

Novel quinazoline derivatives as highly effective A_{2A} adenosine receptor antagonists

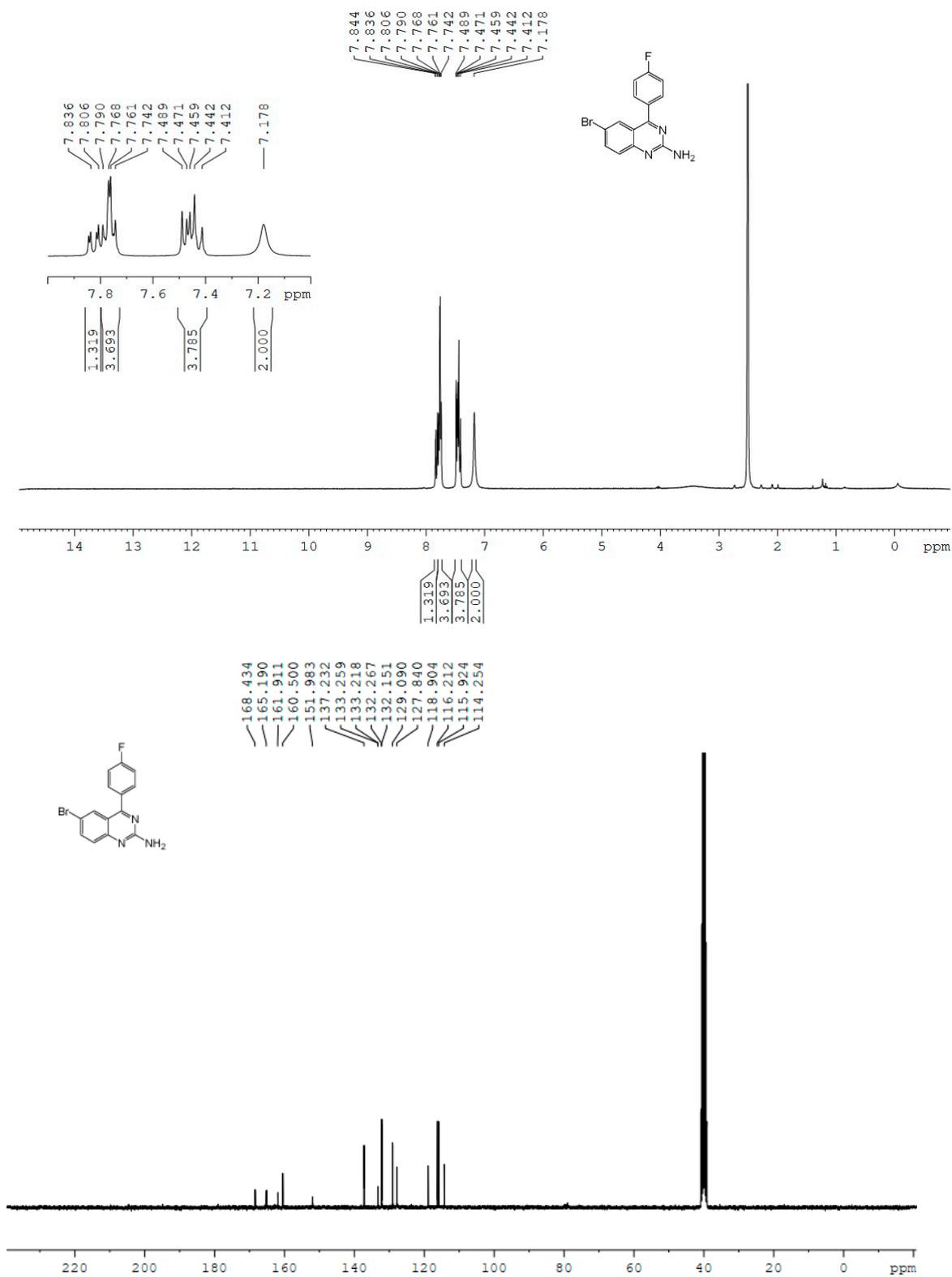
Amélie Laversin, Robin Dufosse[†], Raphaël Bolteau[†], Romain Duroux, Séverine Ravez, Sergio Hernandez-Tapia, Martin Fossart, Mathilde Coevoet, Maxime Liberelle, Saïd Yous, Nicolas Lebègue, Patricia Melnyk*

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

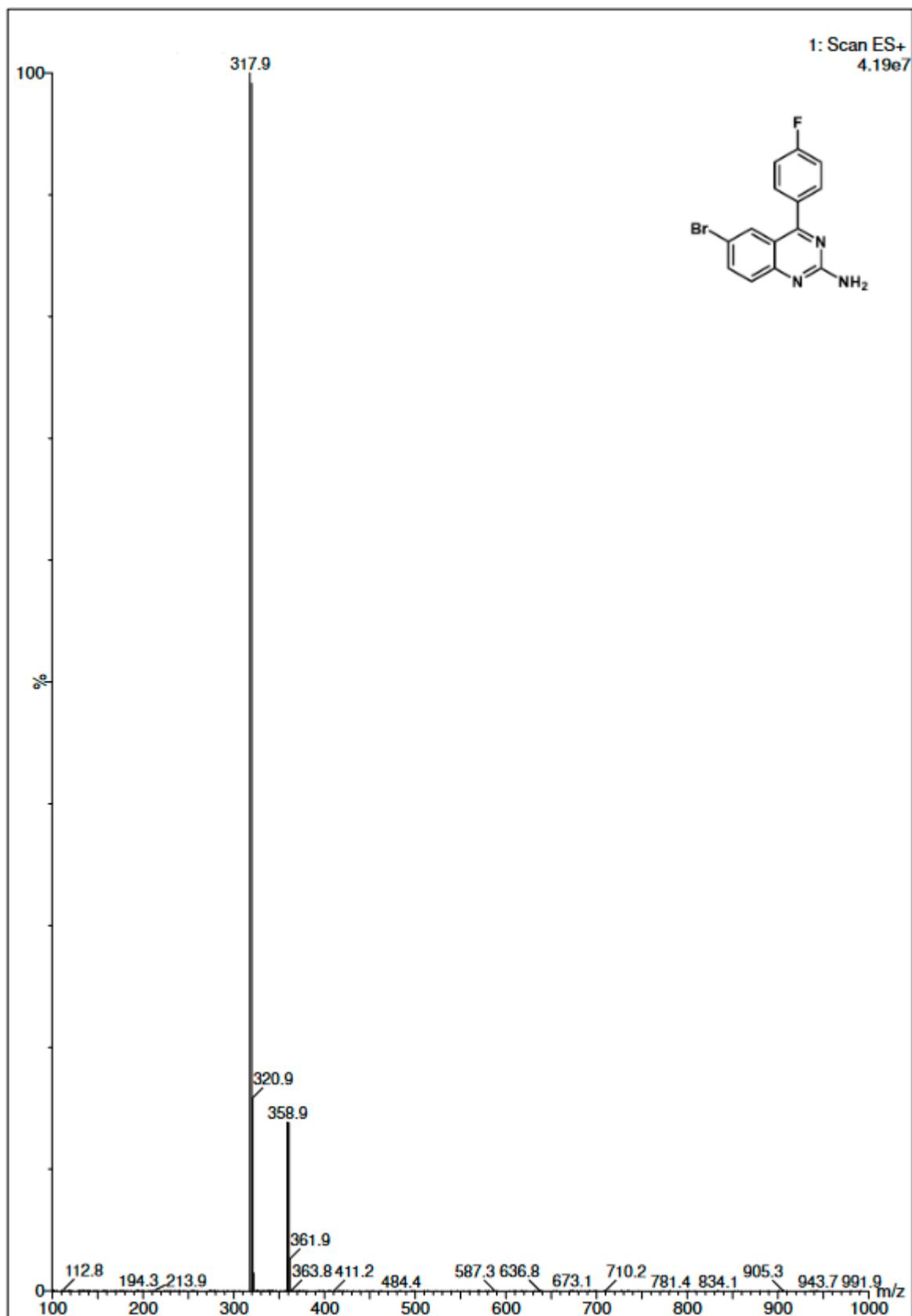
[†]These authors contributed equally

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

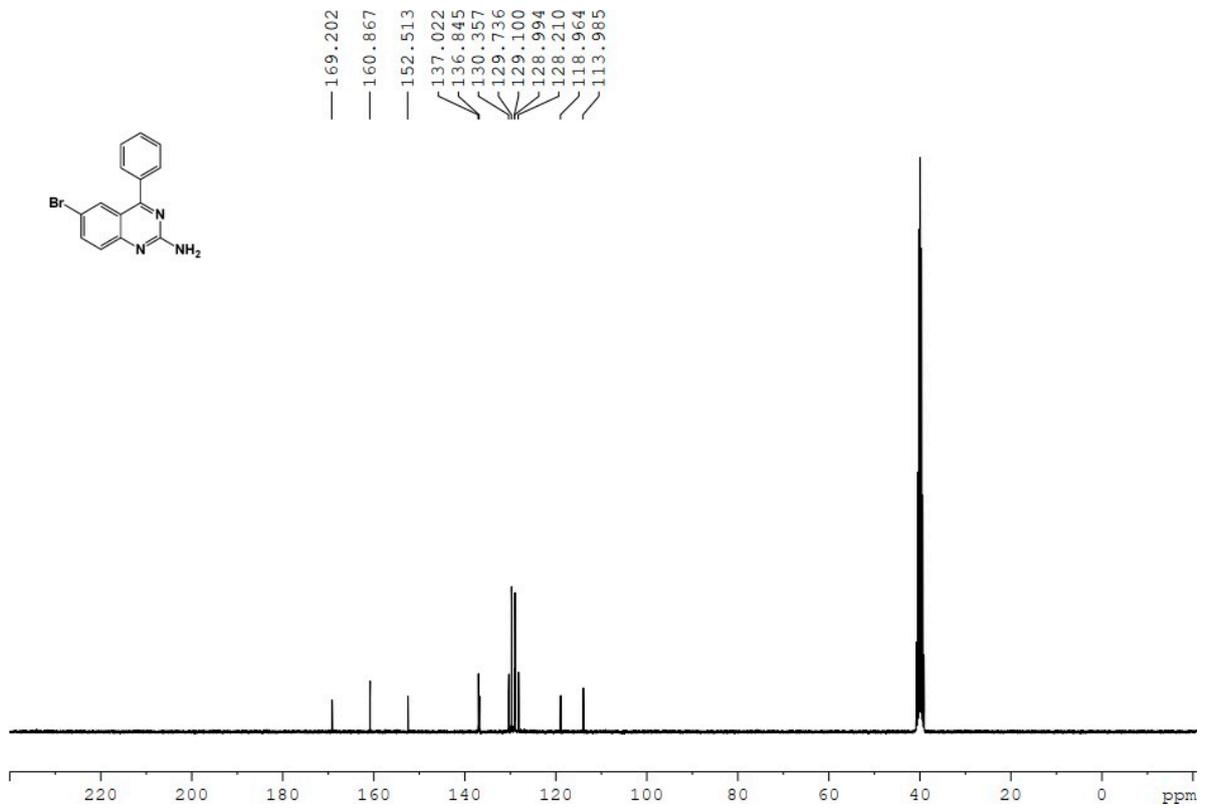
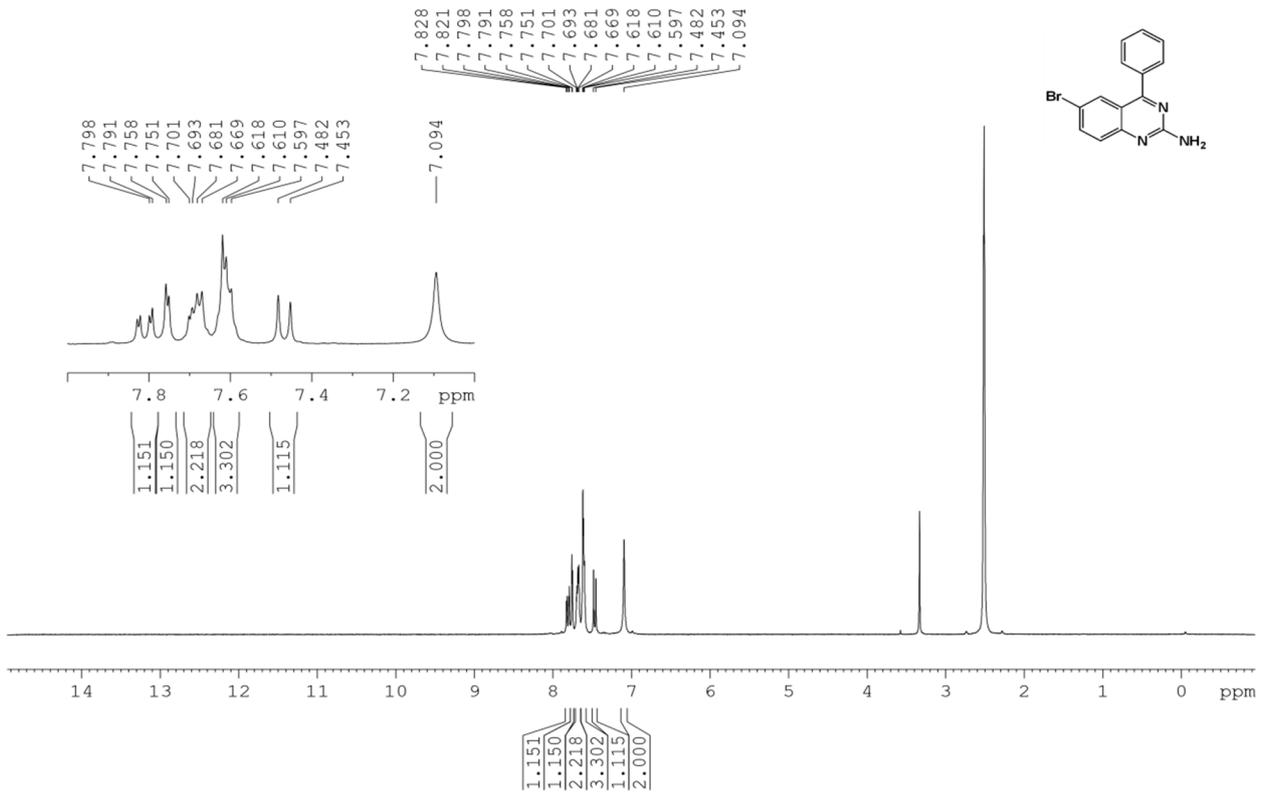
¹H- and ¹³C-NMR Spectra in DMSO-d₆ of compound 5a



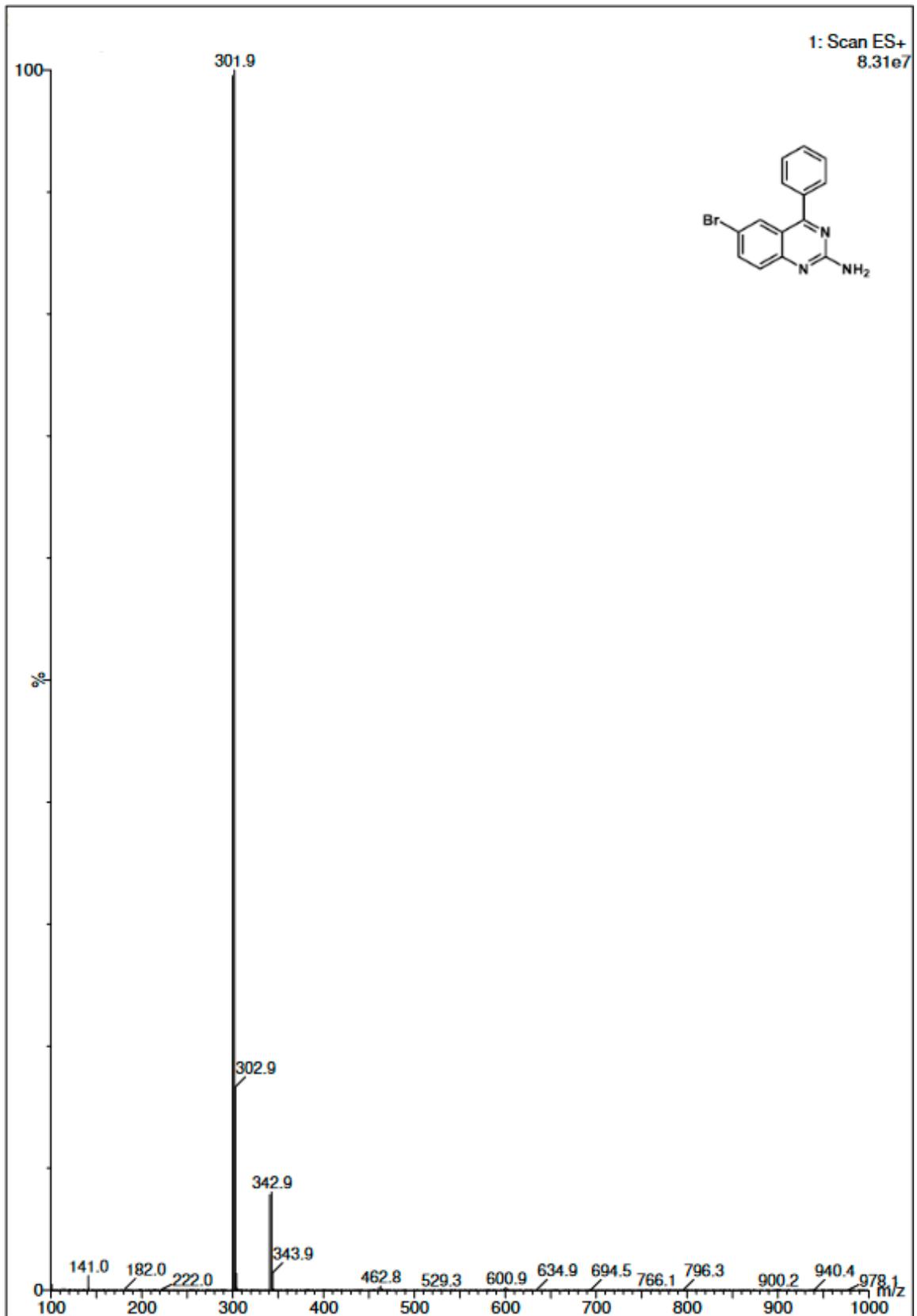
LC-MS mass spectrum of compound 5a



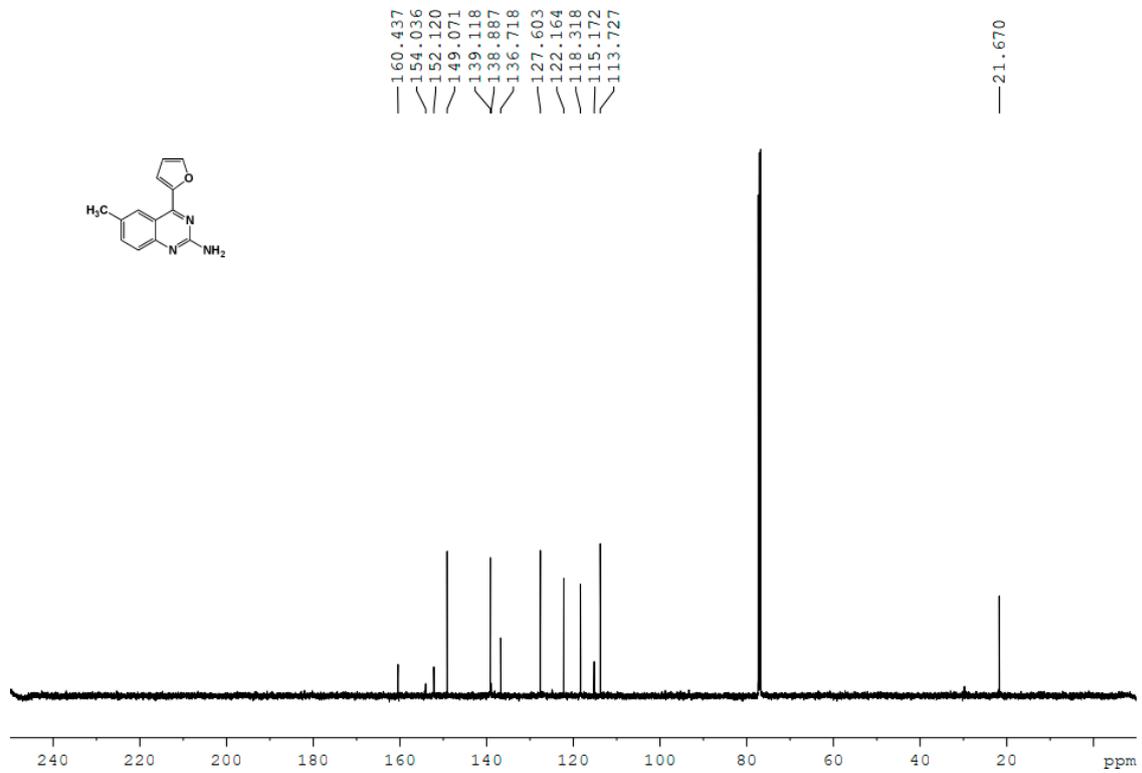
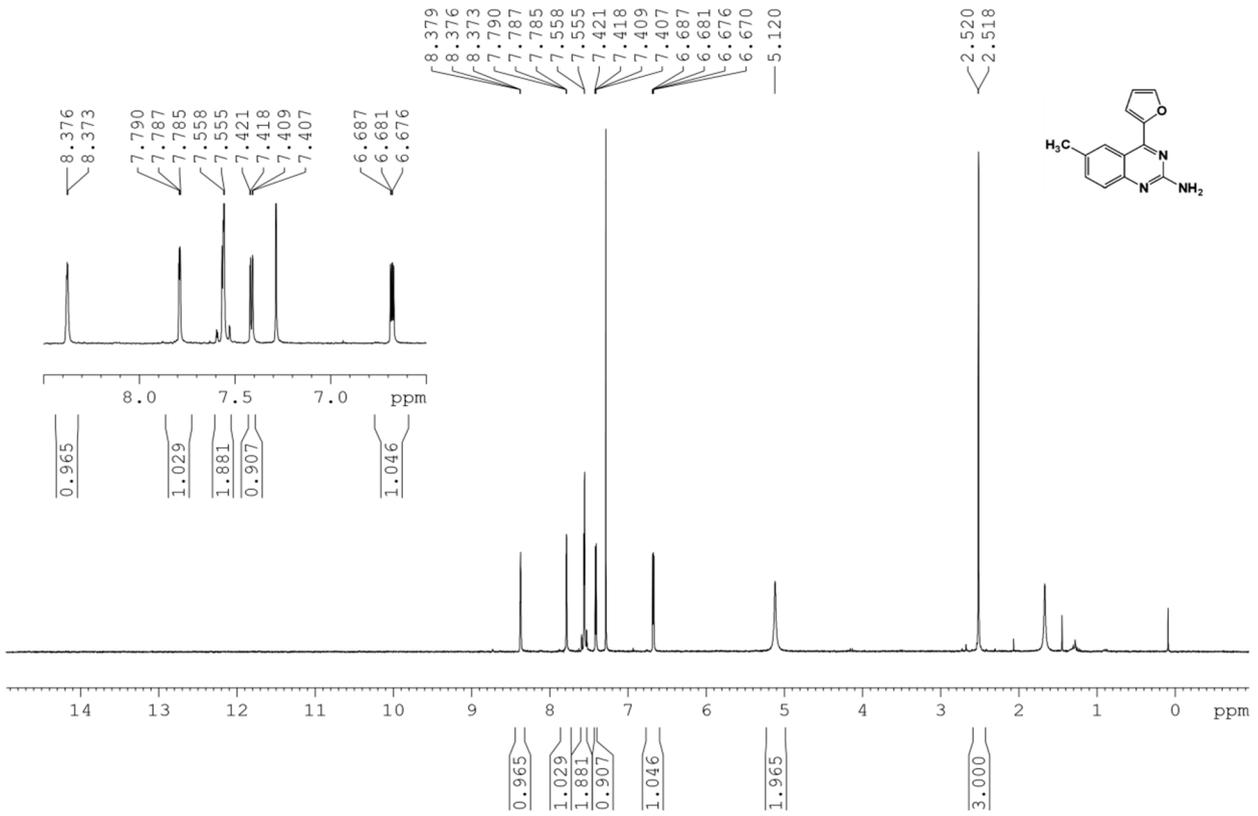
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5b



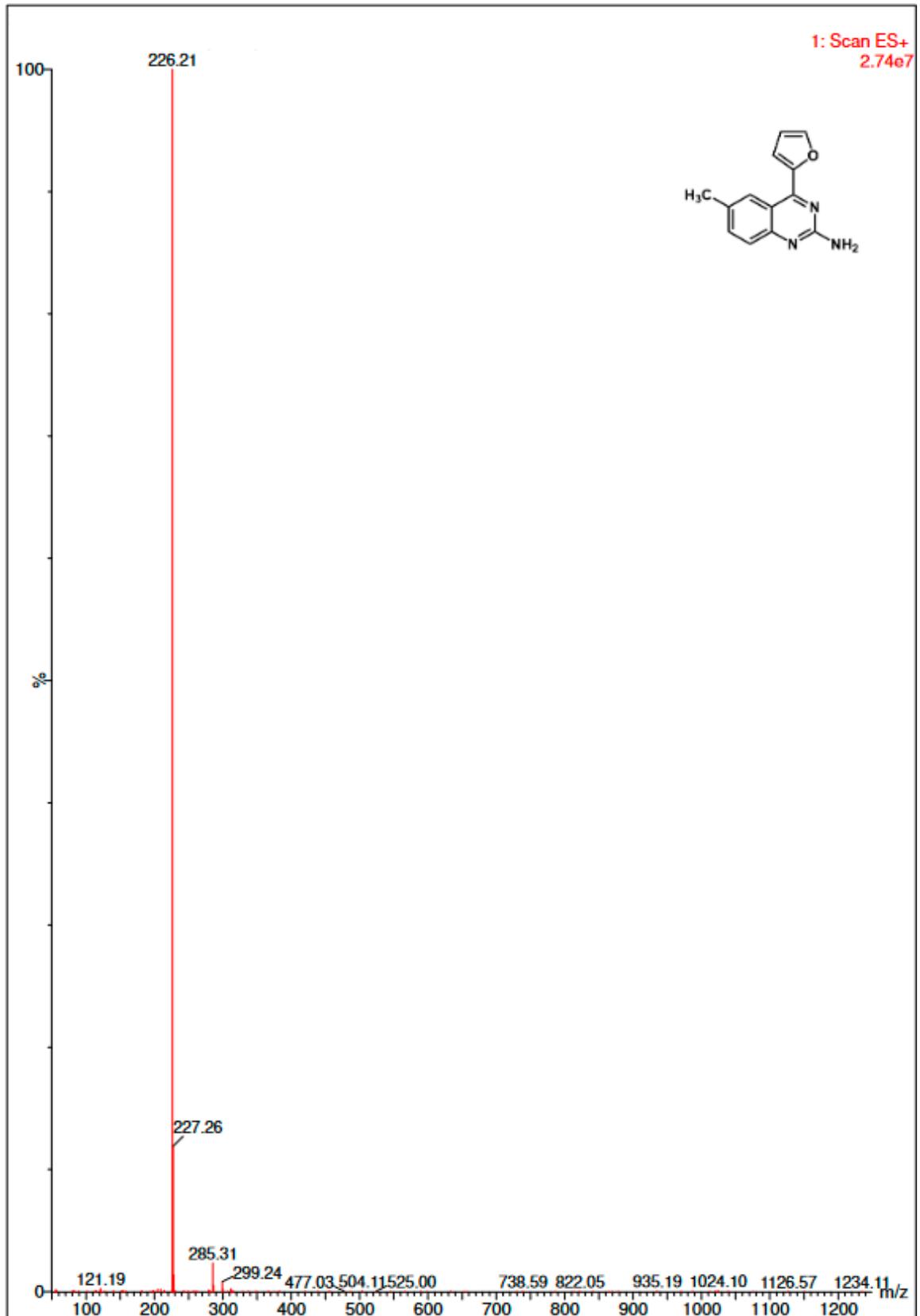
LC-MS mass spectrum of compound 5b



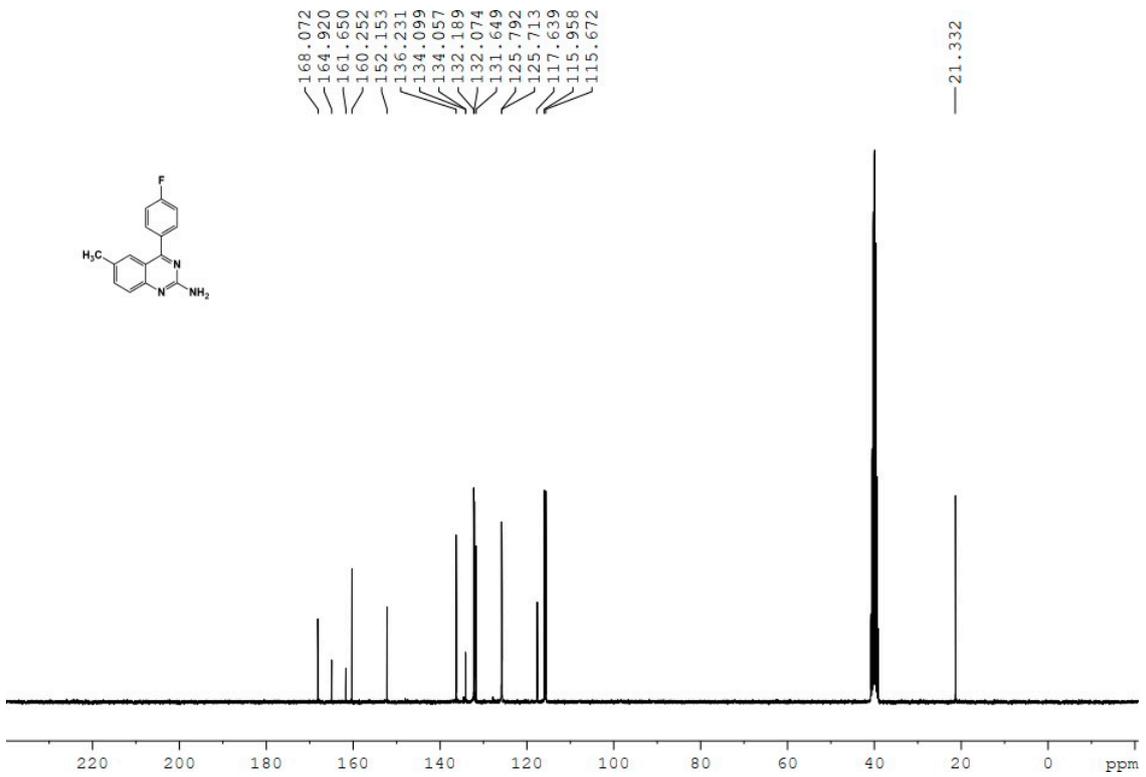
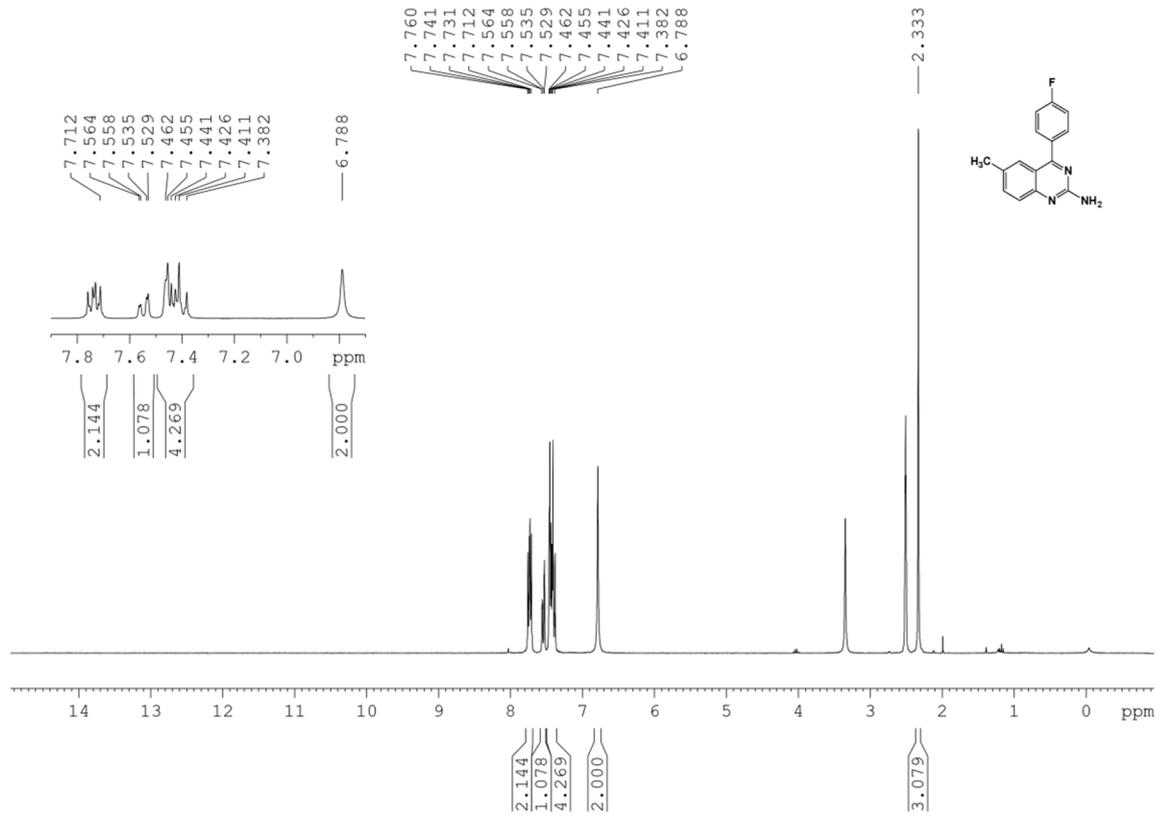
1H- and 13C-NMR Spectra in CDCl₃ of compound 5c



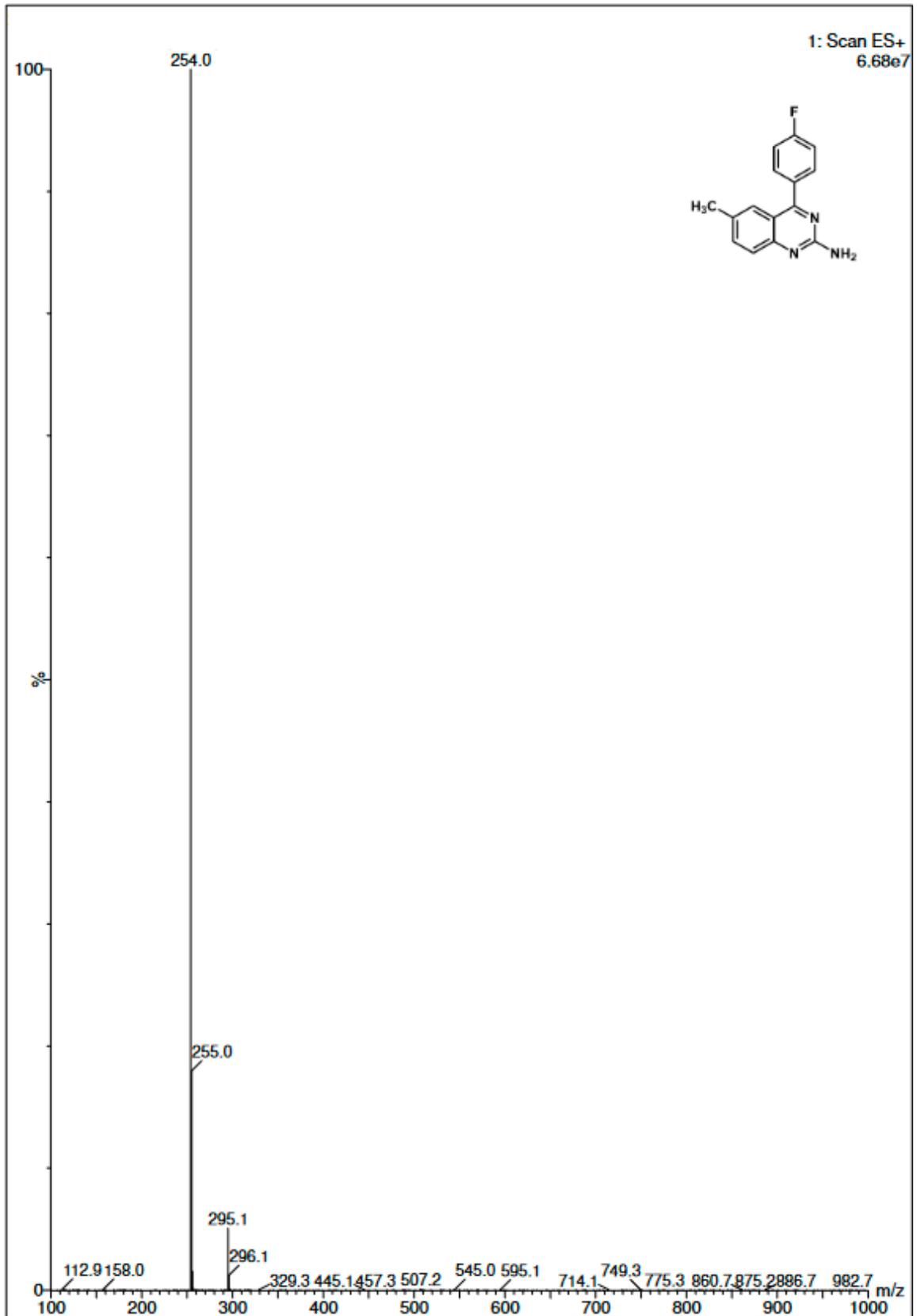
LC-MS mass spectrum of compound 5c



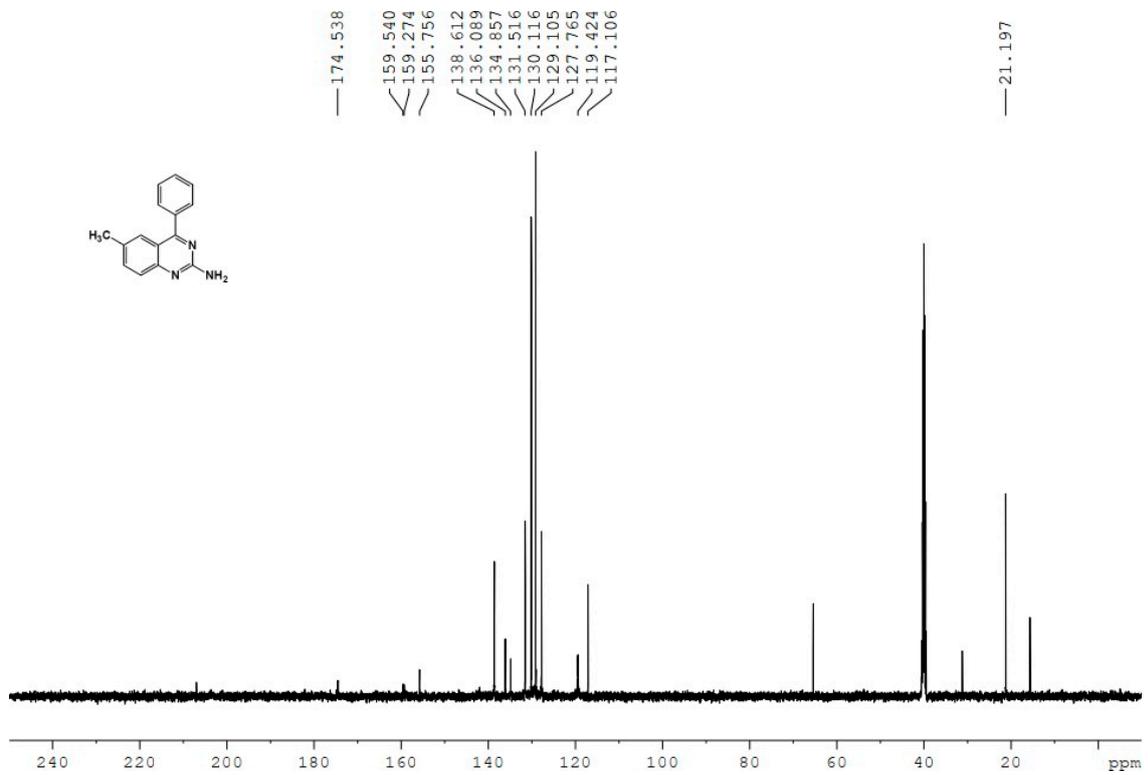
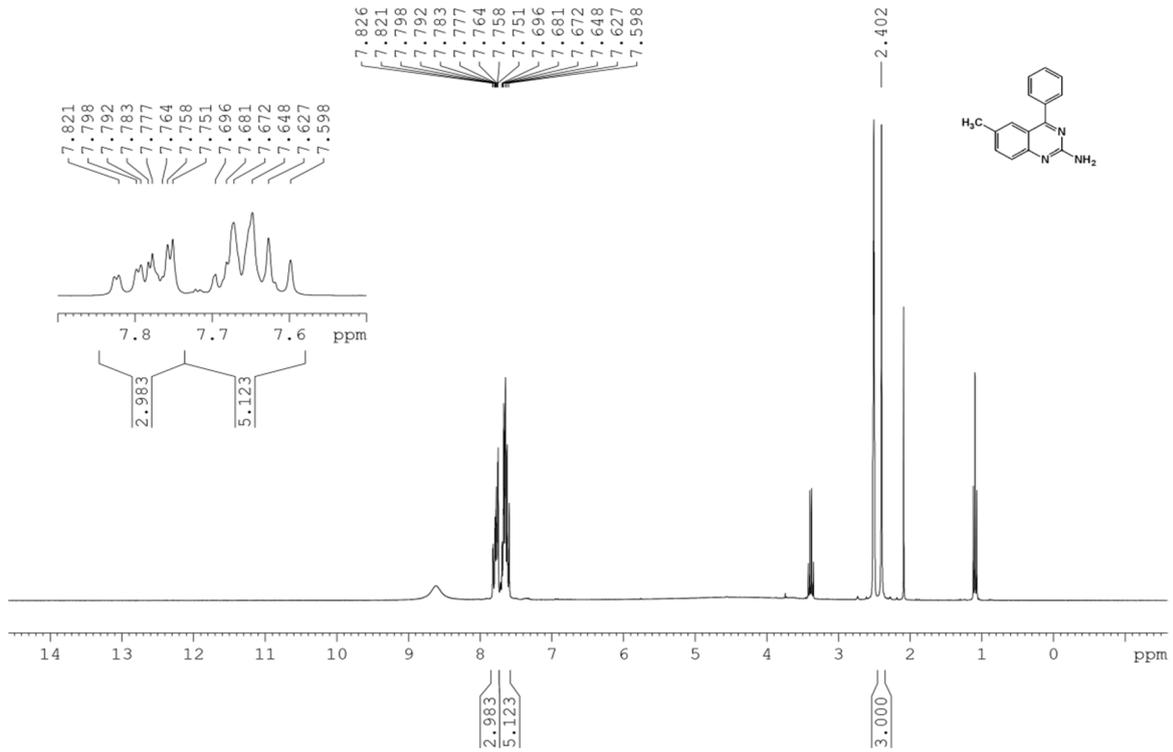
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5d



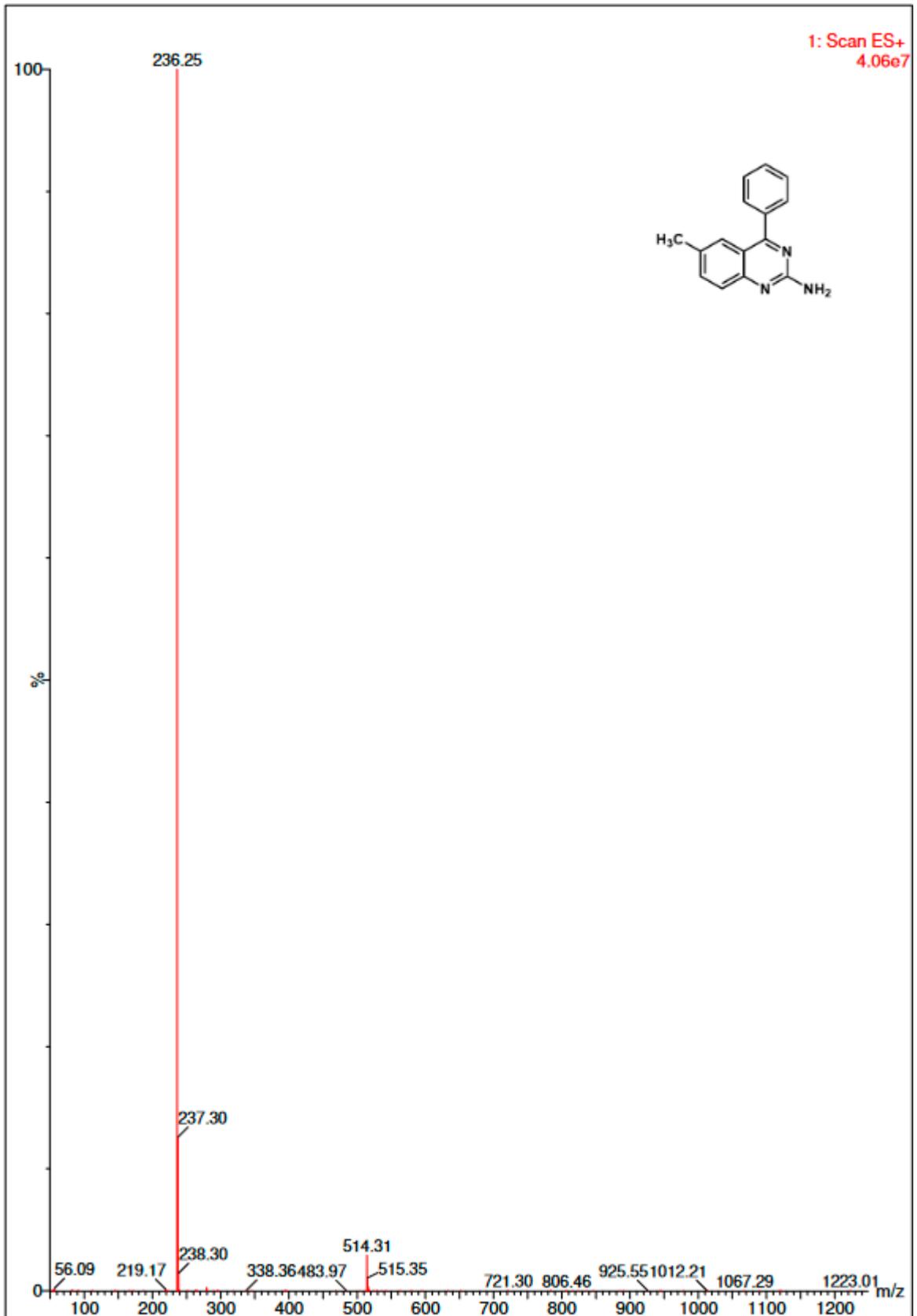
LC-MS mass spectrum of compound 5d



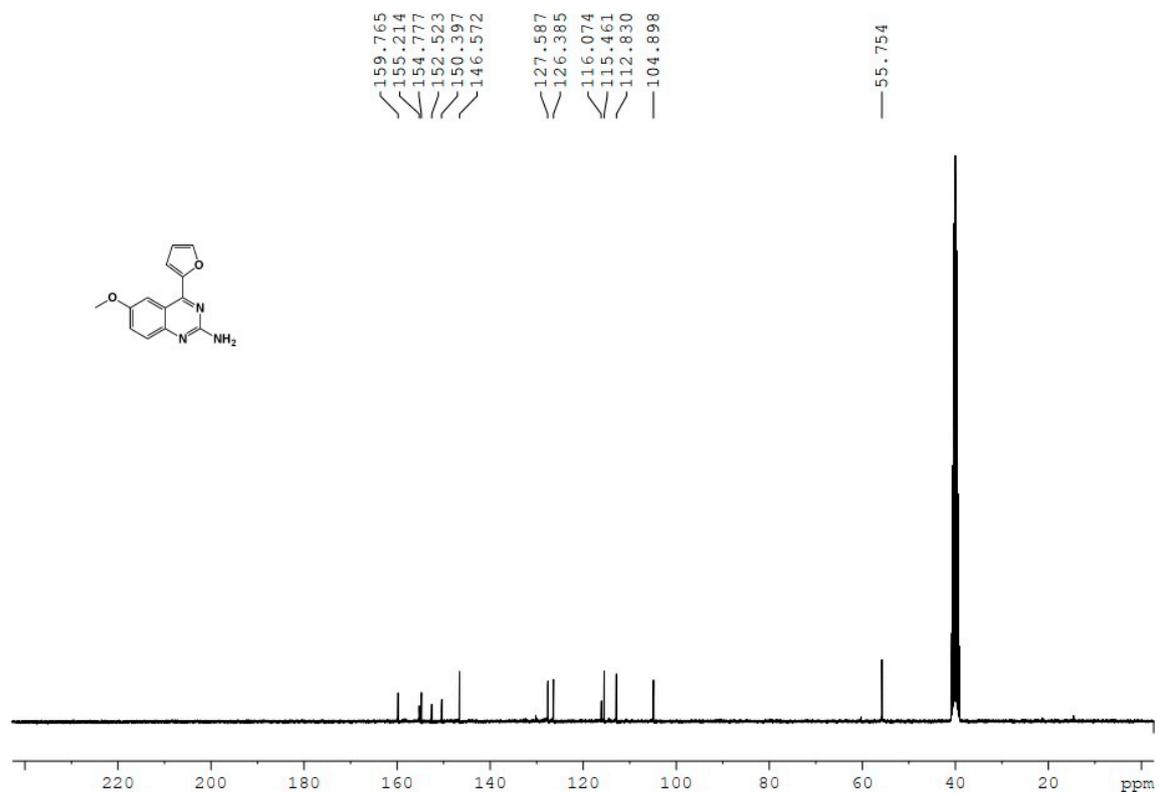
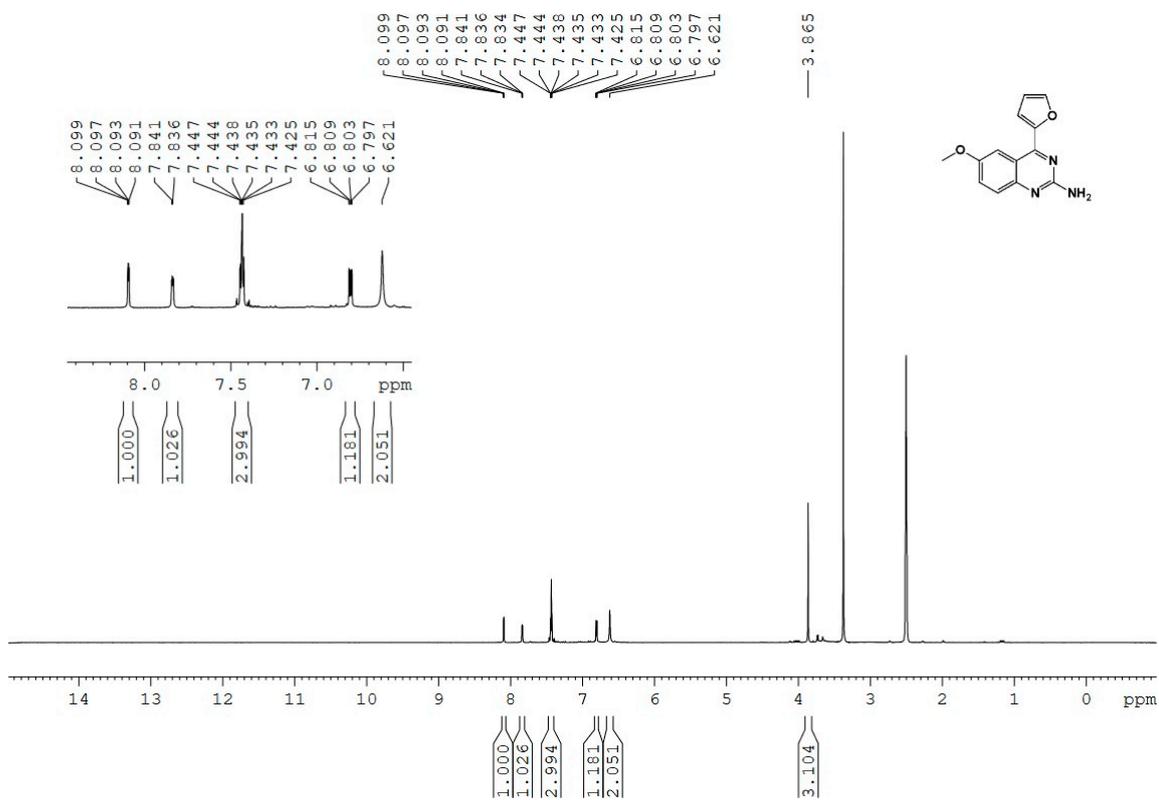
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5e



