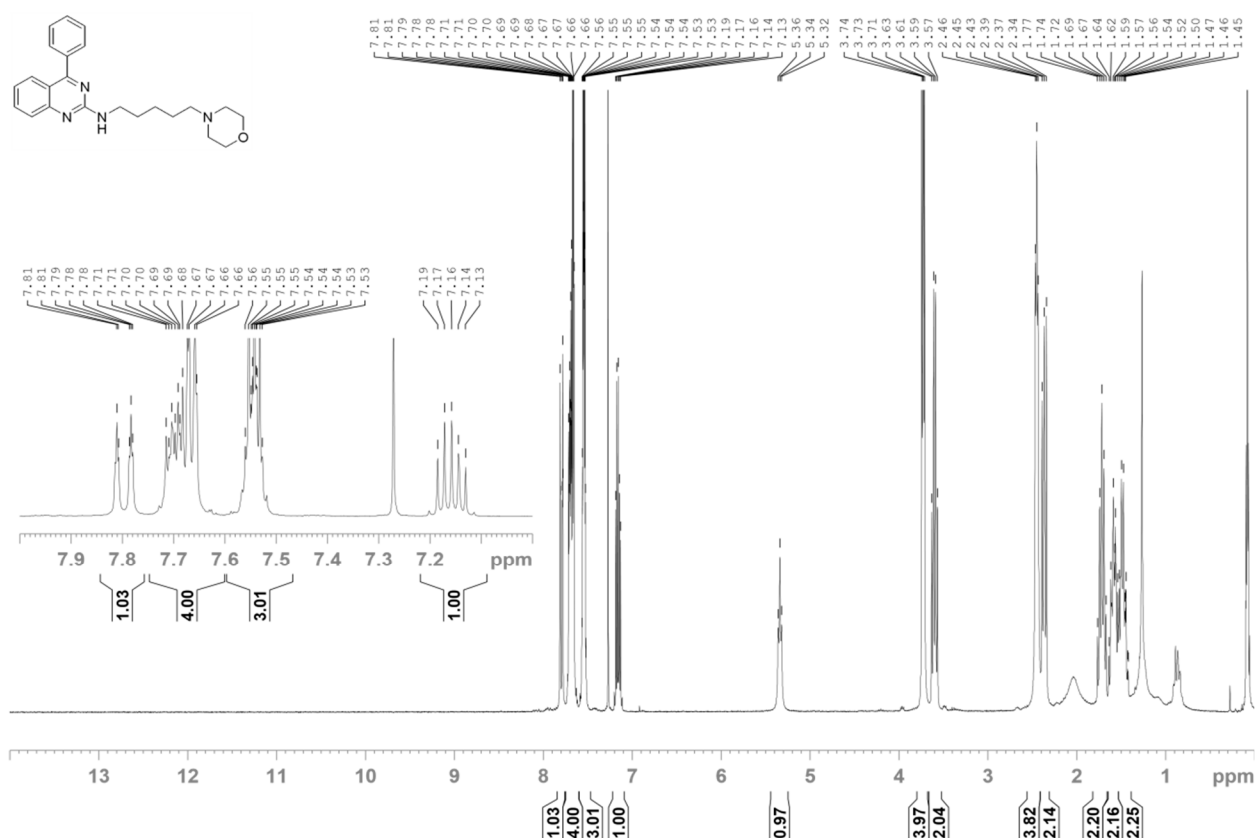




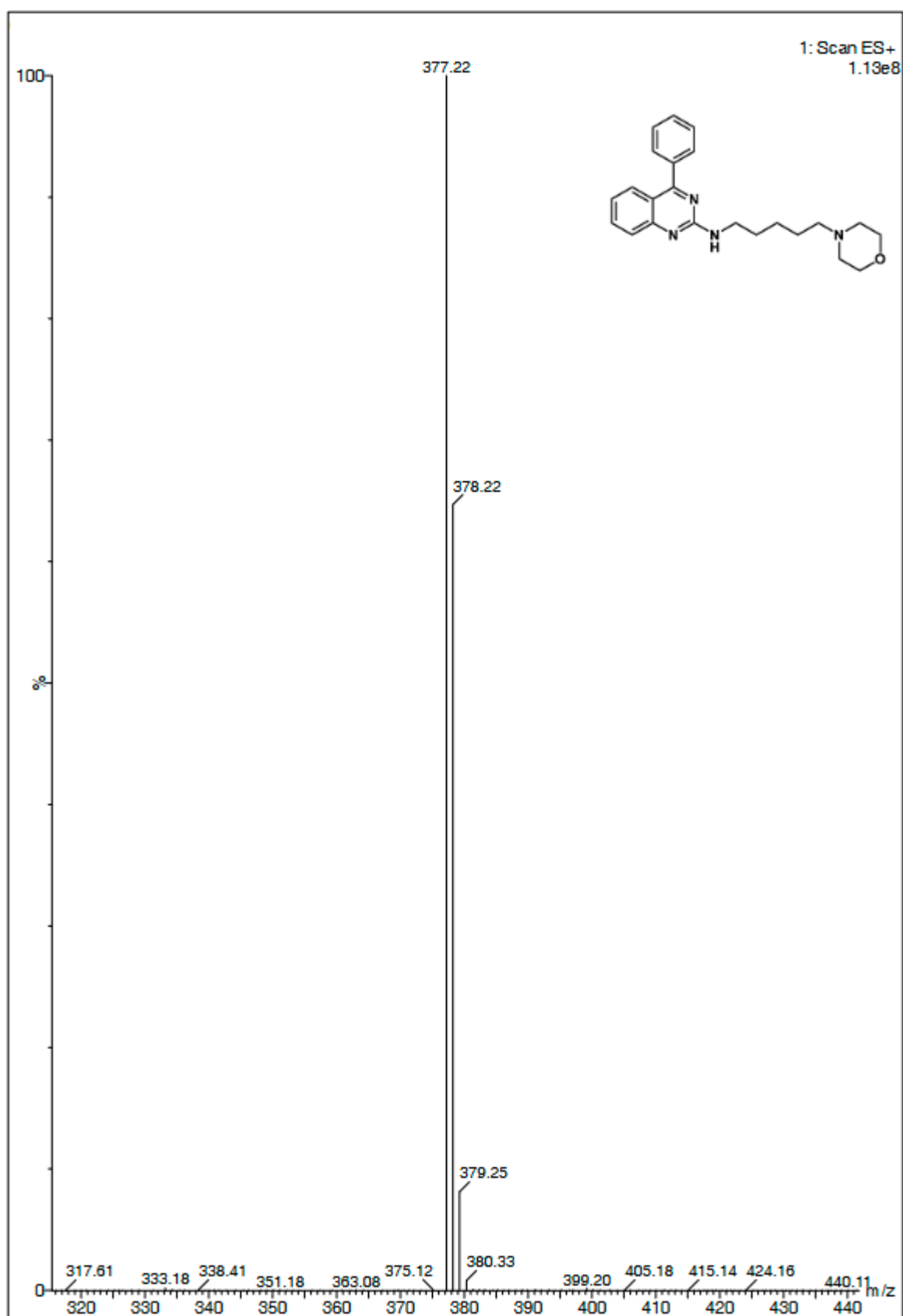
LC-MS mass spectrum of compound 9j



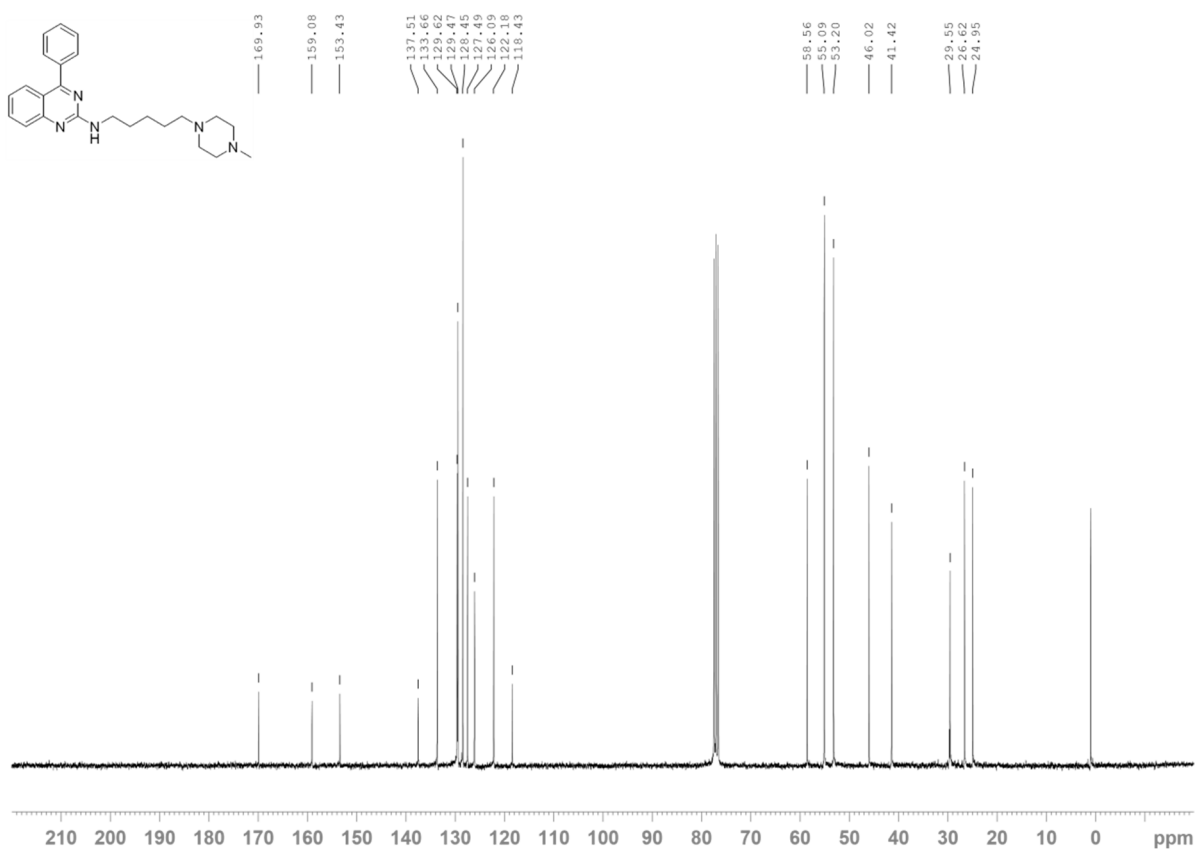
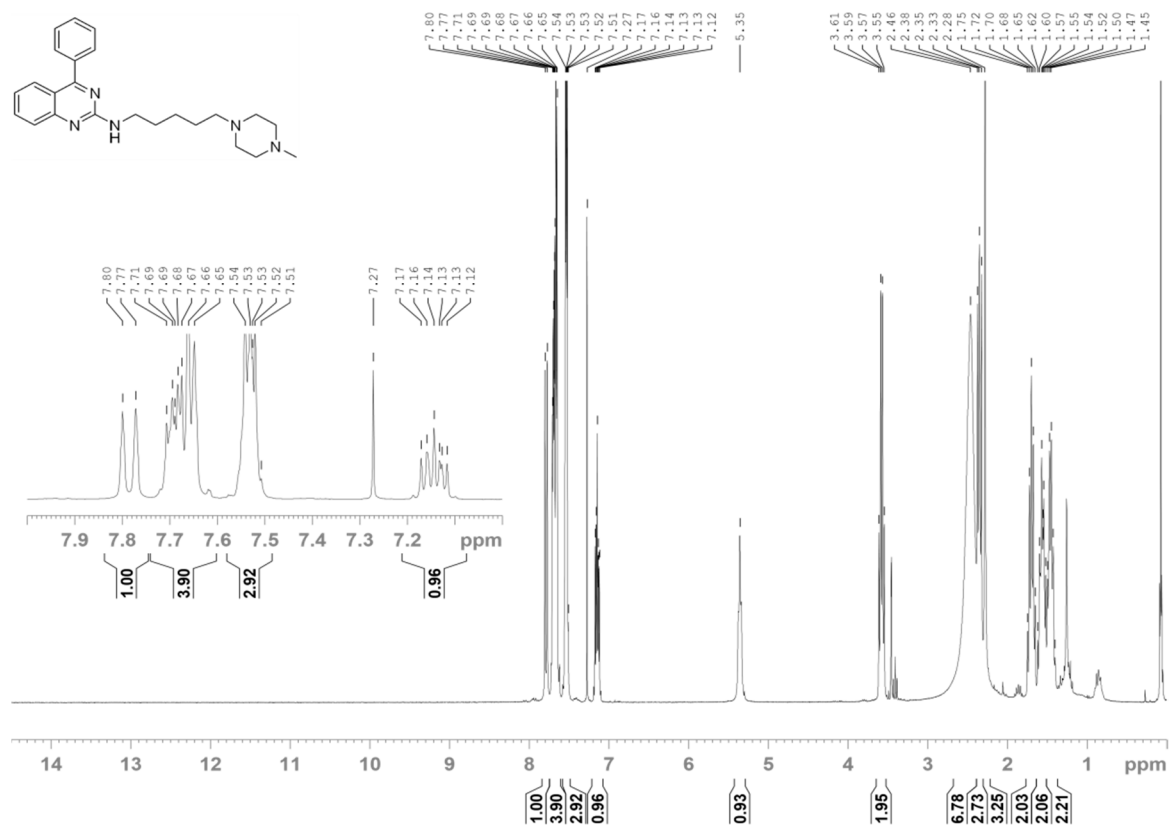
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9k**



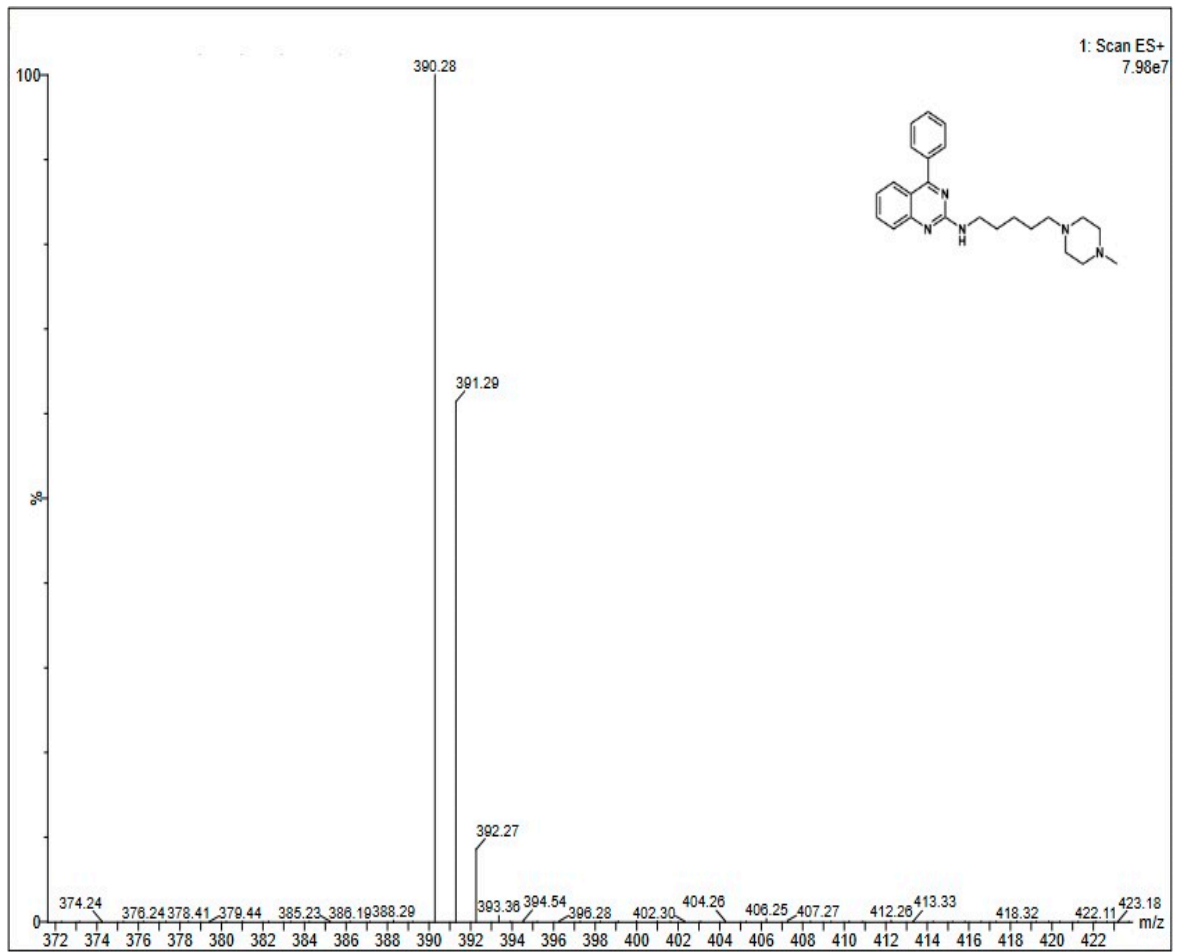
LC-MS mass spectrum of compound 9k



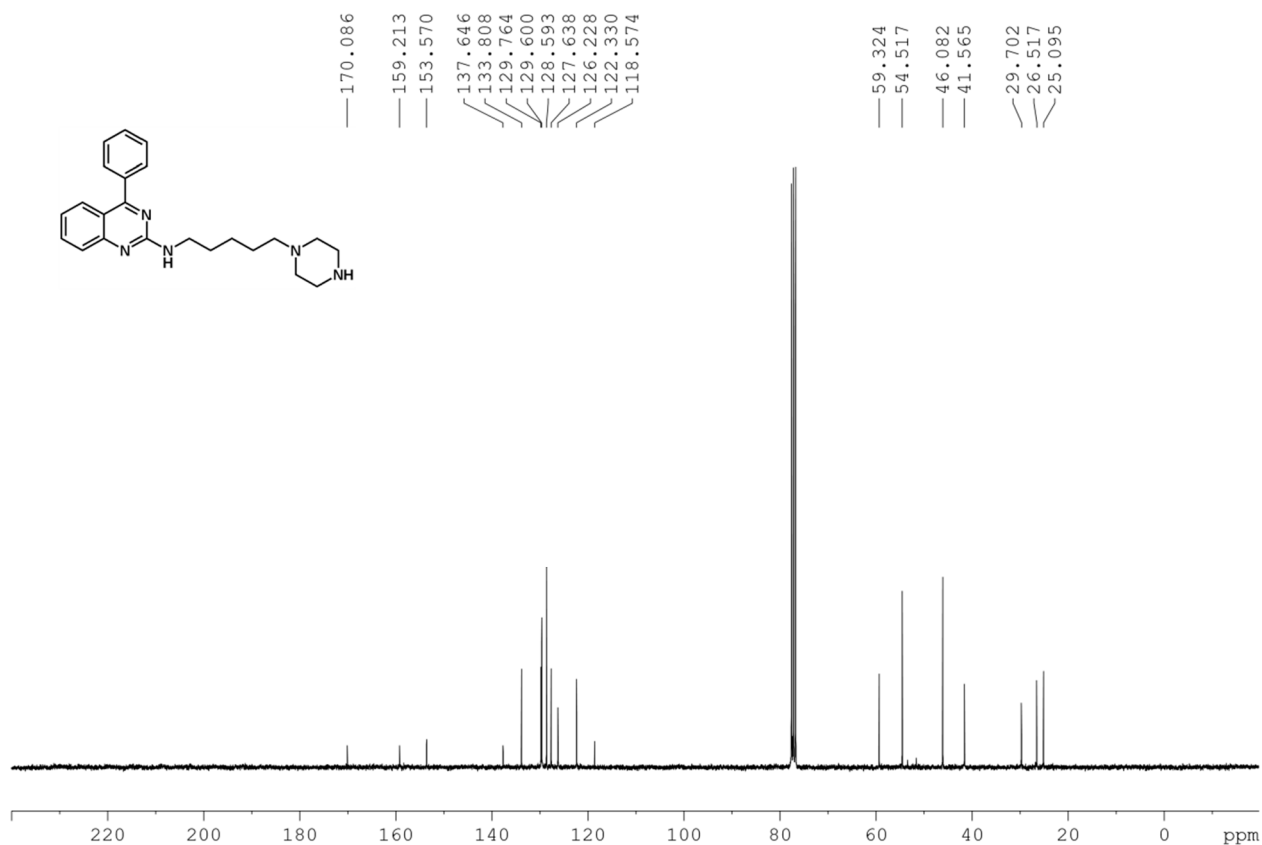
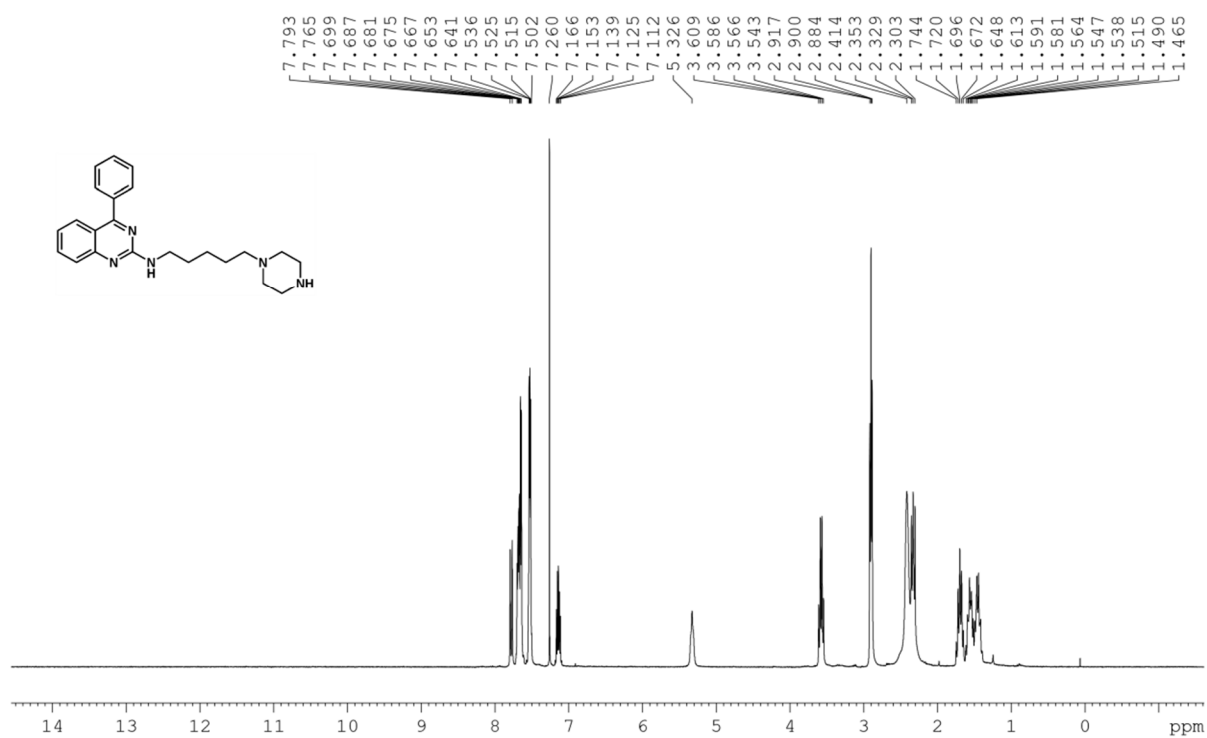
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9I**



