Supporting Information

Discovery of Novel Thioquinazoline-*N*-aryl-acetamide/*N*-arylacetohydrazide Hybrids as Anti-SARS-CoV-2 Agents: Synthesis, *In vitro* Biological Evaluation, and Molecular Docking Studies

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NMR spectra of thioquinazoline-*N*-aryl-acetamide / *N*-arylacetohydrazide hybrids (Fig. 1-20).

2-(2-((4-Oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)benzoic acid (**11a**)

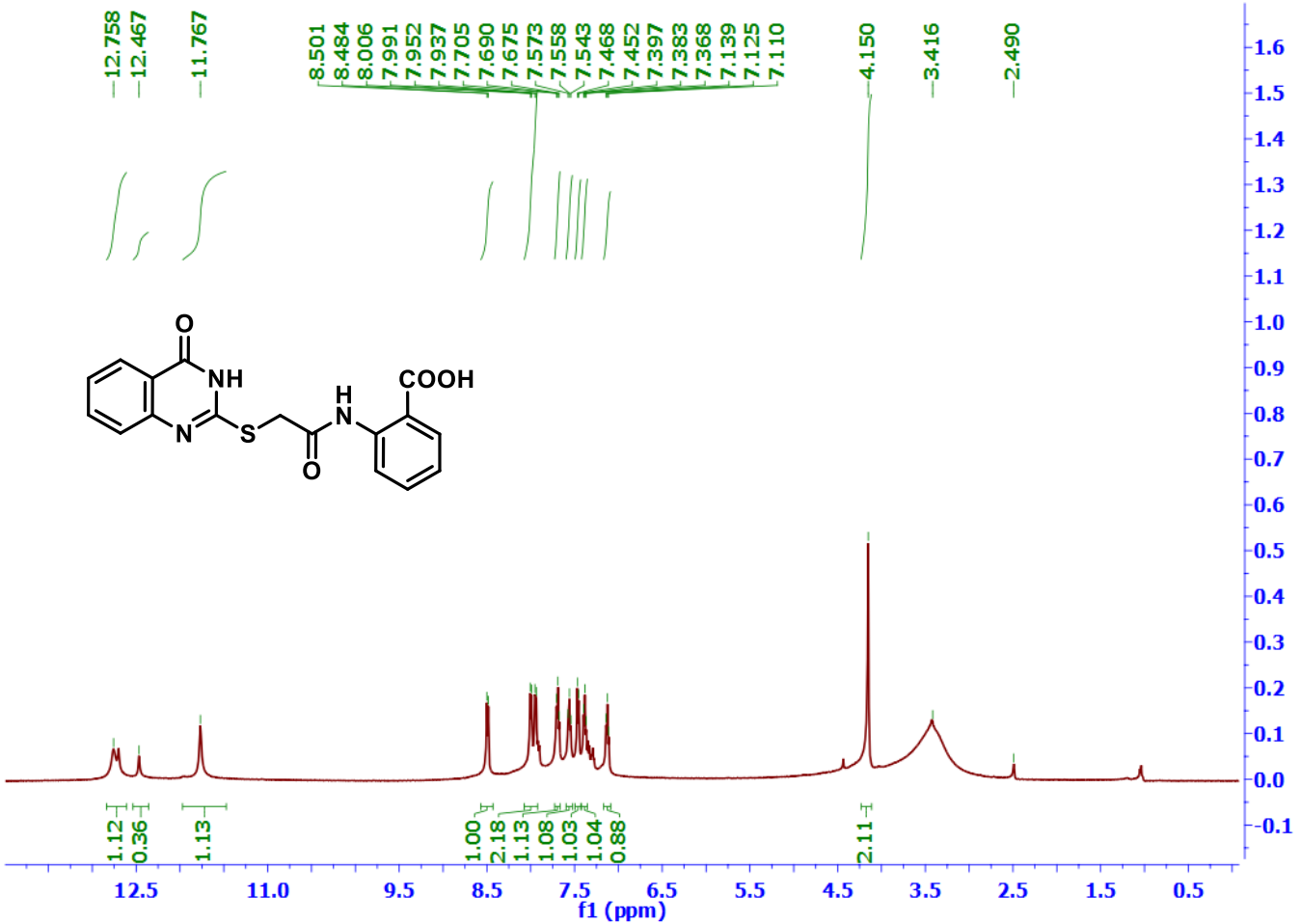

Fig. 1. ^{1}H (500 MHz) NMR spectrum of **11a** in DMSO-d_6

2-(2-((4-Oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)benzoic acid (**11a**)

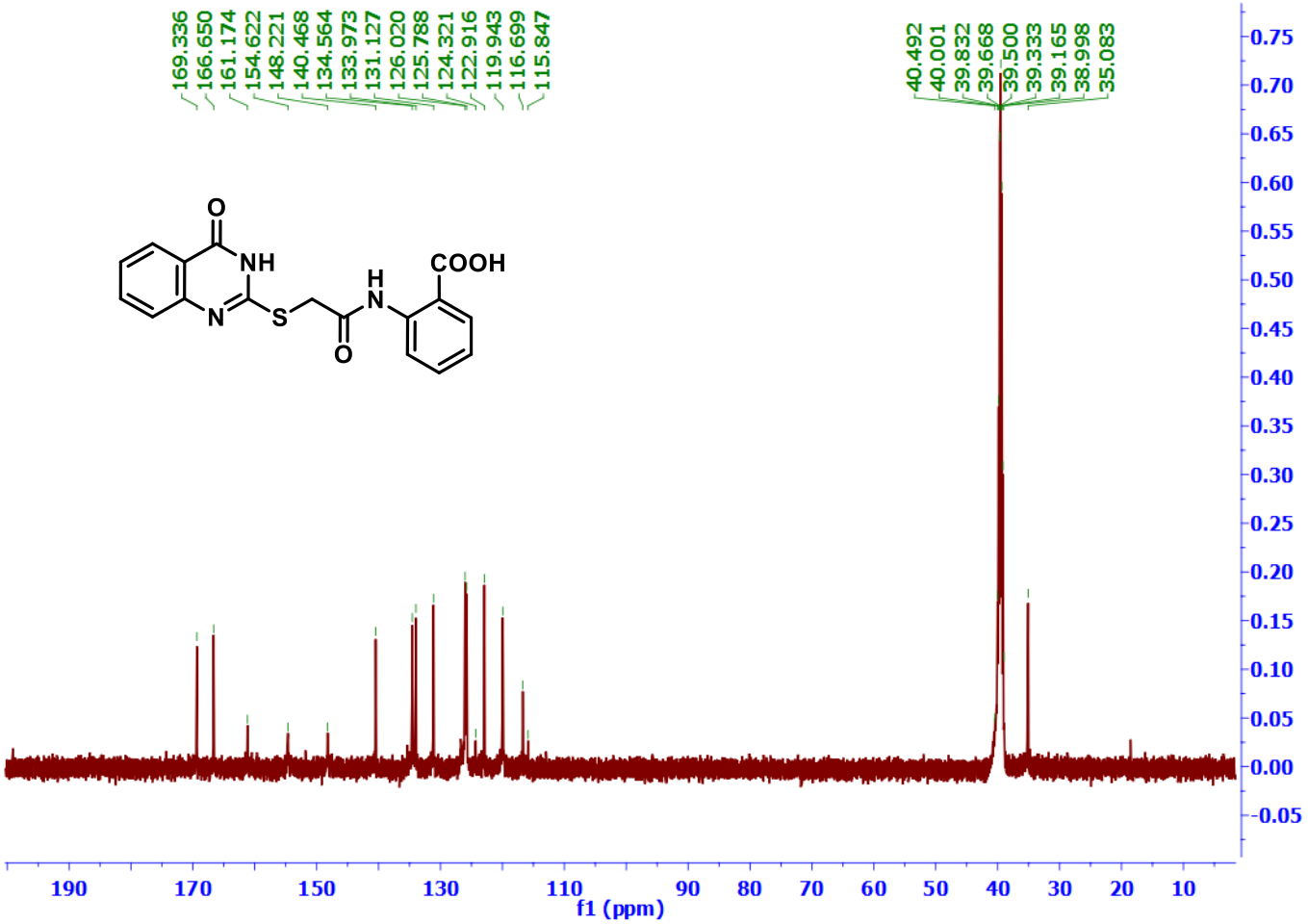

Fig. 2. ^{13}C (125 MHz) NMR spectrum of **11a** in DMSO-d_6

3-(2-((4-Oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)benzoic acid (**11b**)

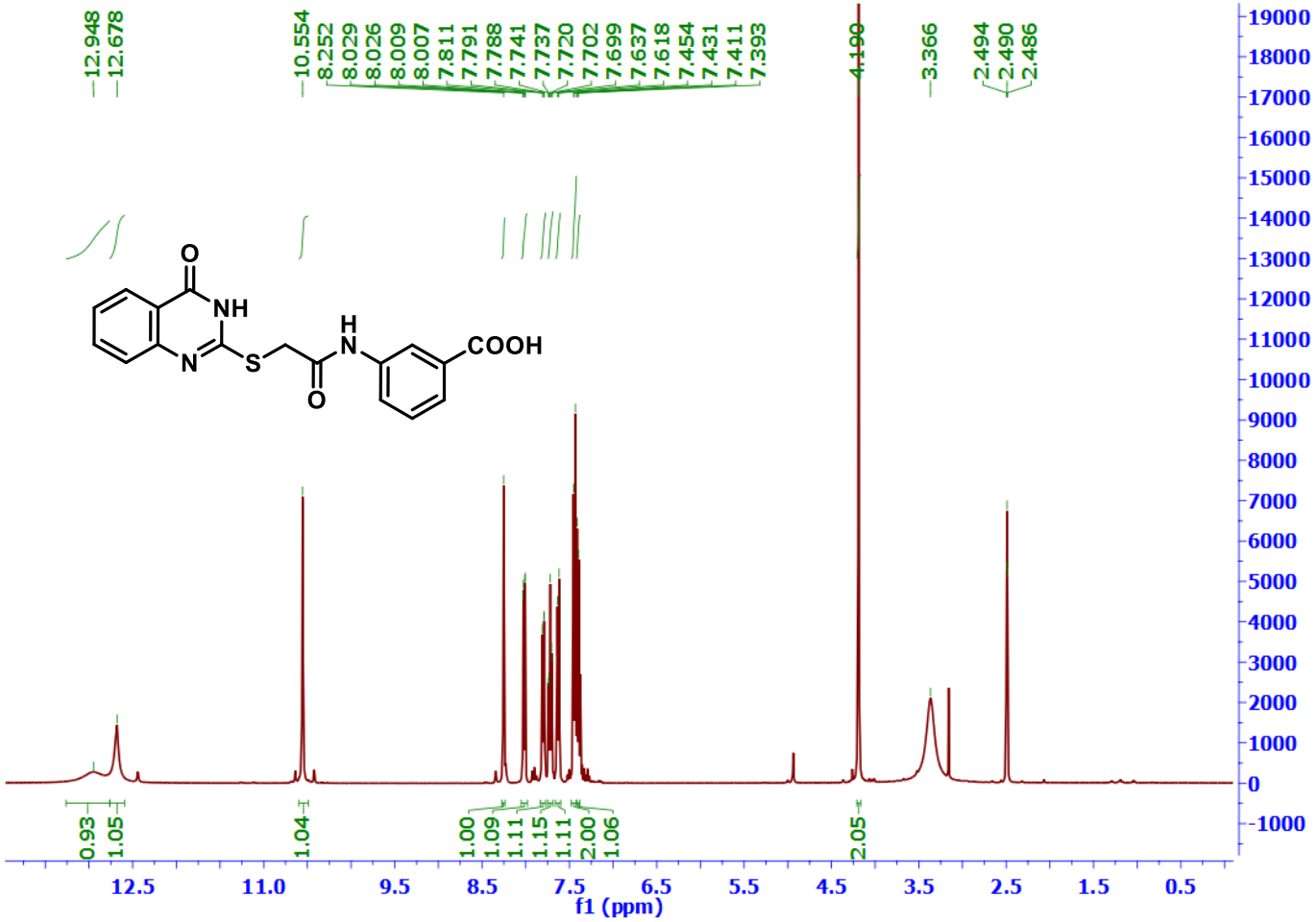

Fig. 3. ^{1}H (400 MHz) NMR spectrum of **11b** in DMSO-d_6

3-(2-((4-Oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)benzoic acid (**11b**)

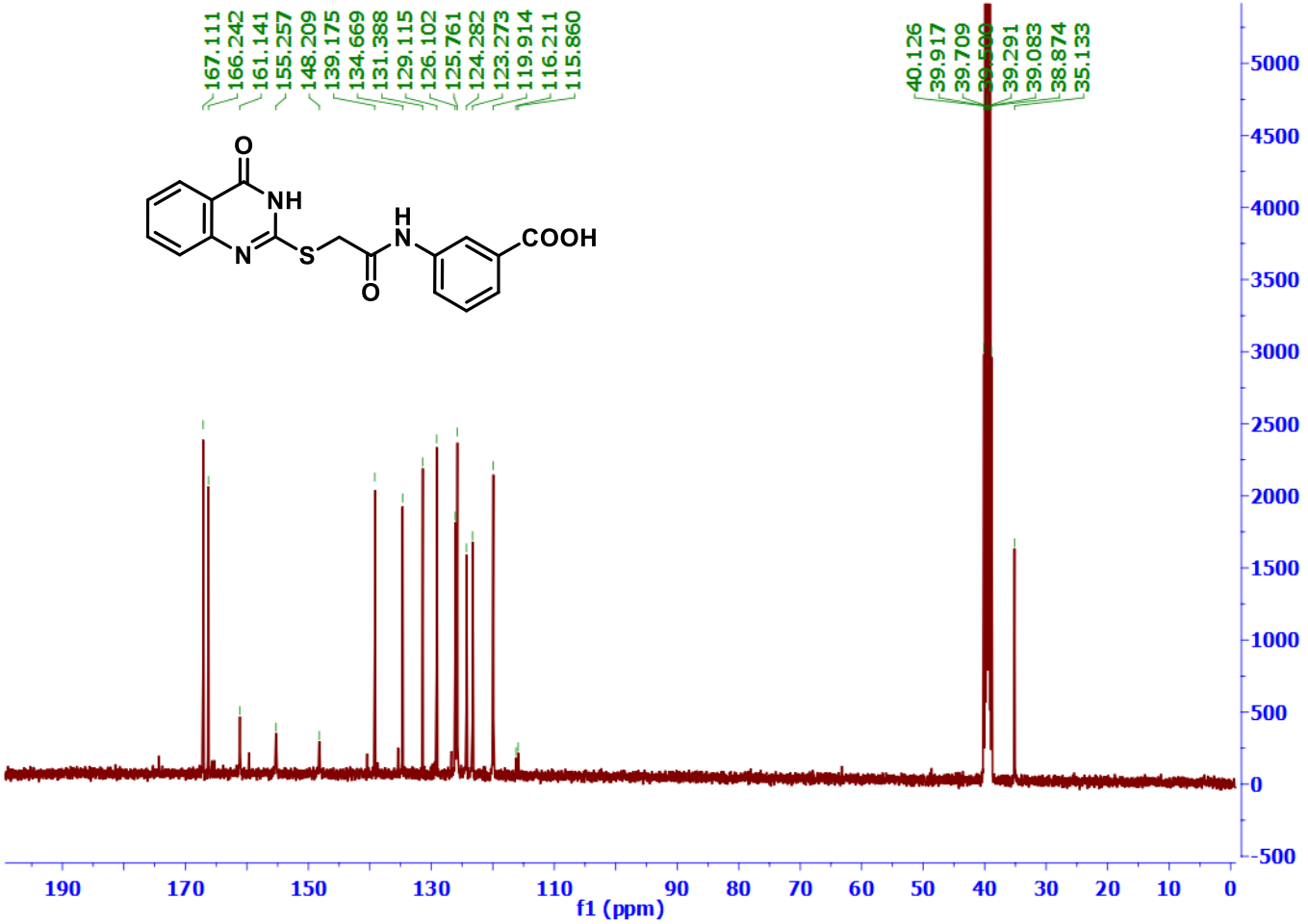

Fig. 4. ^{13}C (100 MHz) NMR spectrum of **11b** in DMSO-d_6

4-(2-((4-Oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)benzoic acid (**11c**)

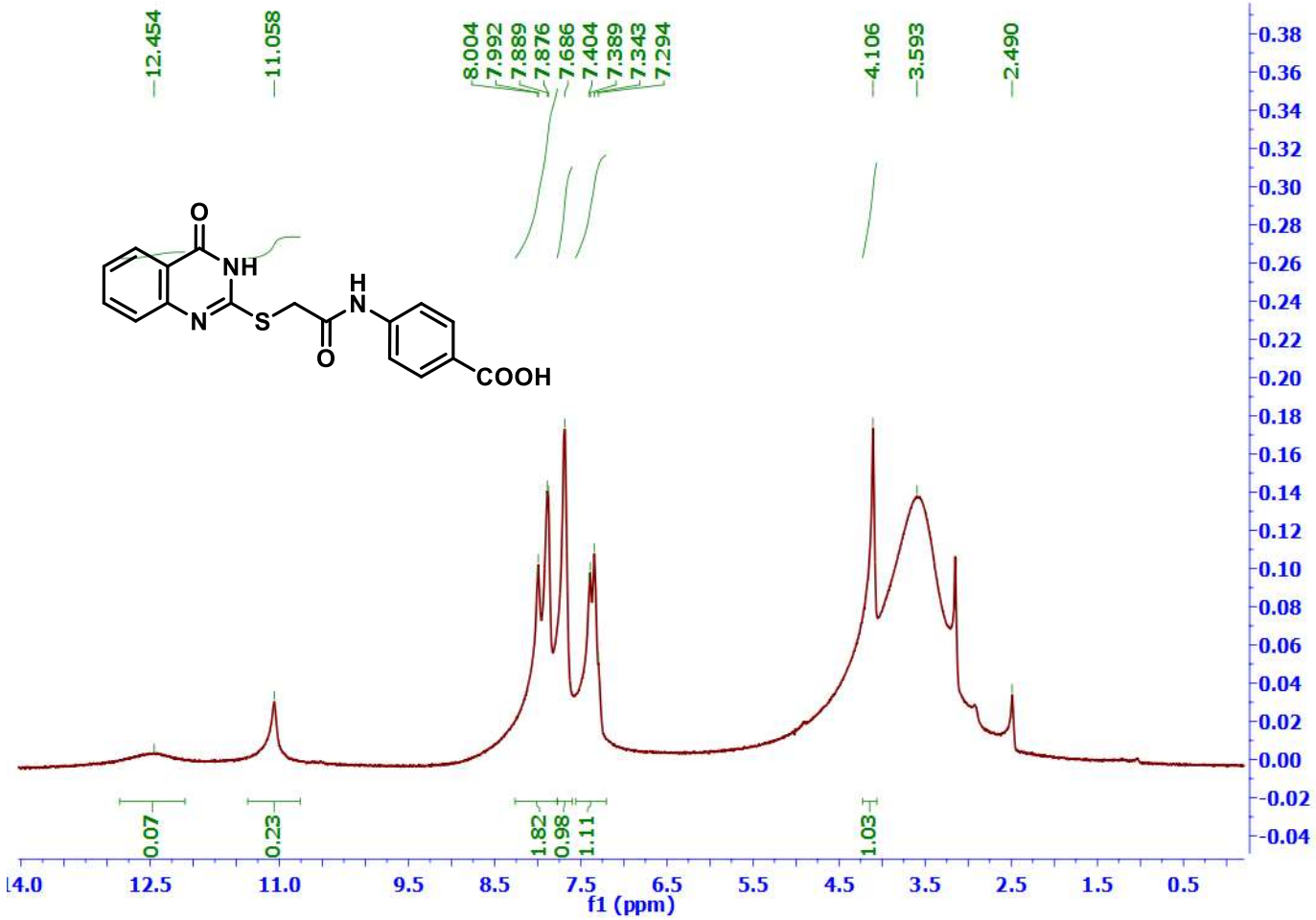

Fig. 5. ^{1}H (500 MHz) NMR spectrum of **11c** in DMSO-d_6

2-(2-((4-Oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetamido)benzoic acid (**12a**)

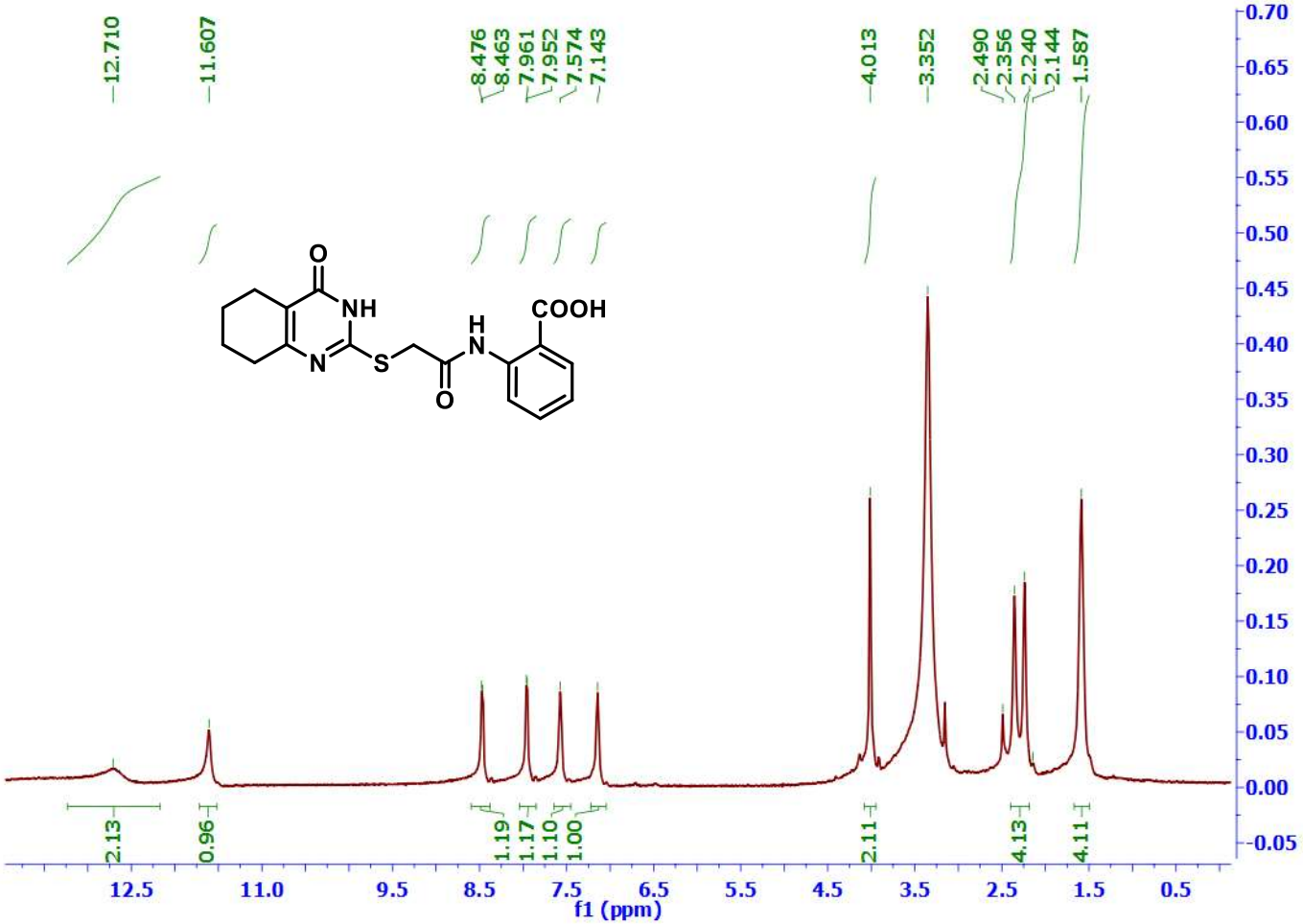

Fig. 6. ^{1}H (500 MHz) NMR spectrum of **12a** in DMSO-d_6

2-(2-((4-Oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetamido)benzoic acid (**12a**)