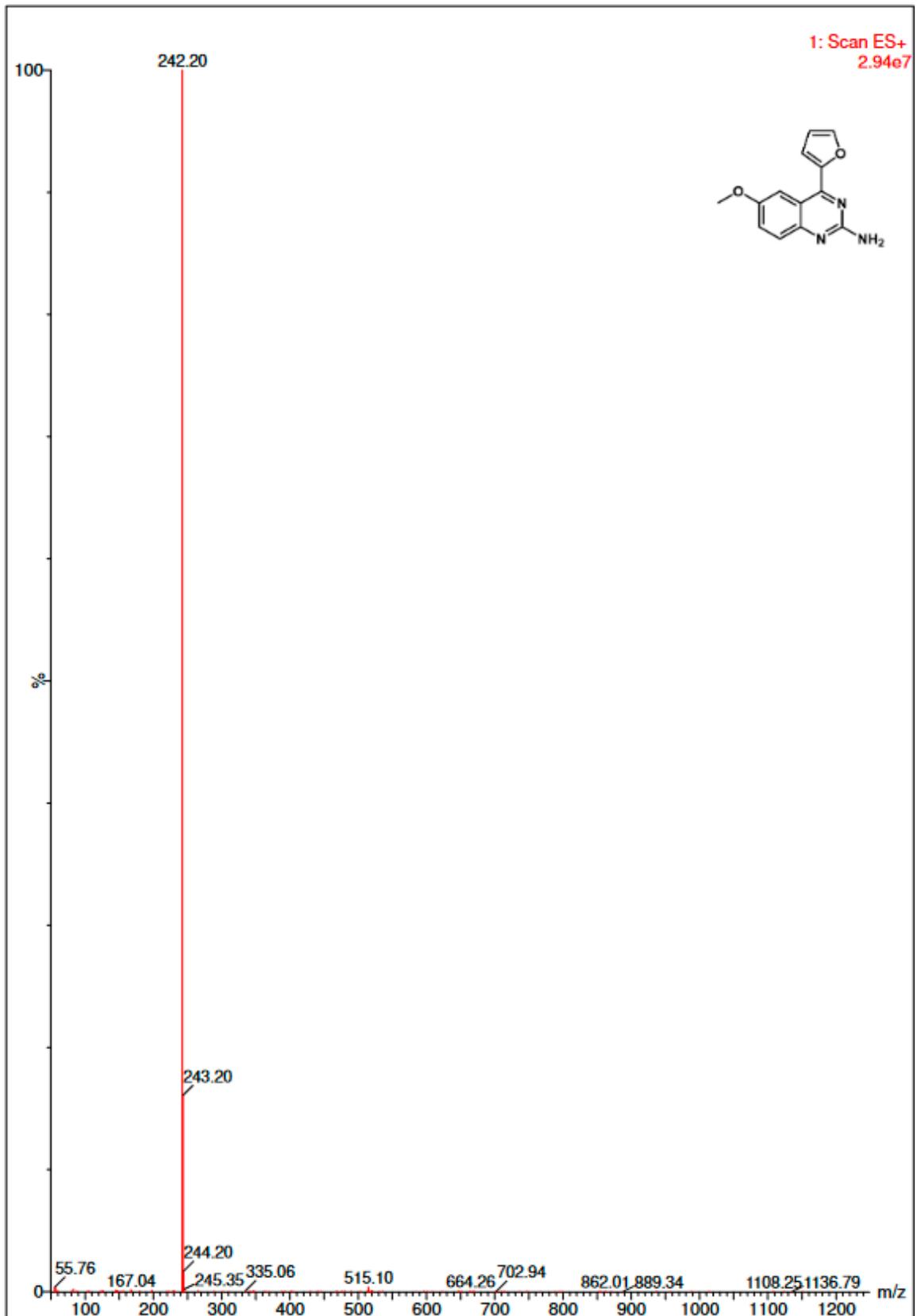
LC-MS mass spectrum of compound 5e



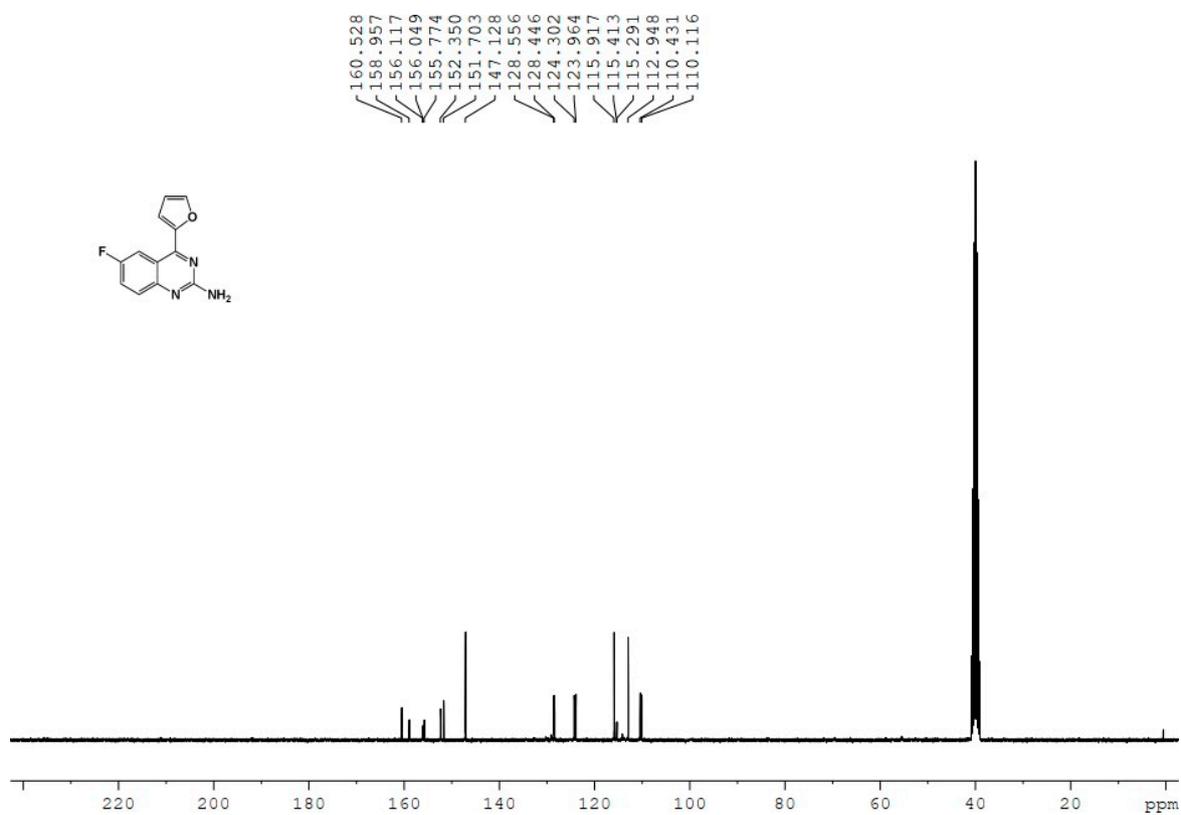
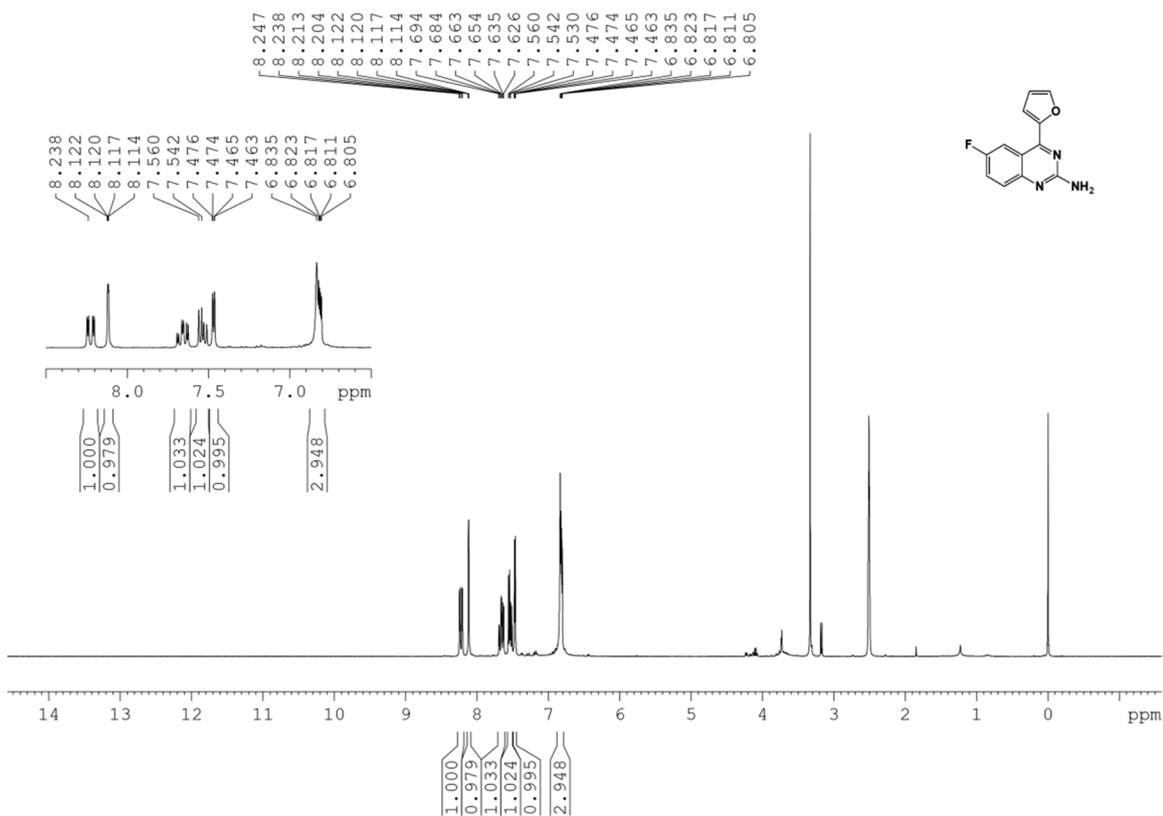
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5f



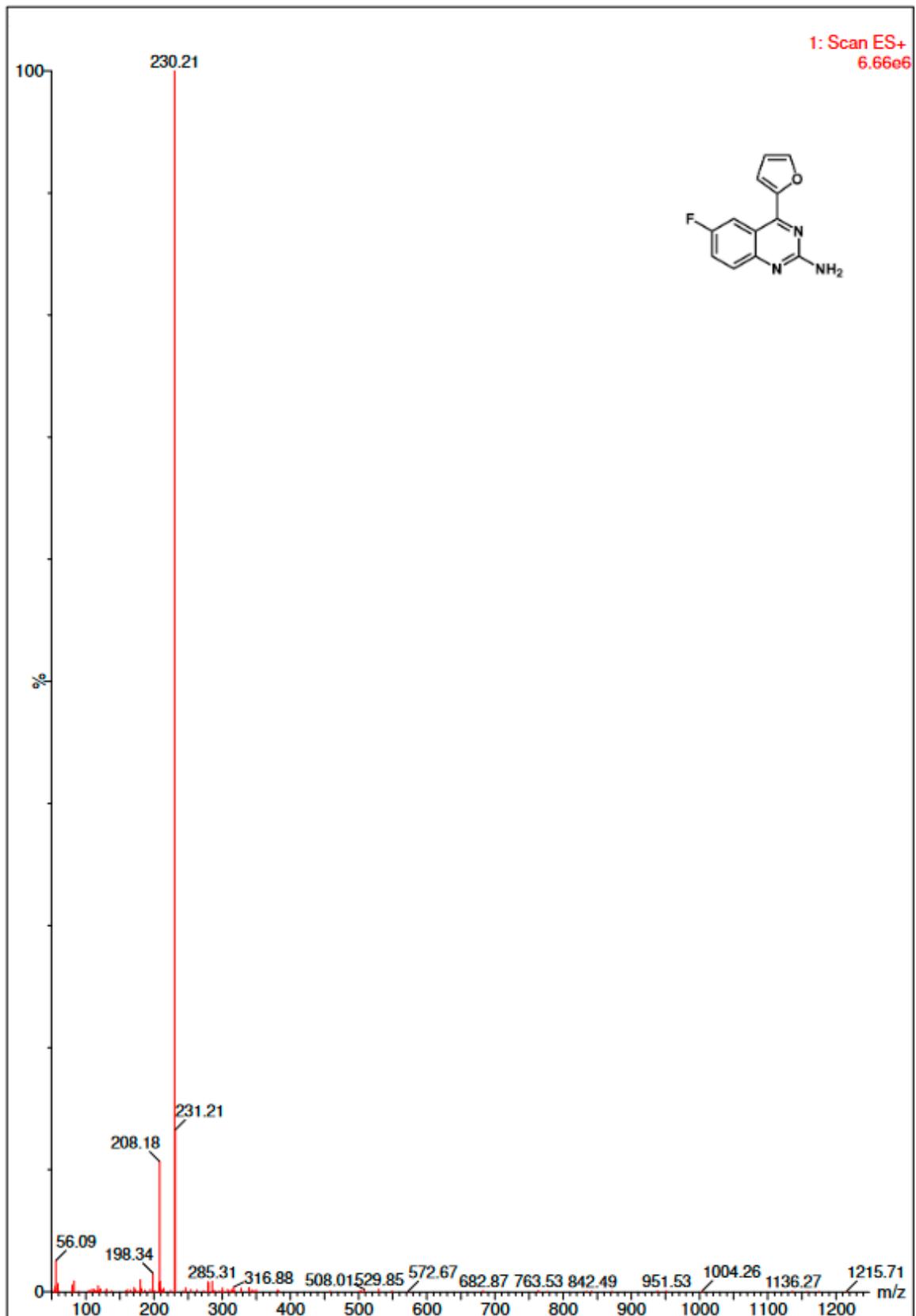
LC-MS mass spectrum of compound 5f



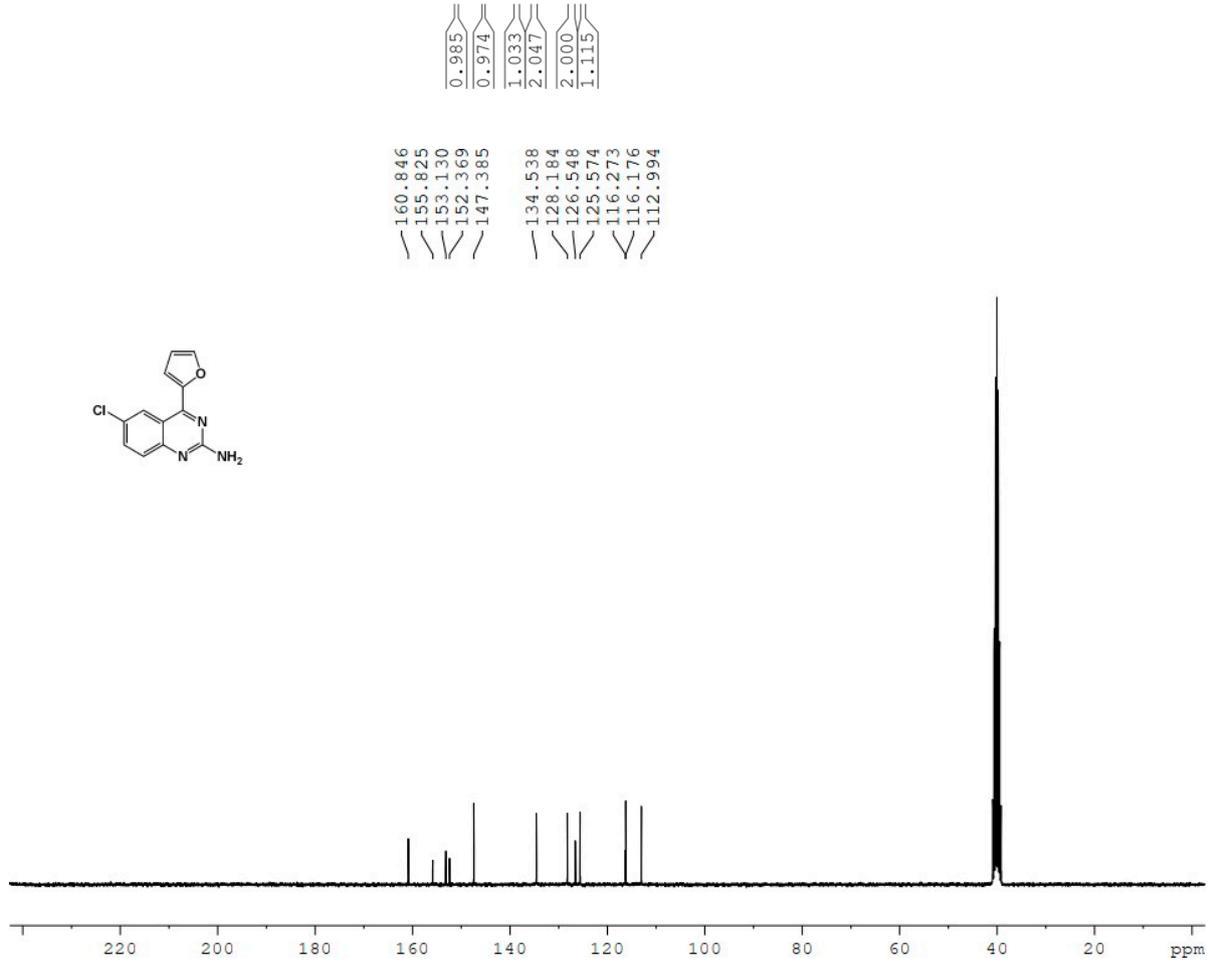
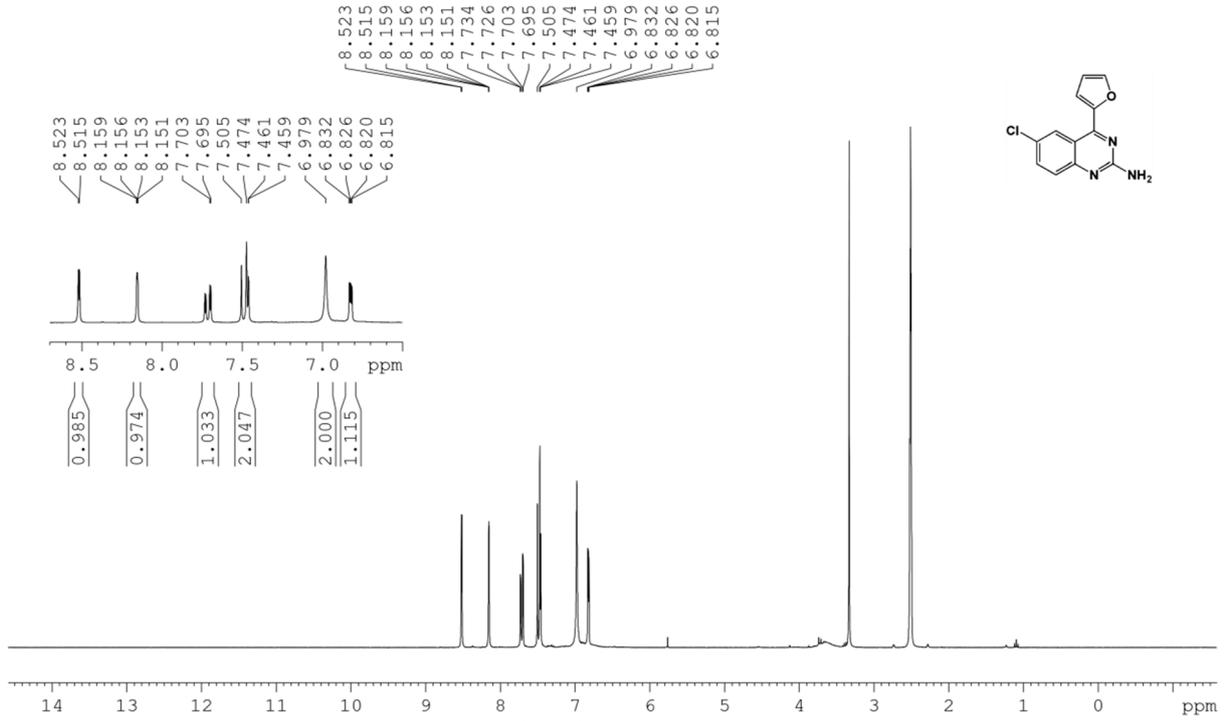
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5g



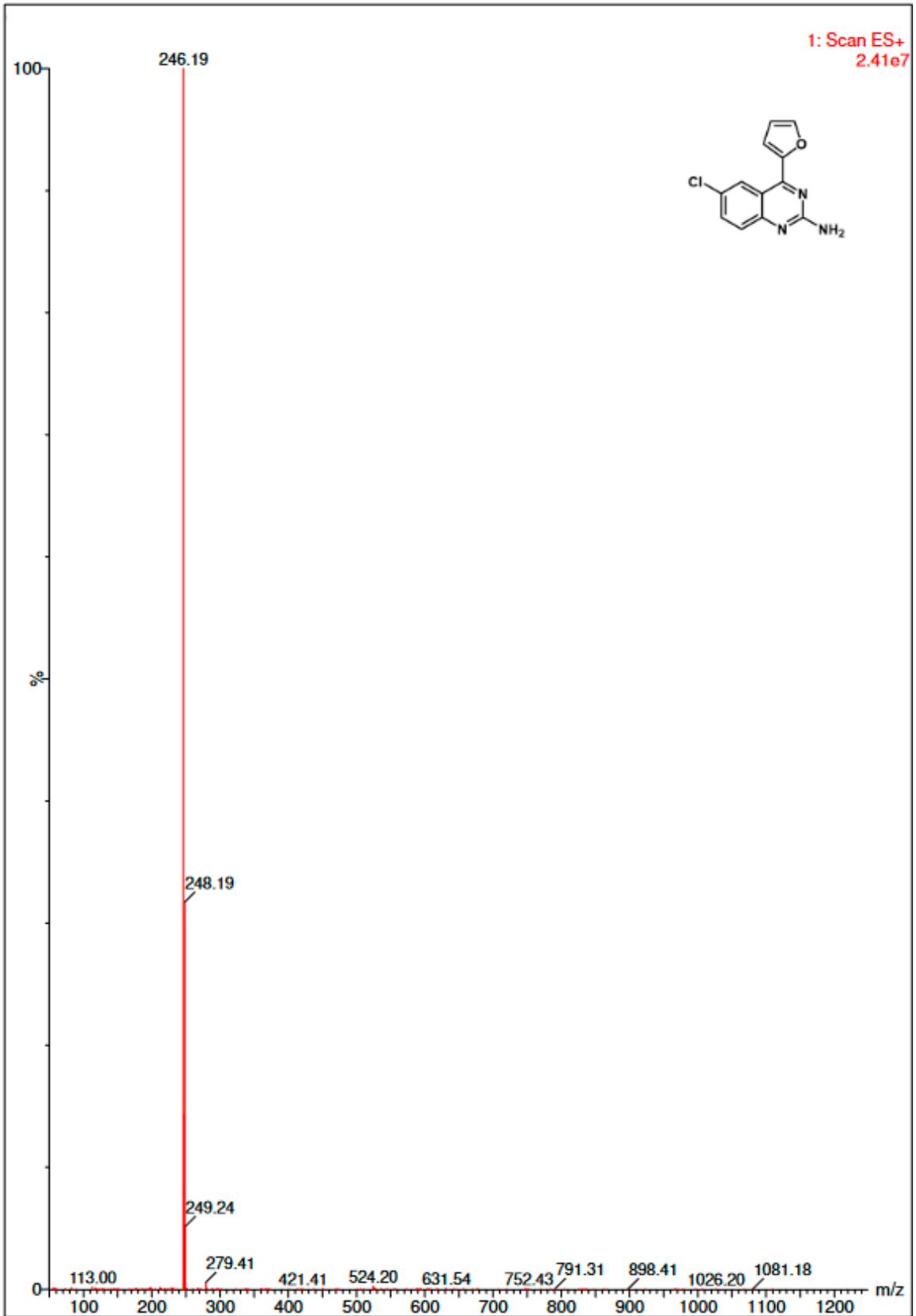
LC-MS mass spectrum of compound 5g



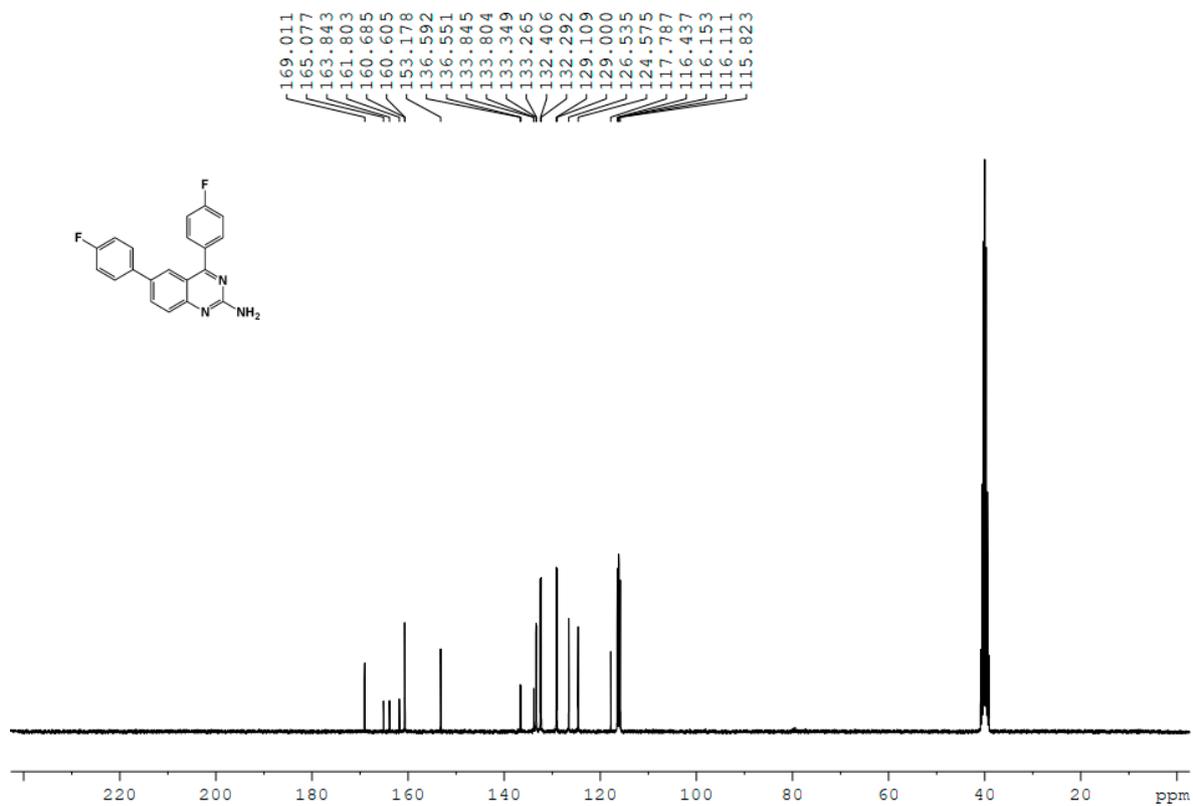
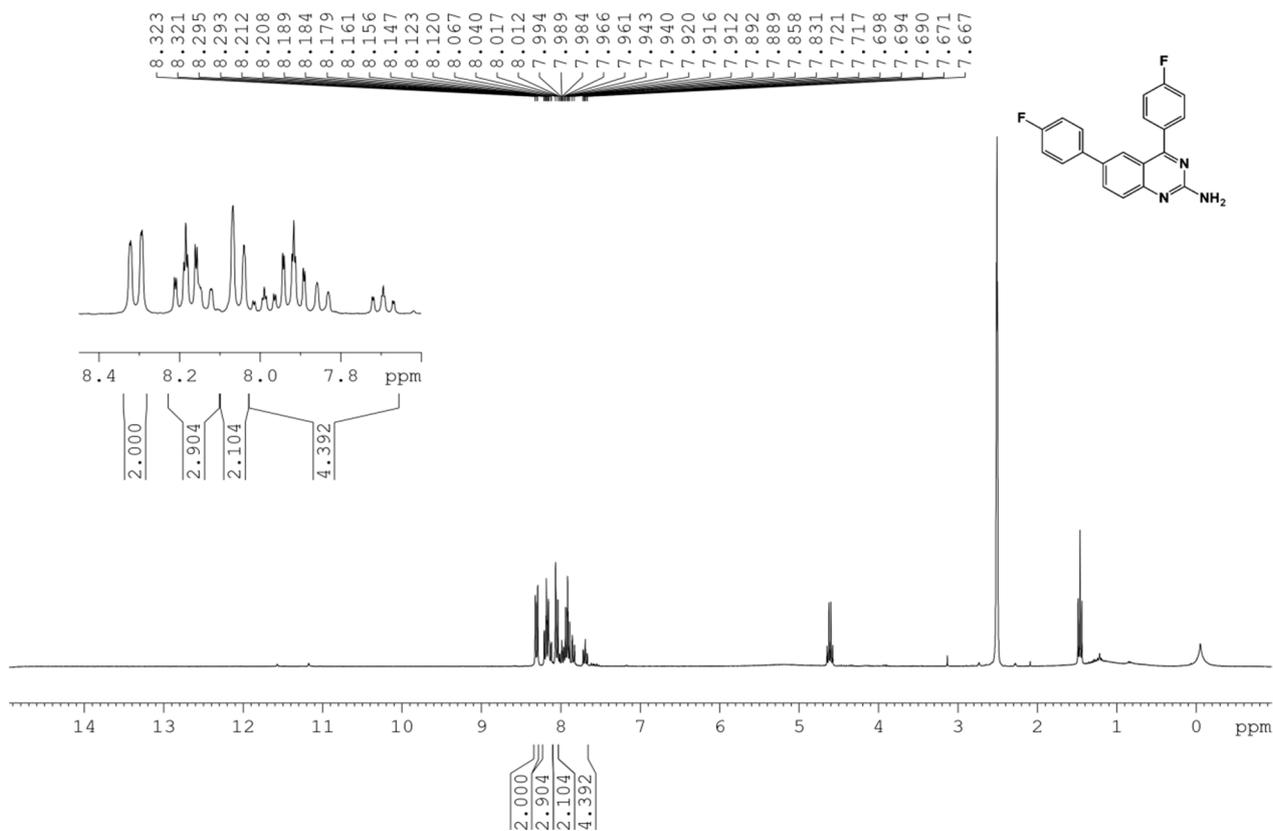
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5h



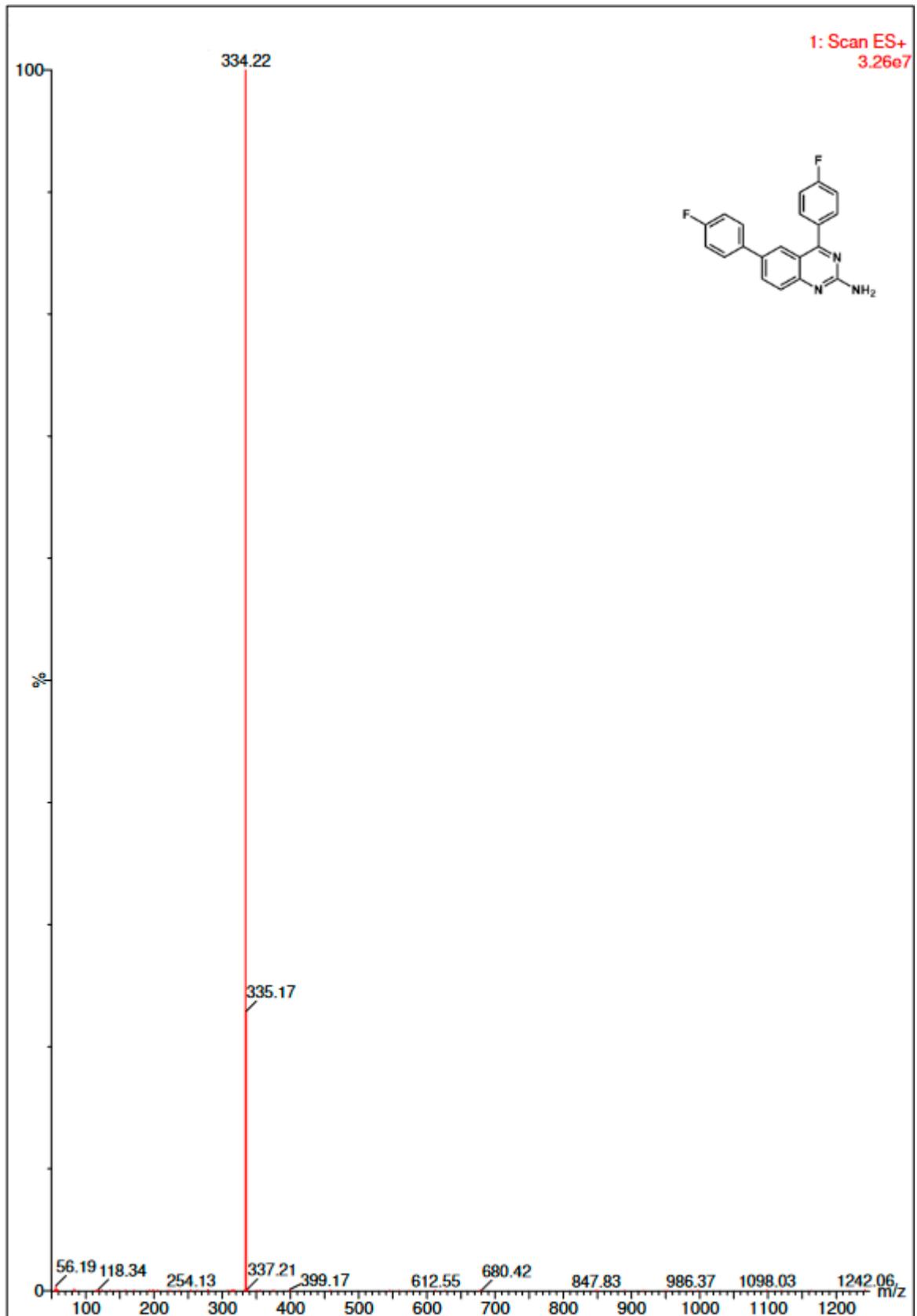
LC-MS mass spectrum of compound 5h



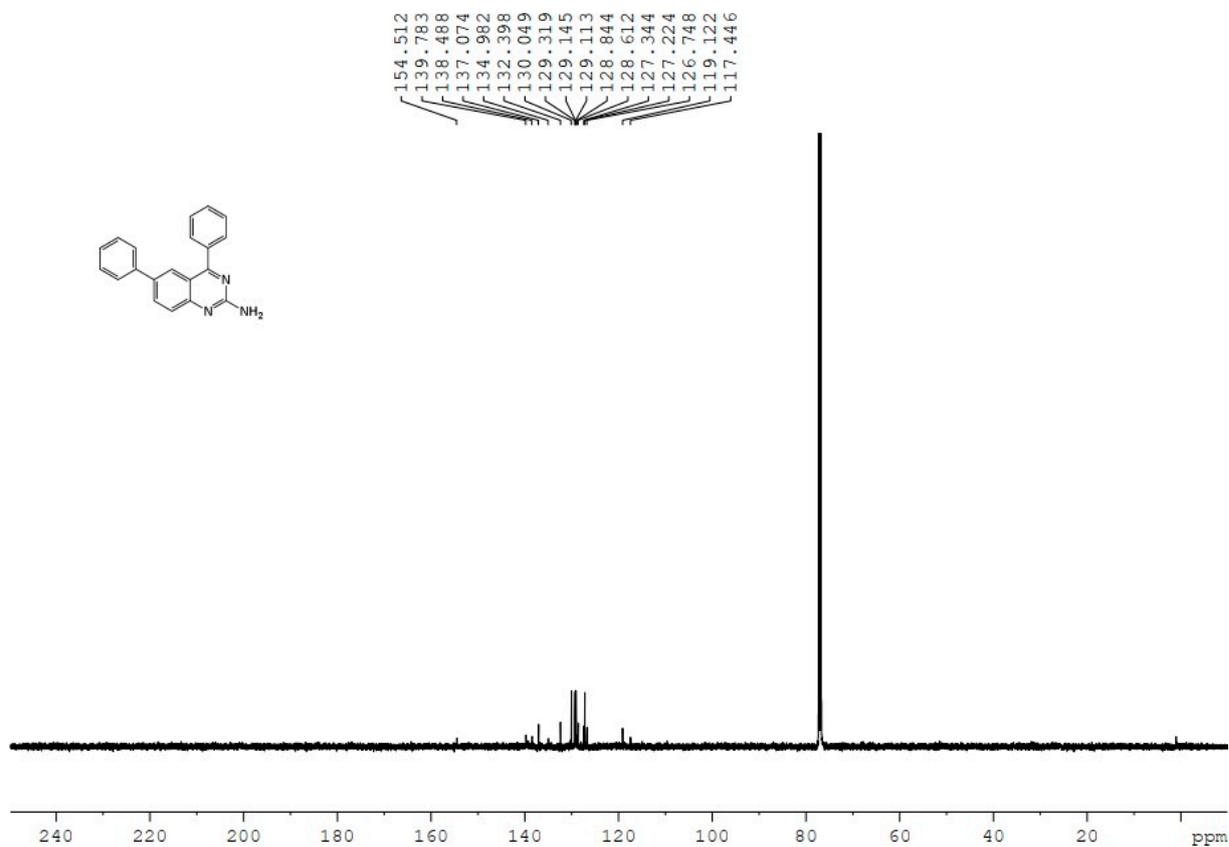
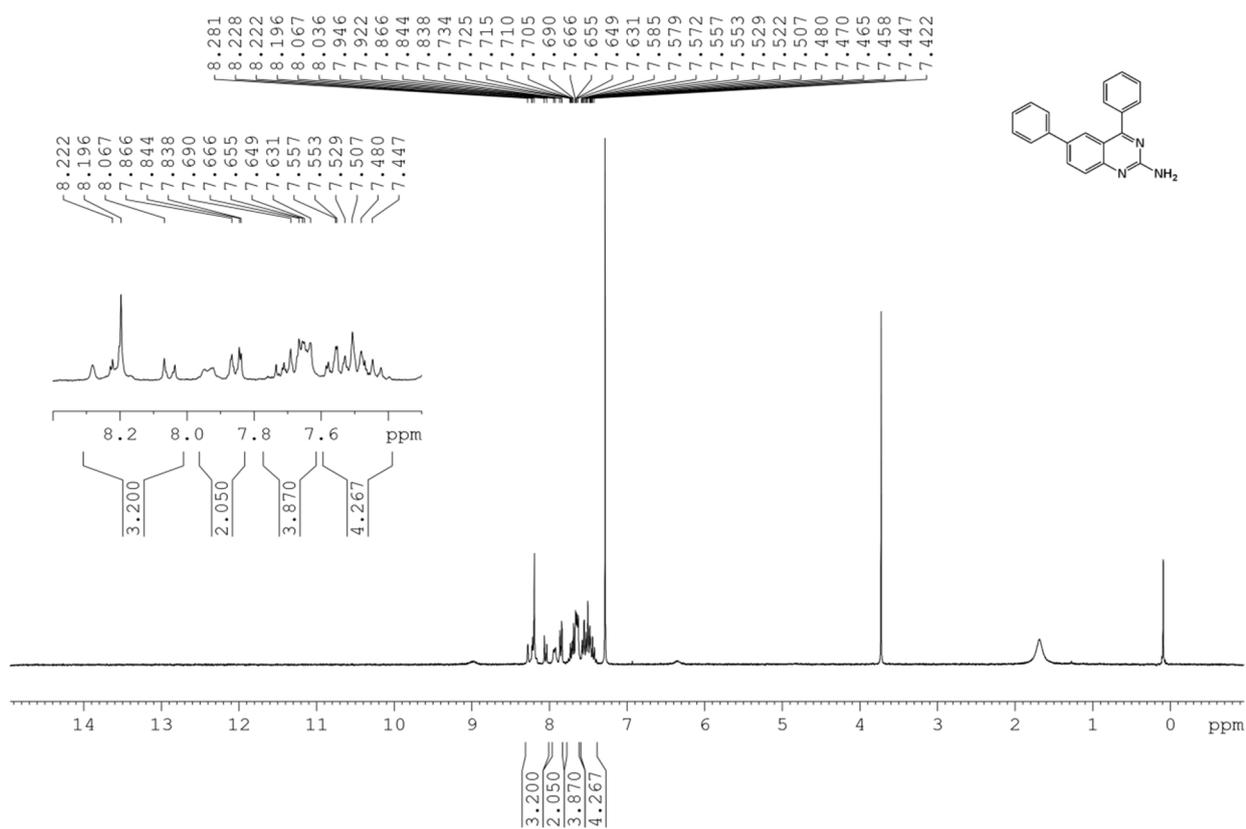
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5i



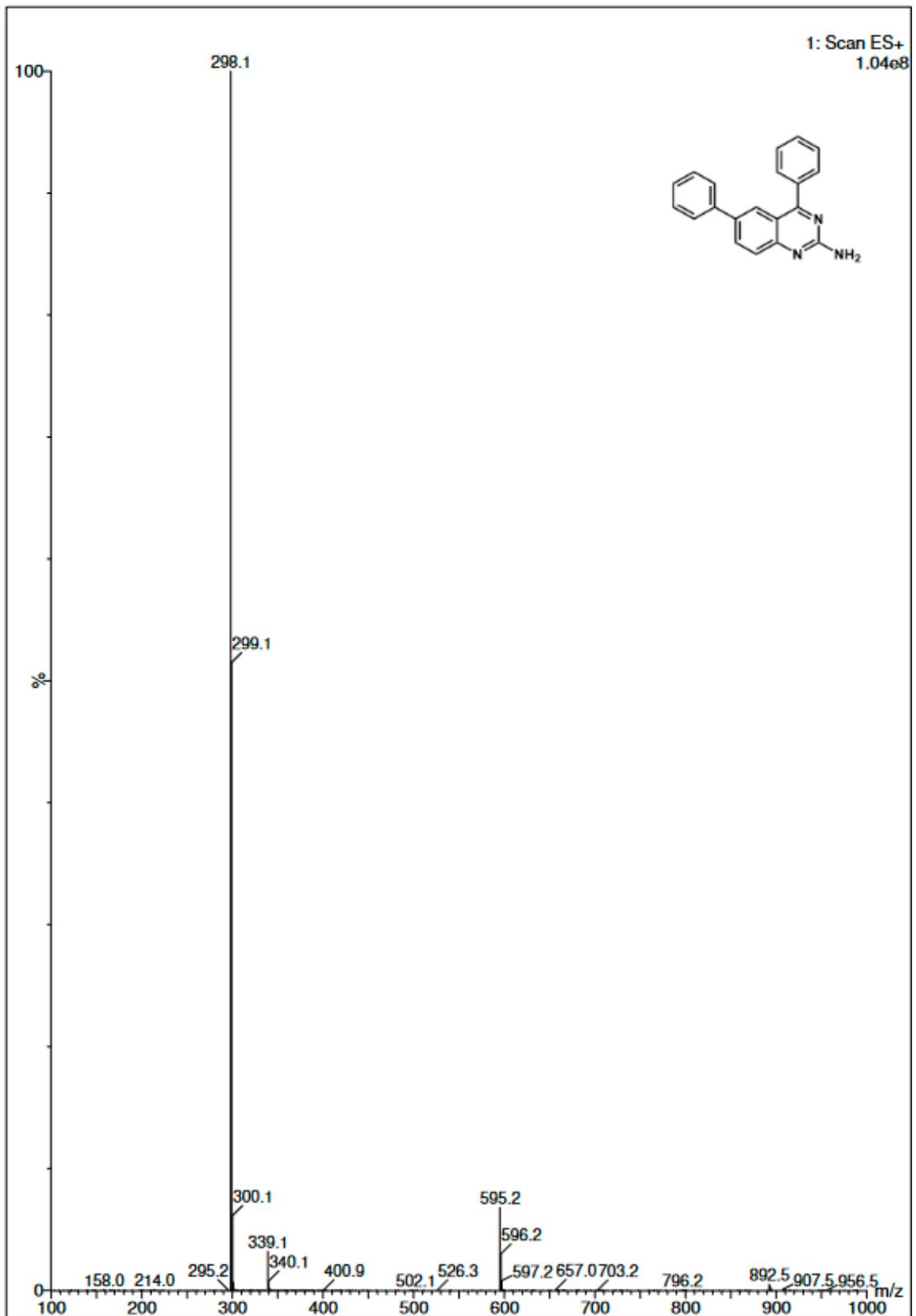
LC-MS mass spectrum of compound 5i



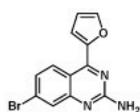
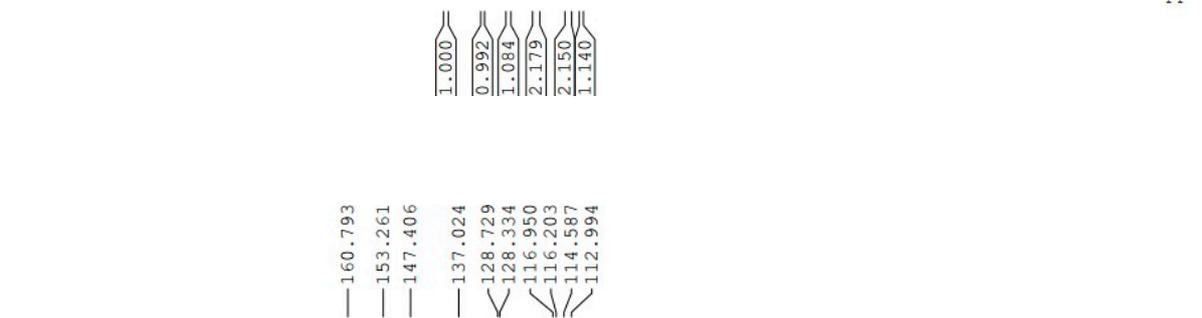
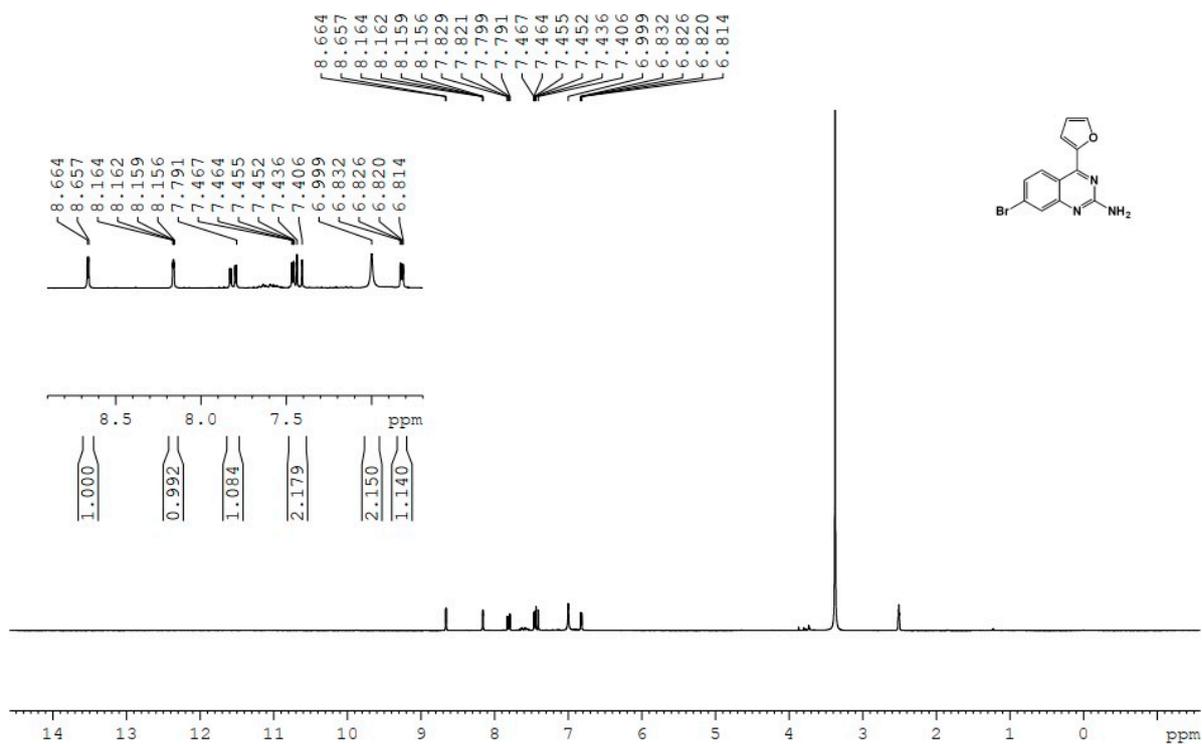
1H- and 13C-NMR Spectra in CDCl₃ of compound 5j



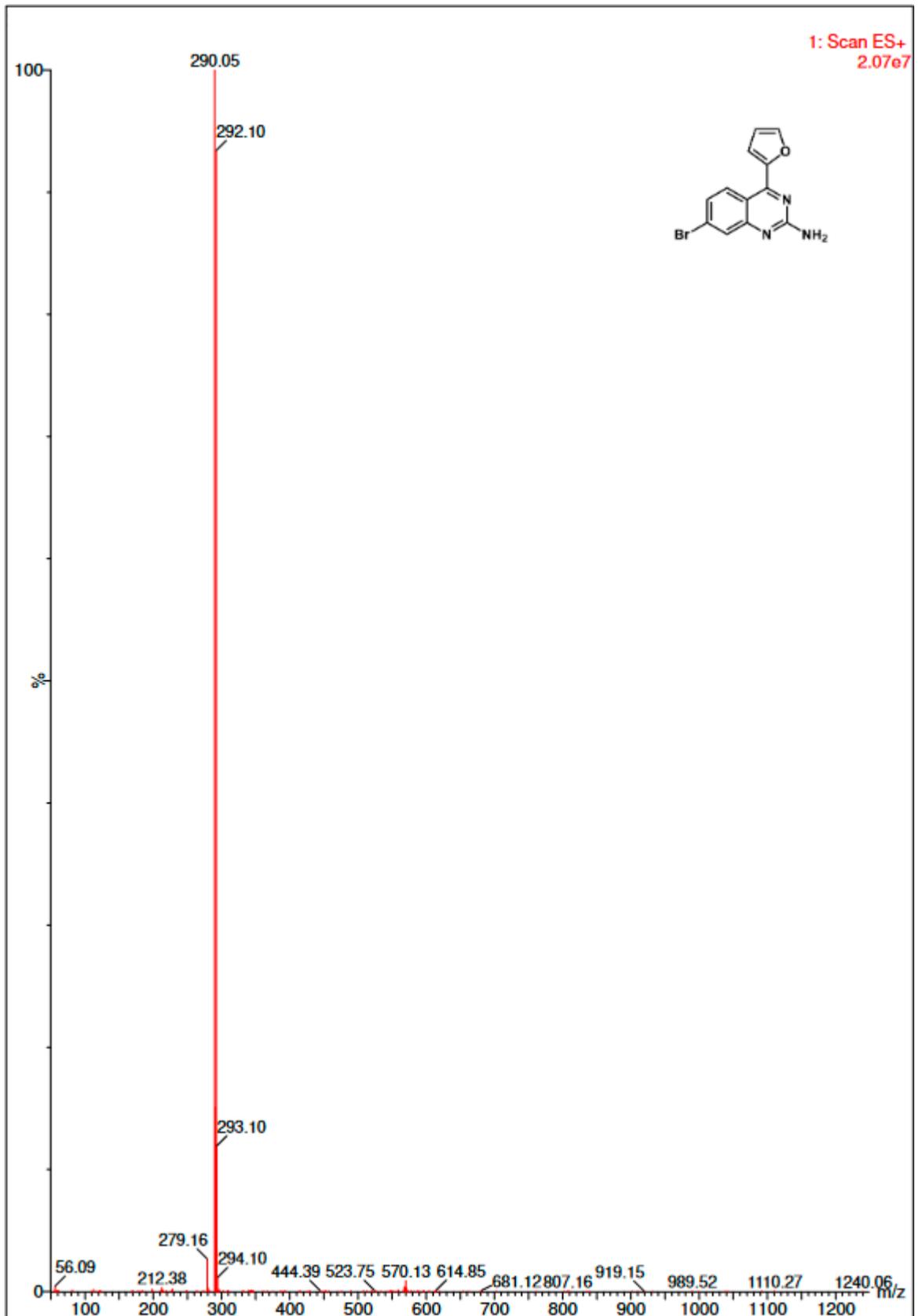
LC-MS mass spectrum of compound 5j



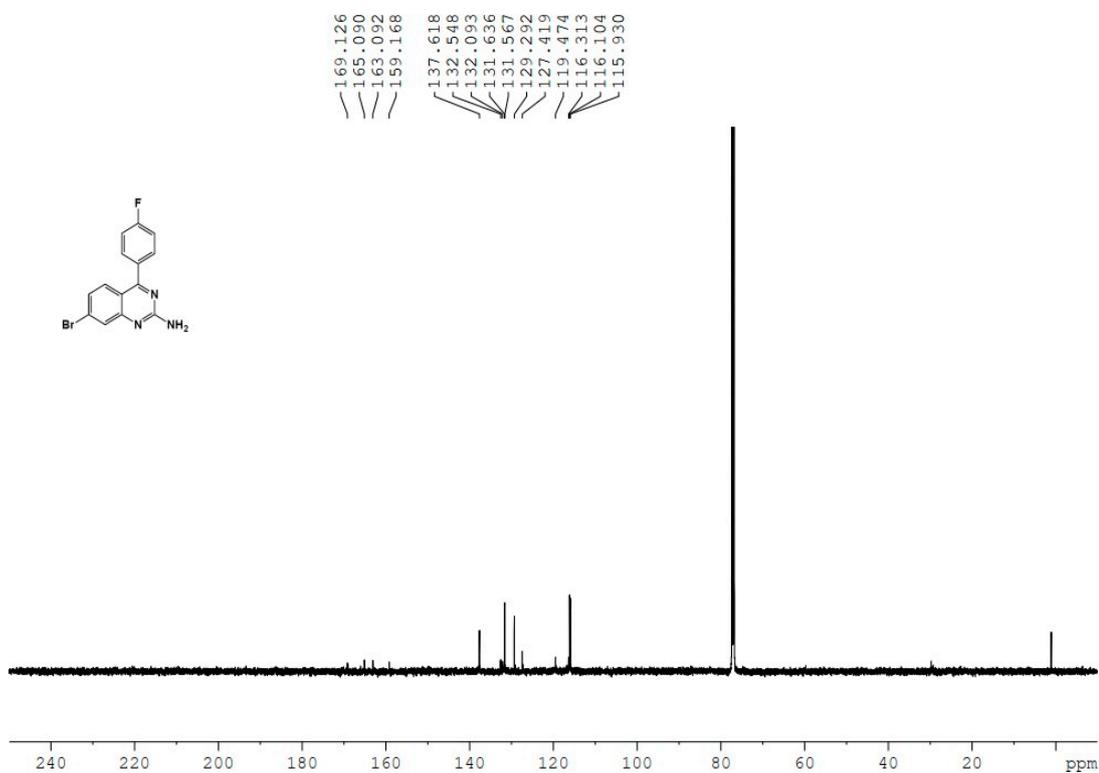
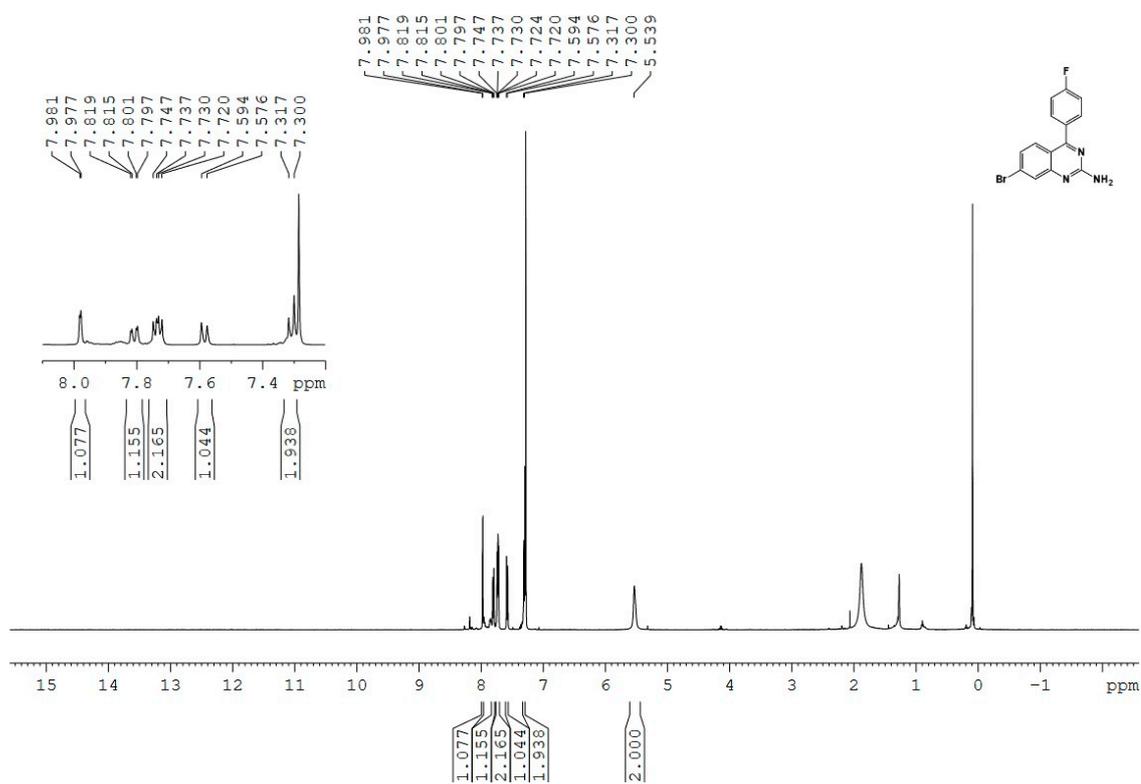
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5k



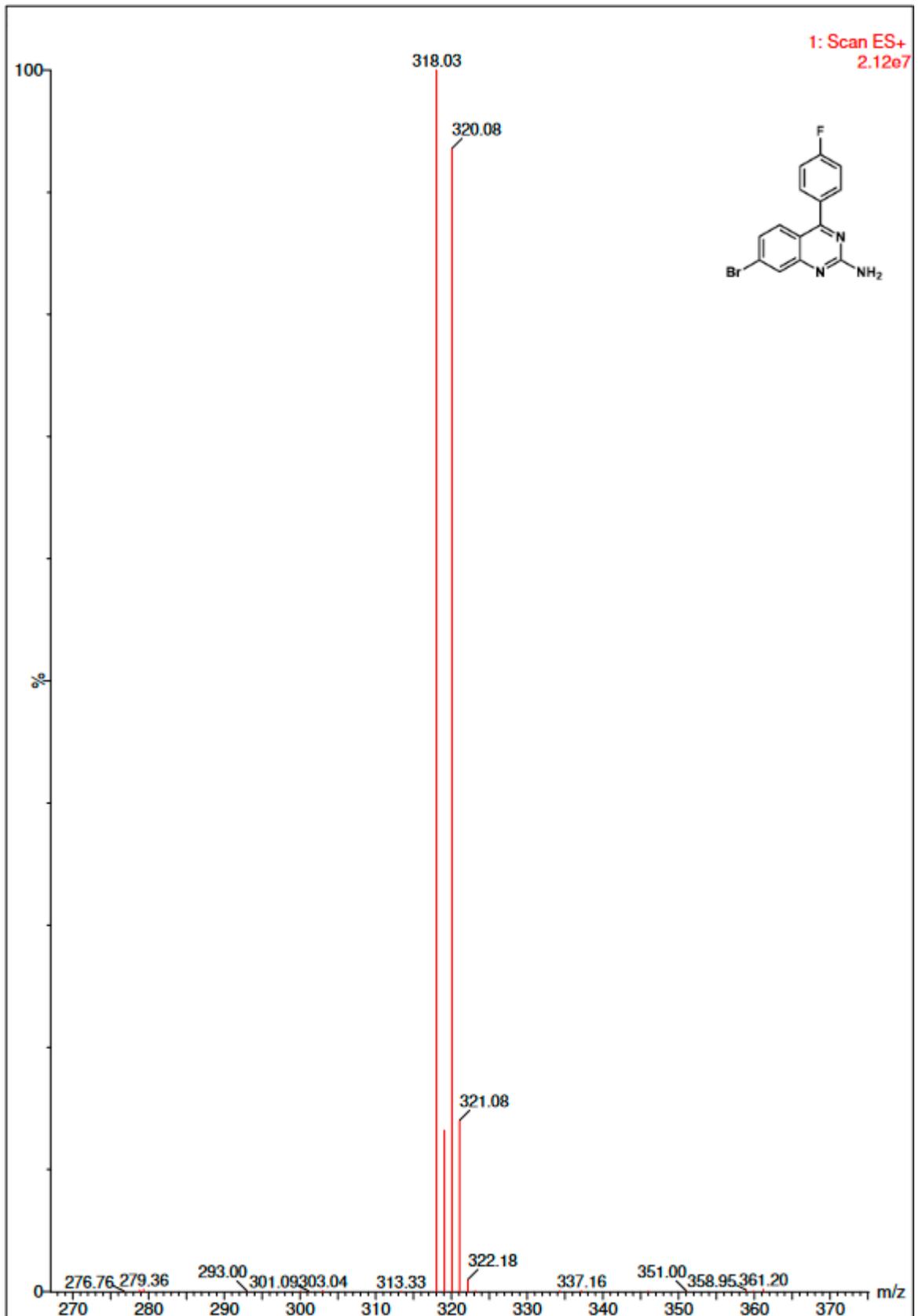
LC-MS mass spectrum of compound 5k



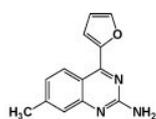
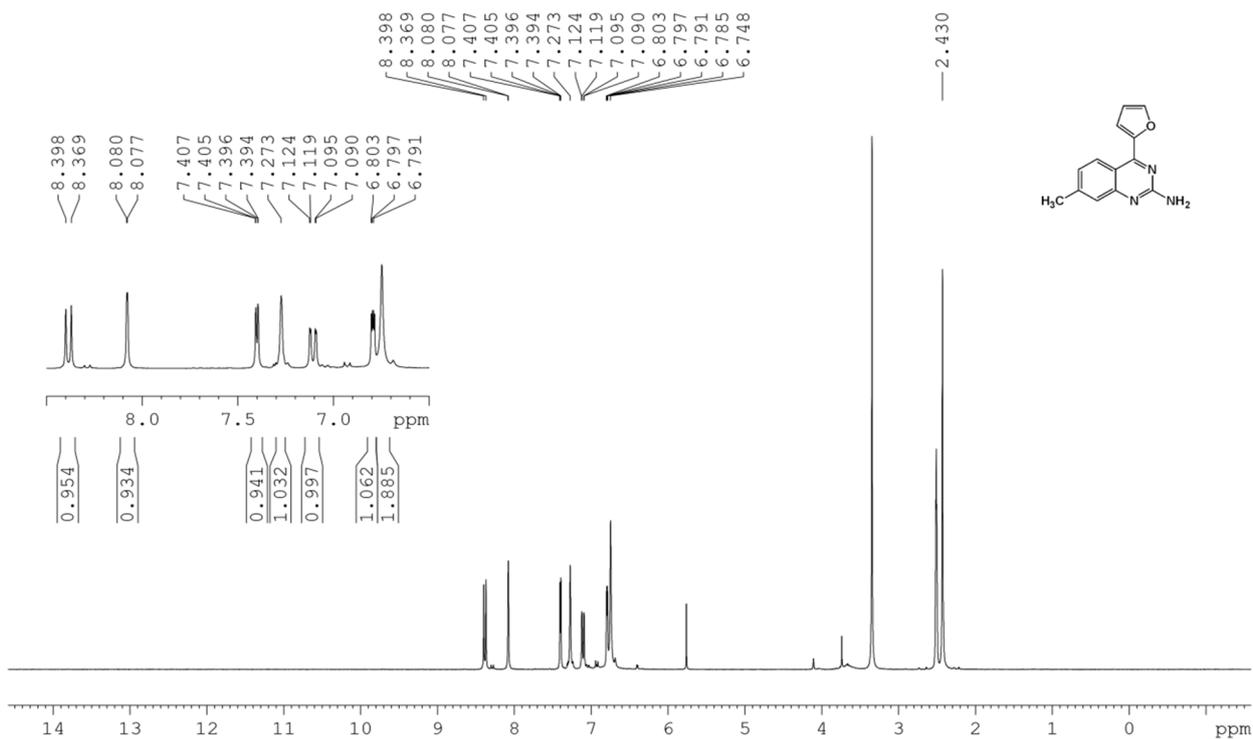
1H- and 13C-NMR Spectra in CDCl₃ of compound 5I