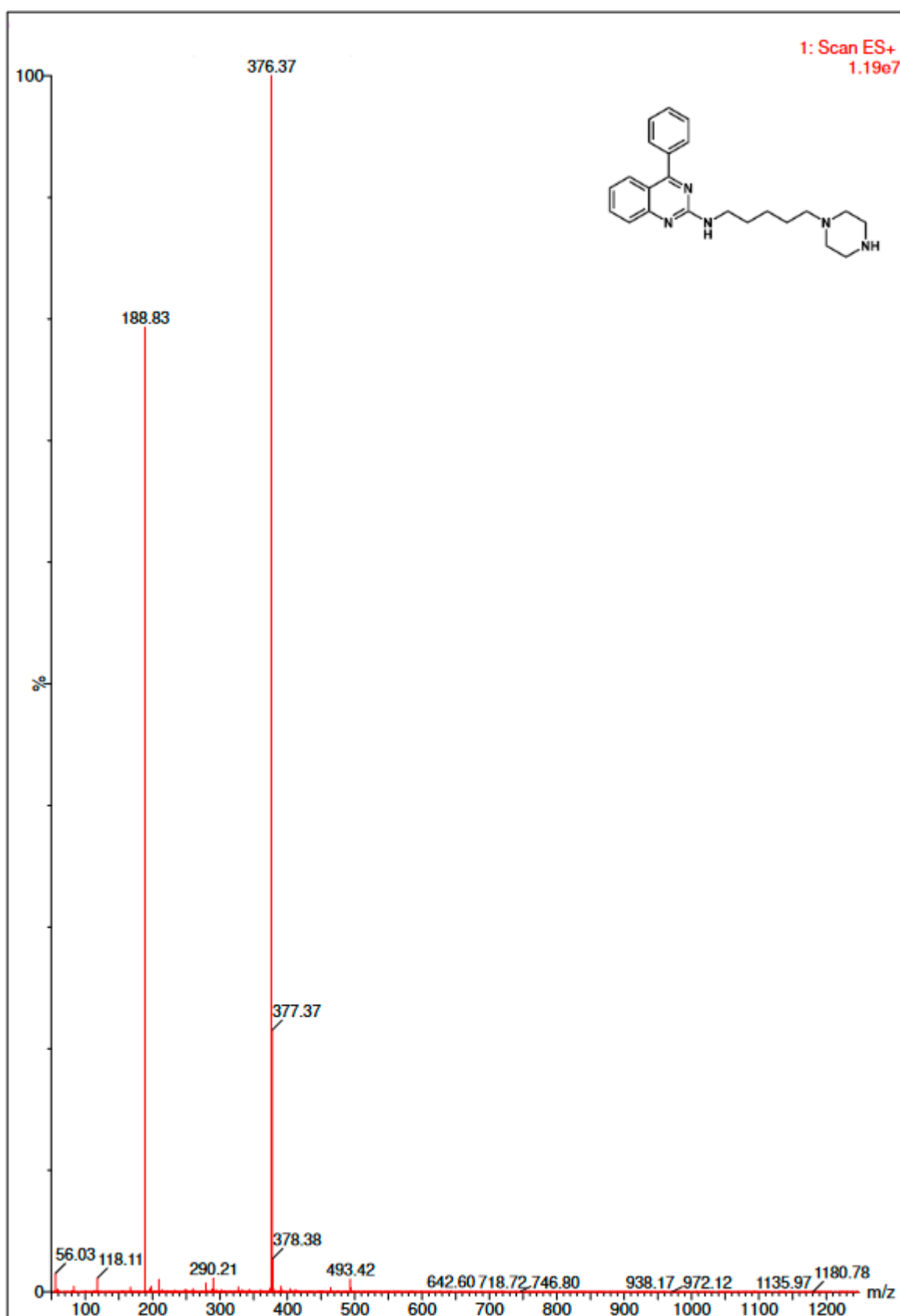
LC-MS mass spectrum of compound 9l



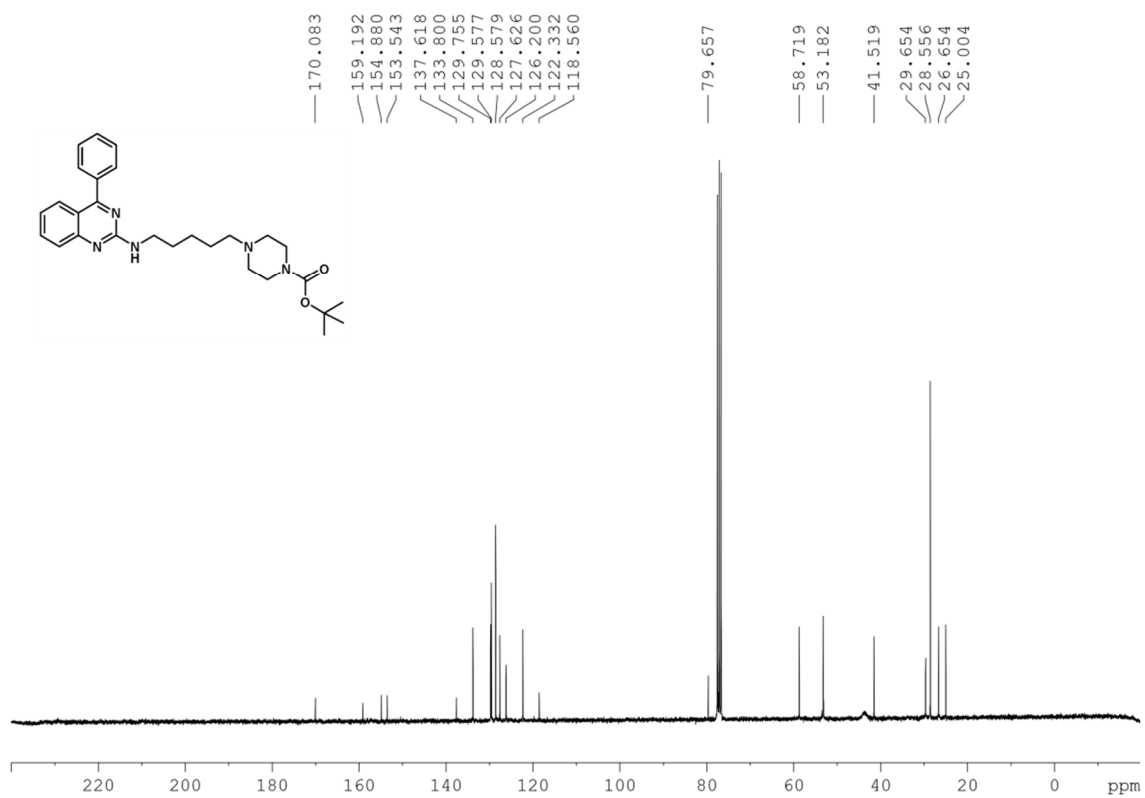
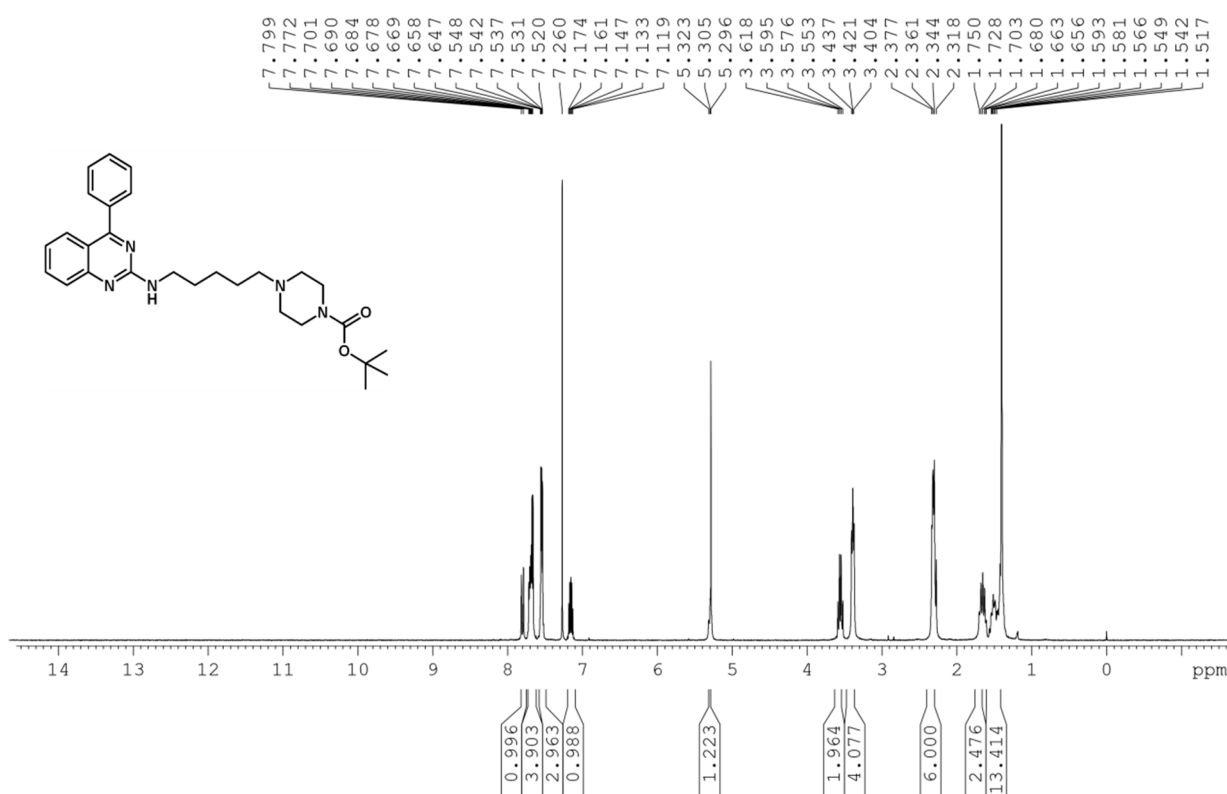
# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9m



LC-MS mass spectrum of compound 9m

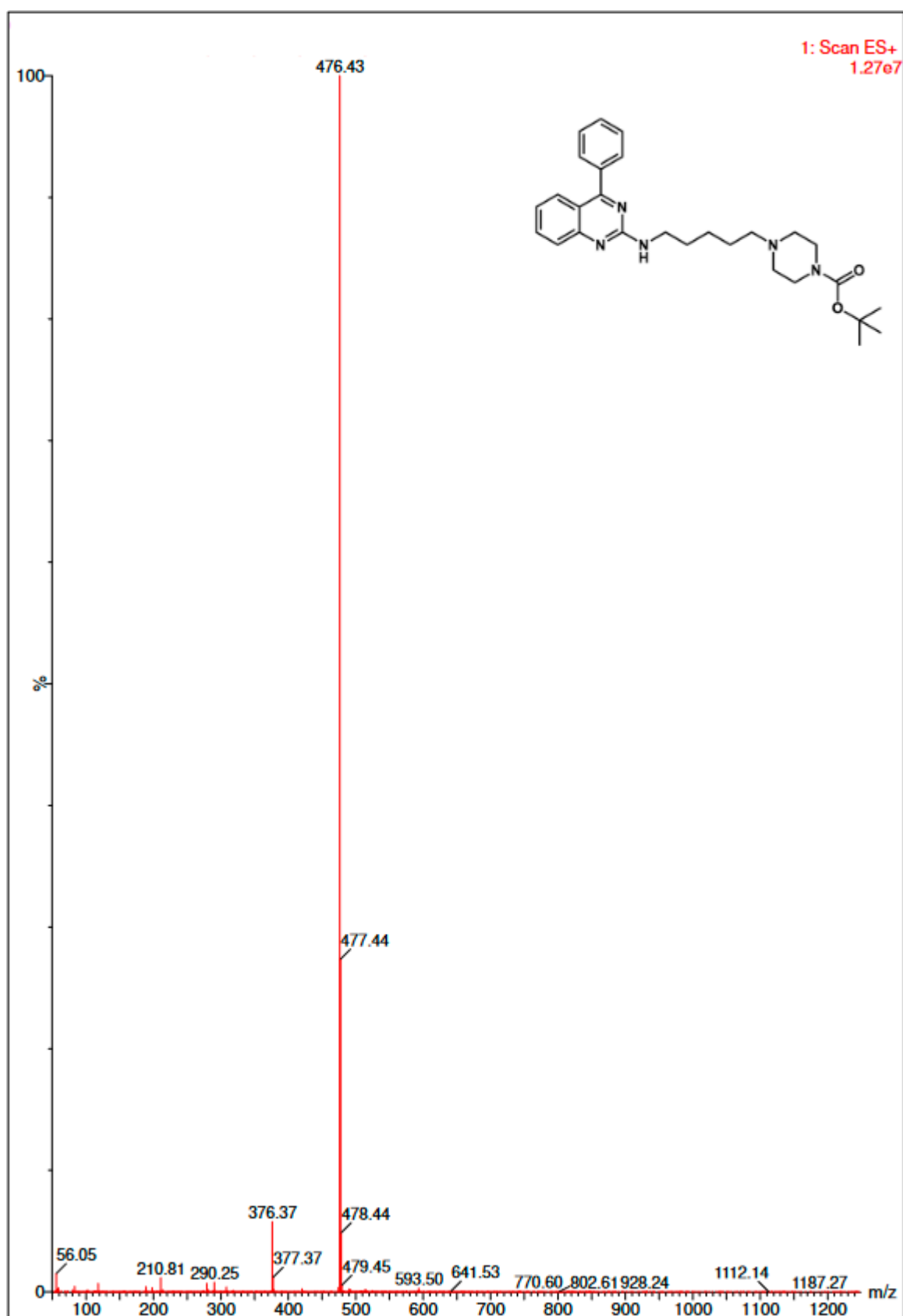


# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9n

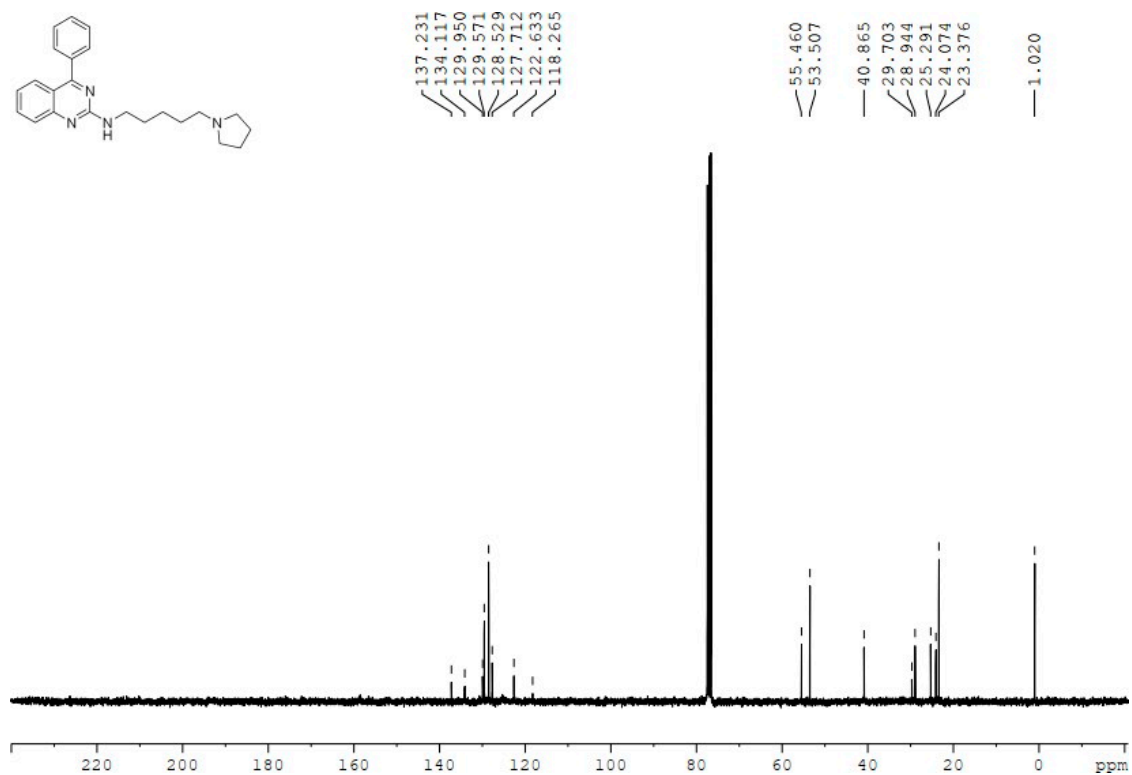
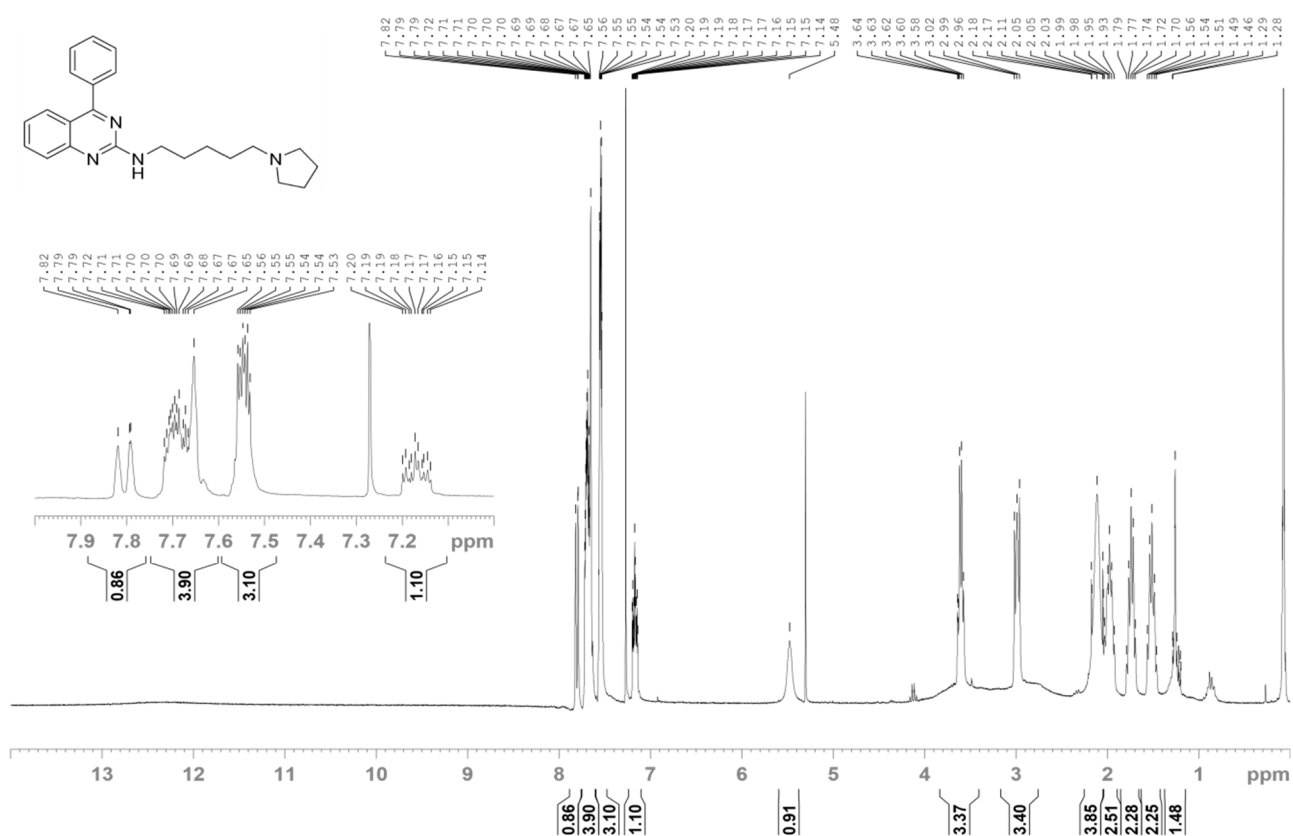




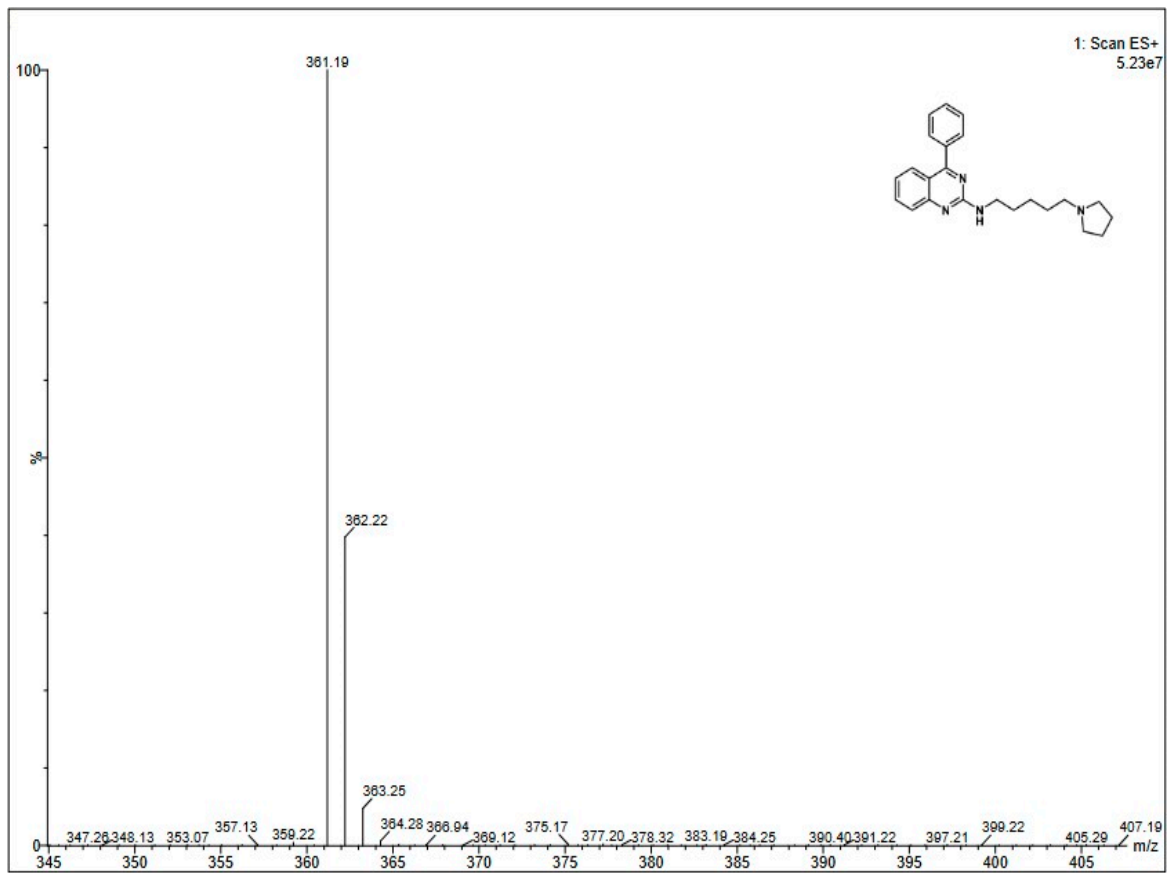
LC-MS mass spectrum of compound 9n



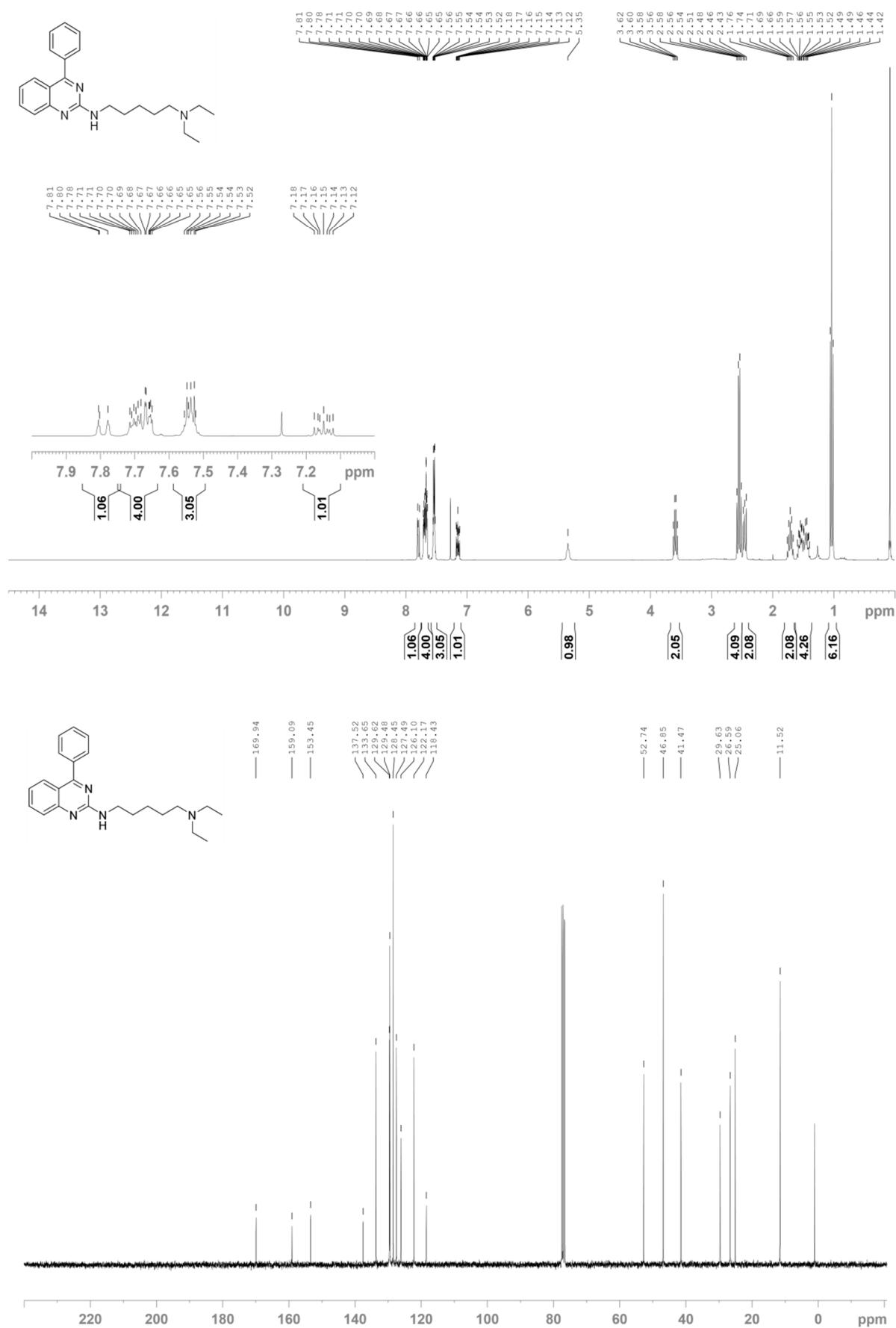
# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9o