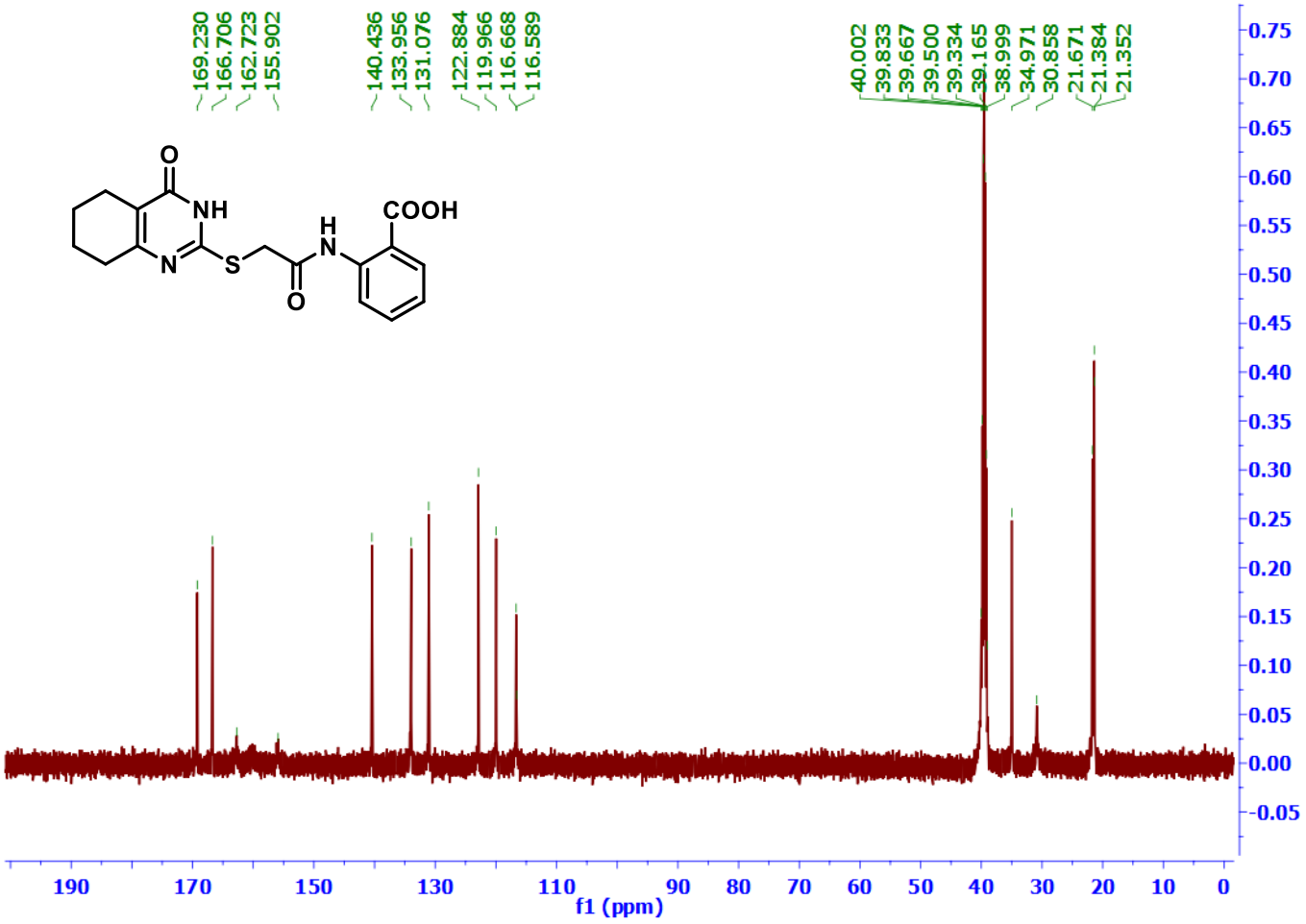

Fig. 7. ^{13}C (125 MHz) NMR spectrum of **12a** in DMSO-d_6

3-(2-((4-Oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetamido)benzoic acid (**12b**)

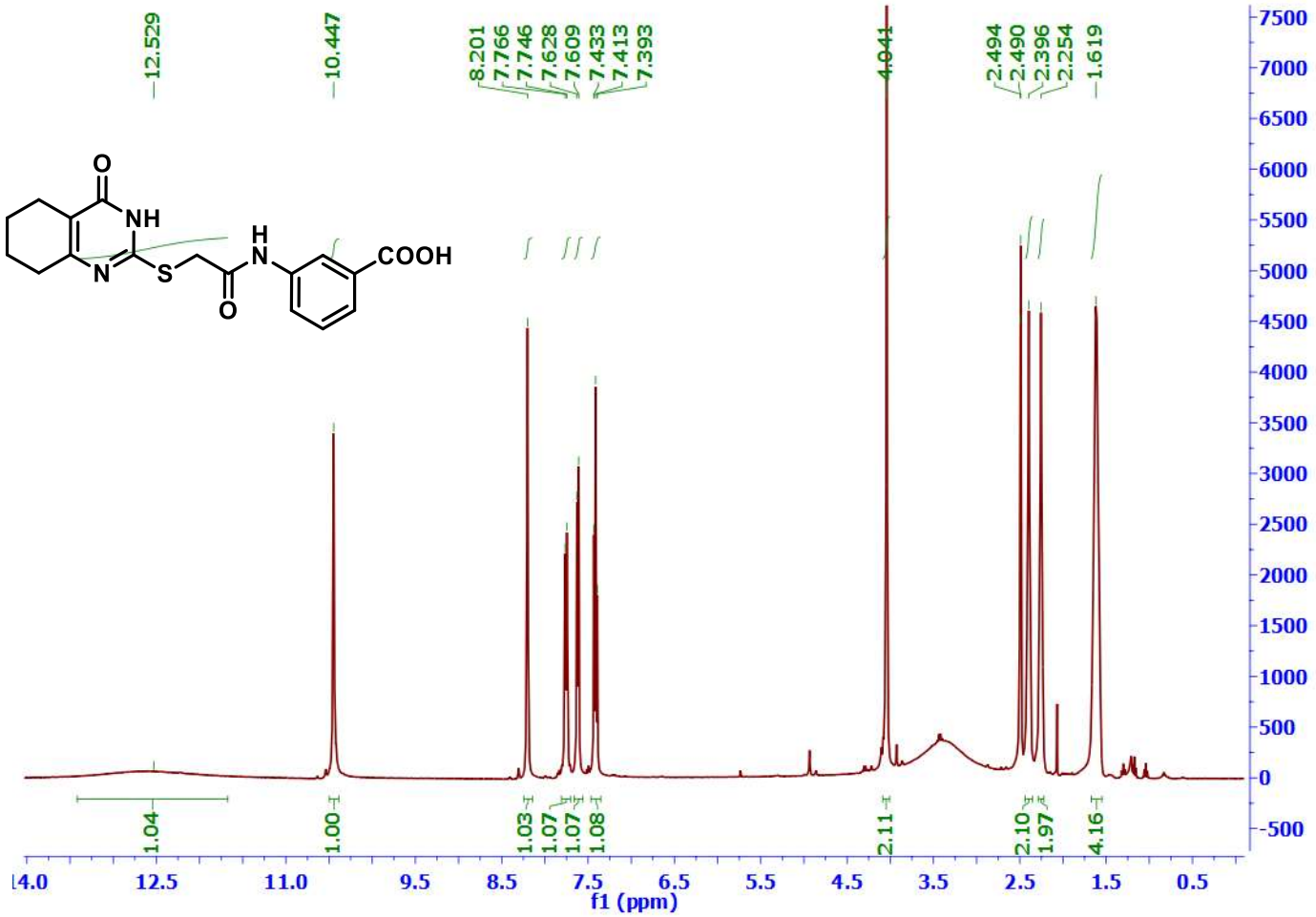

Fig. 8. ^{1}H (400 MHz) NMR spectrum of **12b** in DMSO-d_6

3-(2-((4-Oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetamido)benzoic acid (**12b**)

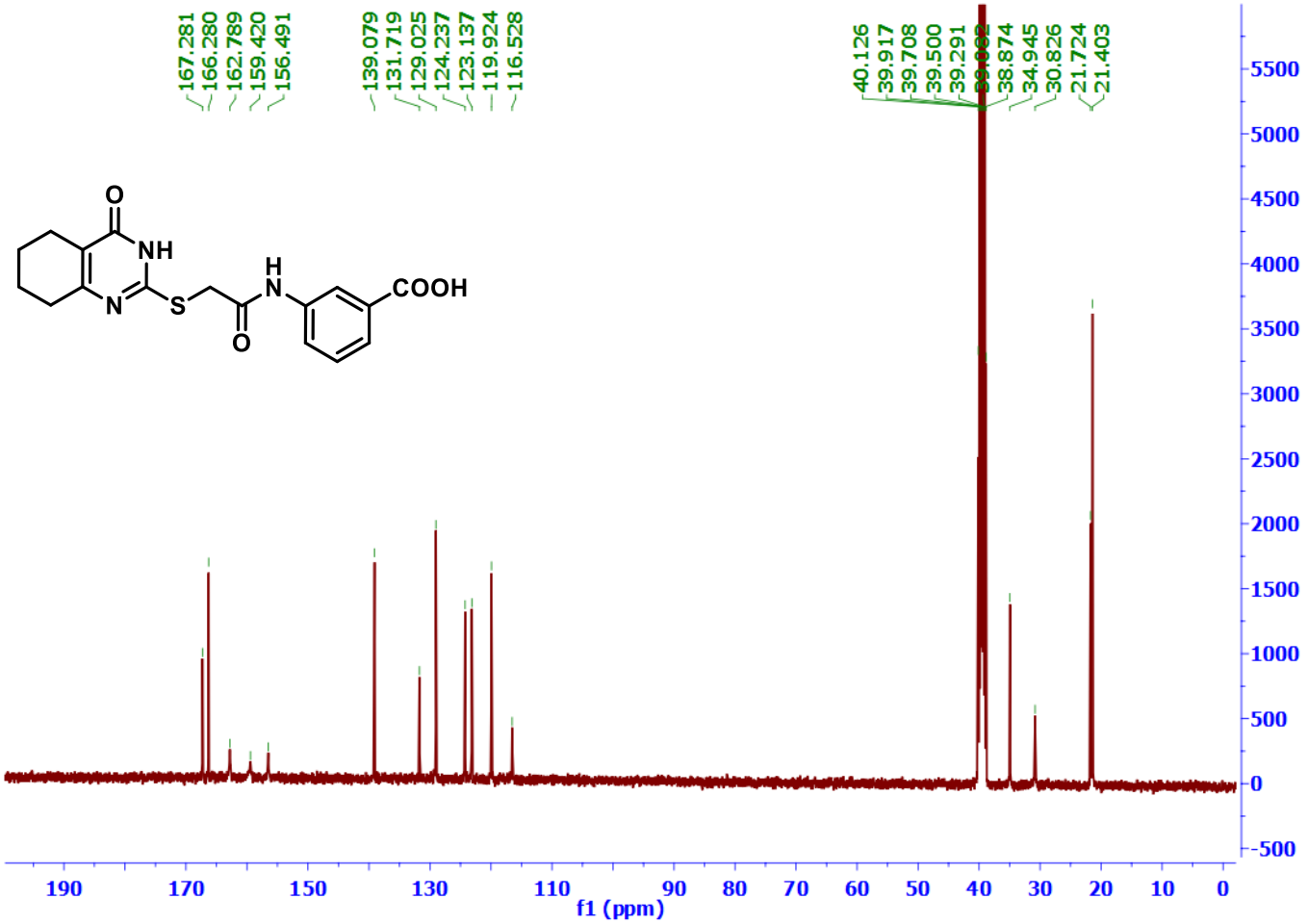

Fig. 9. ^{13}C (100 MHz) NMR spectrum of **12b** in DMSO-d_6

4-(2-((4-Oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetamido)benzoic acid (**12c**)

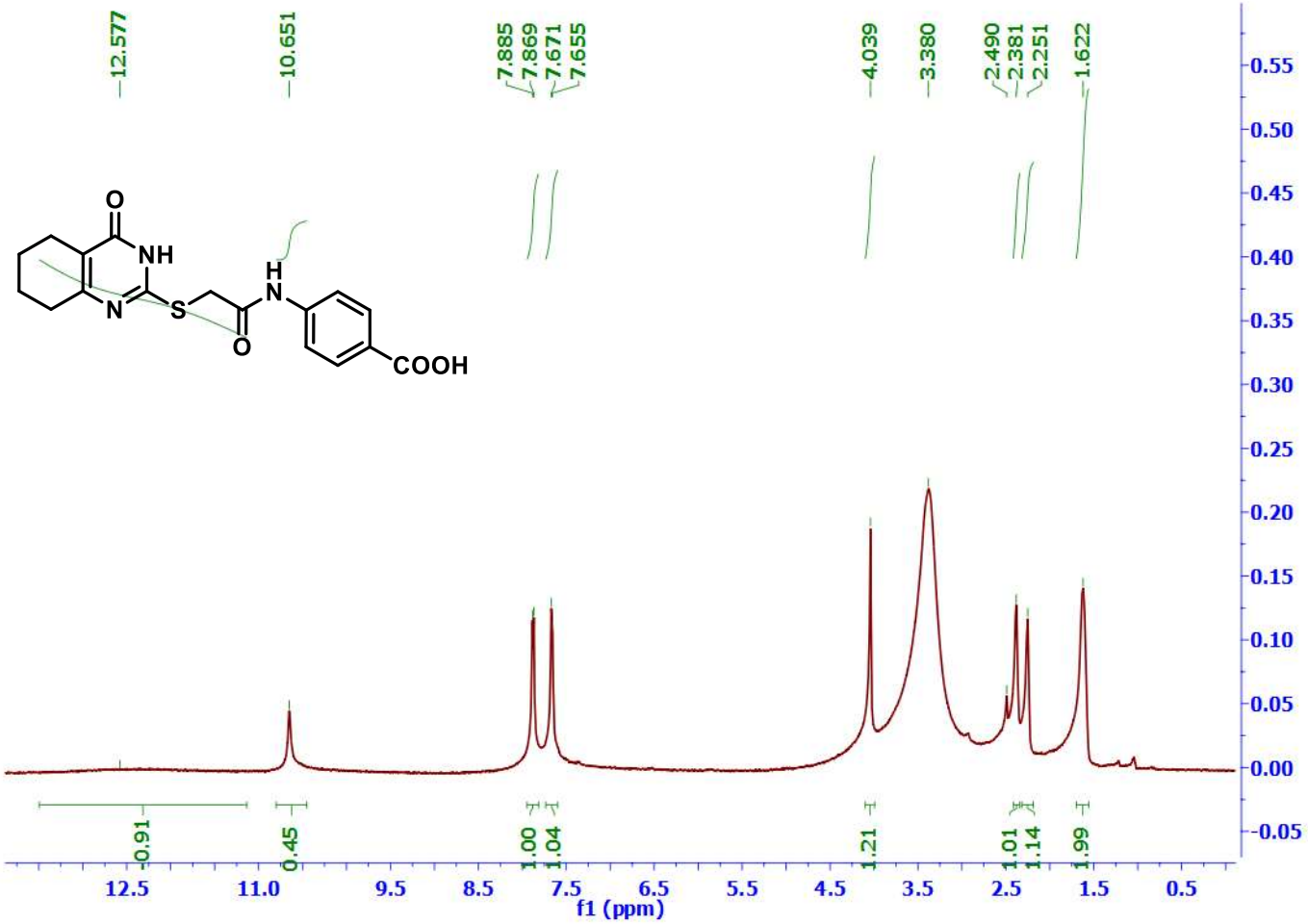

Fig. 10. ^{1}H (500 MHz) NMR spectrum of **12c** in DMSO-d_6

4-(2-((4-Oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetamido)benzoic acid (**12c**)

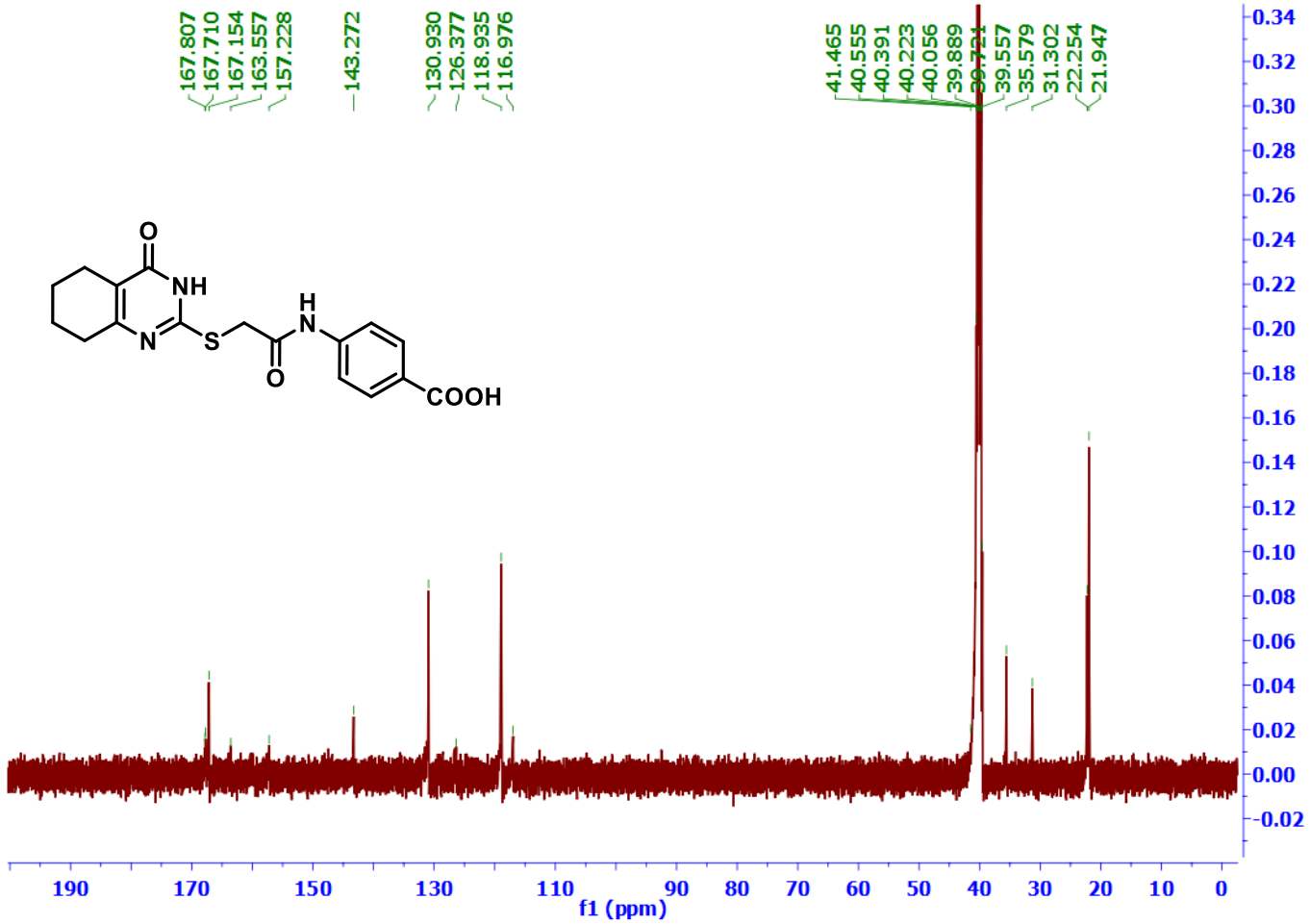

Fig. 11. ^{13}C (125 MHz) NMR spectrum of **12c** in DMSO-d_6

N'-(2-((4-Oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17a**)