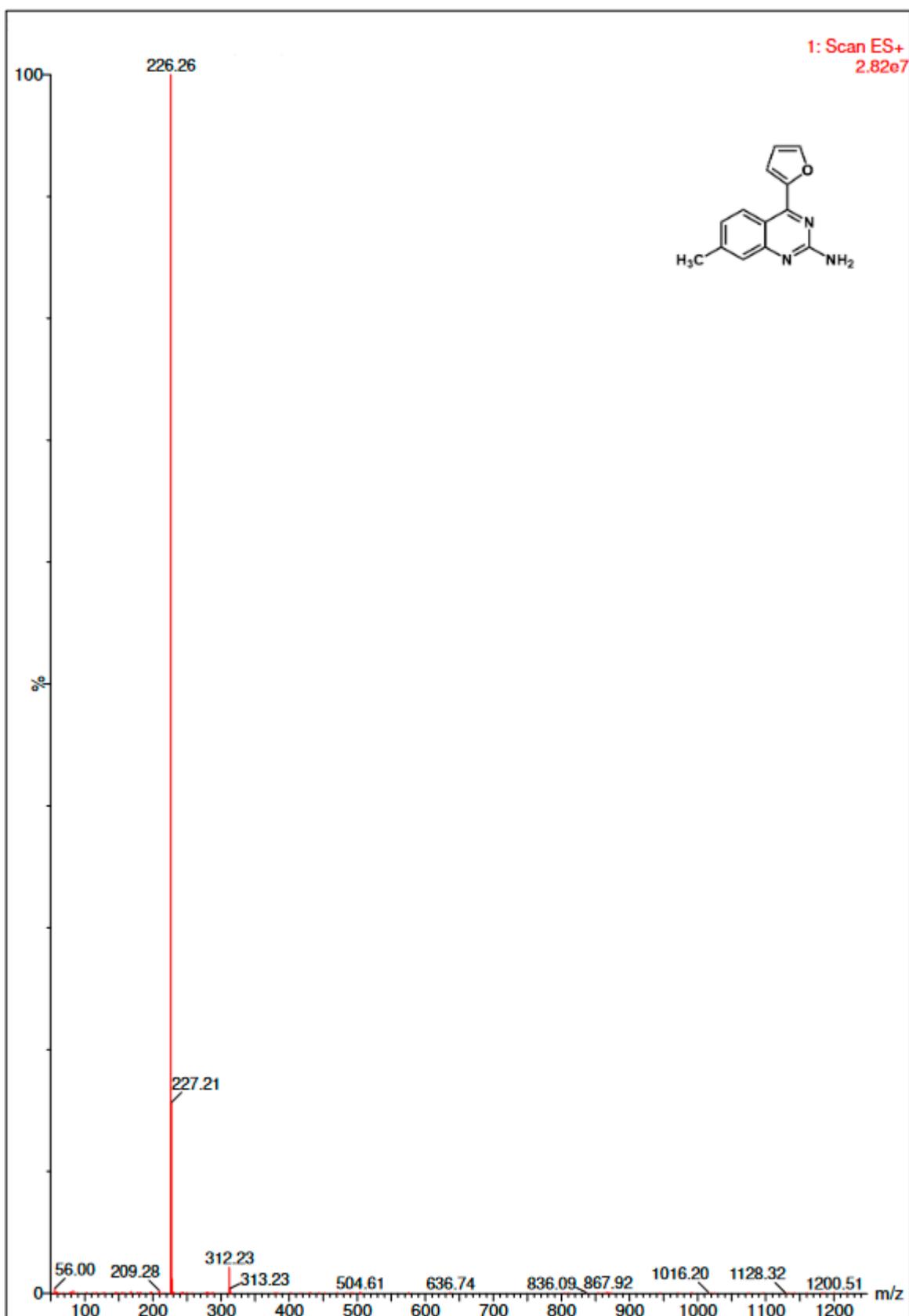
LC-MS mass spectrum of compound 5I



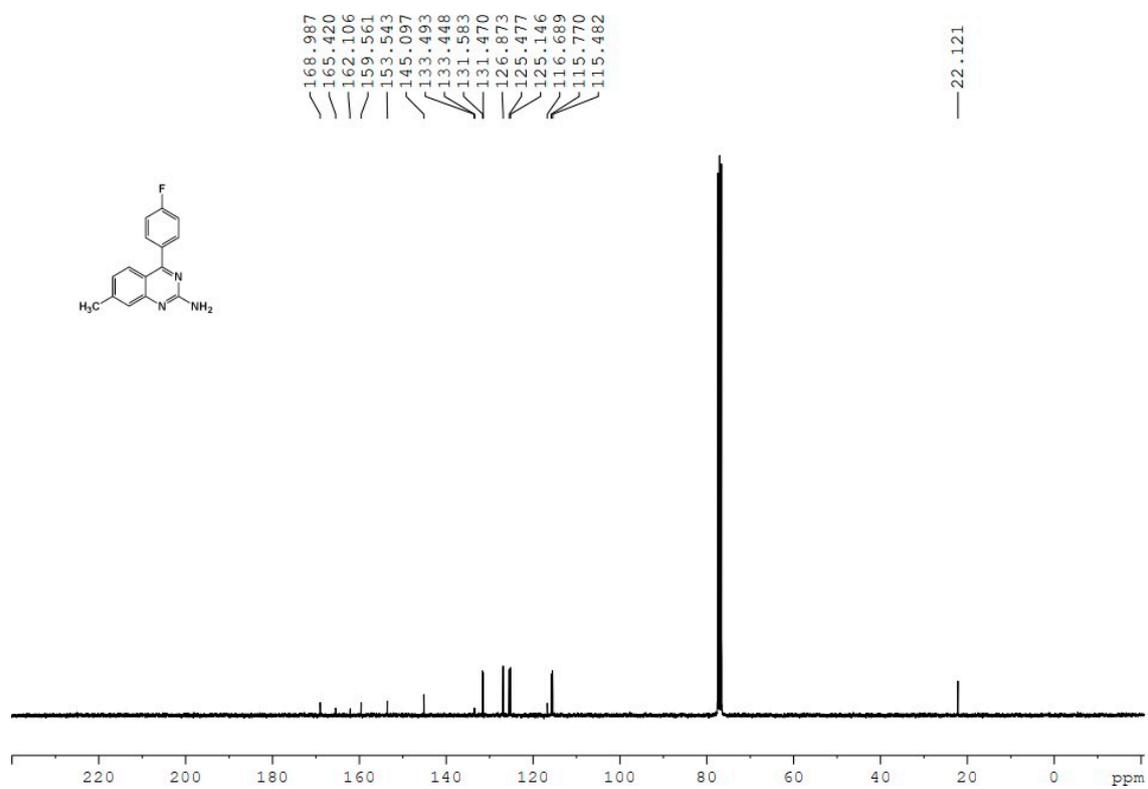
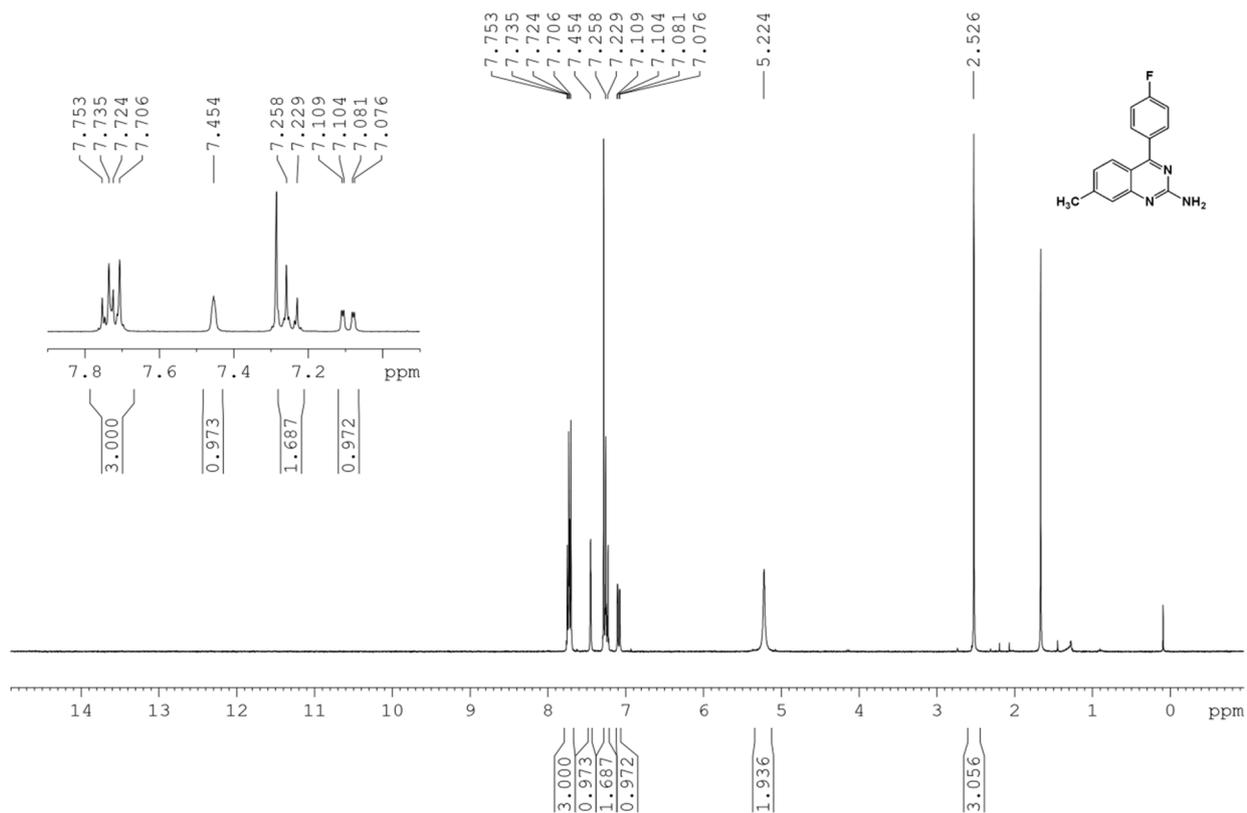
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5m



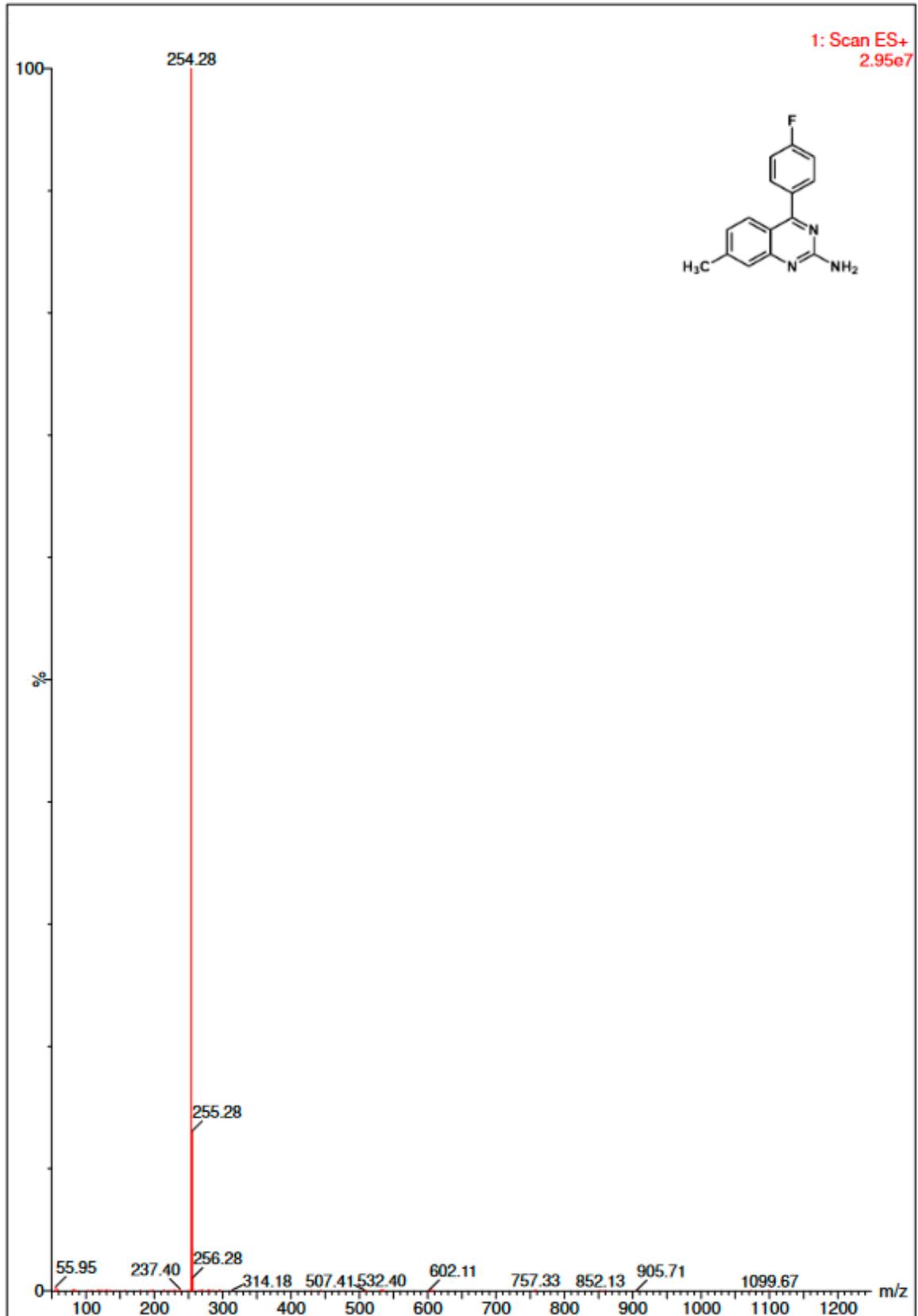
LC-MS mass spectrum of compound 5m



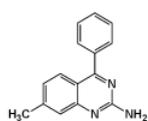
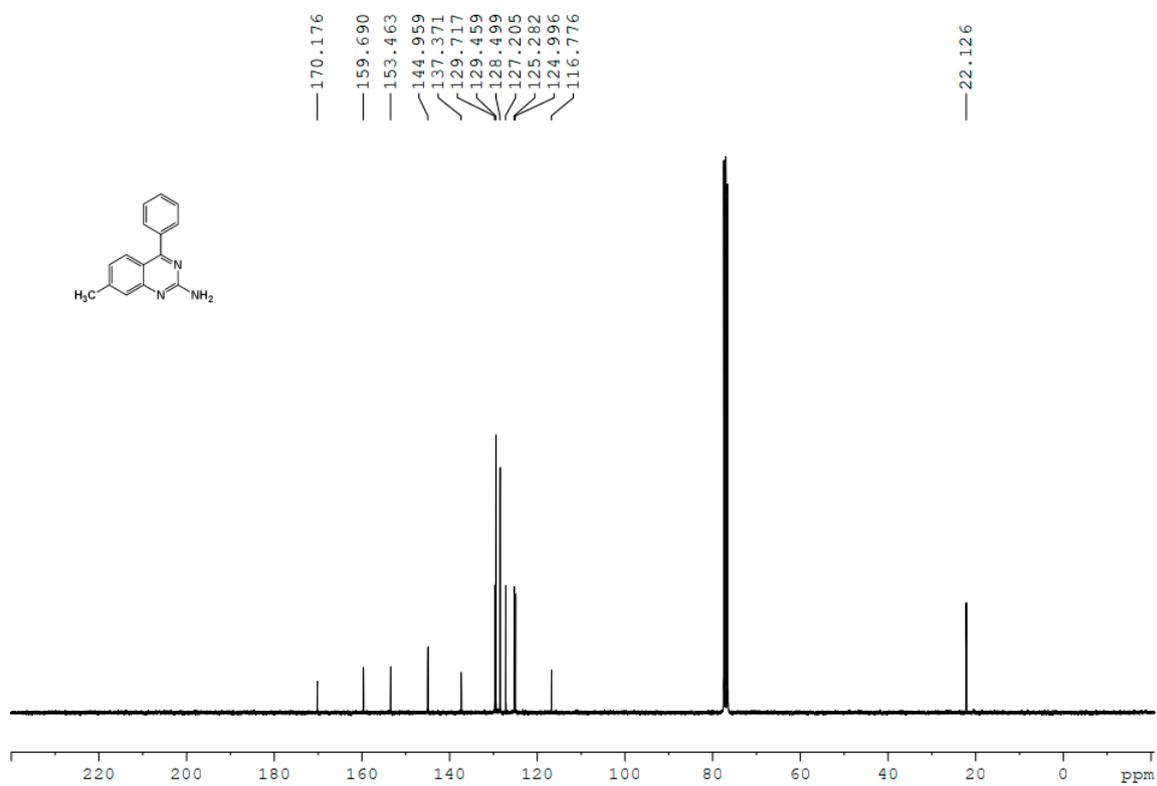
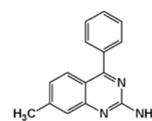
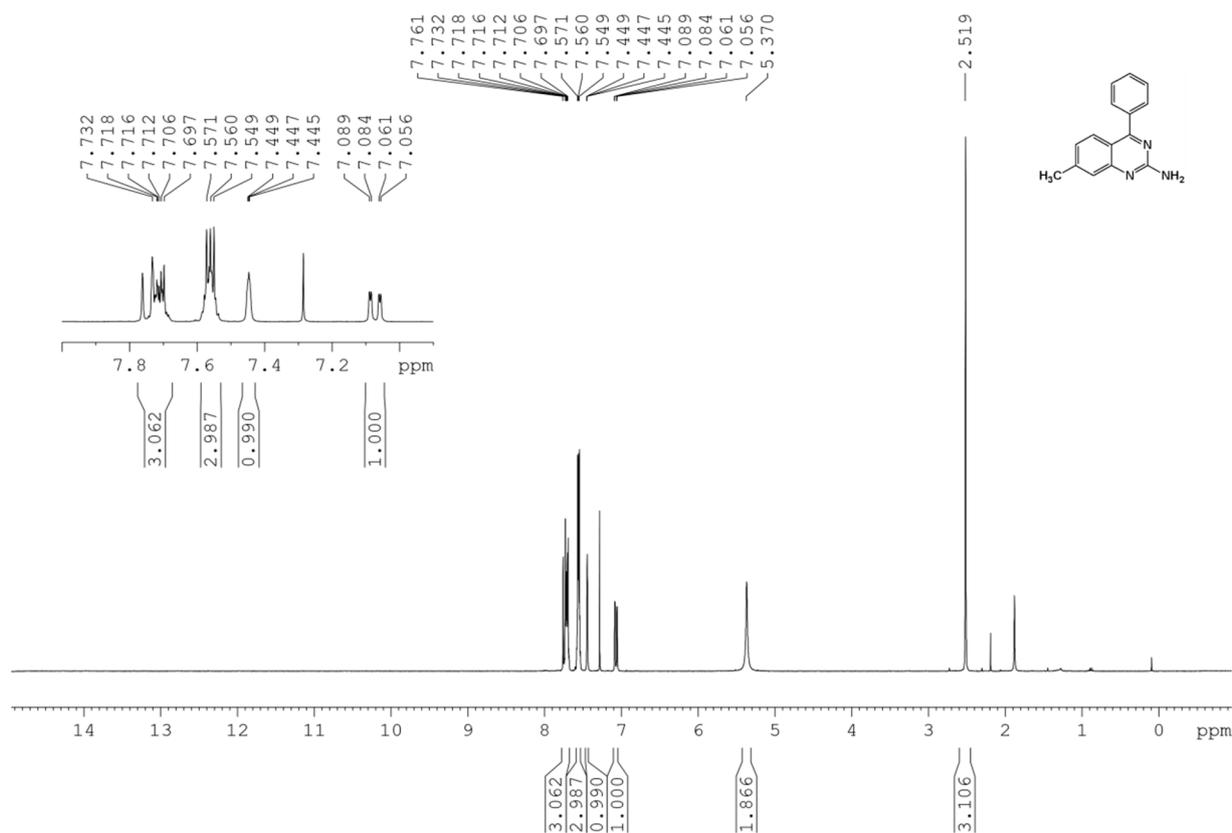
1H- and 13C-NMR Spectra in CDCl₃ of compound 5n



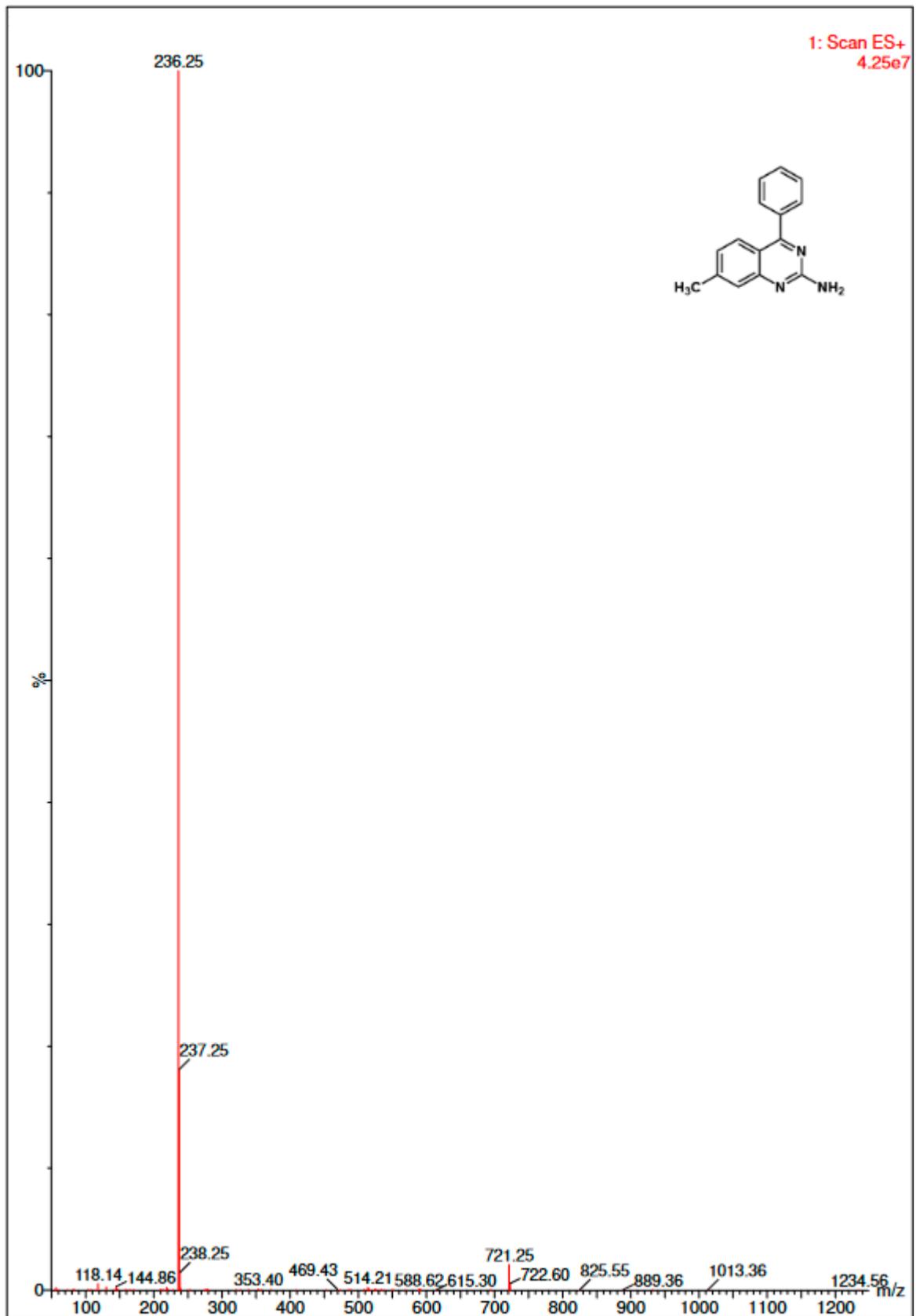
LC-MS mass spectrum of compound 5n



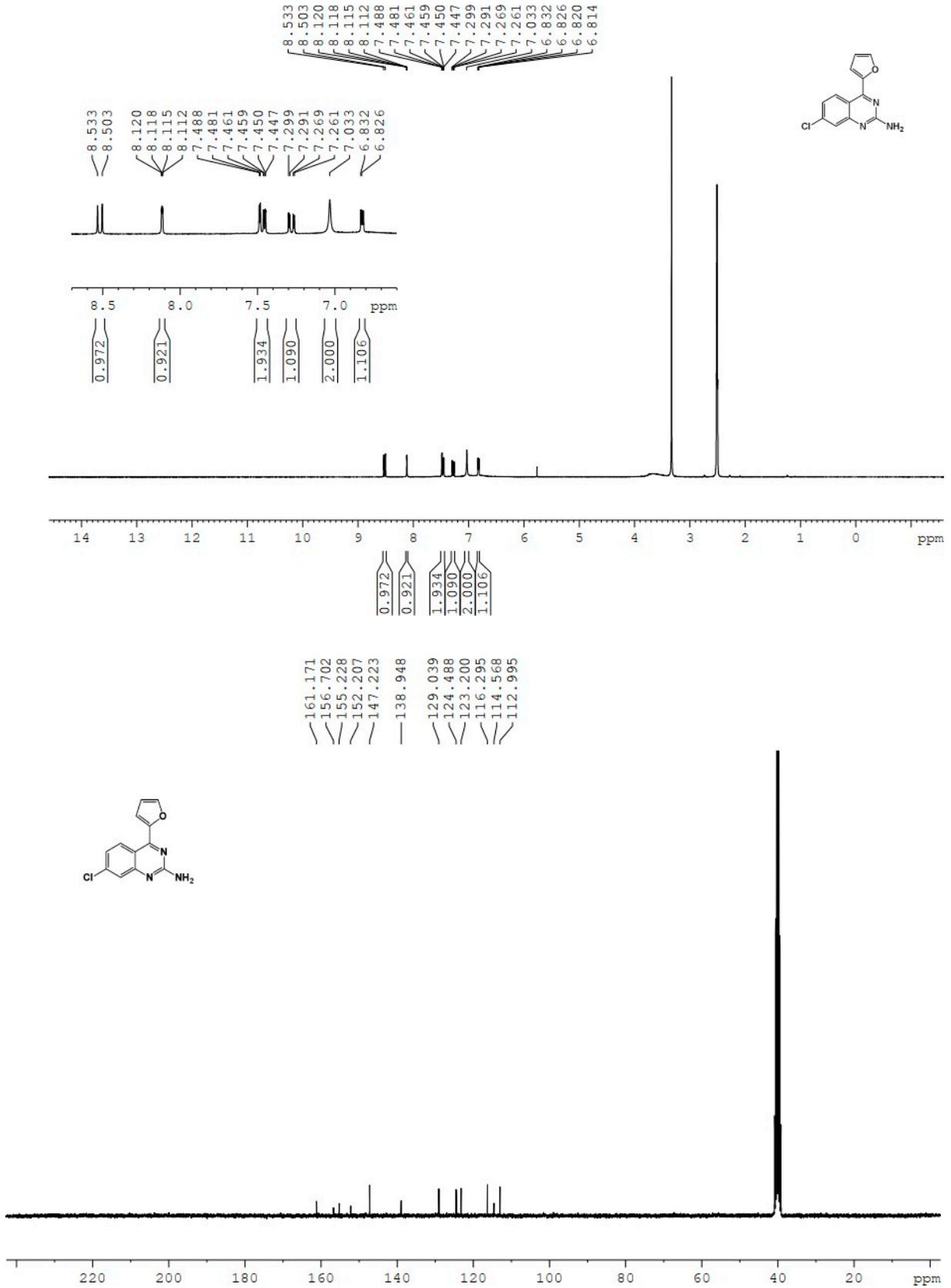
1H- and 13C-NMR Spectra in CDCl₃ of compound 5o



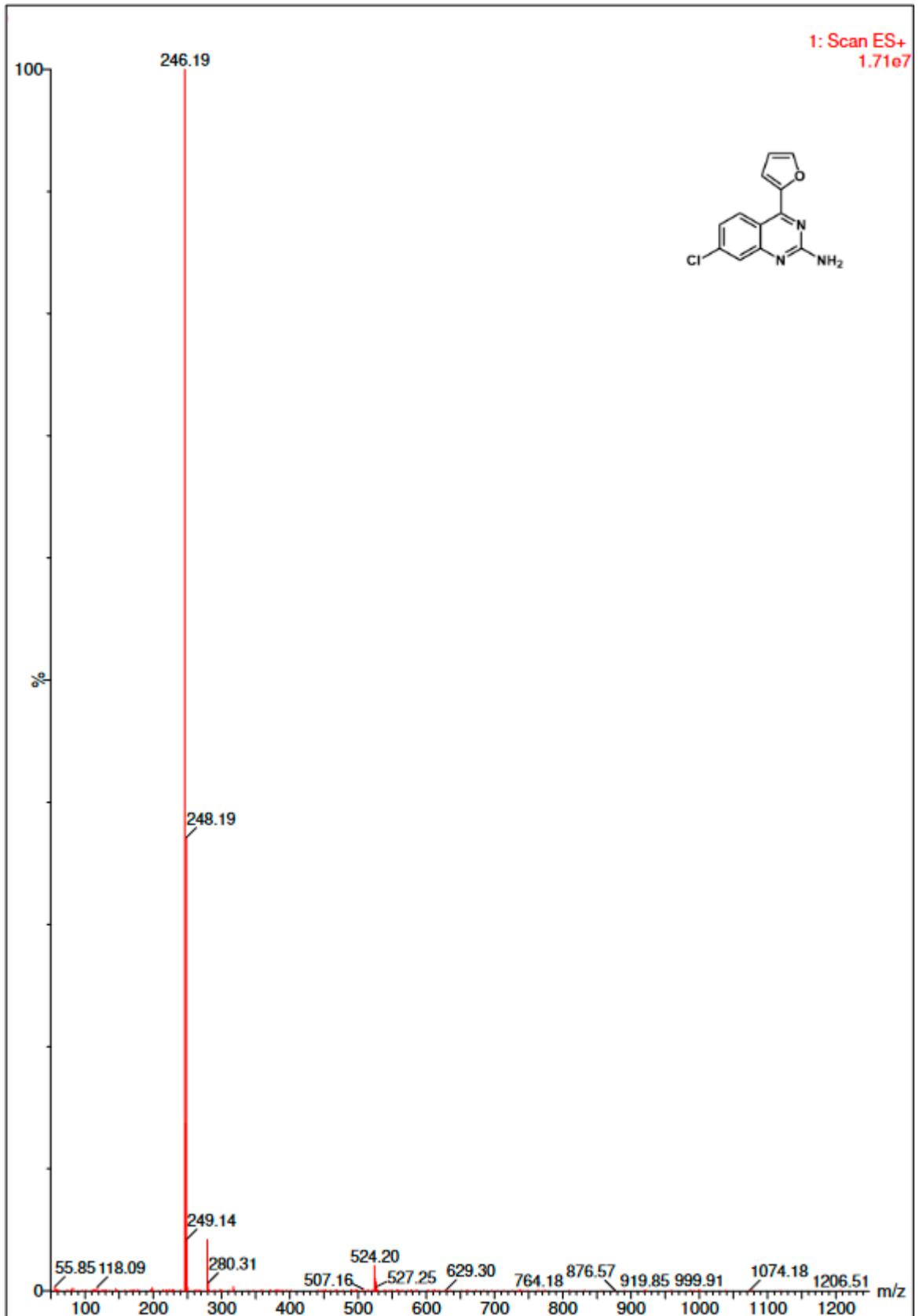
LC-MS mass spectrum of compound 5o



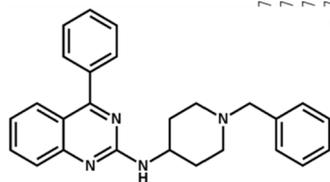
1H- and 13C-NMR Spectra in DMSO-d₆ of compound 5p



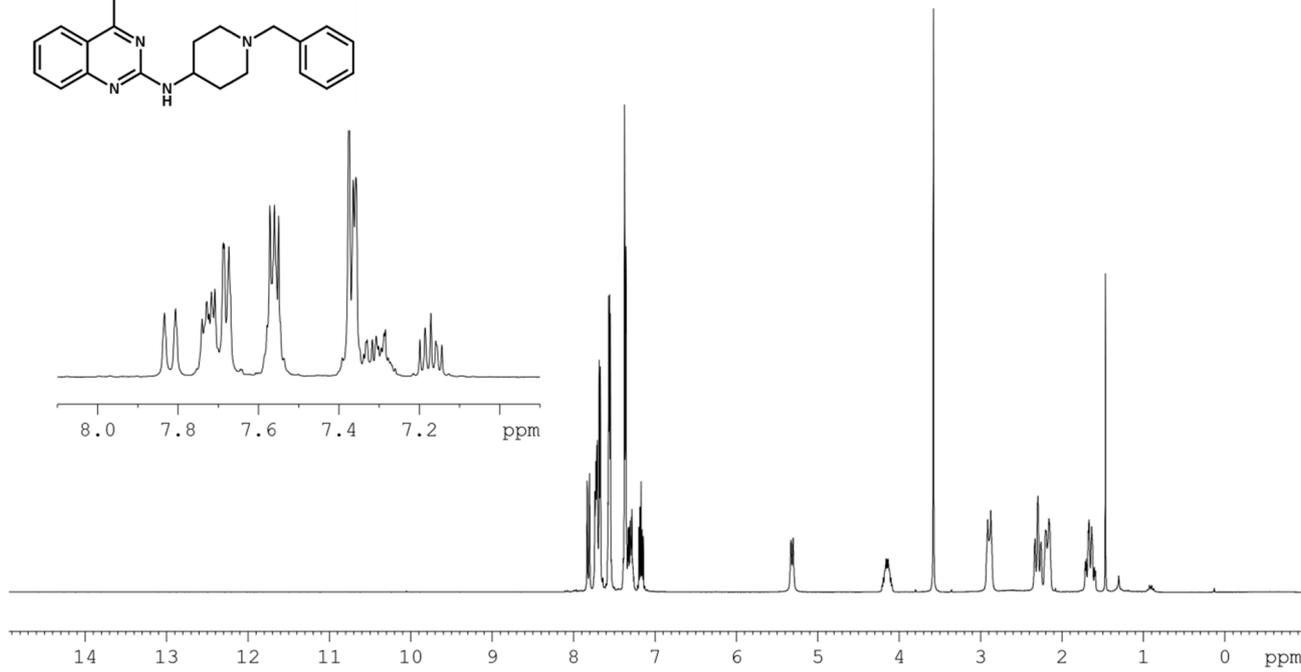
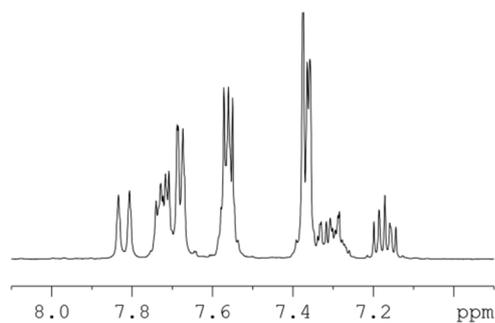
LC-MS mass spectrum of compound 5p



1H- and 13C-NMR Spectra in CDCl₃ of compound 9a

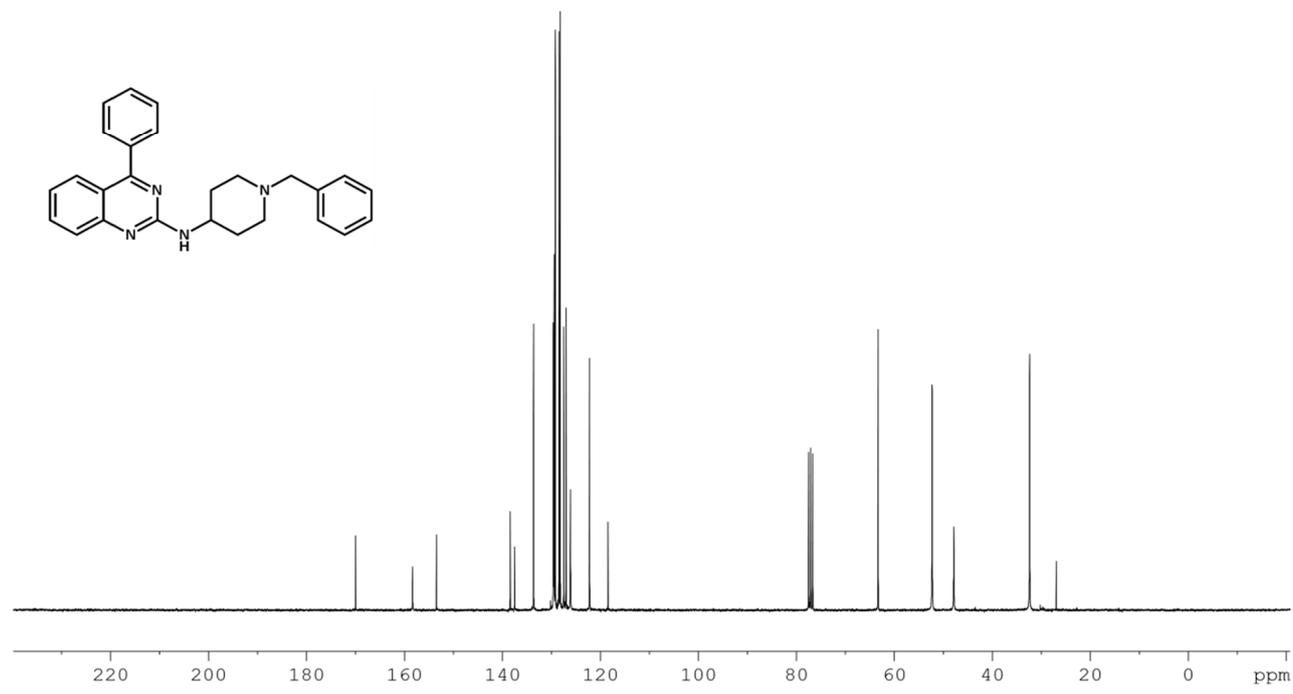
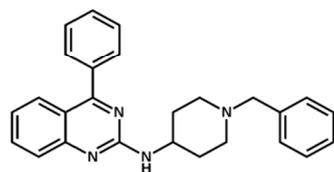


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7.375
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7.308
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5.304
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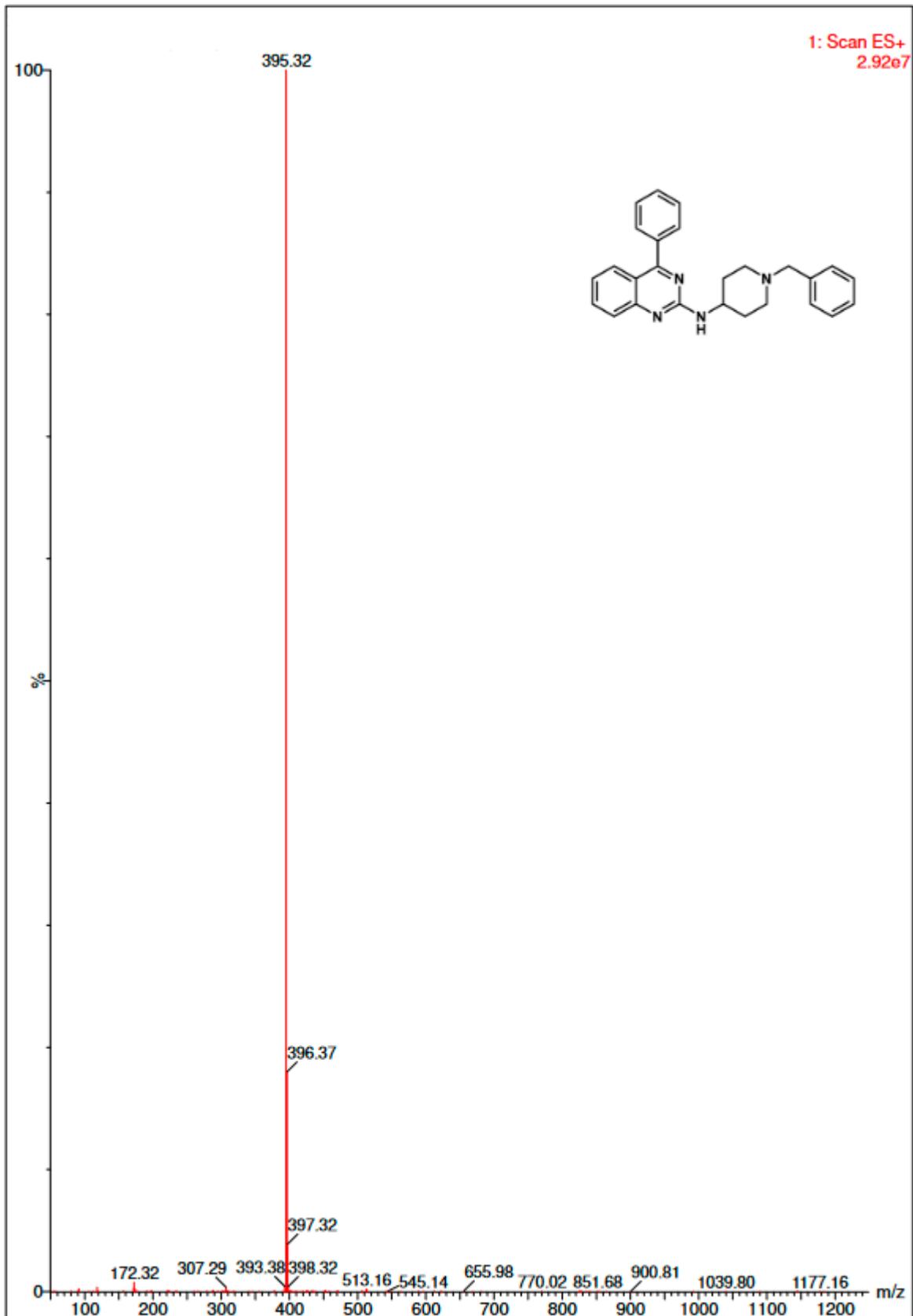


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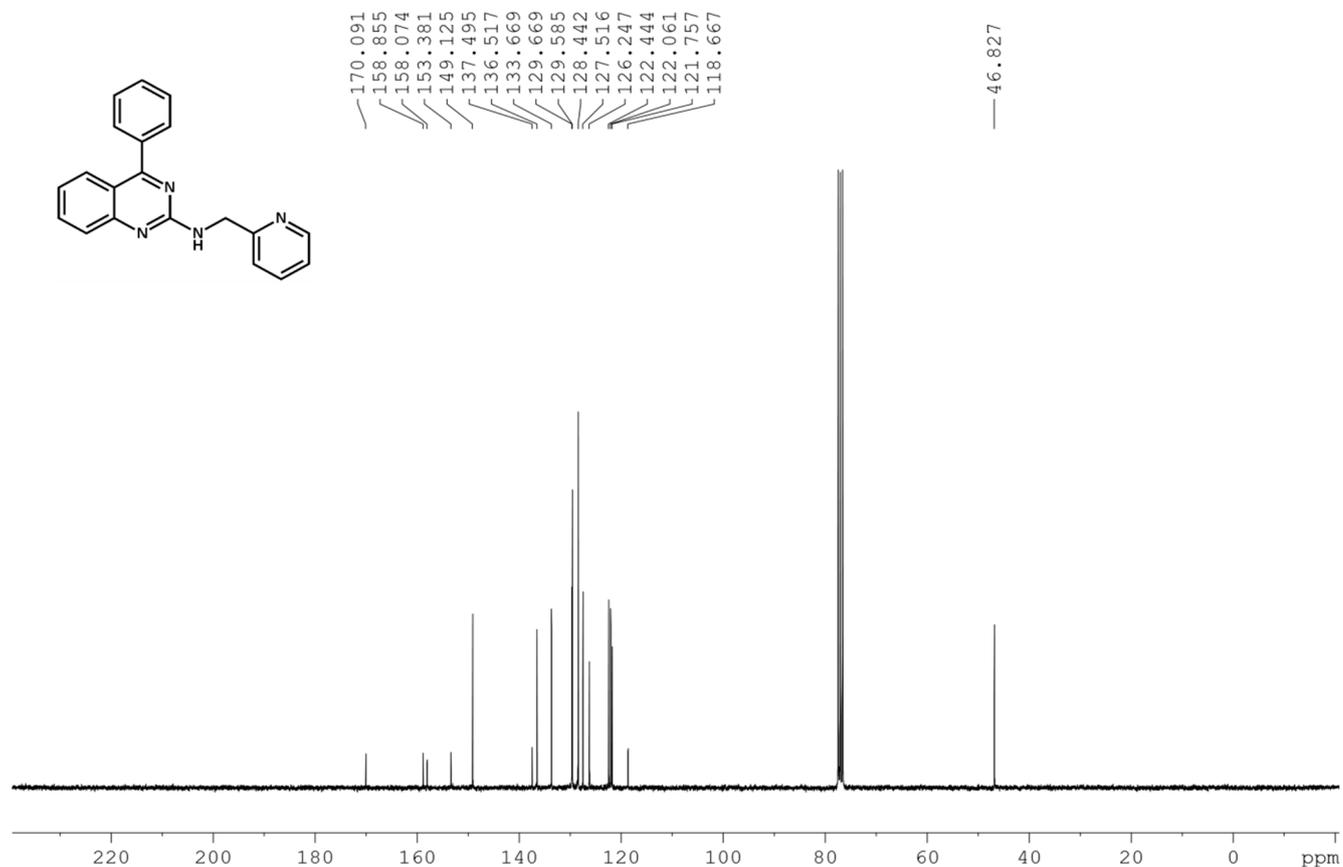
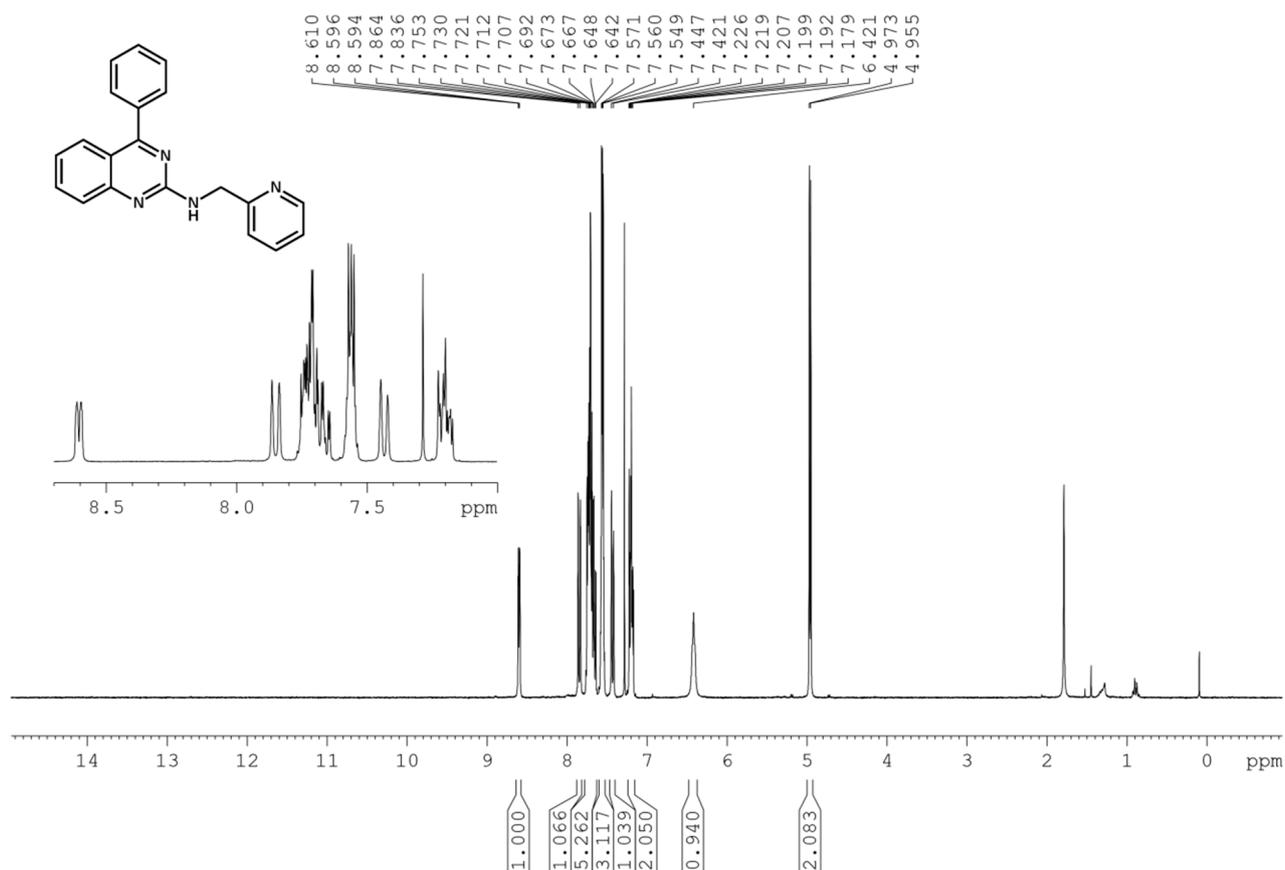
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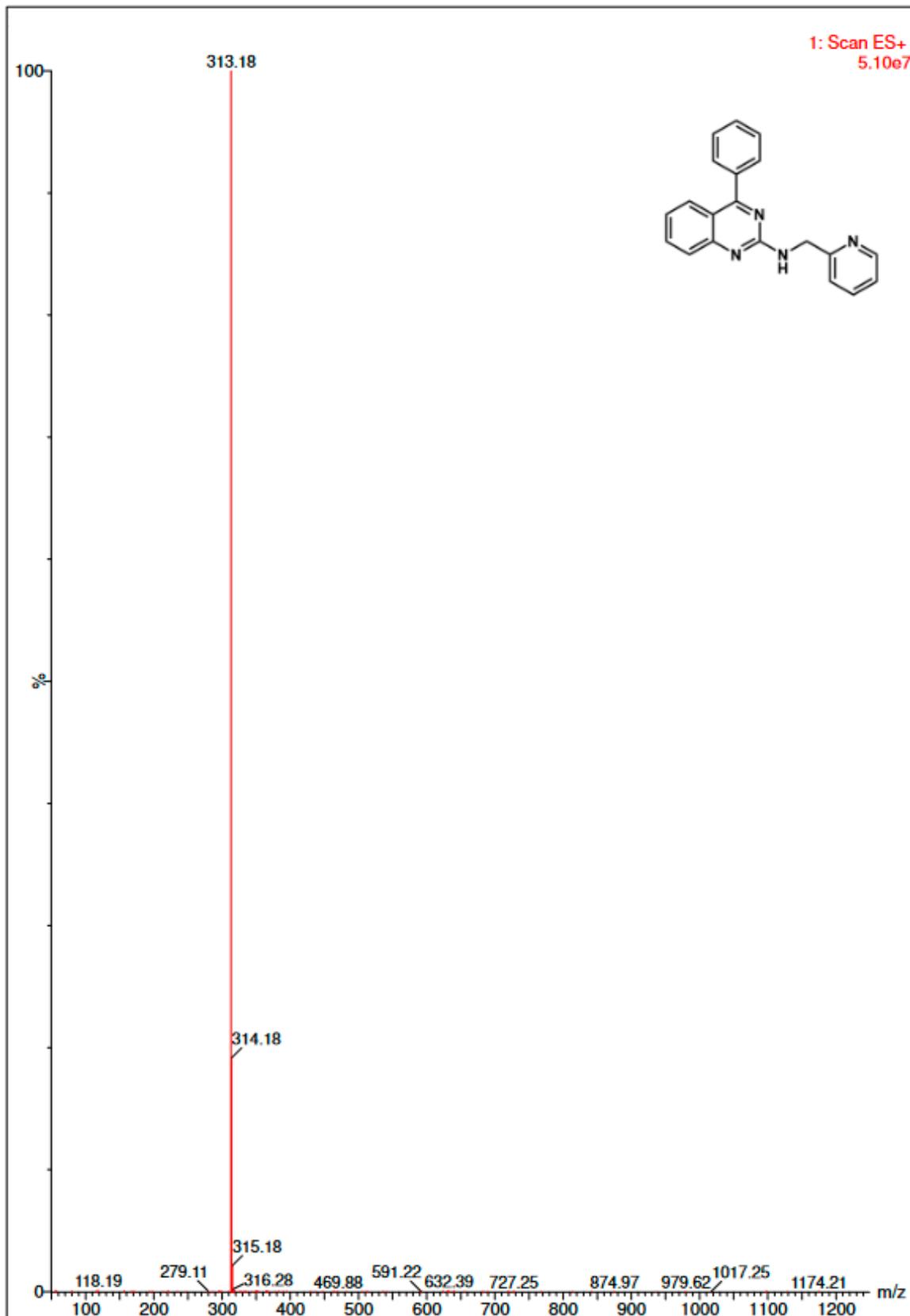
LC-MS mass spectrum of compound 9a



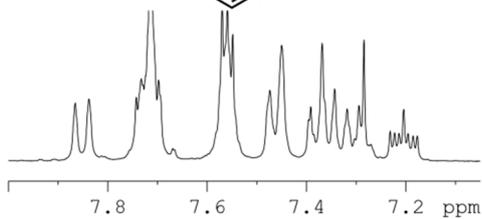
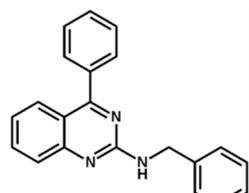
1H- and 13C-NMR Spectra in CDCl₃ of compound 9b



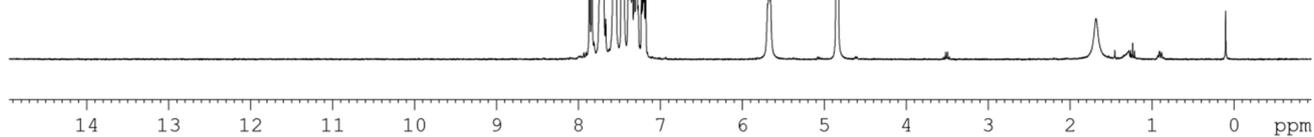
LC-MS mass spectrum of compound 9b



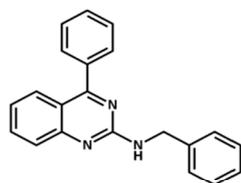
1H- and 13C-NMR Spectra in CDCl₃ of compound 9c



