

SUPPLEMENTARY DATA

Cinnamoyl-*N*-acylhydrazone-donepezil hybrids: synthesis and evaluation of novel multifunctional ligands against neurodegenerative diseases

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All compounds were characterized by IR, NMR and HRMS techniques, also the purity was determined by HPLC (**Fig. 37**). The spectra of the synthesized compounds as well as their intermediates are shown below.

Spectrum data of compounds intermediates 6a-j

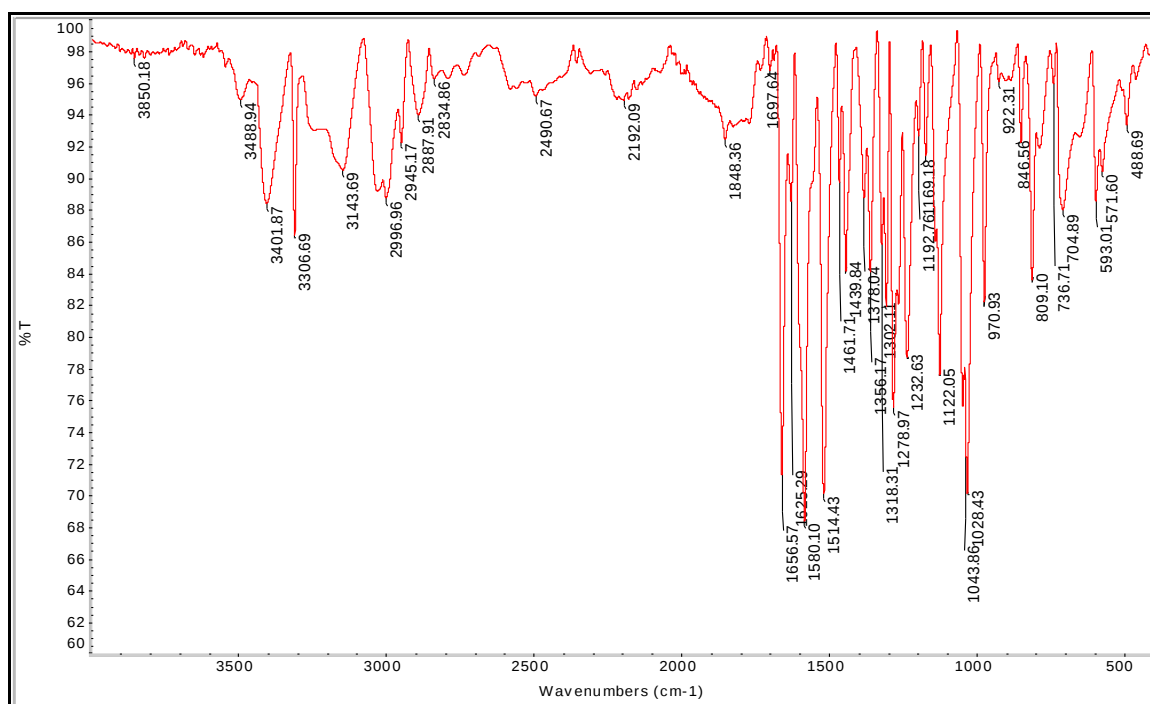


Figure 1. Absorption spectra in the infrared region of (*E*)-3-(4-hydroxy-3-methylphenyl)acrylohydrazide (**6a**) (ATR).

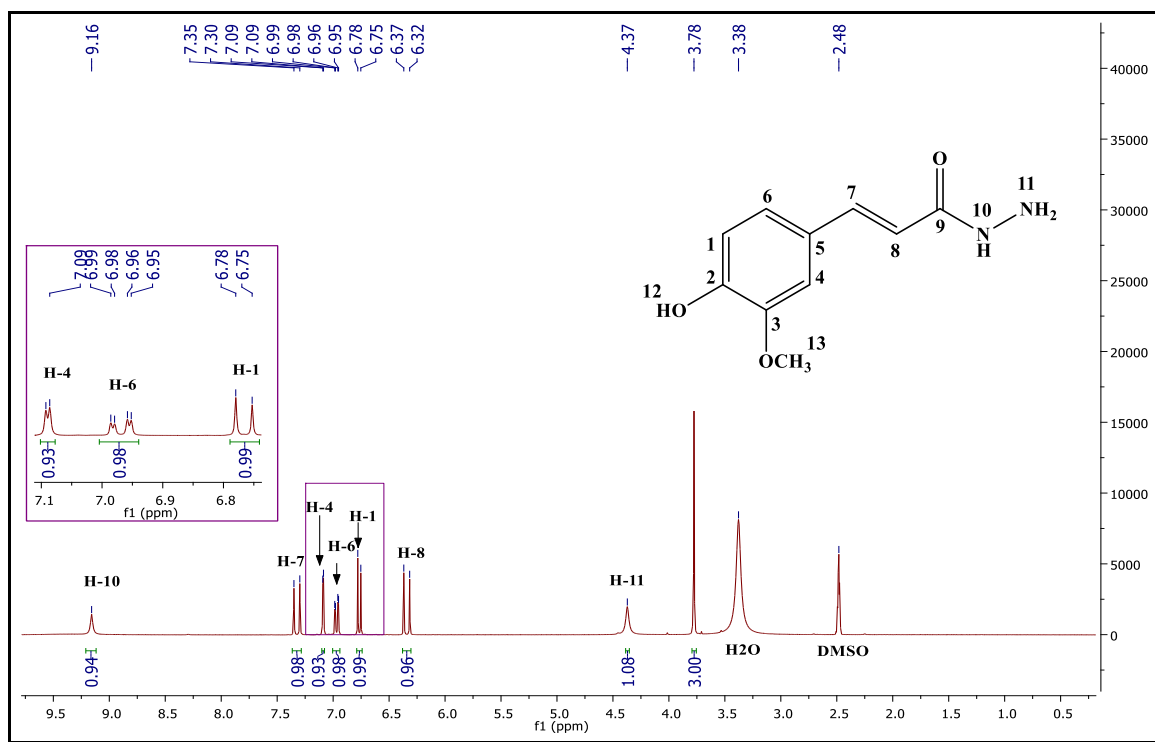


Figure 2. ^1H NMR spectra of (*E*)-3-(4-hydroxy-3-methylphenyl)acrylohydrazide (**6a**) (300 MHz, $\text{DMSO}-d_6$).