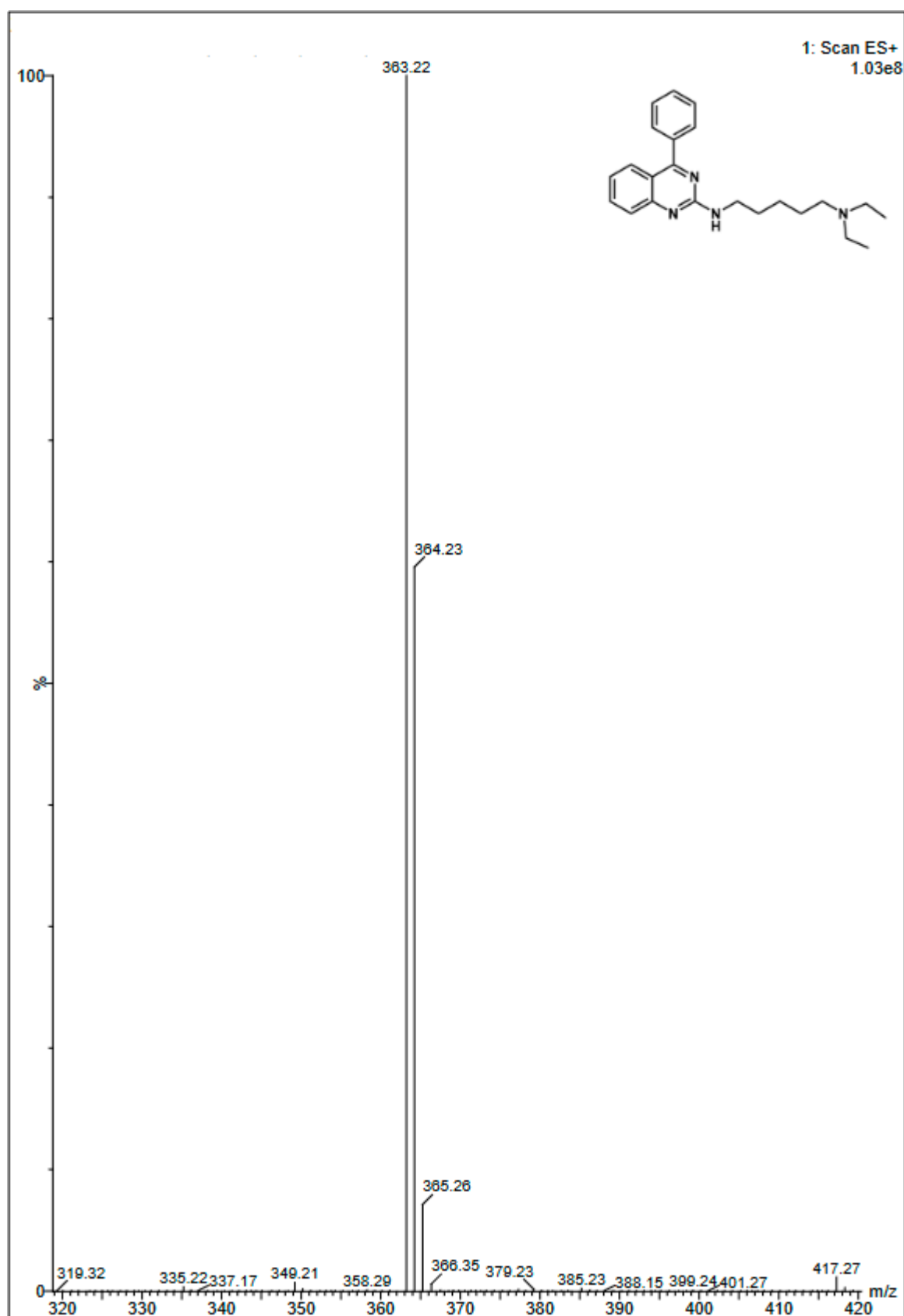
LC-MS mass spectrum of compound 9o



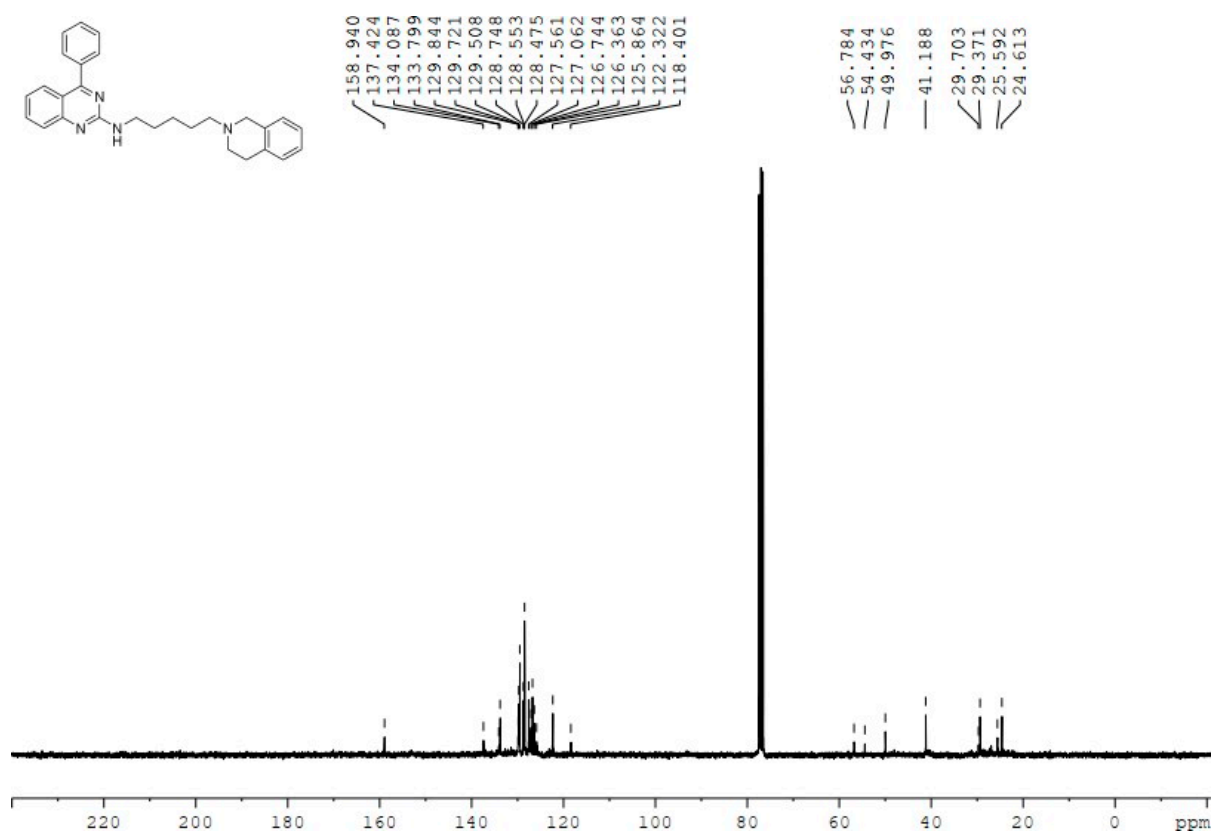
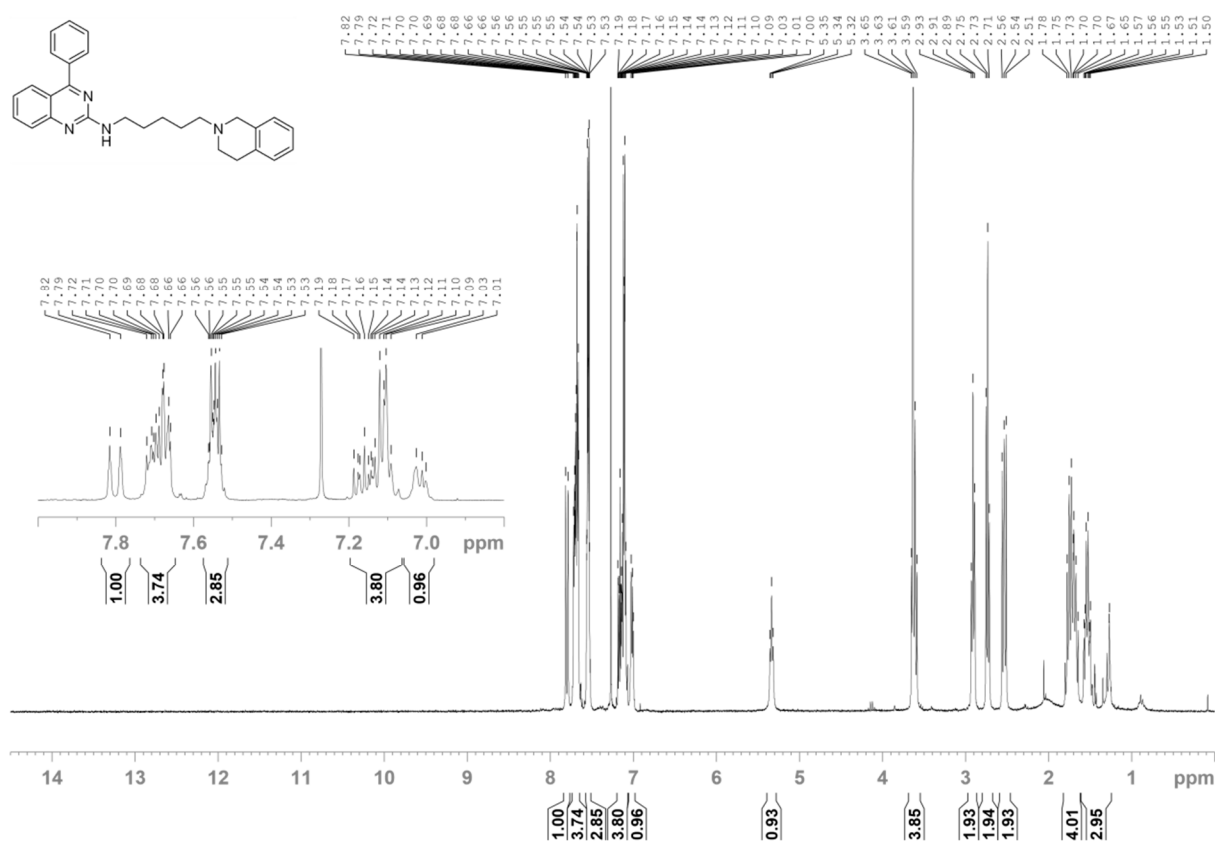
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9p**



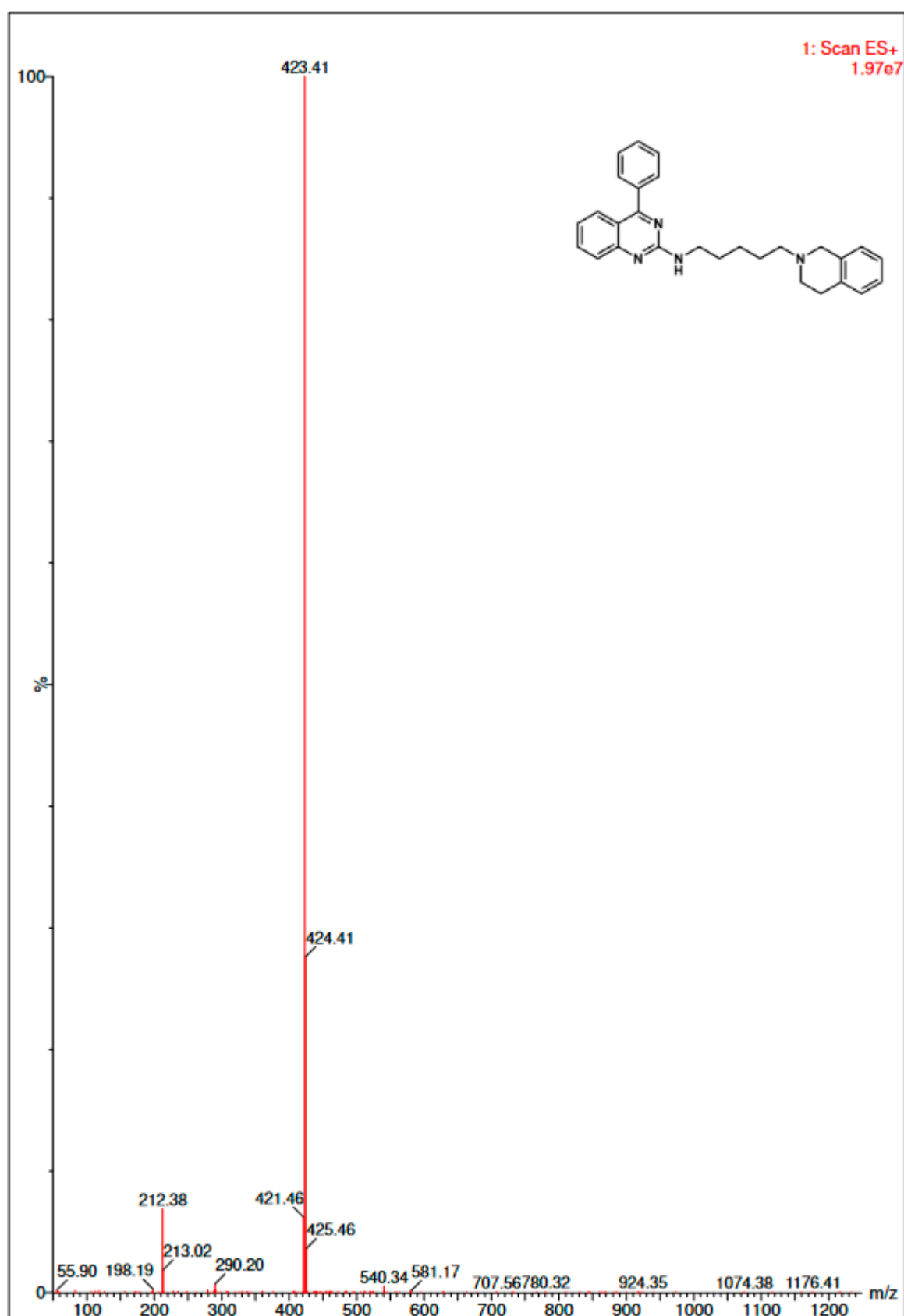
LC-MS mass spectrum of compound 9p



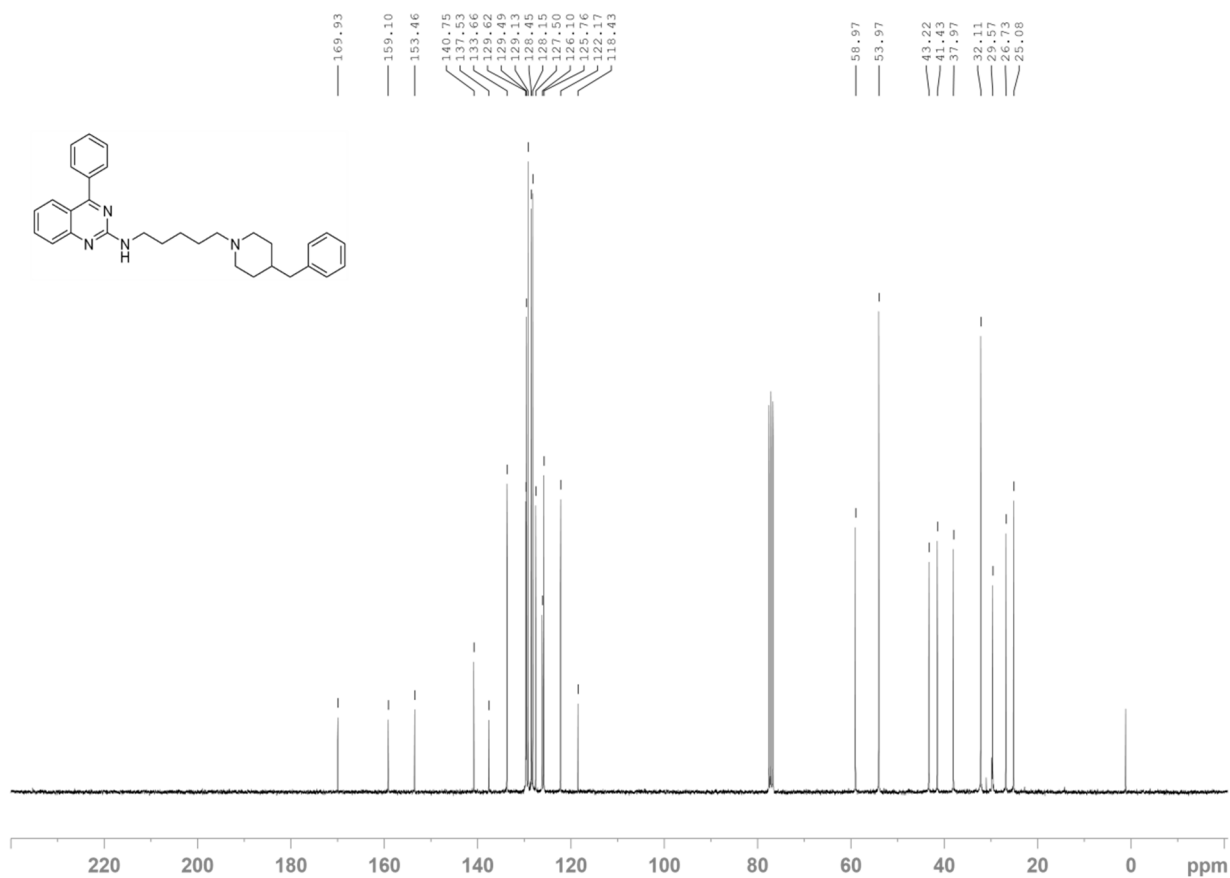
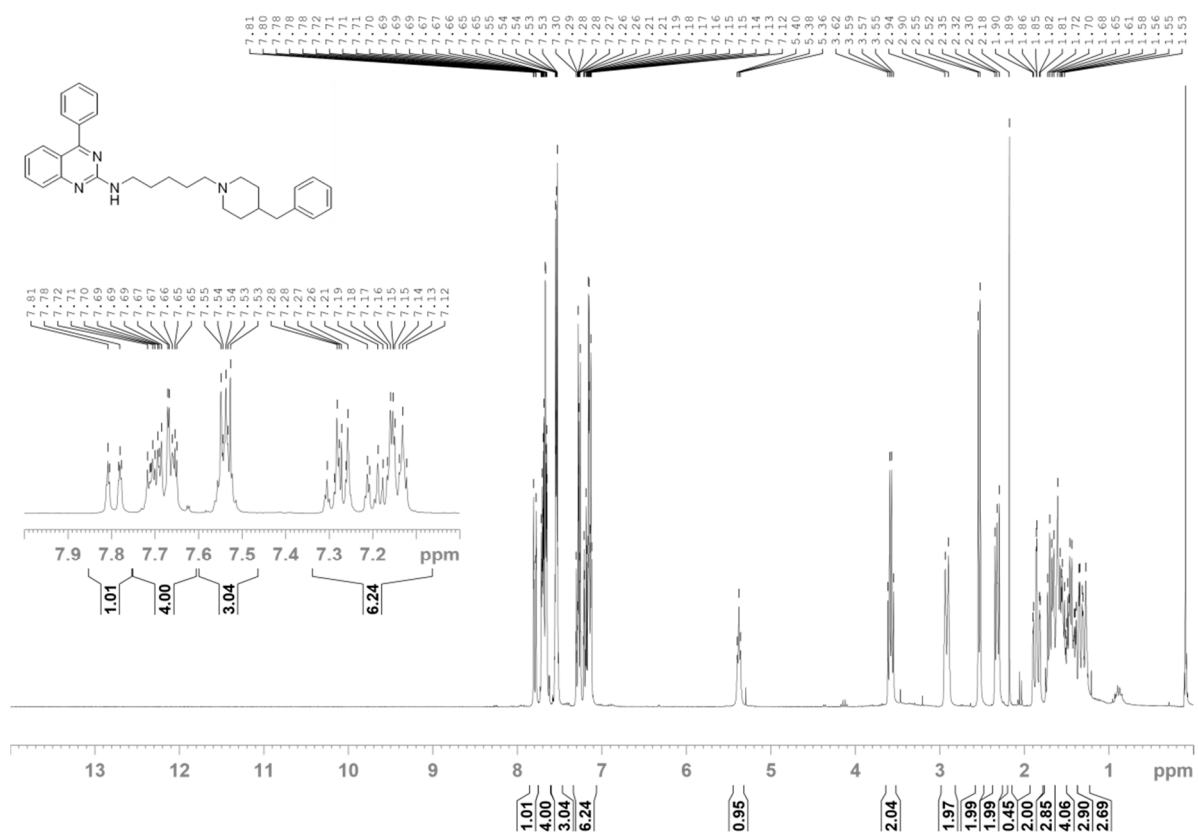
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9q**