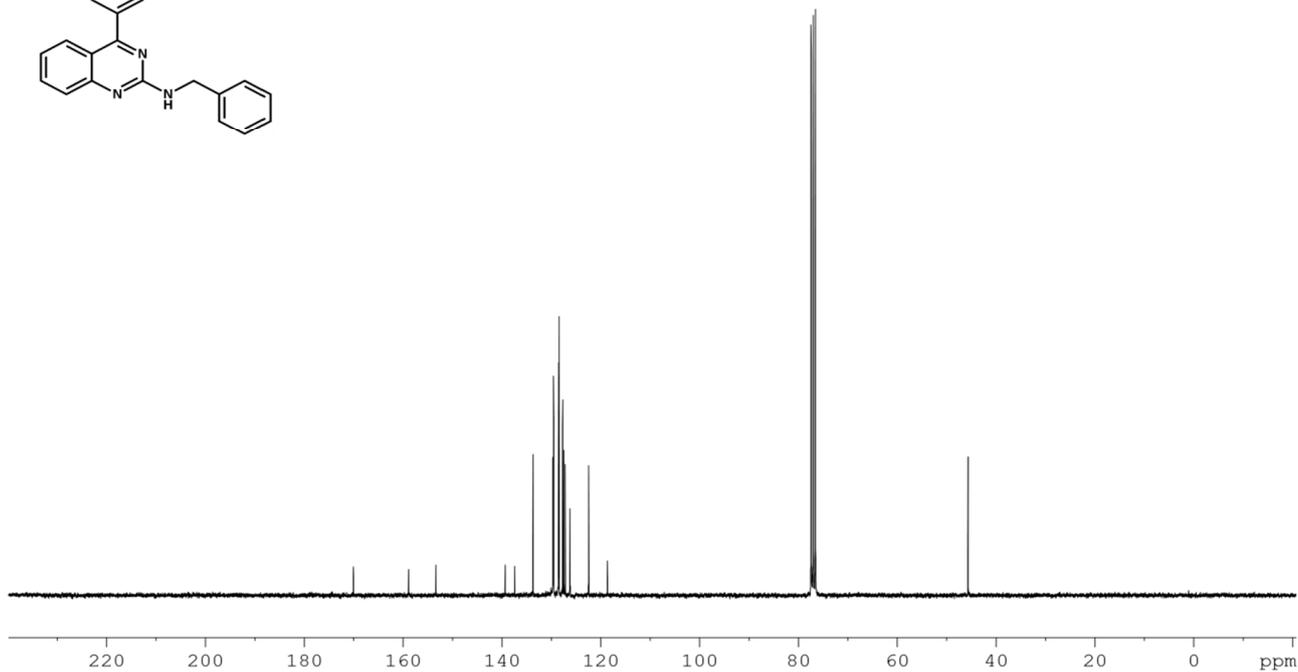
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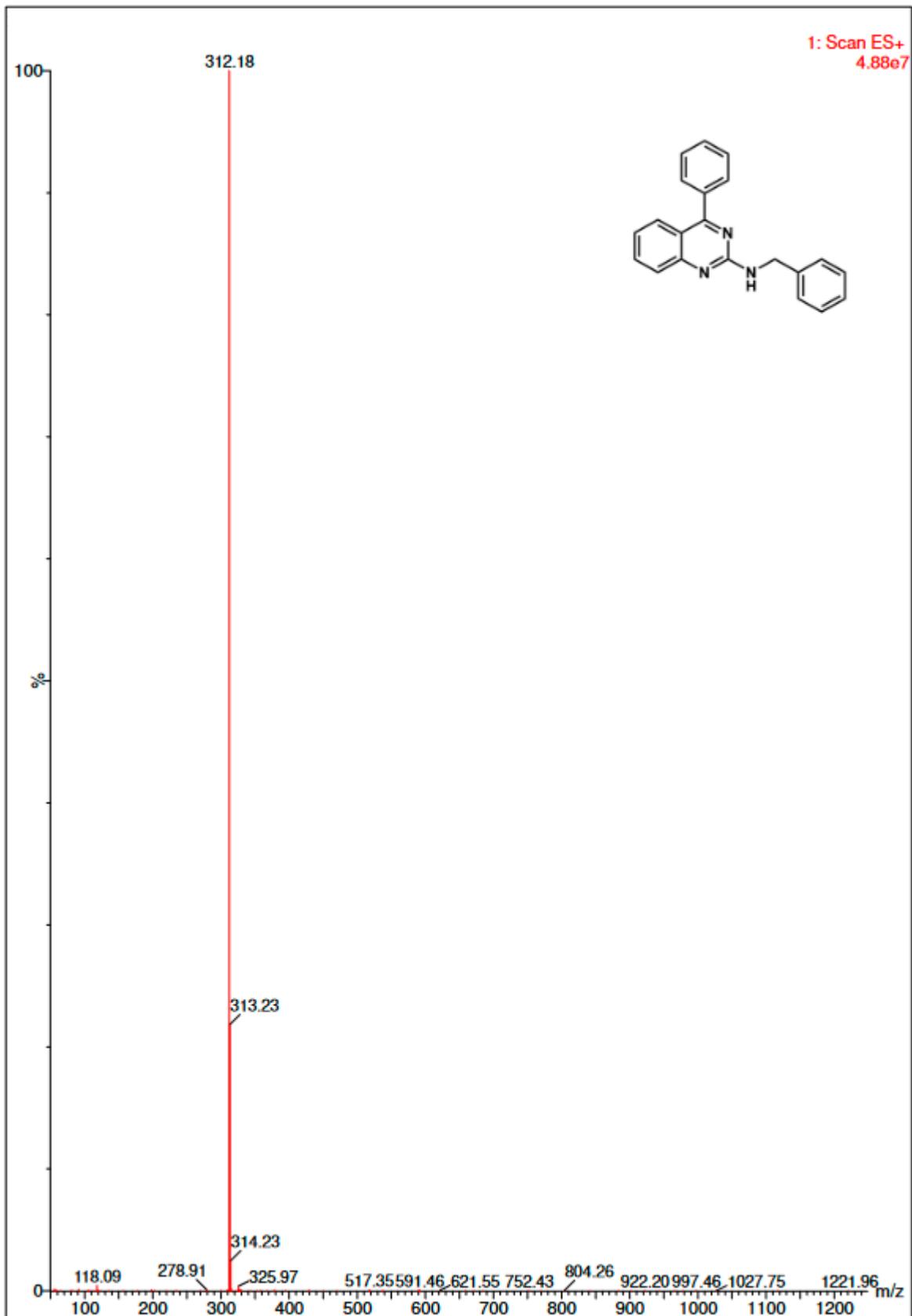
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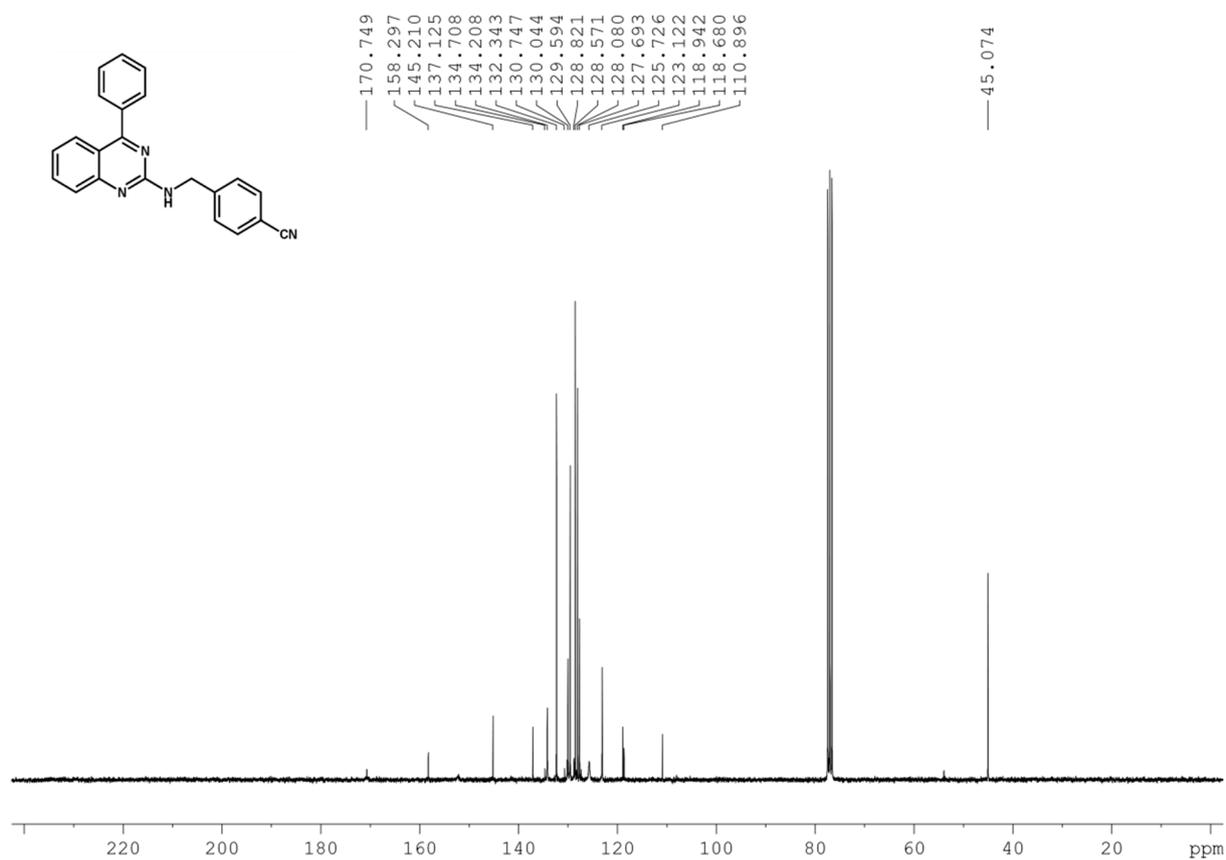
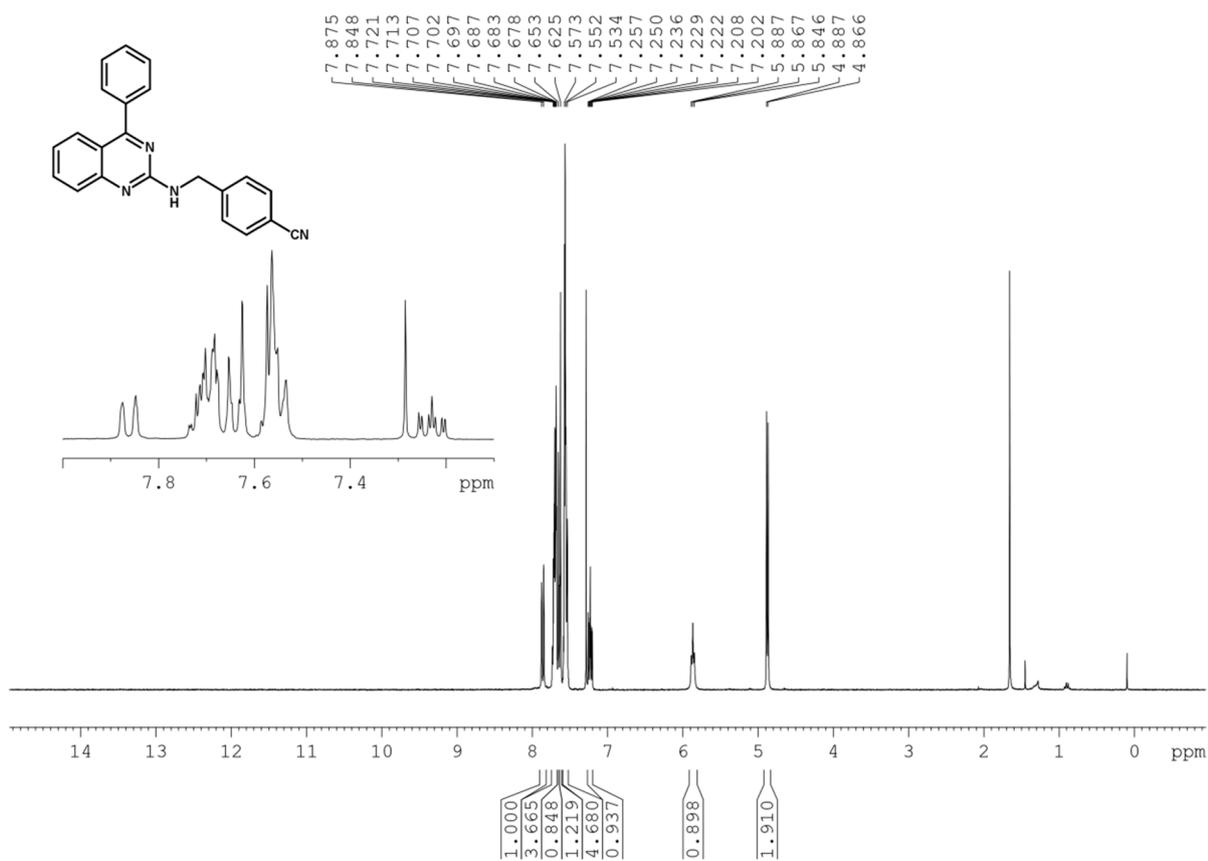
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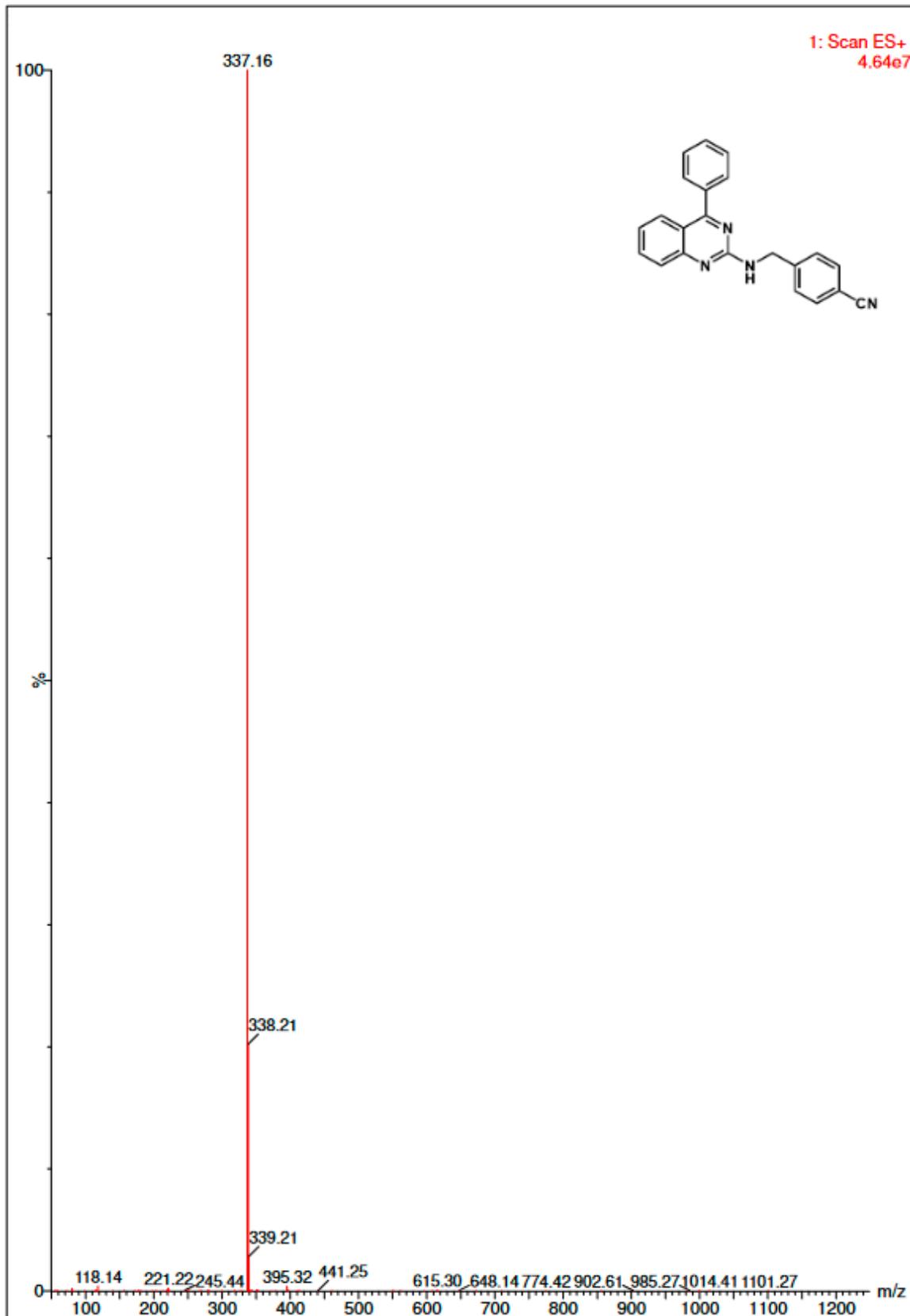
LC-MS mass spectrum of compound 9c



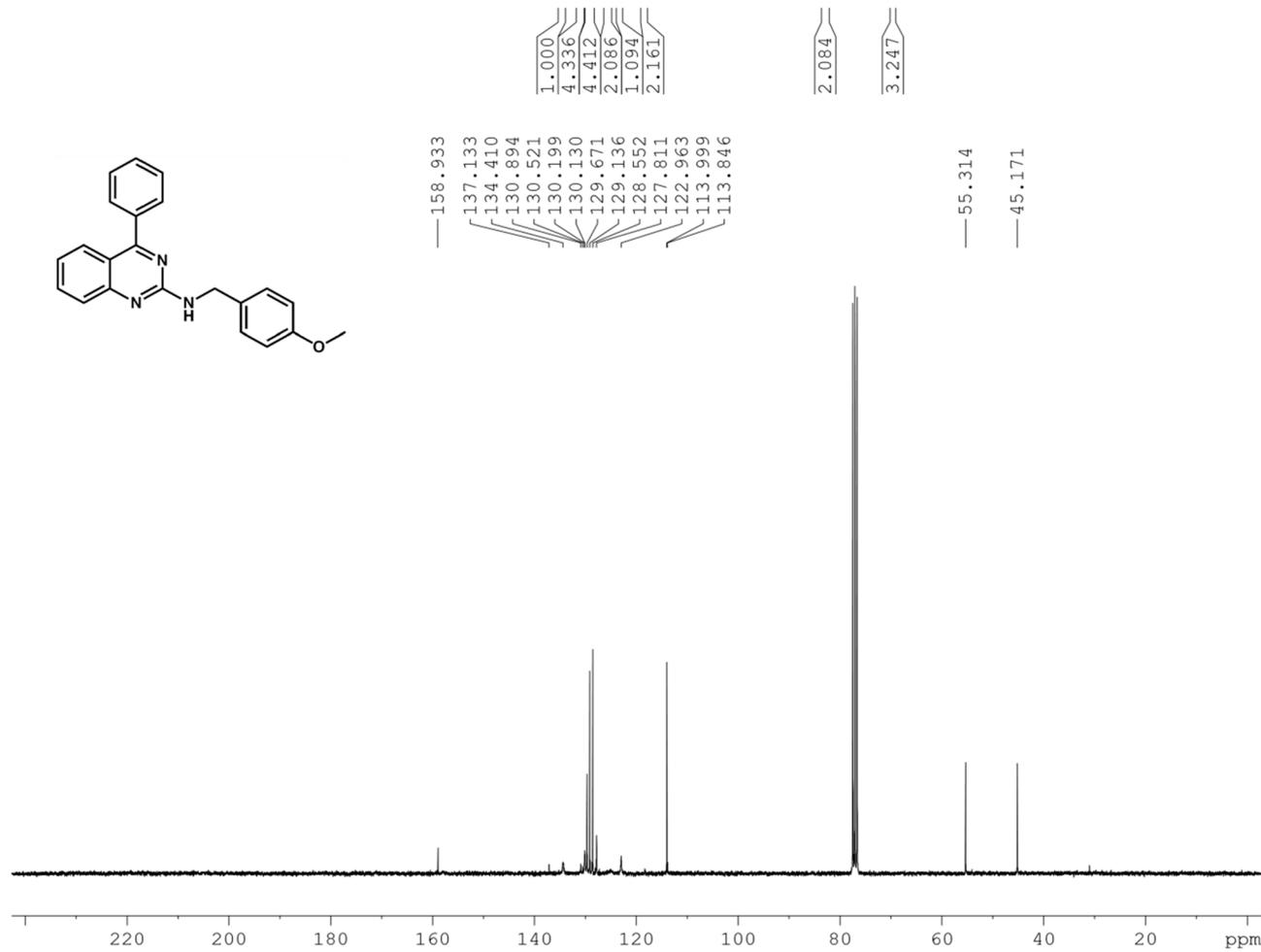
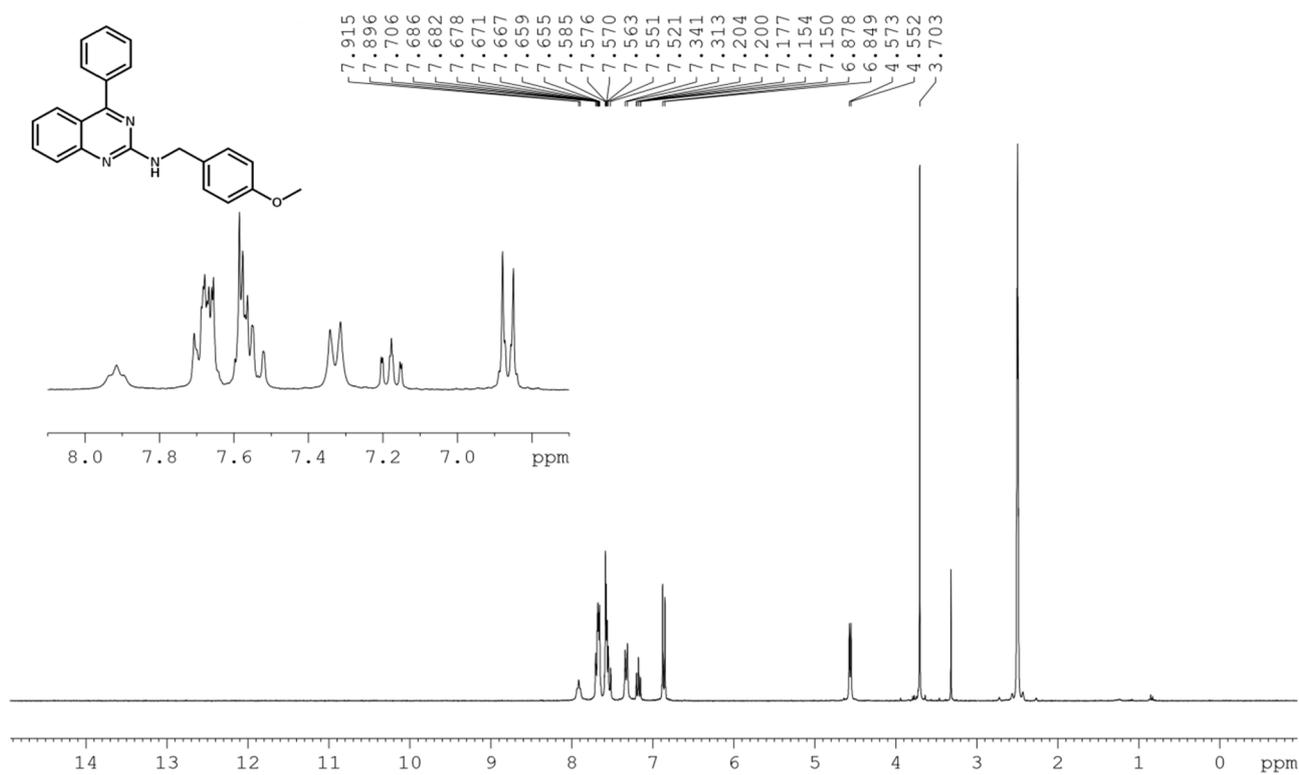
1H- and 13C-NMR Spectra in CDCl₃ of compound 9d



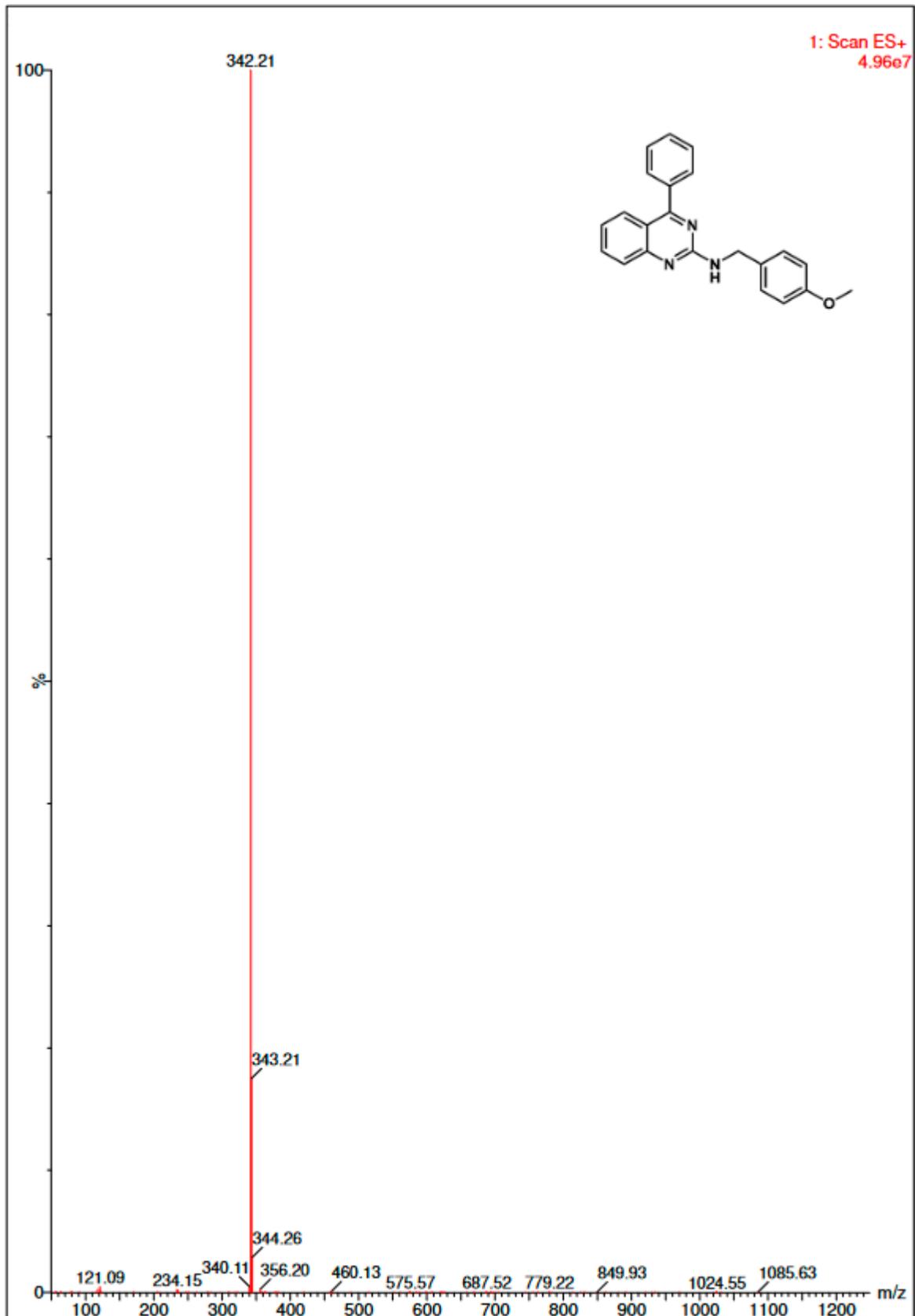
LC-MS mass spectrum of compound 9d



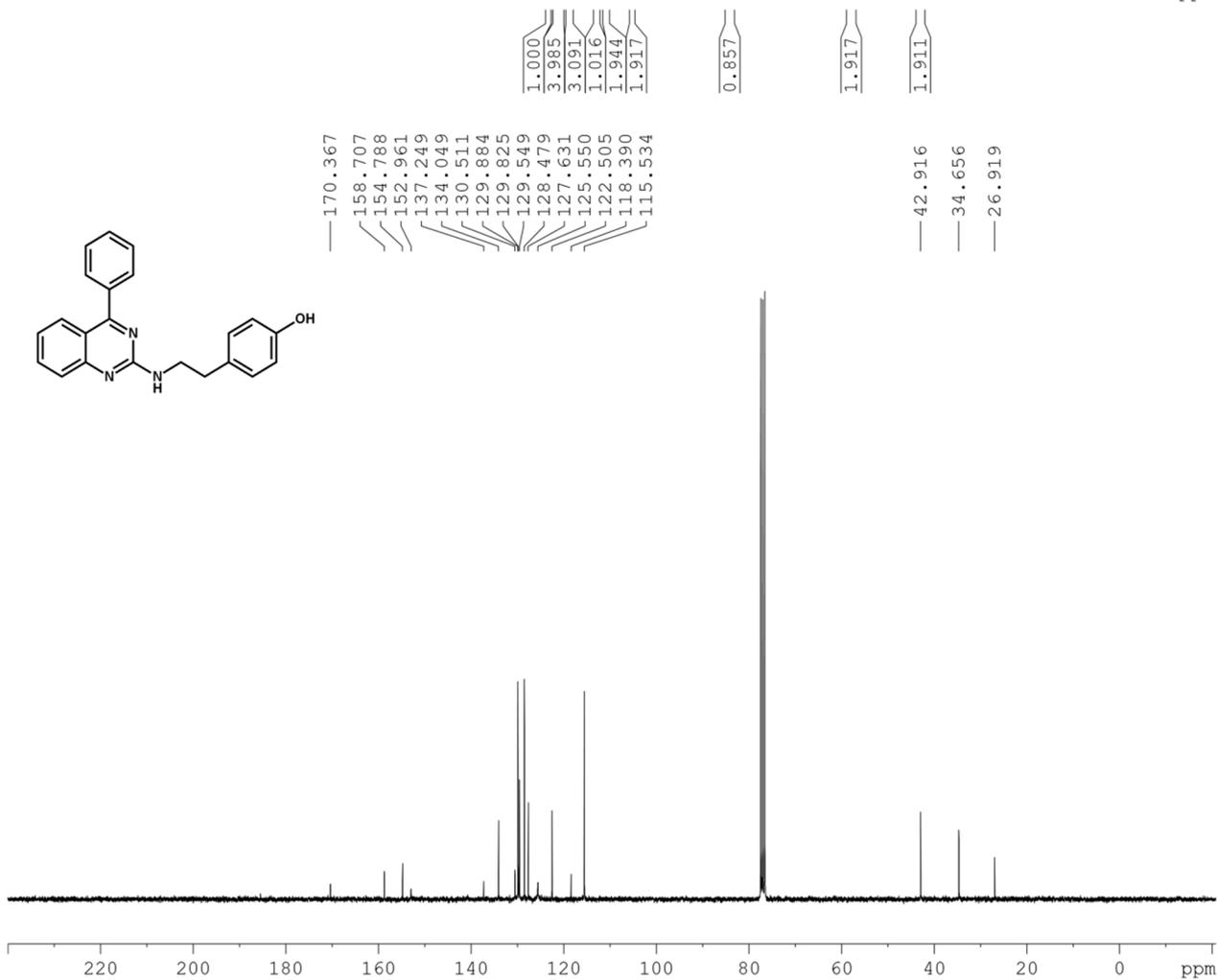
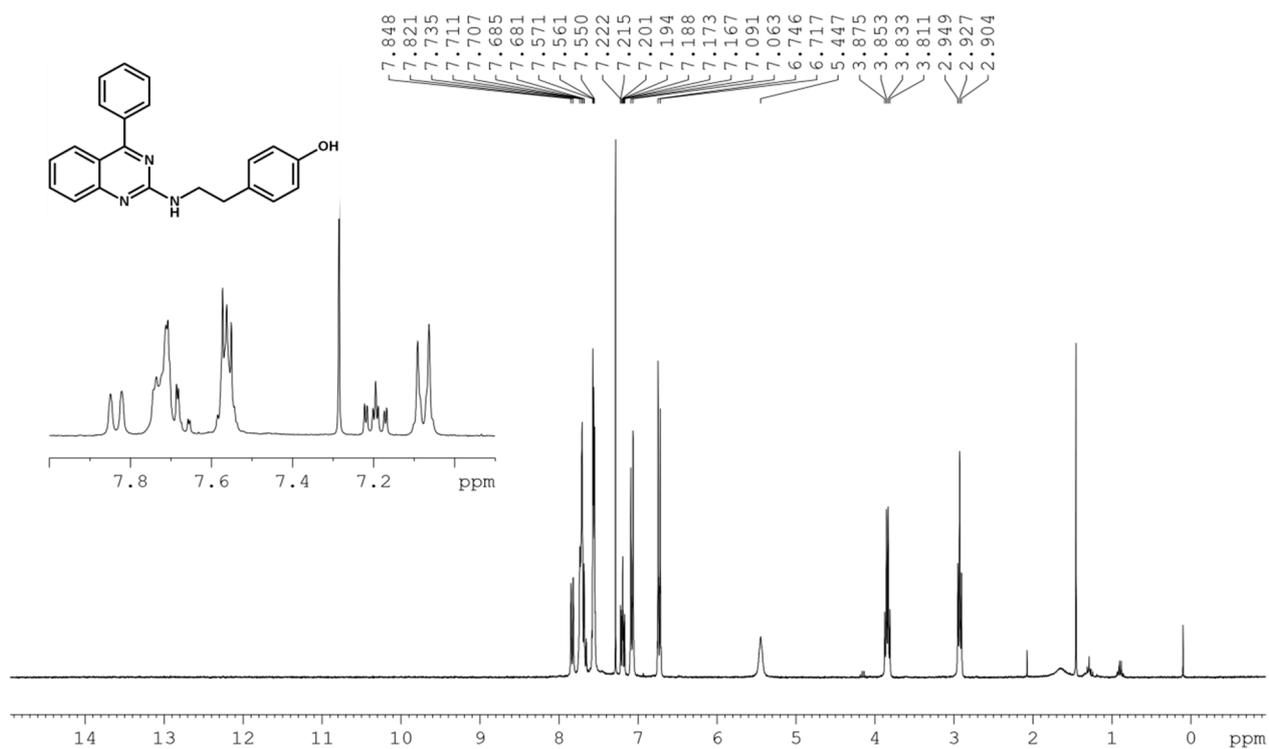
¹H-NMR Spectra in DMSO-d₆ and ¹³C-NMR Spectra in CDCl₃ of compound 9e



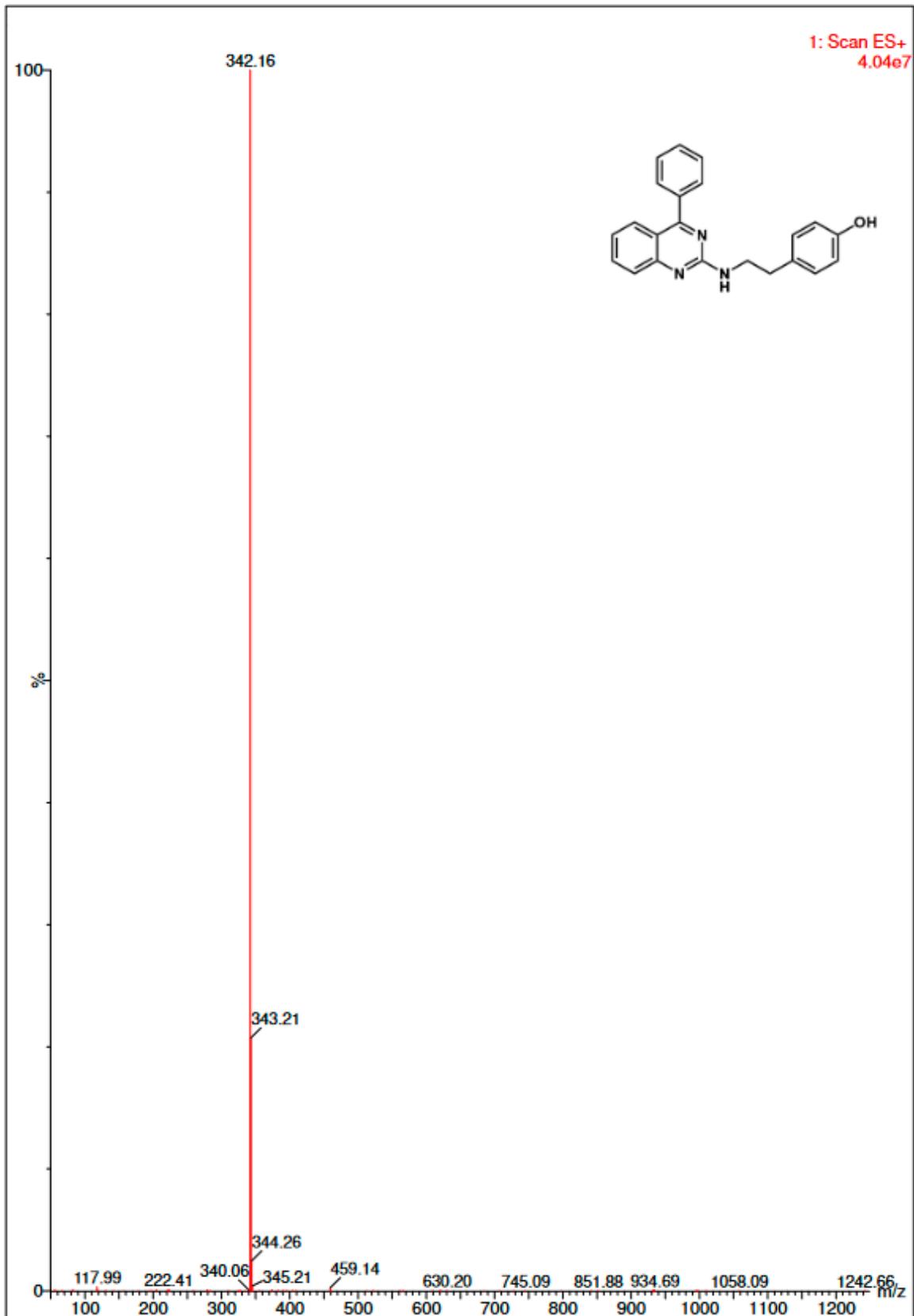
LC-MS mass spectrum of compound 9e



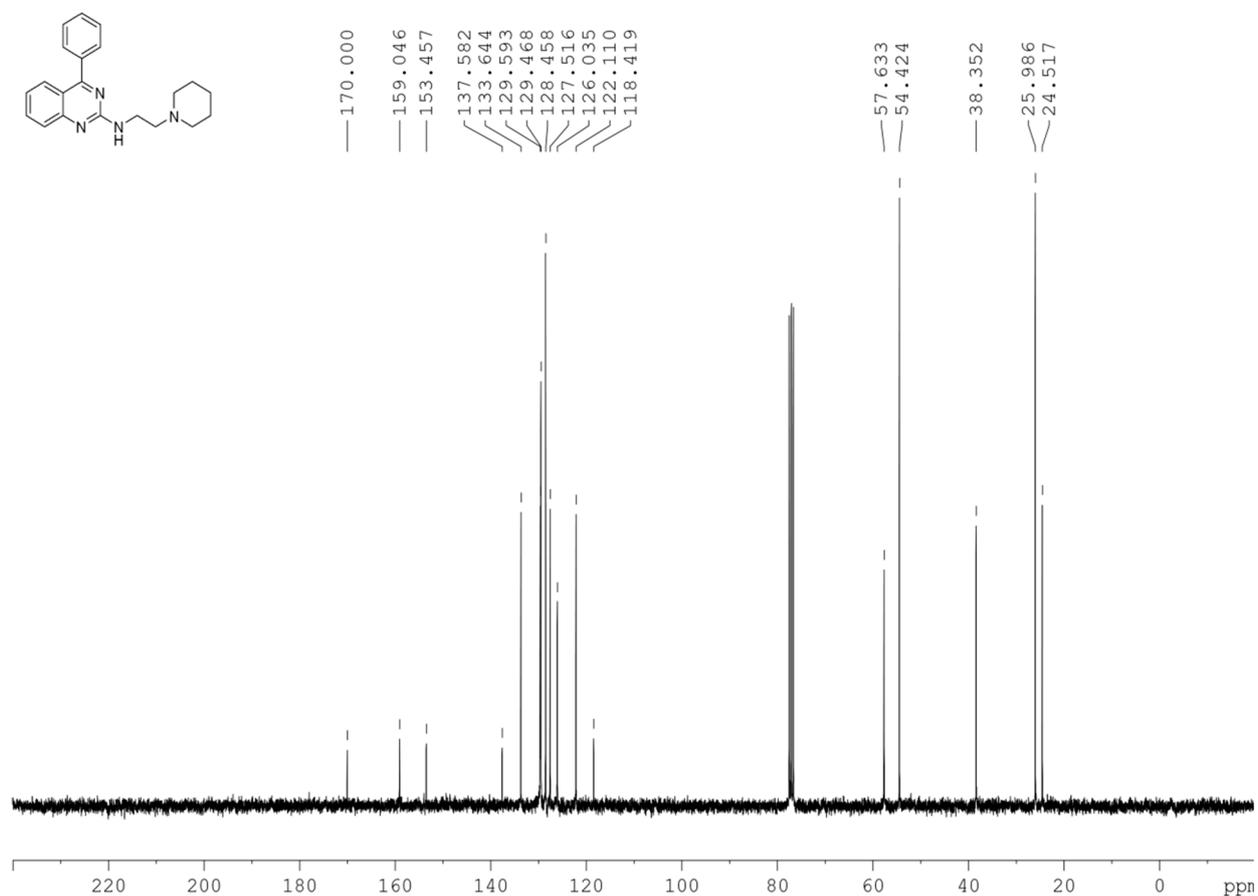
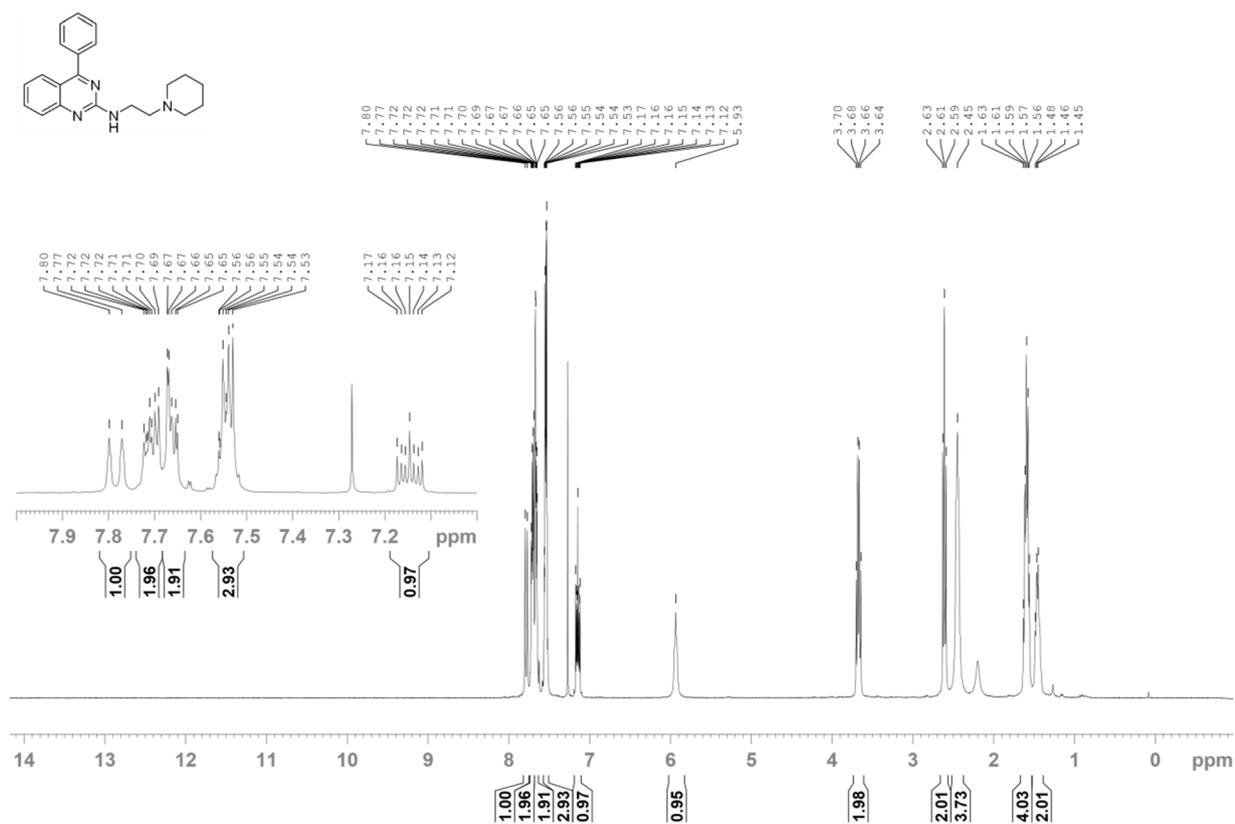
1H- and 13C-NMR Spectra in CDCl₃ of compound 9f



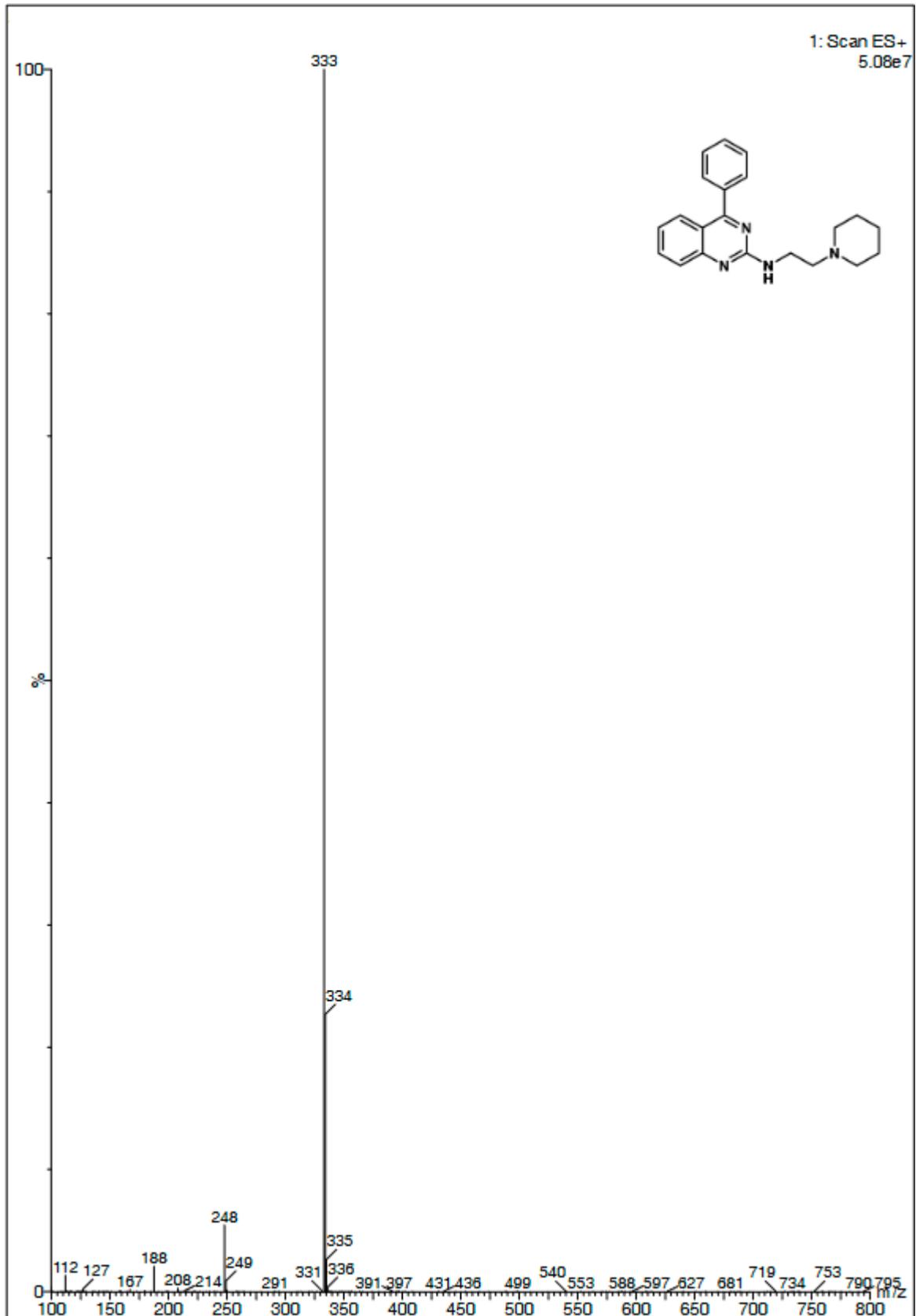
LC-MS mass spectrum of compound 9f



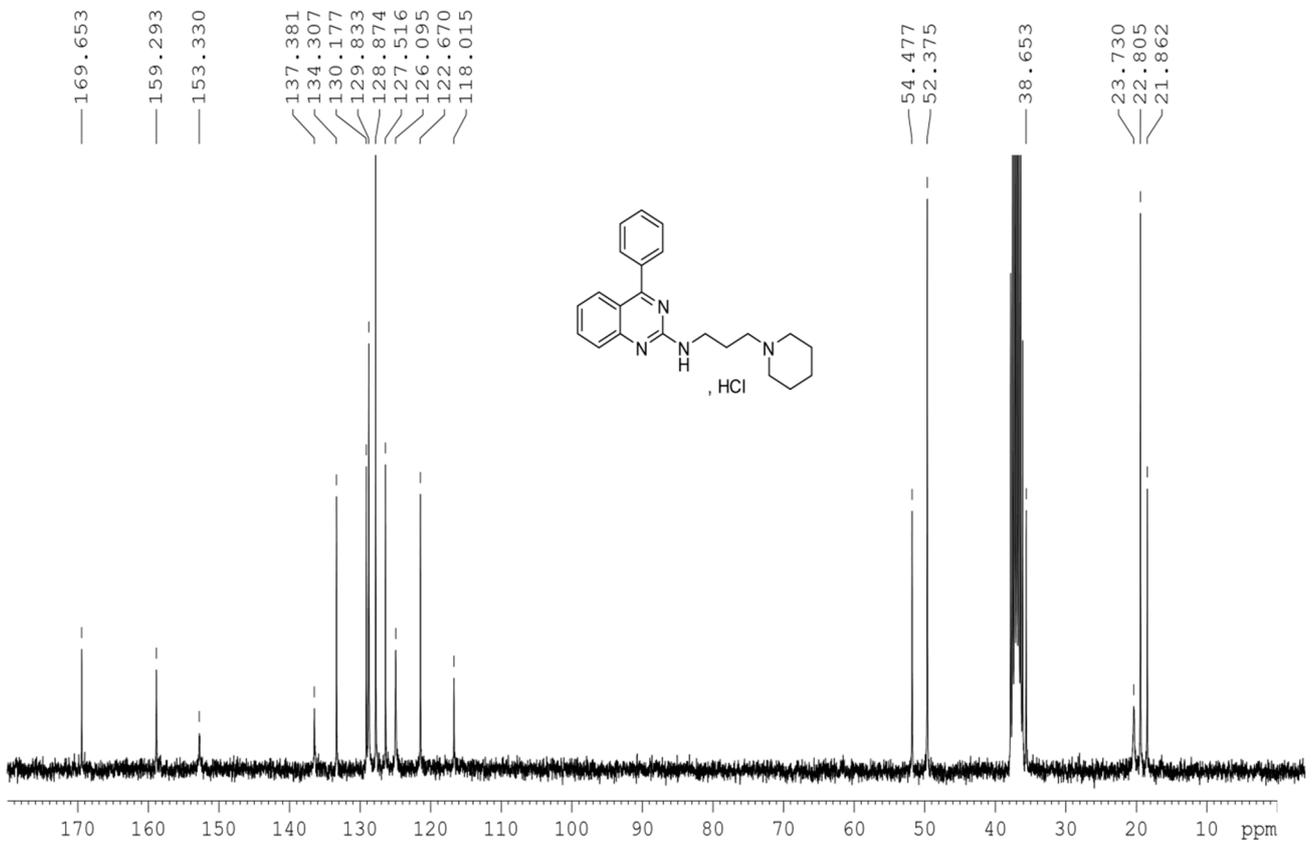
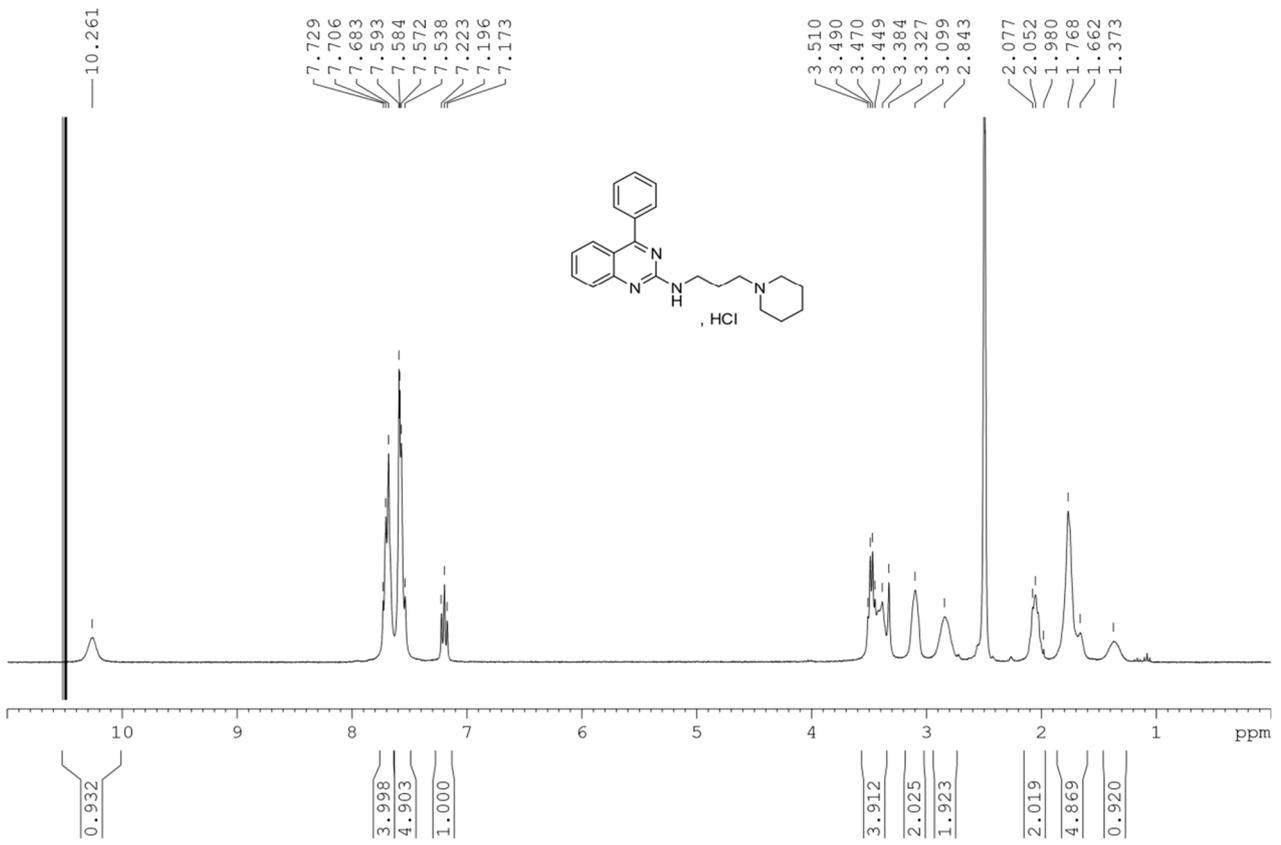
1H- and 13C-NMR Spectra in CDCl₃ of compound 9g