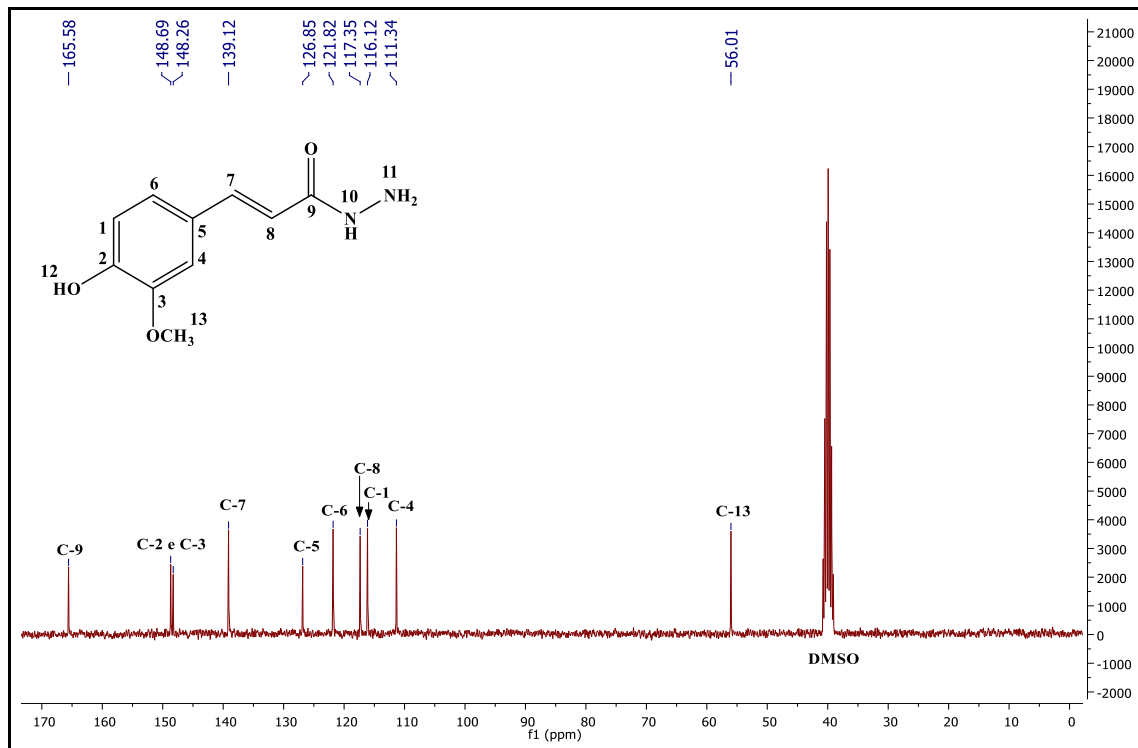


Figure 3. ^{13}C NMR spectra of (*E*)-3-(4-hydroxy-3-methylphenyl)acrylohydrazide (**6a**) (75 MHz, $\text{DMSO}-d_6$).

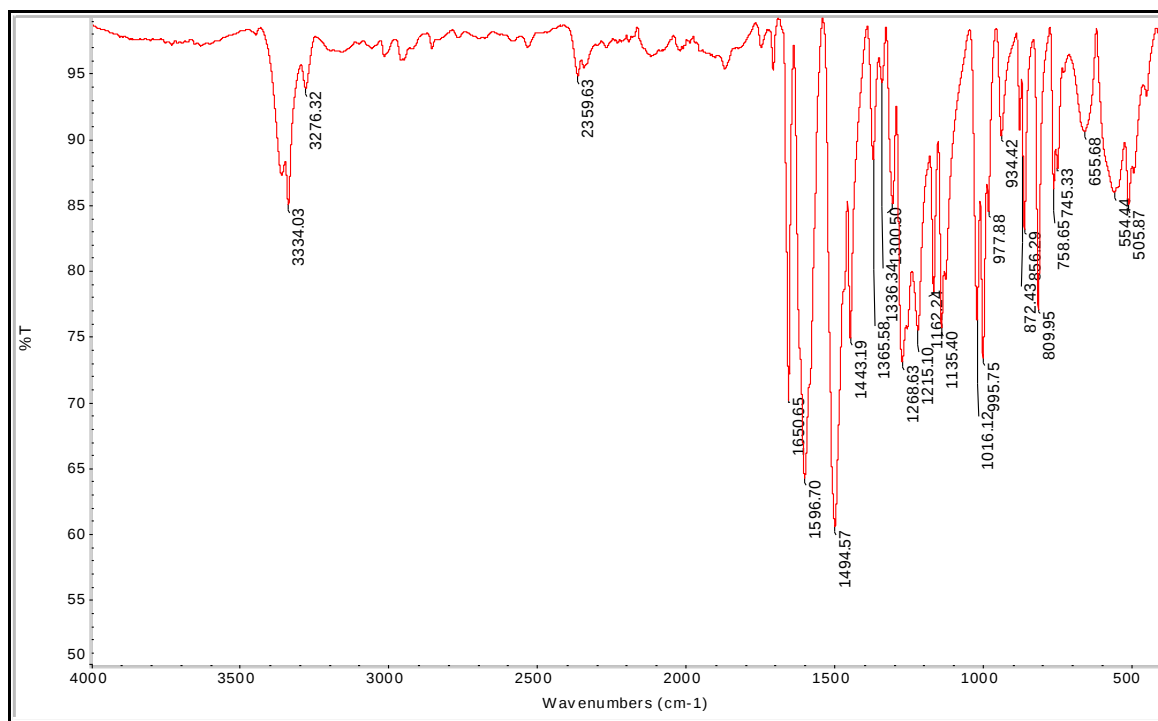


Figure 4. Absorption spectra in the infrared region of (*E*)-3-(3-hydroxy-4-methoxyphenyl)acrylohydrazide (**6b**) (ATR).