LC-MS mass spectrum of compound 9q

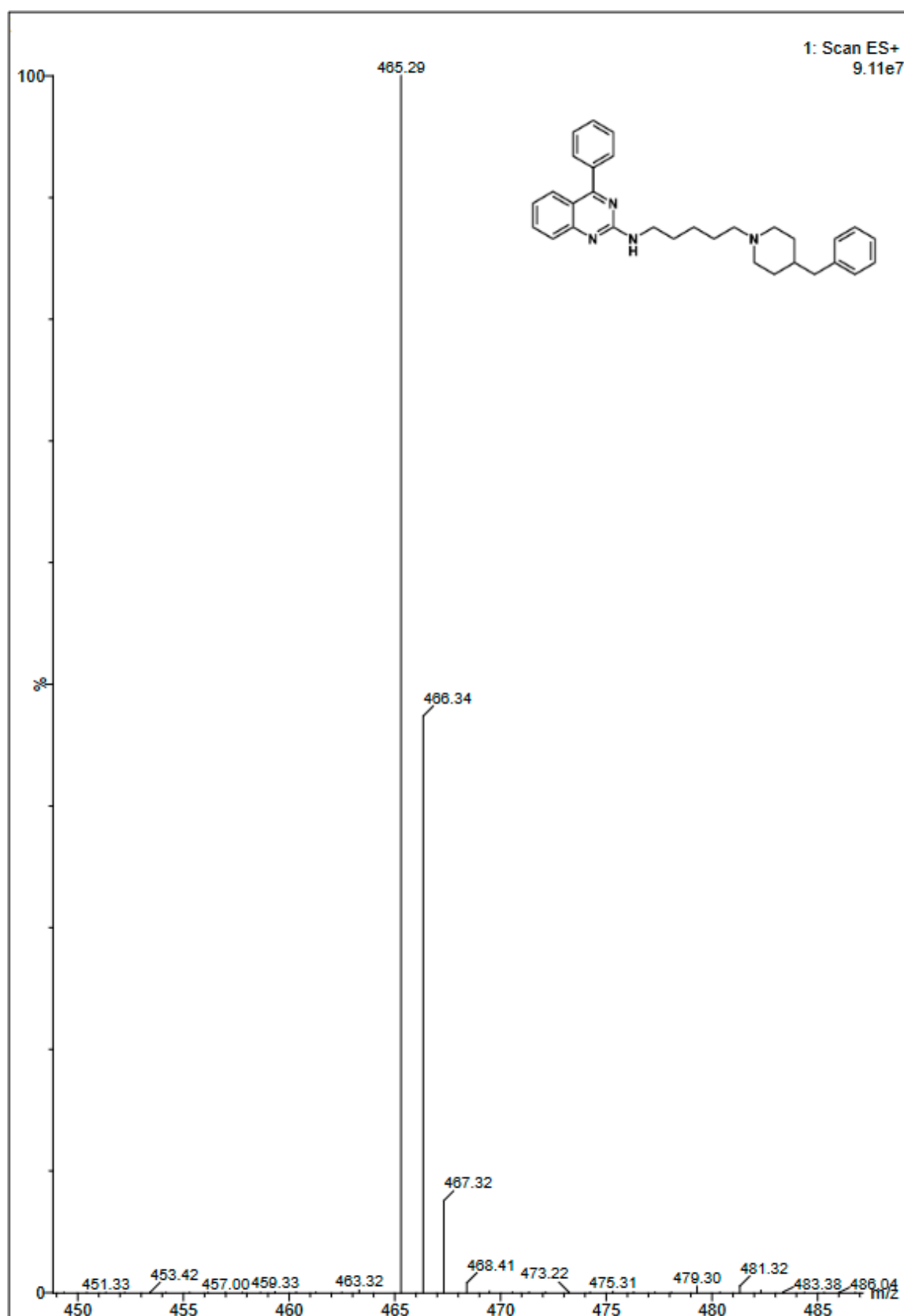


# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9r

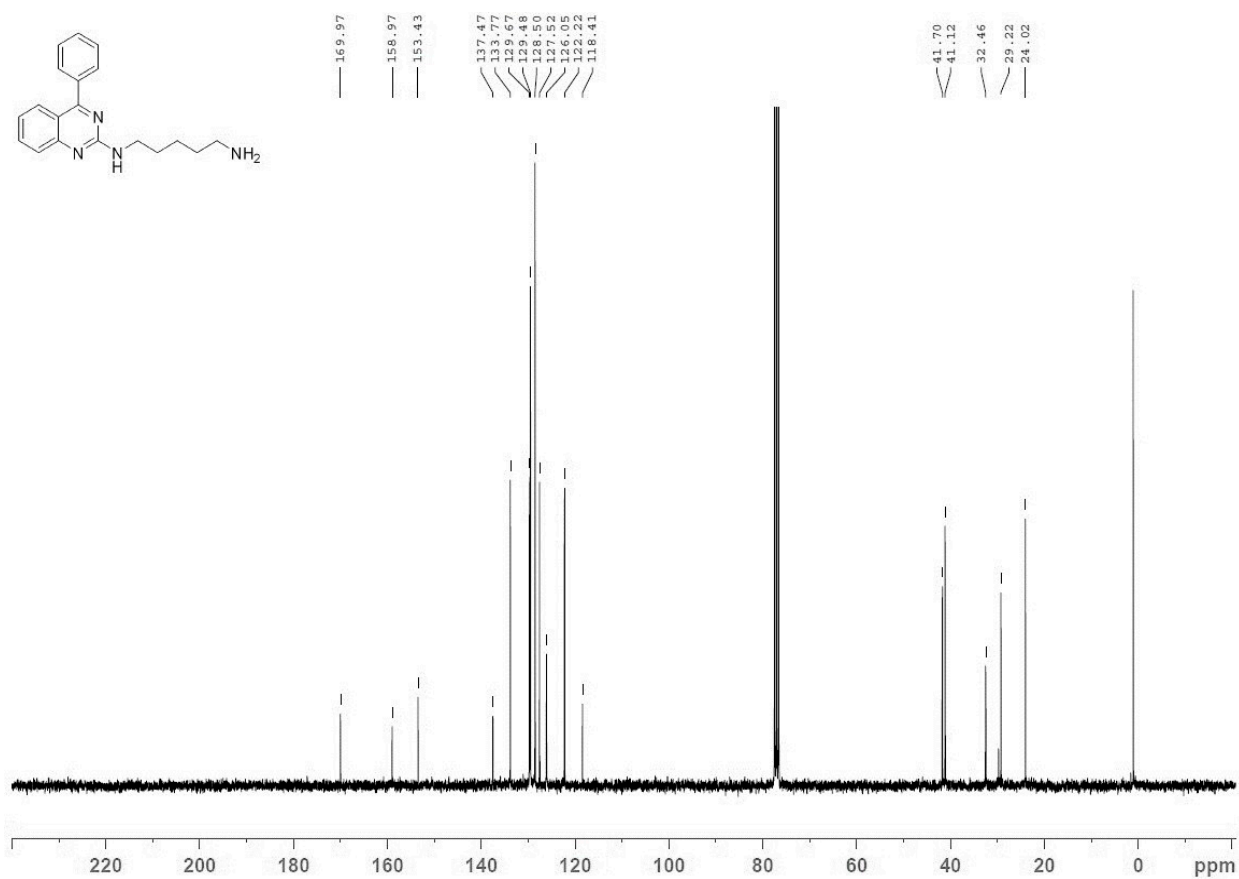
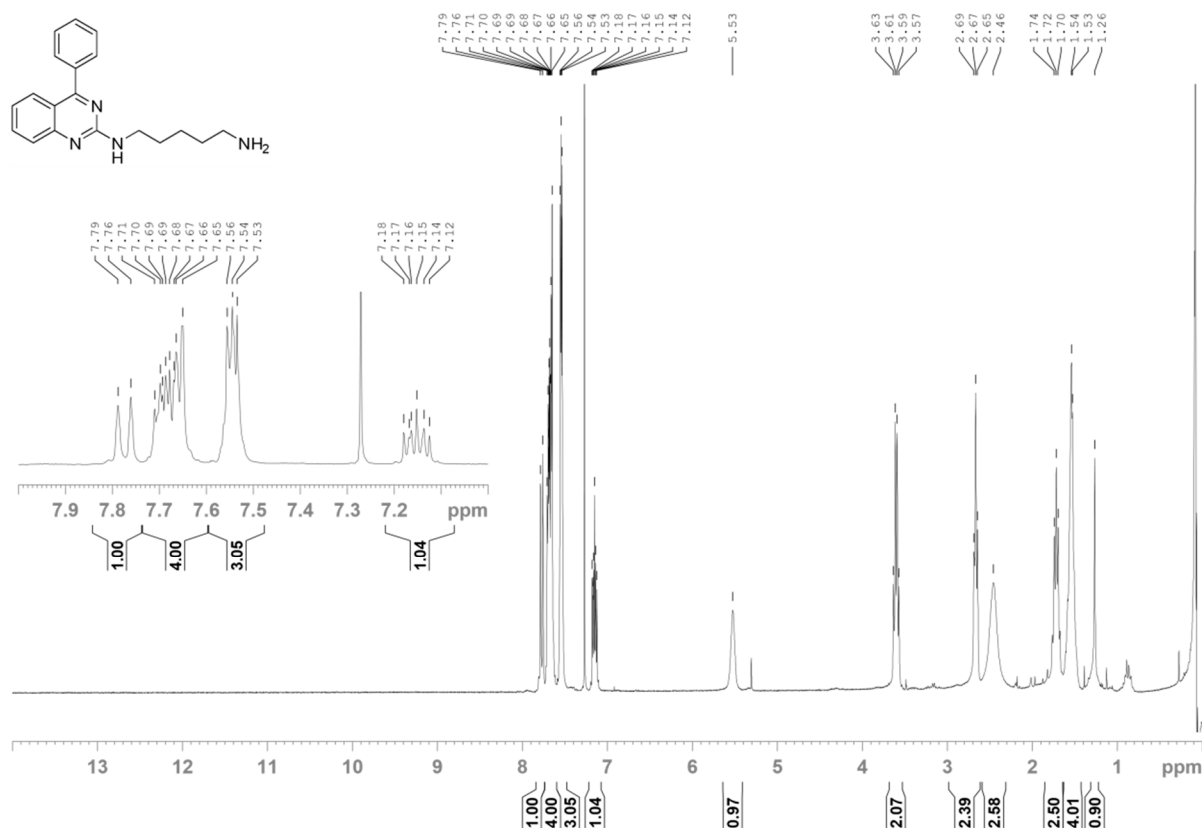




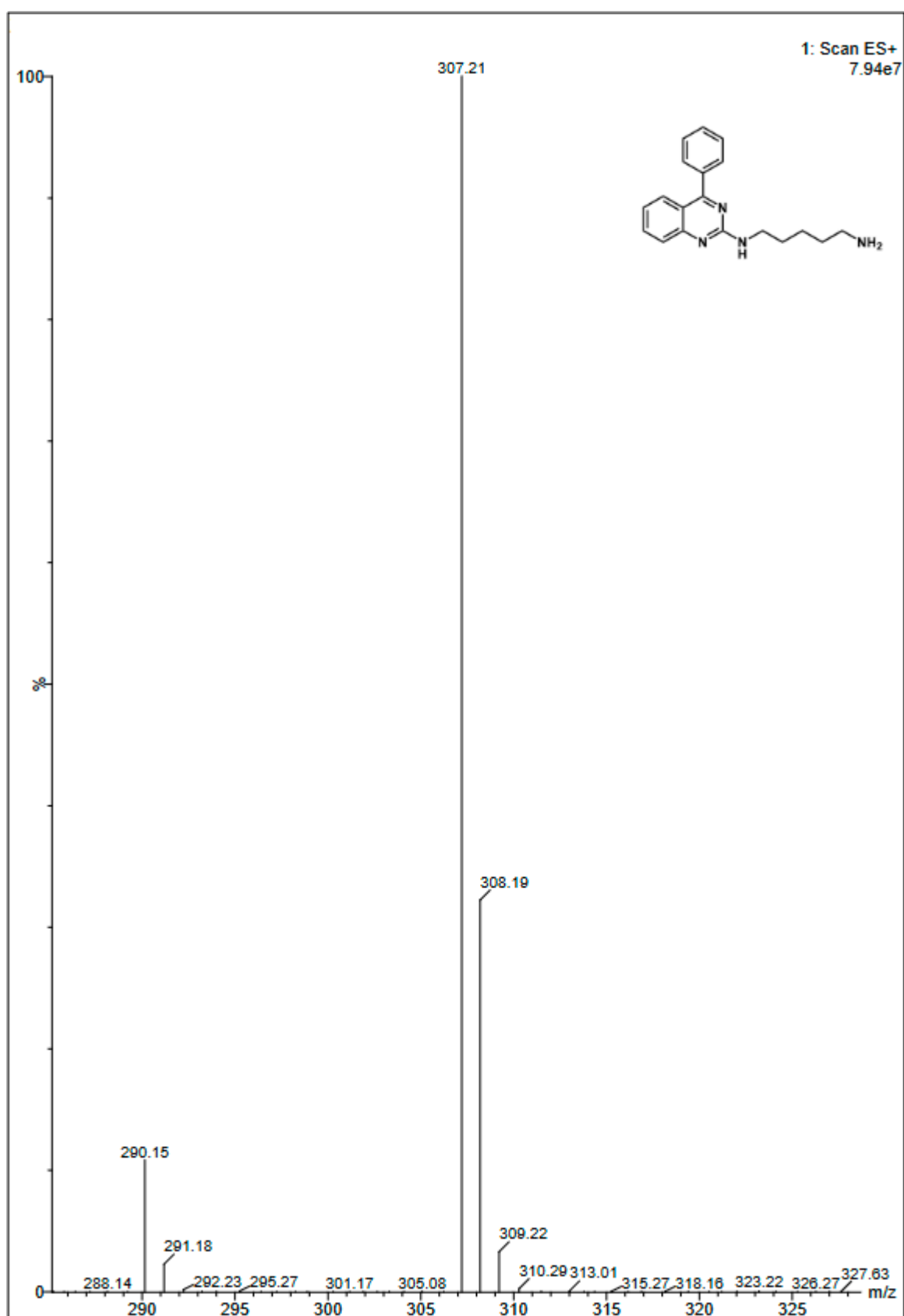
LC-MS mass spectrum of compound 9r



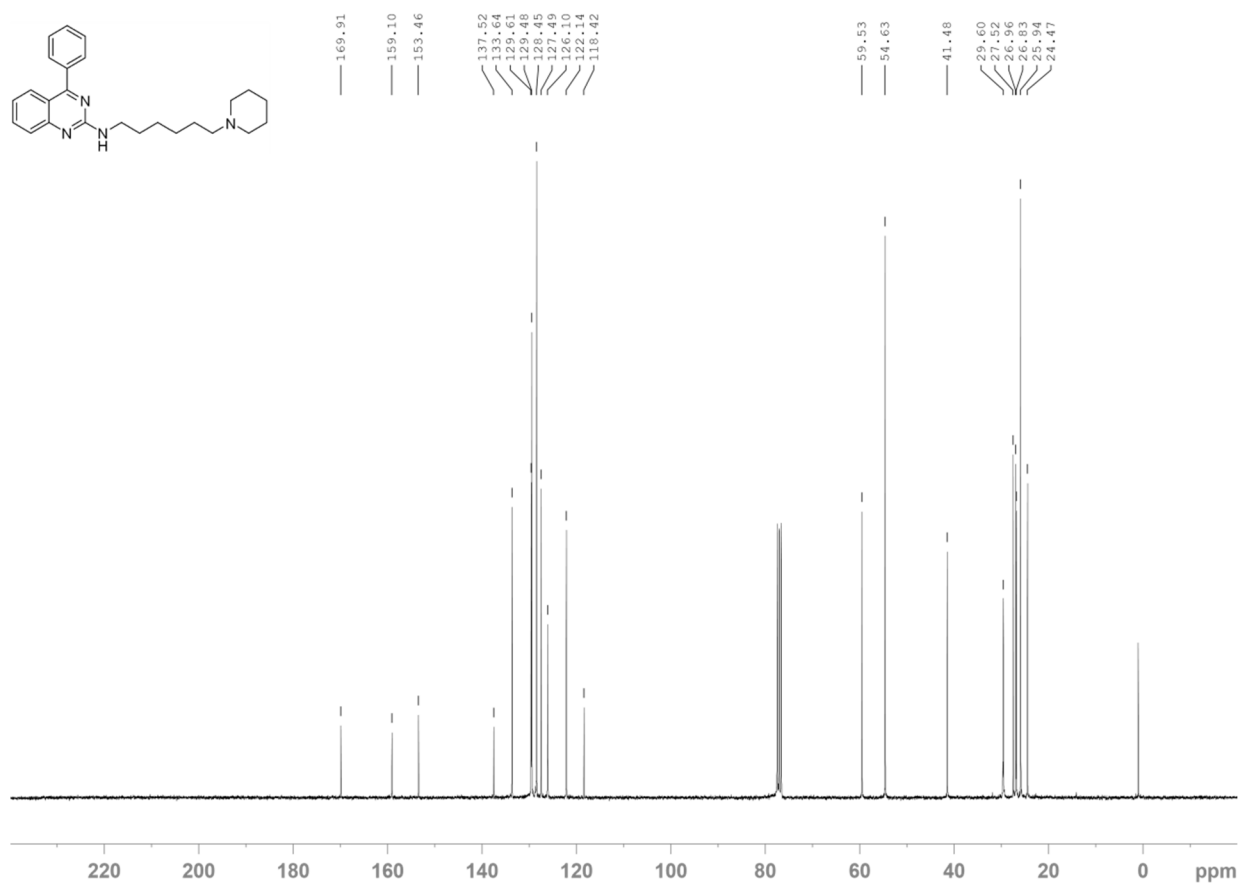
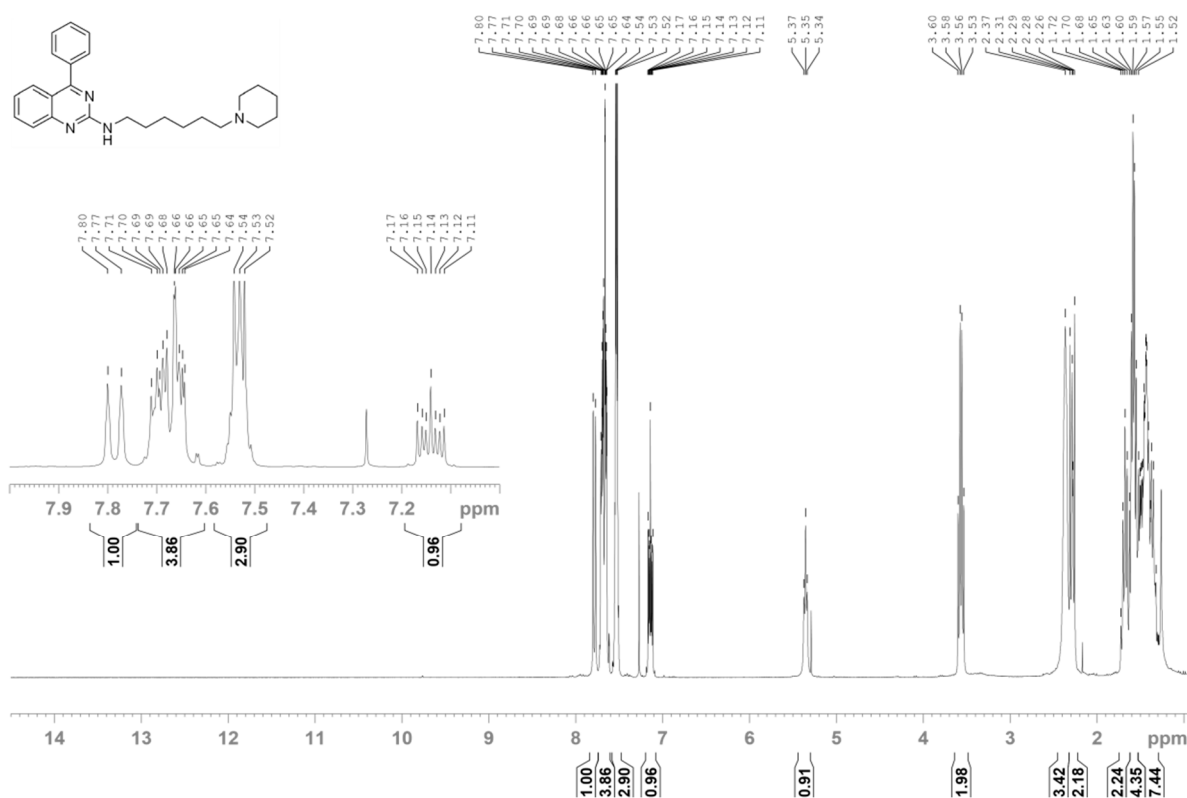
# 1H- and 13C-NMR Spectra in CDCl<sub>3</sub> of compound 9s



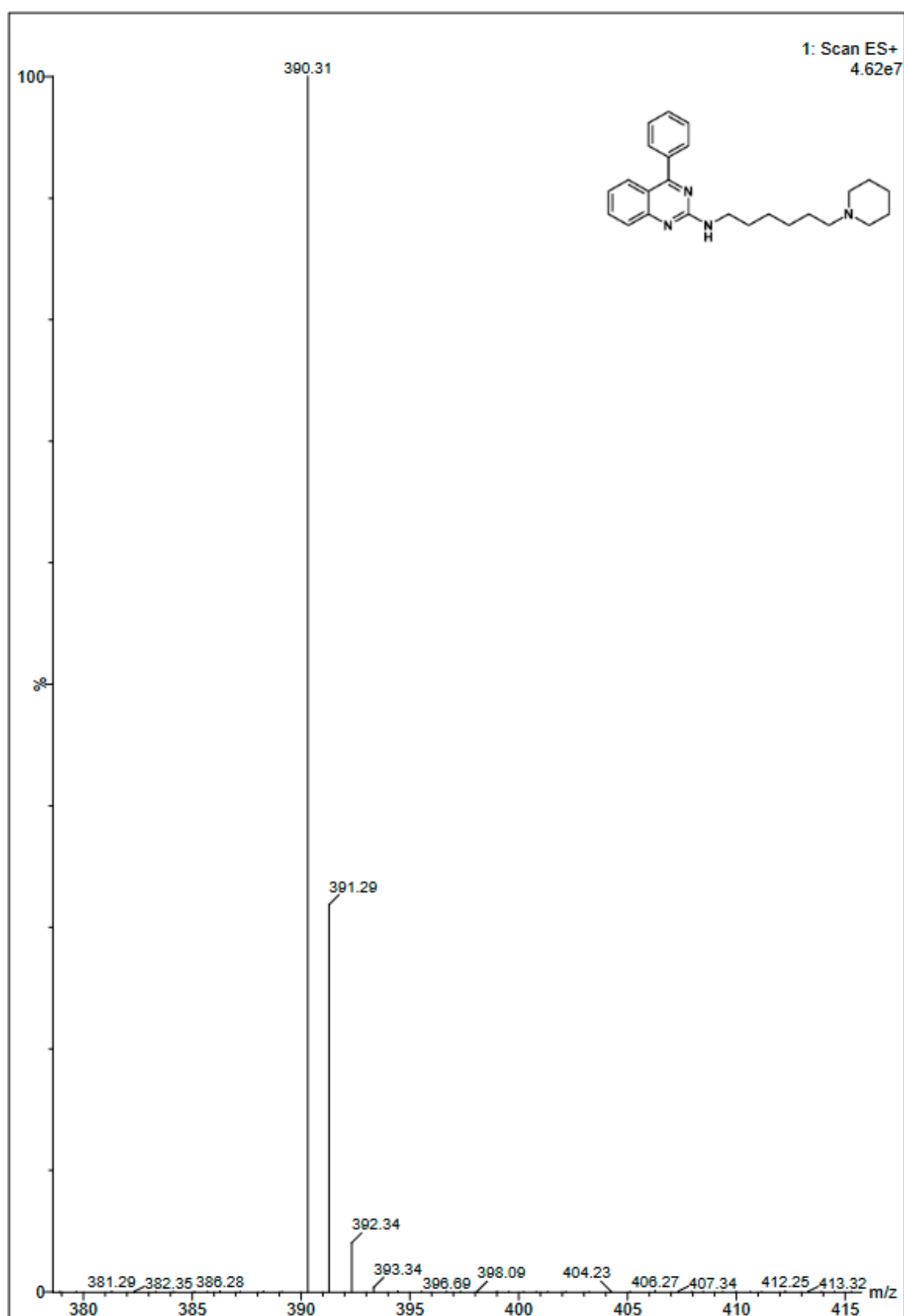
LC-MS mass spectrum of compound 9s



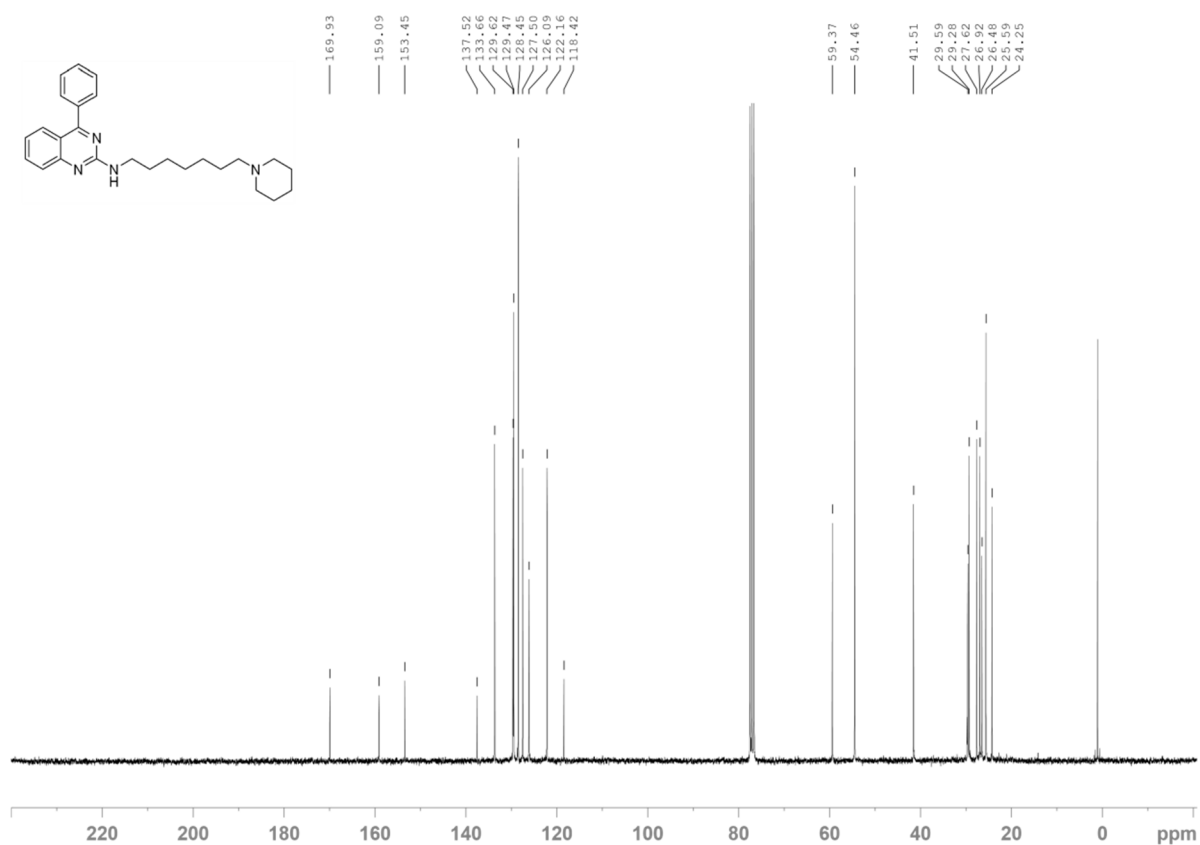
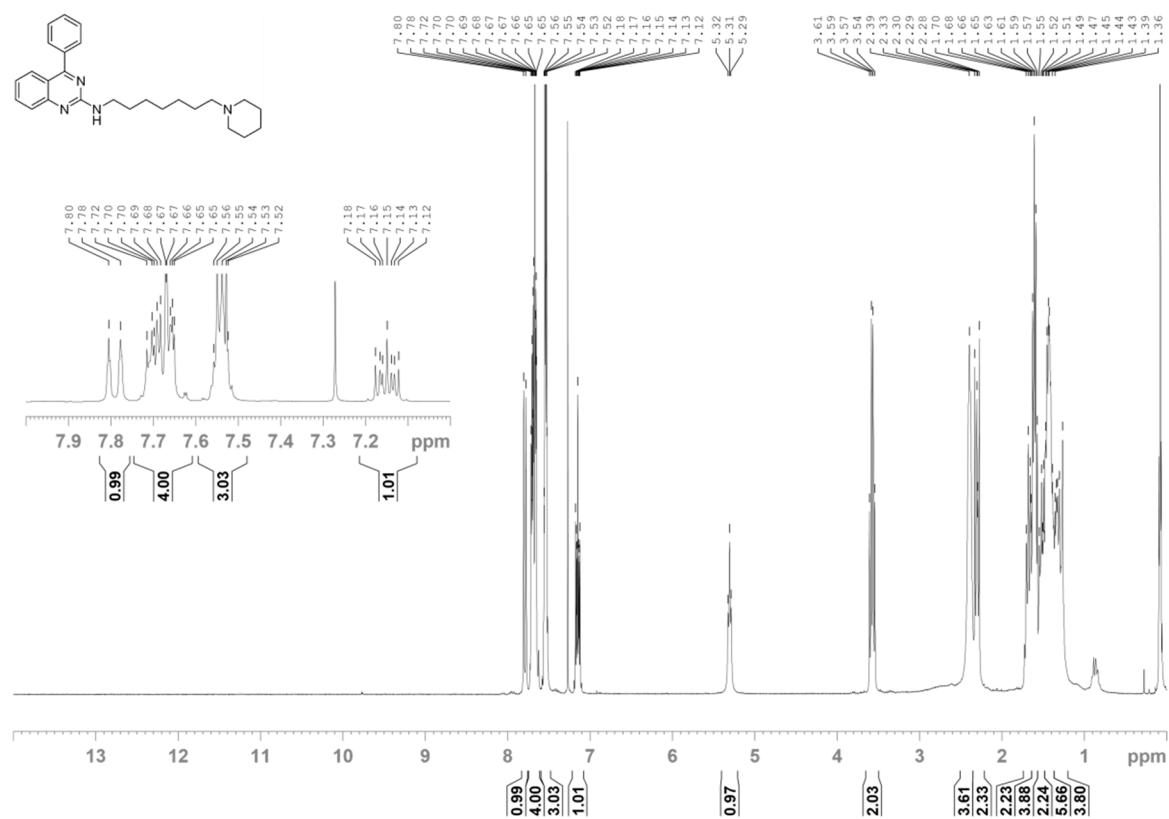
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9t**