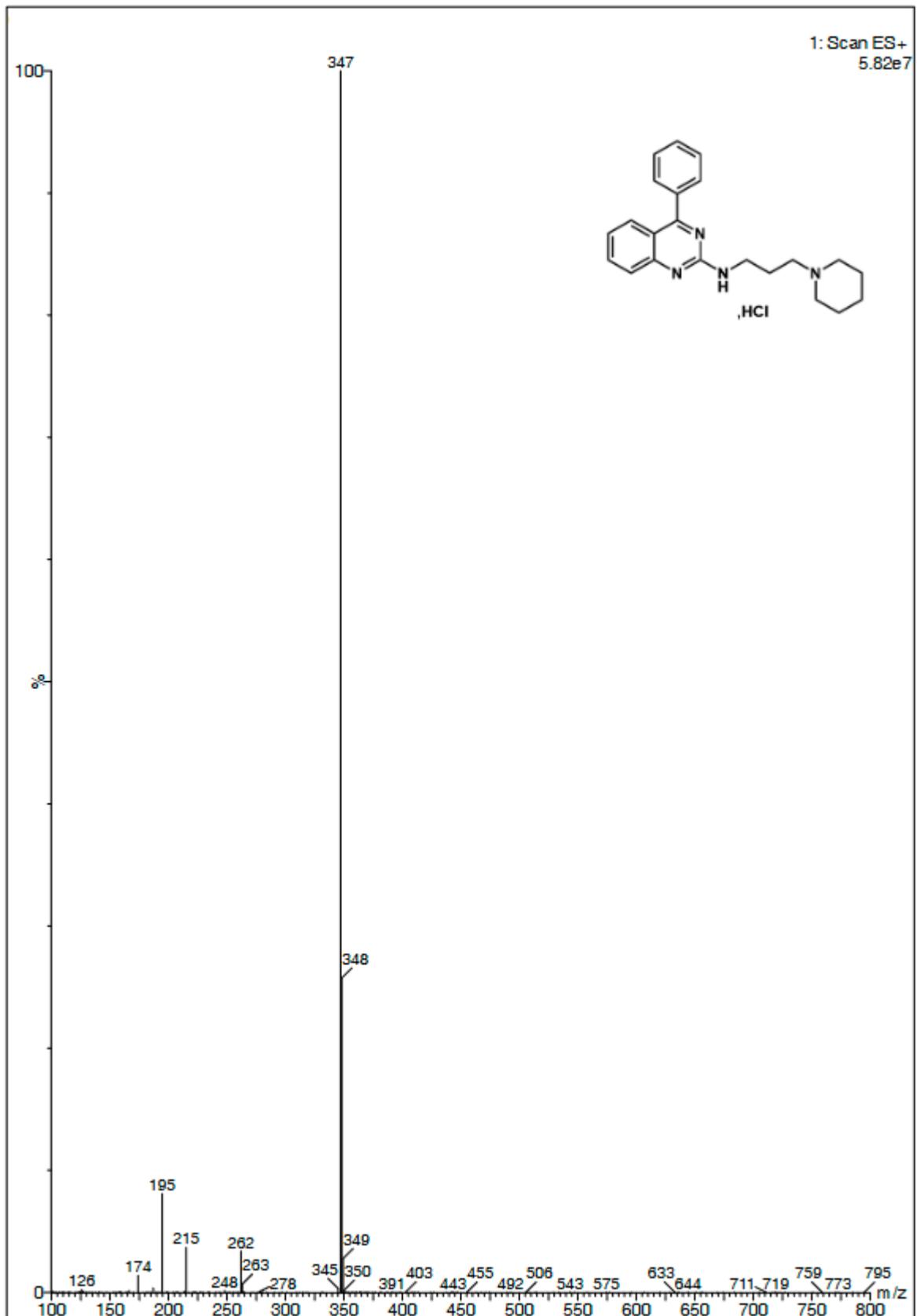
LC-MS mass spectrum of compound 9g



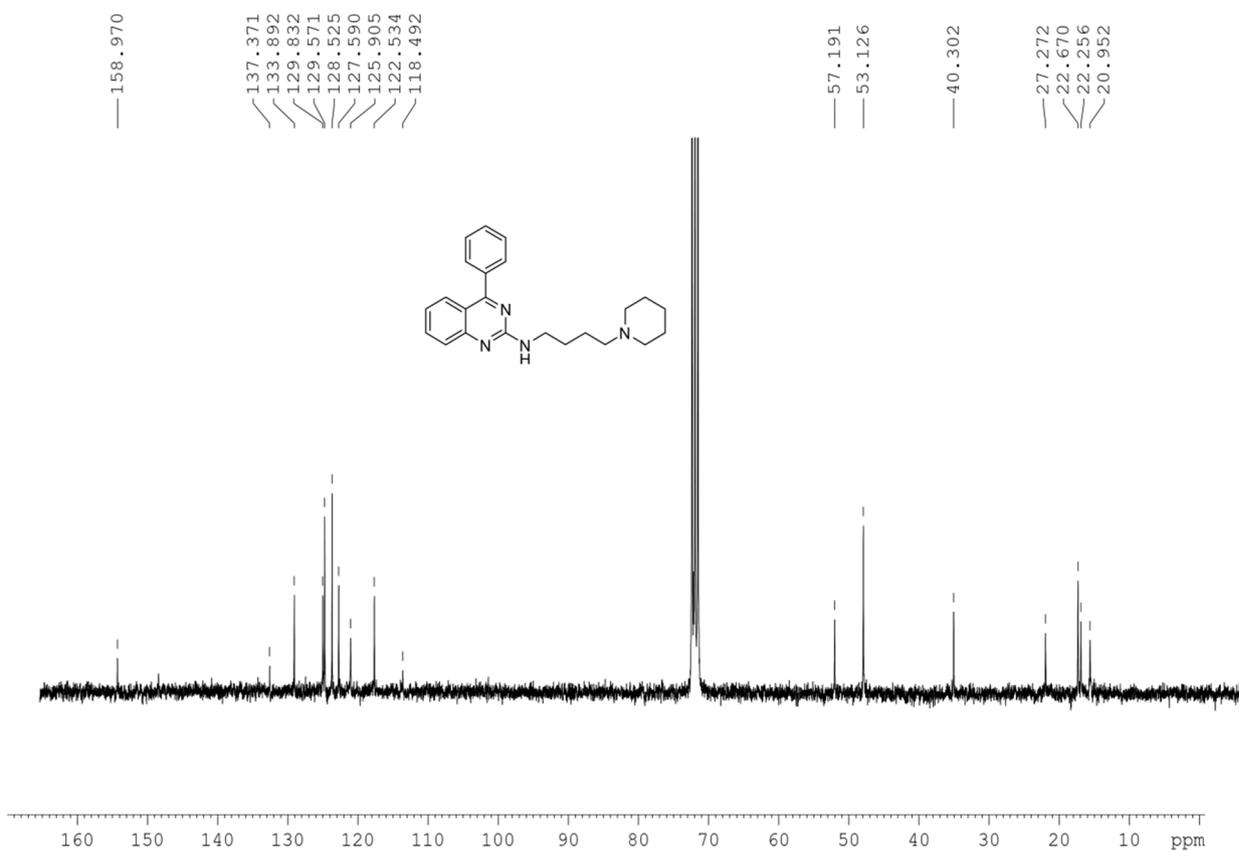
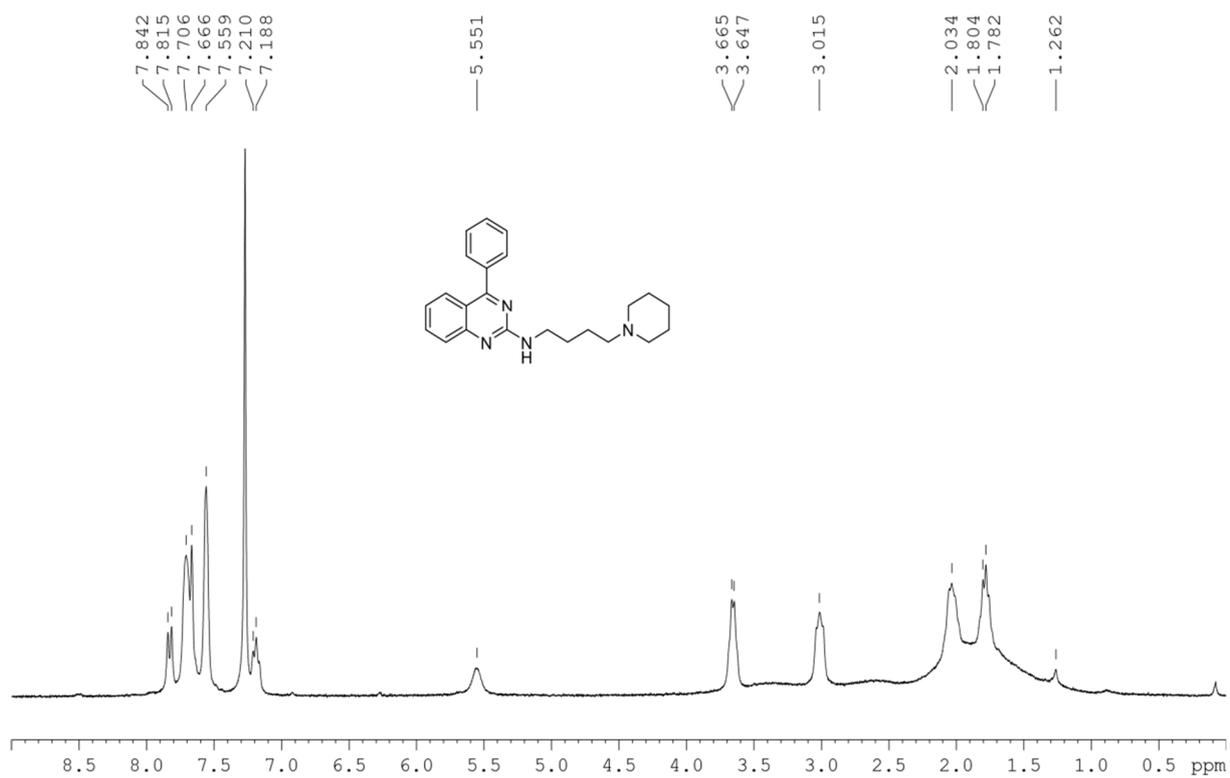
1H- and 13C-NMR Spectra in DMSO-d6 of compound 9h



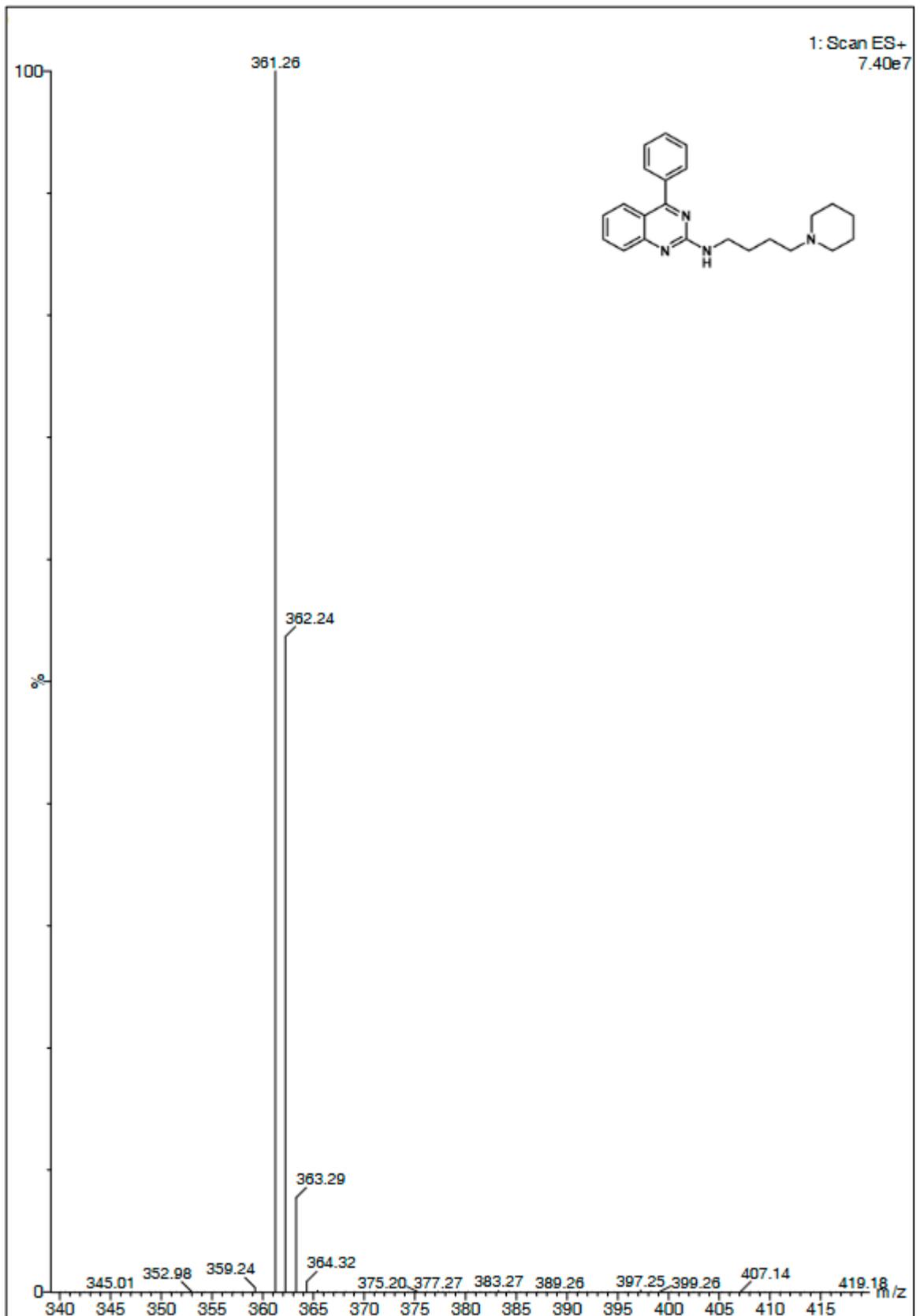
LC-MS mass spectrum of compound 9h



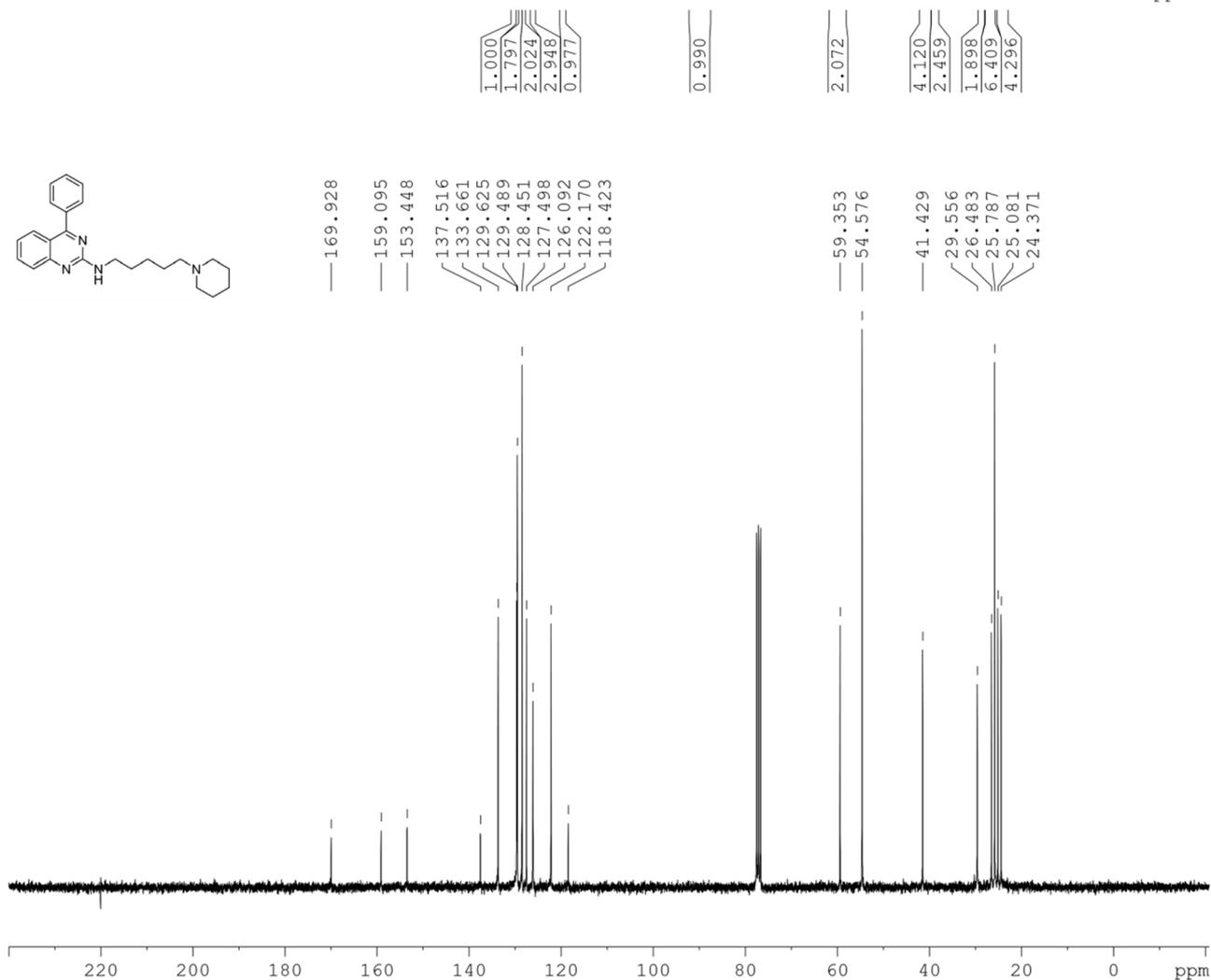
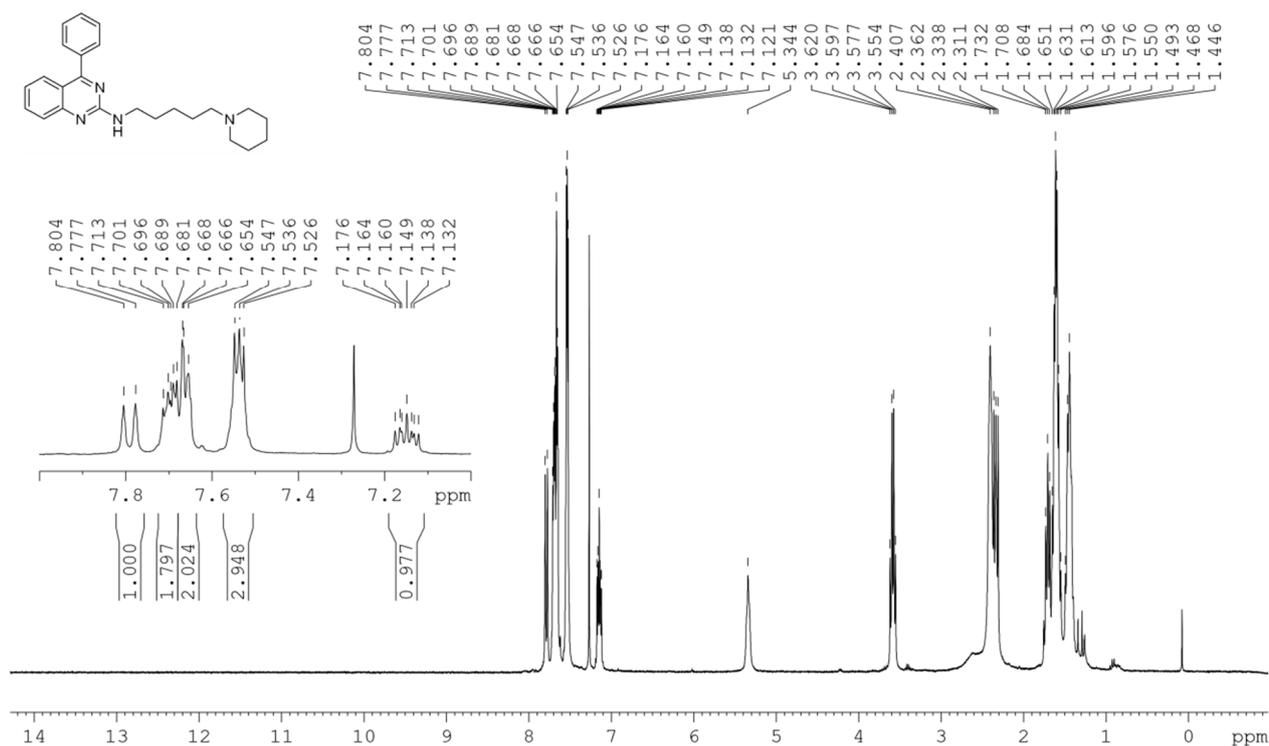
1H- and 13C-NMR Spectra in CDCl₃ of compound 9i



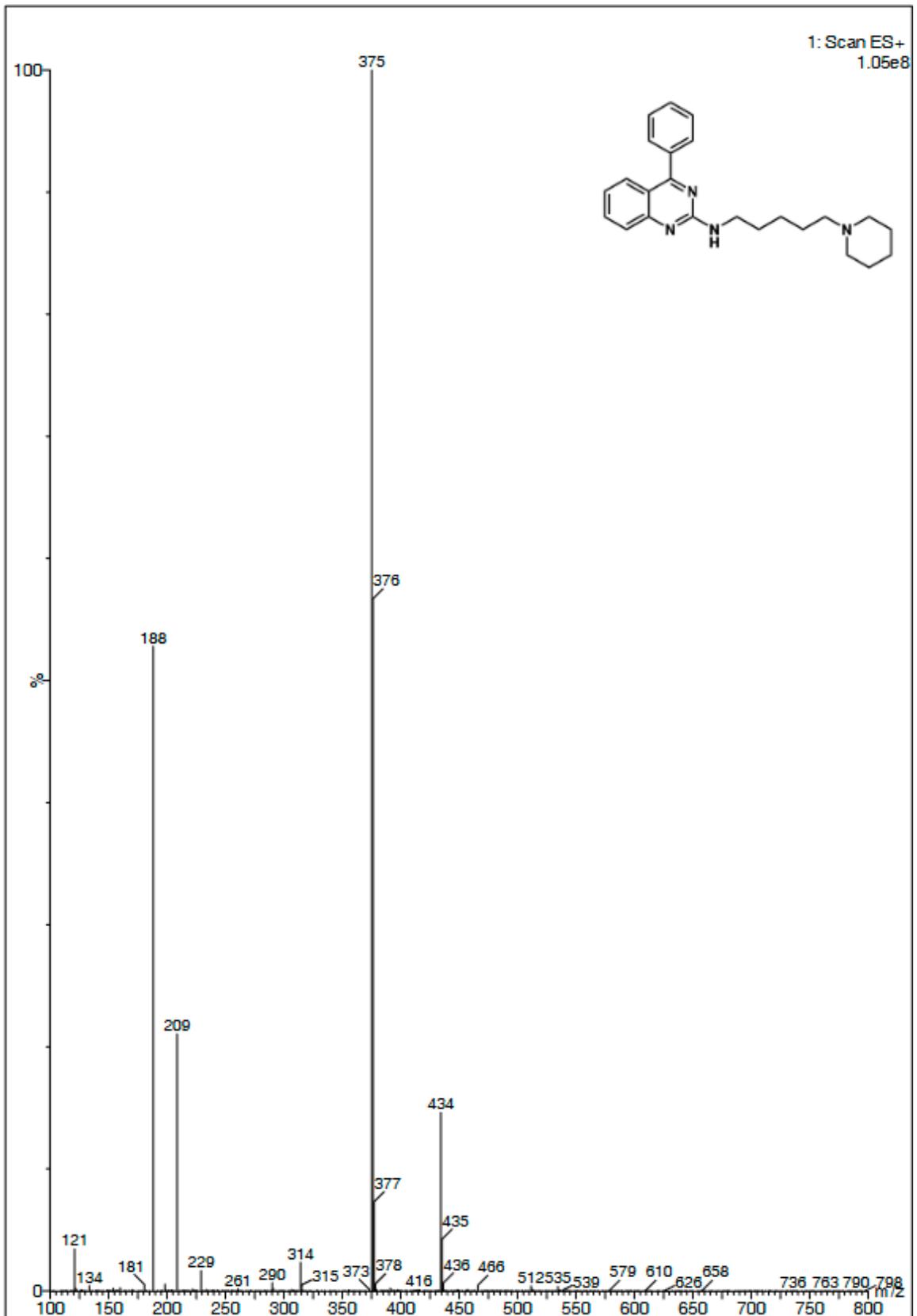
LC-MS mass spectrum of compound 9i



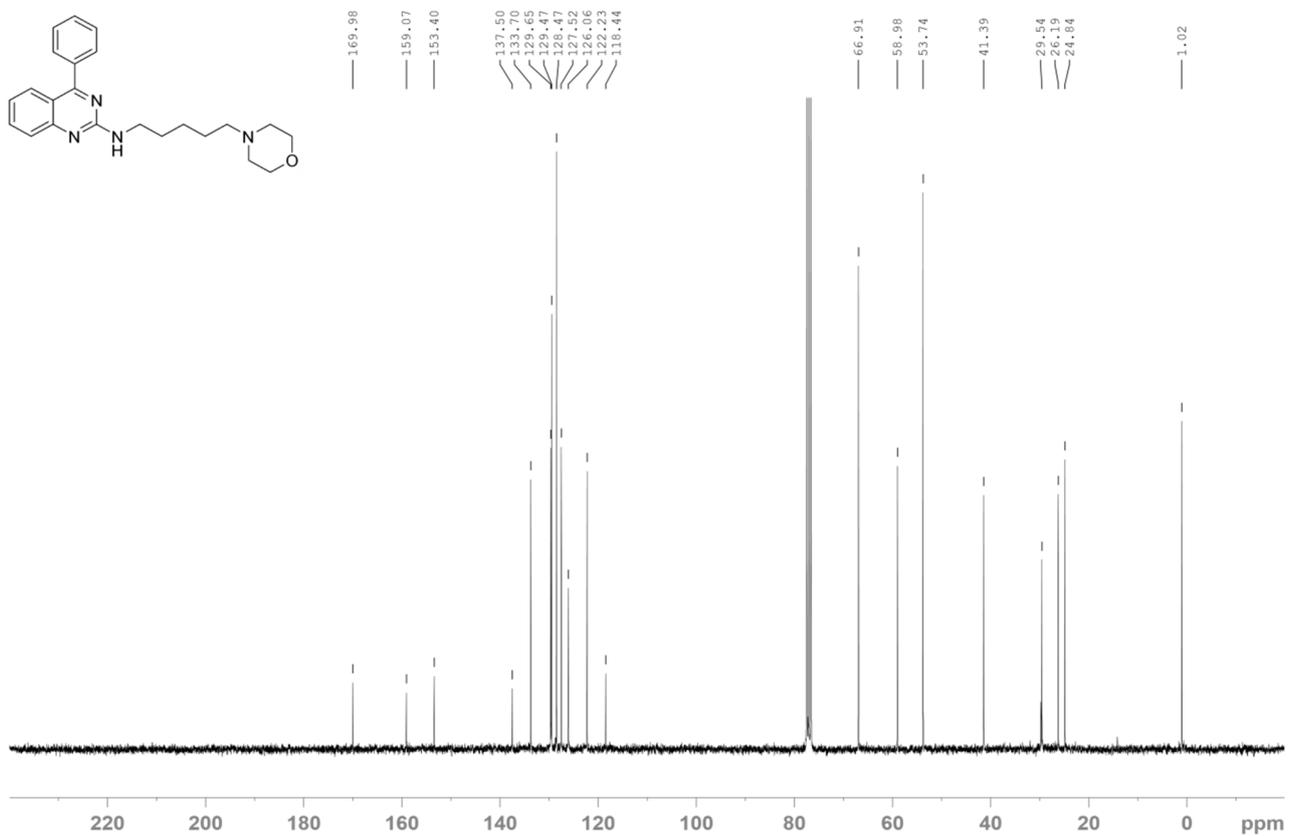
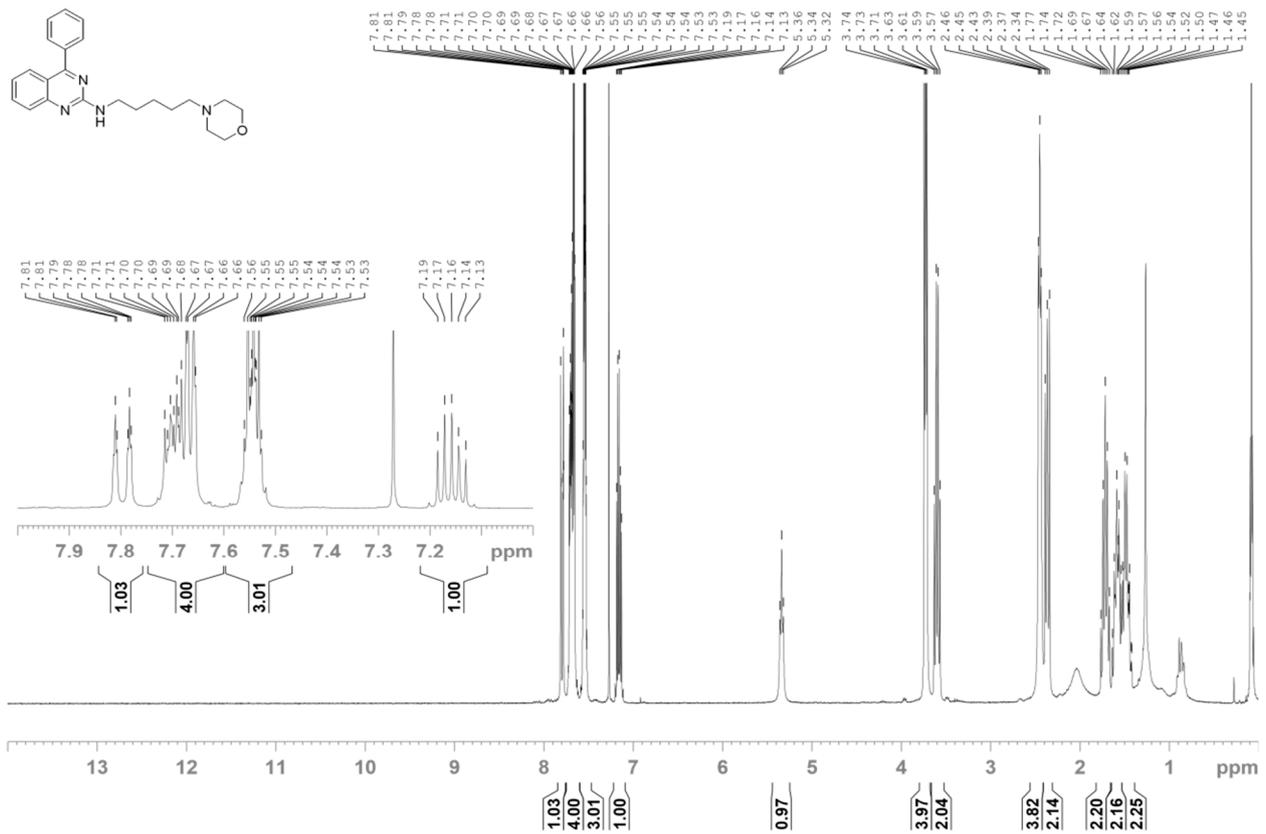
1H- and 13C-NMR Spectra in CDCl₃ of compound 9j



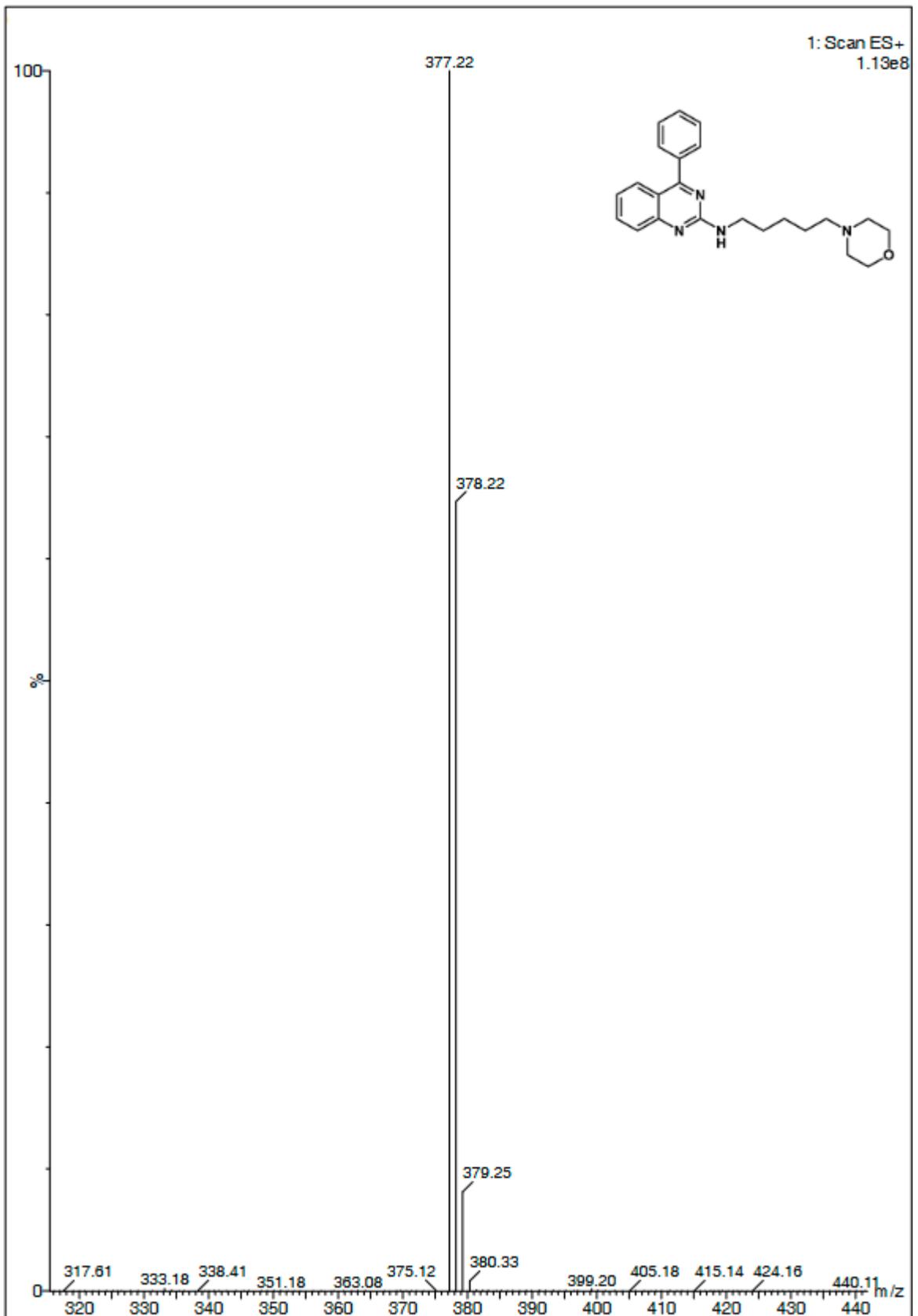
LC-MS mass spectrum of compound 9j



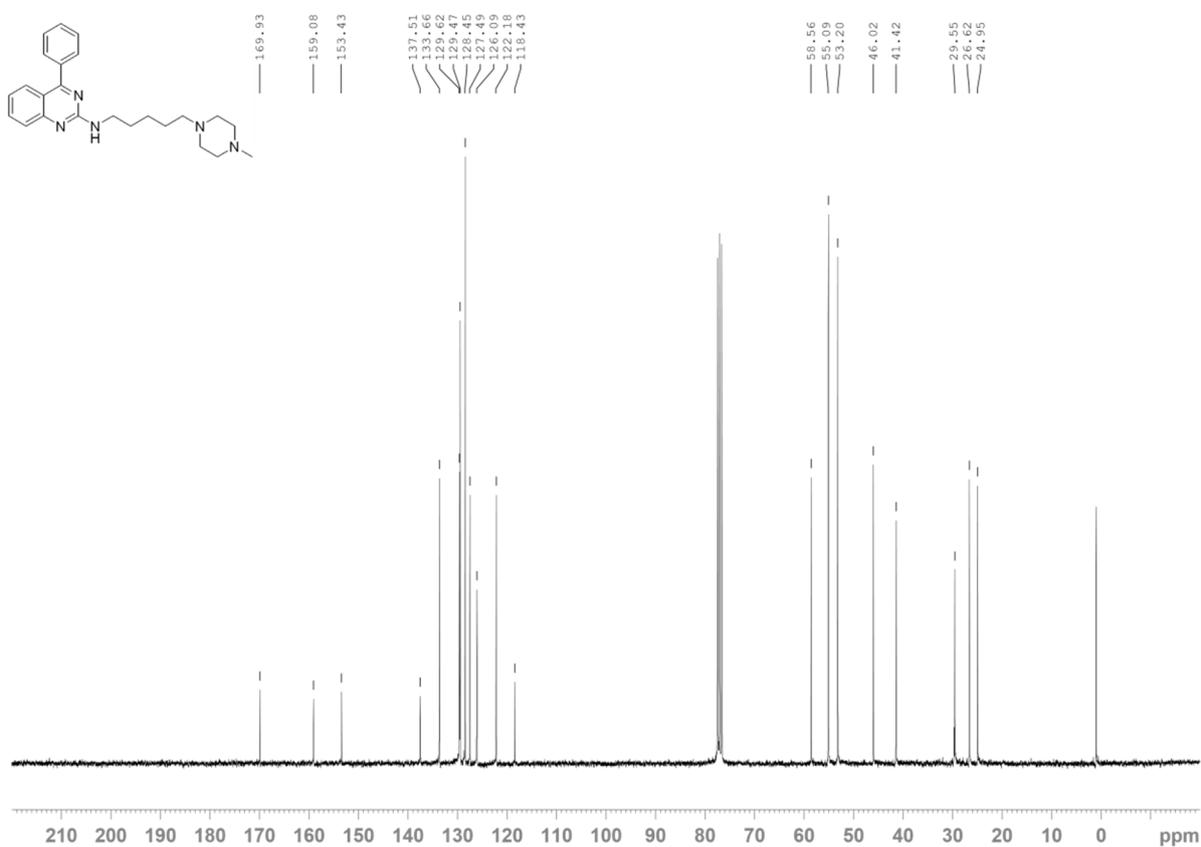
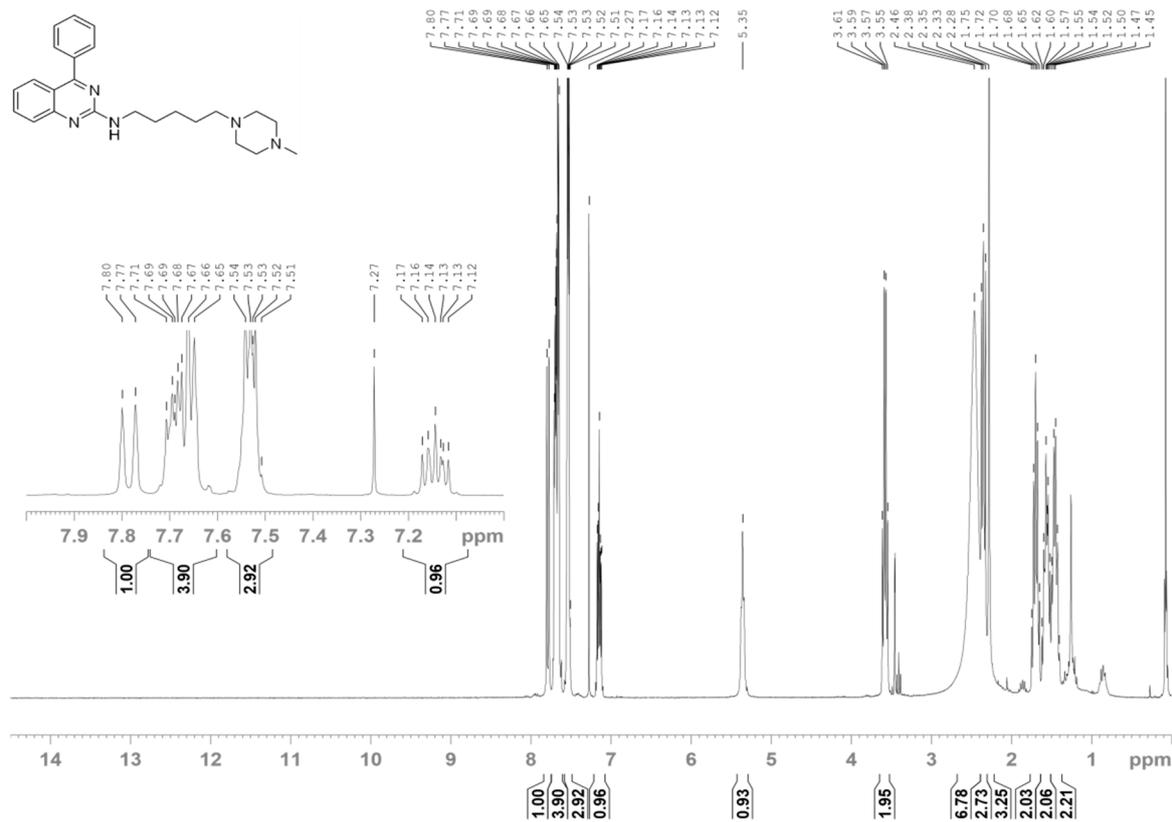
1H- and 13C-NMR Spectra in CDCl₃ of compound 9k



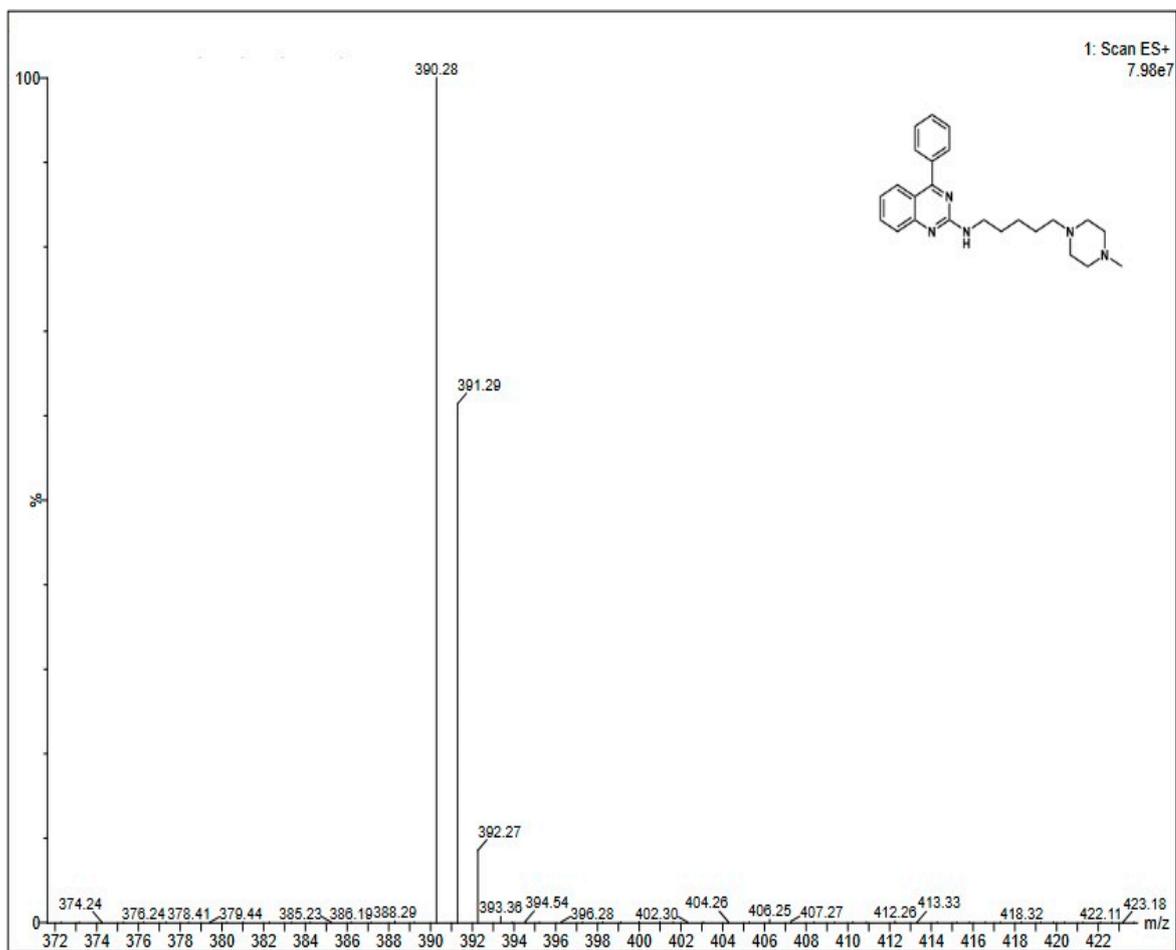
LC-MS mass spectrum of compound 9k



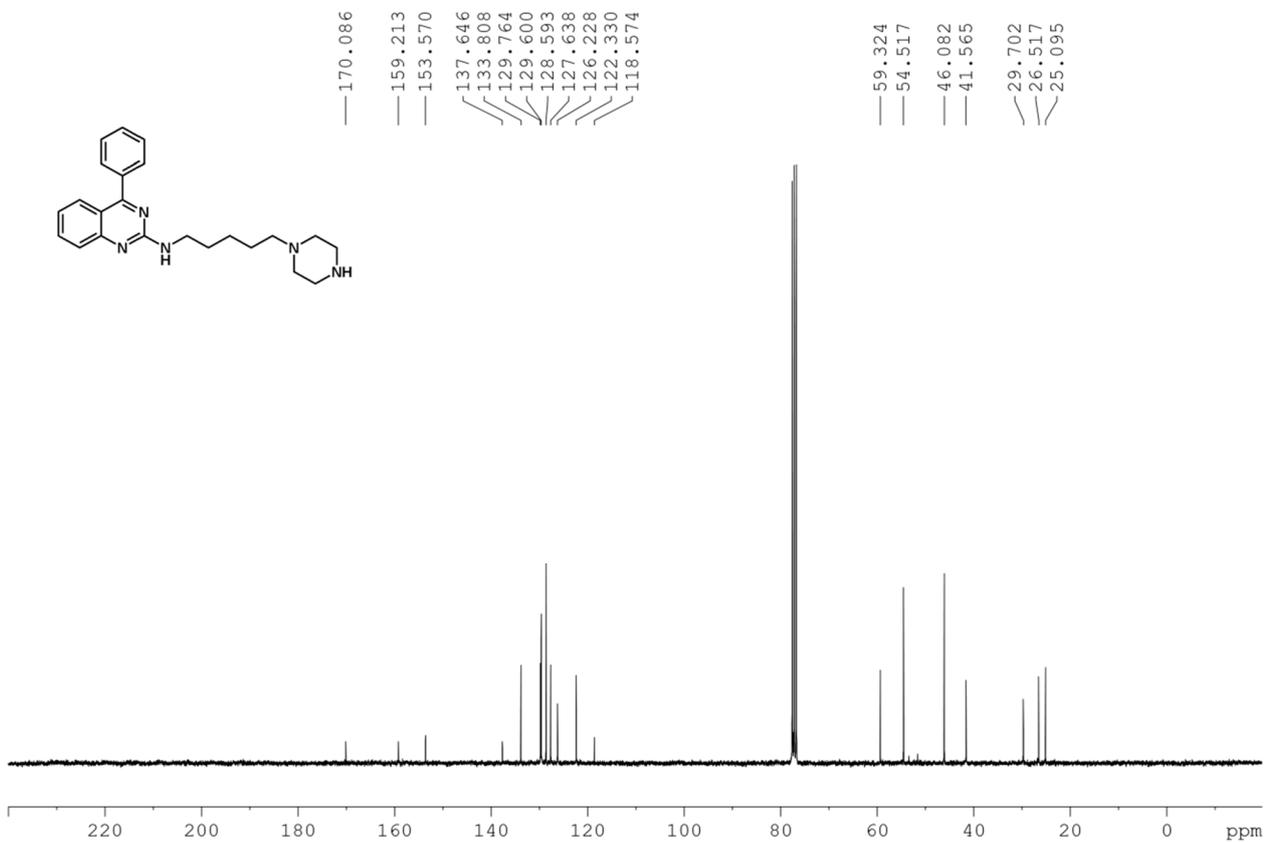
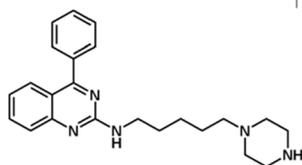
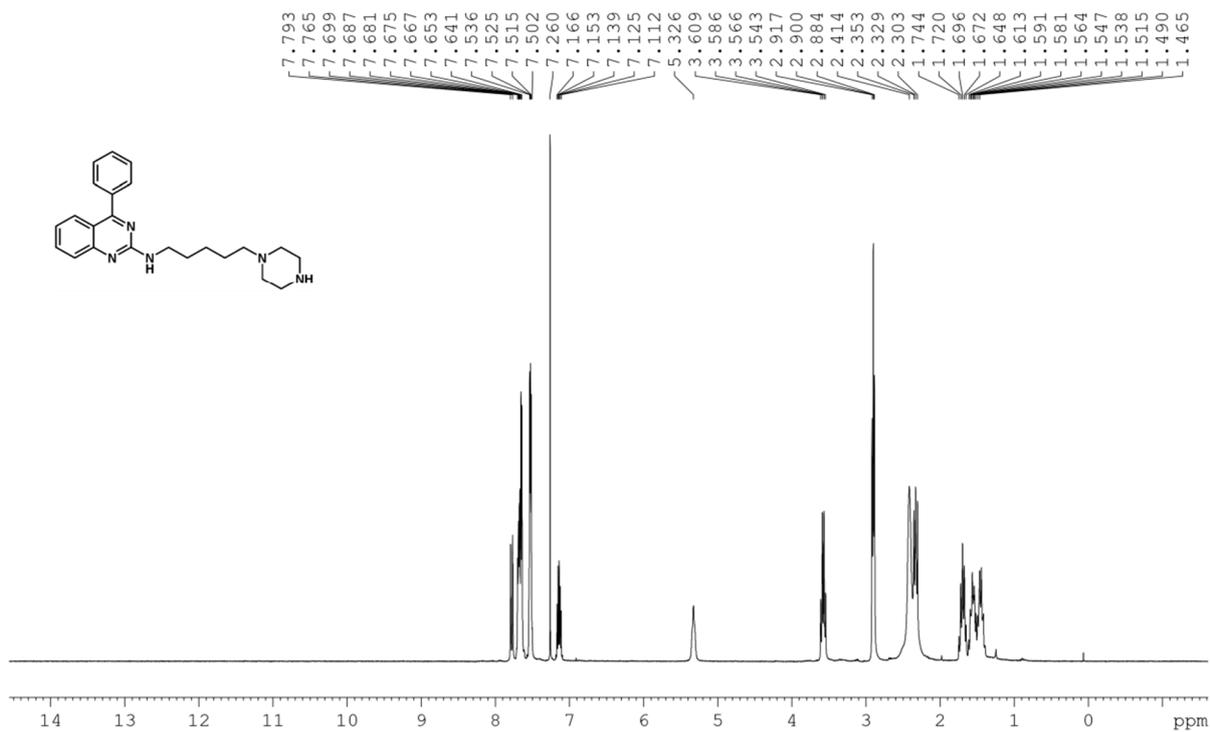
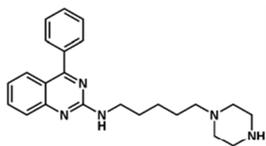
1H- and 13C-NMR Spectra in CDCl₃ of compound 9I



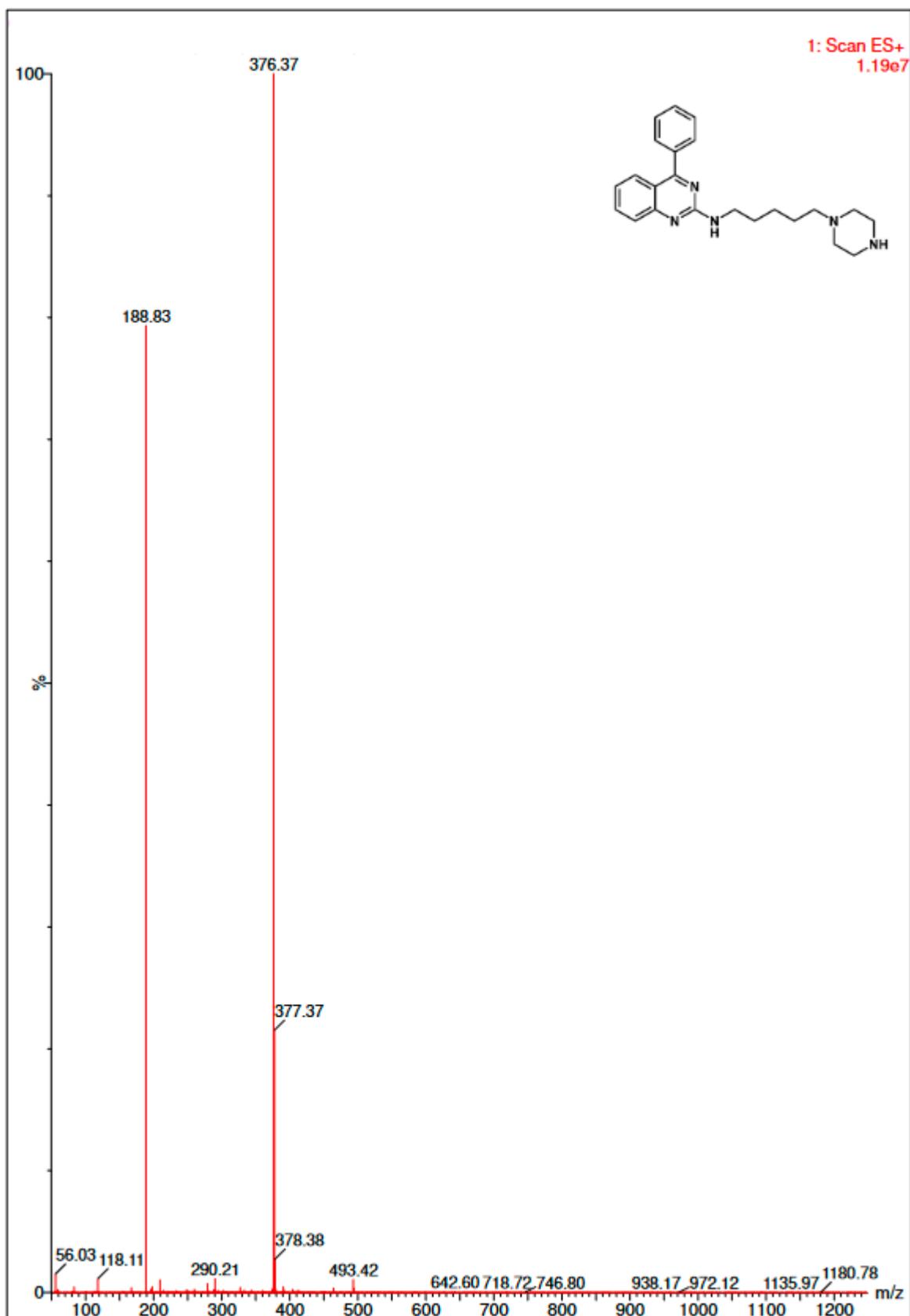
LC-MS mass spectrum of compound 9I



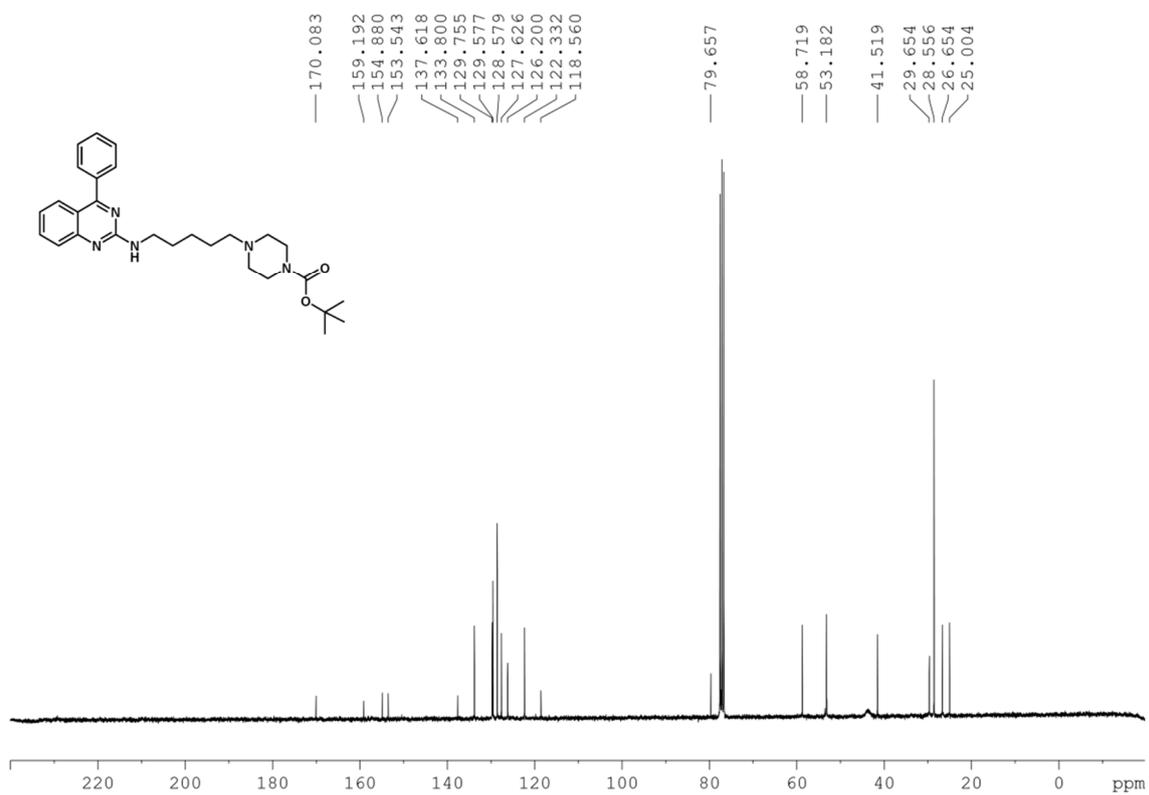
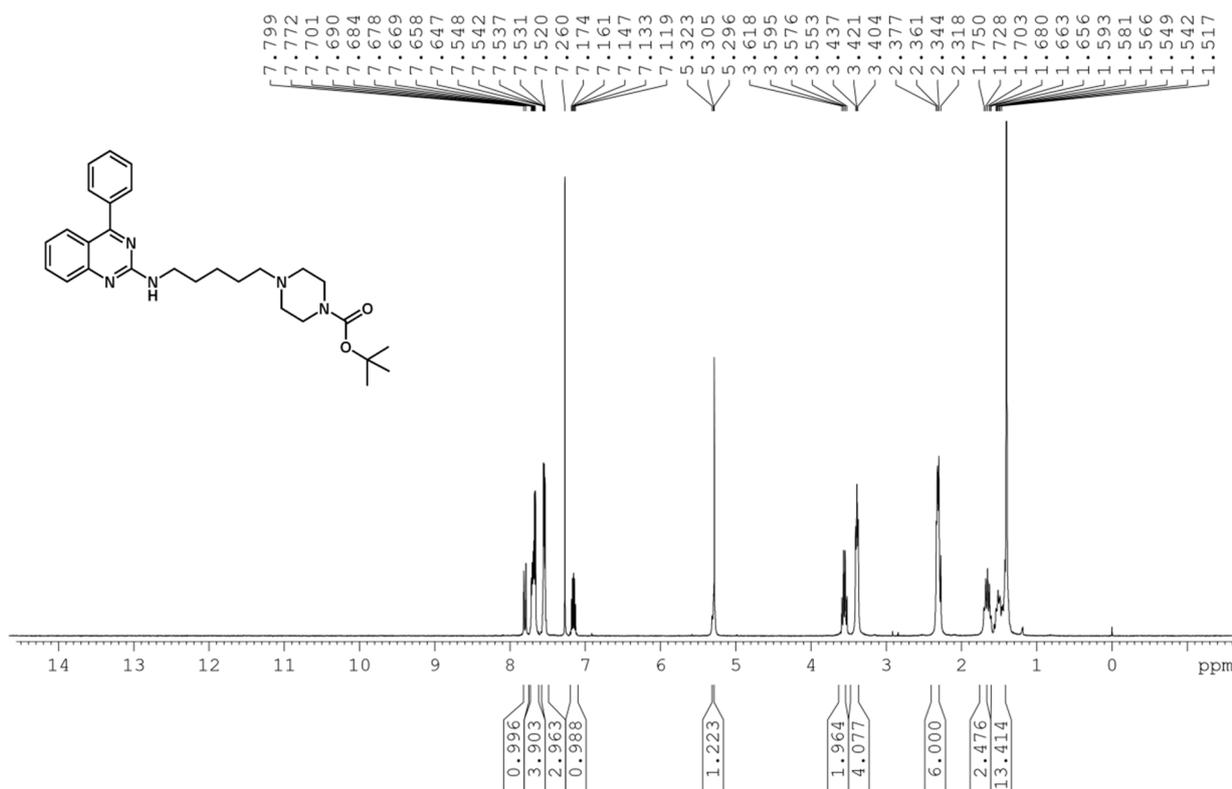
1H- and 13C-NMR Spectra in CDCl₃ of compound 9m