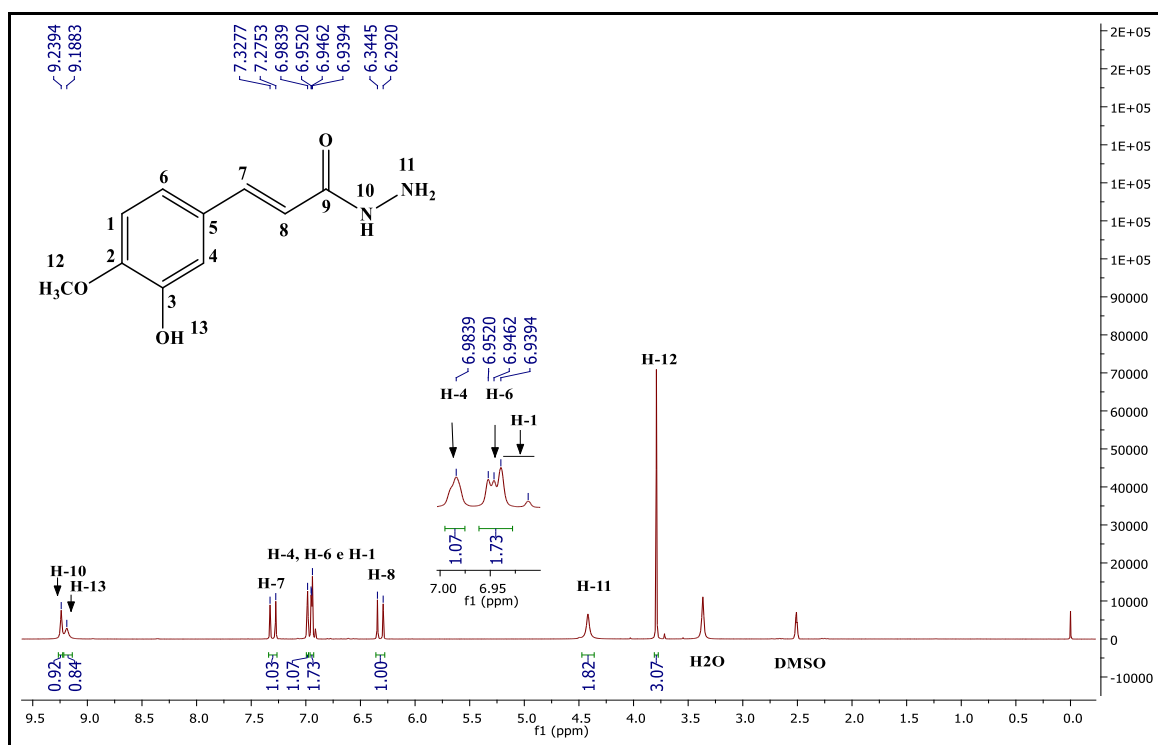


Figure 5. ¹H NMR spectra of (*E*)-3-(3-hydroxy-4-methoxyphenyl)acrylohydrazide (**6b**) (300 MHz, DMSO-*d*₆).

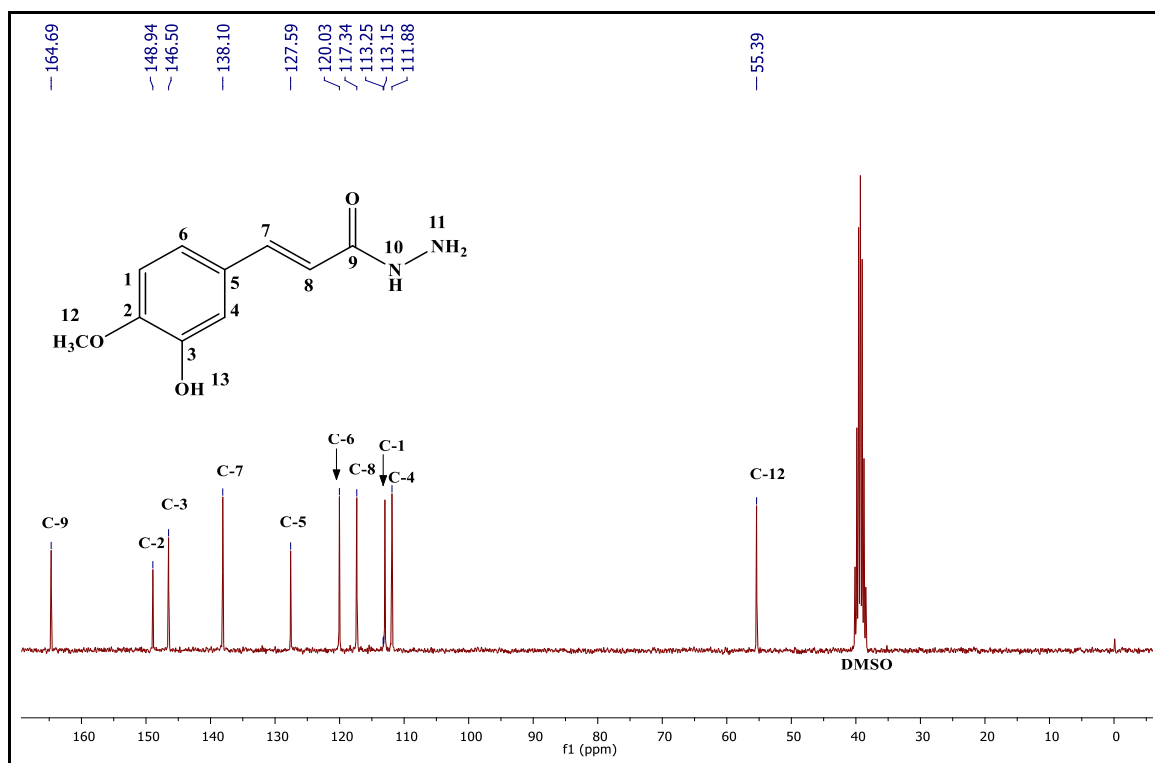


Figure 6. ¹³C NMR spectra of (*E*)-3-(3-hydroxy-4-methoxyphenyl)acrylohydrazide (**6b**) (75 MHz, DMSO-*d*₆).

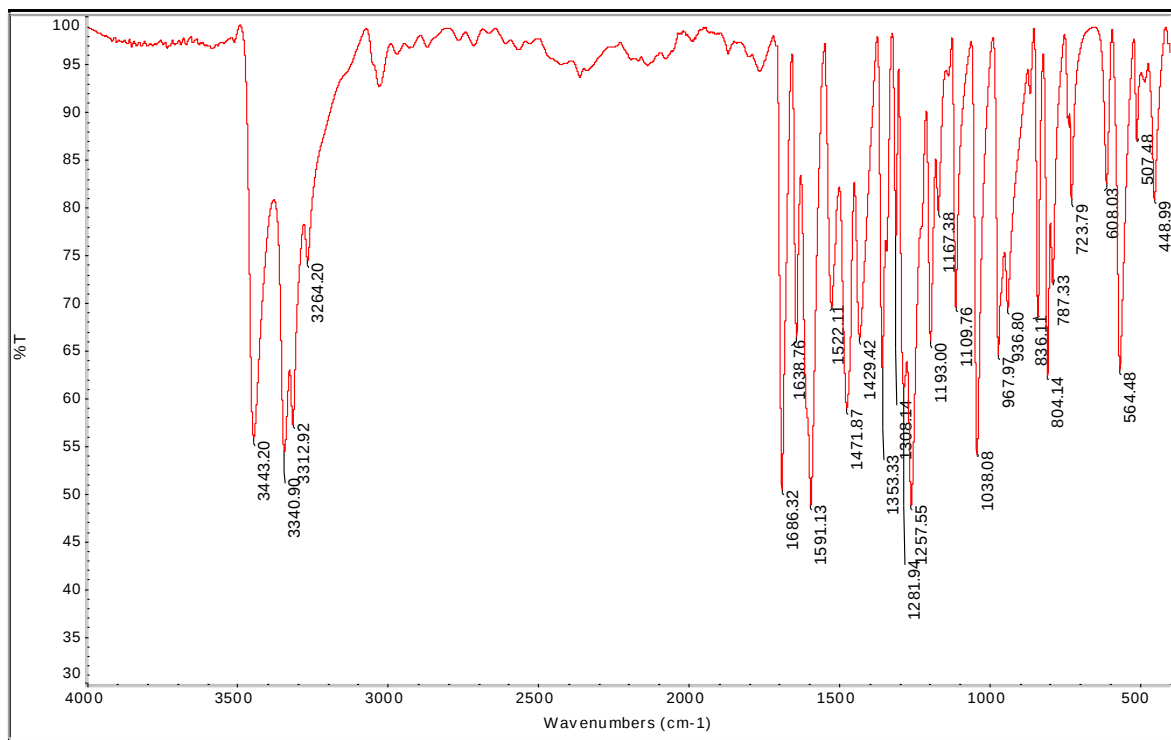


Figure 7. Absorption spectra in the infrared region of (*E*)-3-(3,4-dihydroxyphenyl)acrylohydrazide (**6c**) (ATR).