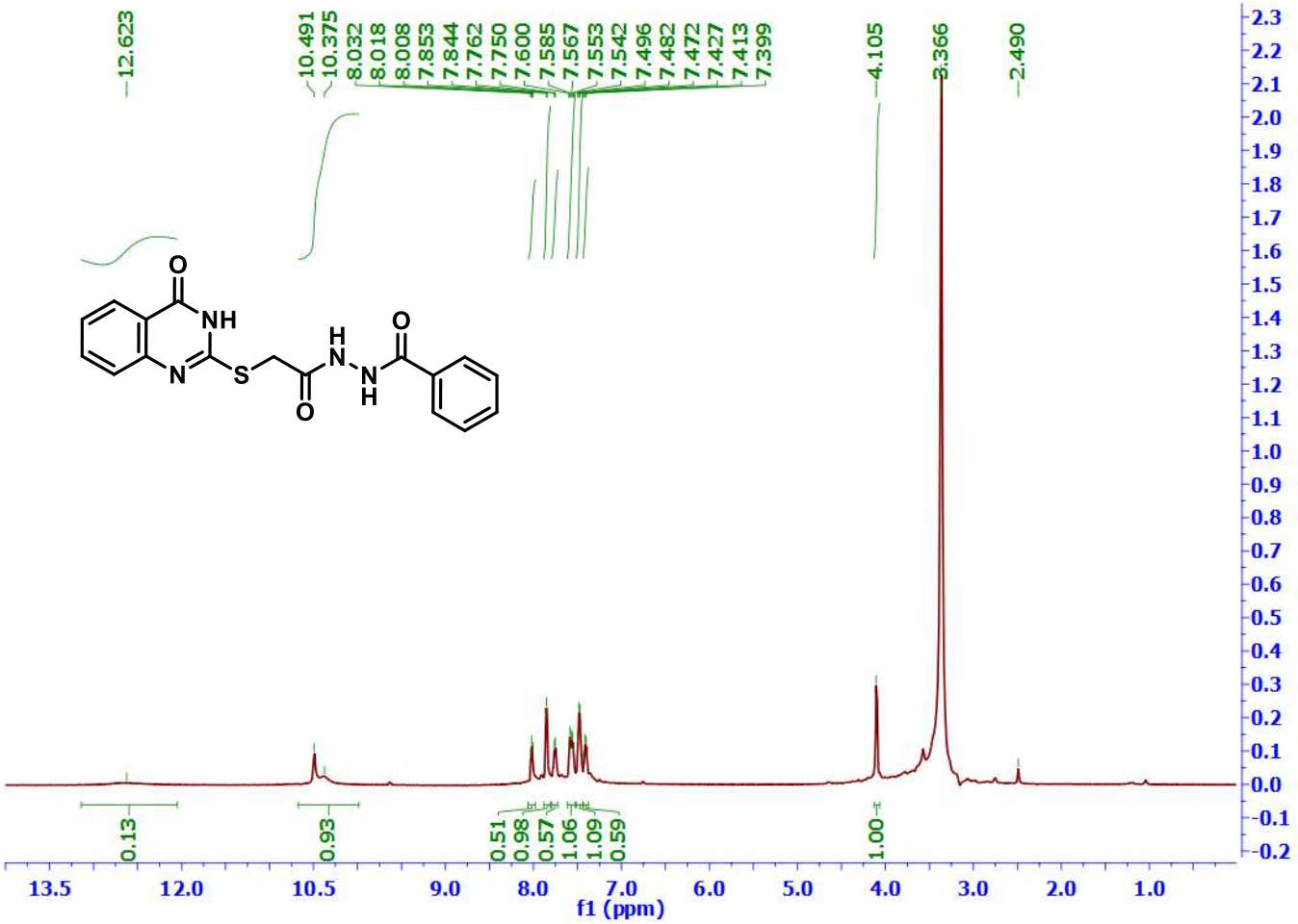

Fig. 12. ^{1}H (500 MHz) NMR spectrum of **17a** in DMSO-d_6

4-Methyl-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17b**)

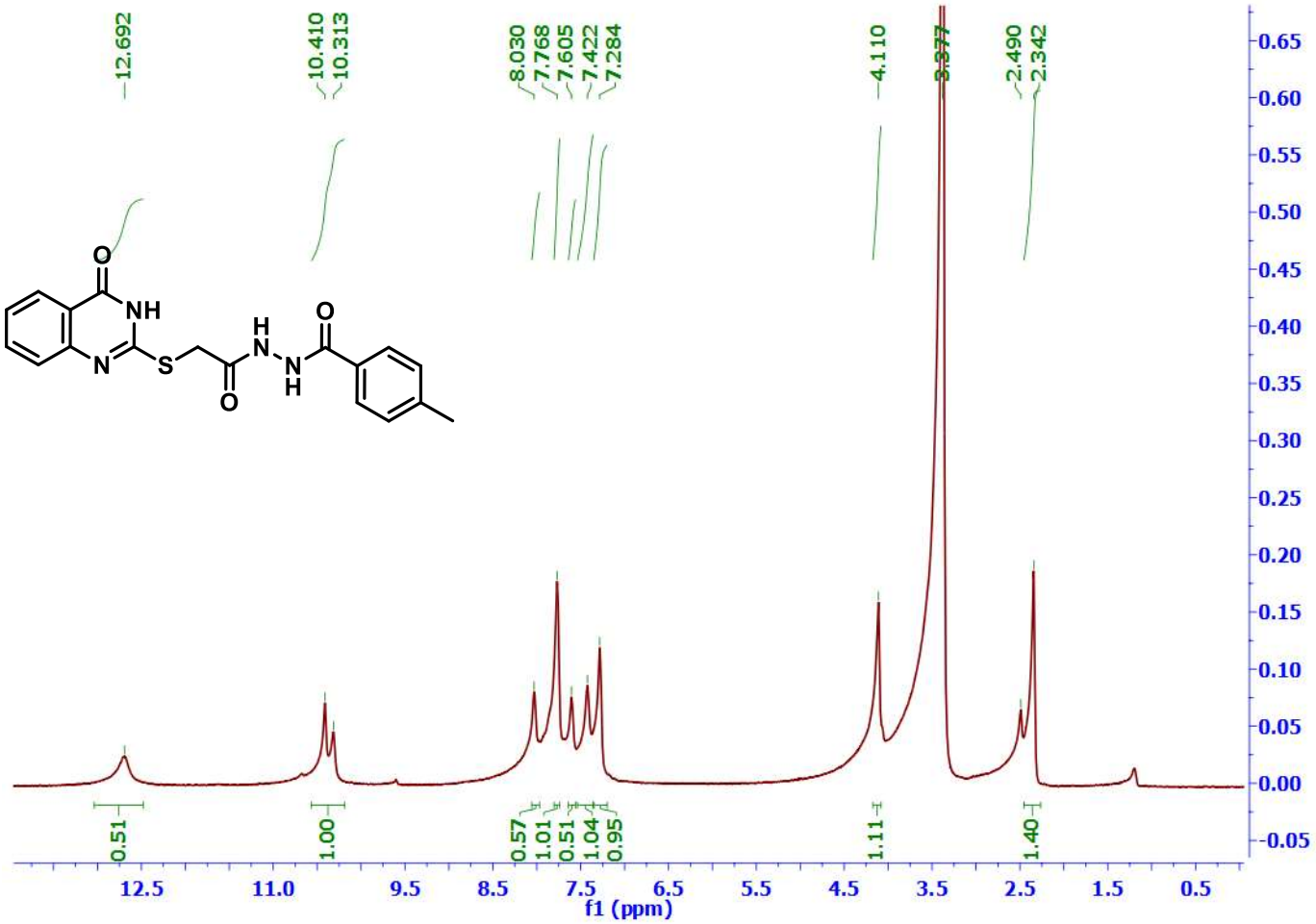

Fig. 13. ^{1}H (500 MHz) NMR spectrum of **17b** in DMSO-d_6

4-Methyl-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17b**)

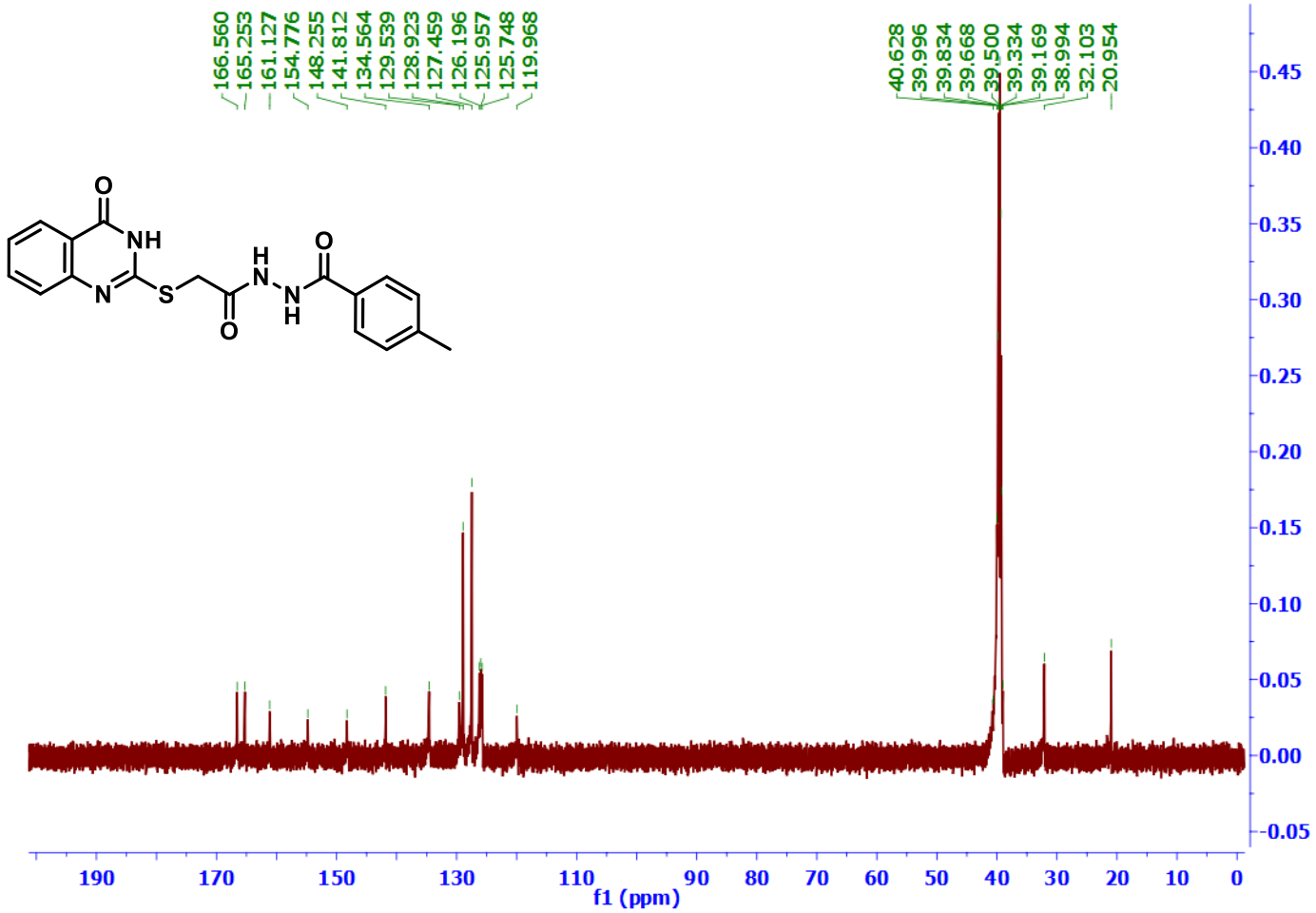

Fig. 14. ^{13}C (125 MHz) NMR spectrum of **17b** in DMSO-d_6

4-Nitro-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17c**)

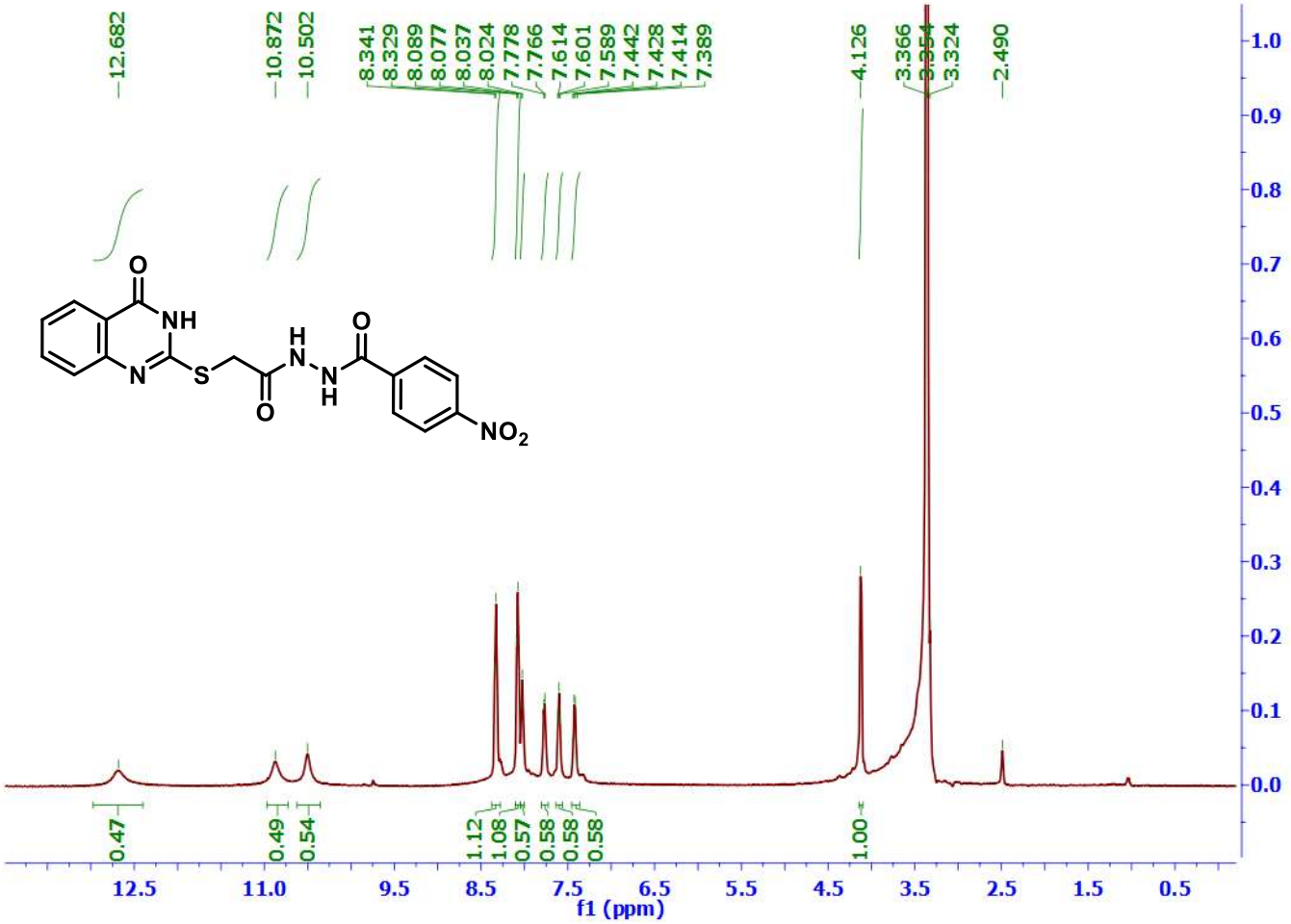

Fig. 15. ^{1}H (500 MHz) NMR spectrum of **17c** in DMSO-d_6

4-Nitro-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17c**)

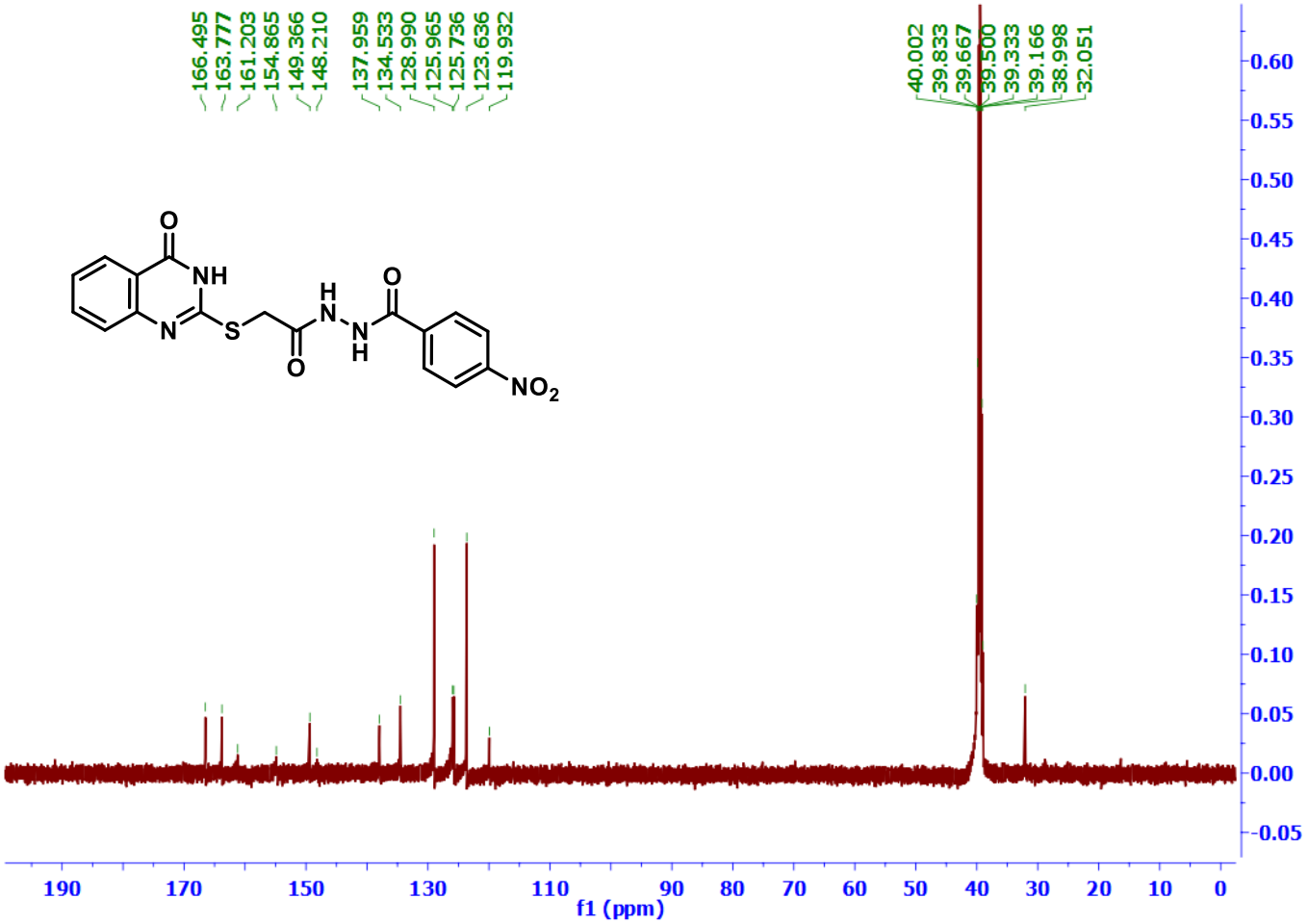

Fig. 16. ^{13}C (125 MHz) NMR spectrum of **17c** in DMSO-d_6

2-Methoxy-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17d**)

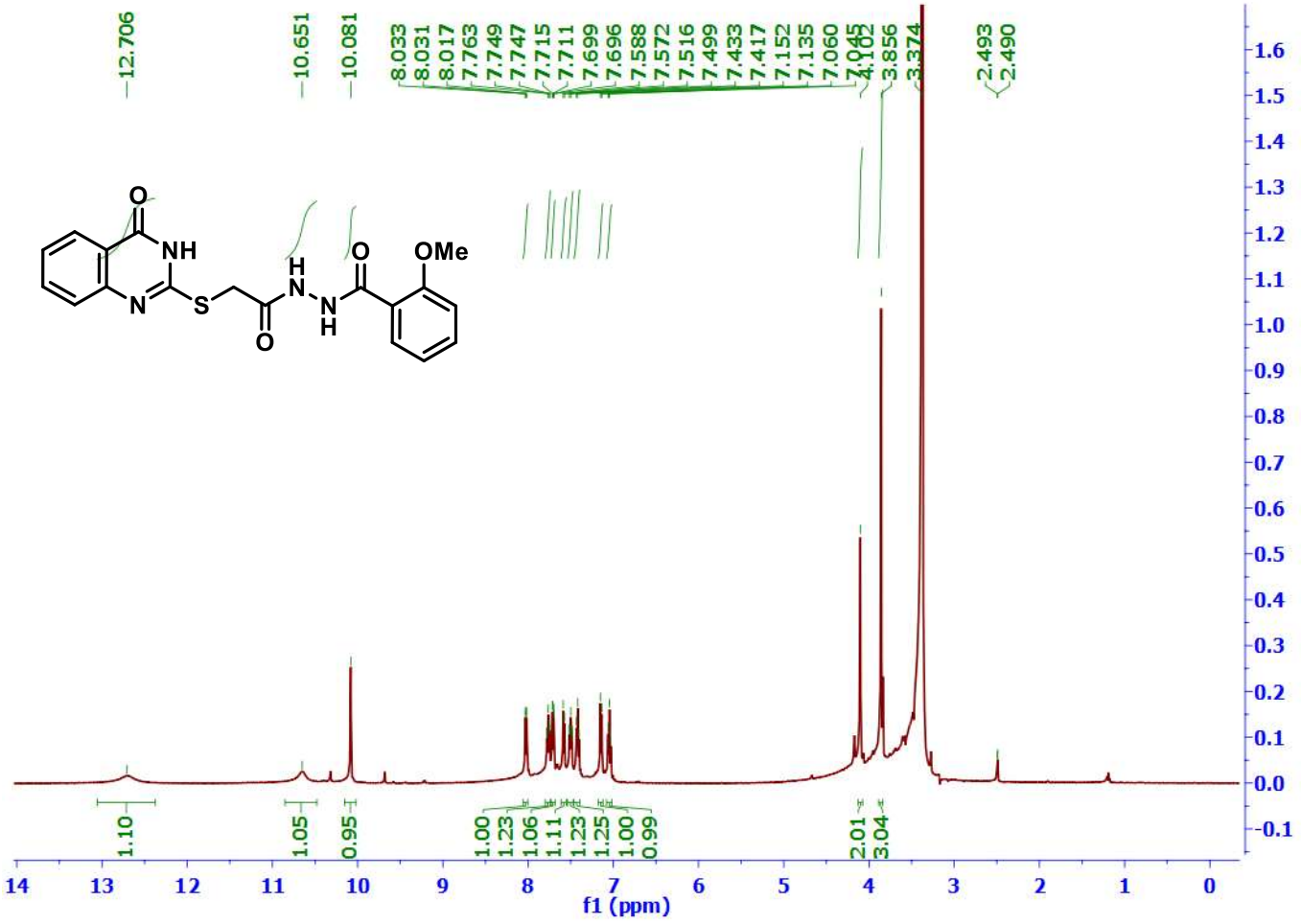

Fig. 17. ^{1}H (500 MHz) NMR spectrum of **17d** in DMSO-d_6

2-Methoxy-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17d**)