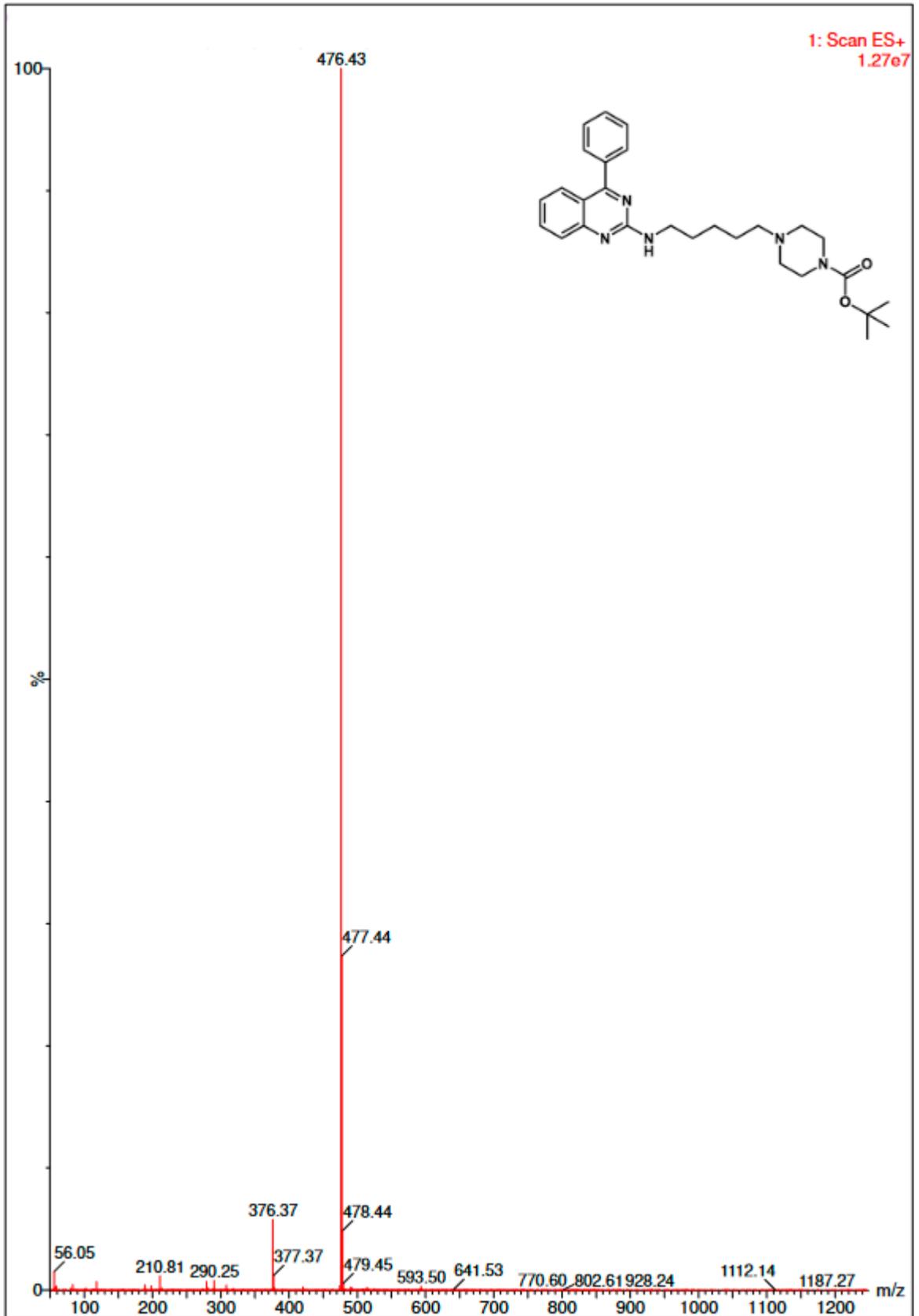
LC-MS mass spectrum of compound 9m



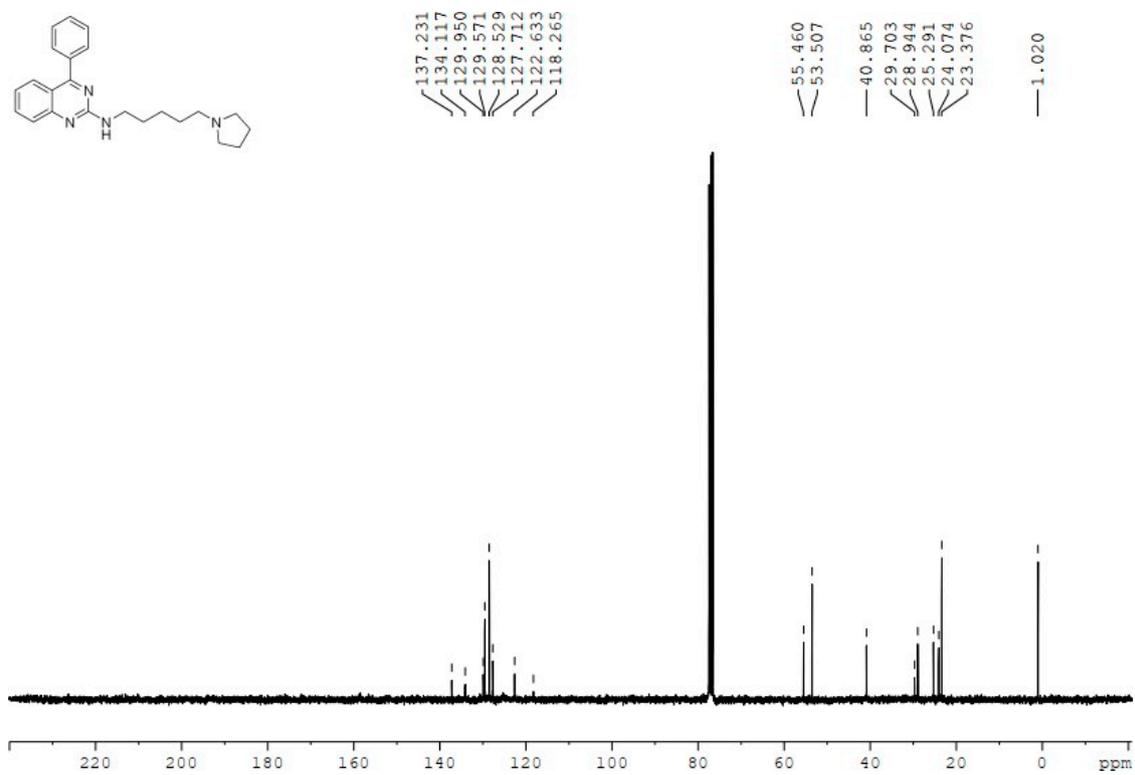
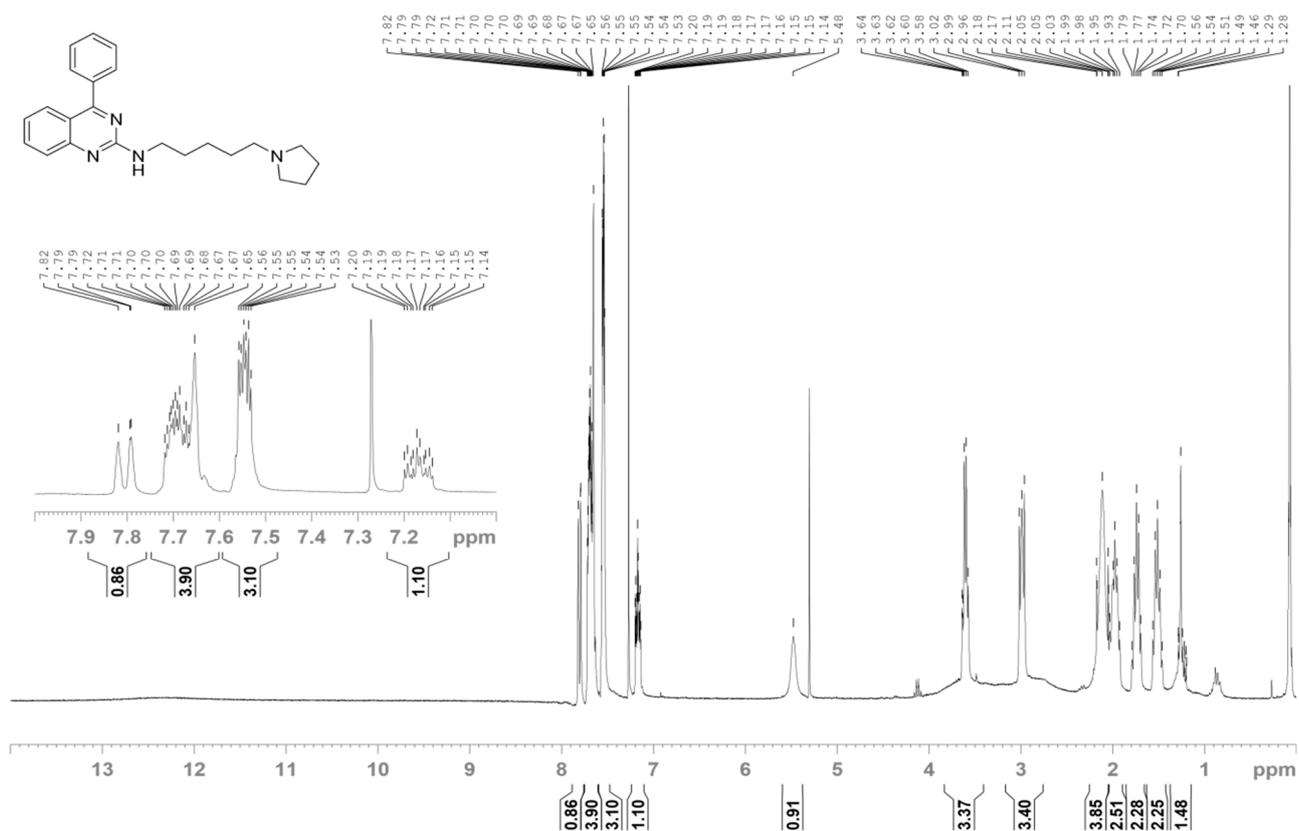
1H- and 13C-NMR Spectra in CDCl₃ of compound 9n



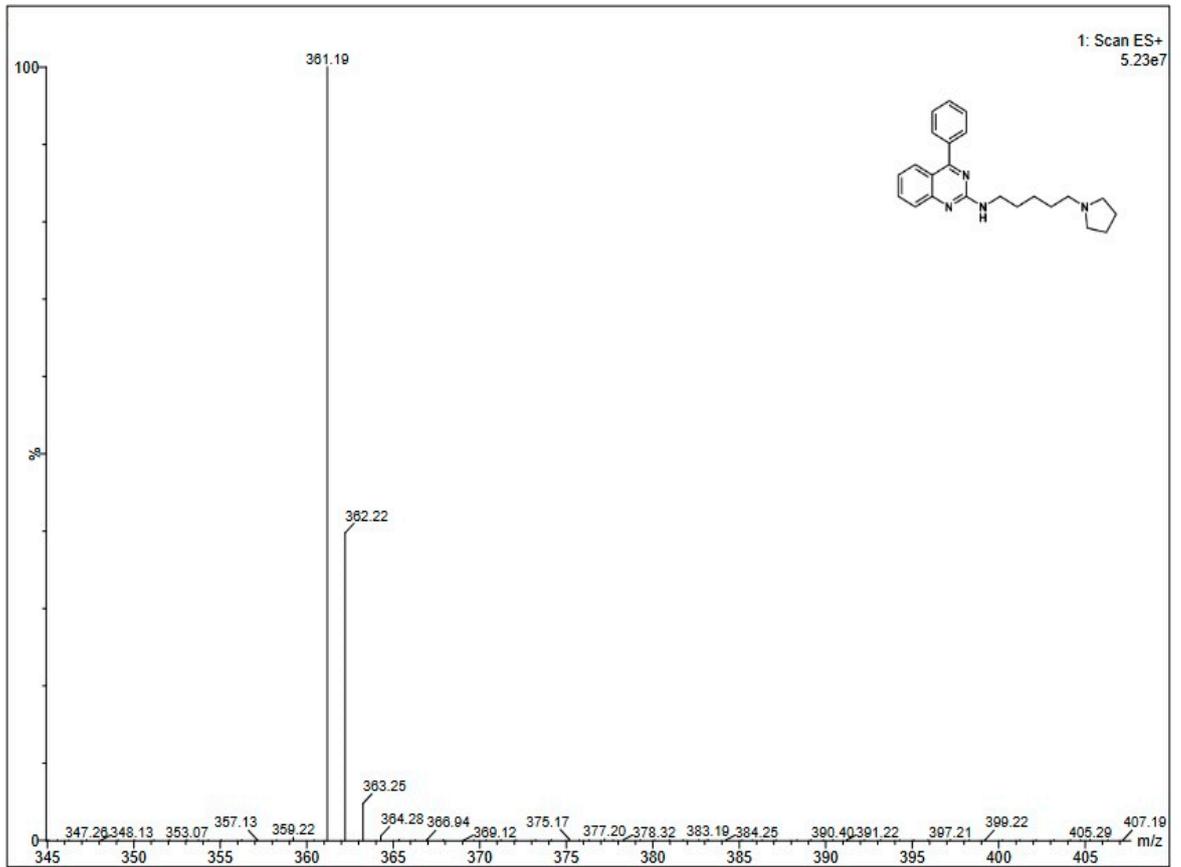
LC-MS mass spectrum of compound 9n



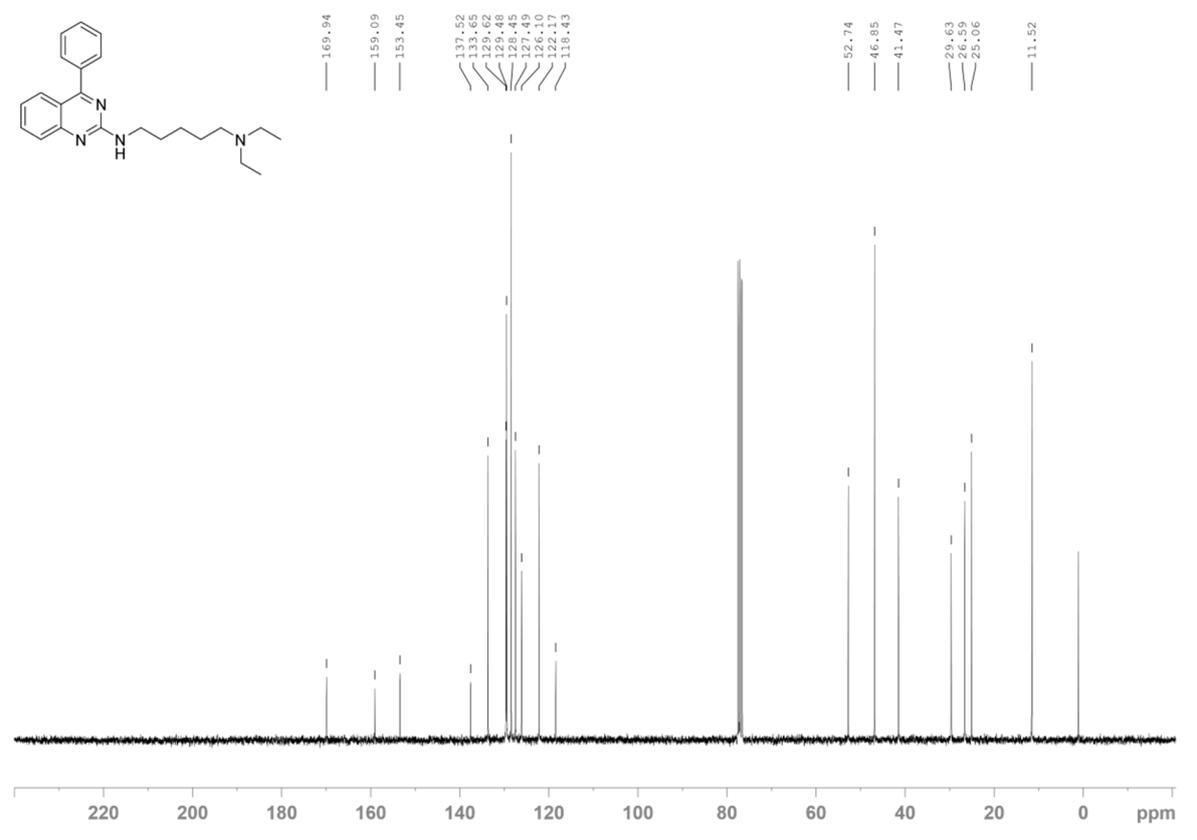
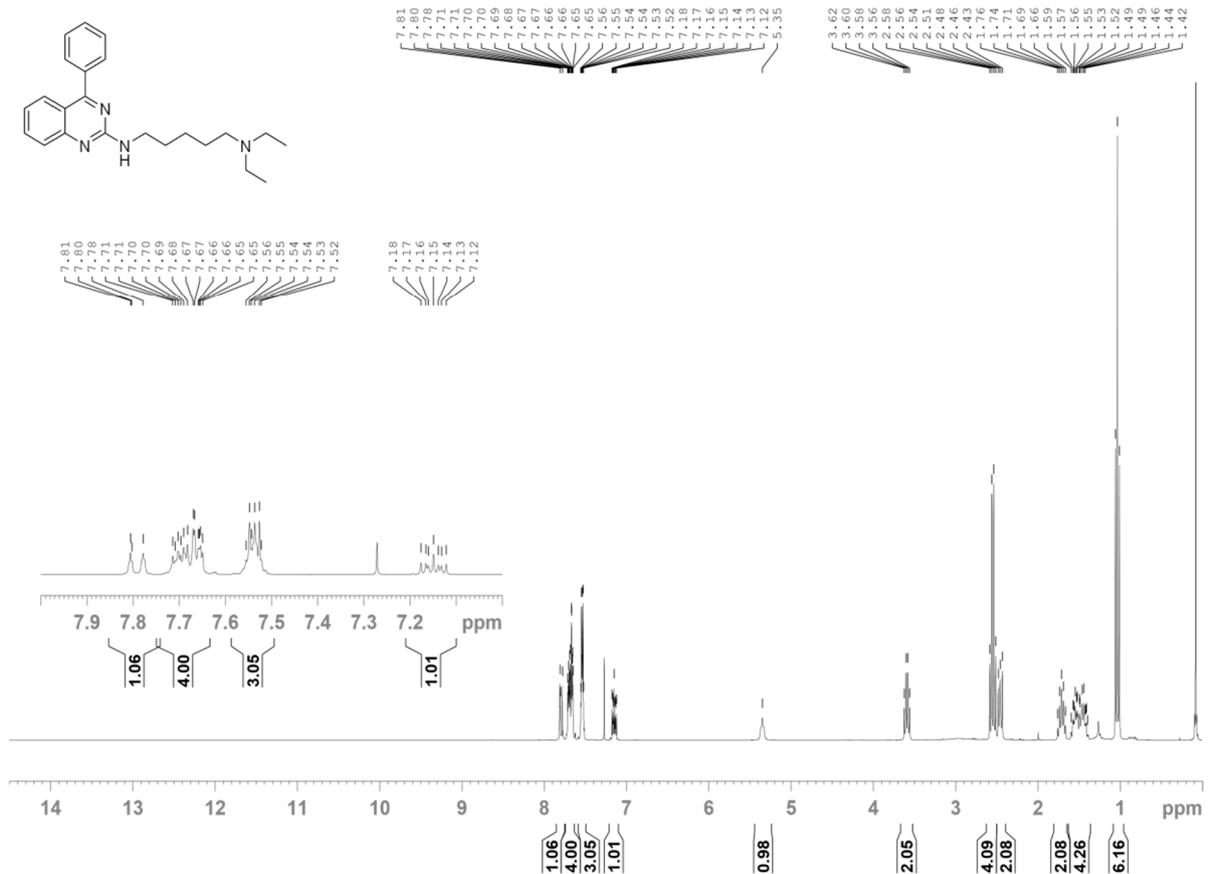
1H- and 13C-NMR Spectra in CDCl₃ of compound 9o



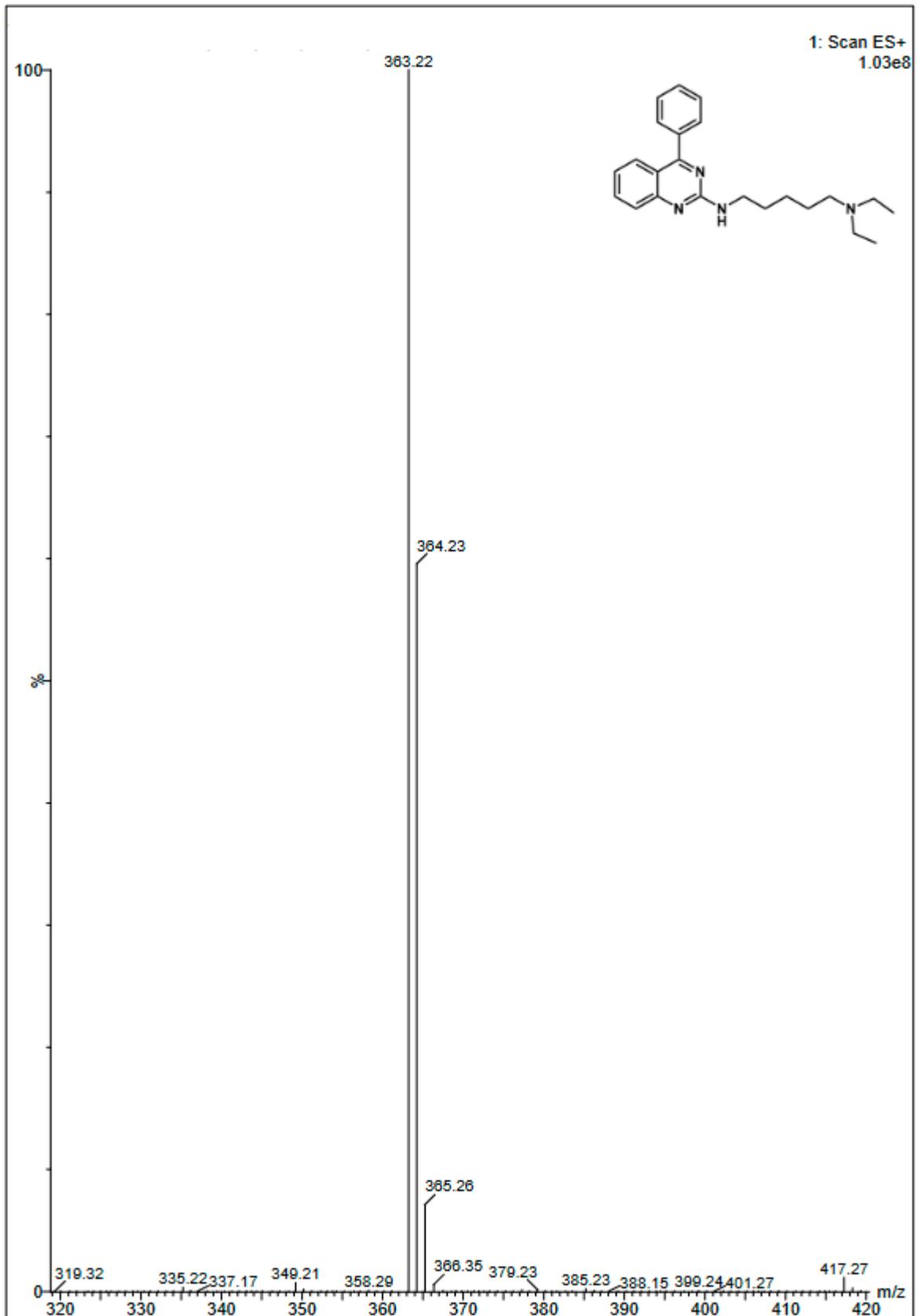
LC-MS mass spectrum of compound 9o



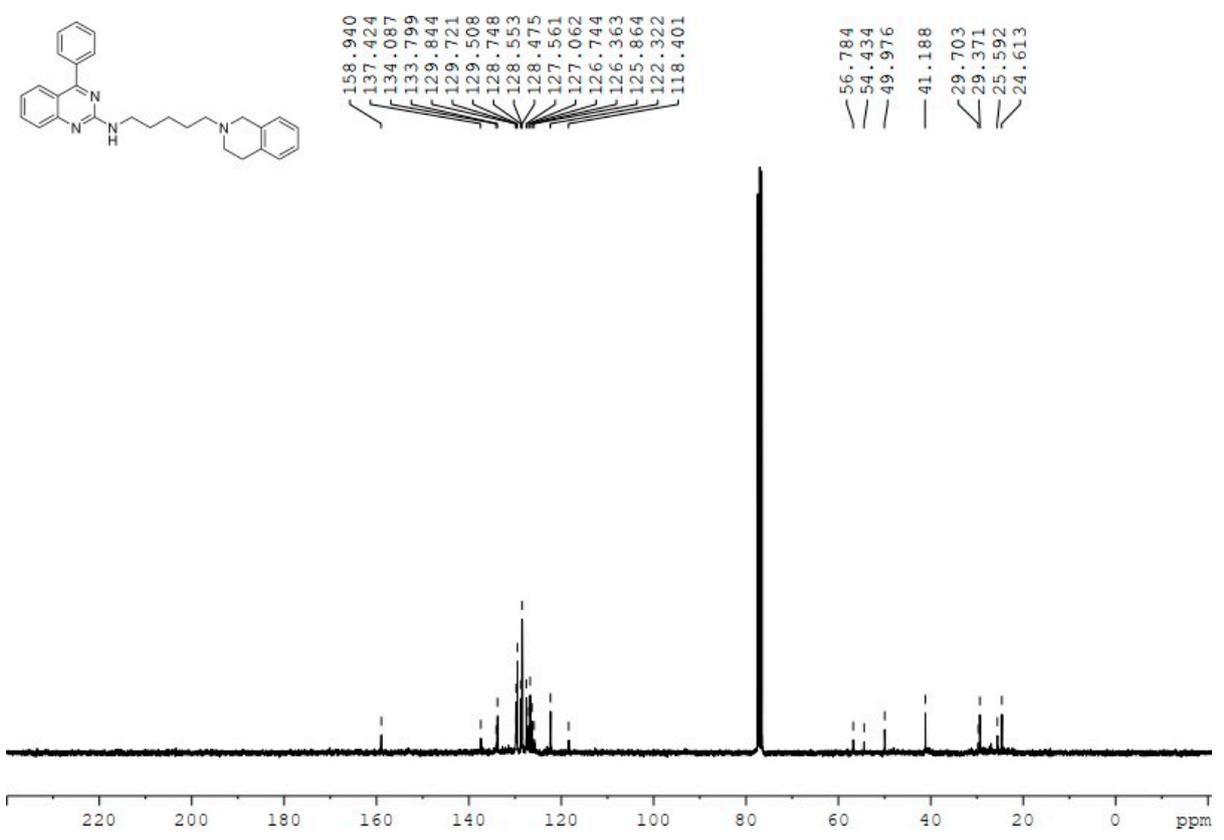
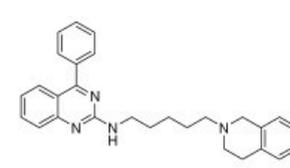
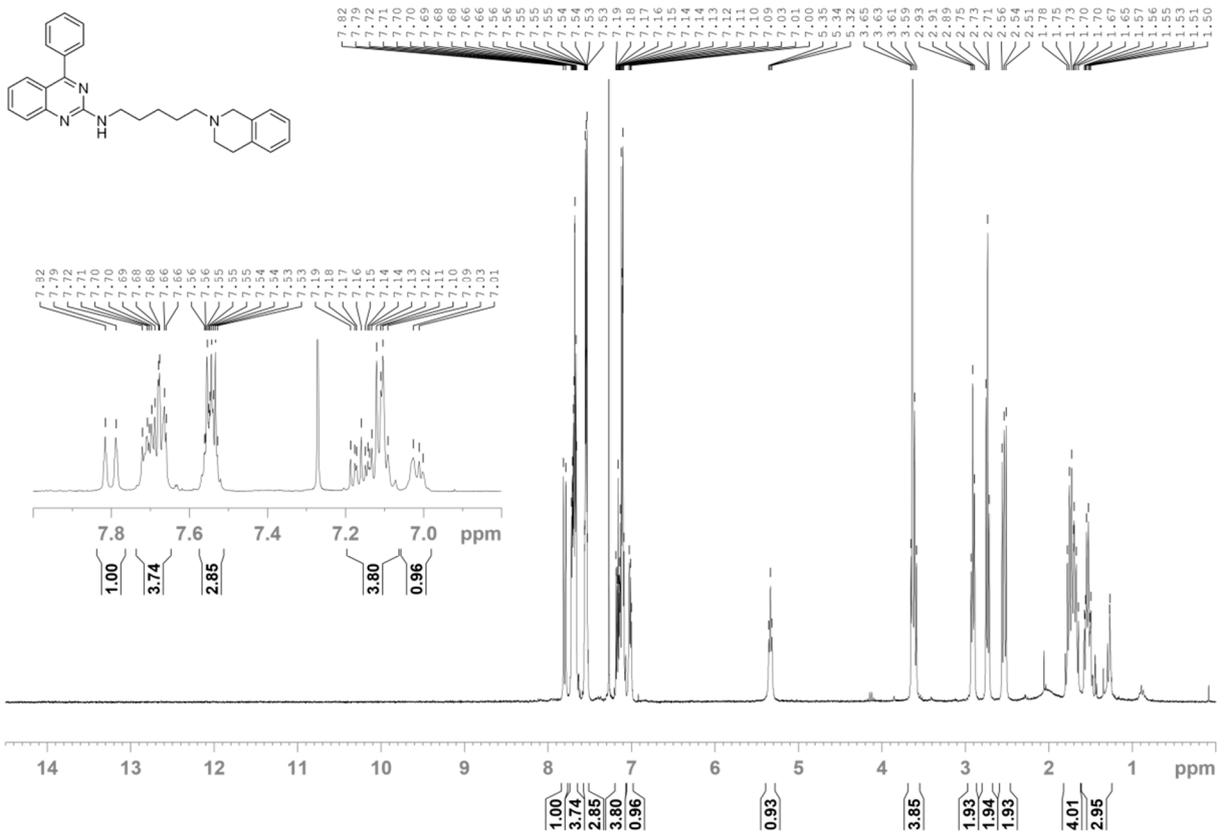
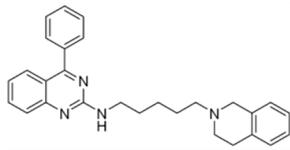
1H- and 13C-NMR Spectra in CDCl₃ of compound 9p



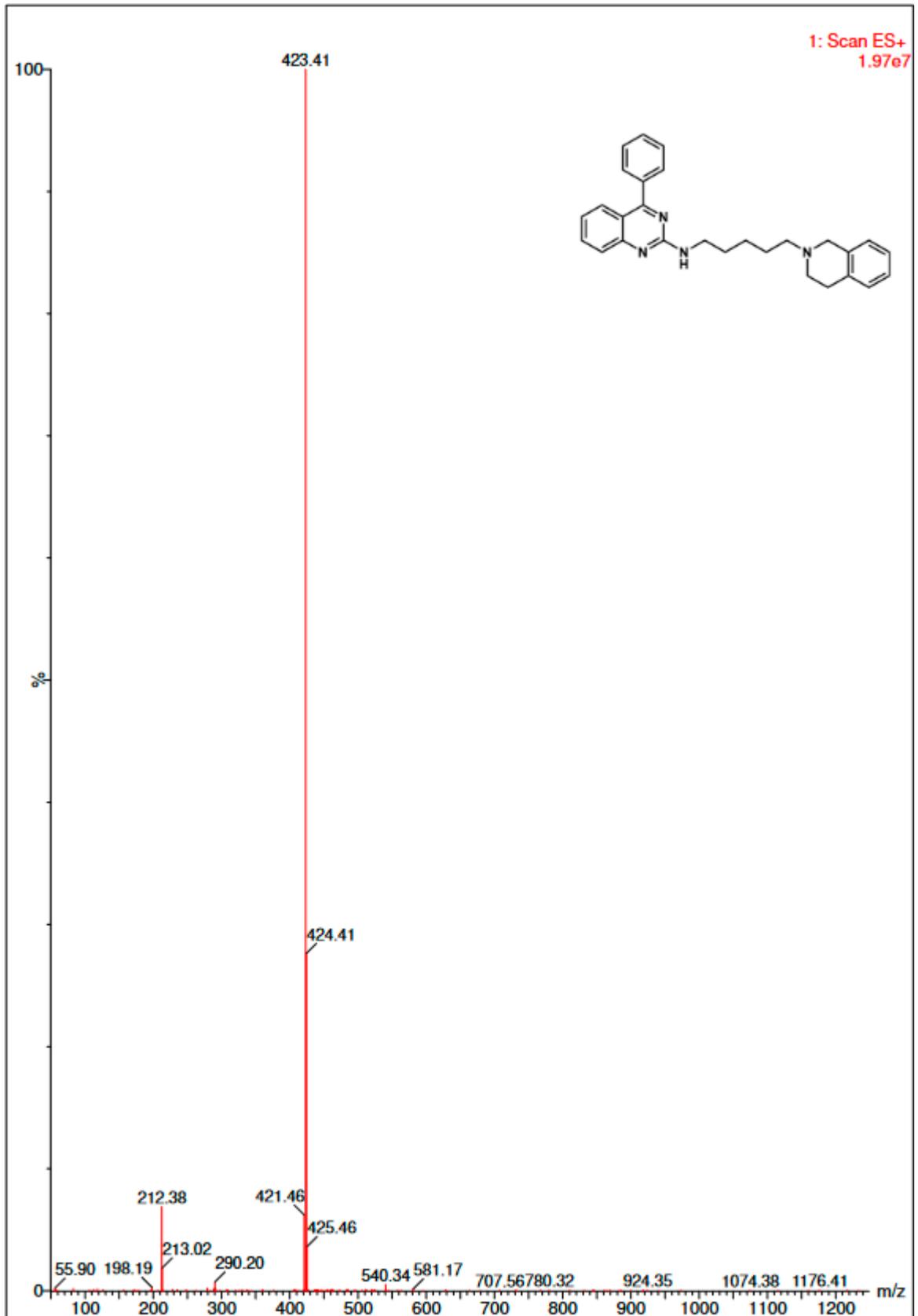
LC-MS mass spectrum of compound 9p



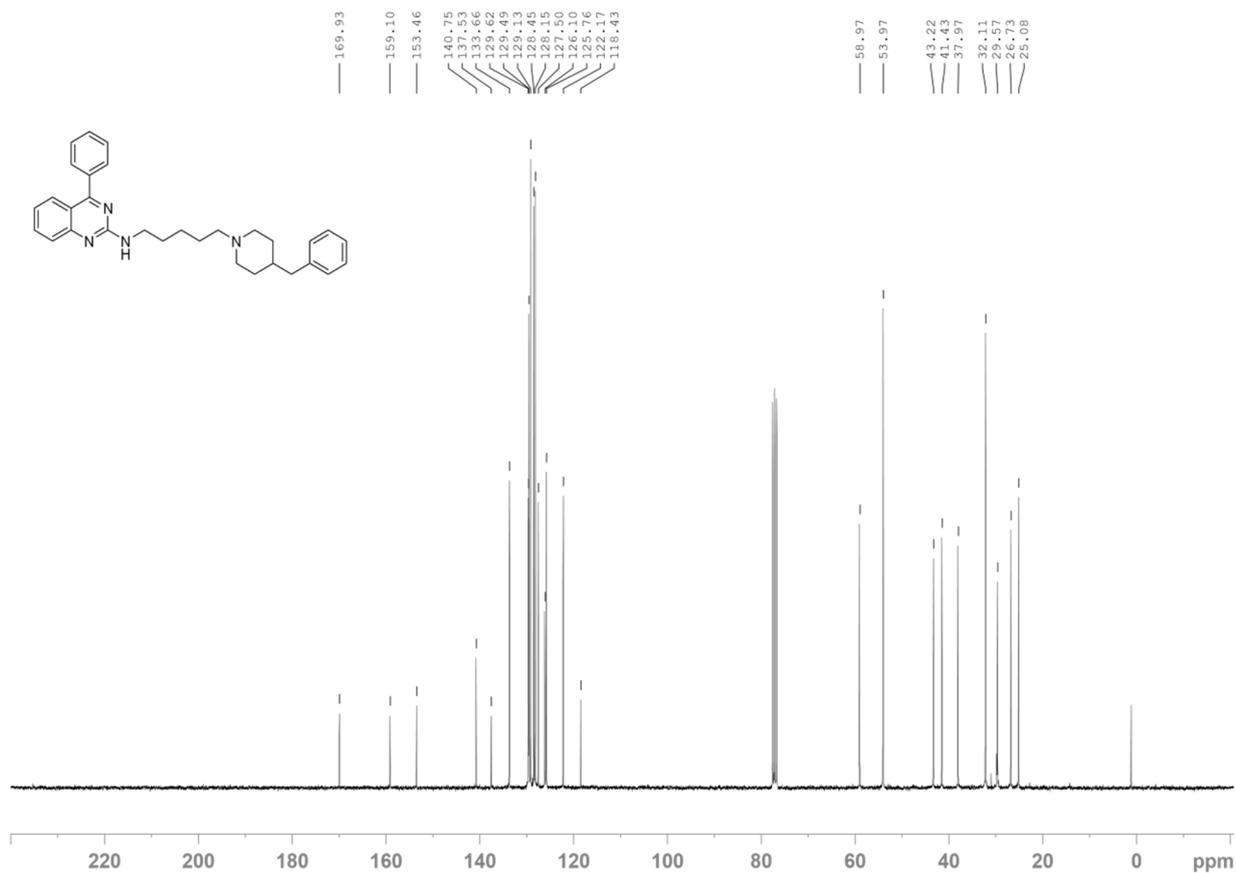
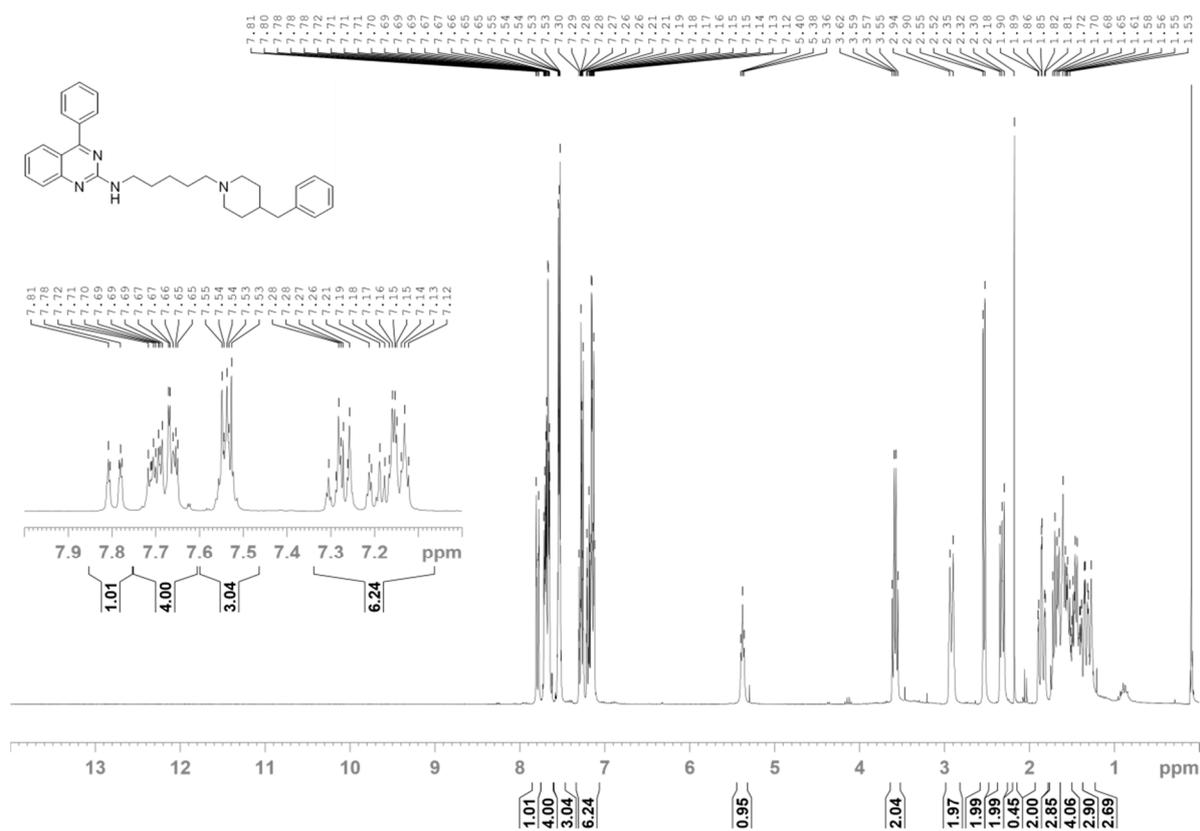
1H- and 13C-NMR Spectra in CDCl₃ of compound 9q



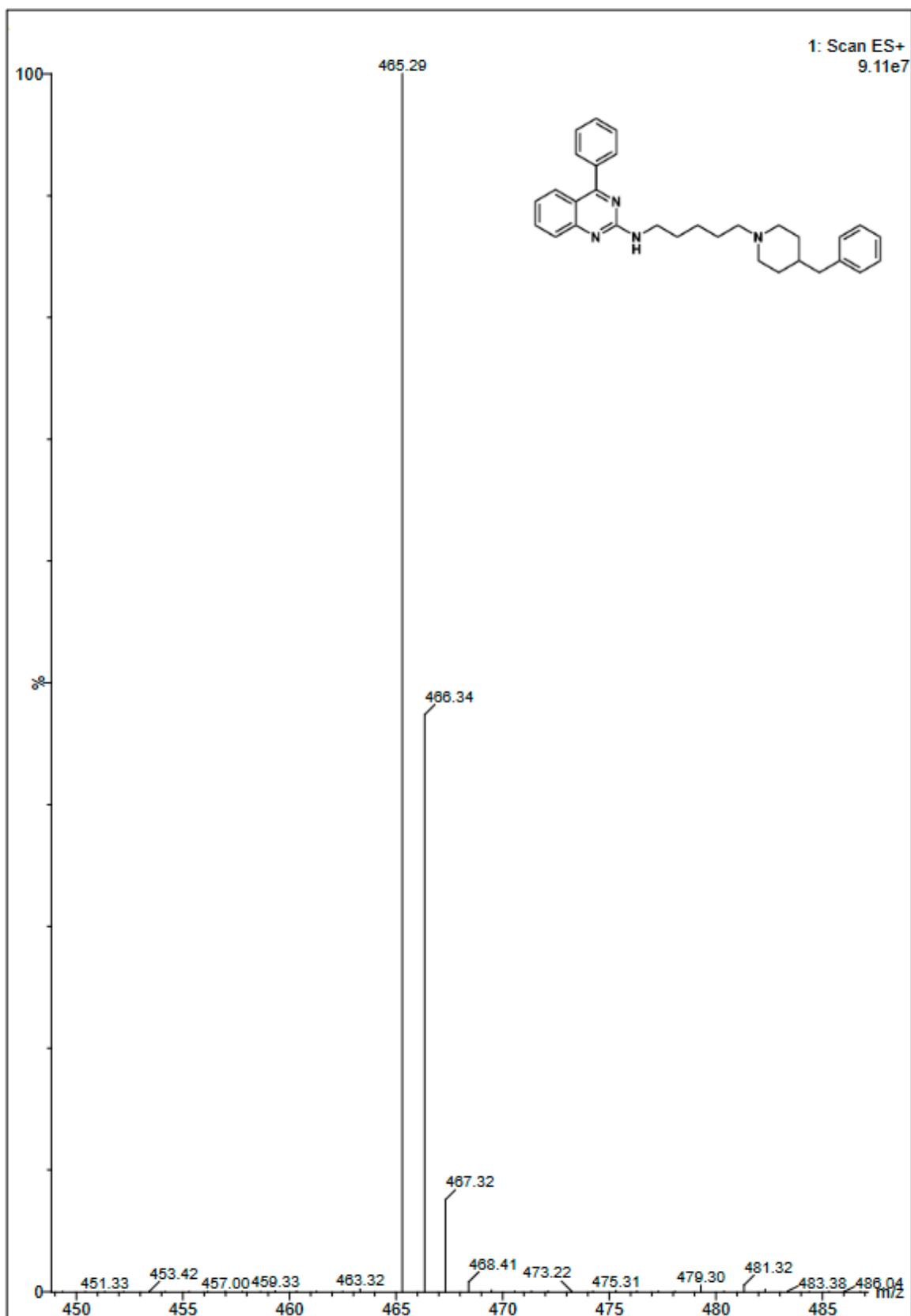
LC-MS mass spectrum of compound 9q



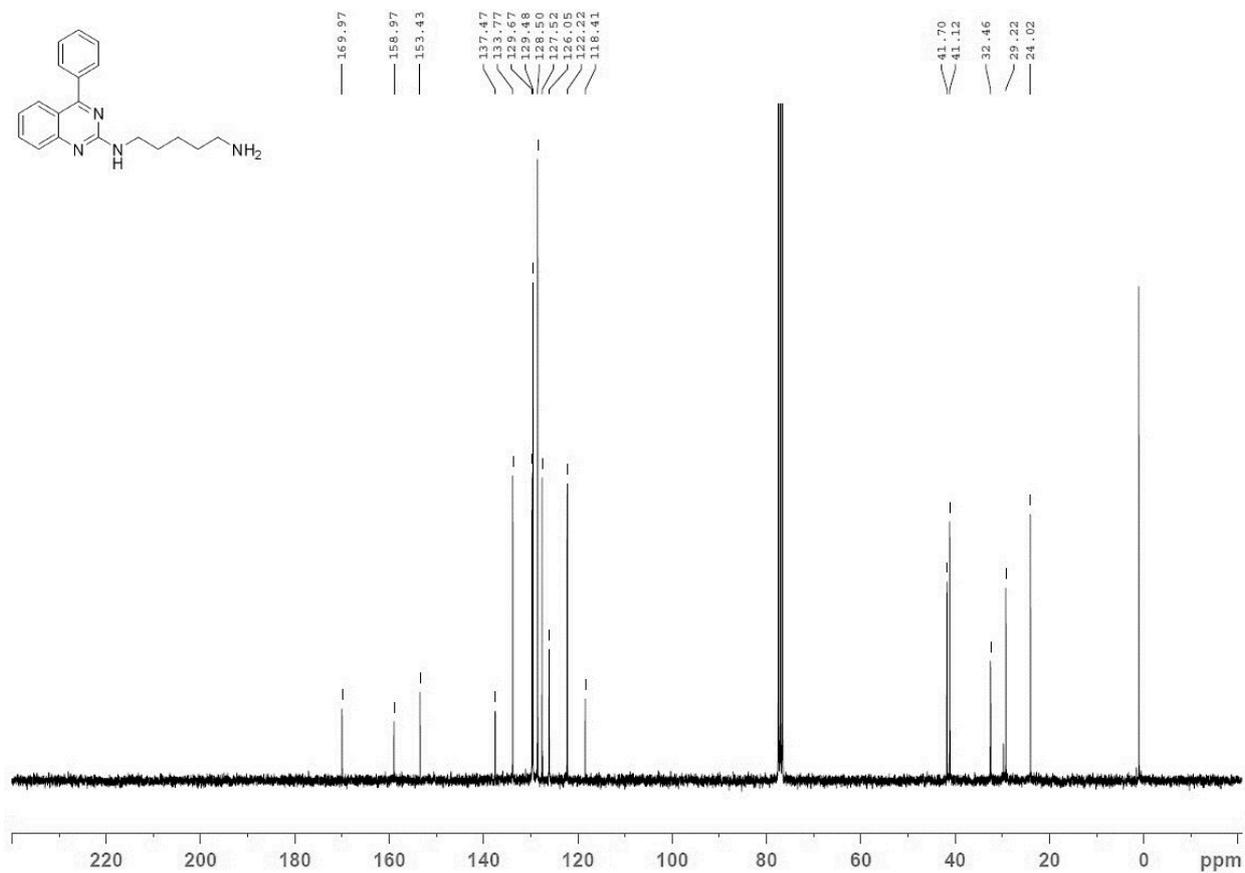
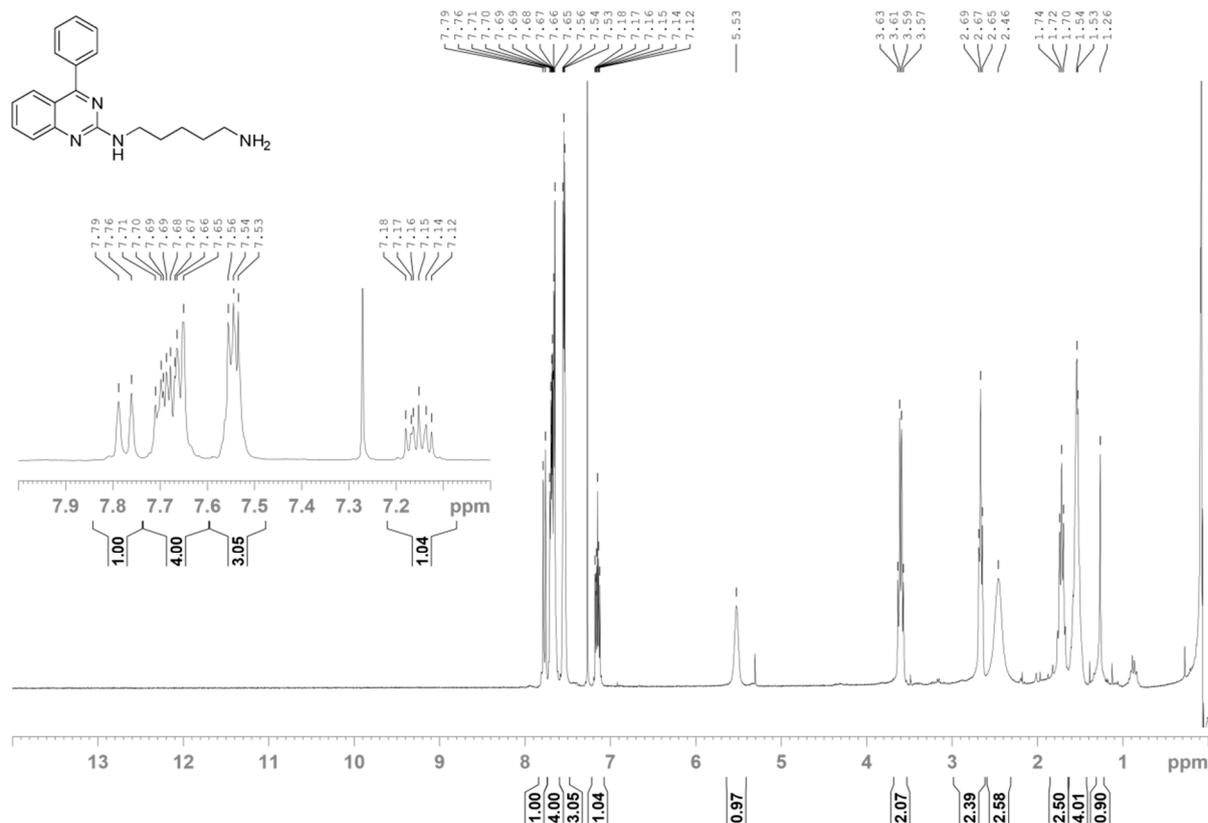
1H- and 13C-NMR Spectra in CDCl₃ of compound 9r