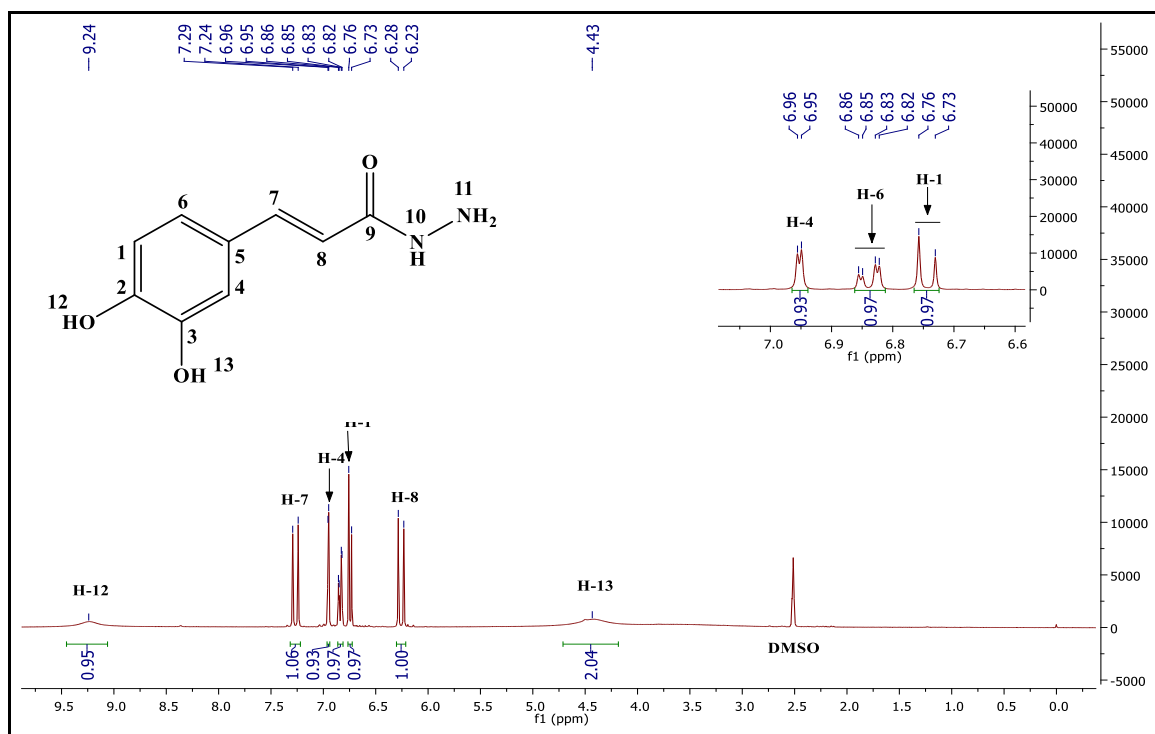


Figure 8. ¹H NMR spectra of (*E*)-3-(3,4-dihydroxyphenyl)acrylohydrazide (**6c**) (300 MHz, DMSO-*d*₆).

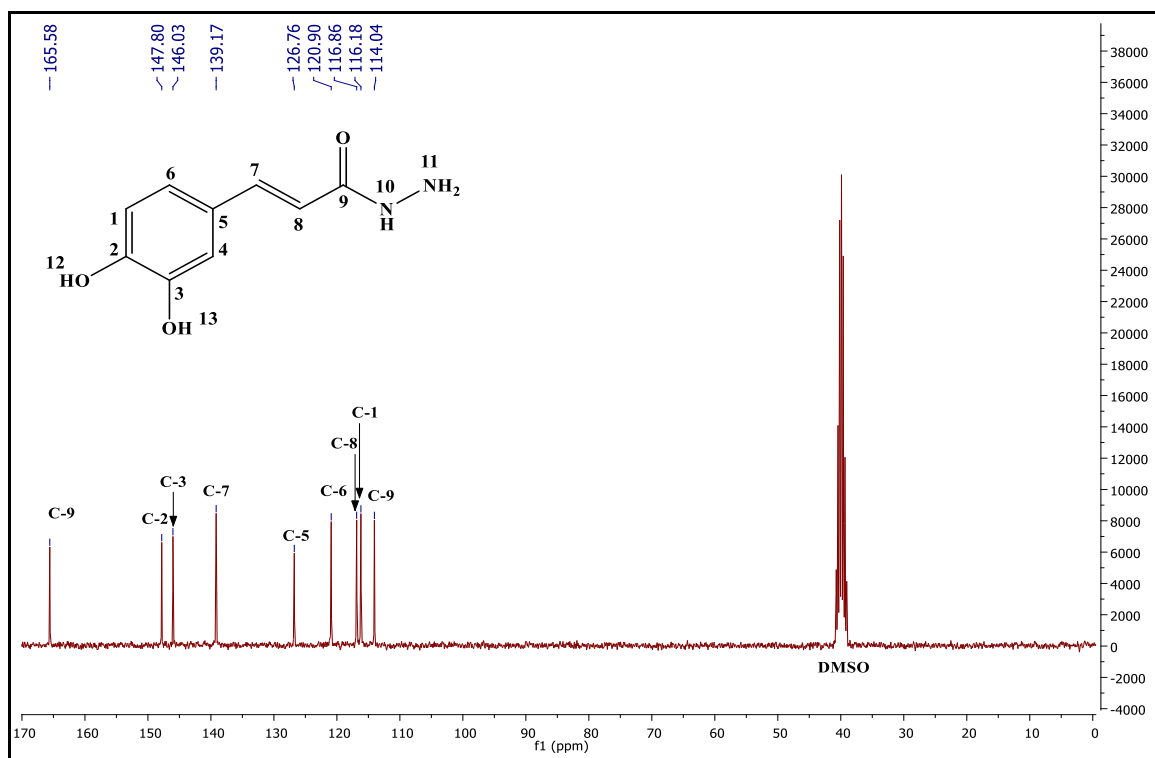


Figure 9. ¹³C NMR spectra of (*E*)-3-(3,4-dihydroxyphenyl)acrylohydrazide (**6c**) (75 MHz, DMSO-*d*₆).