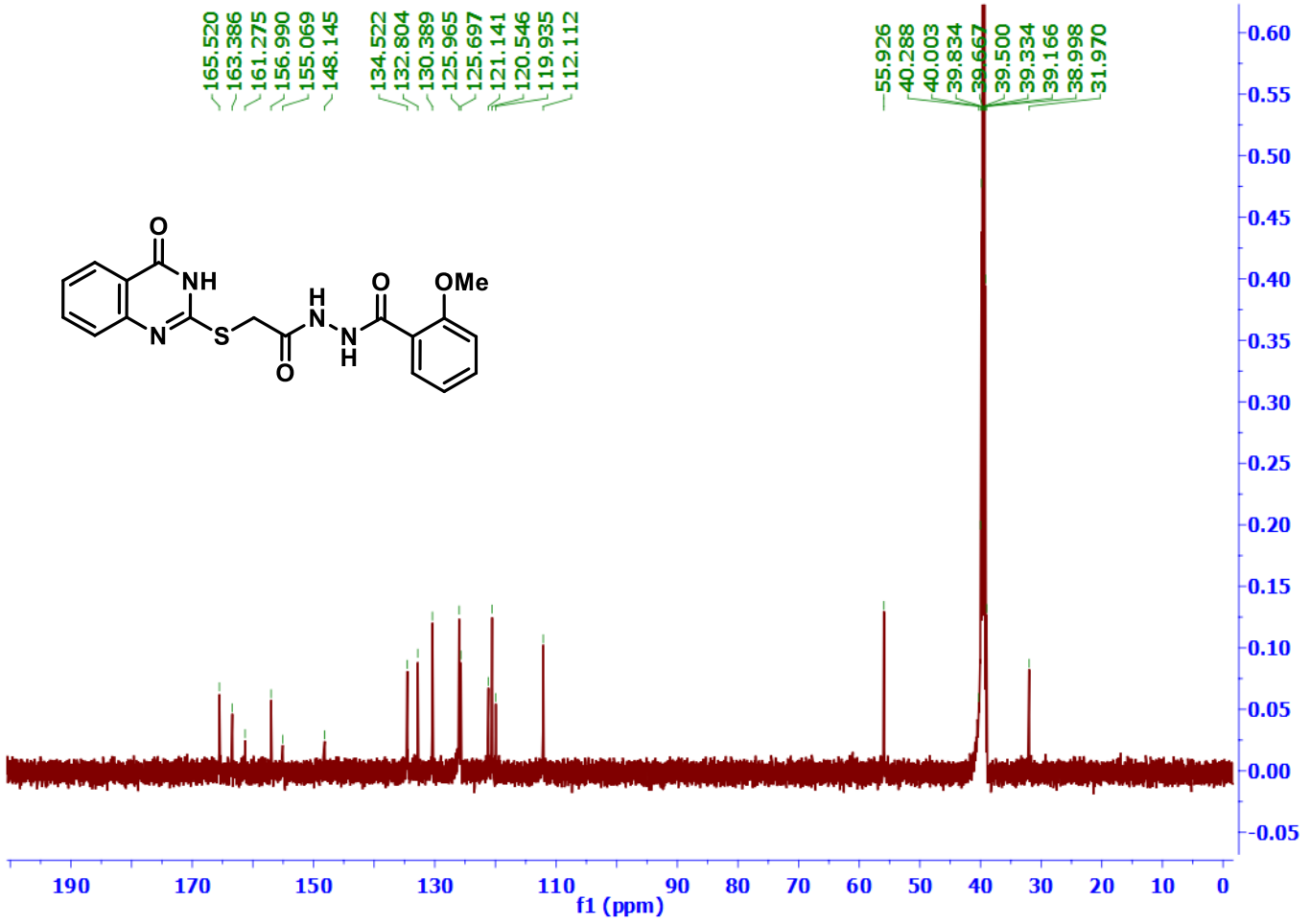

Fig. 18. ^{13}C (125 MHz) NMR spectrum of **17d** in DMSO-d_6

2-Chloro-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17e**)

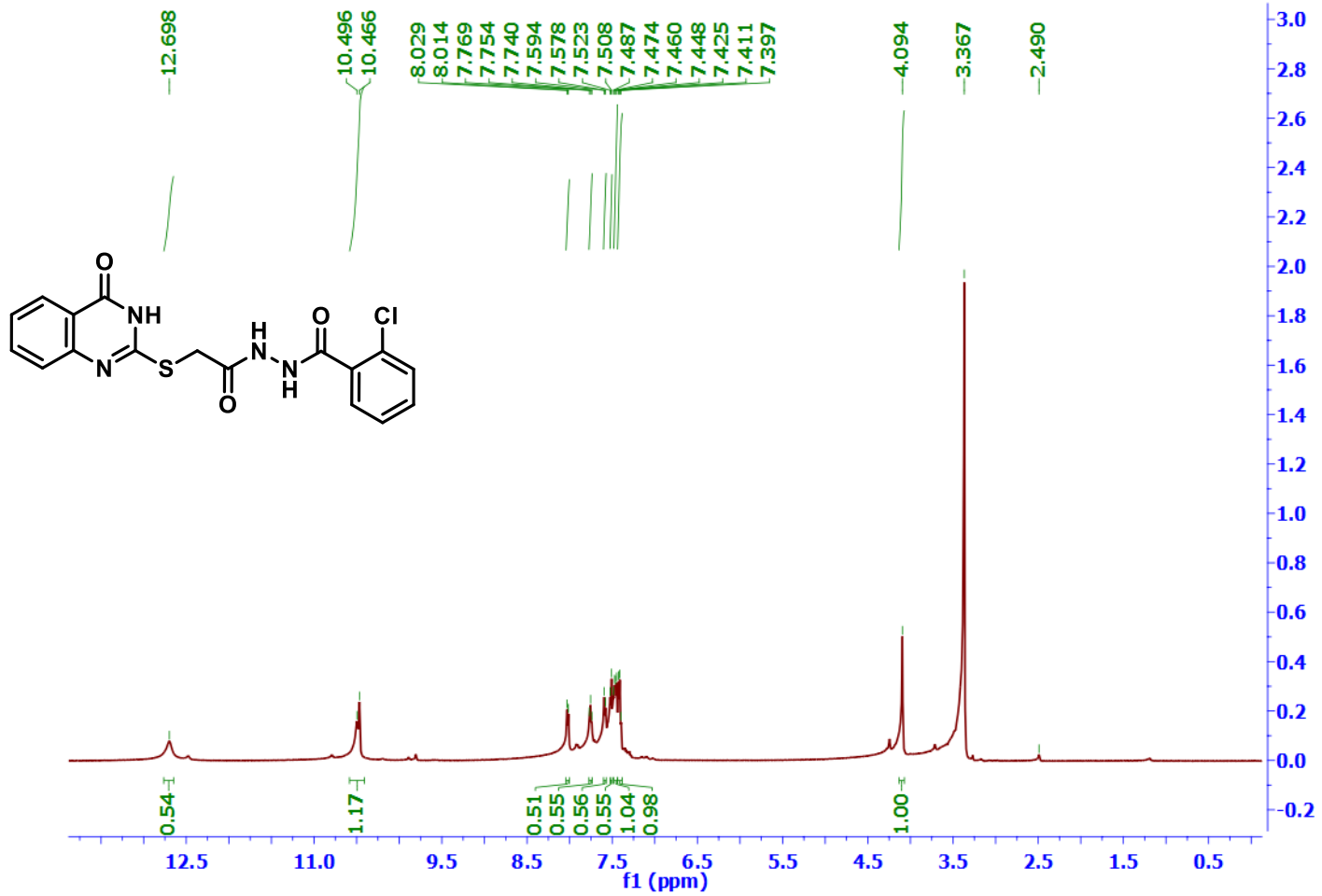

Fig. 19 ^{1}H (500 MHz) NMR spectrum of **17e** in DMSO-d_6

2-Chloro-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17e**)

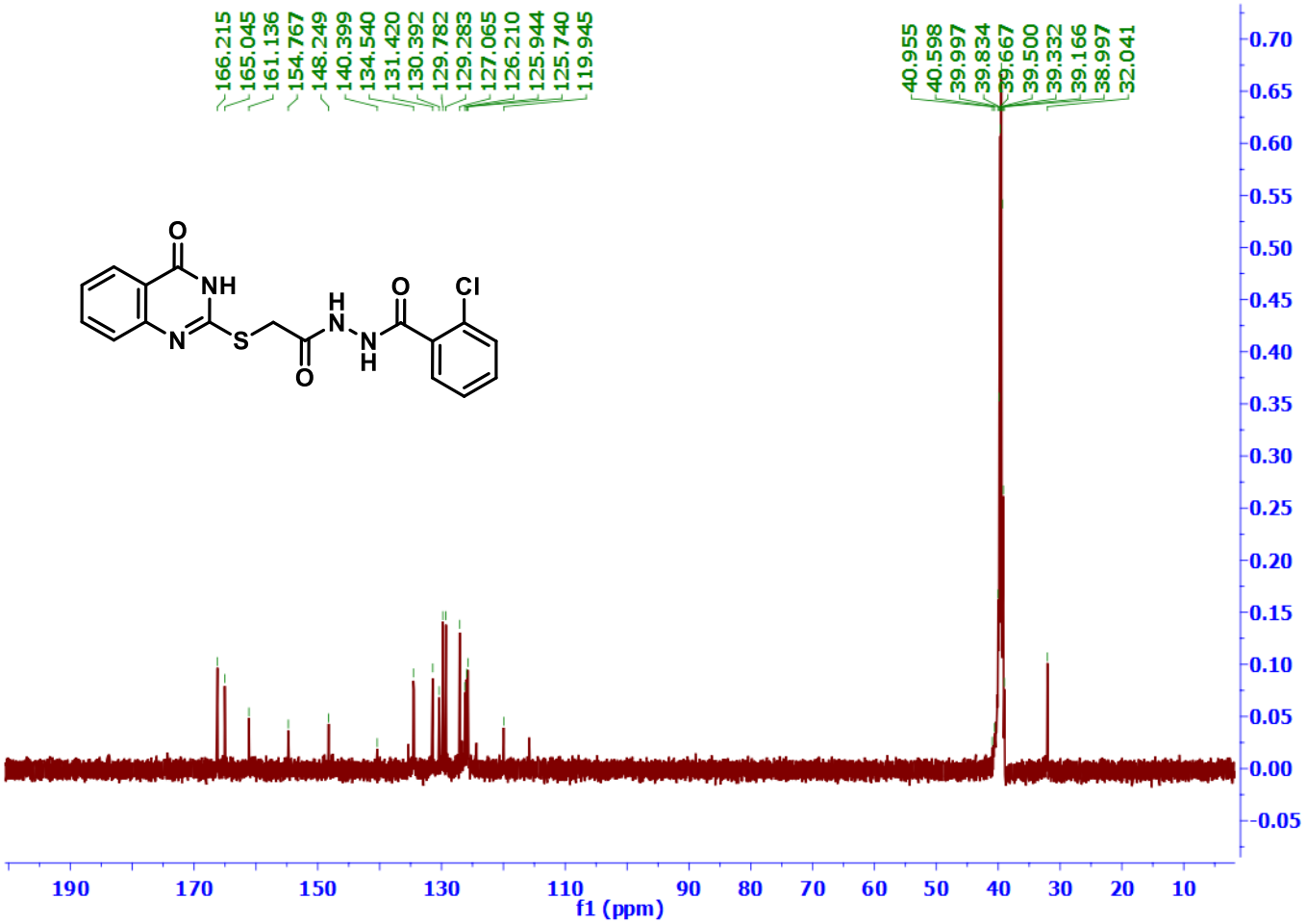

Fig. 20 ^{13}C (125 MHz) NMR spectrum of **17e** in DMSO-d_6

4-Chloro-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17f**)

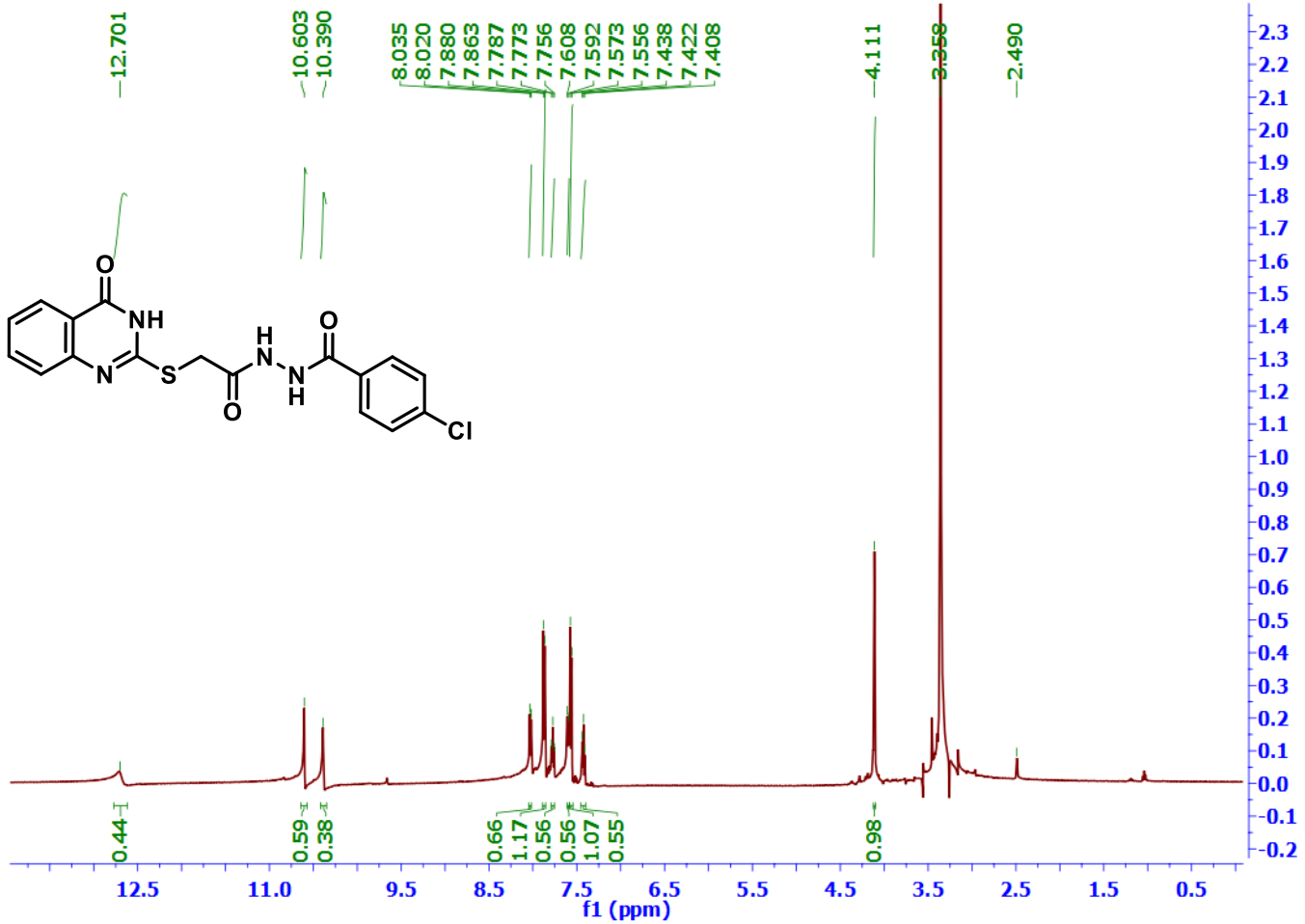

Fig. 21 ^{1}H (500 MHz) NMR spectrum of **17f** in DMSO-d_6

4-Chloro-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17f**)

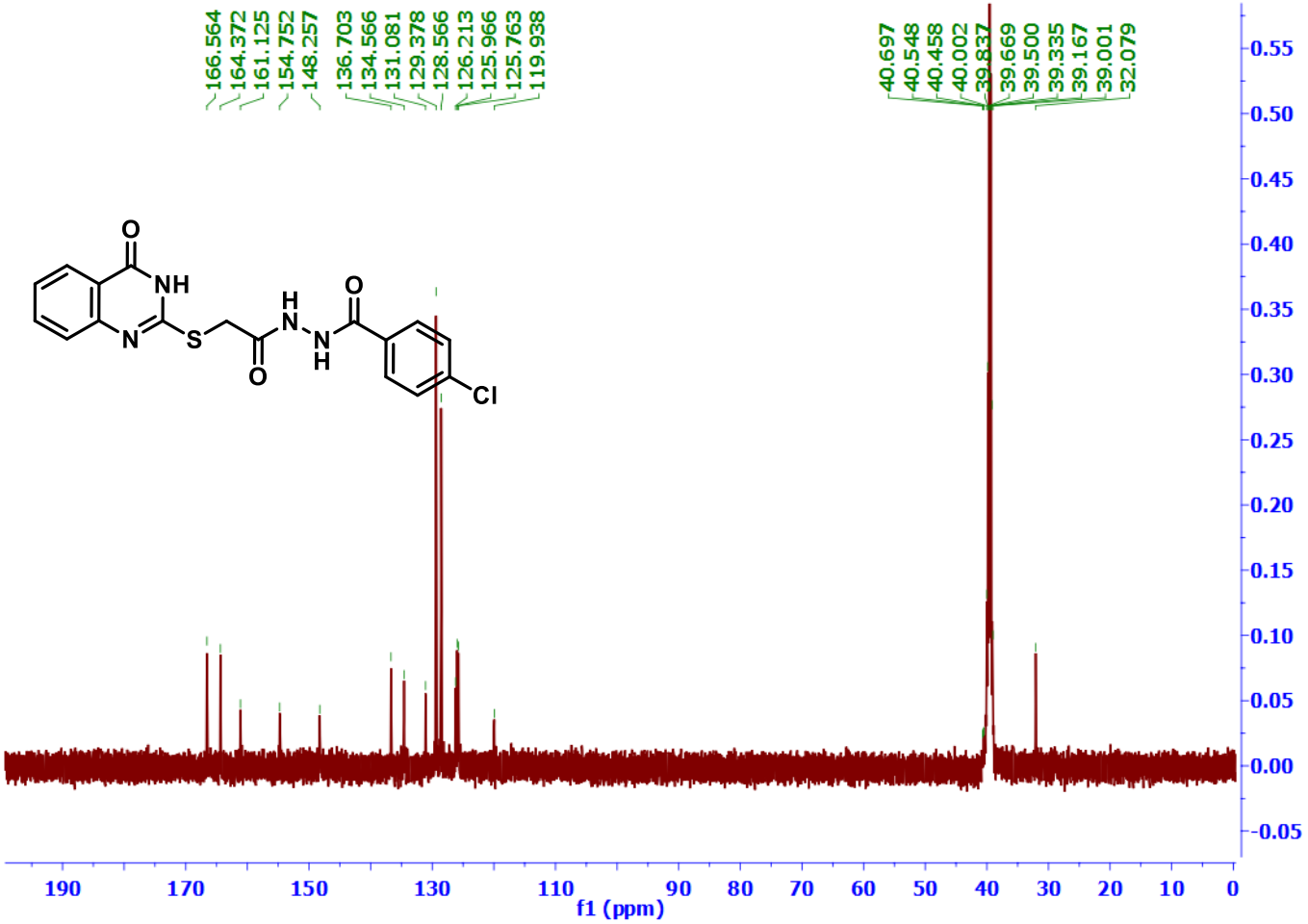

Fig. 22. ^{13}C (125 MHz) NMR spectrum of **17f** in DMSO-d_6

2-Bromo-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17g**)

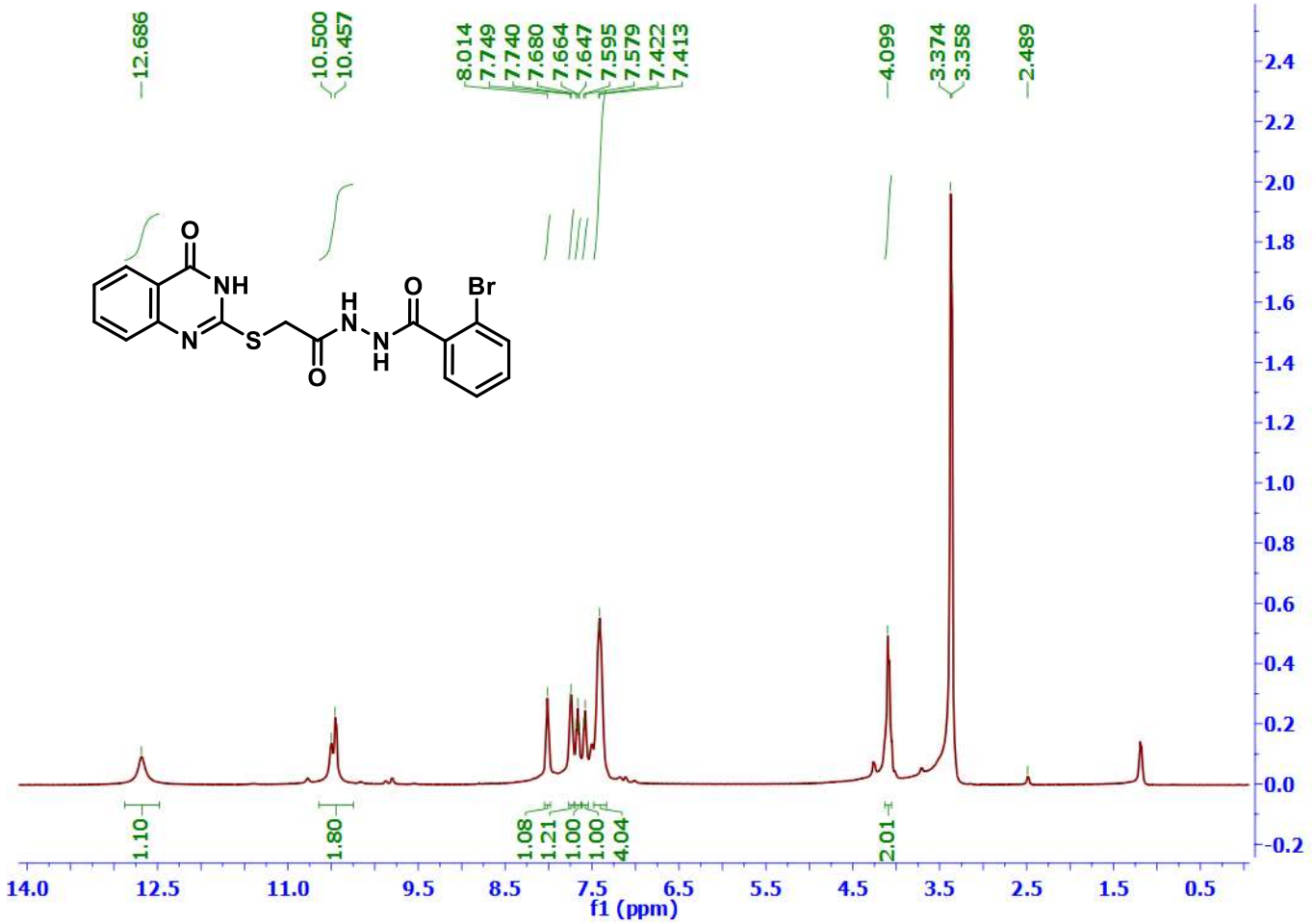

Fig. 23. ^{1}H (500 MHz) NMR spectrum of **17g** in DMSO-d_6

2-Bromo-*N*'-(2-((4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**17g**)