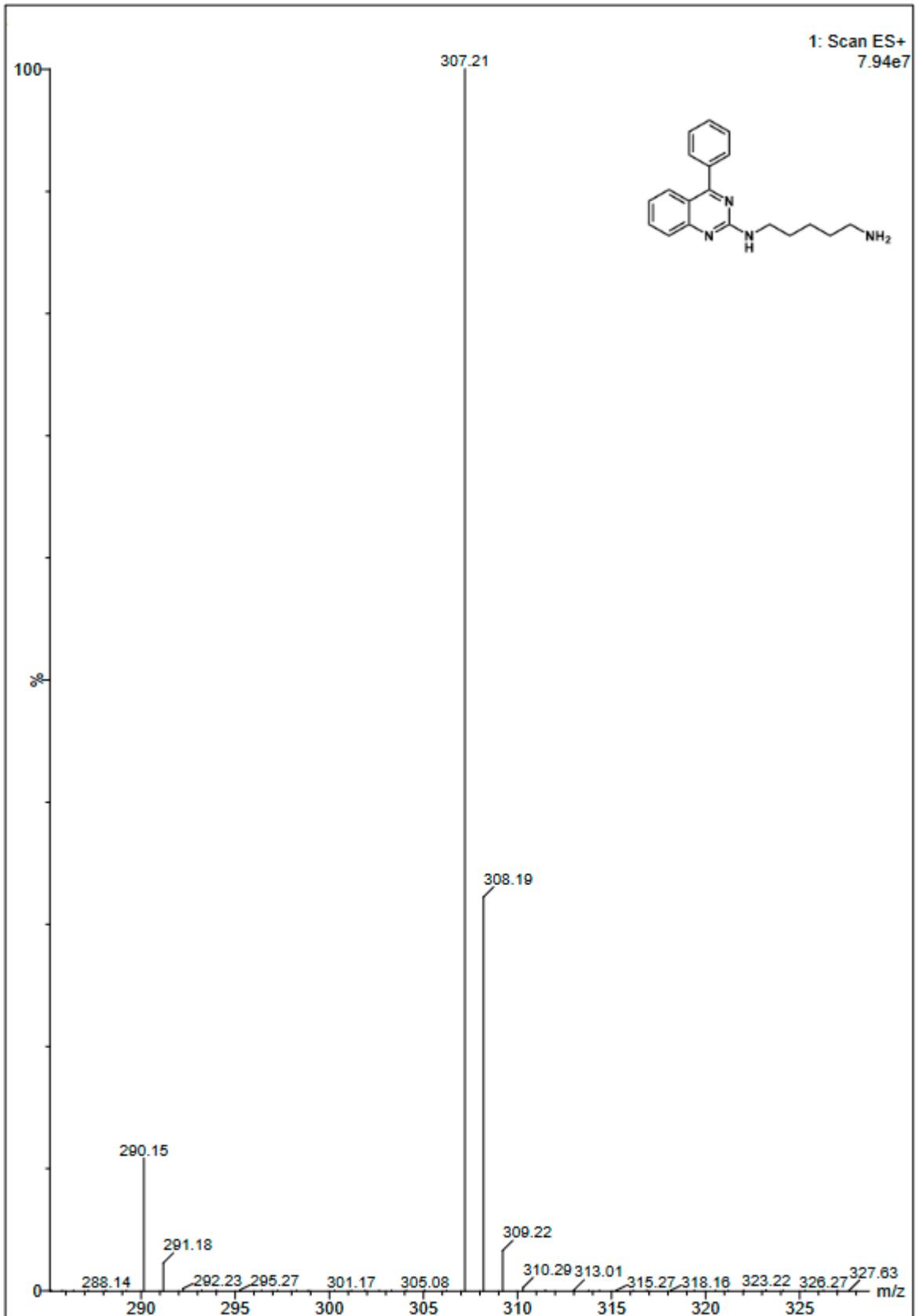
LC-MS mass spectrum of compound 9r



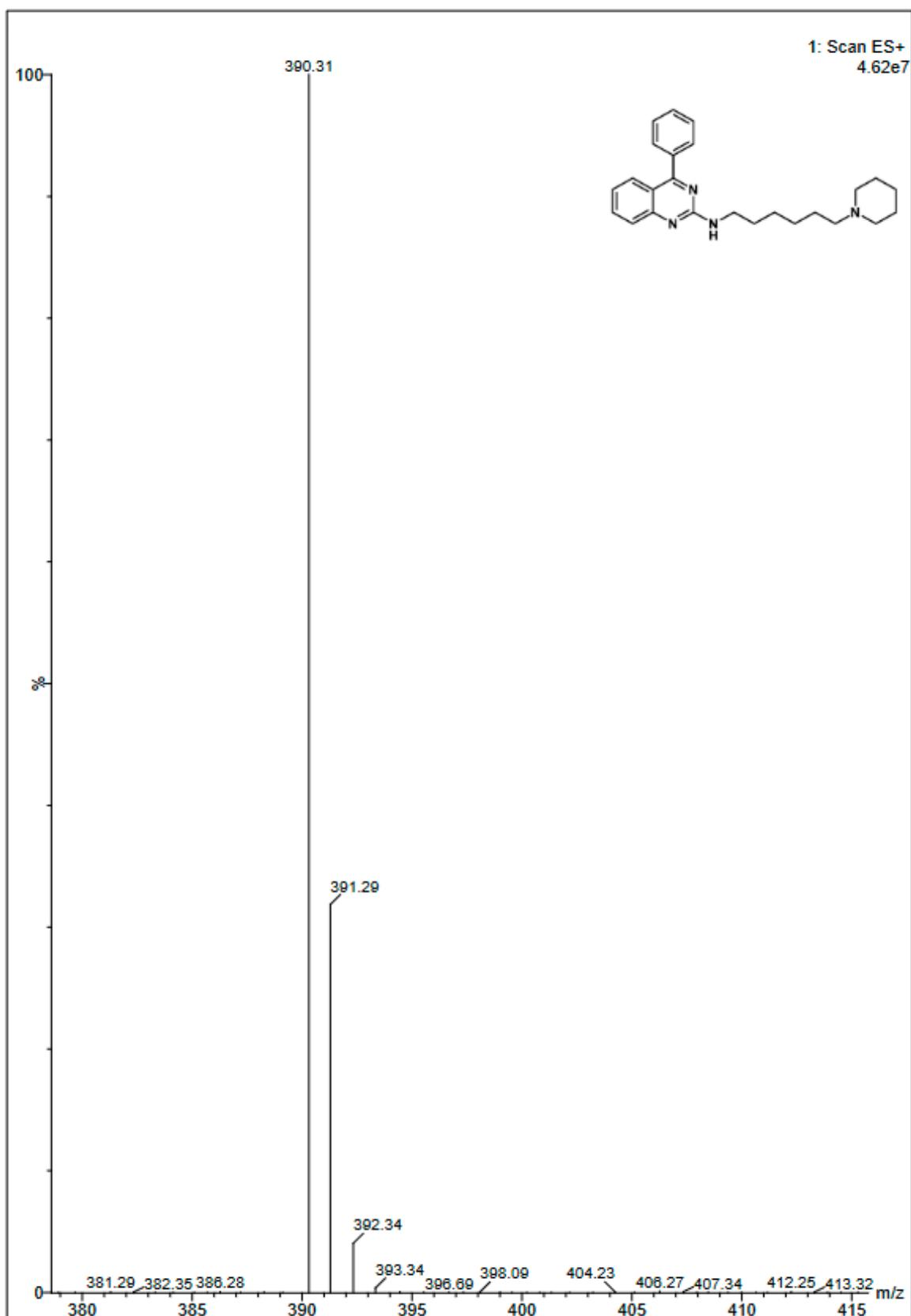
1H- and 13C-NMR Spectra in CDCl₃ of compound 9s



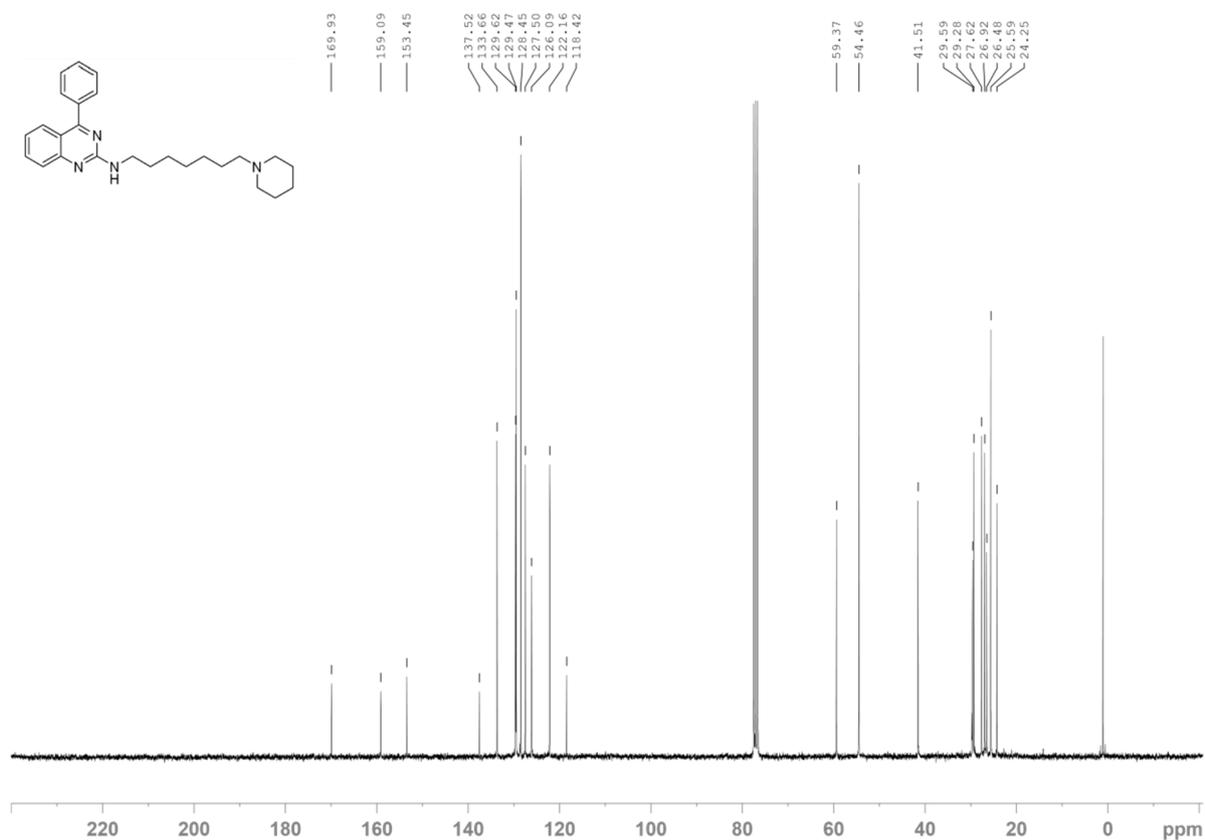
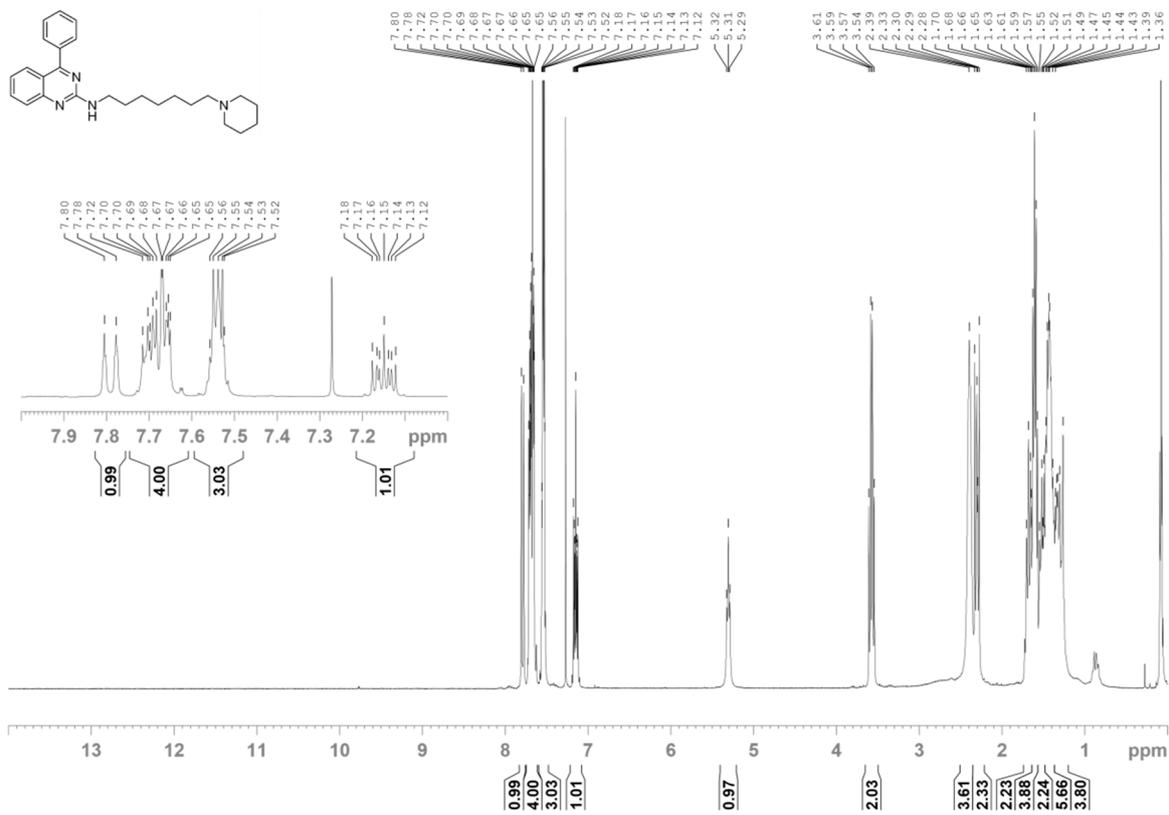
LC-MS mass spectrum of compound 9s



LC-MS mass spectrum of compound 9t



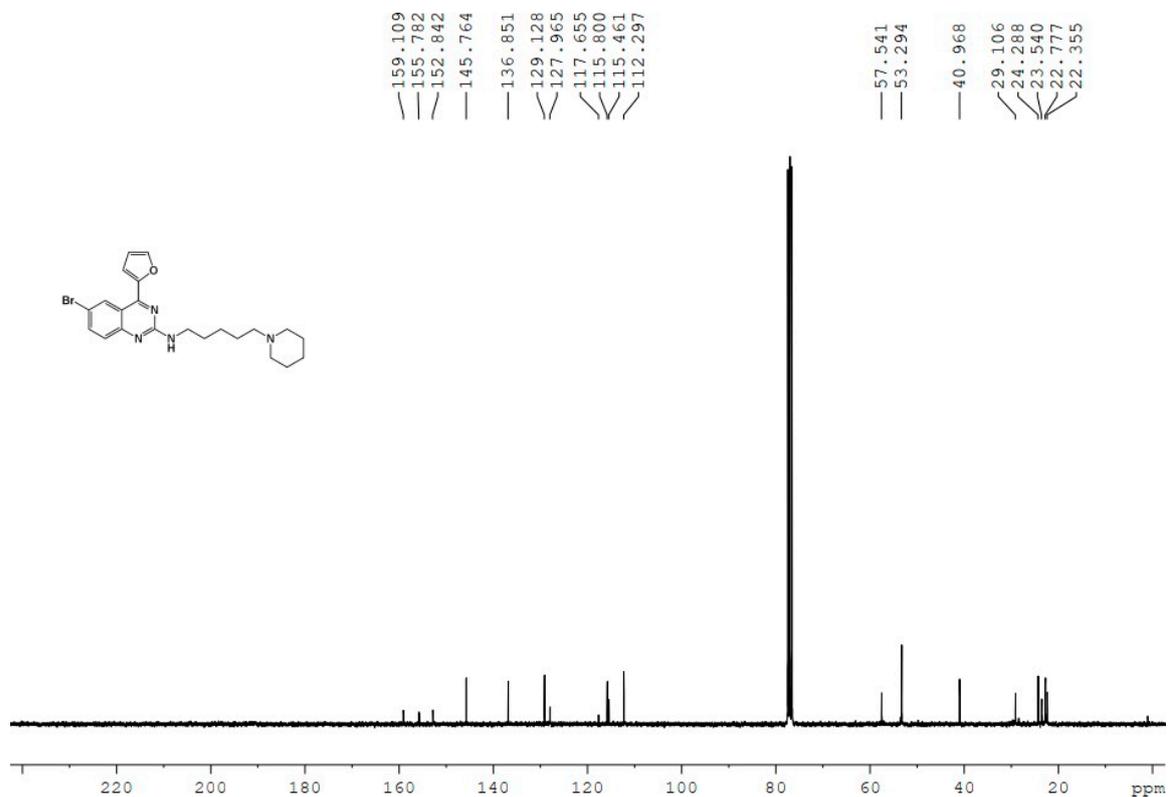
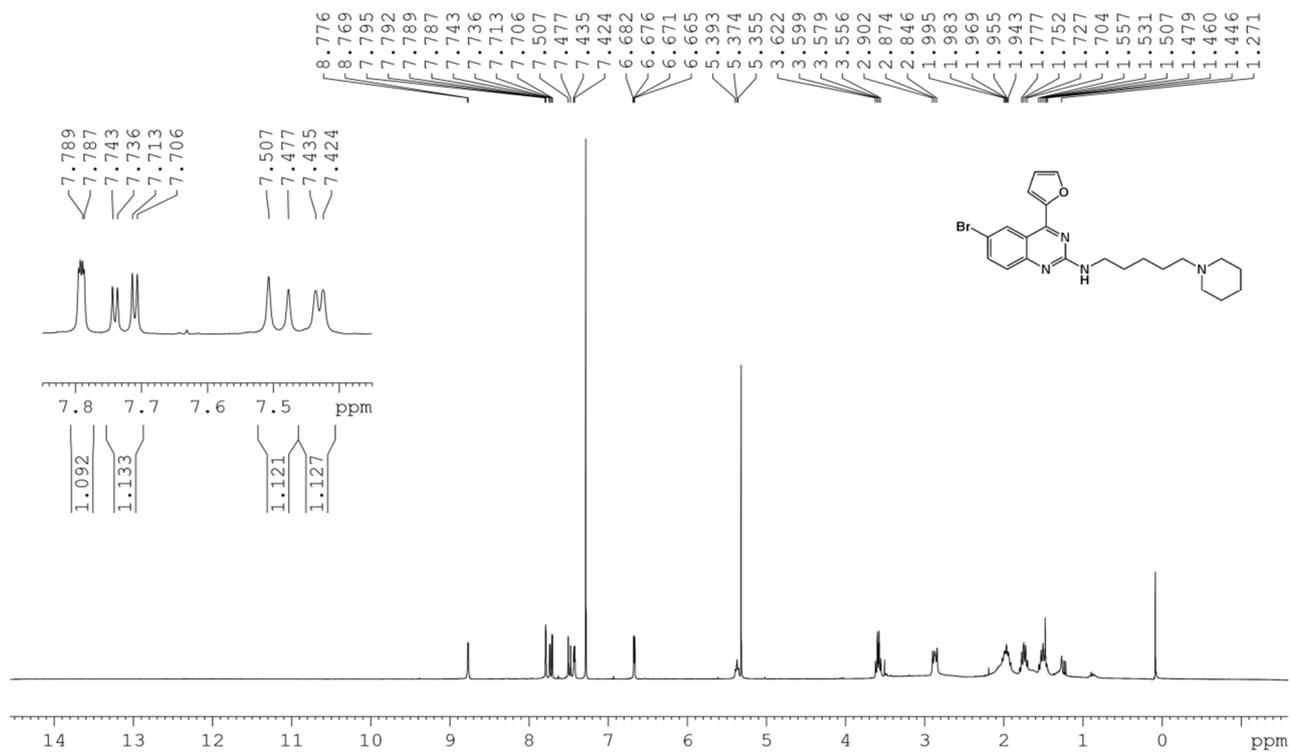
1H- and 13C-NMR Spectra in CDCl₃ of compound 9u



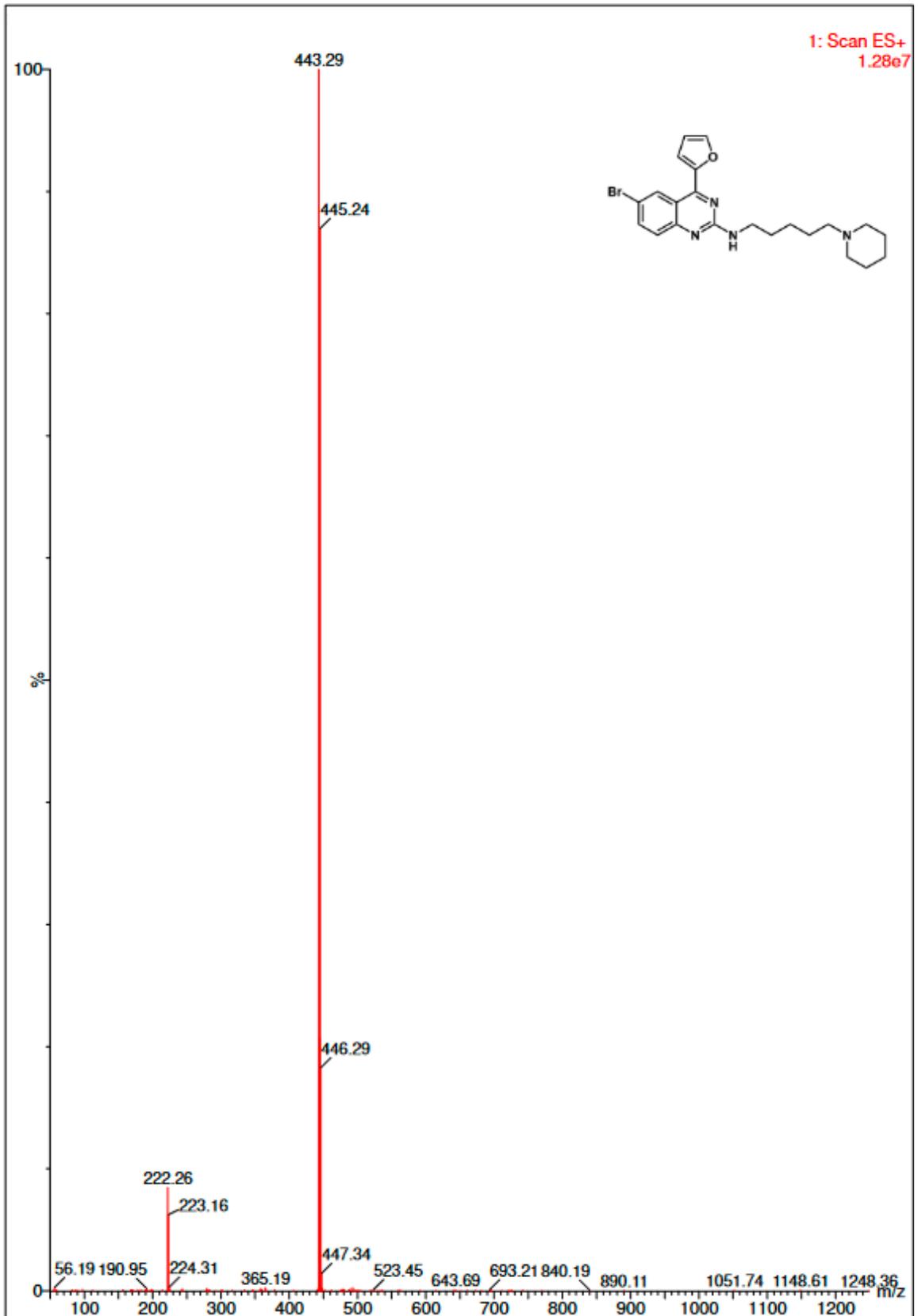
LC-MS mass spectrum of compound 9u



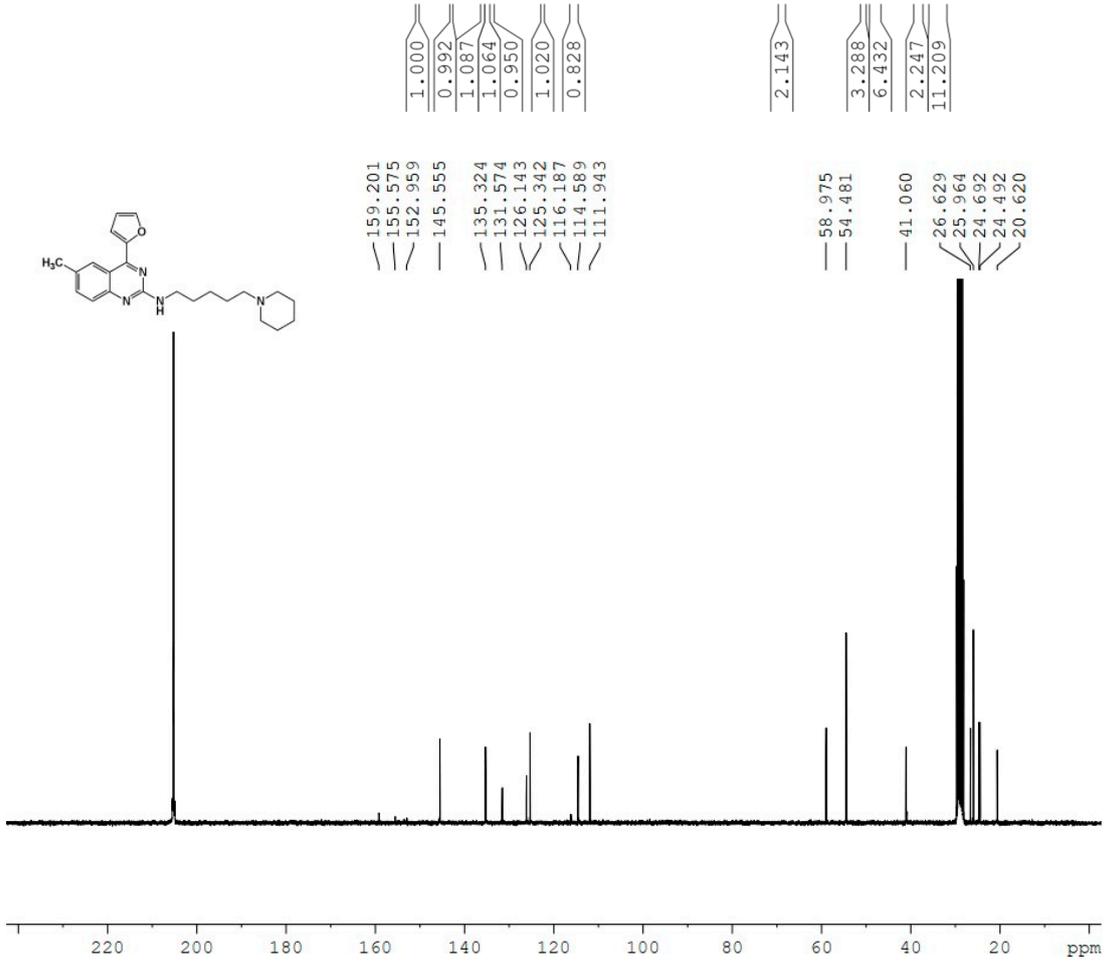
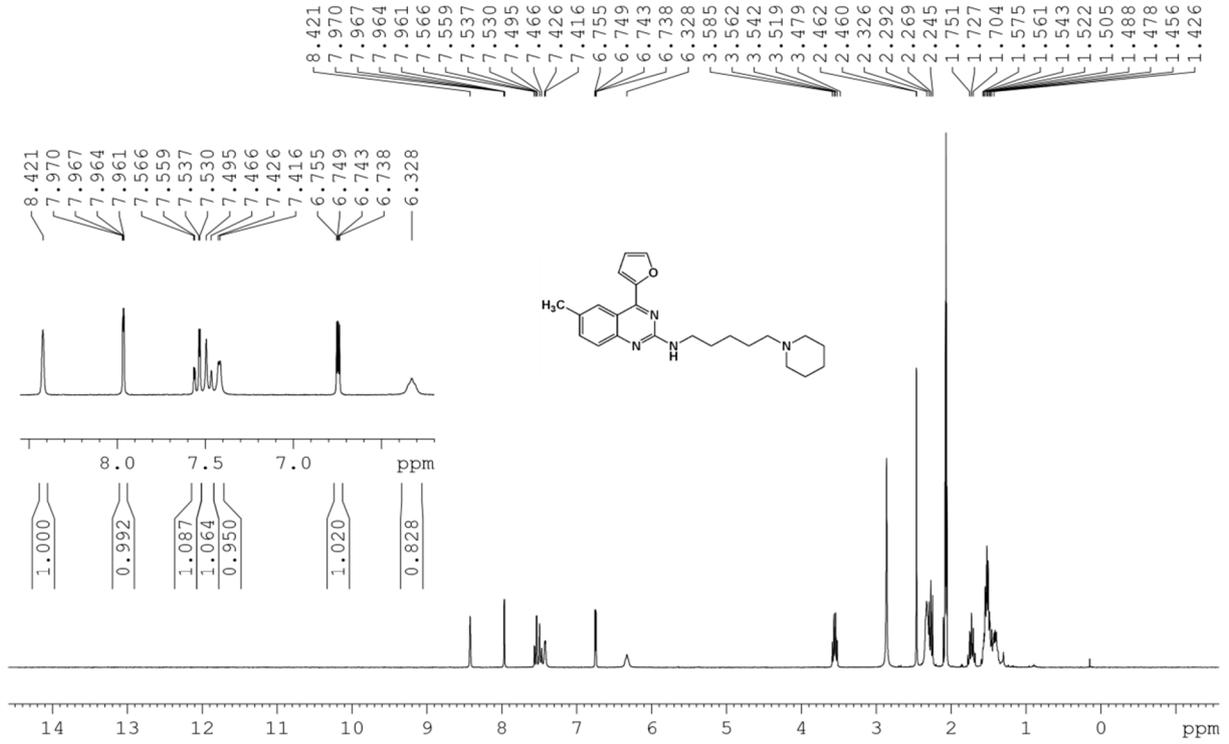
1H- and 13C-NMR Spectra in CDCl₃ of compound 9v



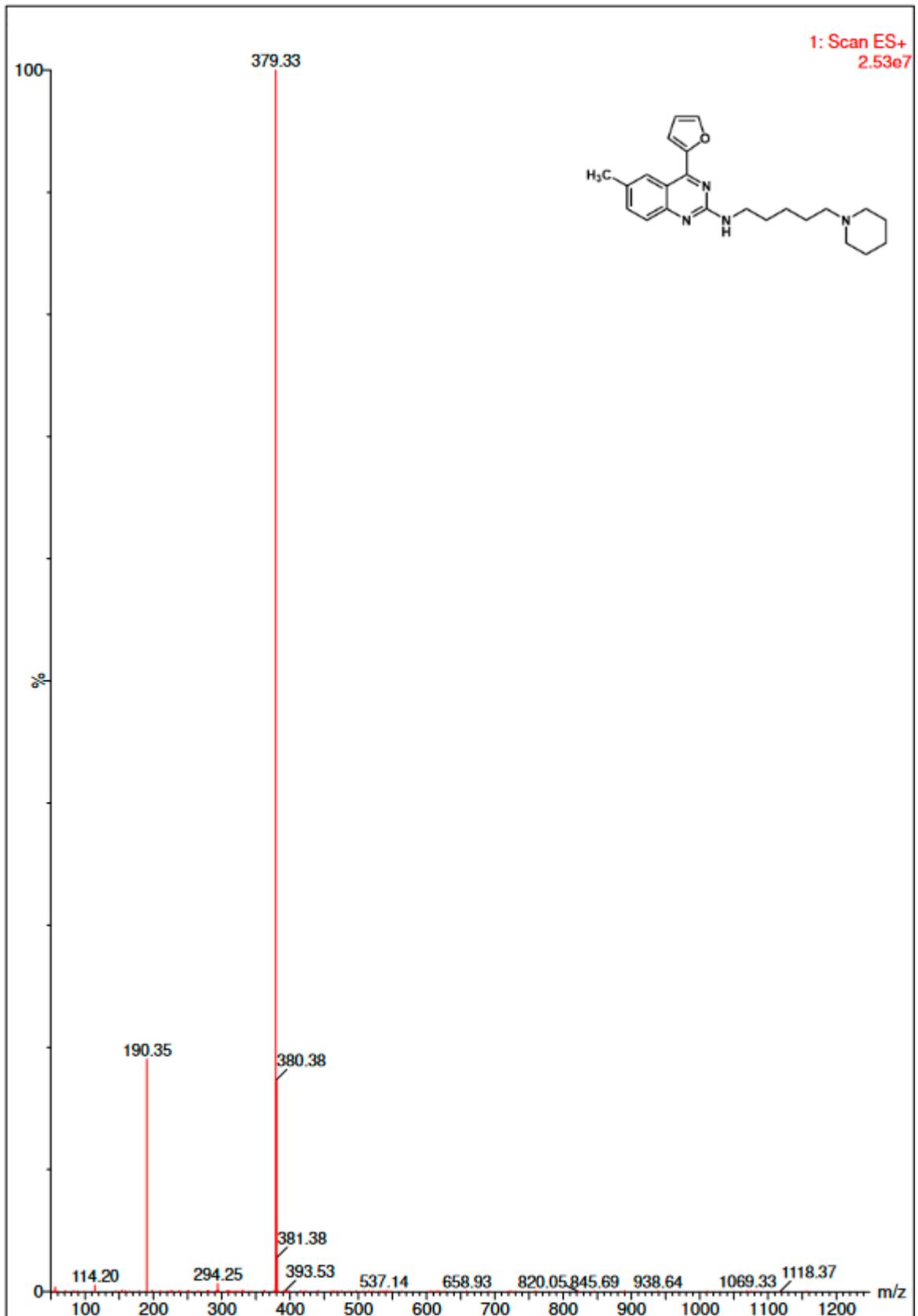
LC-MS mass spectrum of compound 9v



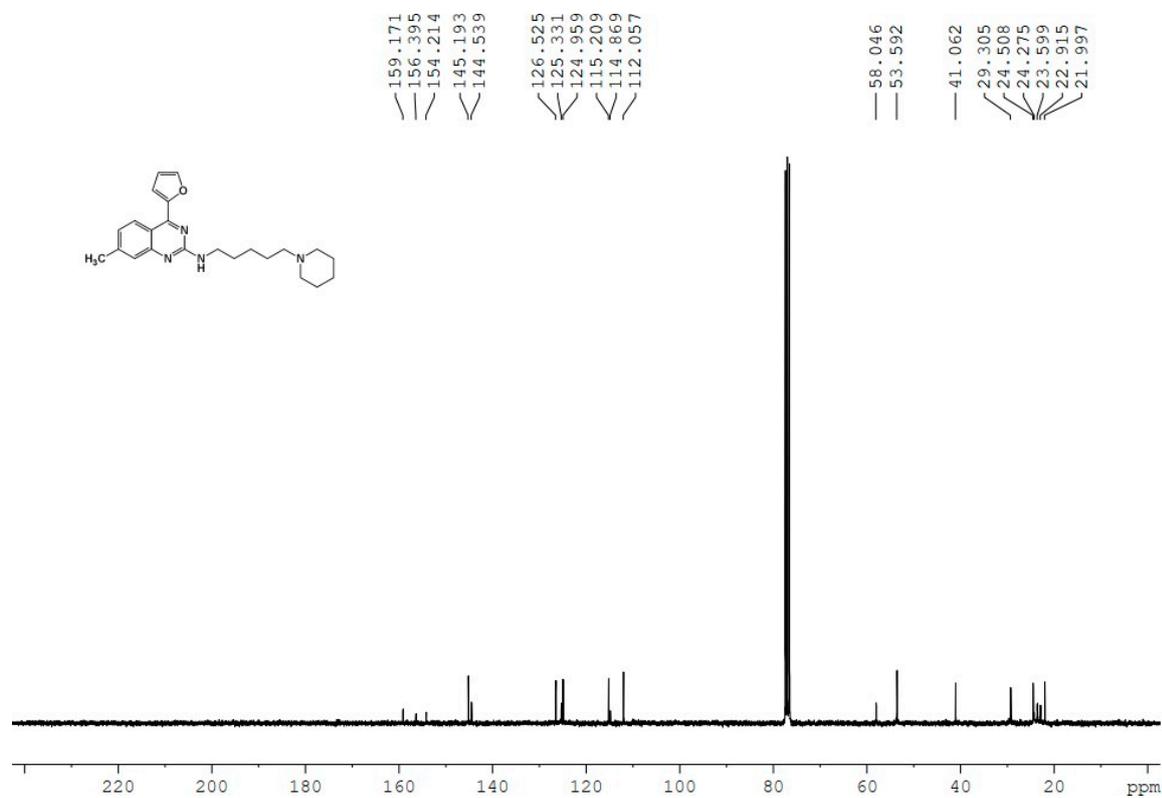
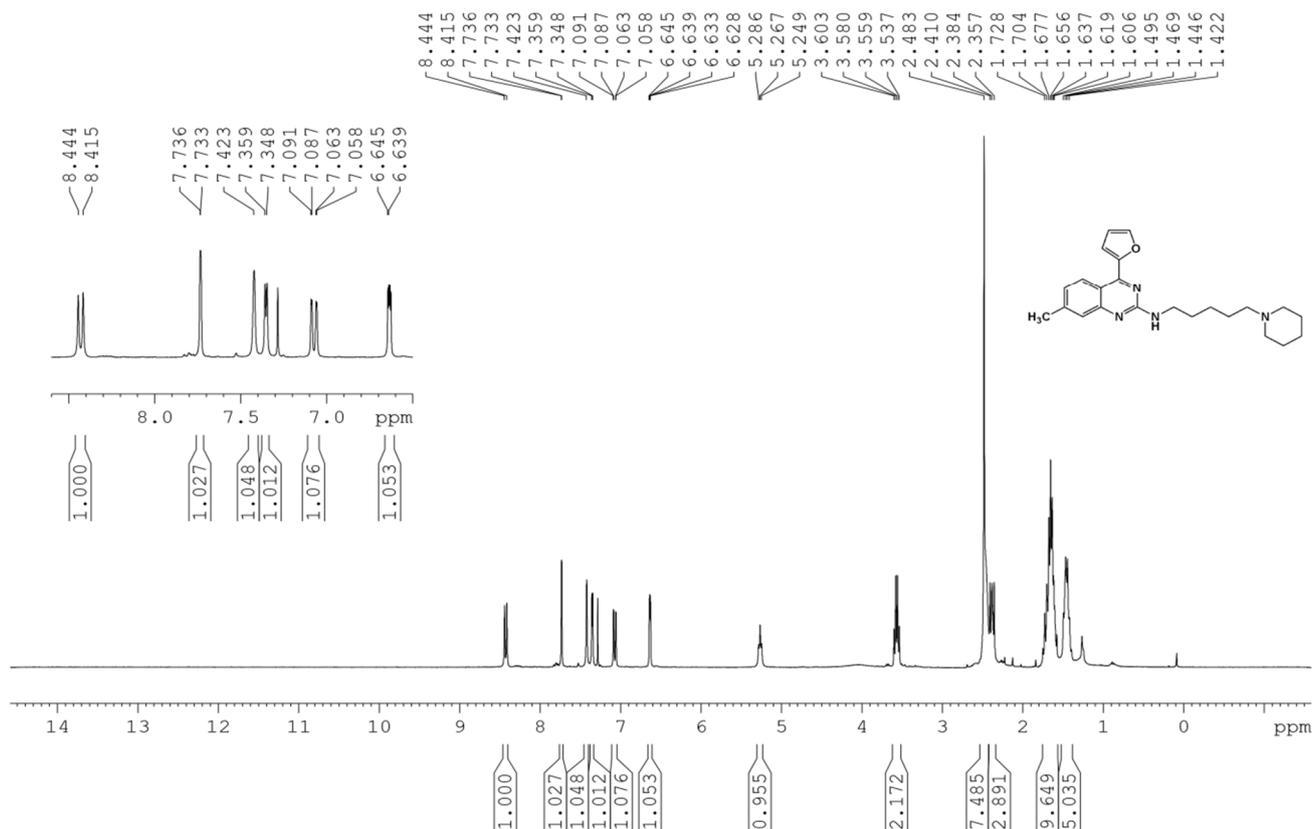
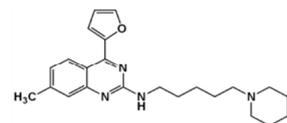
1H- and 13C-NMR Spectra in (CD₃)₂CO of compound 9w



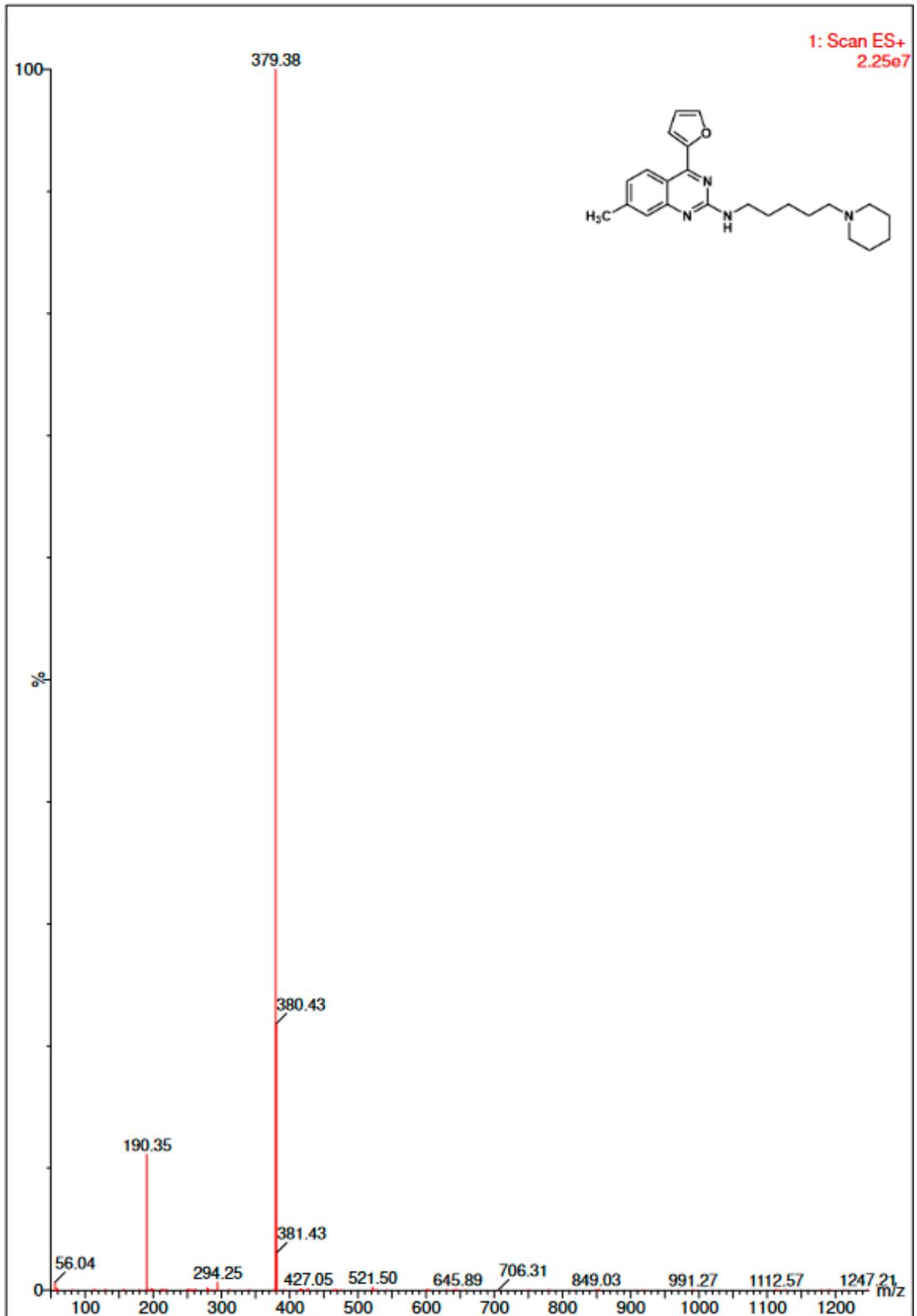
LC-MS mass spectrum of compound 9w



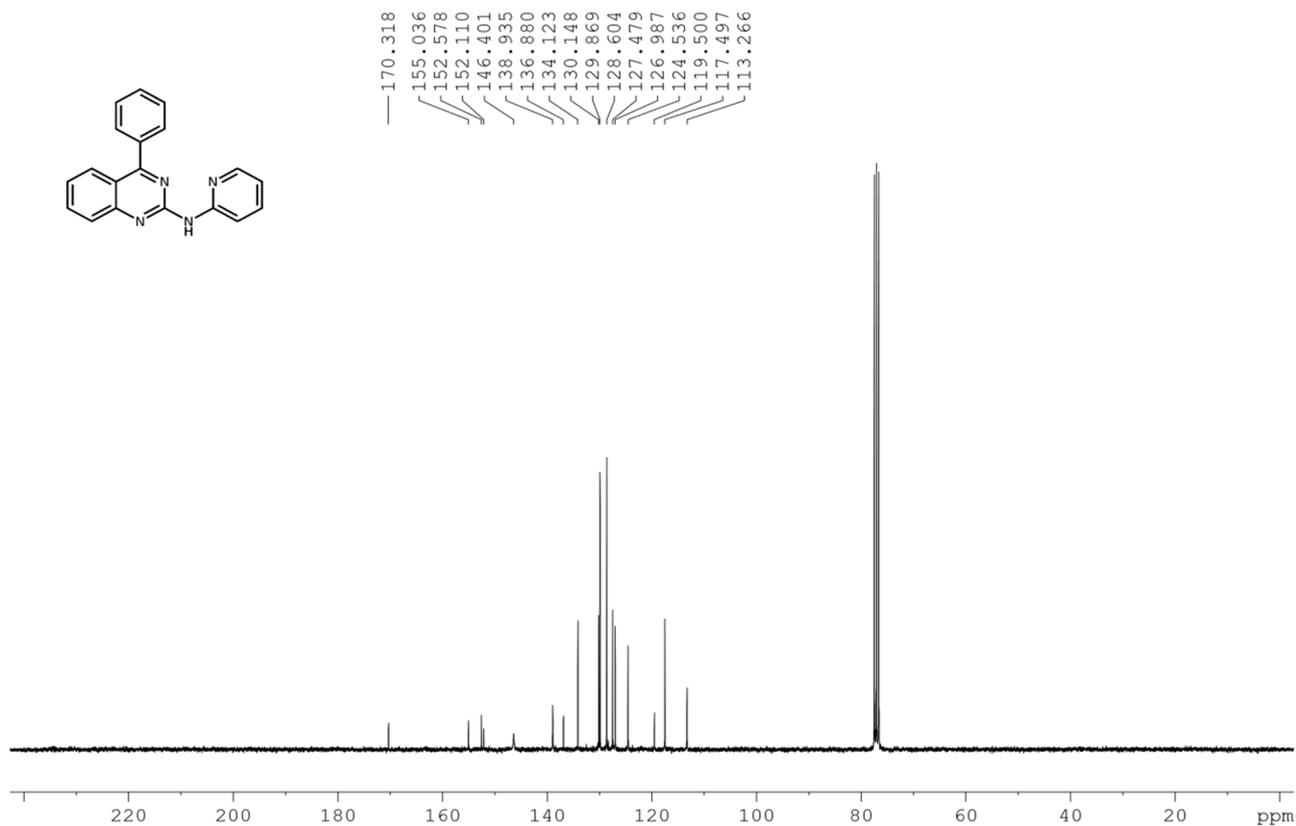
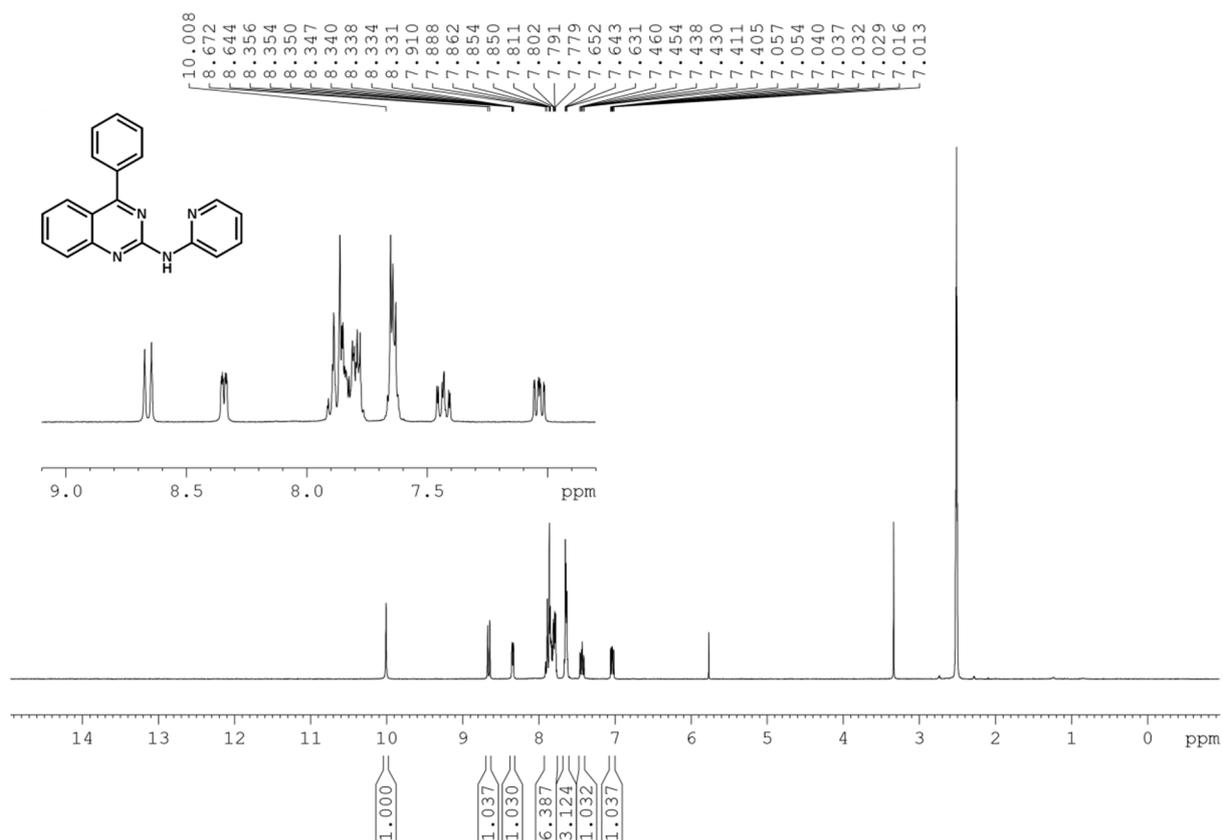
1H- and 13C-NMR Spectra in CDCl₃ of compound 9x



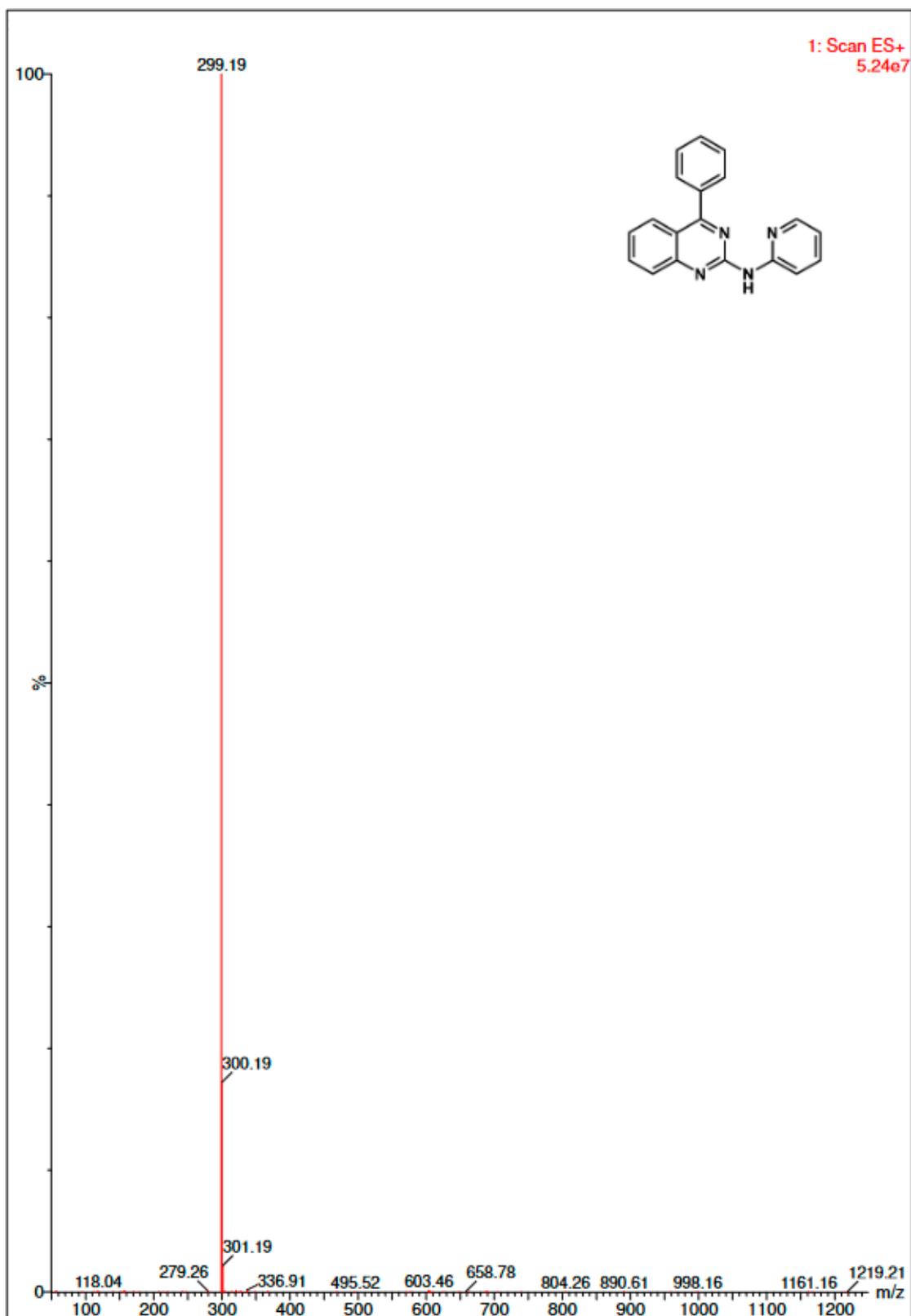
LC-MS mass spectrum of compound 9x



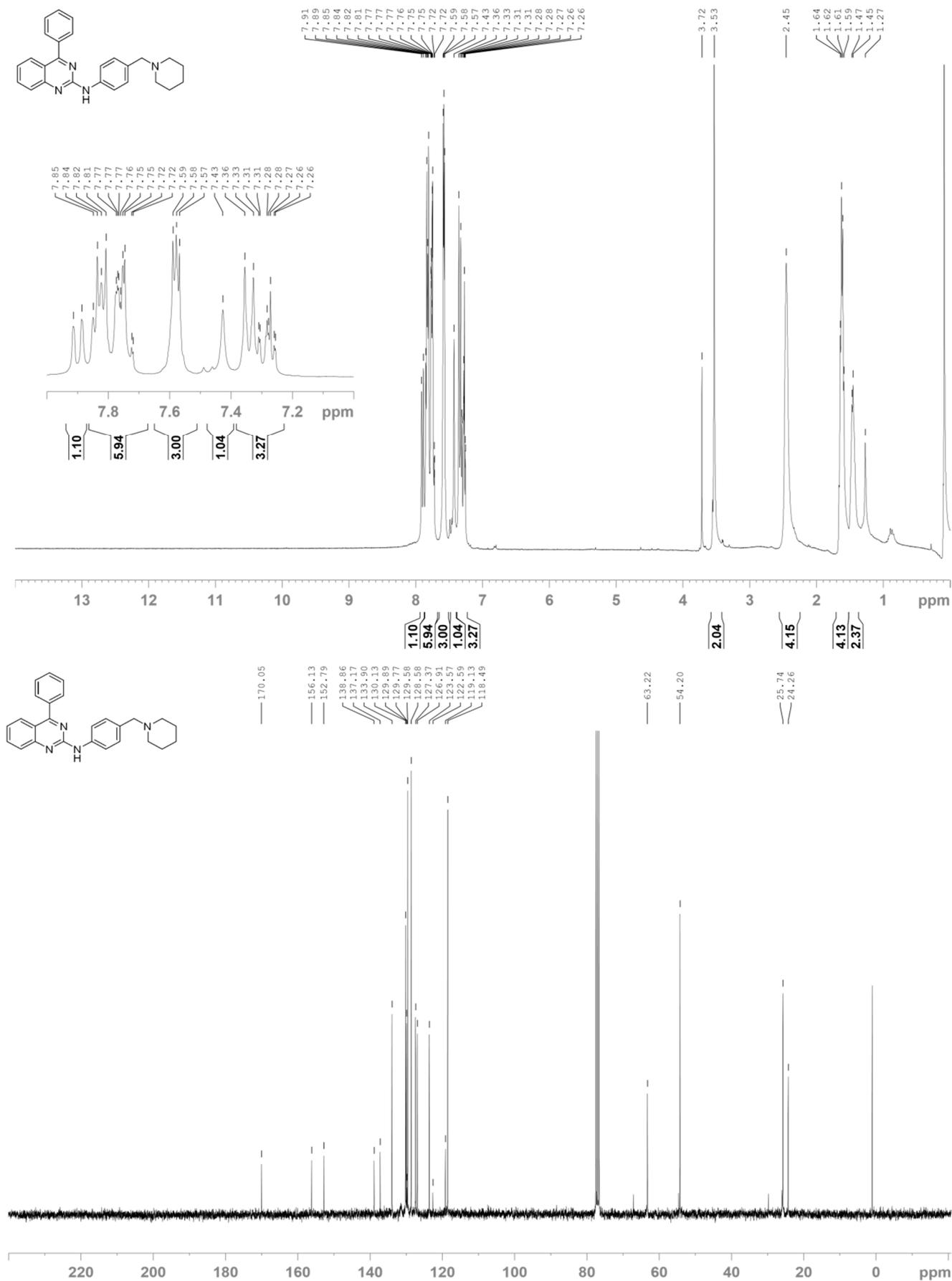
¹H-NMR Spectra in DMSO-d₆ and ¹³C-NMR Spectra in CDCl₃ of compound 10a