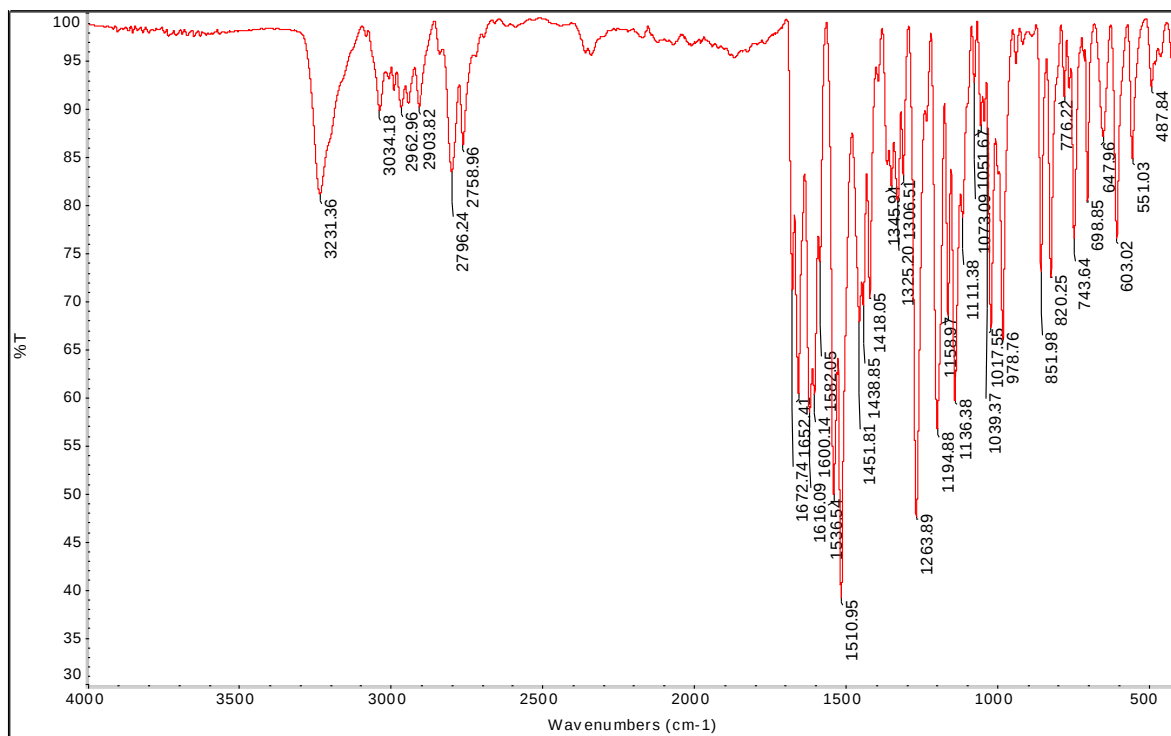


Figure 10. Absorption spectra in the infrared region of (*E*)-3-(3,4-dimethoxyphenyl)acrylohydrazide (**6d**) (ATR).

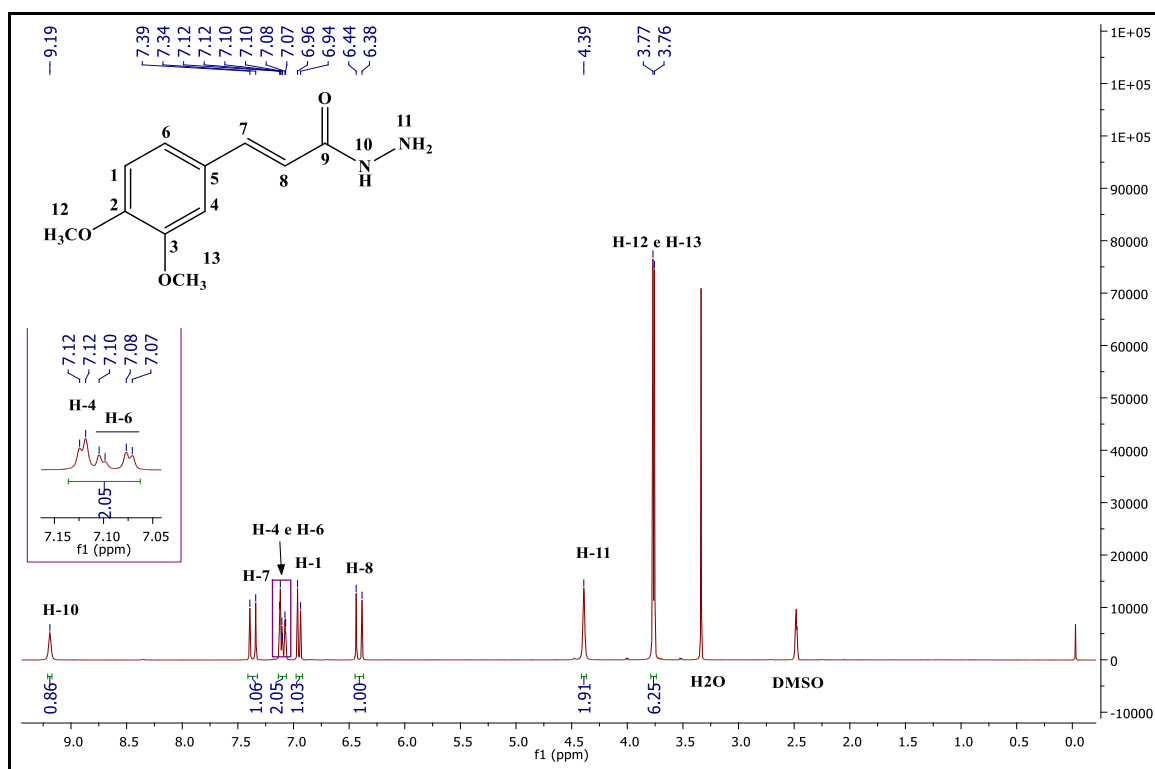


Figure 11. ¹H NMR spectra of (*E*)-3-(3,4-dimethoxyphenyl)acrylohydrazide (**6d**) (300 MHz, DMSO-*d*₆).