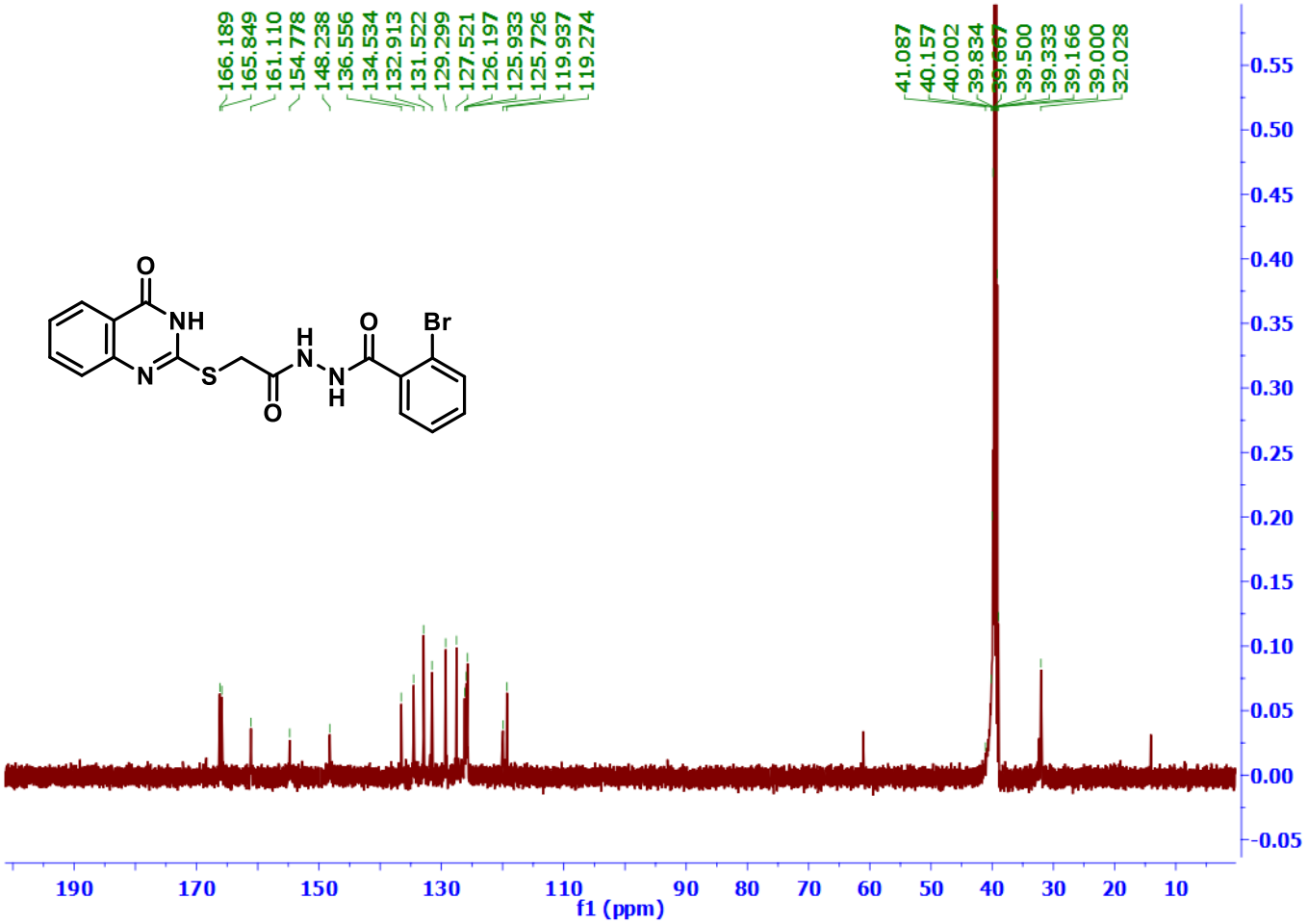

Fig. 24. ^{13}C (125 MHz) NMR spectrum of **17g** in DMSO-d_6

N'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18a**)

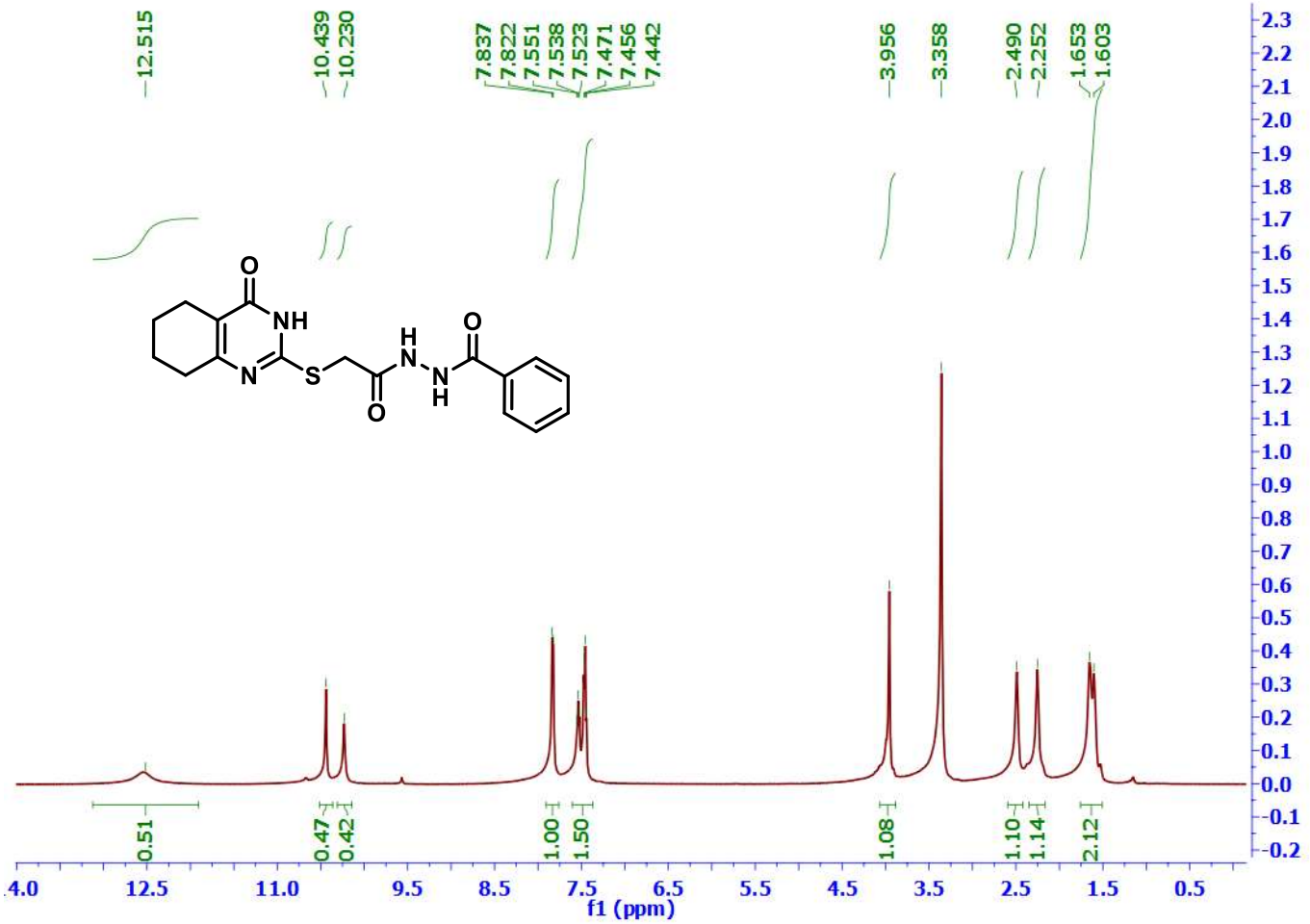

Fig. 25. ^{13}C (125 MHz) NMR spectrum of **18a** in DMSO-d_6

N'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18a**)

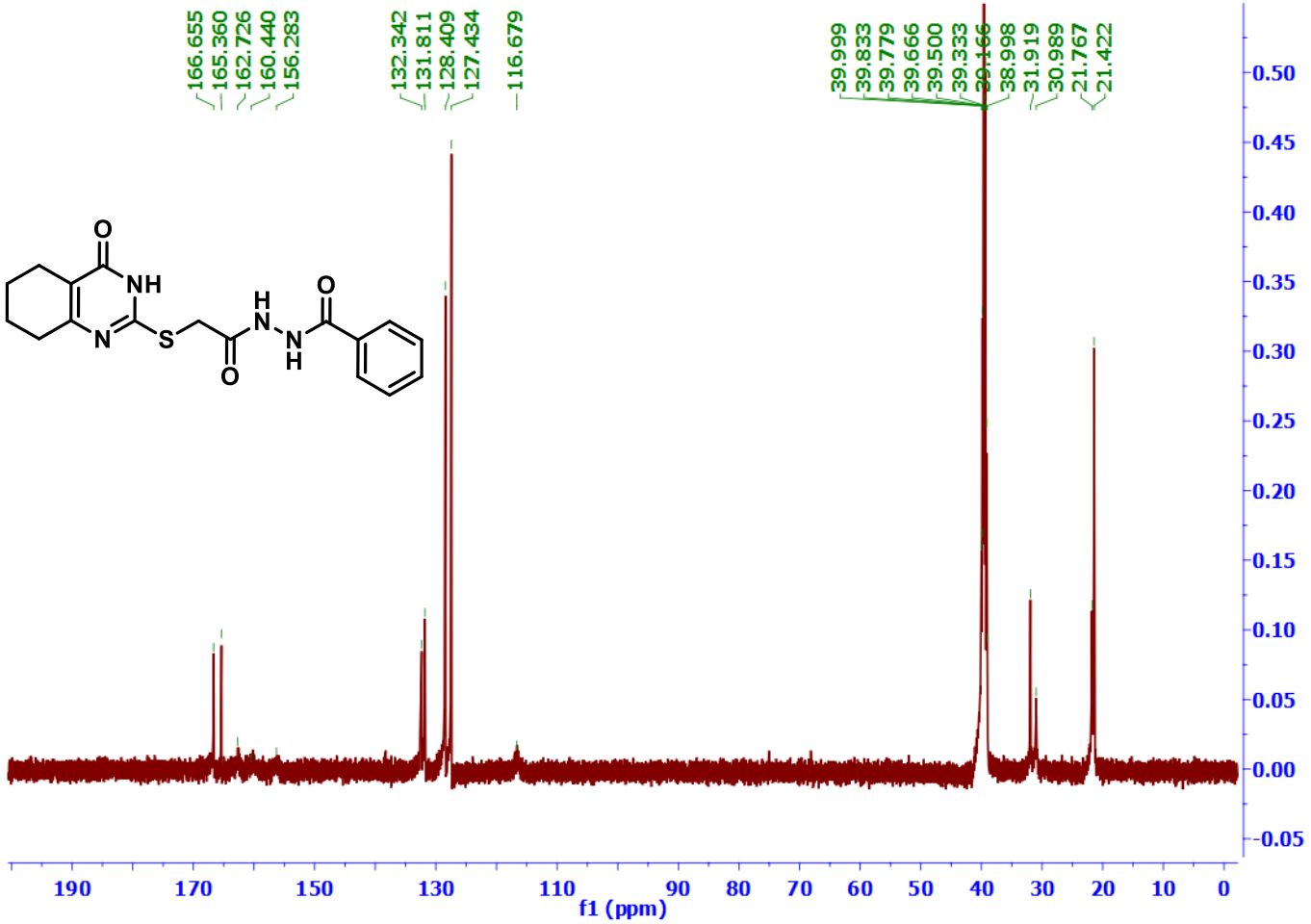

Fig. 26. ^{13}C (125 MHz) NMR spectrum of **18a** in DMSO-d_6

4-Methyl-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18b**)

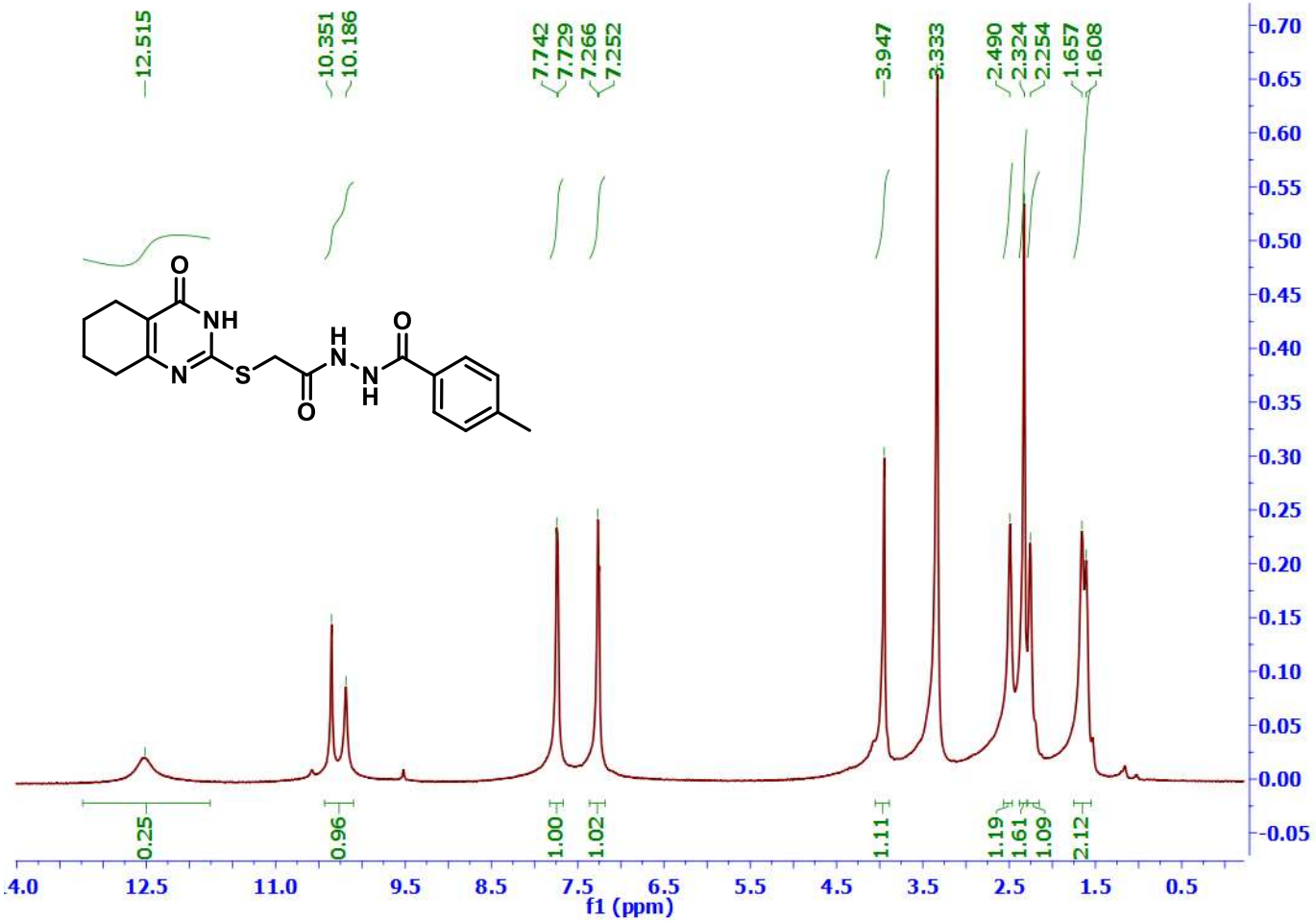

Fig. 27. ^{1}H (500 MHz) NMR spectrum of **18b** in DMSO-d_6

4-Methyl-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18b**)

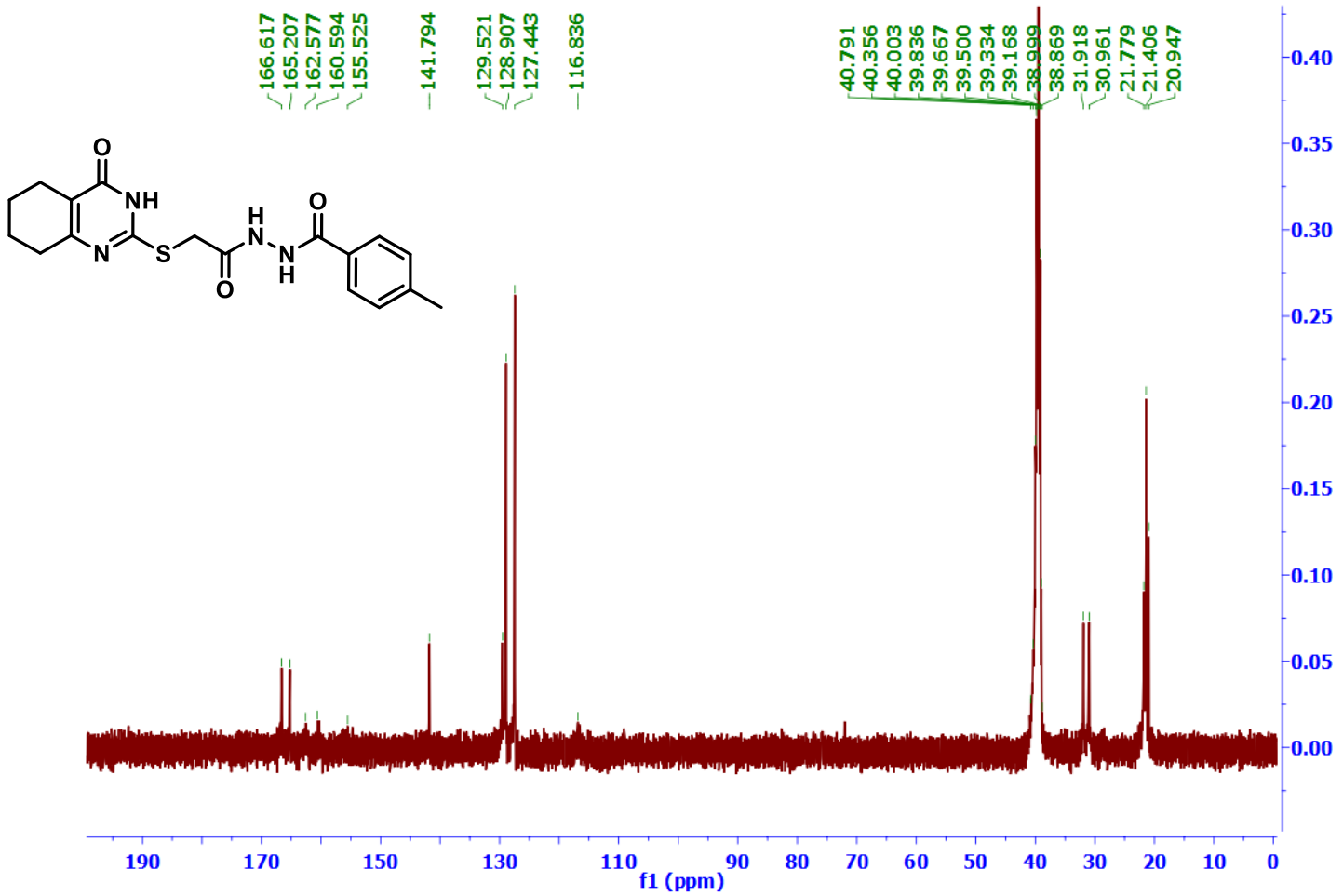

Fig. 28. ^{13}C (125 MHz) NMR spectrum of **18b** in DMSO-d_6

4-Nitro-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18c**)

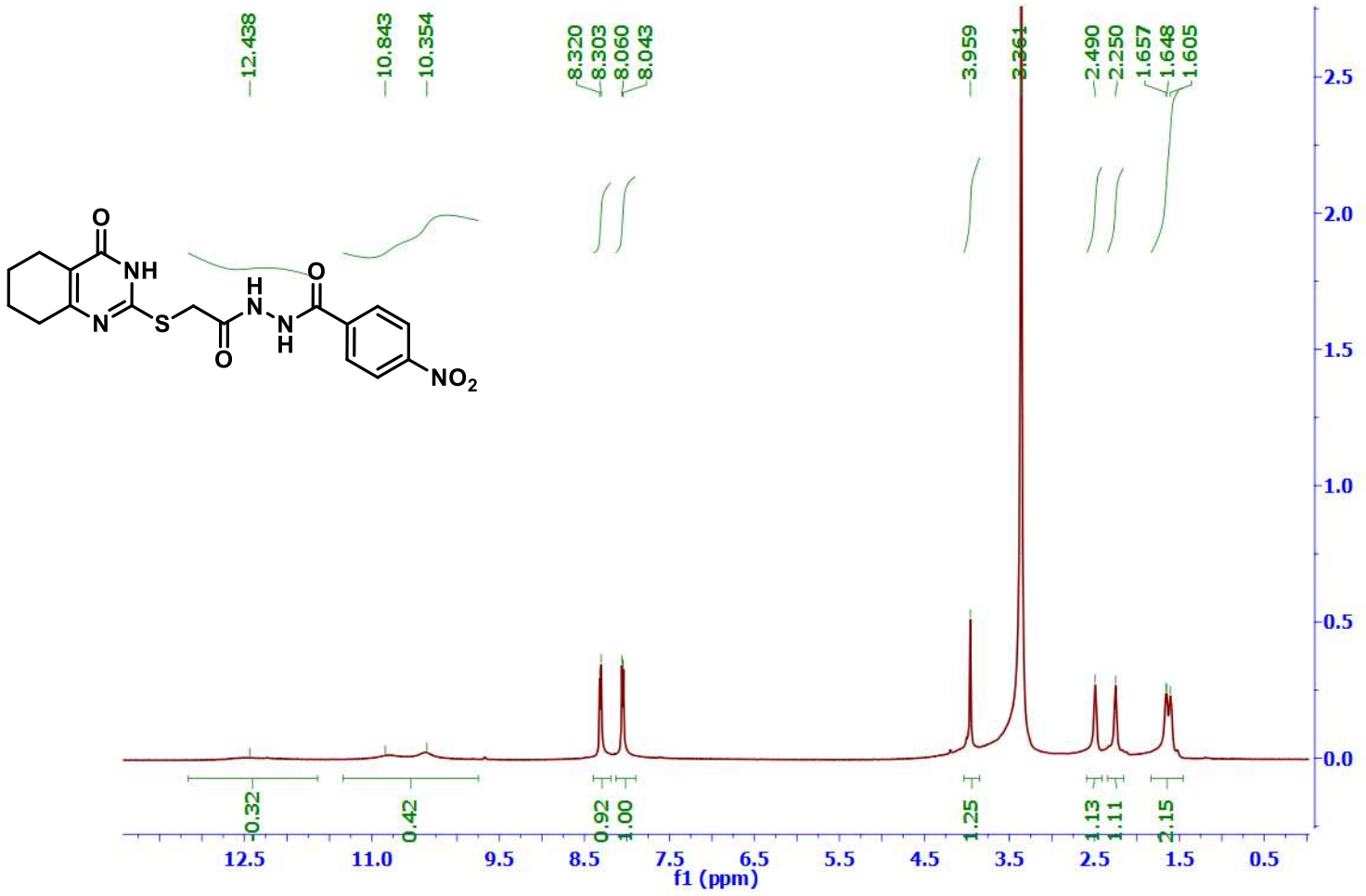

Fig. 29. ^{1}H (500 MHz) NMR spectrum of **18c** in DMSO-d_6

4-Nitro-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18c**)