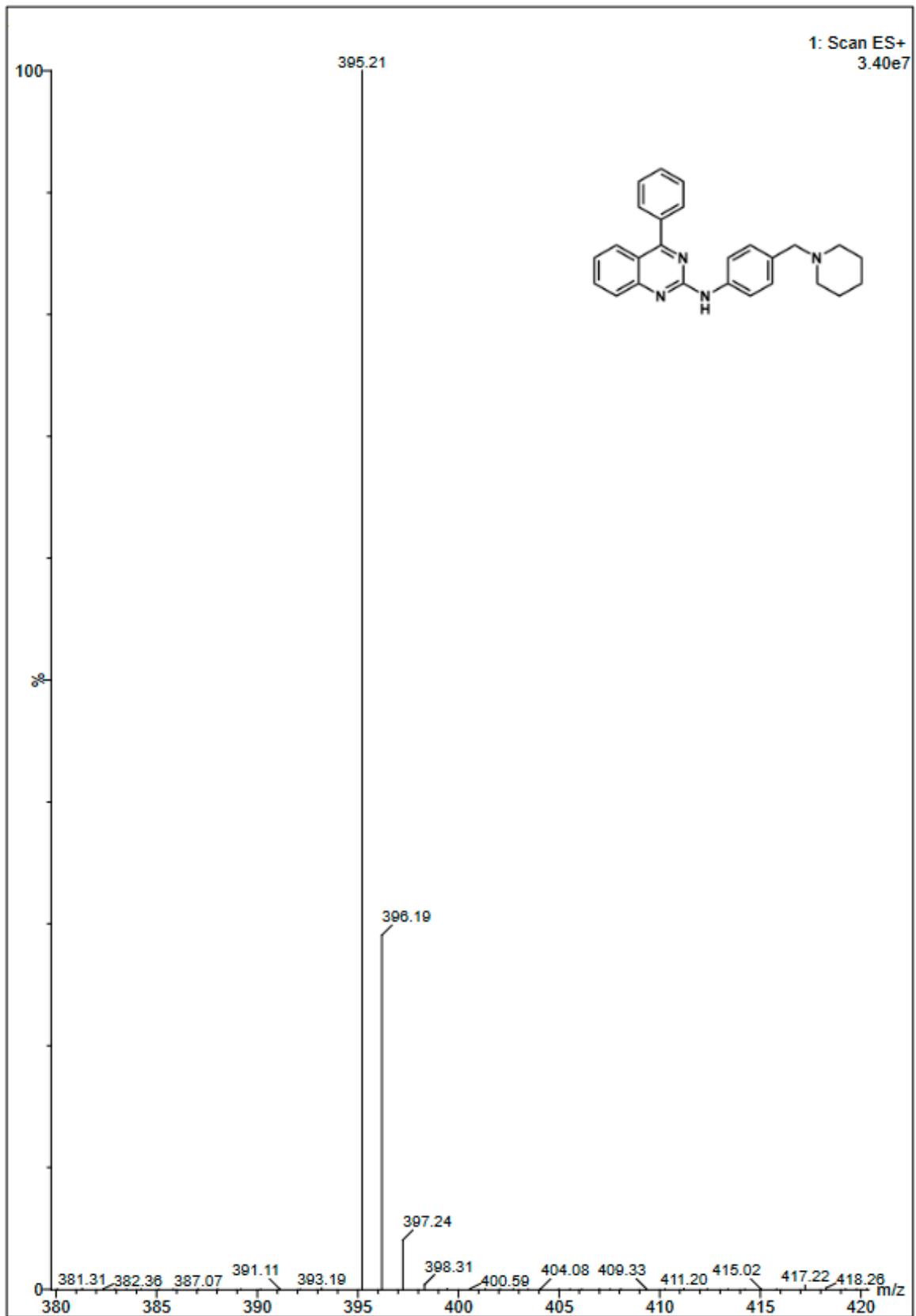
LC-MS mass spectrum of compound 10a



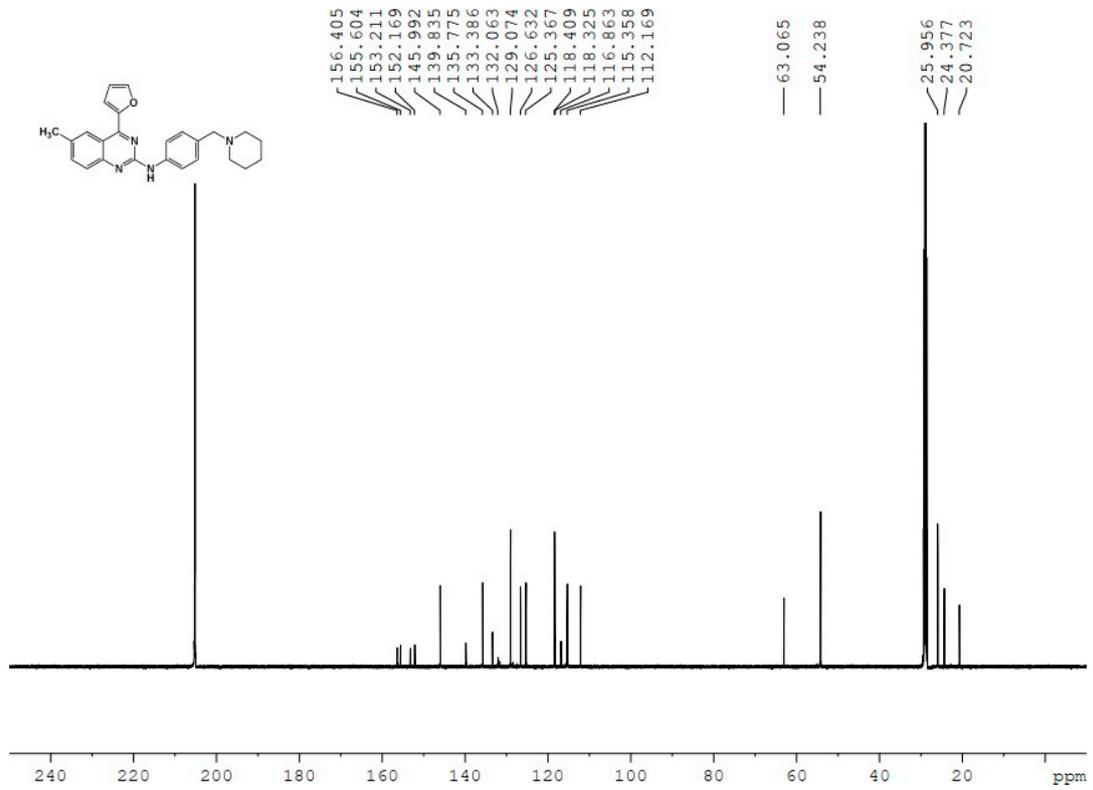
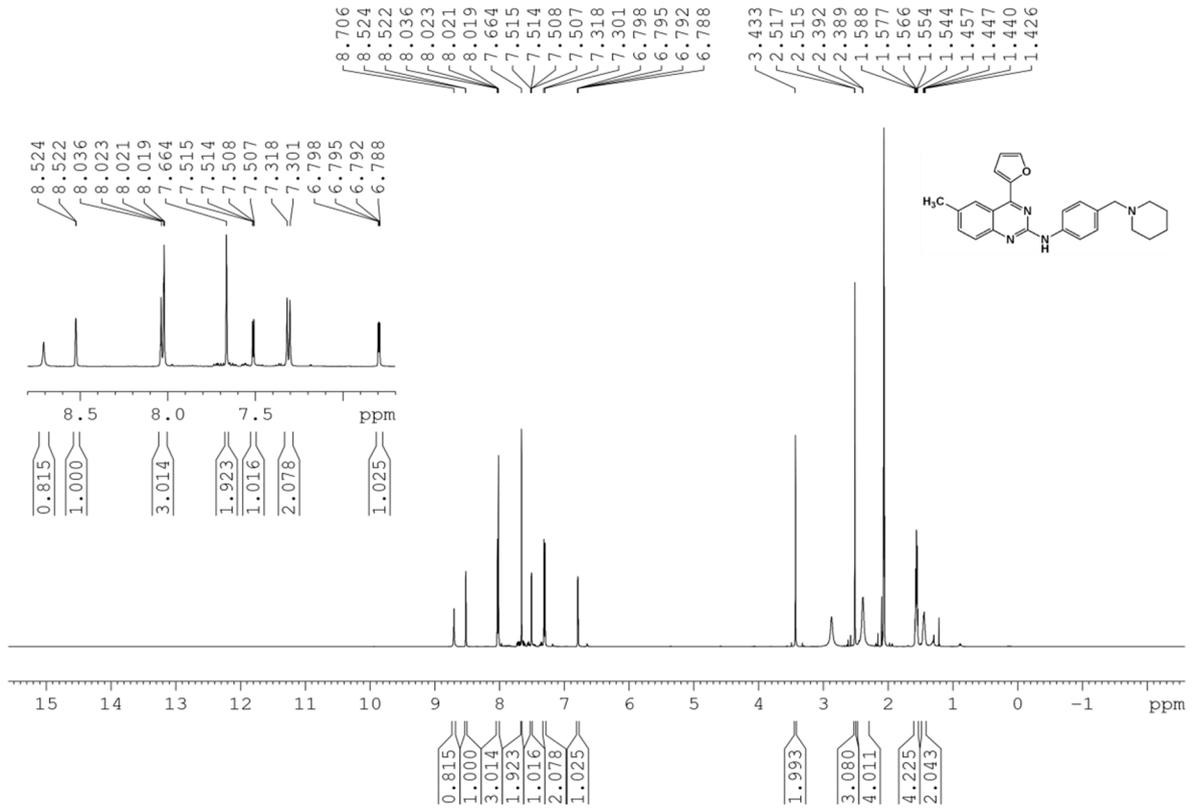
1H-NMR Spectra in DMSO-d6 and 13C-NMR Spectra in CDCl3 of compound 10b



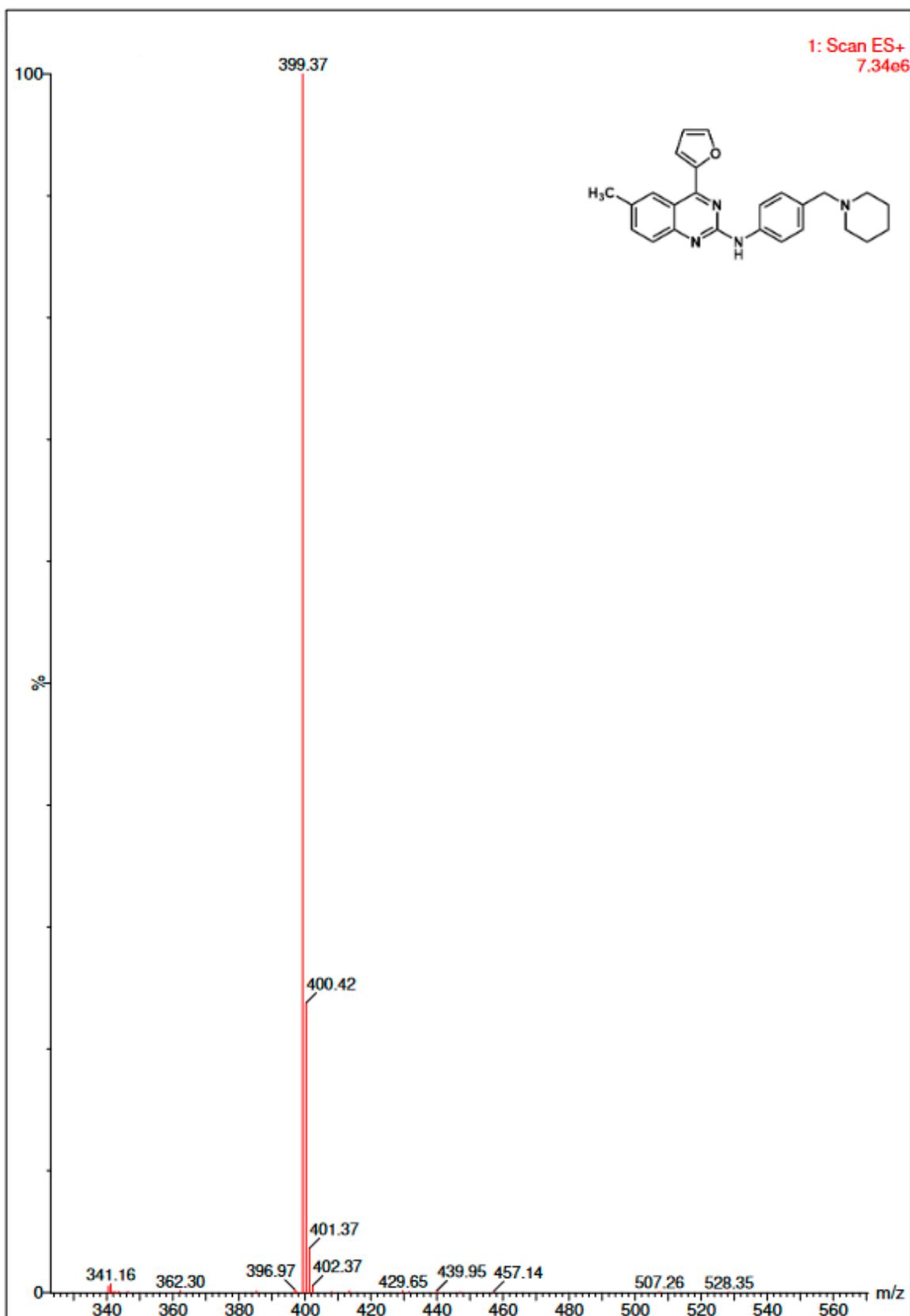
LC-MS mass spectrum of compound 10b



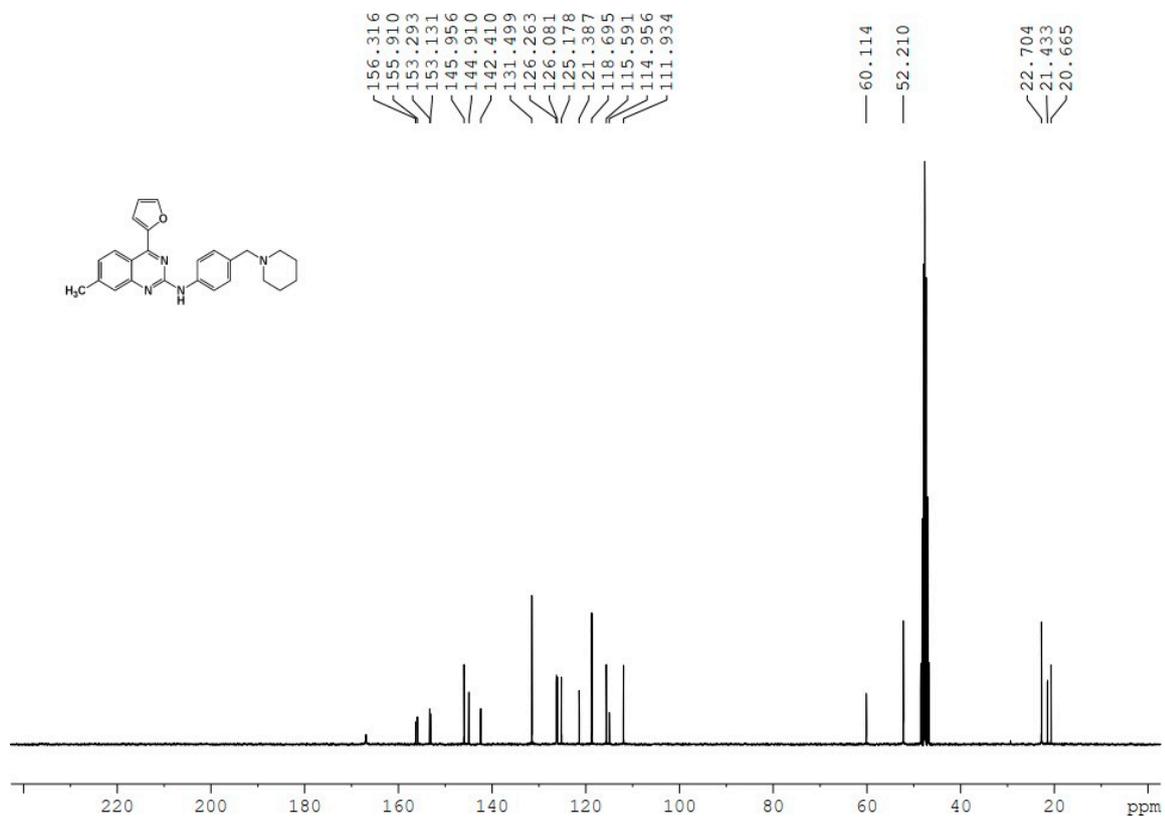
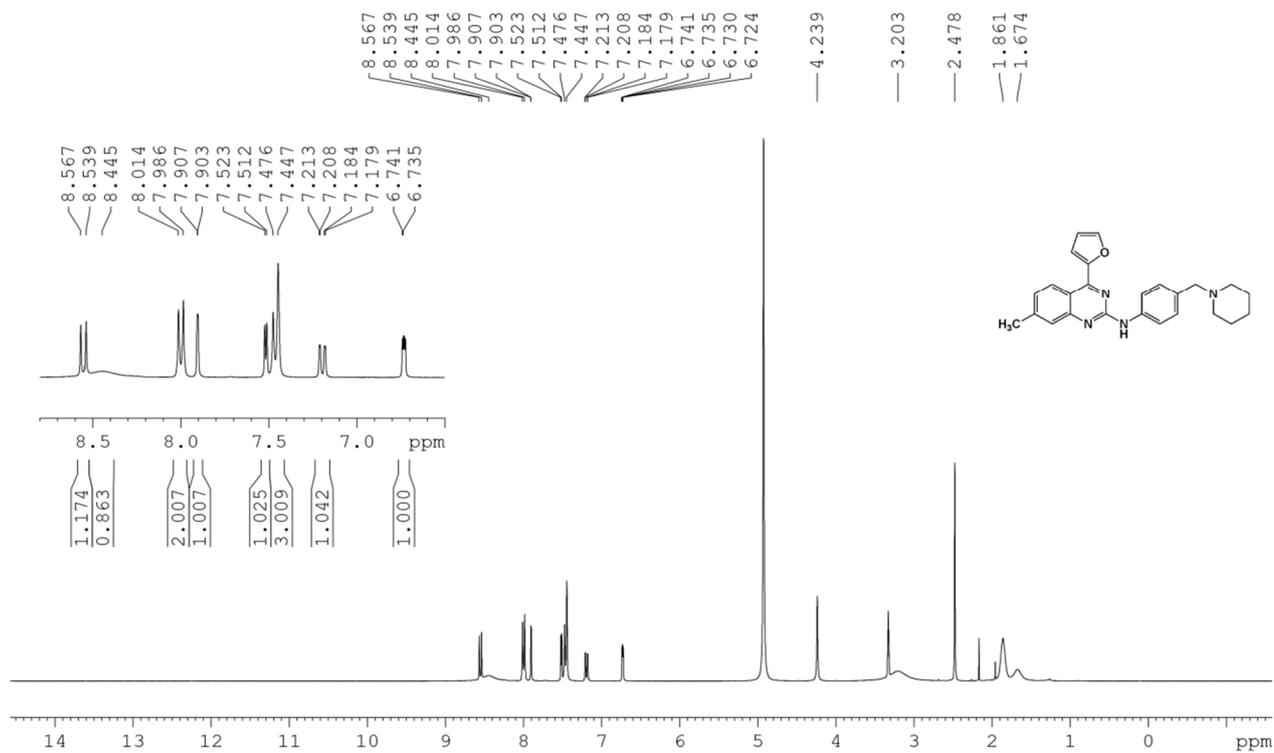
1H- and 13C-NMR Spectra in (CD₃)₂CO of compound 10c



LC-MS mass spectrum of compound 10c



1H- and 13C-NMR Spectra in CD₃OD of compound 10d



LC-MS mass spectrum of compound 10d

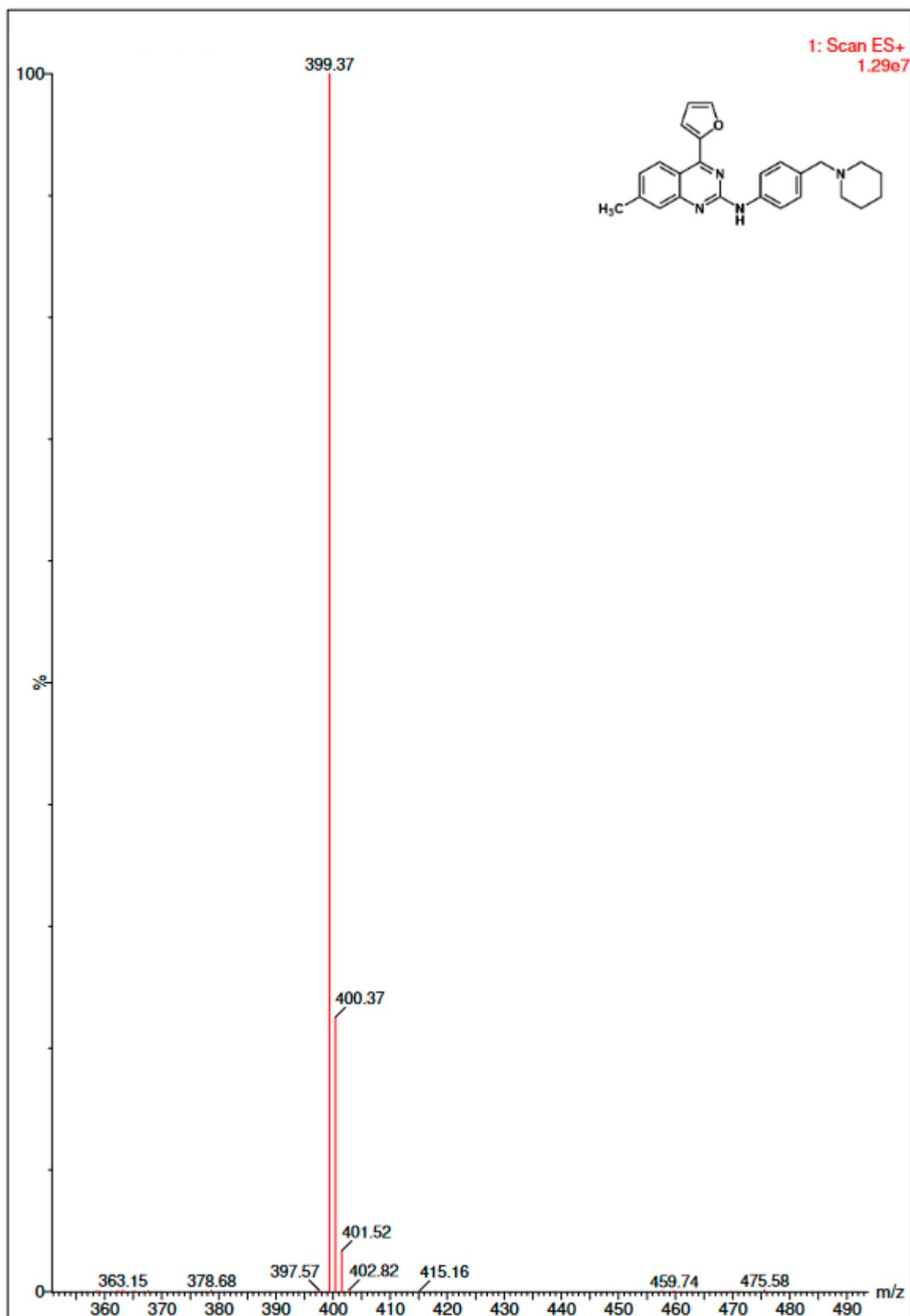


Figure S2. Dose-response curve of ZM241385

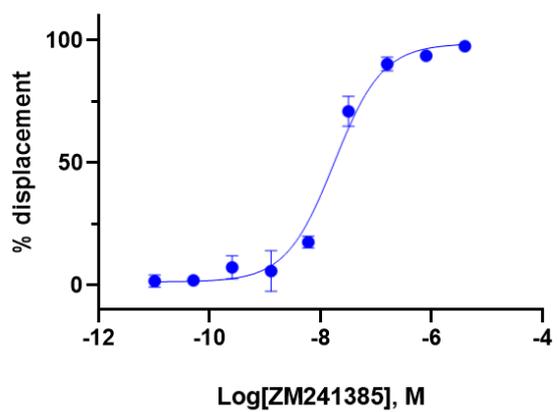
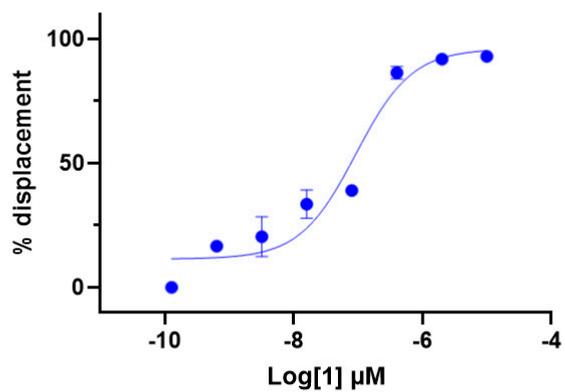
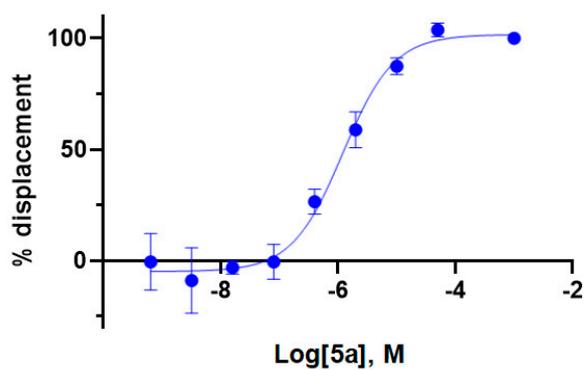


Figure S3. FP competition binding experiments with compound 1 and some final compounds

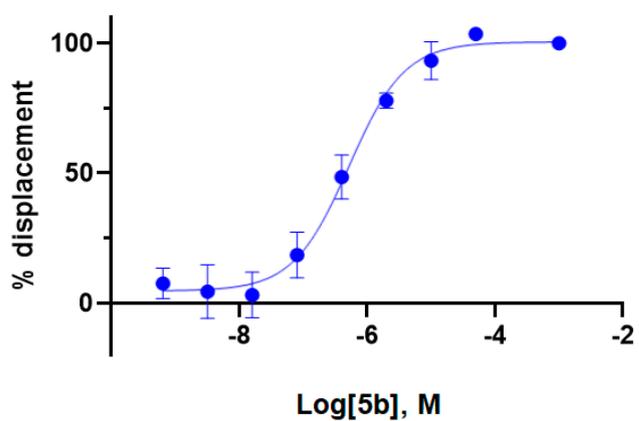
FP competition binding experiment with 1



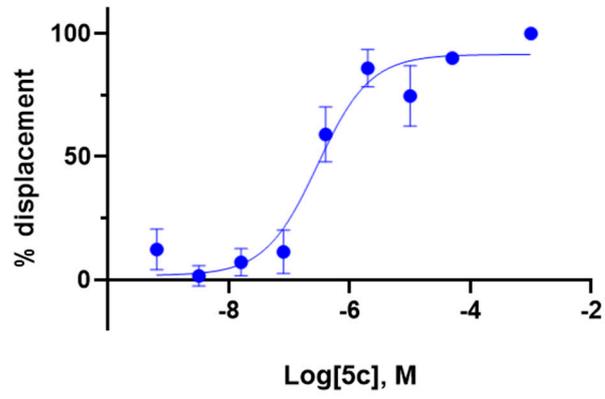
FP competition binding experiment with 5a



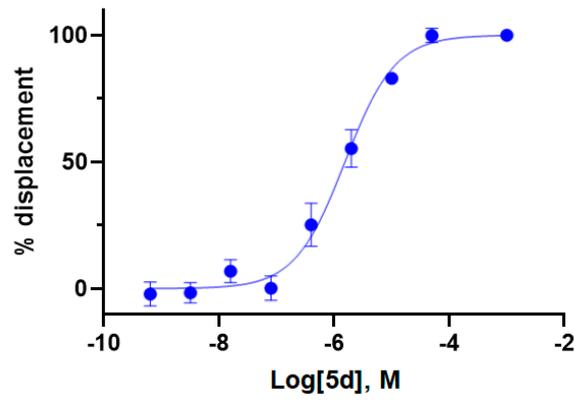
FP competition binding experiment with 5b



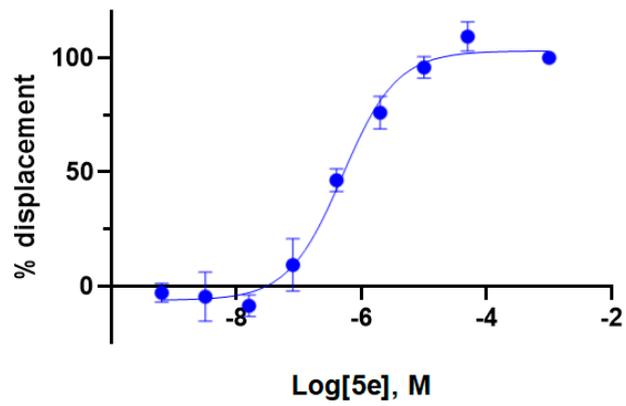
FP competition binding experiment with 5c



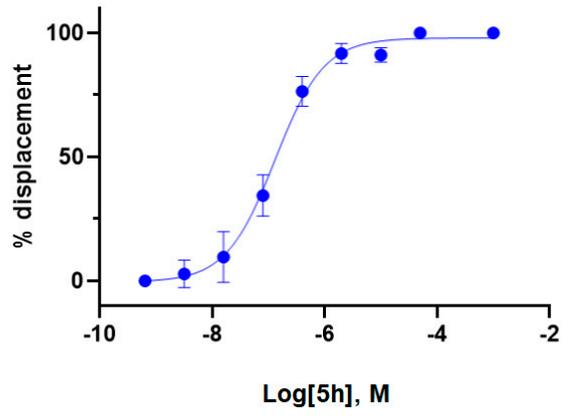
FP competition binding experiment with 5d



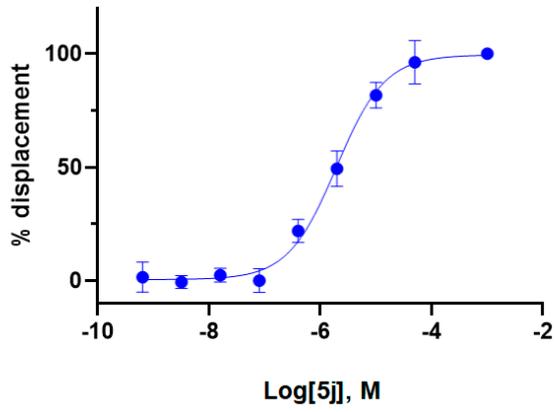
FP competition binding experiment with 5e



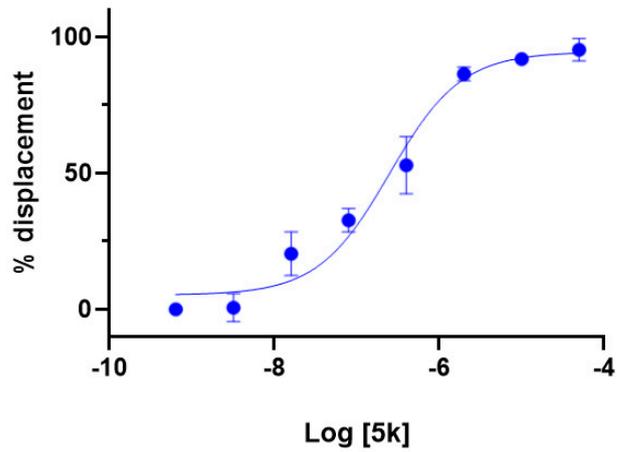
FP competition binding experiment with 5h



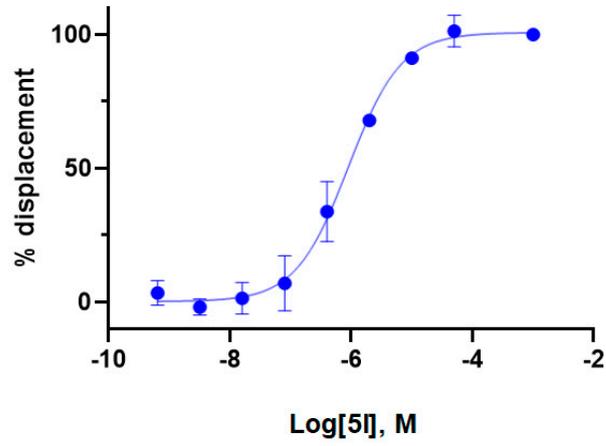
FP competition binding experiment with 5j



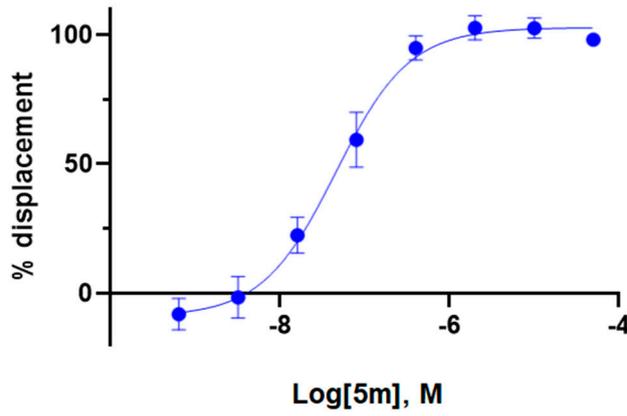
FP competition binding experiment with 5k



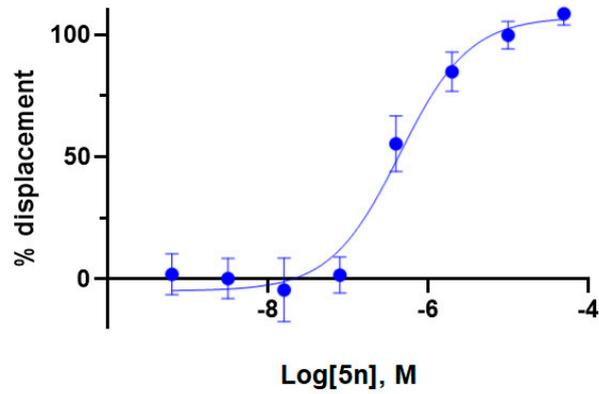
FP competition binding experiment with 5l



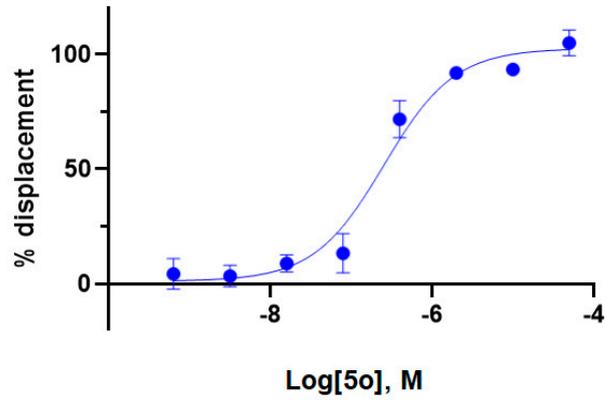
FP competition binding experiment with 5m



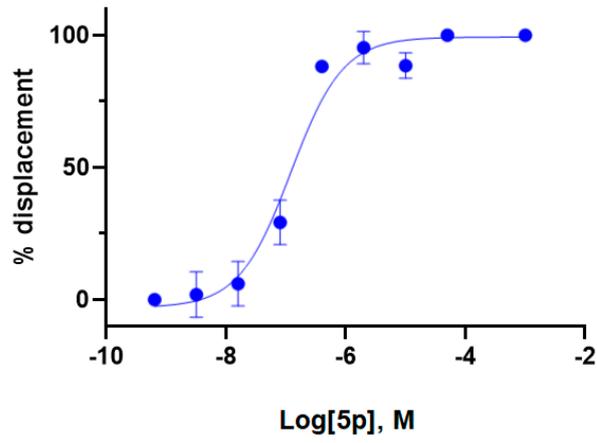
FP competition binding experiment with 5n



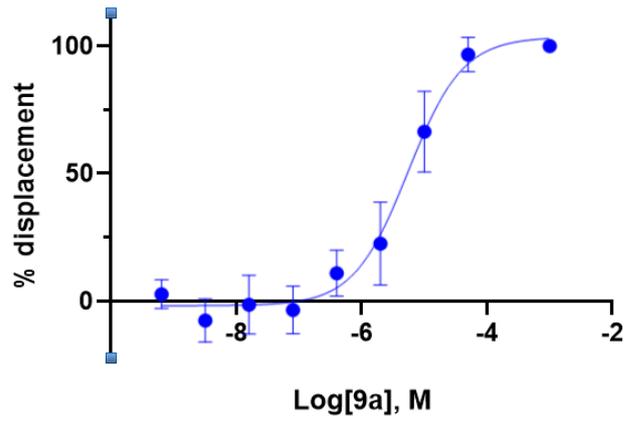
FP competition binding experiment with 5o



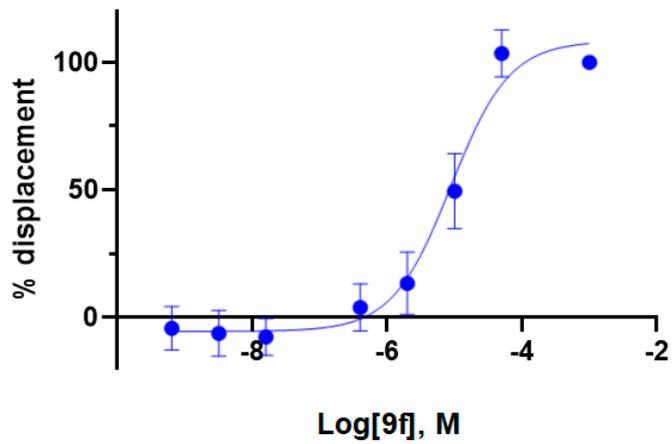
FP competition binding experiment with 5p



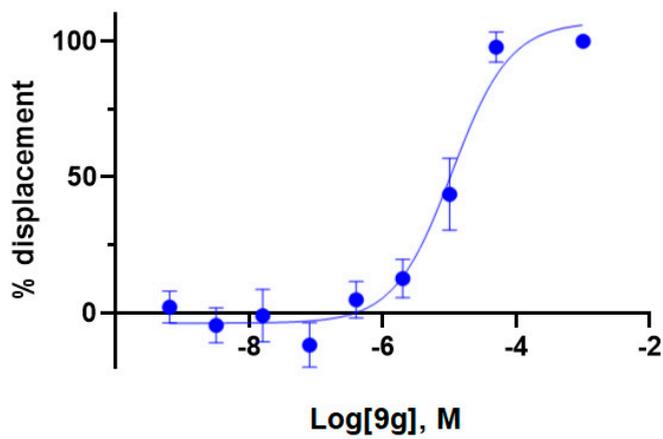
FP competition binding experiment with 9a



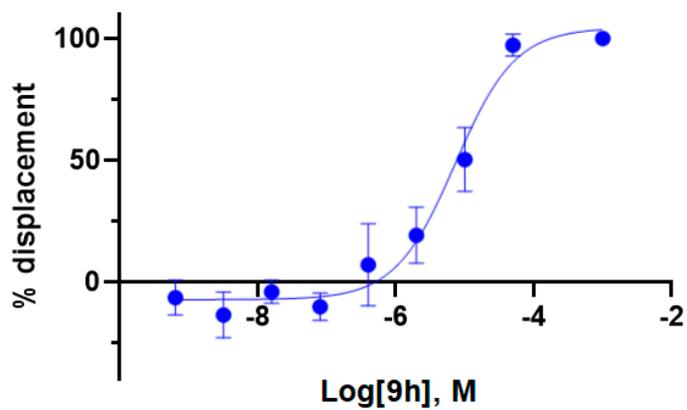
FP competition binding experiment with 9f



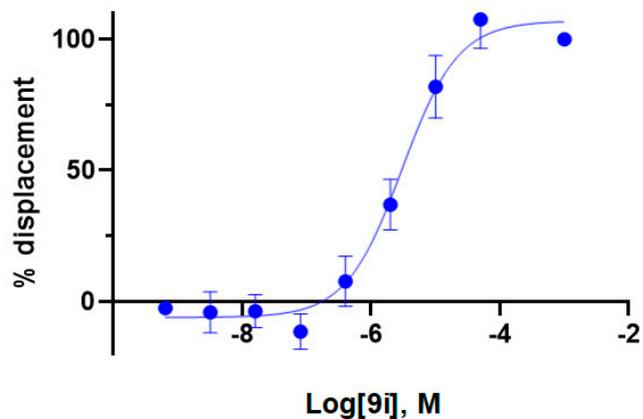
FP competition binding experiment with 9g



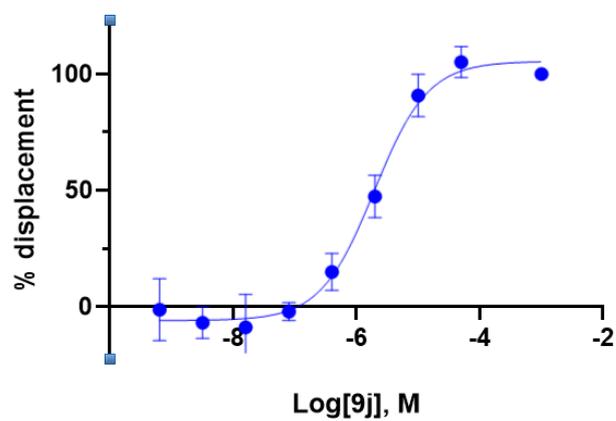
FP competition binding experiment with 9h



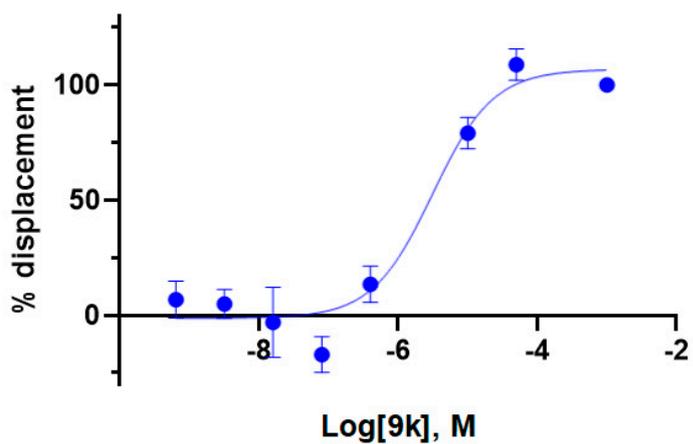
FP competition binding experiment with 9i



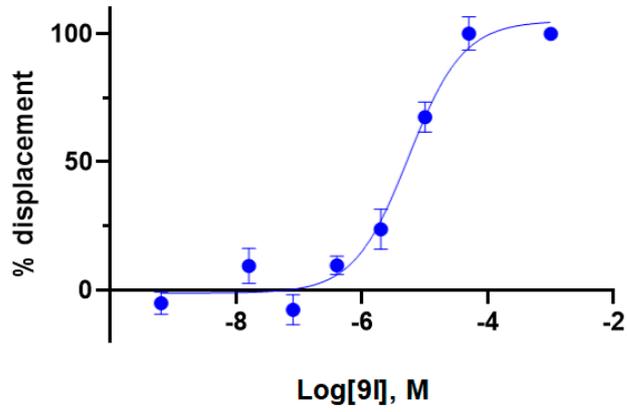
FP competition binding experiment with 9j



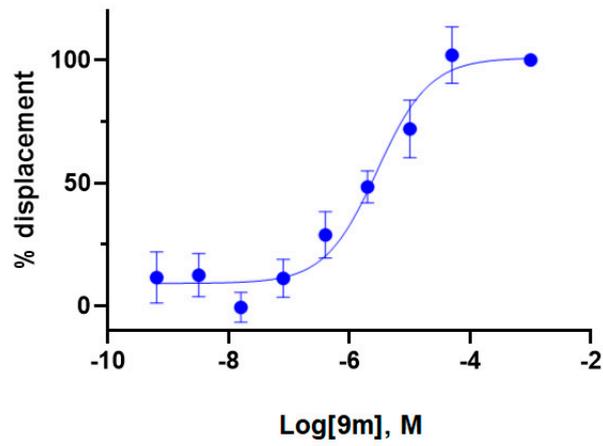
FP competition binding experiment with 9k



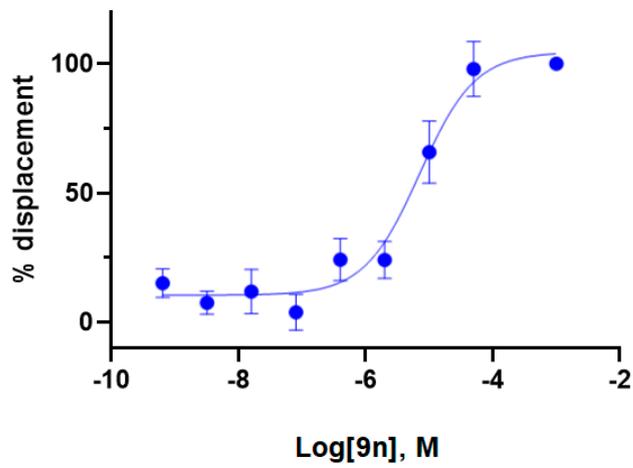
FP competition binding experiment with 9l



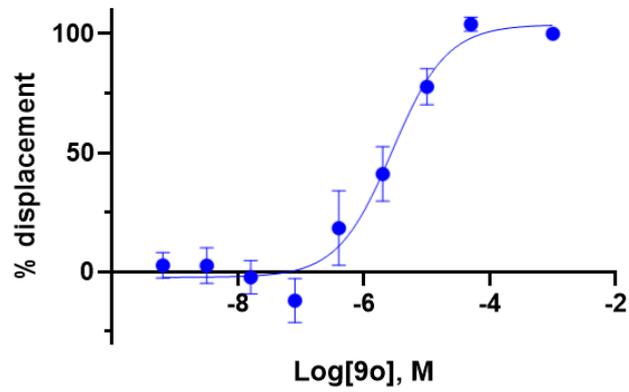
FP competition binding experiment with 9m



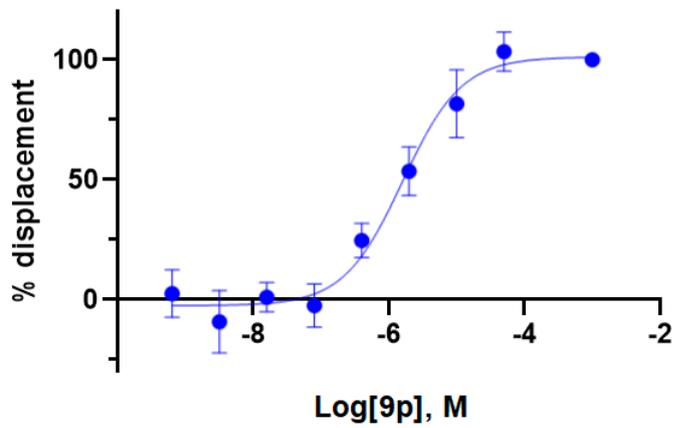
FP competition binding experiment with 9n



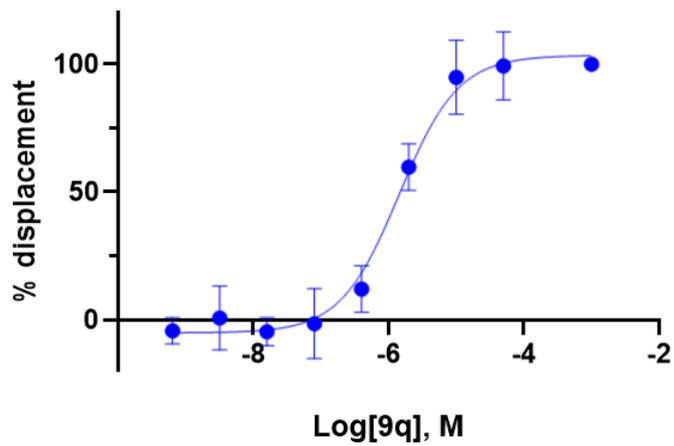
FP competition binding experiment with 9o



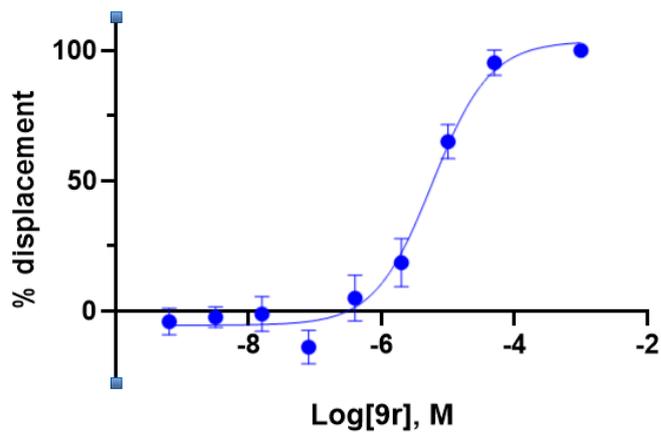
FP competition binding experiment with 9p



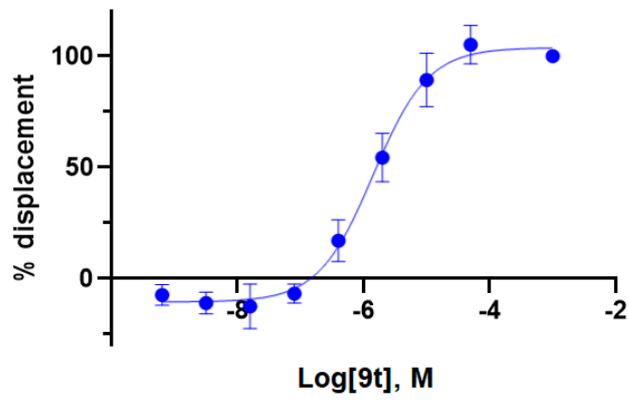
FP competition binding experiment with 9q



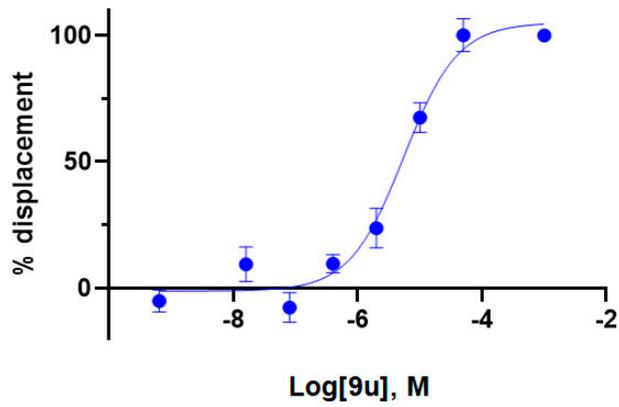
FP competition binding experiment with 9r



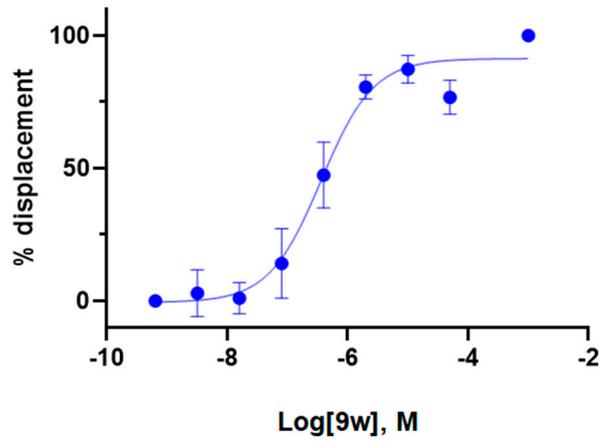
FP competition binding experiment with 9t



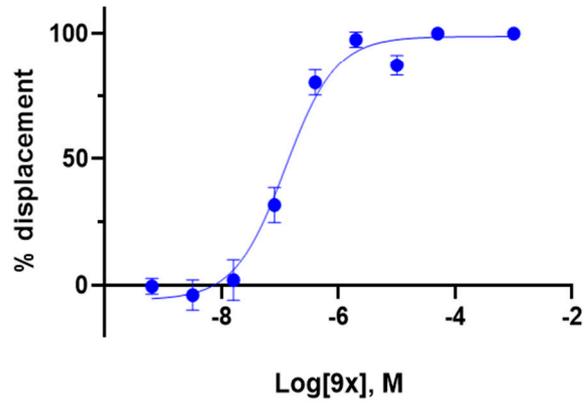
FP competition binding experiment with 9u



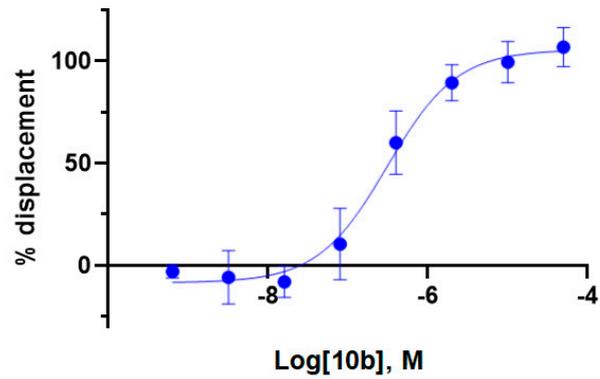
FP competition binding experiment with 9w



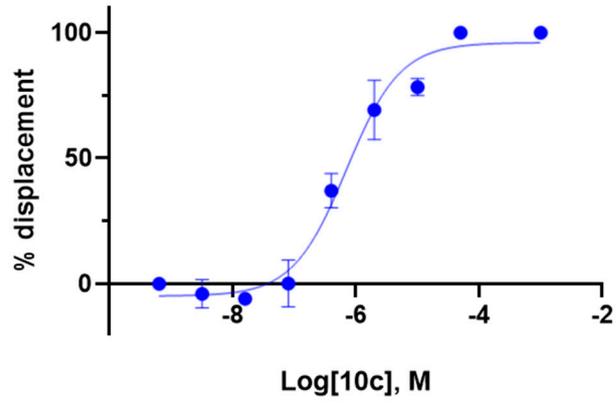
FP competition binding experiment with 9x



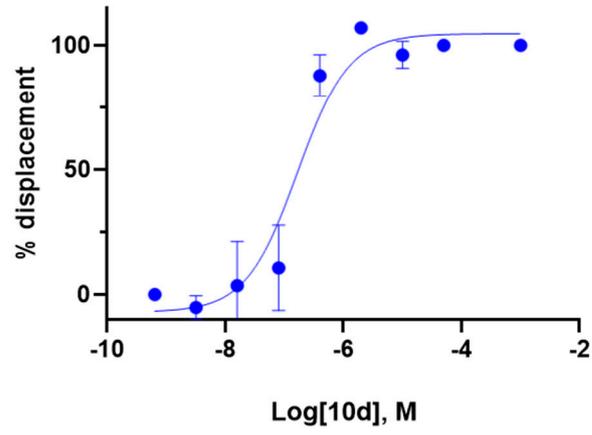
FP competition binding experiment with 10b



FP competition binding experiment with 10c



FP competition binding experiment with 10d



FP competition binding experiment with 11

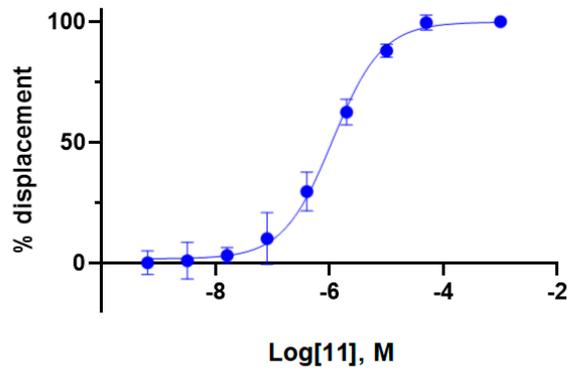
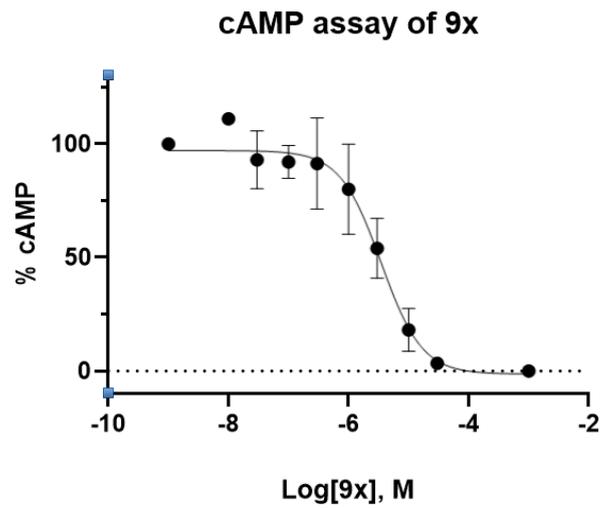
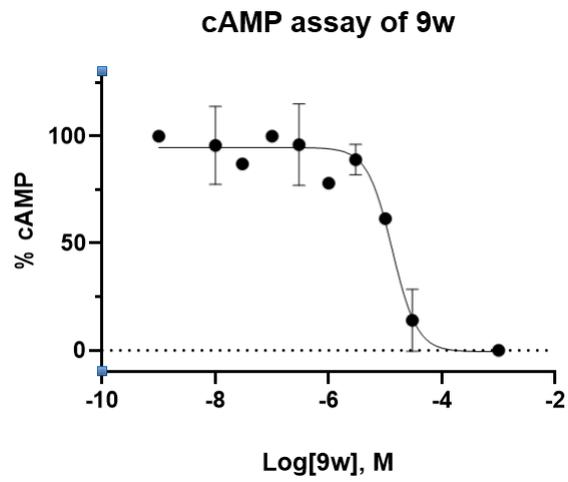
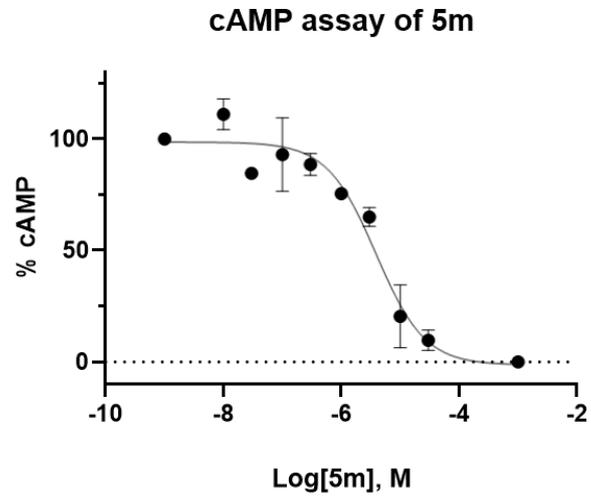
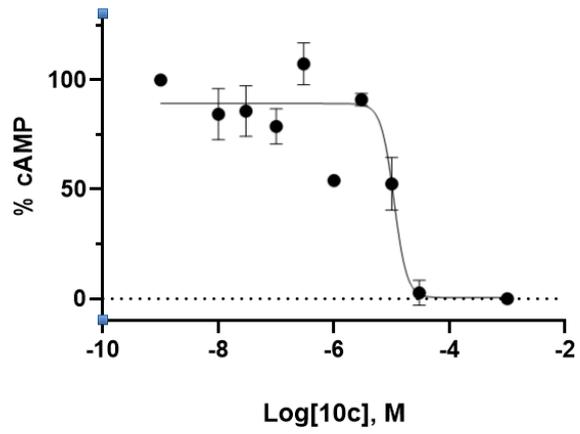


Figure S4. cAMP assays of compounds 5m, 9w, 9x, 10c, 10d



cAMP assay of 10c



cAMP assay of 10d