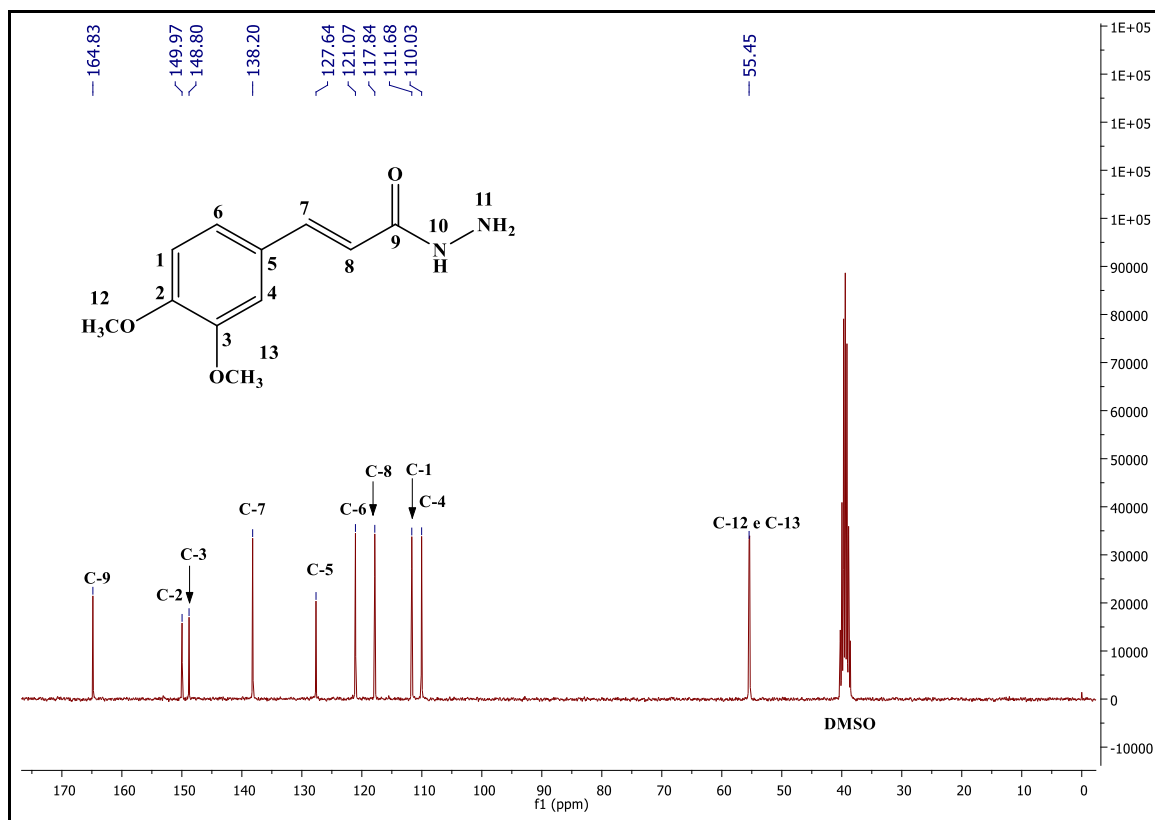


Figure 12. ^{13}C NMR spectra of (E)-3-(3,4-dimethoxyphenyl) acrylohydrazide (**6d**) (75 MHz, DMSO- d_6).

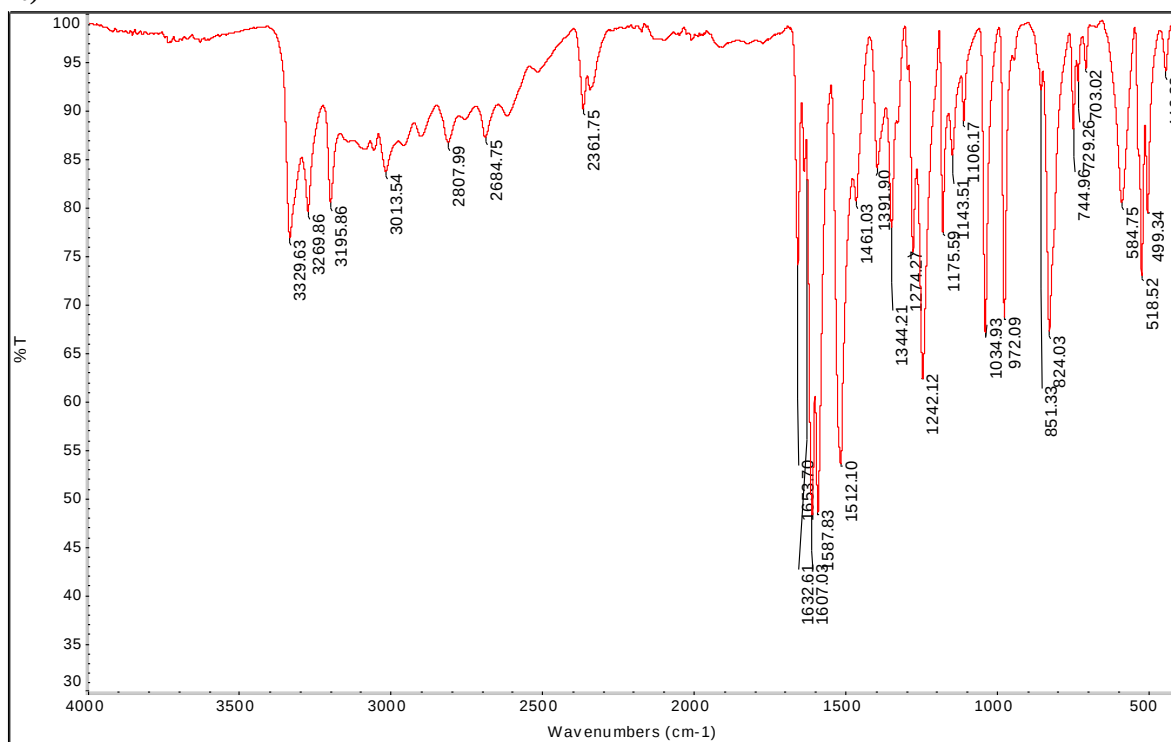


Figure 13. Absorption spectra in the infrared region of (E)-3-(4-methoxyphenyl)acrylohydrazide (**6e**) (ATR).