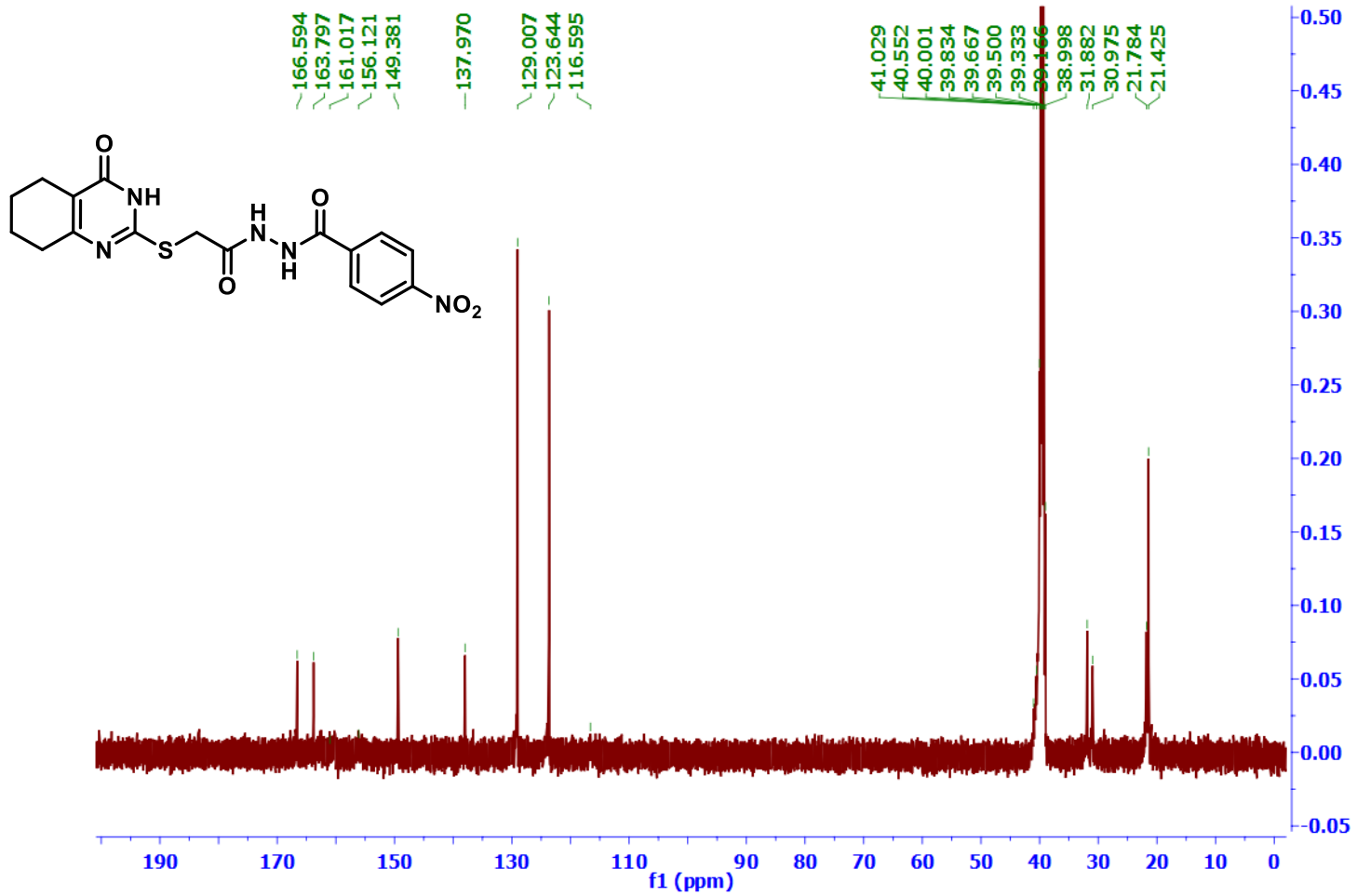

Fig. 30. ^{13}C (125 MHz) NMR spectrum of **18c** in DMSO-d_6

2-Methoxy-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18d**)

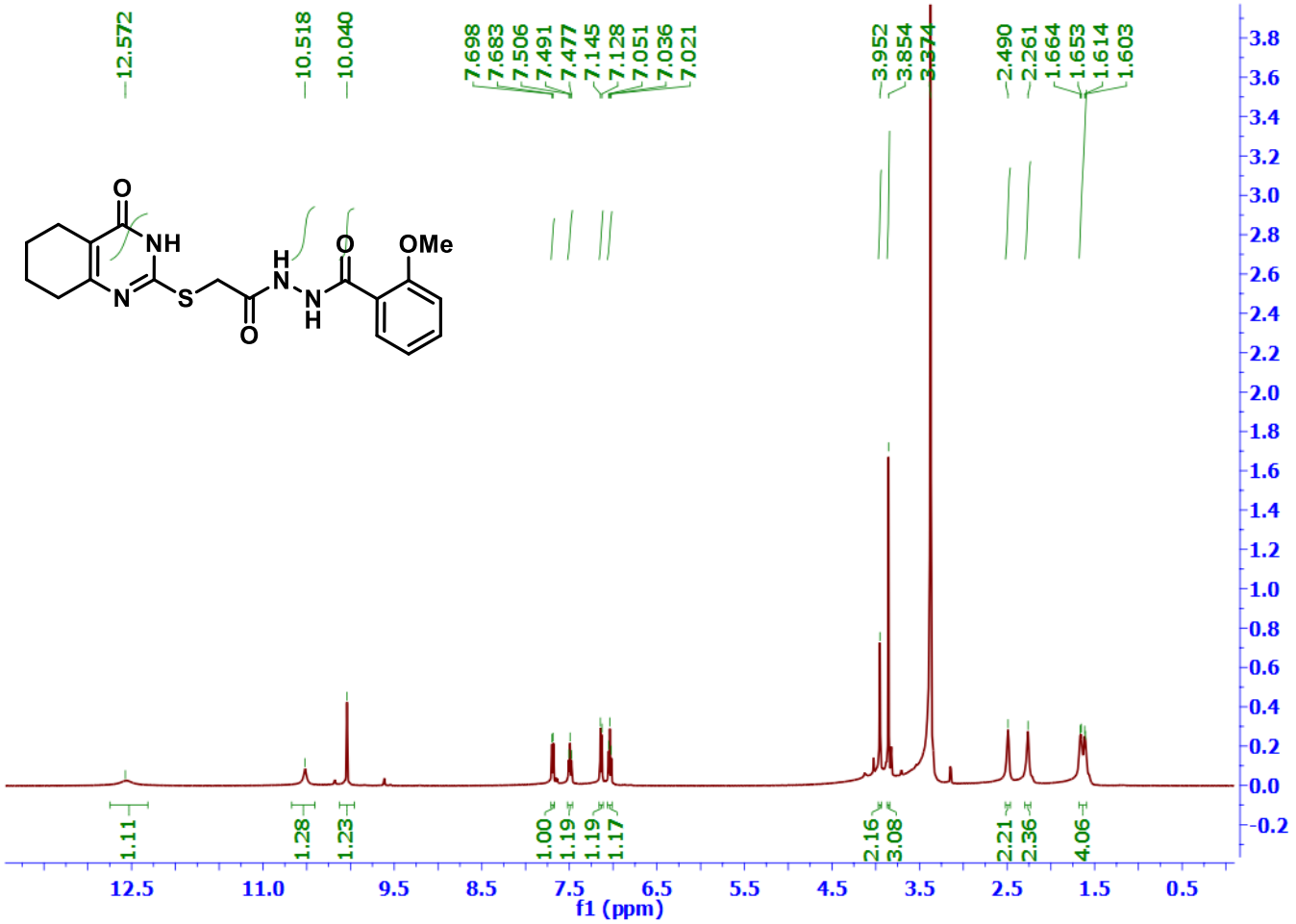

Fig. 31. ^{1}H (500 MHz) NMR spectrum of **18d** in DMSO-d_6

2-Methoxy-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18d**)

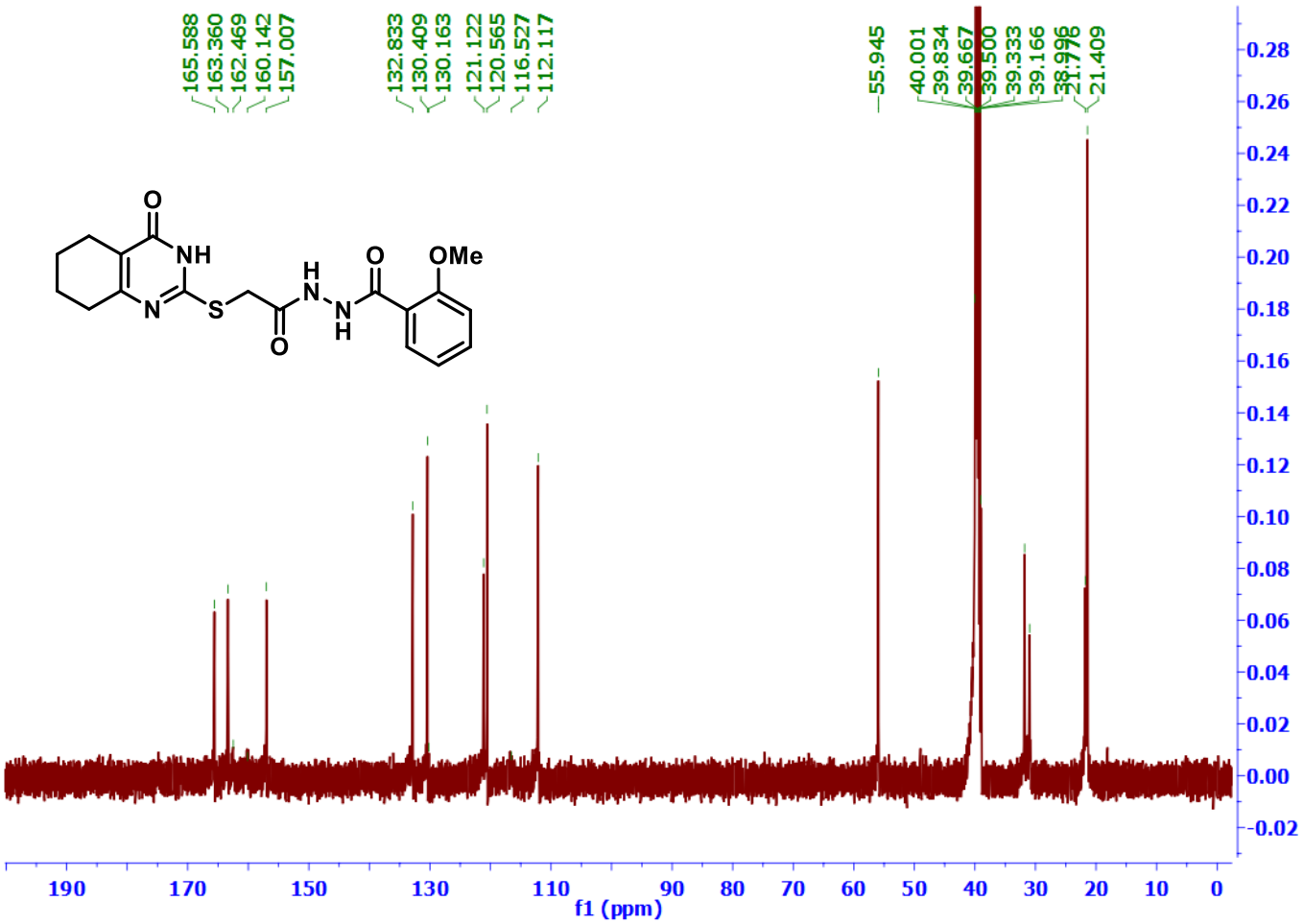

Fig. 32. ^{13}C (125 MHz) NMR spectrum of **18d** in DMSO-d_6

2-Chloro-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18e)**

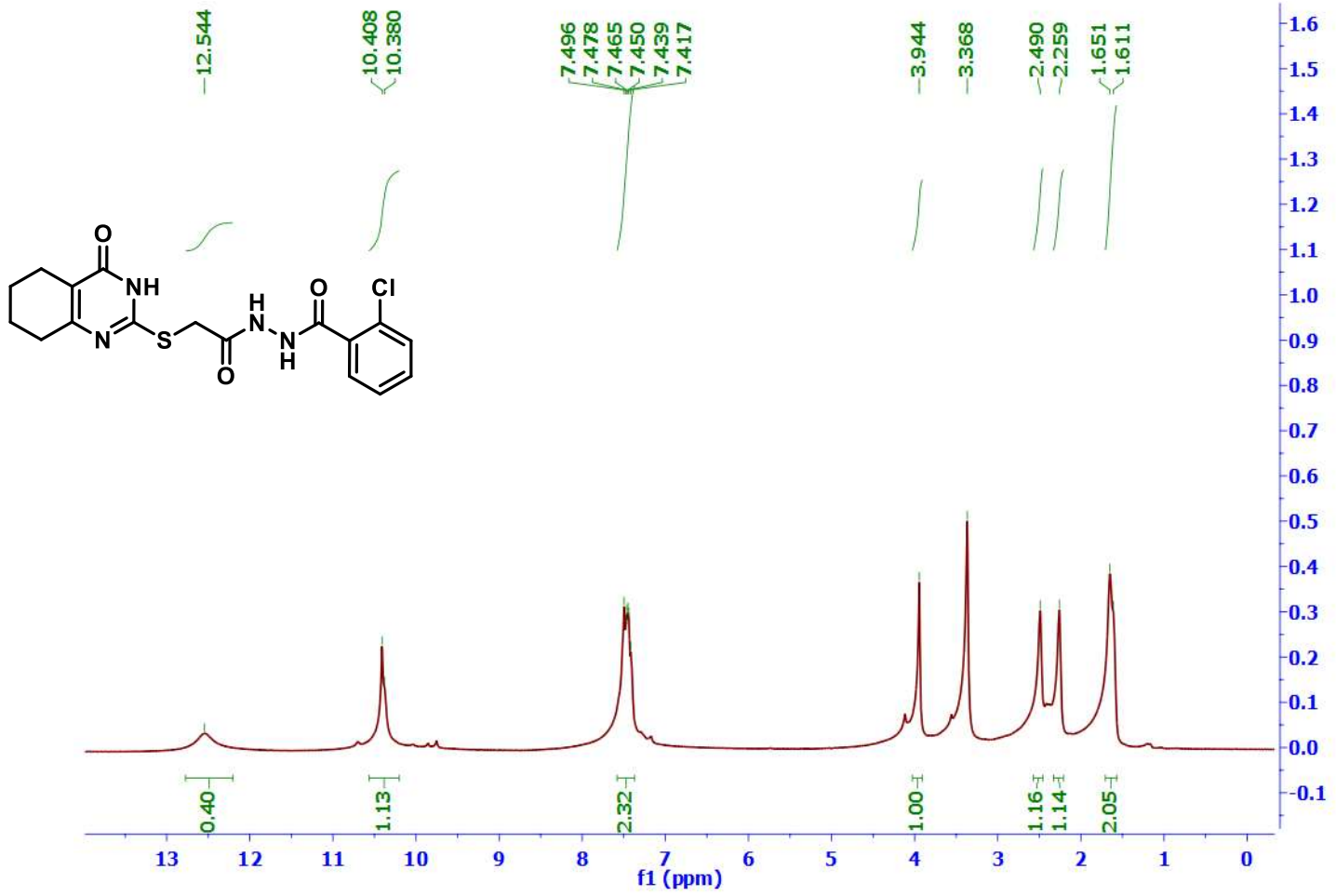

Fig. 33. ^{1}H (500 MHz) NMR spectrum of **18e** in DMSO-d_6

2-Chloro-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18e)**

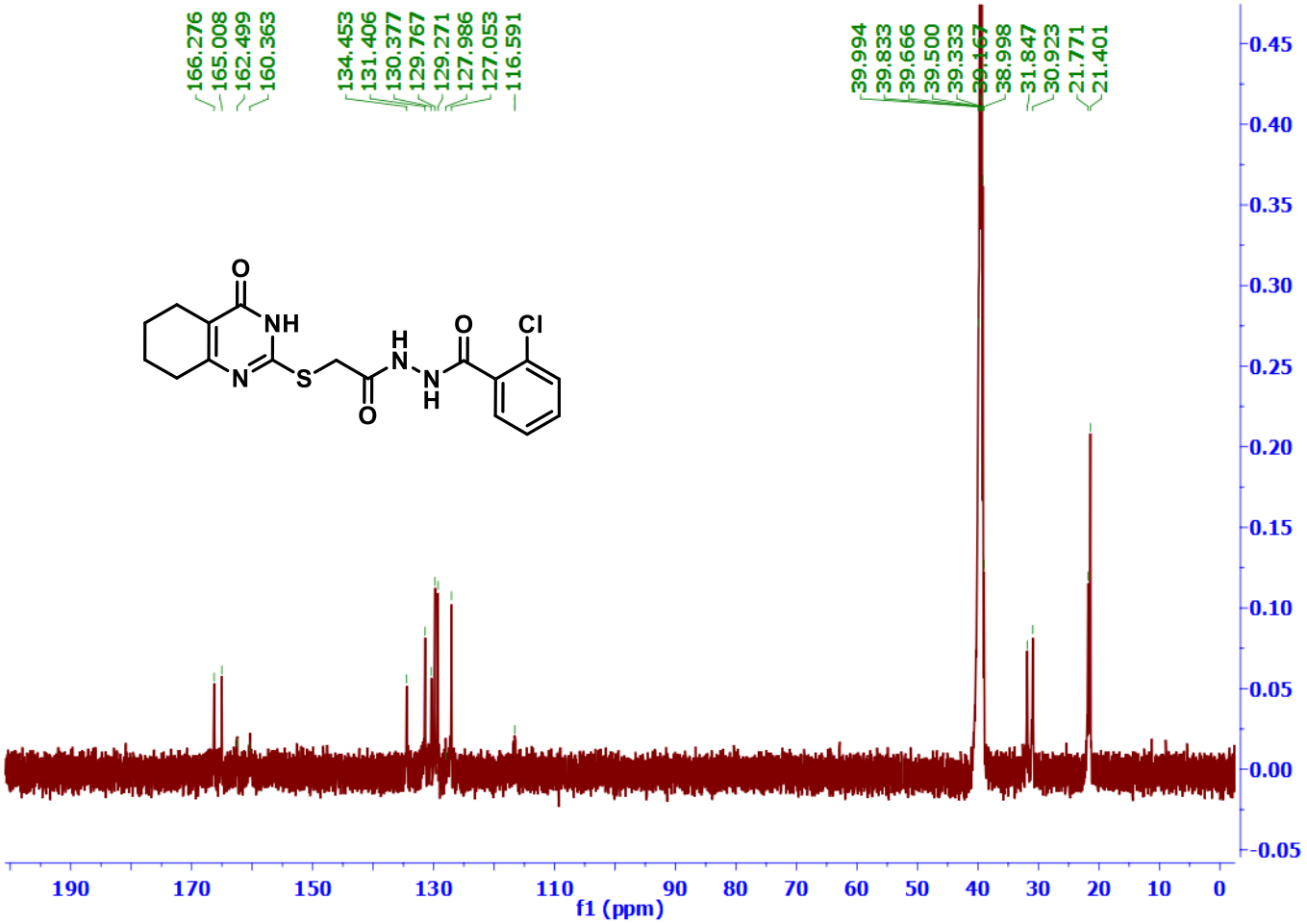

Fig. 34. ^{13}C (125 MHz) NMR spectrum of **18e** in DMSO-d_6

4-Chloro-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18f**)