LC-MS mass spectrum of compound 9t



# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9u**



LC-MS mass spectrum of compound 9u

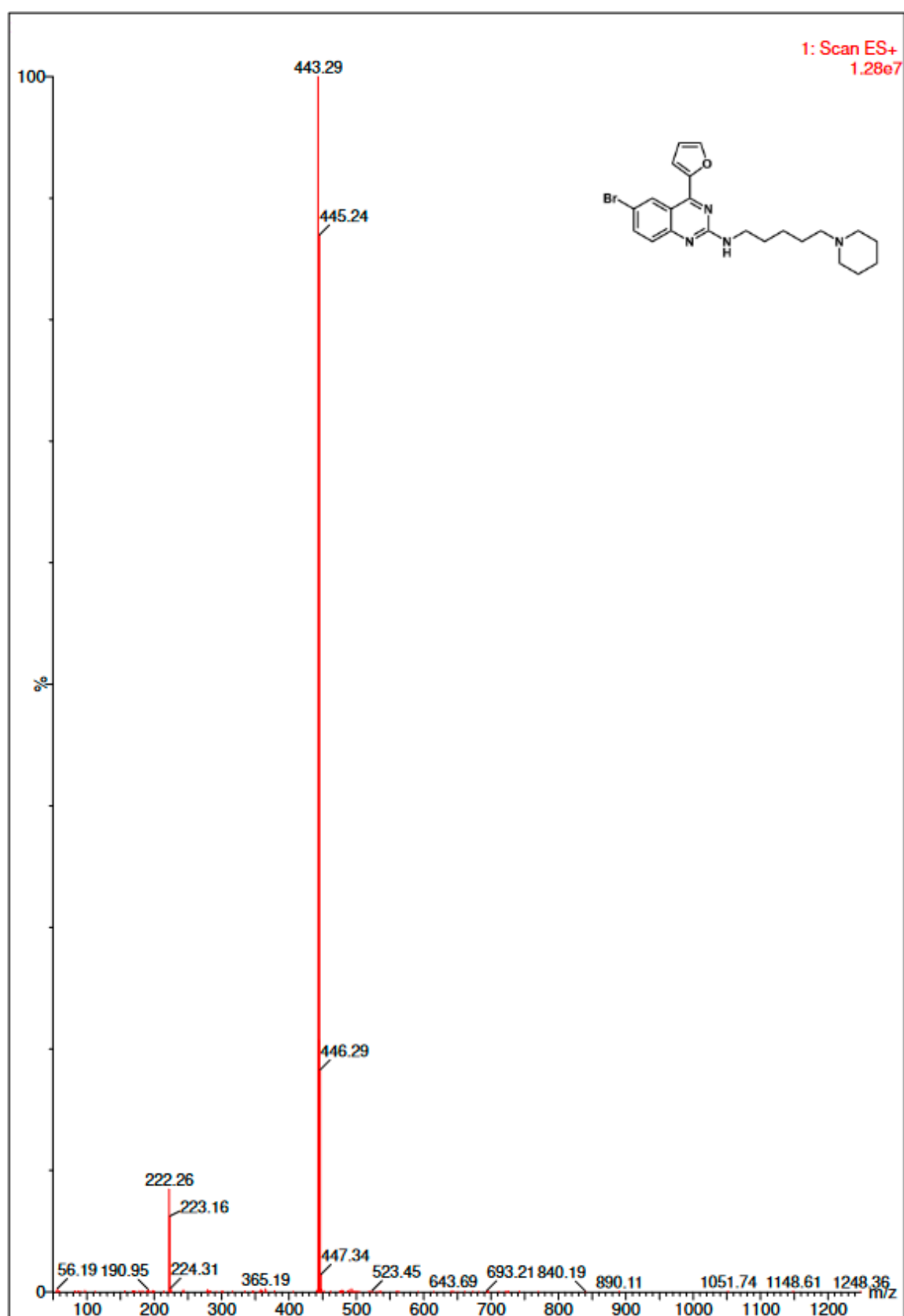


# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9v**

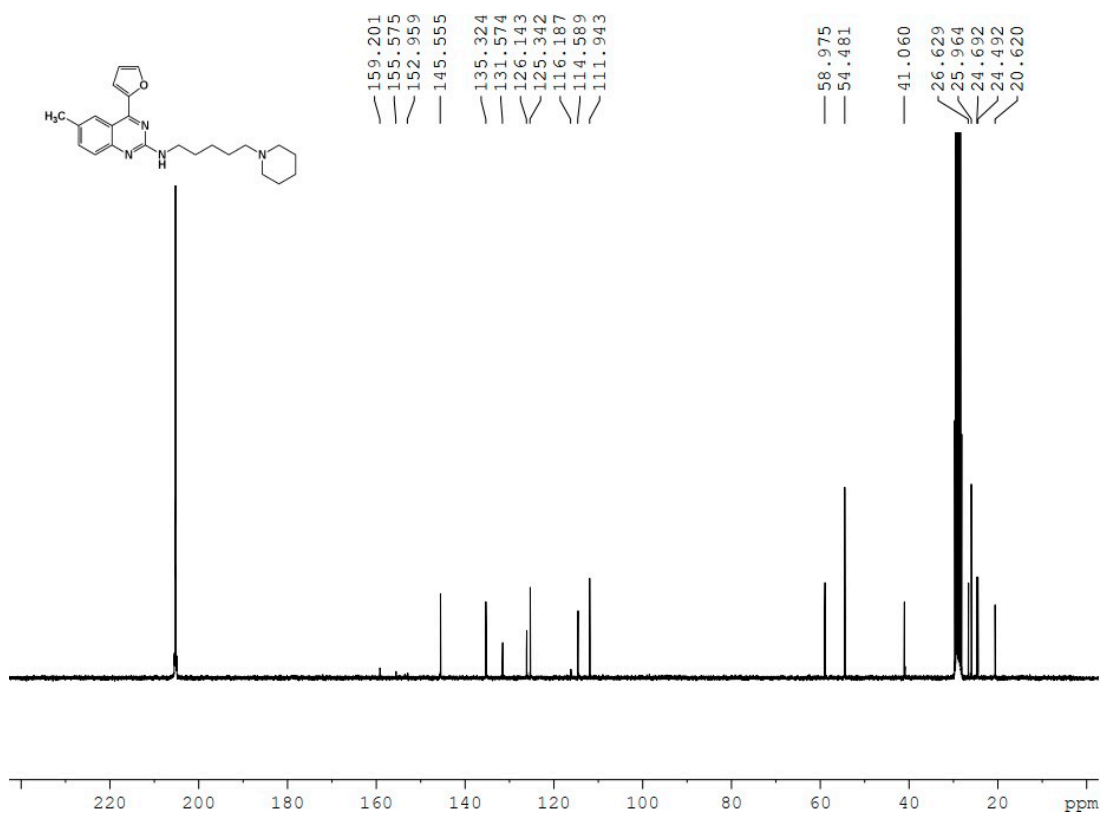
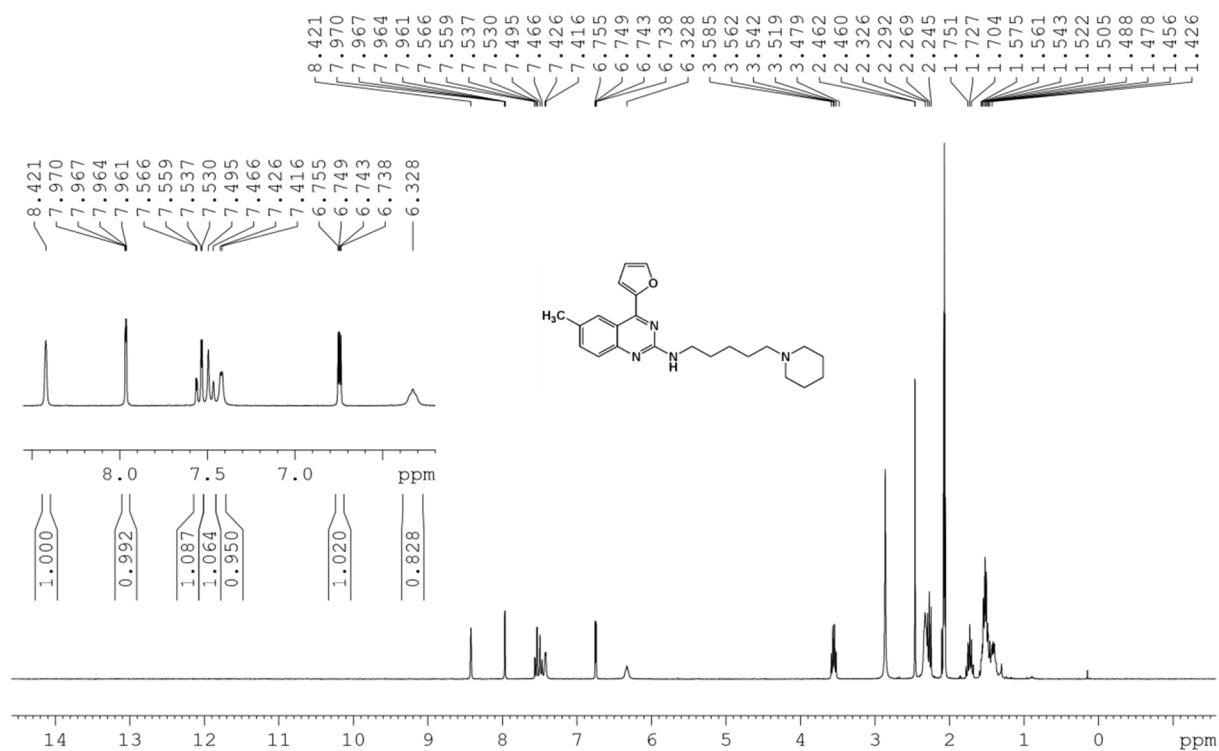




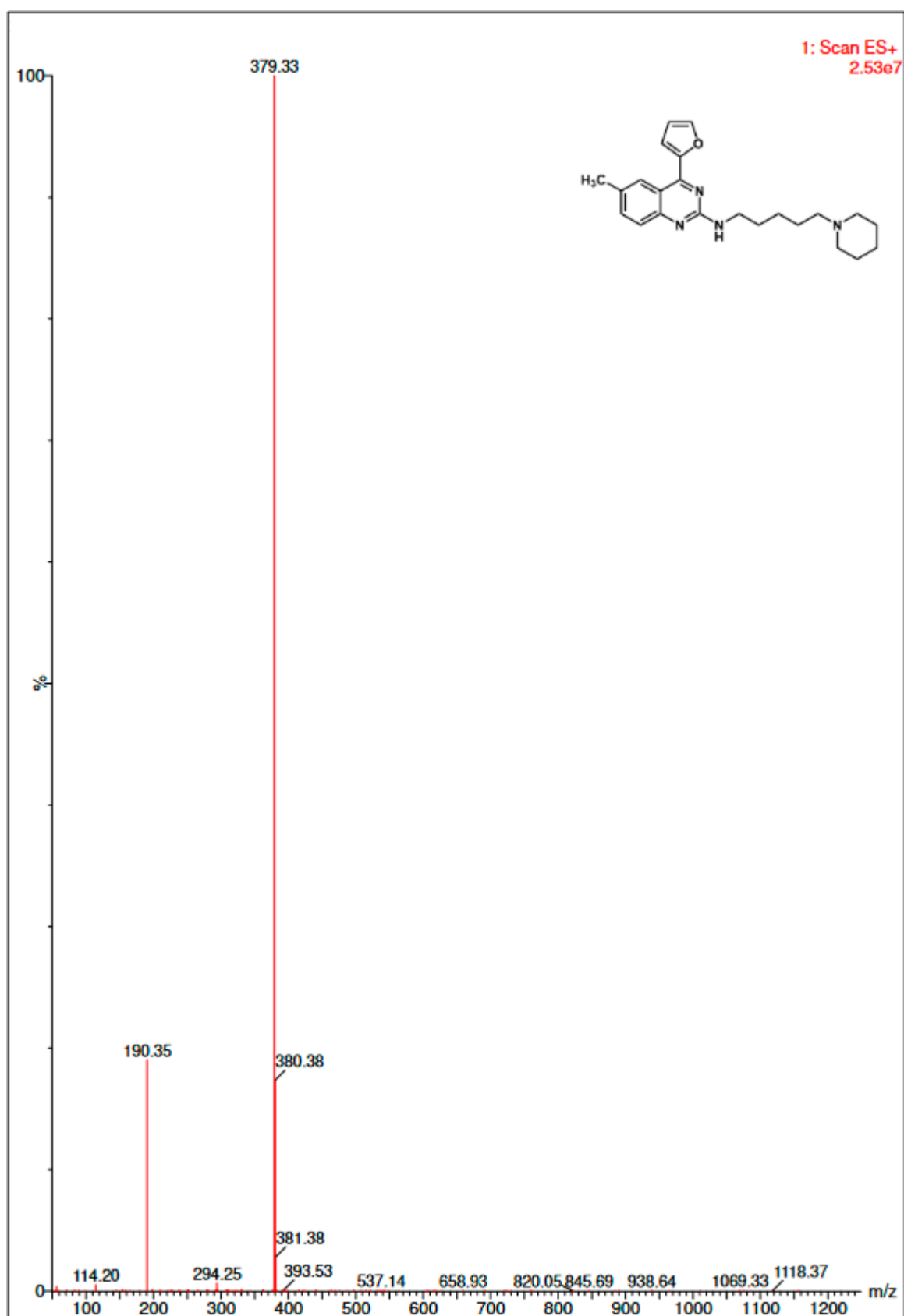
LC-MS mass spectrum of compound 9v



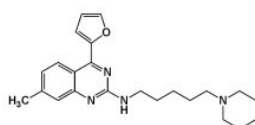
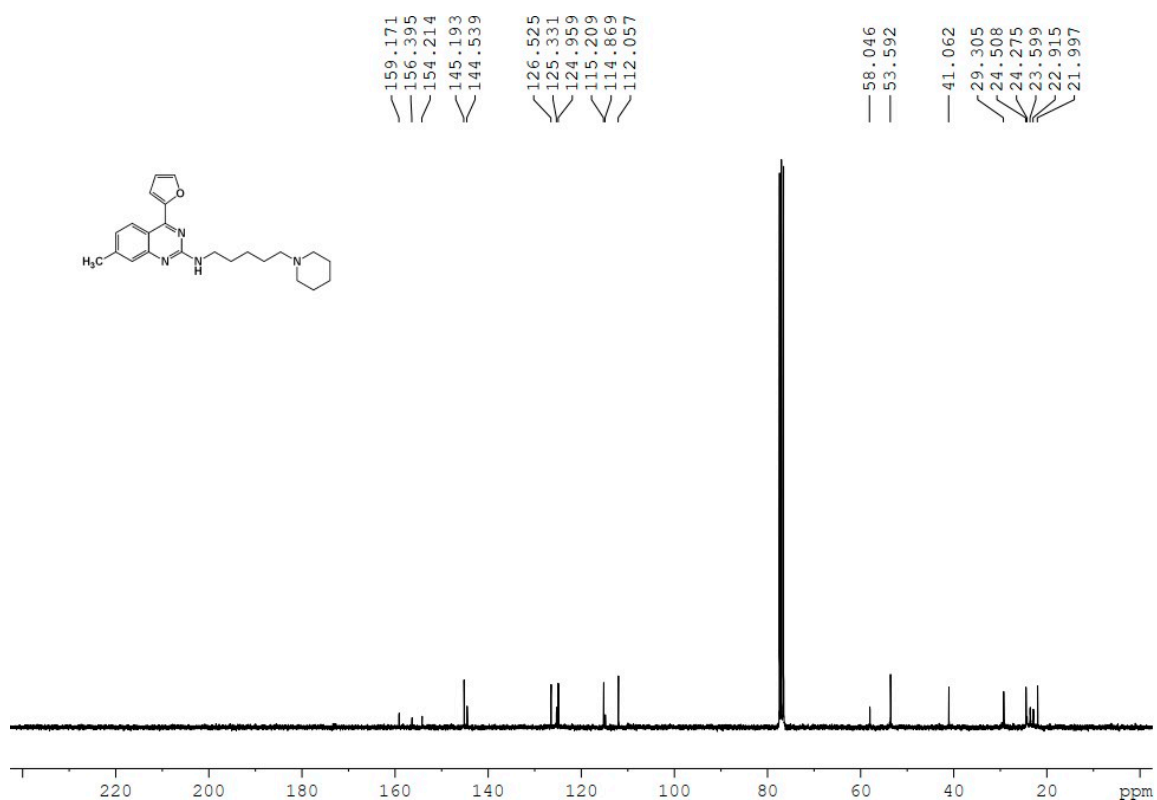
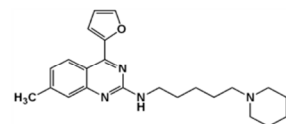
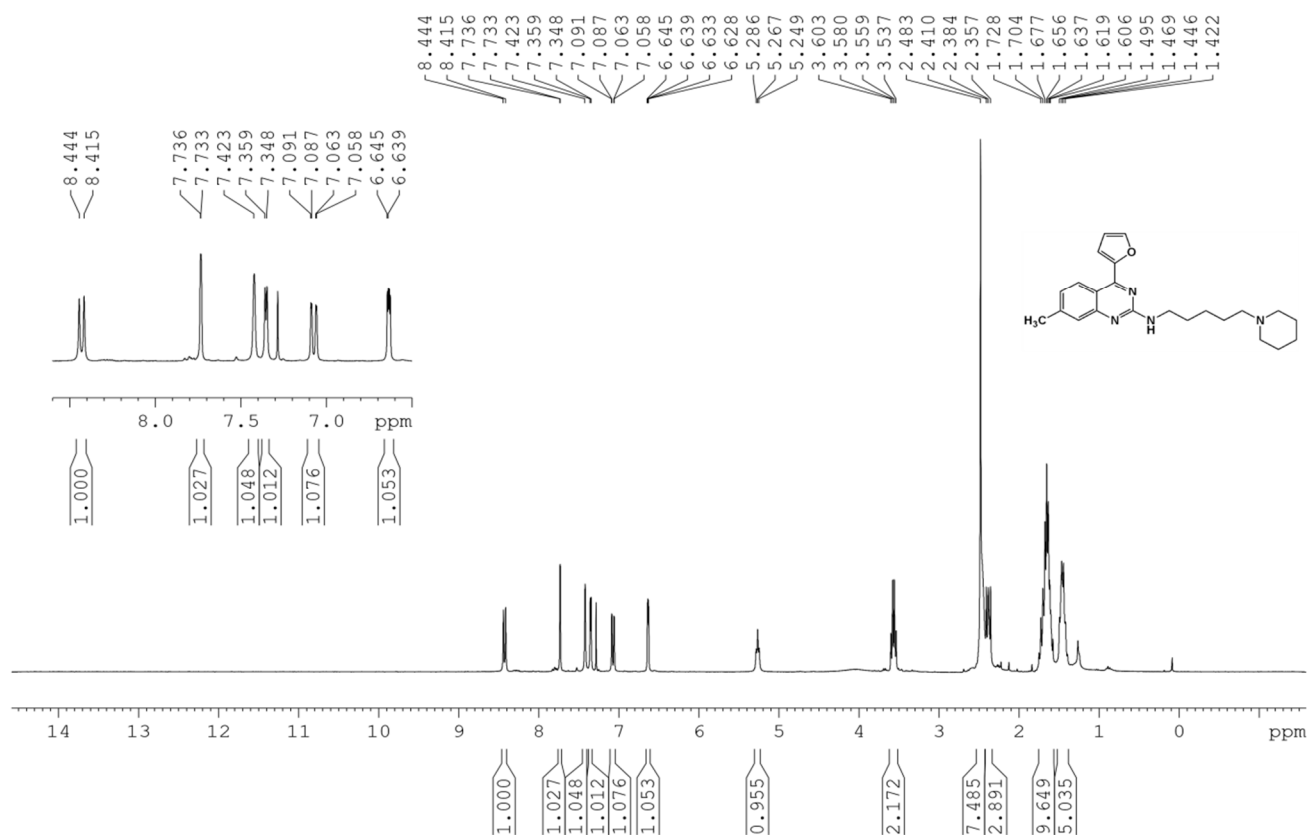
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in (CD<sub>3</sub>)<sub>2</sub>CO of compound 9w**