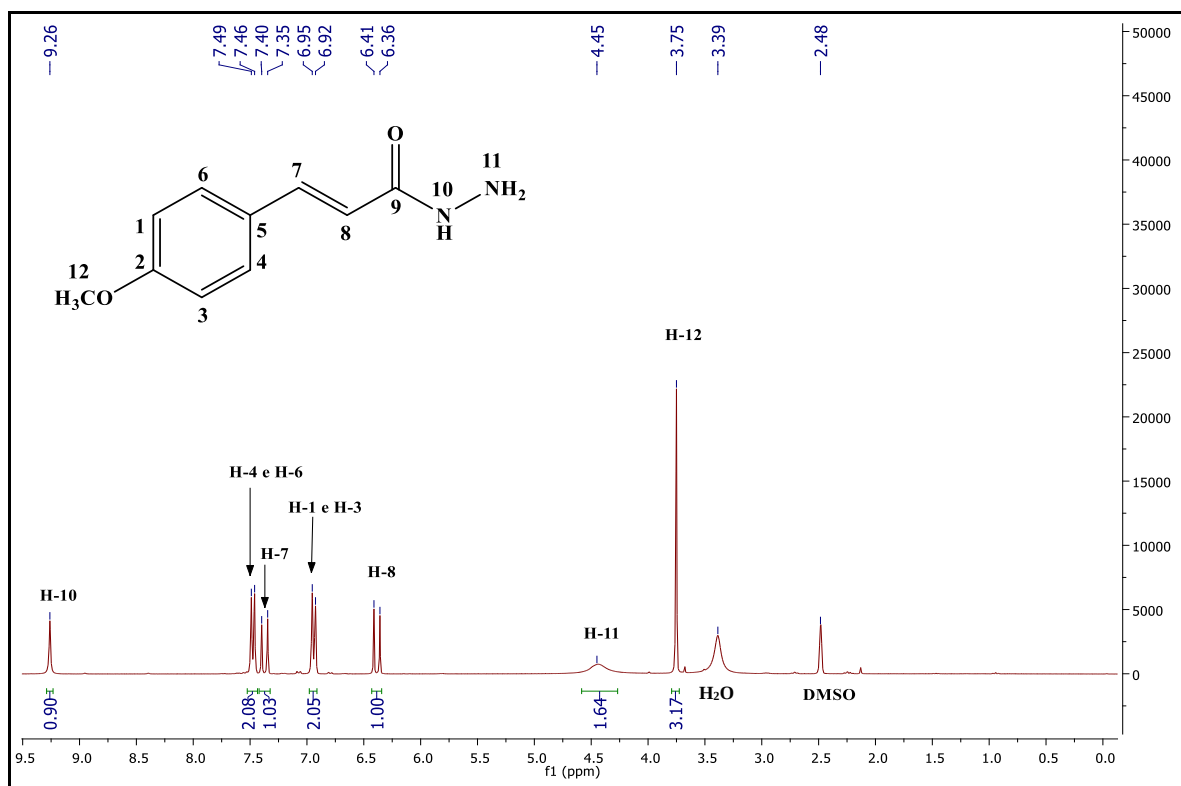


Figure 14. ¹H NMR spectra of (*E*)-3-(4-methoxyphenyl)acrylohydrazide (**6e**) (300 MHz, DMSO-*d*₆).

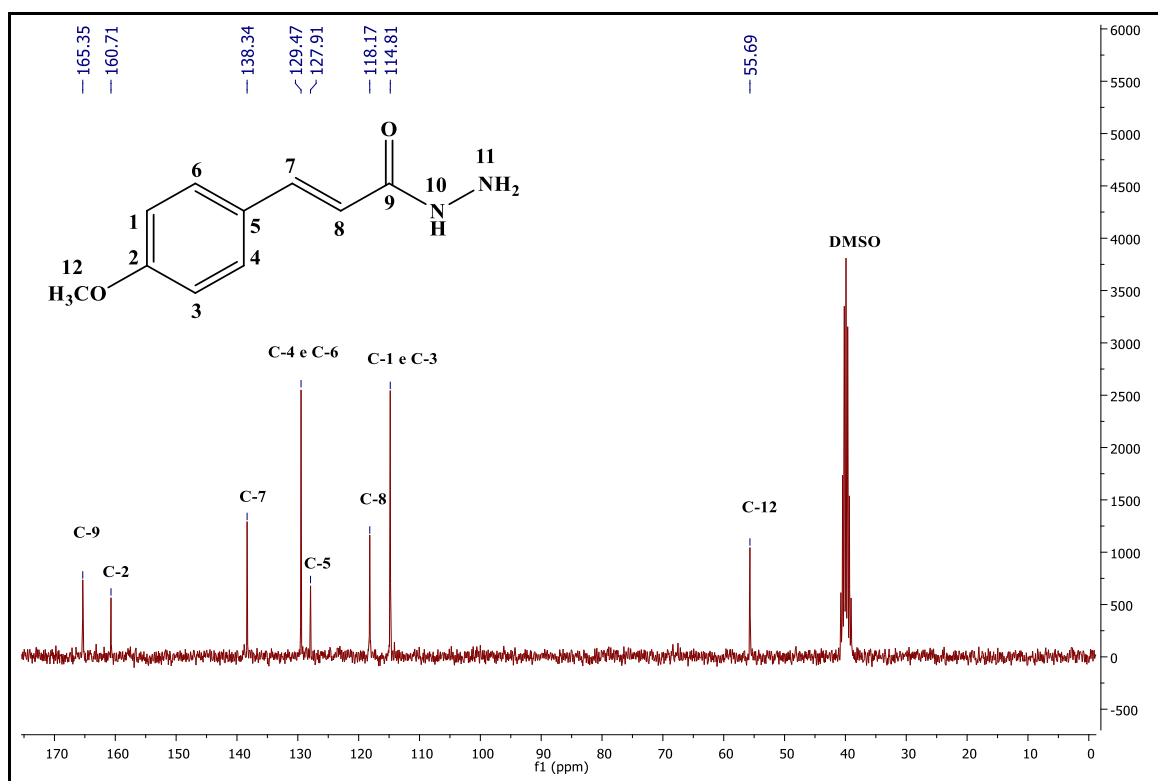


Figure 15. ¹³C NMR spectra of (*E*)-3-(4-methoxyphenyl)acrylohydrazide (**6e**) (75 MHz, DMSO-*d*₆).

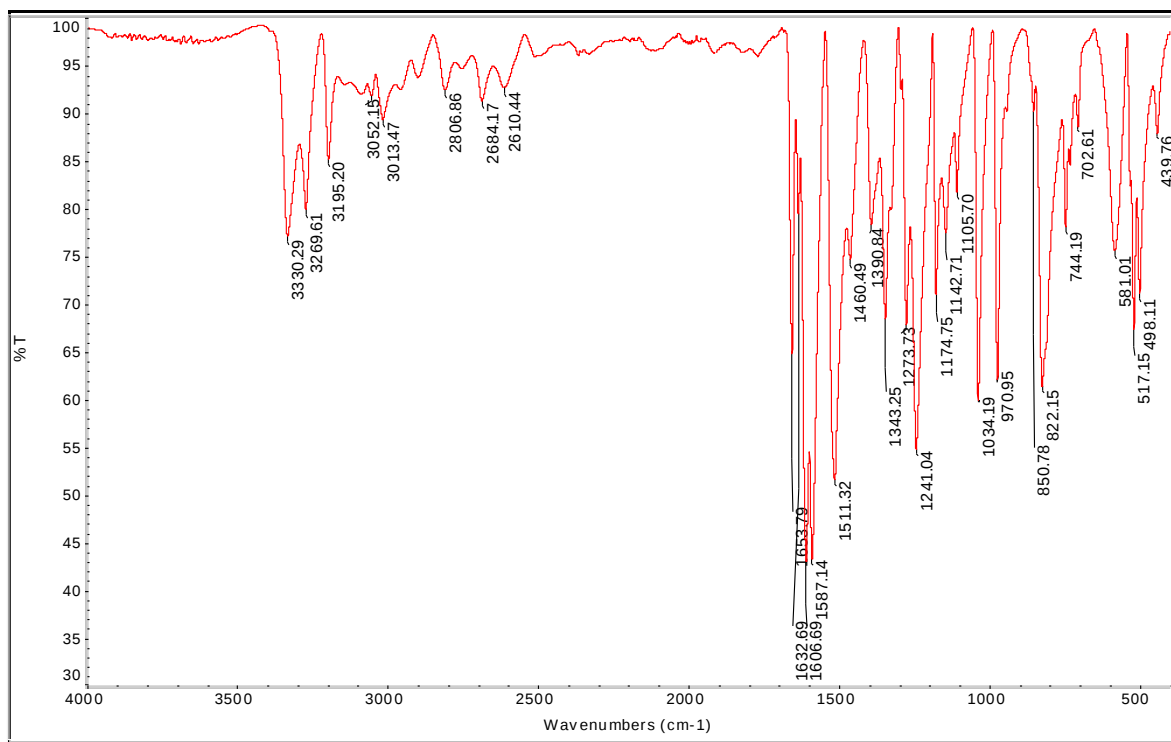


Figure 16. Absorption spectra in the infrared region of (*E*)-3-(4-hydroxyphenyl)acrylohydrazide (**6f**) (ATR).