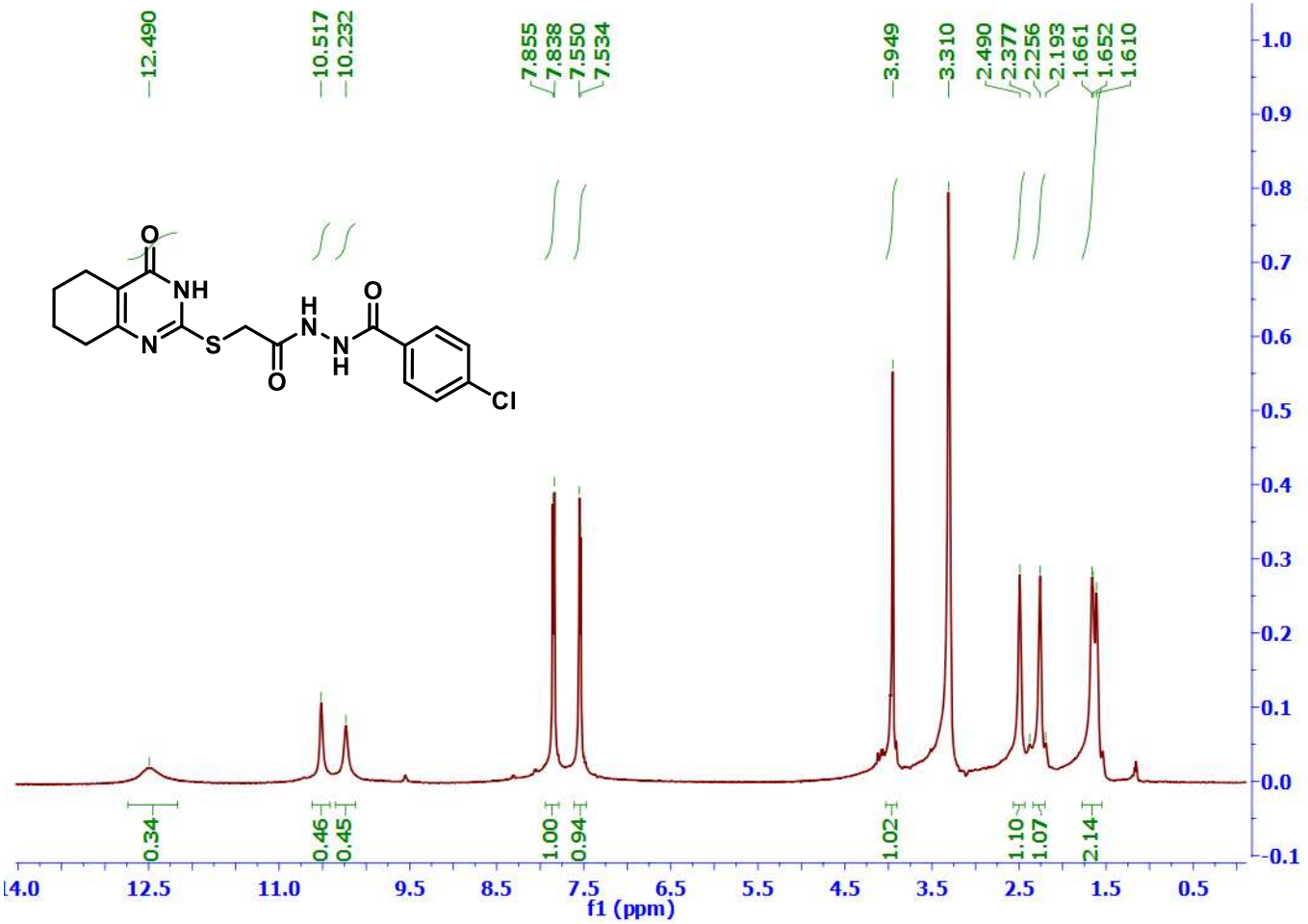

Fig. 35. ^{1}H (500 MHz) NMR spectrum of **18f** in DMSO-d_6

4-Chloro-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18f**)

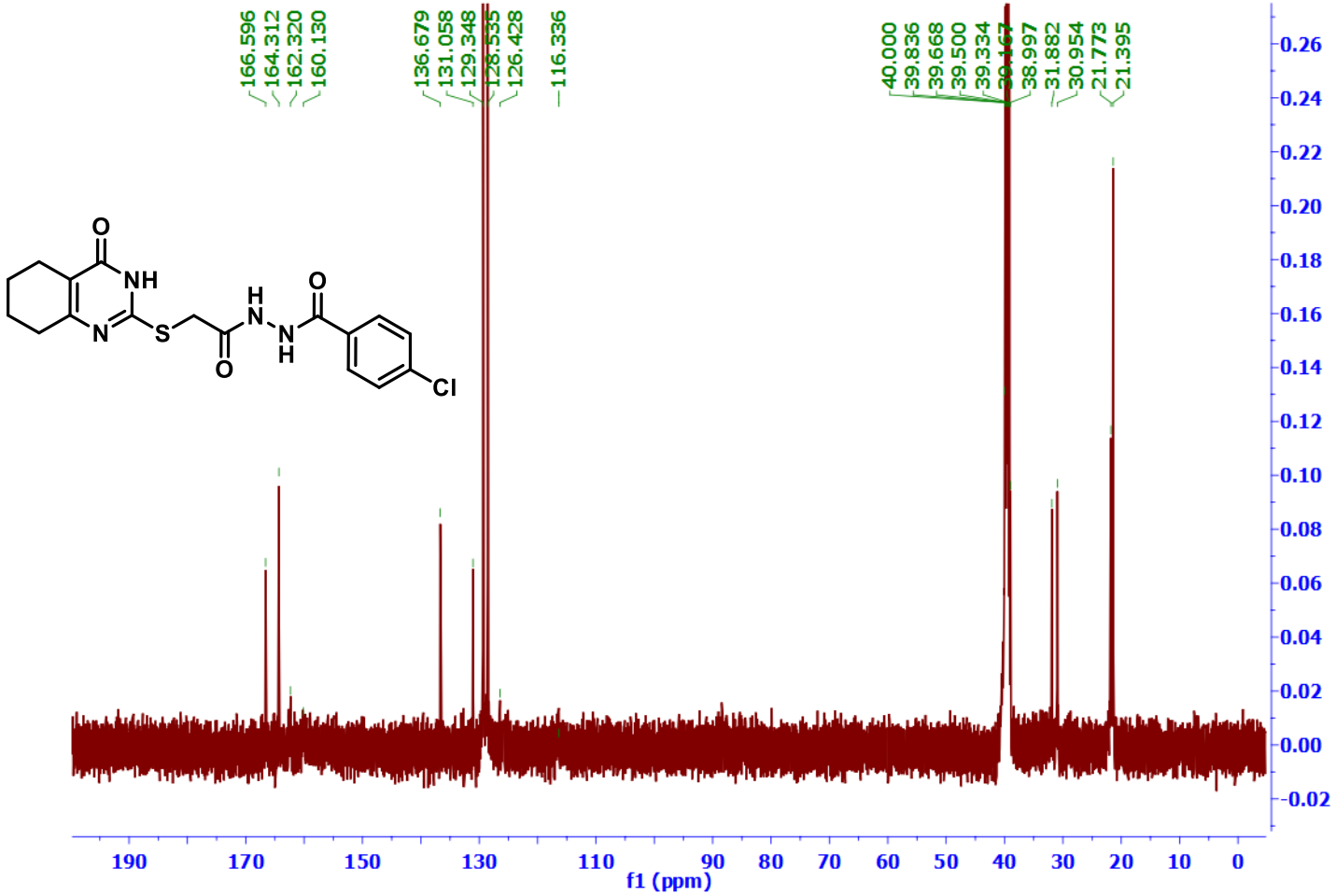

Fig. 36 ^{13}C (125 MHz) NMR spectrum of **18f** in DMSO-d_6

2-Bromo-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18g**)

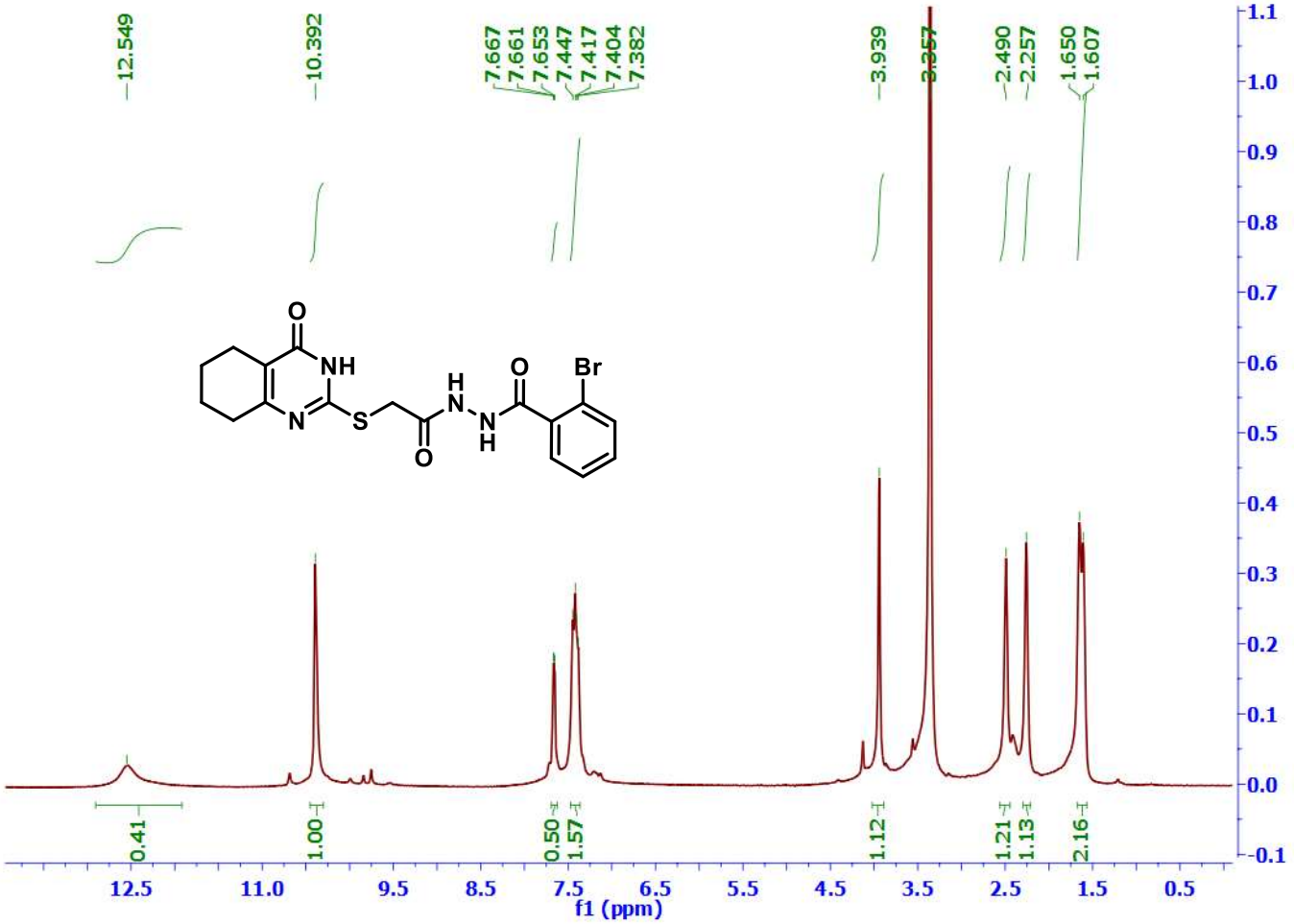

Fig. 37. ^{1}H (500 MHz) NMR spectrum of **18g** in DMSO-d_6

2-Bromo-*N*'-(2-((4-oxo-3,4,5,6,7,8-hexahydroquinazolin-2-yl)thio)acetyl)benzohydrazide (**18g**)

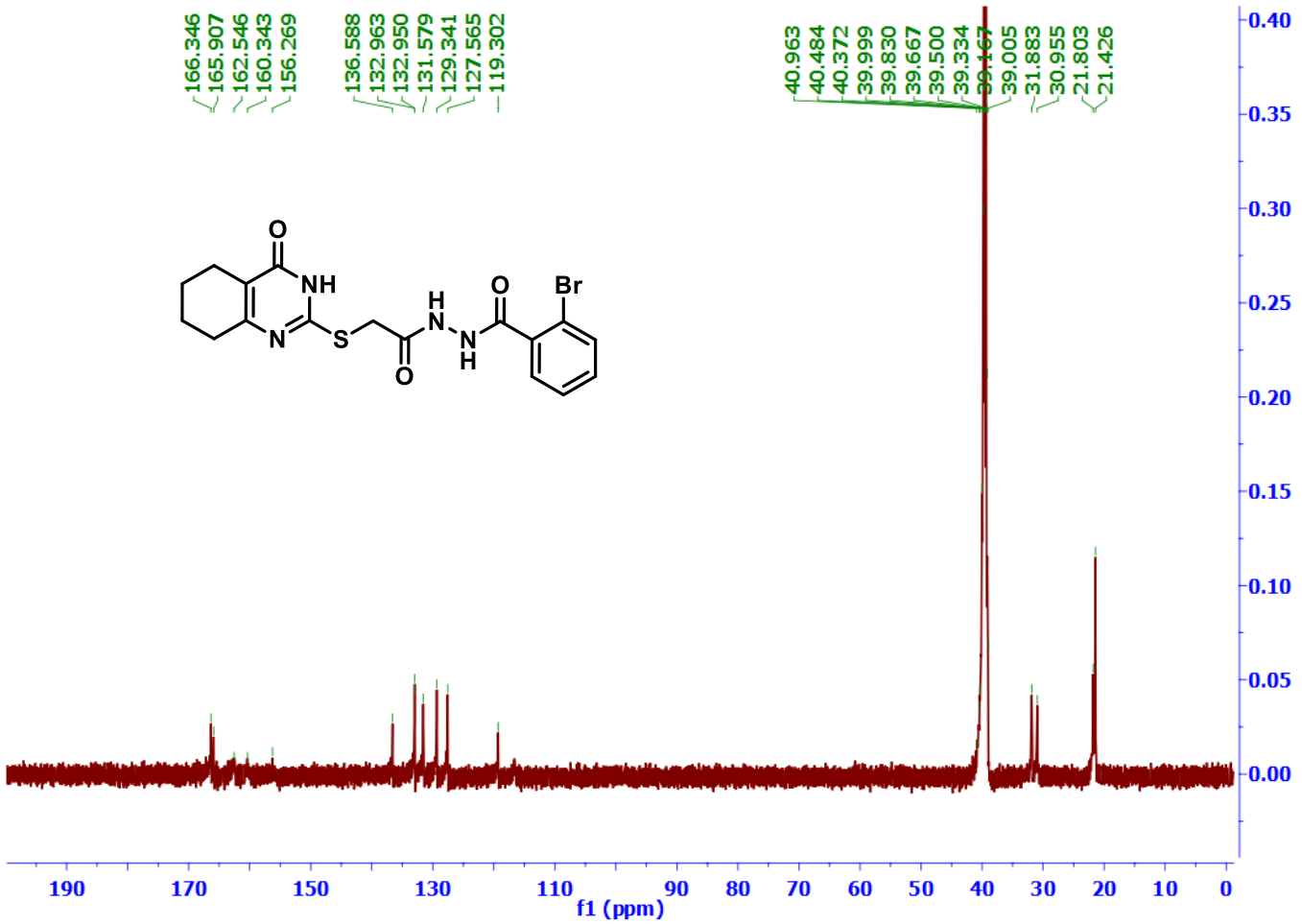

Fig. 38. ^{13}C (125 MHz) NMR spectrum of **18g** in DMSO-d_6

2. Dose-inhibition curves of the synthesized derivatives against NRC-03-nhCoV and Vero-E6 cells (Fig. 39)

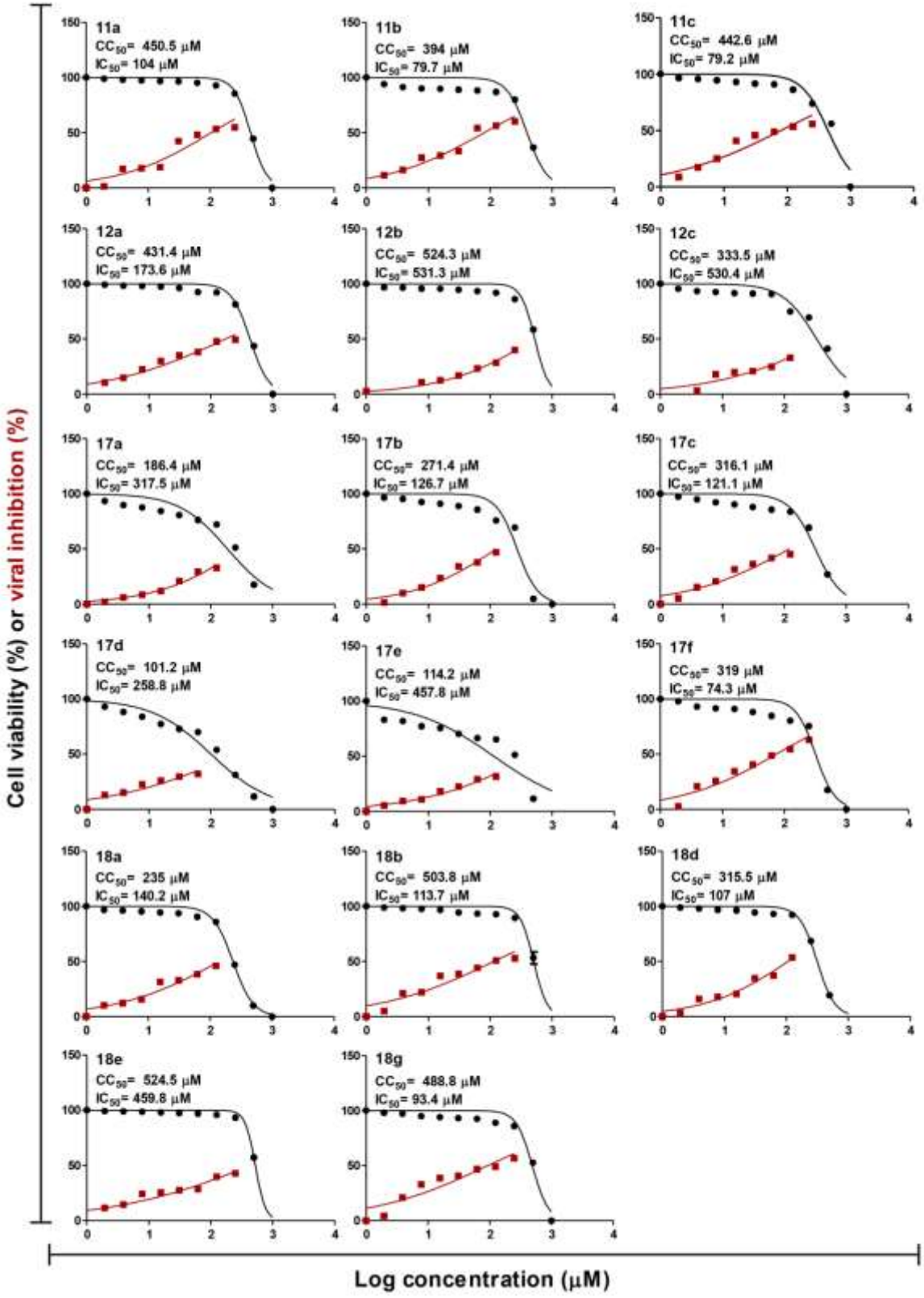

Fig. 39. Dose-inhibition curves of the synthesized derivatives against NRC-03-nhCoV and Vero-E6 cells

3. 2D diagrams of the synthesized compounds showing their interactions in M^{pro} active site (PDB ID: 7LTJ) (Fig. 40-59).