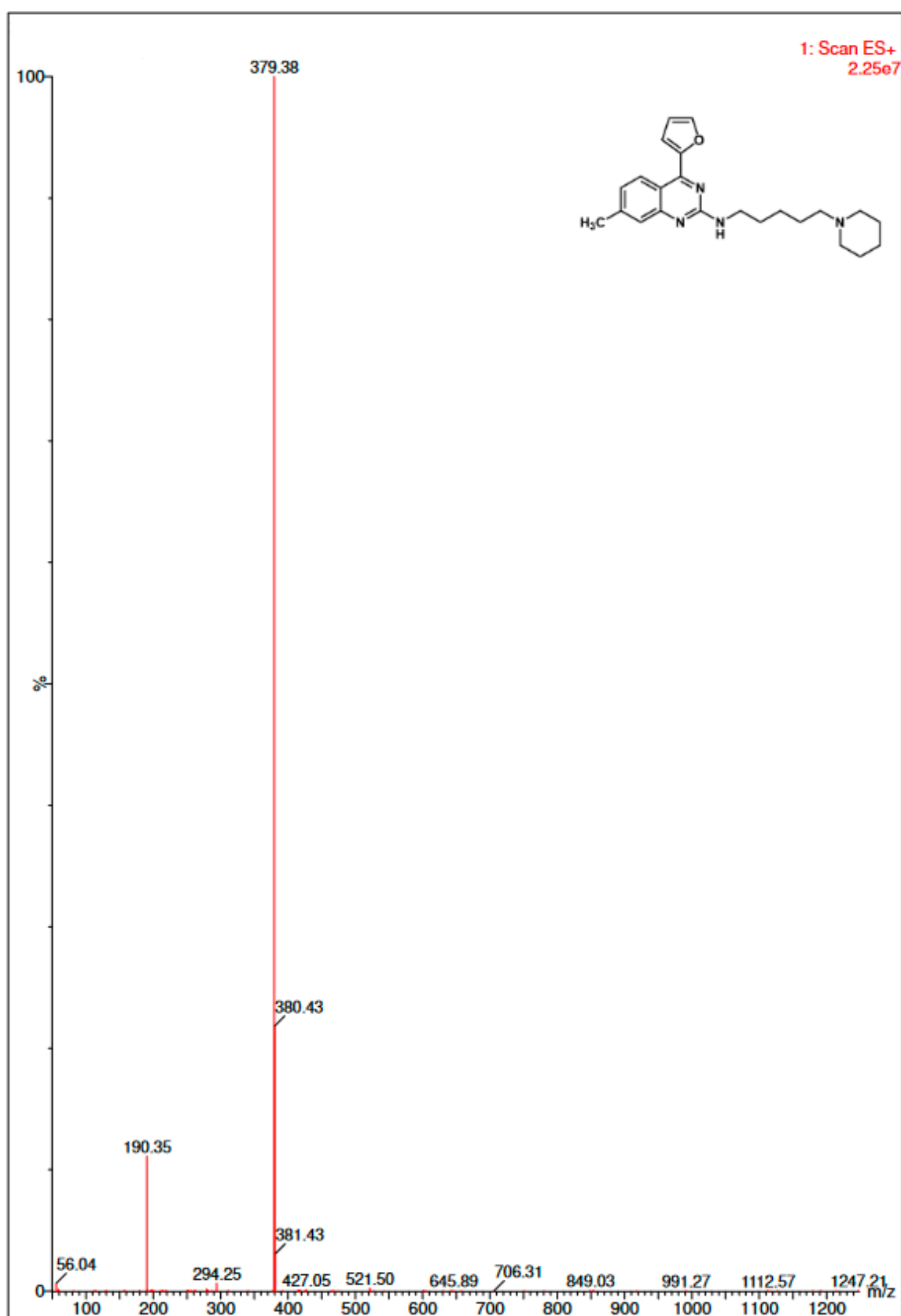
LC-MS mass spectrum of compound 9w



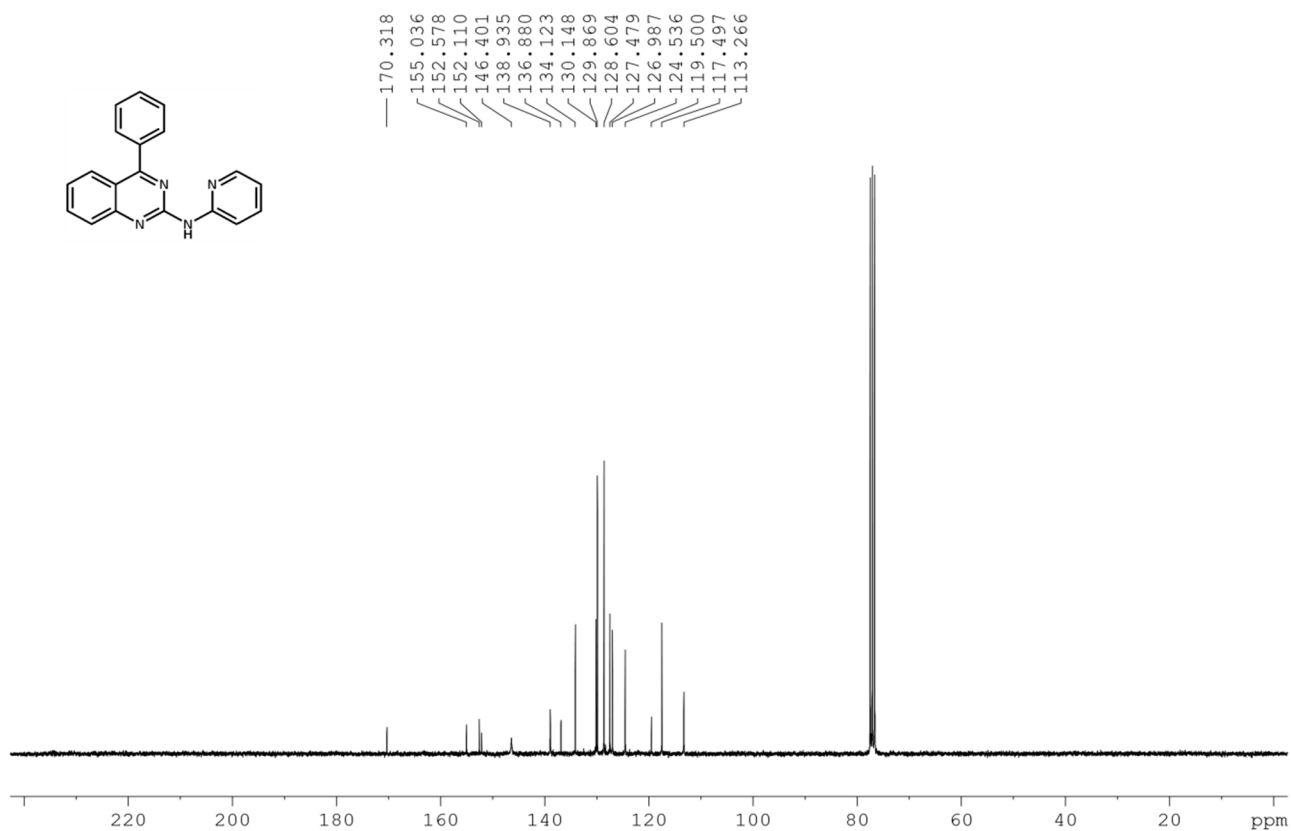
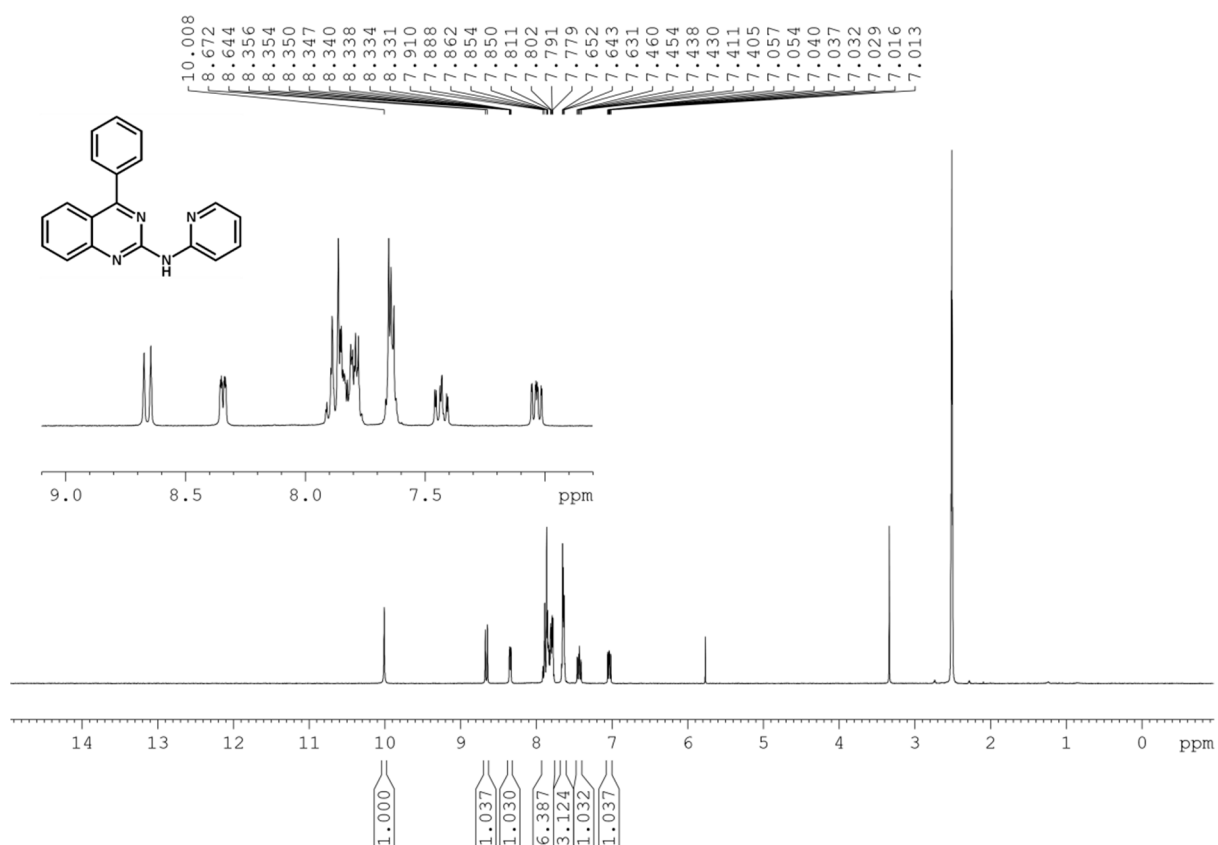
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 9x**



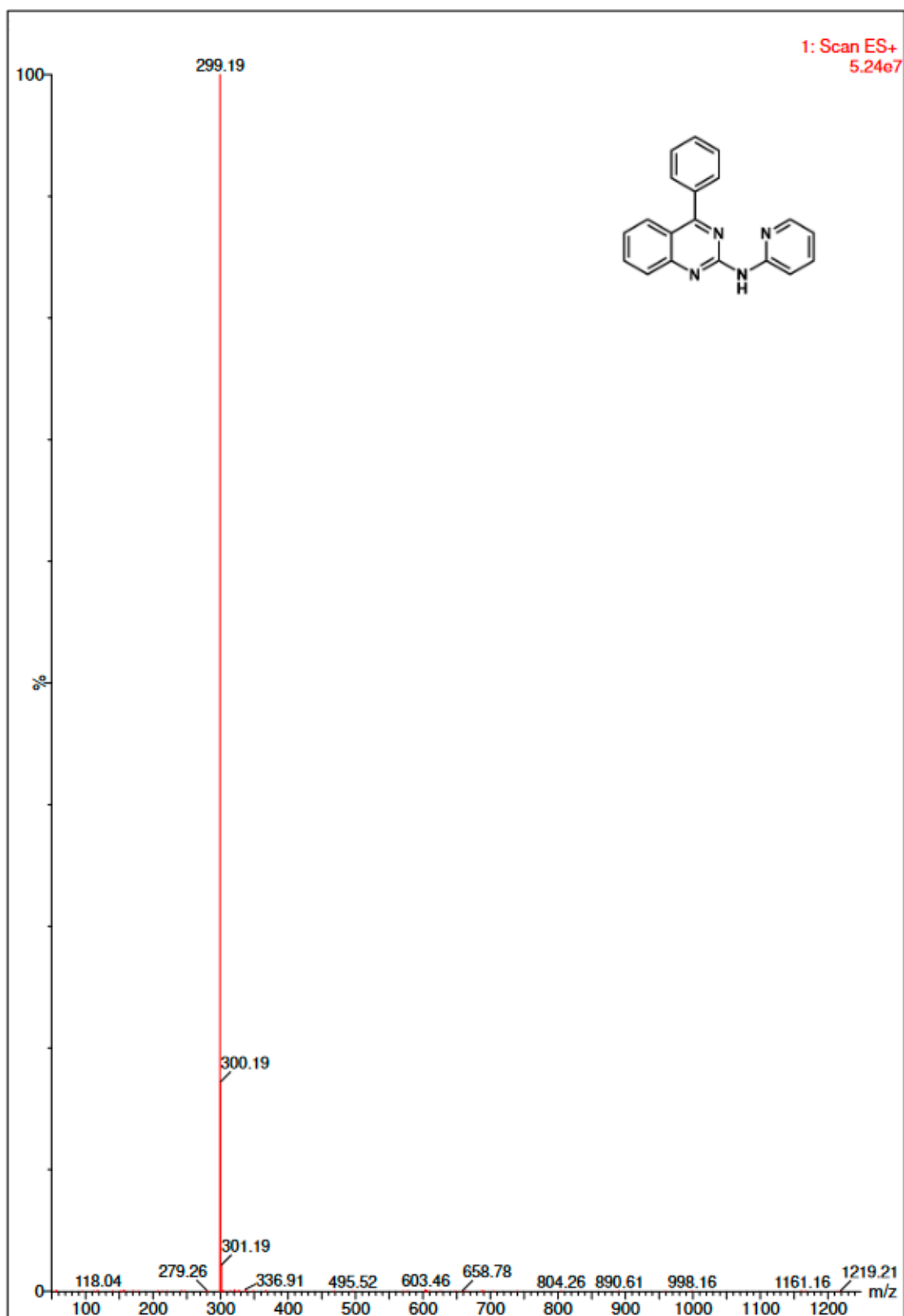
LC-MS mass spectrum of compound 9x



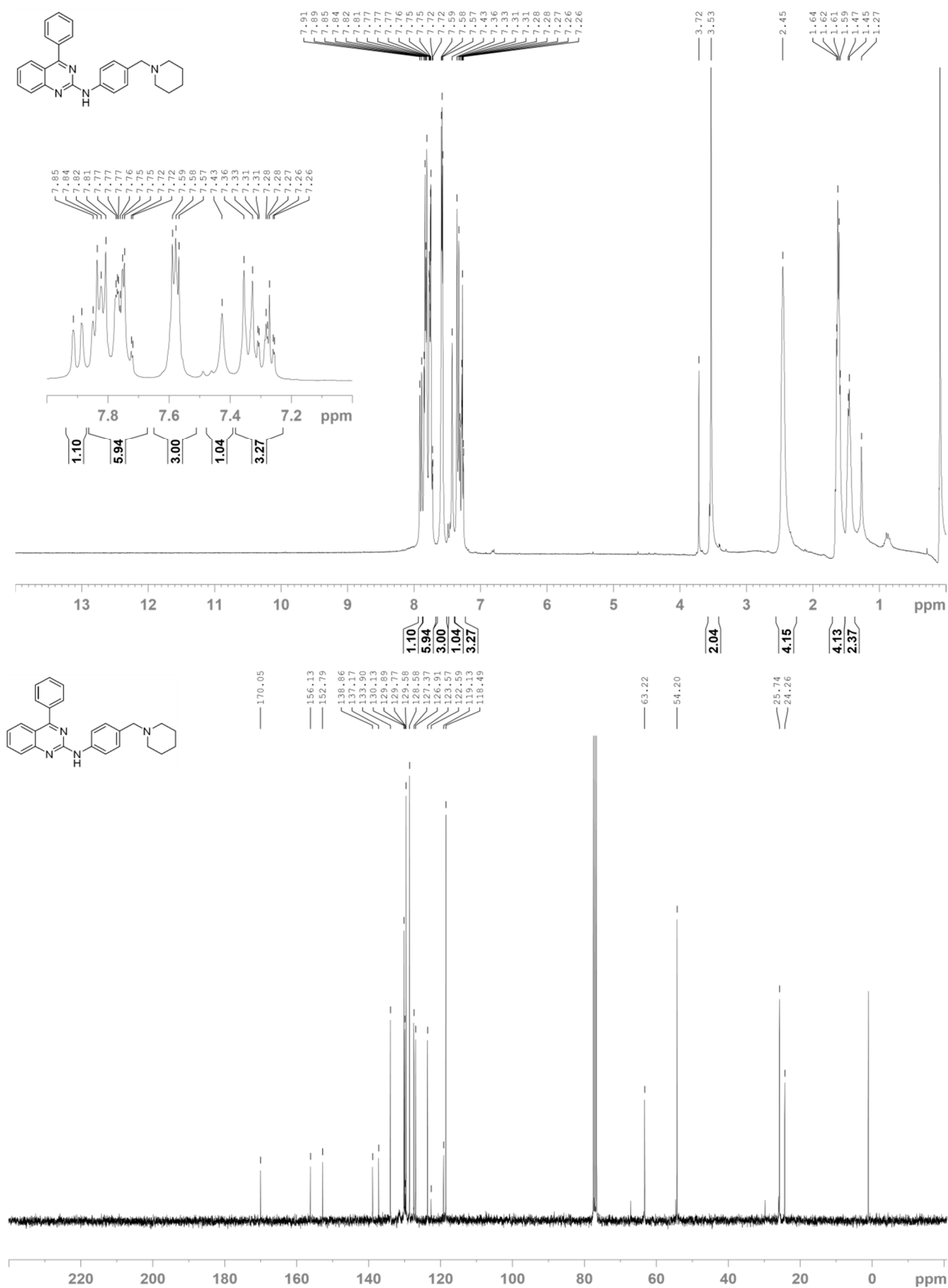
# **<sup>1</sup>H-NMR Spectra in DMSO-d<sub>6</sub> and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 10a**



LC-MS mass spectrum of compound 10a

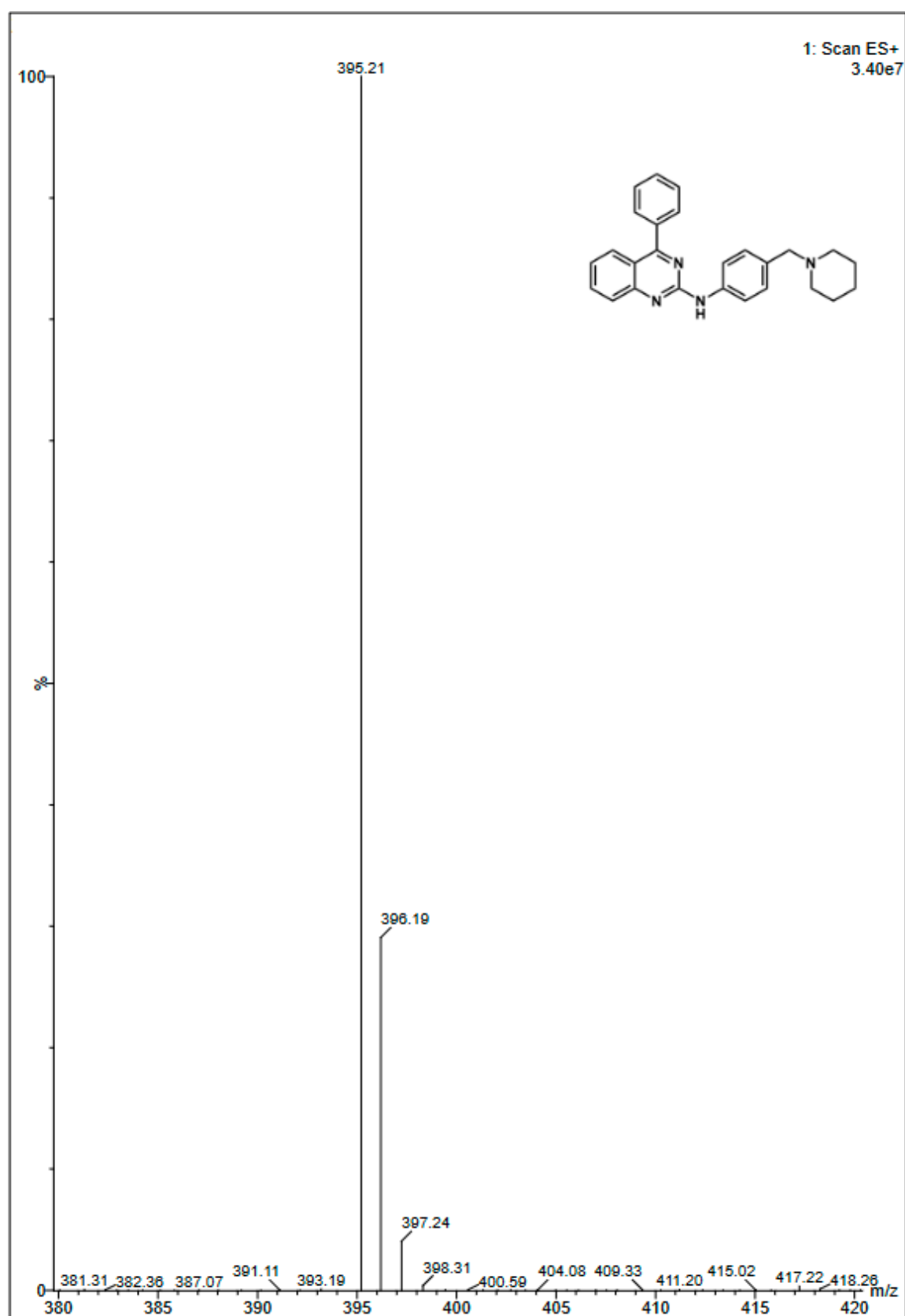


# **<sup>1</sup>H-NMR Spectra in DMSO-d<sub>6</sub> and <sup>13</sup>C-NMR Spectra in CDCl<sub>3</sub> of compound 10b**

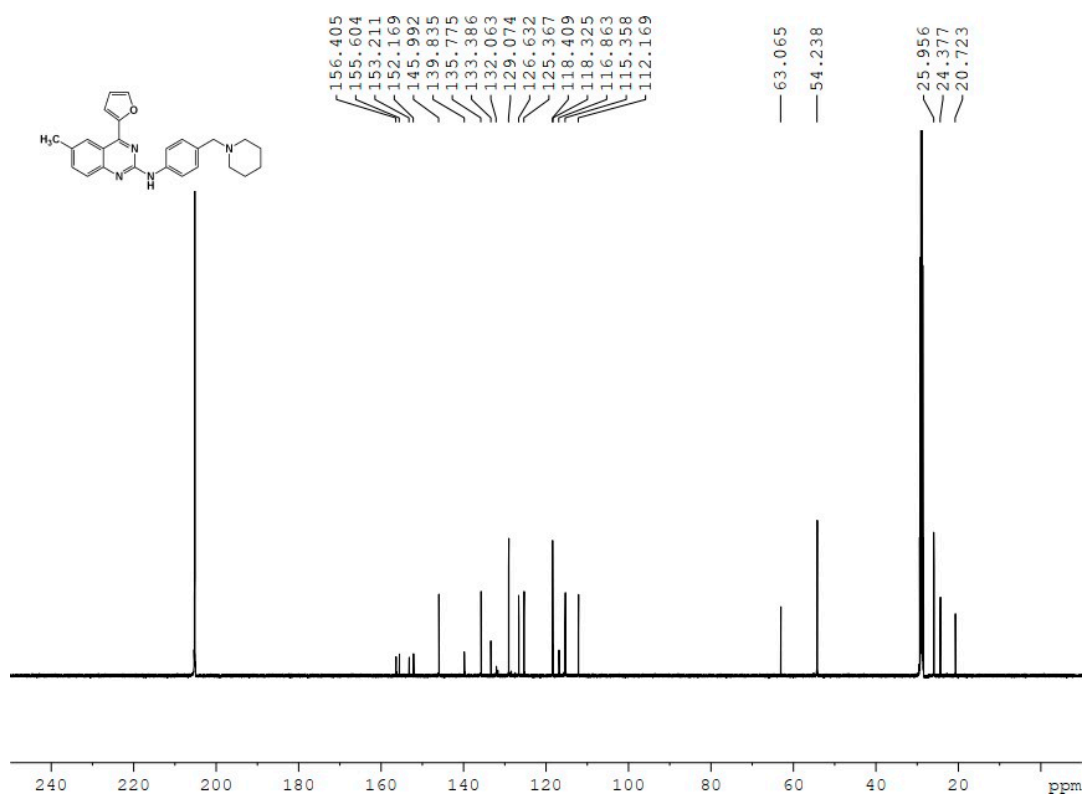
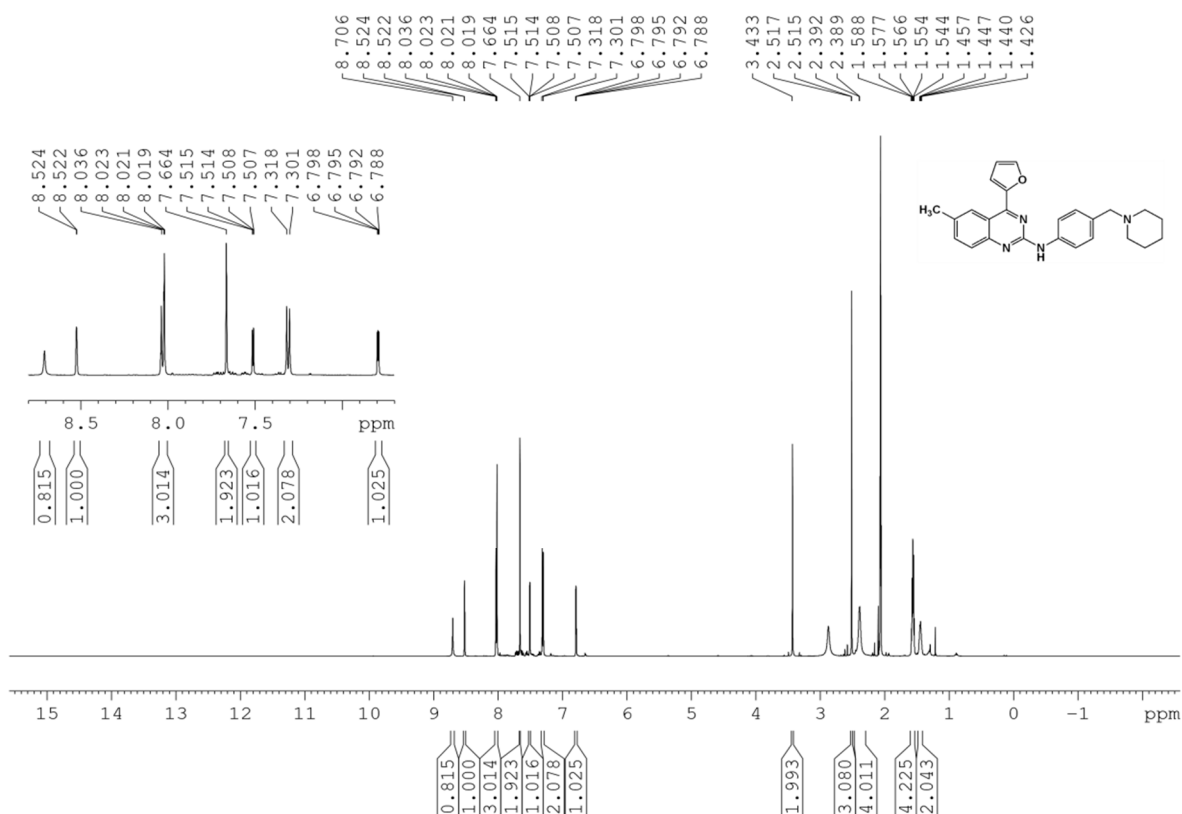




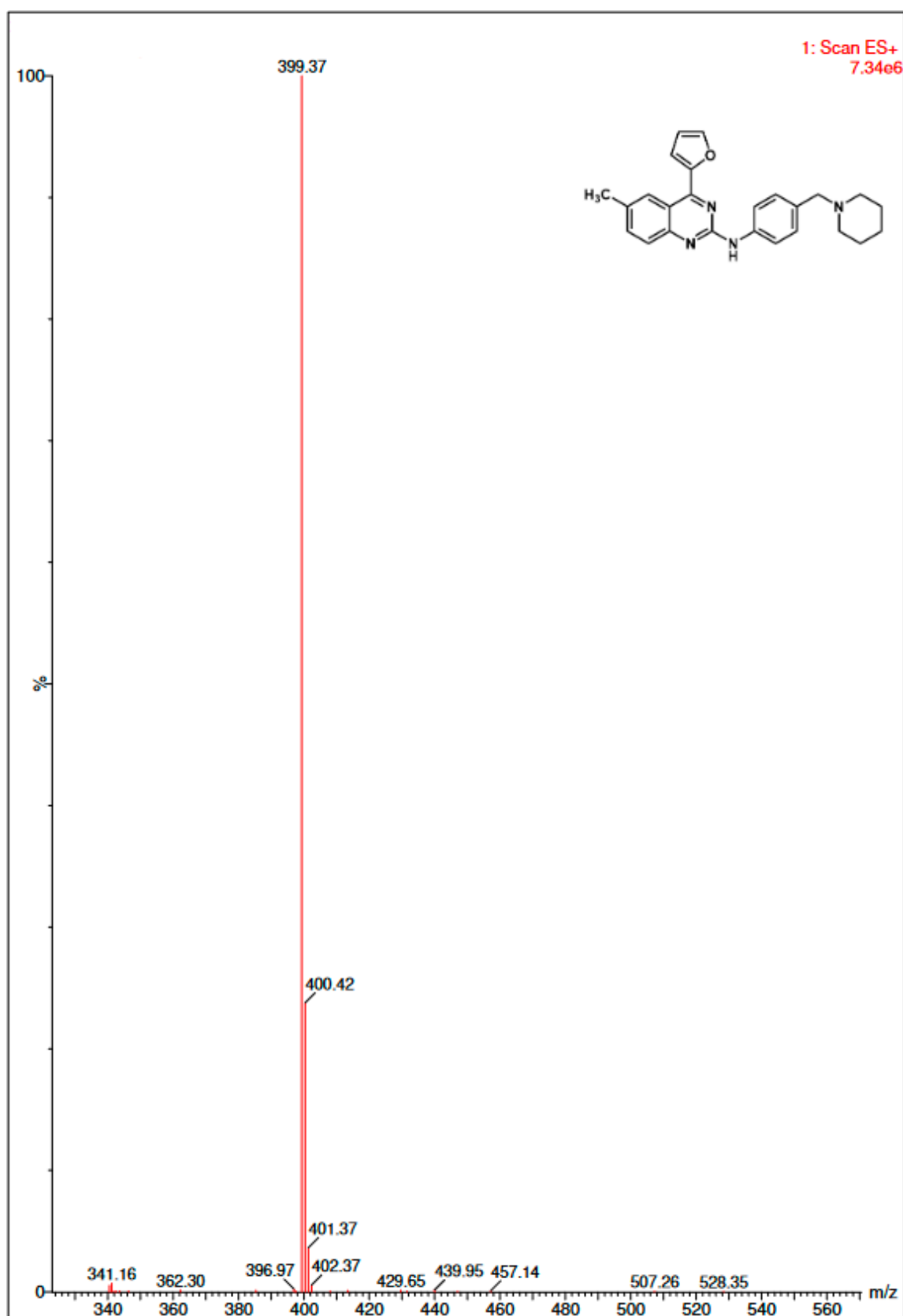
LC-MS mass spectrum of compound 10b



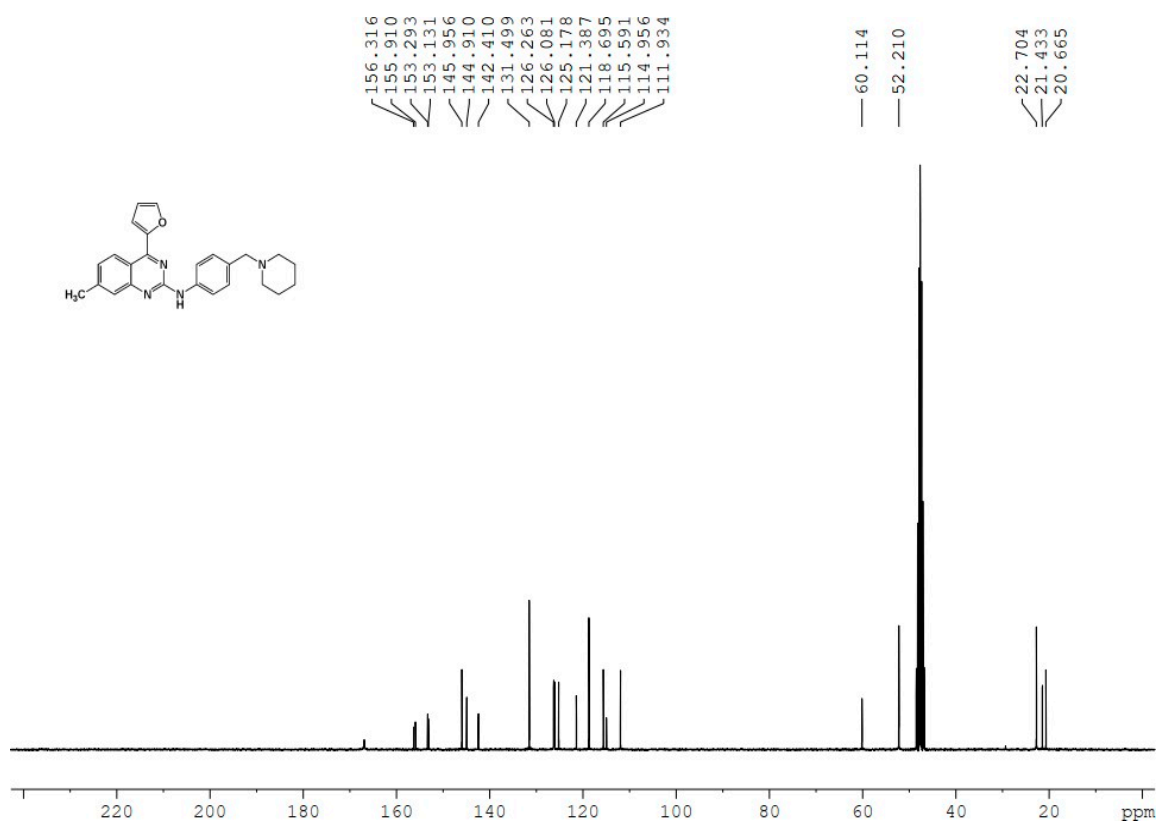
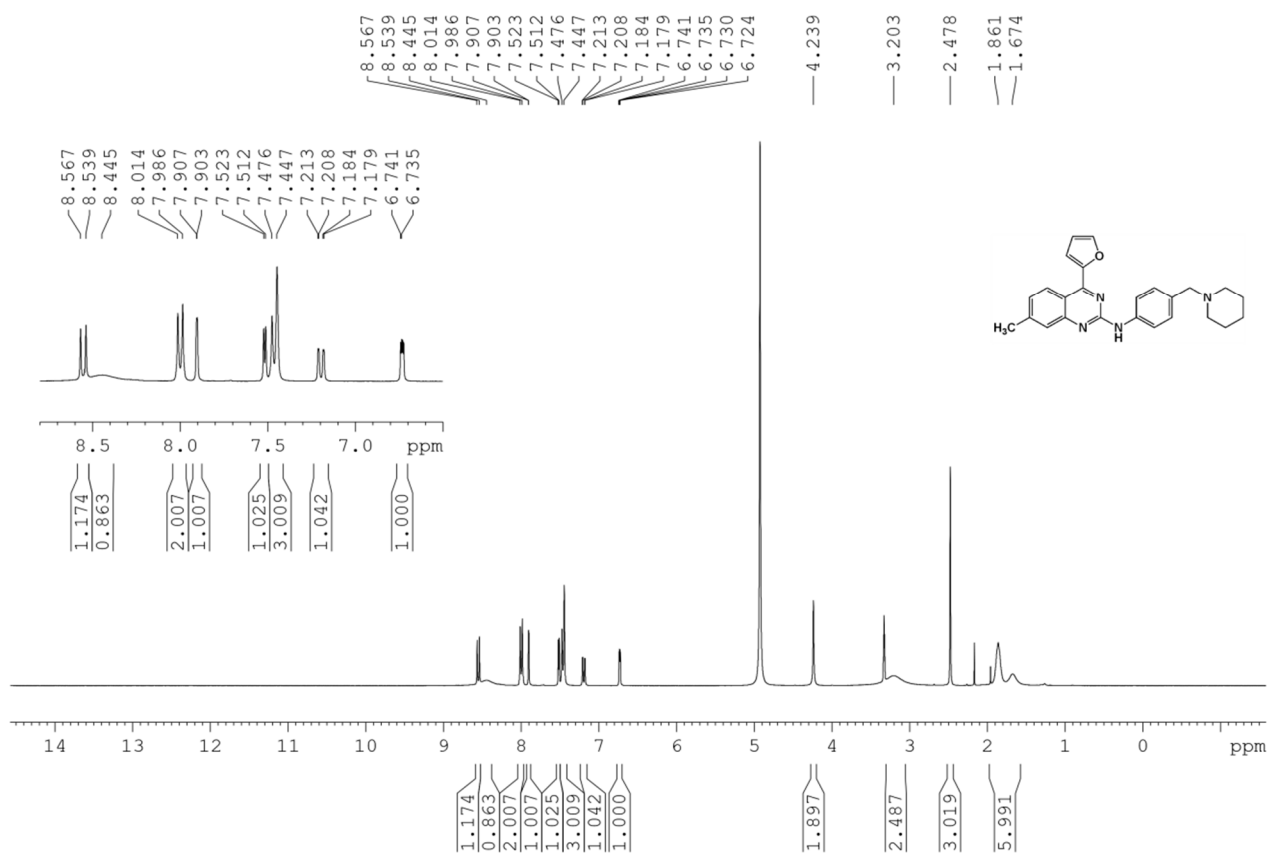
# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in (CD<sub>3</sub>)<sub>2</sub>CO of compound 10c**



LC-MS mass spectrum of compound 10c



# **<sup>1</sup>H- and <sup>13</sup>C-NMR Spectra in CD<sub>3</sub>OD of compound 10d**



LC-MS mass spectrum of compound 10d

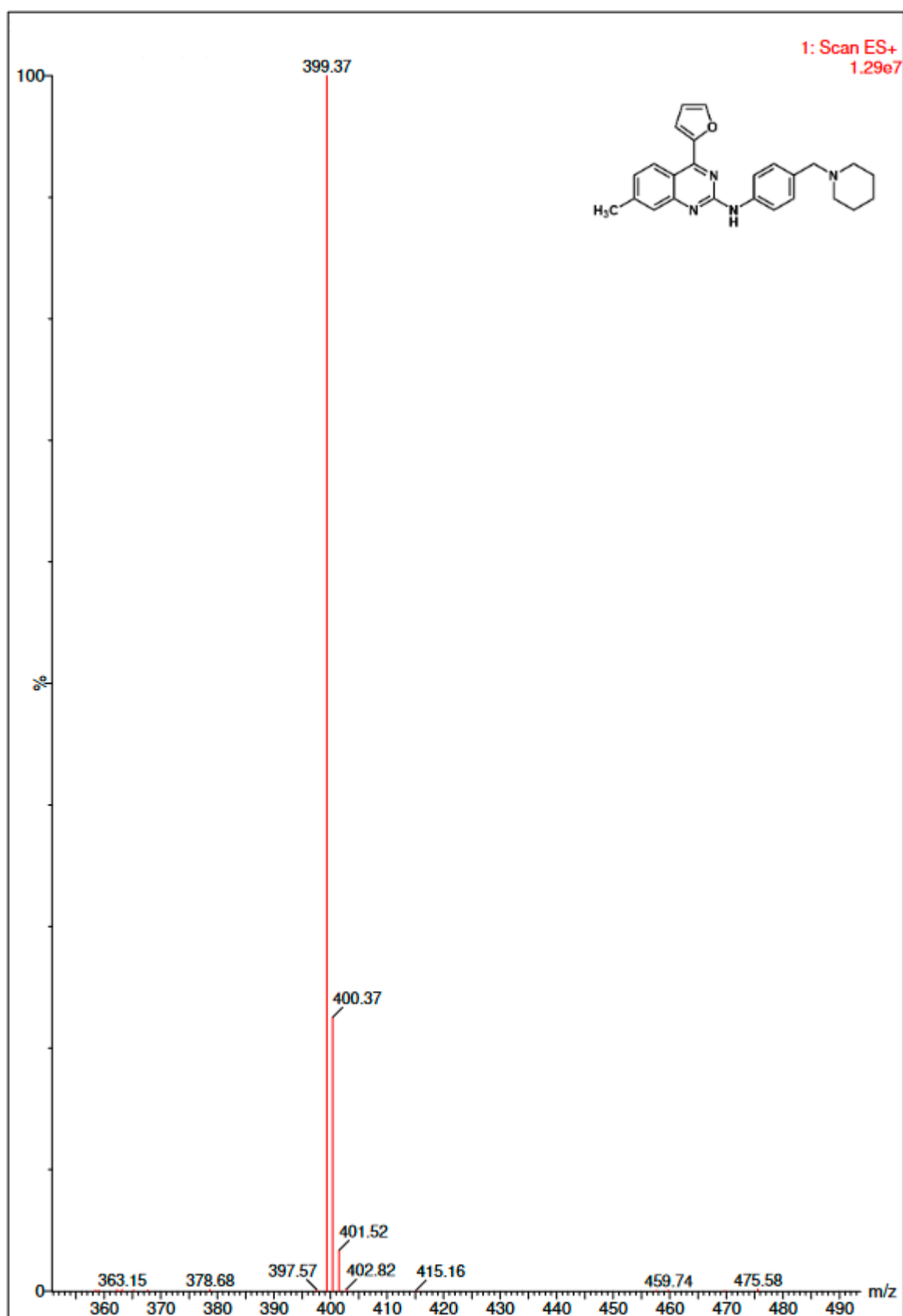


Figure S2. Dose-response curve of ZM241385

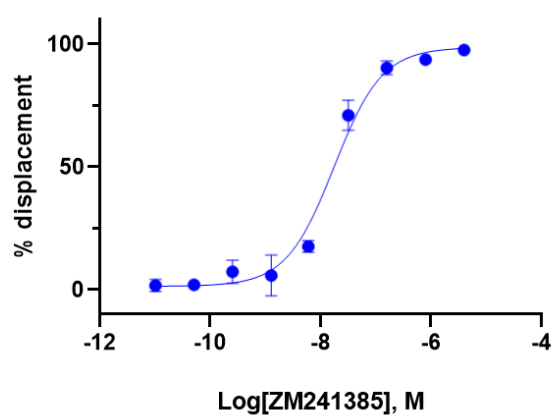
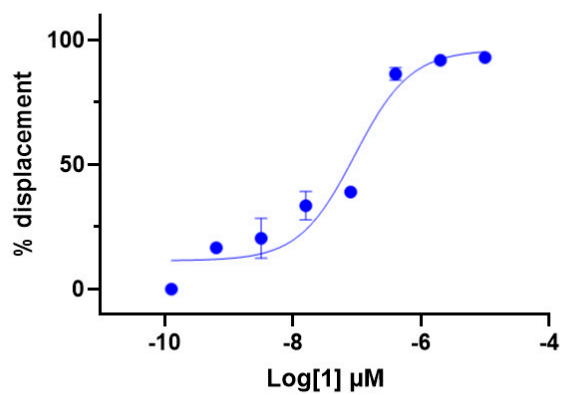
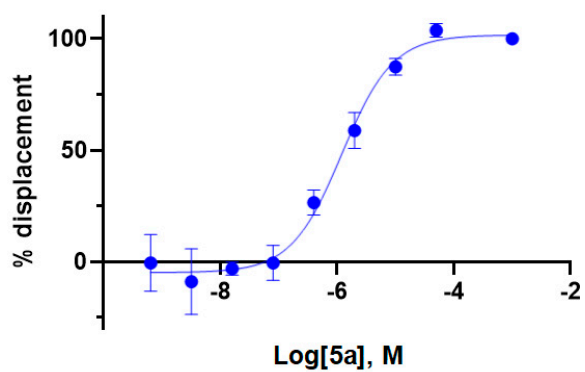


Figure S3. FP competition binding experiments with compound 1 and some final compounds

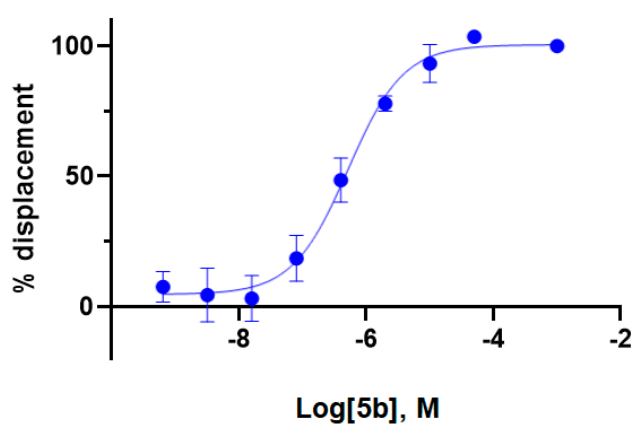
FP competition binding experiment with 1



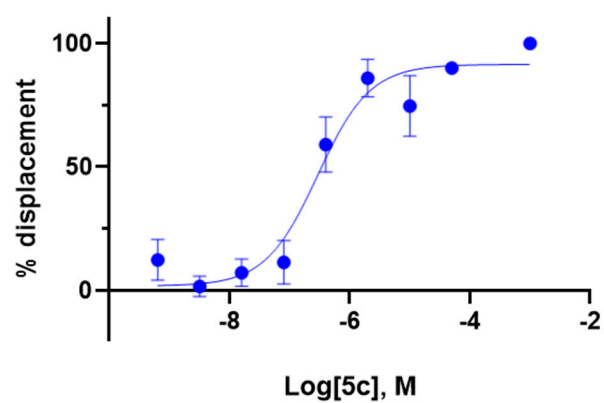
FP competition binding experiment with 5a



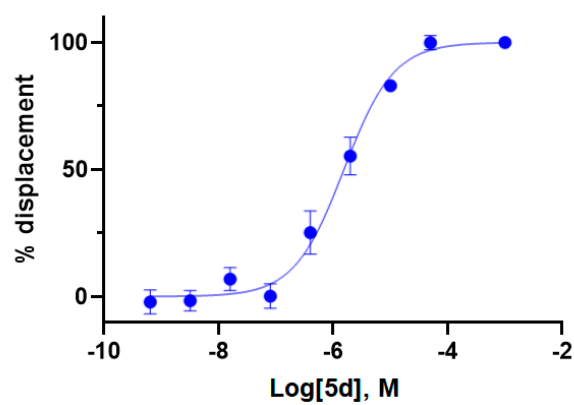
FP competition binding experiment with 5b



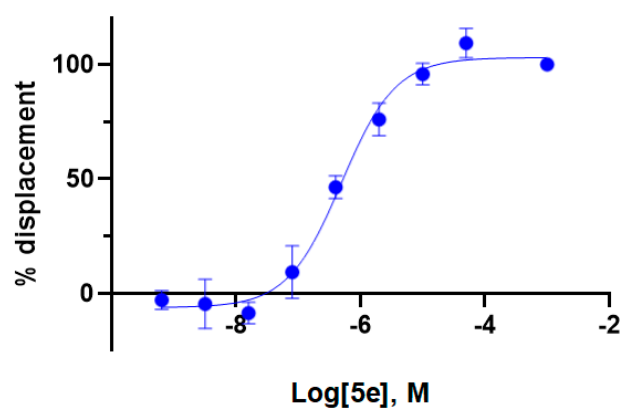
FP competition binding experiment with 5c



FP competition binding experiment with 5d

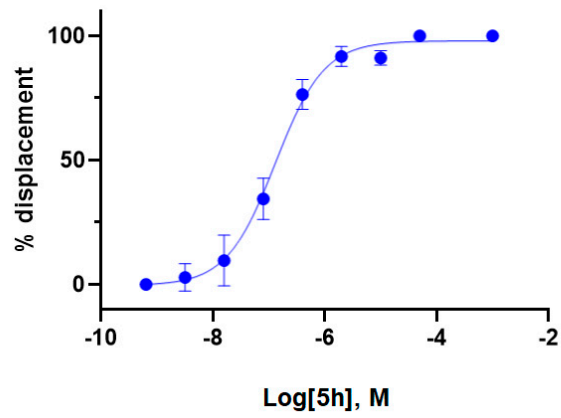


FP competition binding experiment with 5e

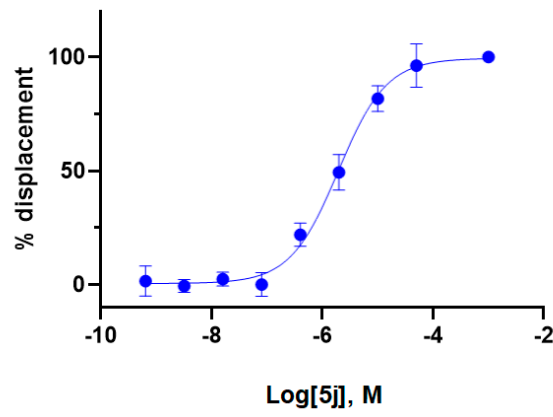




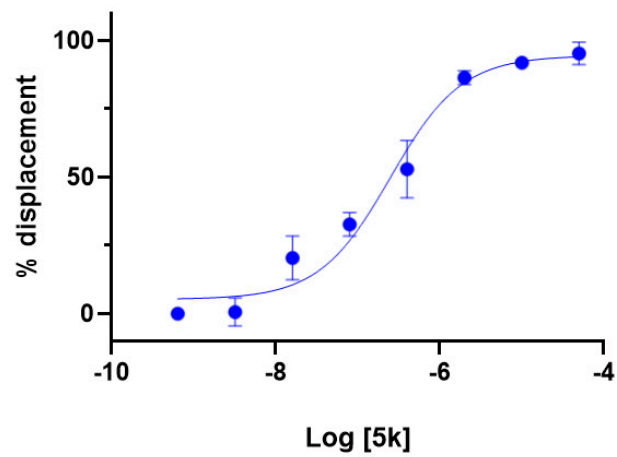
FP competition binding experiment with 5h



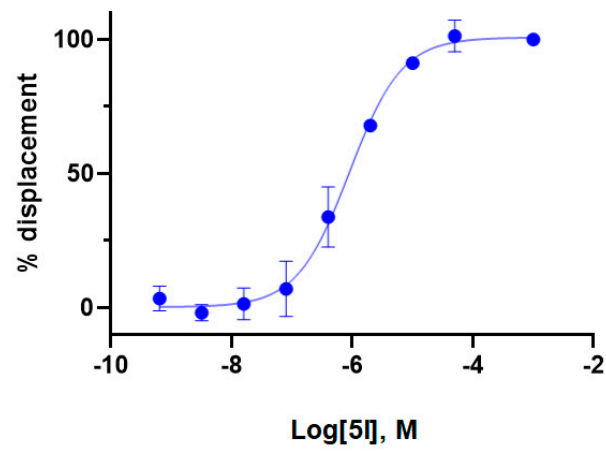
FP competition binding experiment with 5j



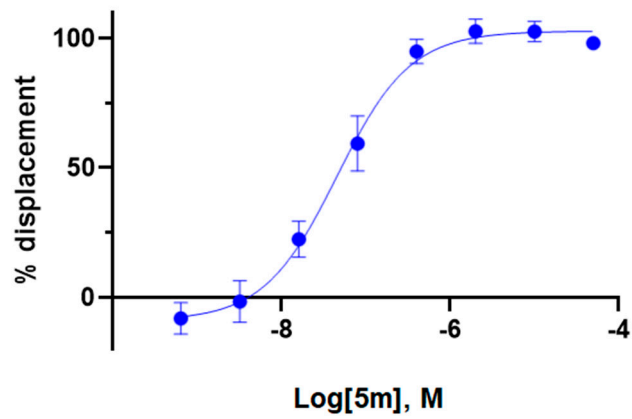
FP competition binding experiment with 5k



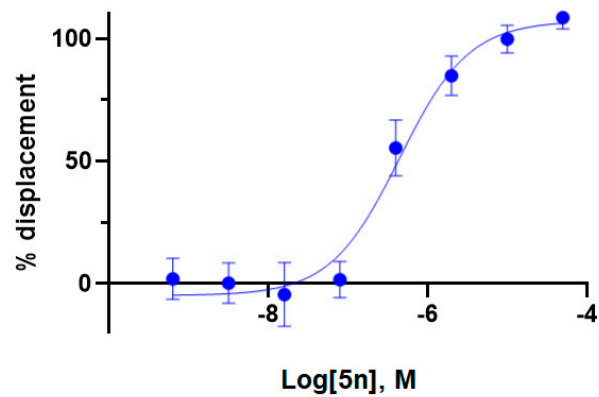
**FP competition binding experiment with 5l**



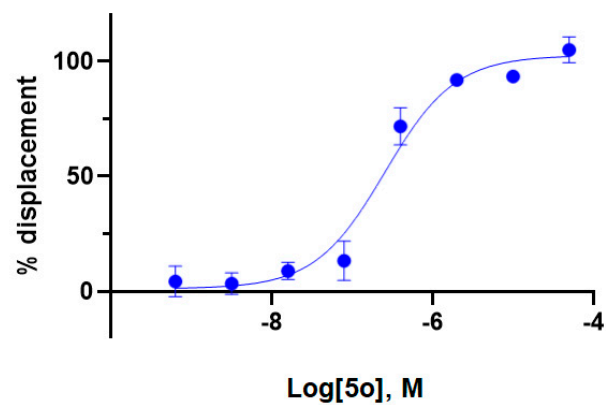
**FP competition binding experiment with 5m**