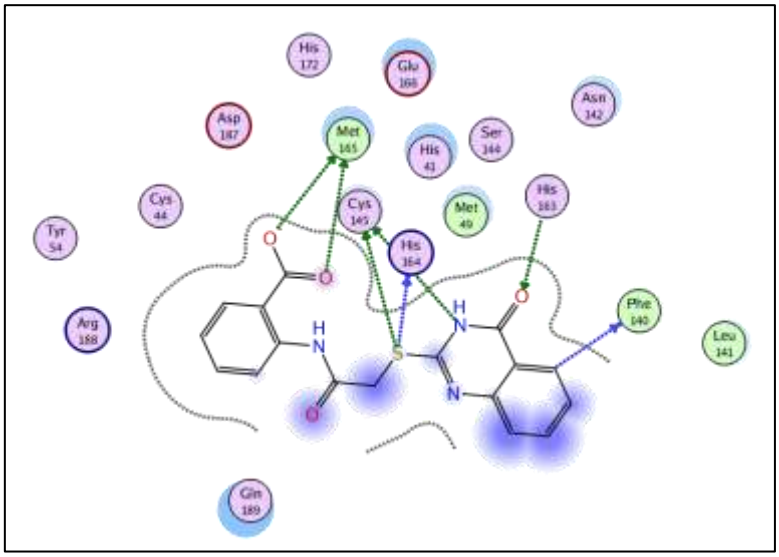

Fig. 40. 2D diagram **11a** showing its interaction in M^{pro} active site

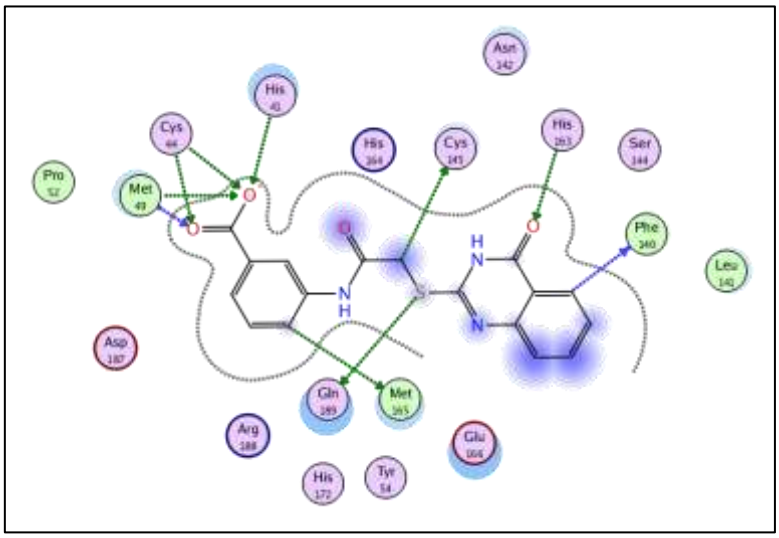

Fig. 41. 2D diagram **11b** showing its interaction in M^{pro} active site

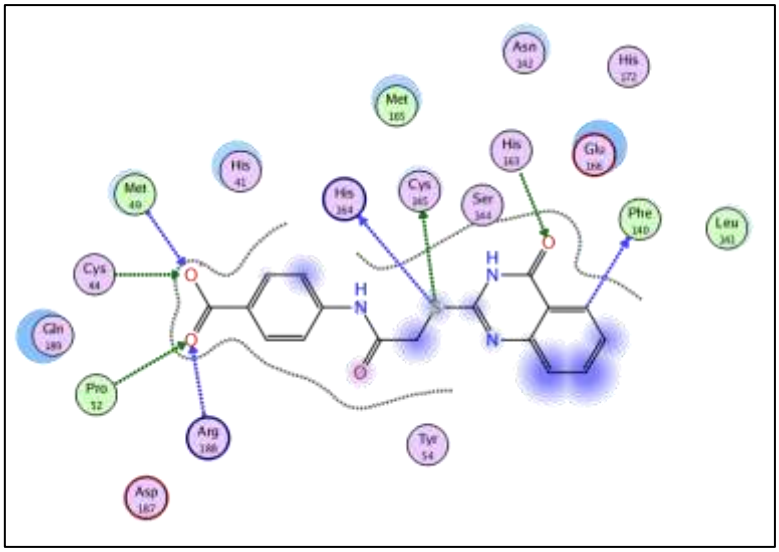

Fig. 42. 2D diagram **11c** showing its interaction in M^{pro} active site

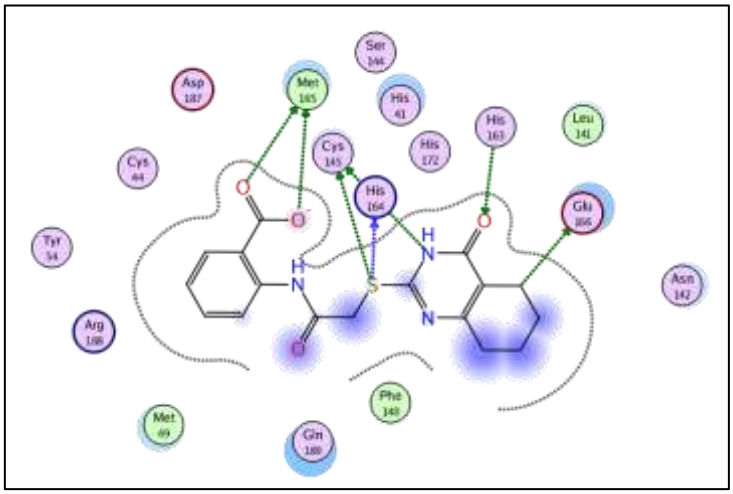

Fig. 43. 2D diagram **12a** showing its interaction in M^{pro} active site

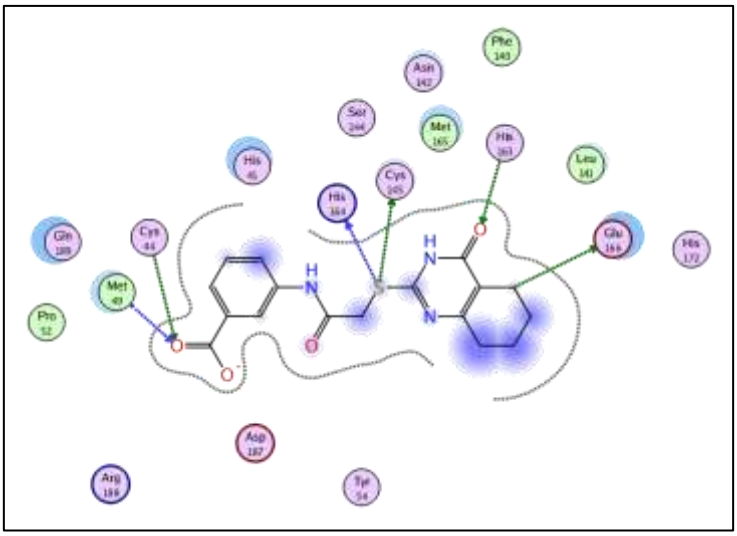

Fig. 44. 2D diagram **12b** showing its interaction in M^{pro} active site

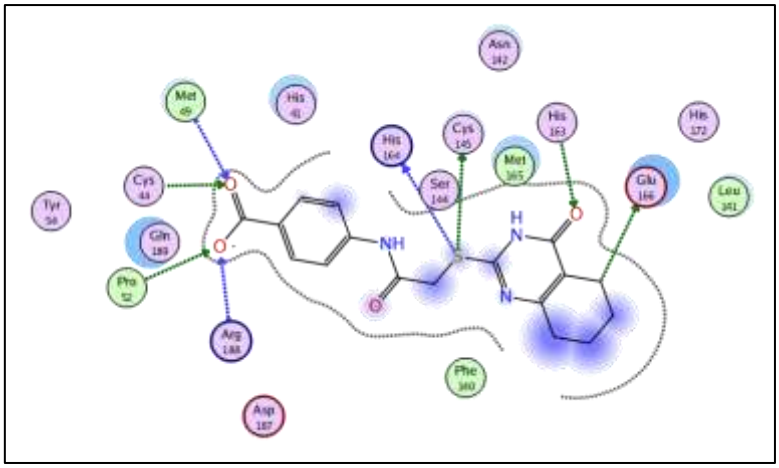

Fig. 45. 2D diagram **12c** showing its interaction in M^{pro} active site

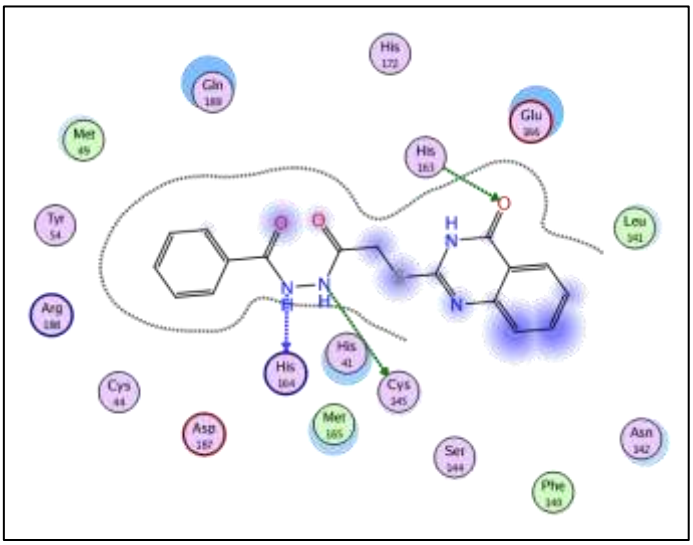

Fig. 46. 2D diagram **17a** showing its interaction in M^{pro} active site

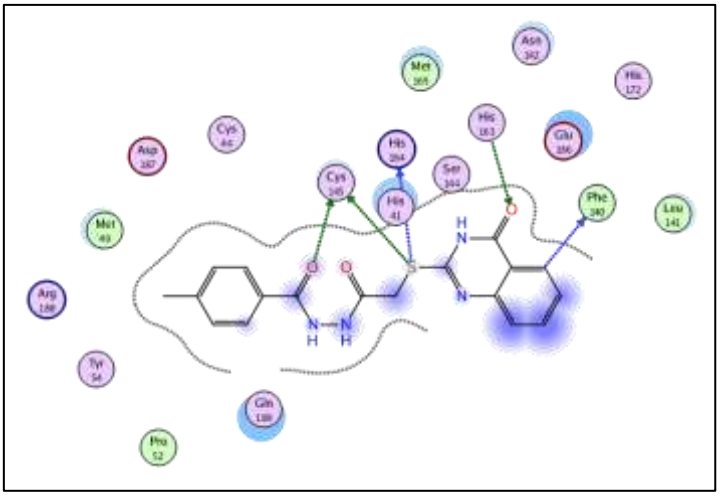

Fig. 47. 2D diagram **17b** showing its interaction in M^{pro} active site

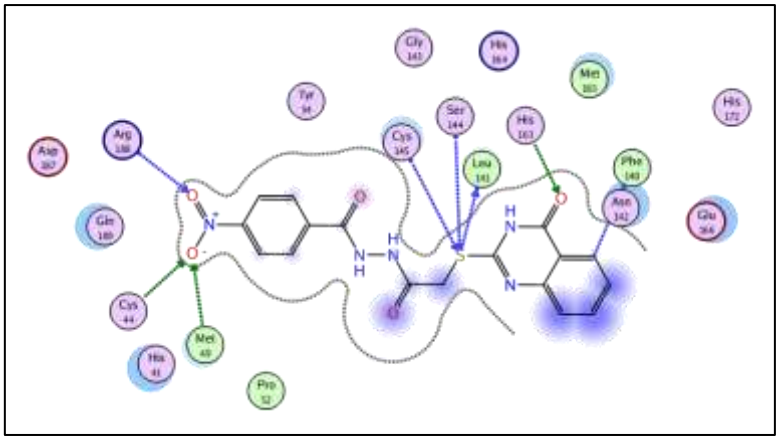

Fig. 48. 2D diagram **17c** showing its interaction in M^{pro} active site

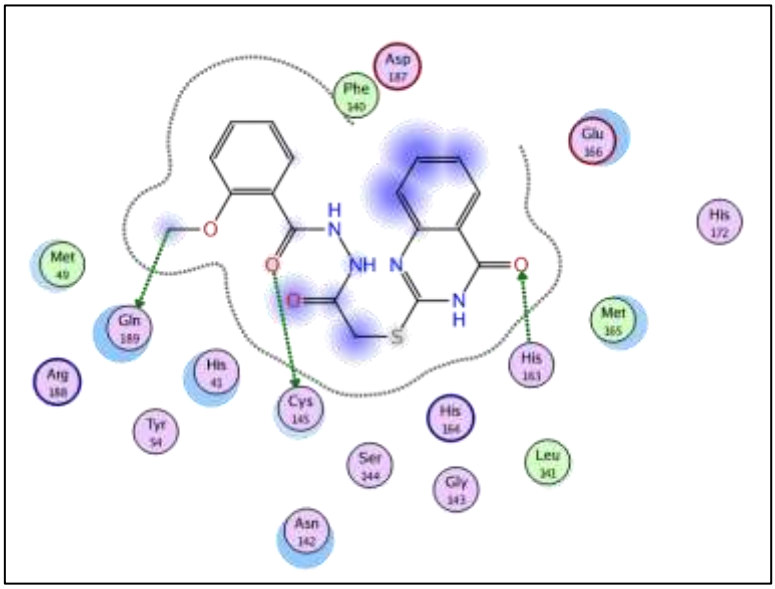

Fig. 49. 2D diagram **17d** showing its interaction in M^{pro} active site

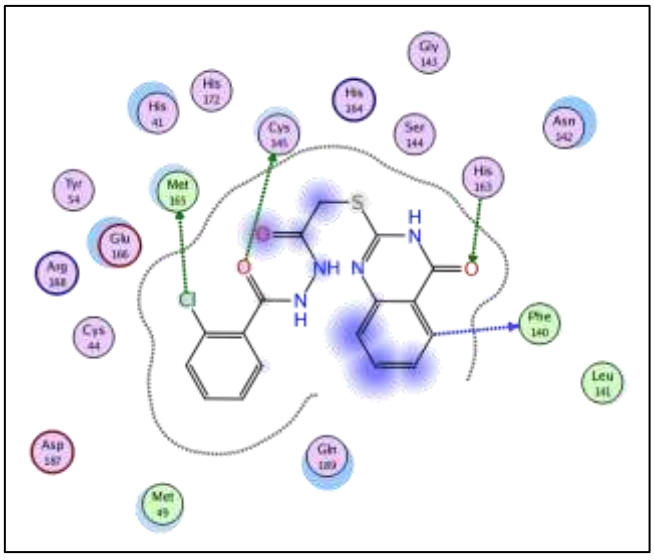

Fig. 50. 2D diagram **17e** showing its interaction in M^{pro} active site

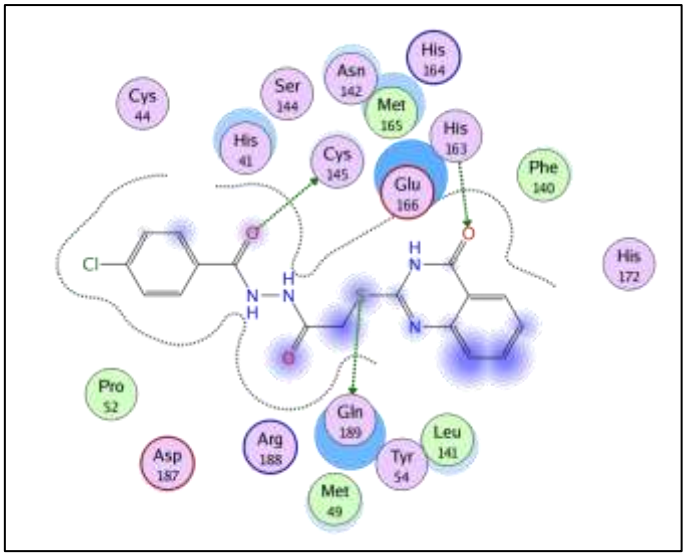

Fig. 51. 2D diagram **17f** showing its interaction in M^{pro} active site

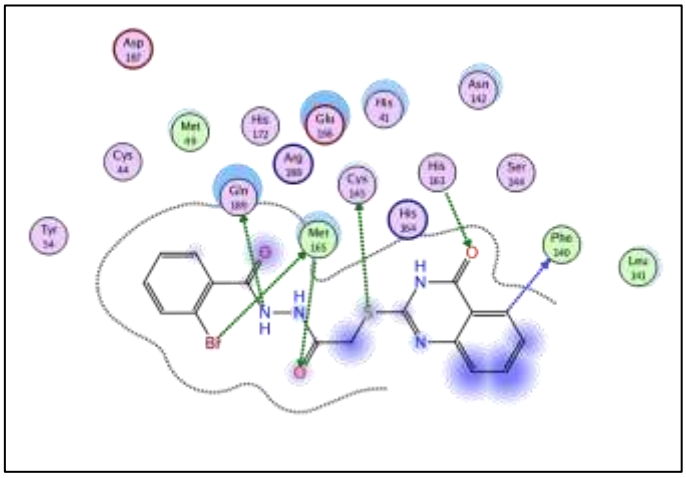

Fig. 52. 2D diagram **17g** showing its interaction in M^{pro} active site

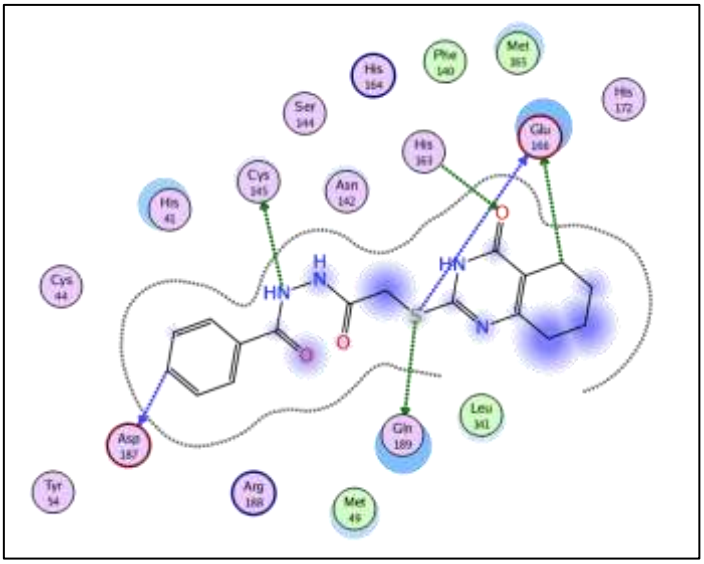

Fig. 53. 2D diagram **18a** showing its interaction in M^{pro} active site

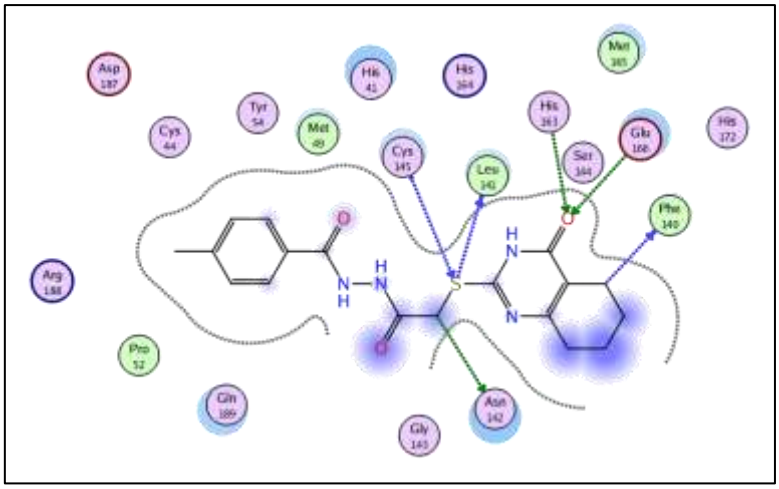

Fig. 54. 2D diagram **18b** showing its interaction in M^{pro} active site

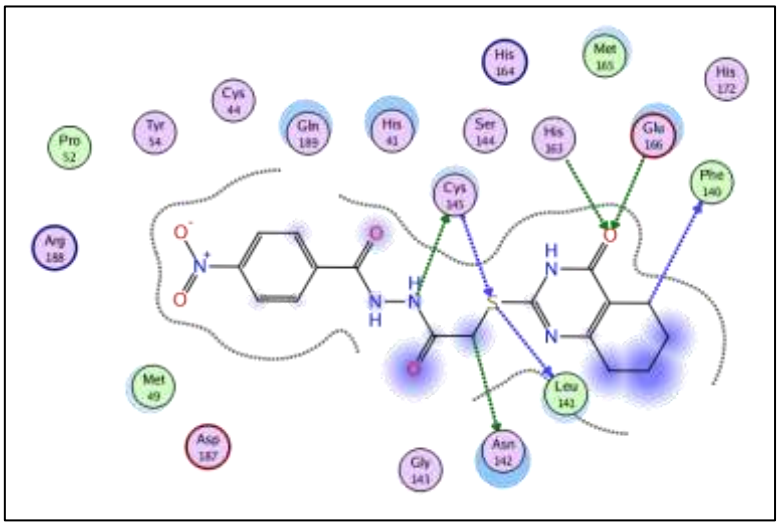

Fig. 55. 2D diagram **18c** showing its interaction in M^{pro} active site

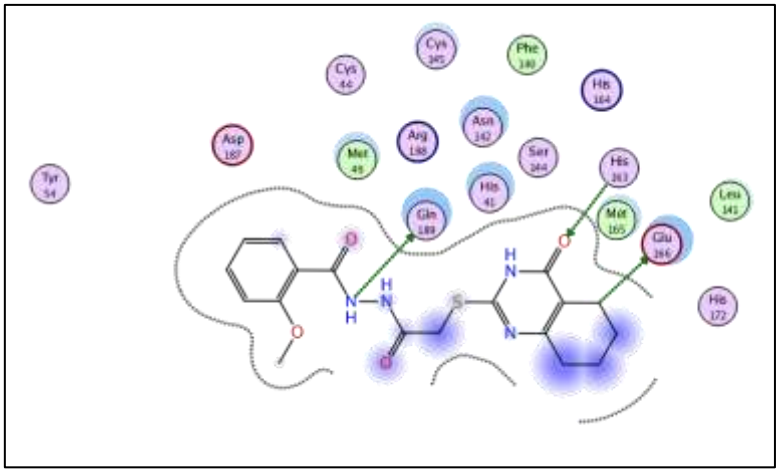

Fig. 56. 2D diagram **18d** showing its interaction in M^{pro} active site

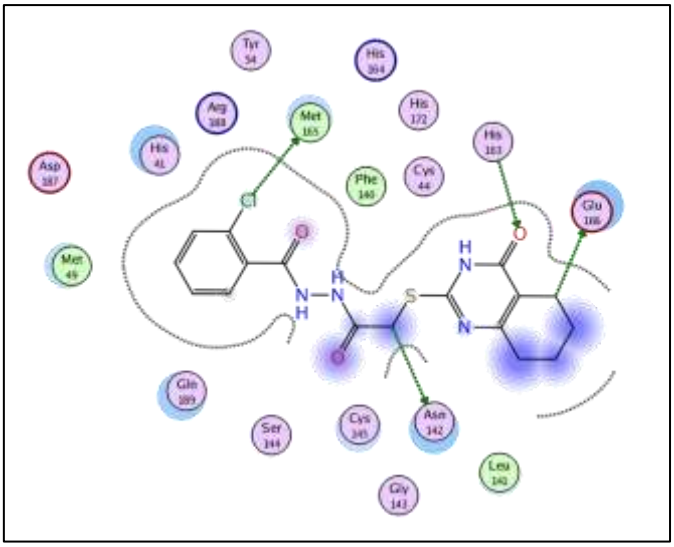

Fig. 57. 2D diagram **18e** showing its interaction in M^{pro} active site

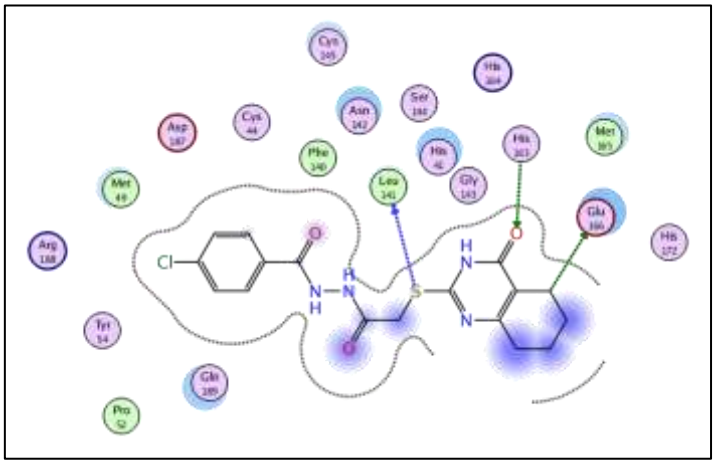

Fig. 58. 2D diagram **18f** showing its interaction in M^{pro} active site

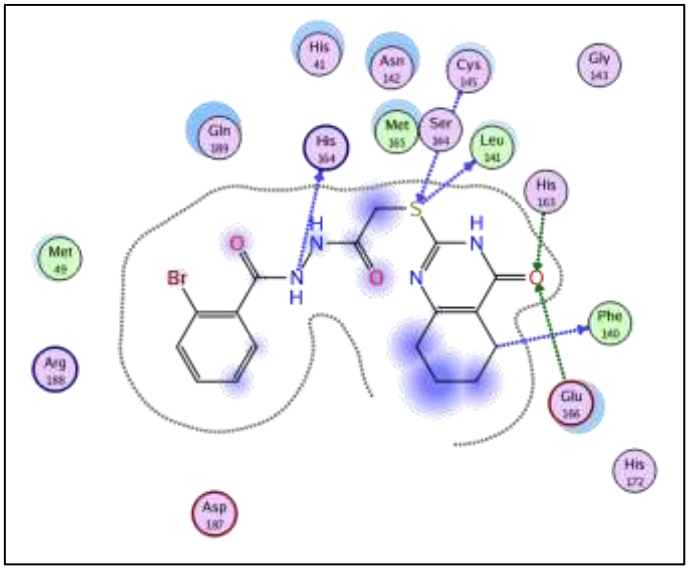

Fig. 59. 2D diagram **18g** showing its interaction in M^{pro} active site