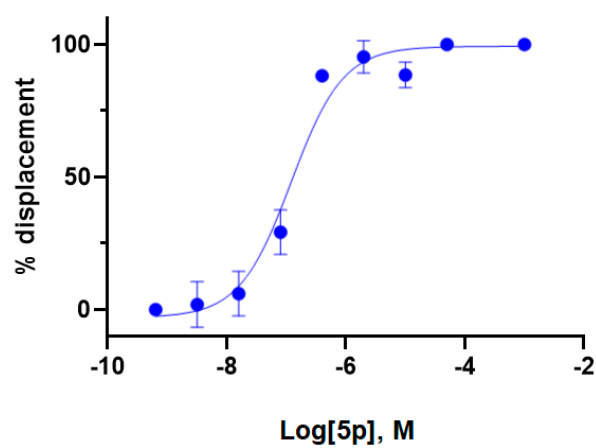
**FP competition binding experiment with 5n**



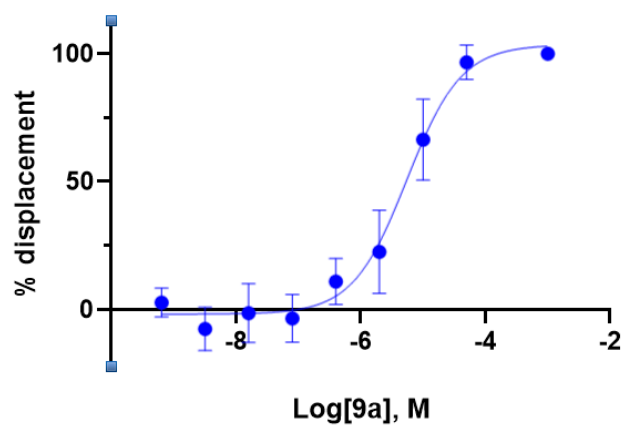
FP competition binding experiment with 5o



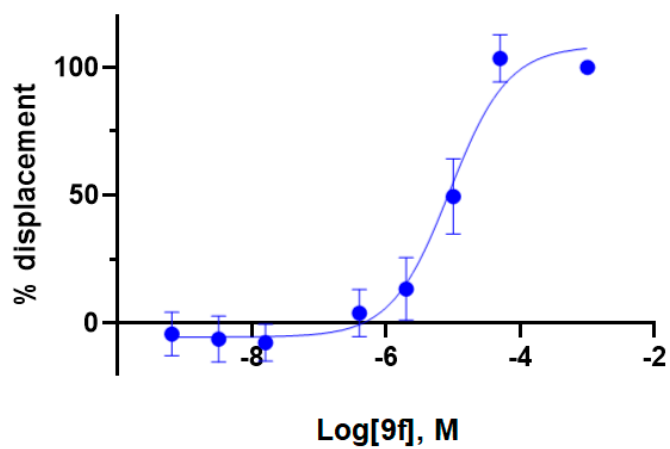
FP competition binding experiment with 5p



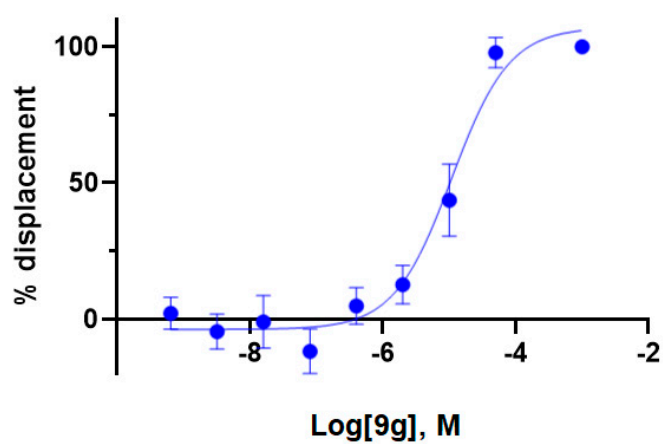
FP competition binding experiment with 9a



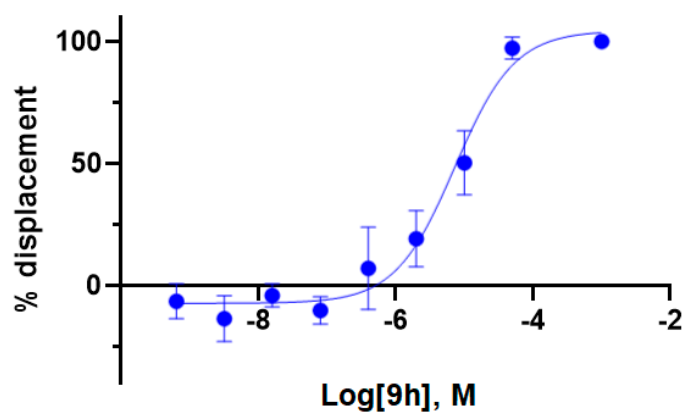
### FP competition binding experiment with 9f



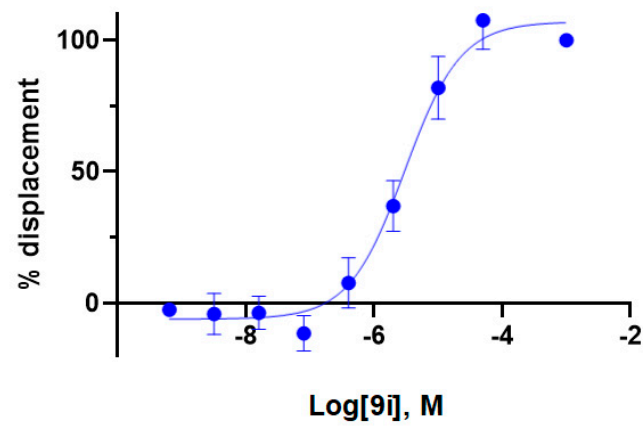
### FP competition binding experiment with 9g



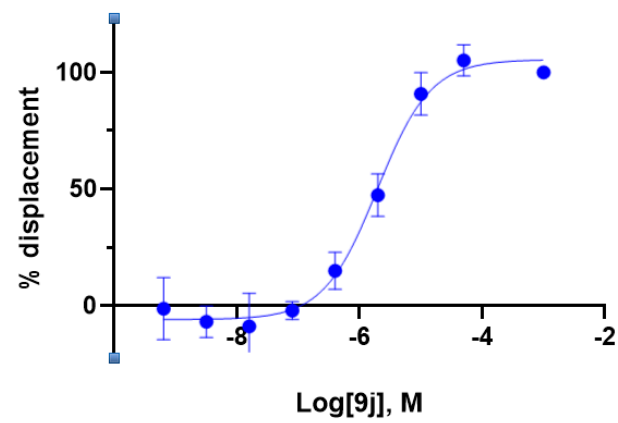
### FP competition binding experiment with 9h



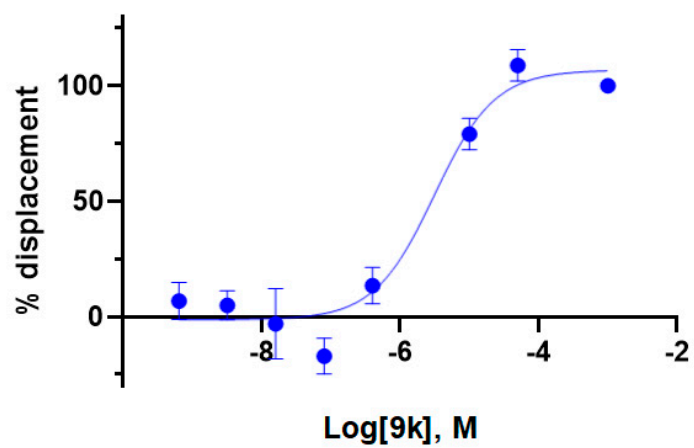
FP competition binding experiment with 9i



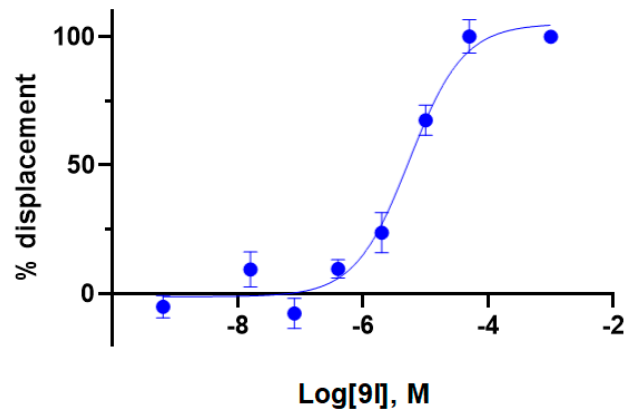
FP competition binding experiment with 9j



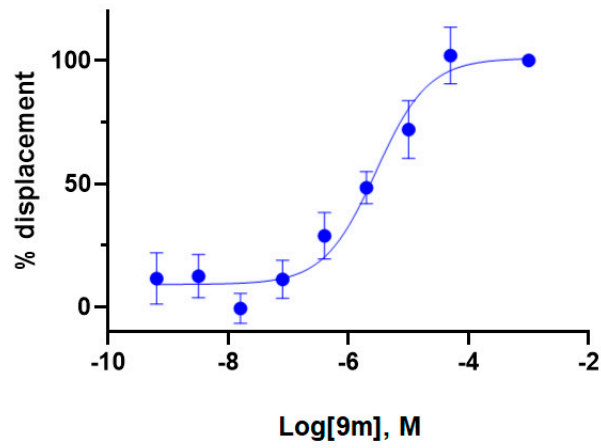
FP competition binding experiment with 9k



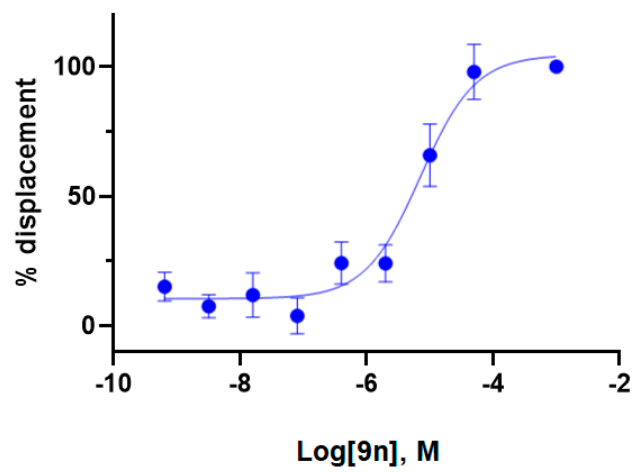
**FP competition binding experiment with 9l**



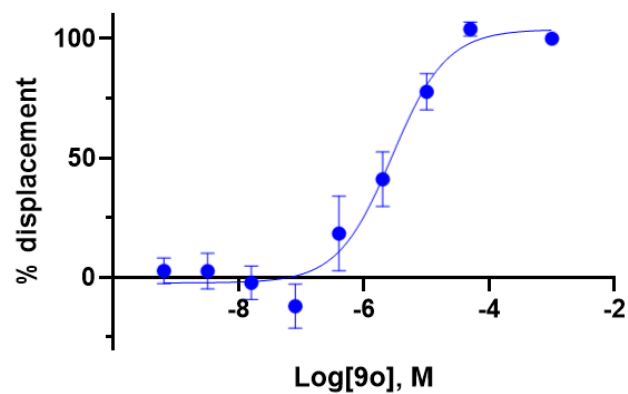
**FP competition binding experiment with 9m**



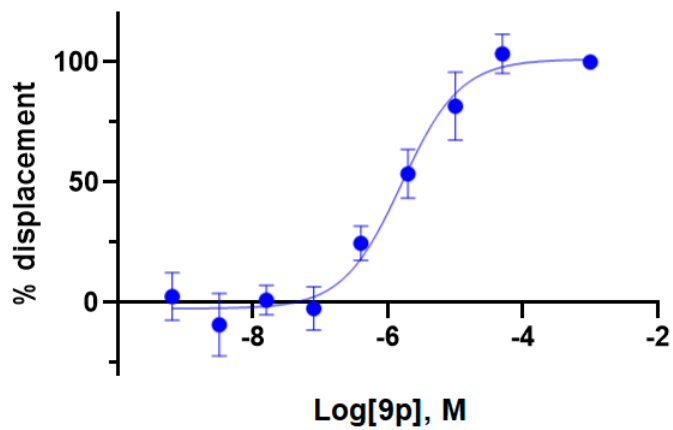
**FP competition binding experiment with 9n**



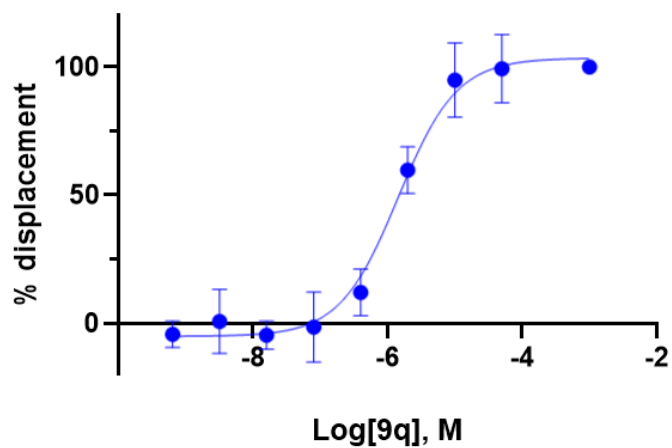
FP competition binding experiment with 9o



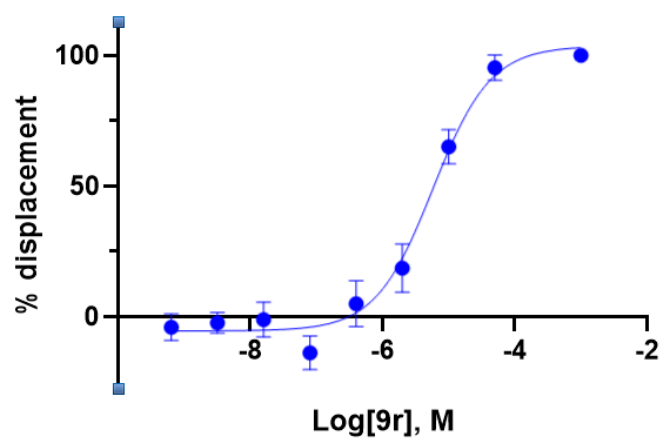
FP competition binding experiment with 9p



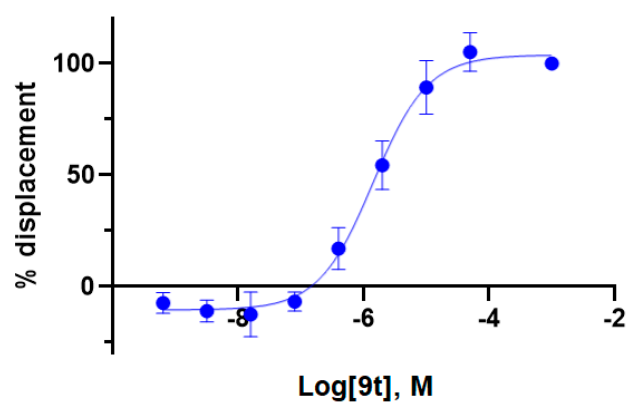
FP competition binding experiment with 9q



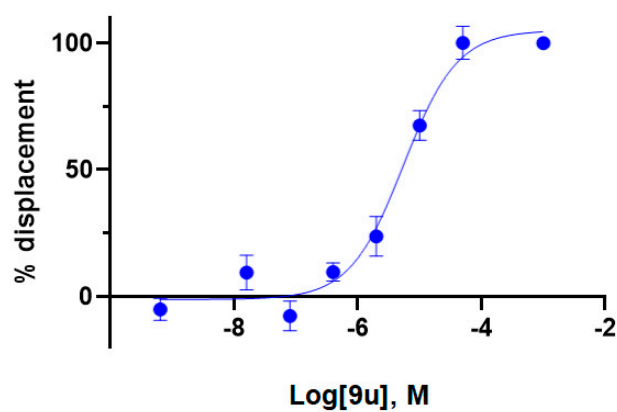
FP competition binding experiment with 9r



FP competition binding experiment with 9t

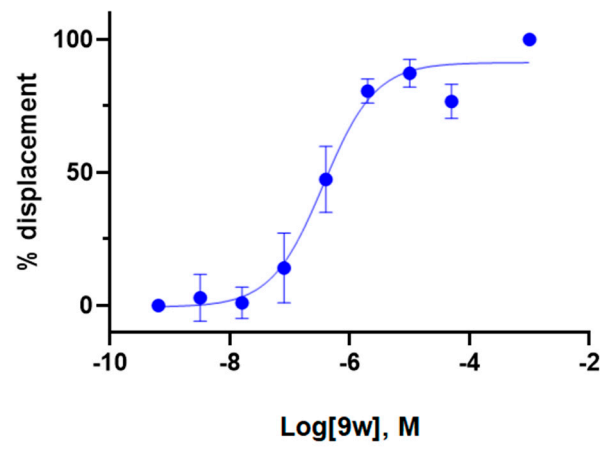


FP competition binding experiment with 9u

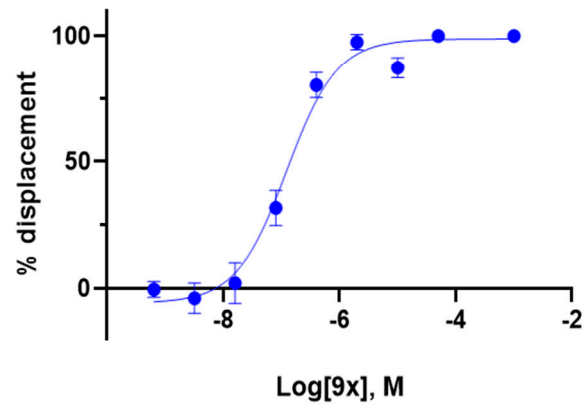




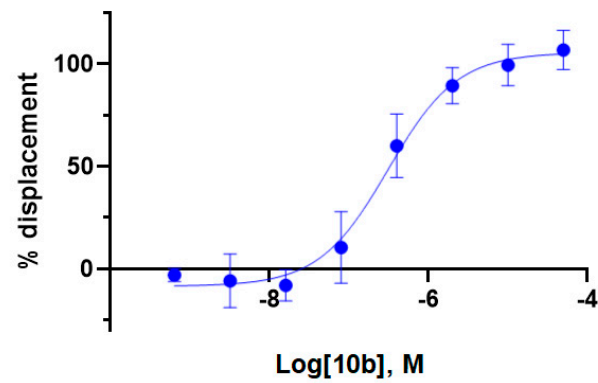
**FP competition binding experiment with 9w**



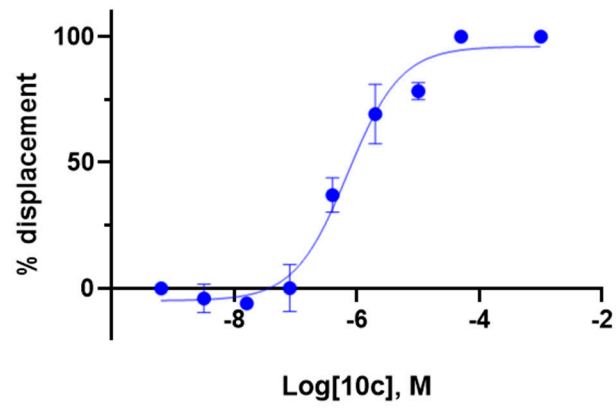
**FP competition binding experiment with 9x**



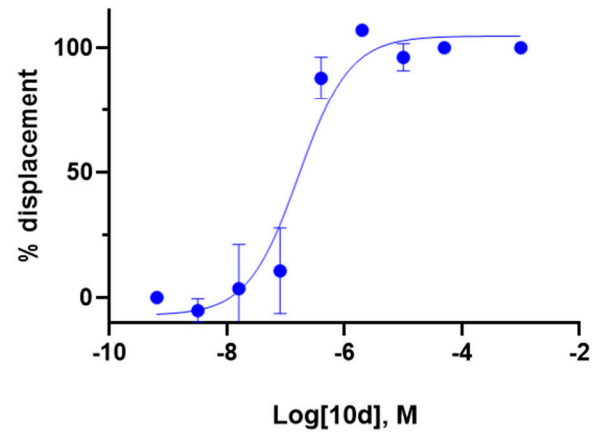
**FP competition binding experiment with 10b**



FP competition binding experiment with 10c



FP competition binding experiment with 10d



FP competition binding experiment with 11

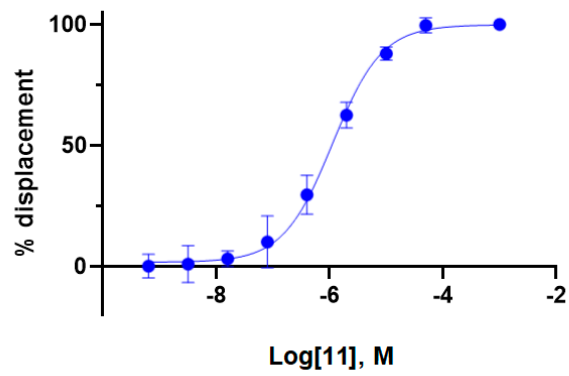
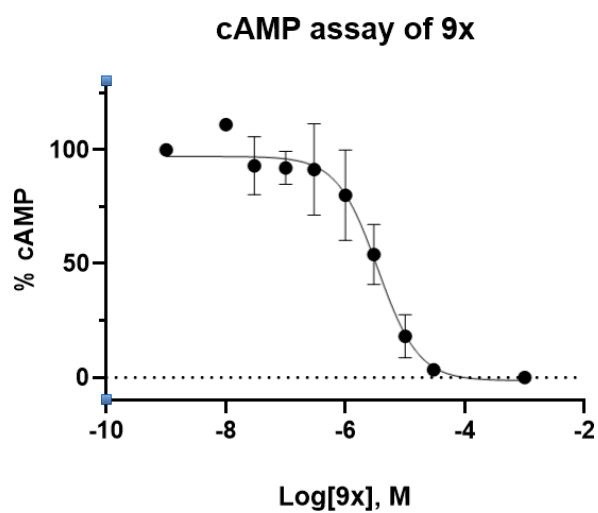
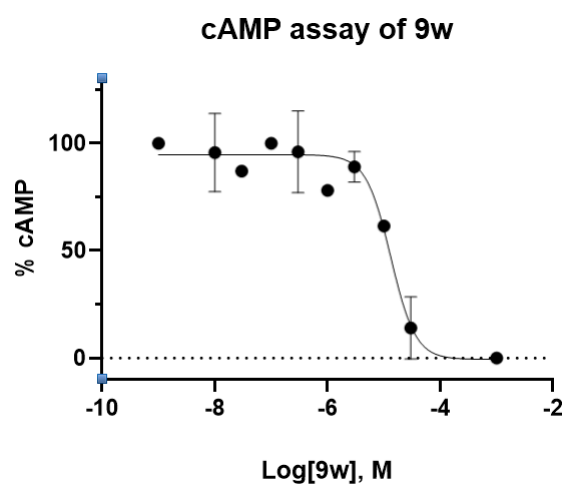
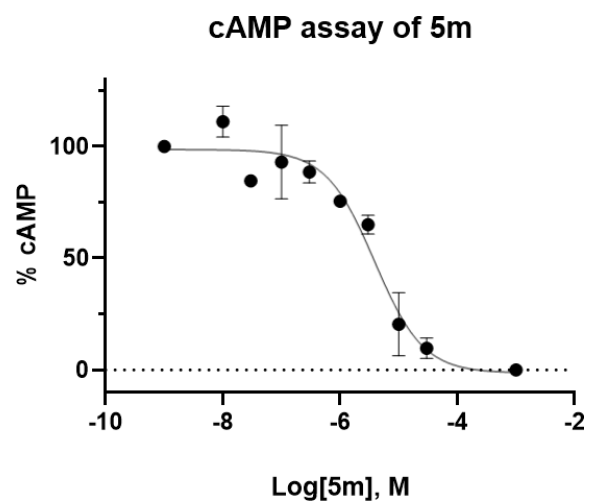
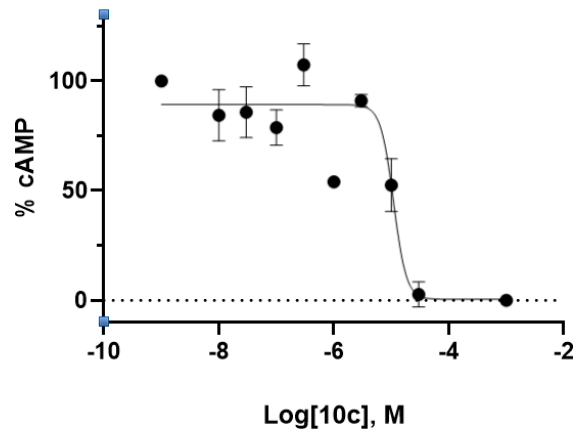


Figure S4. cAMP assays of compounds 5m, 9w, 9x, 10c, 10d



cAMP assay of 10c



cAMP assay of 10d