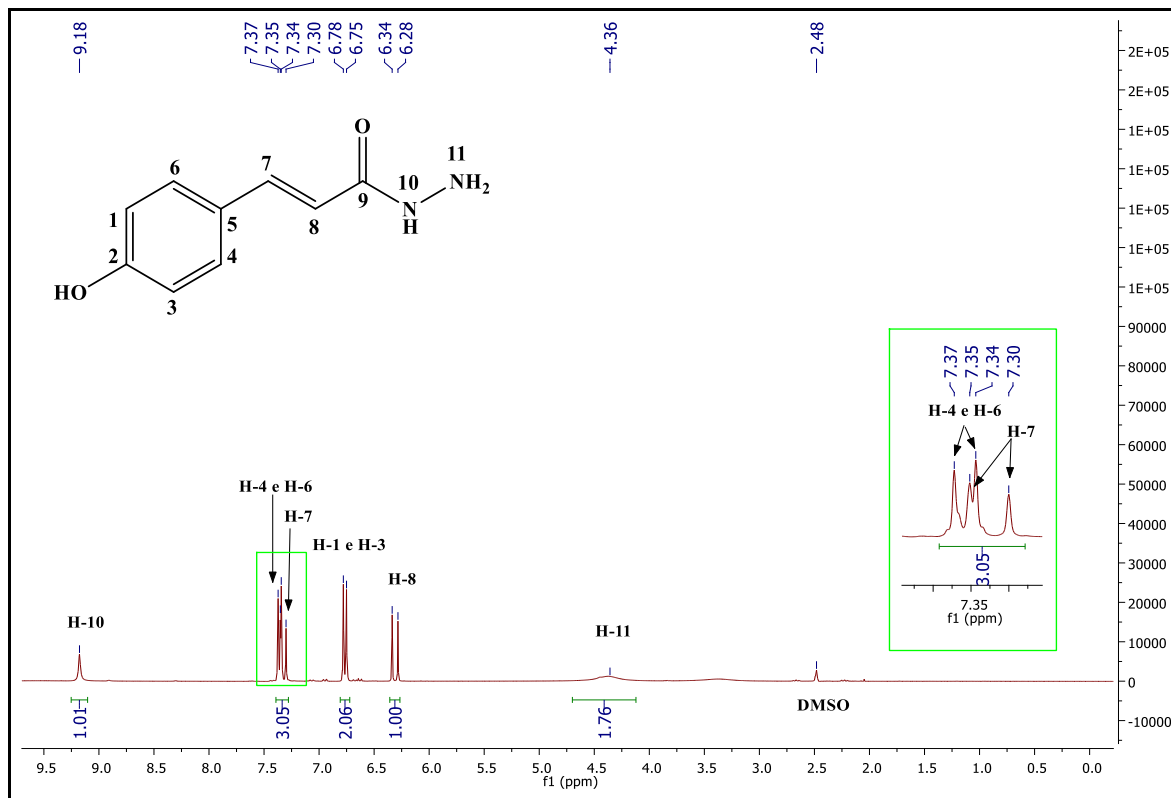


Figure 17. ¹H NMR spectra of (*E*)-3-(4-hydroxyphenyl)acrylohydrazide (**6f**) (300 MHz, DMSO-*d*₆).

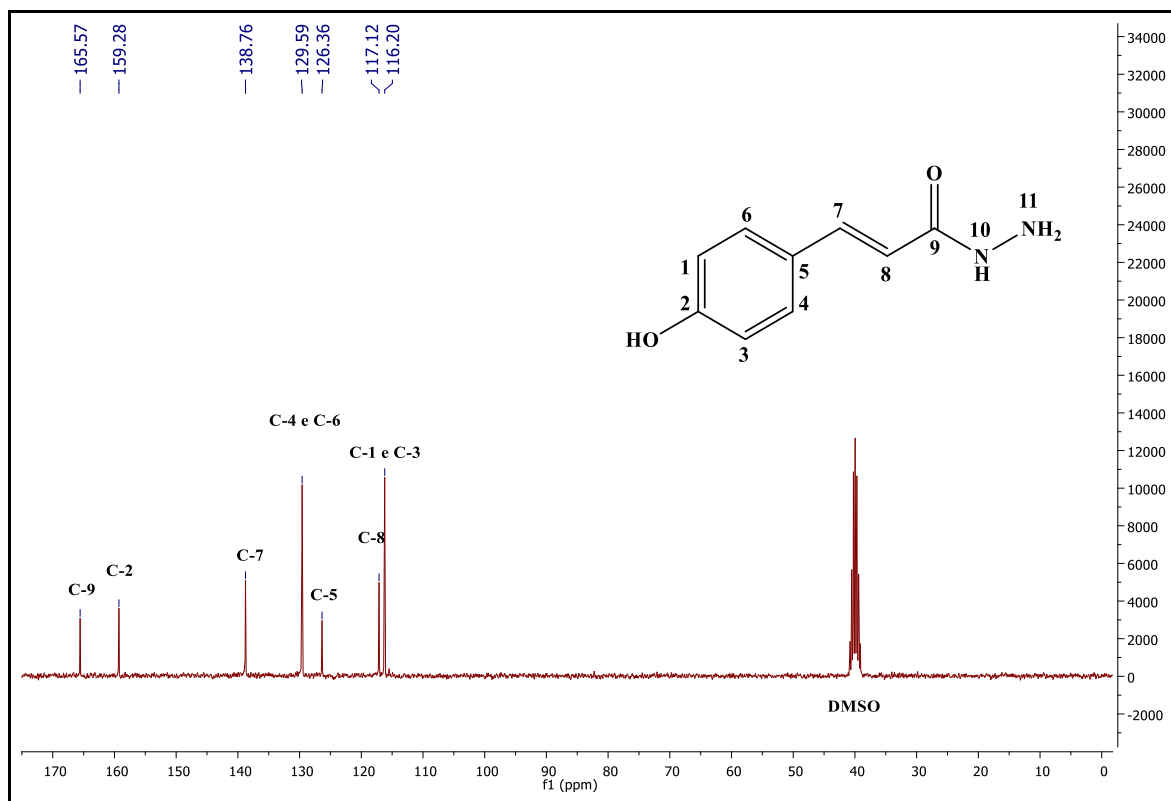


Figure 18. ^{13}C NMR spectra of (*E*)-3-(4-hydroxyphenyl)acrylohydrazide (**6f**) (75 MHz, DMSO- d_6).

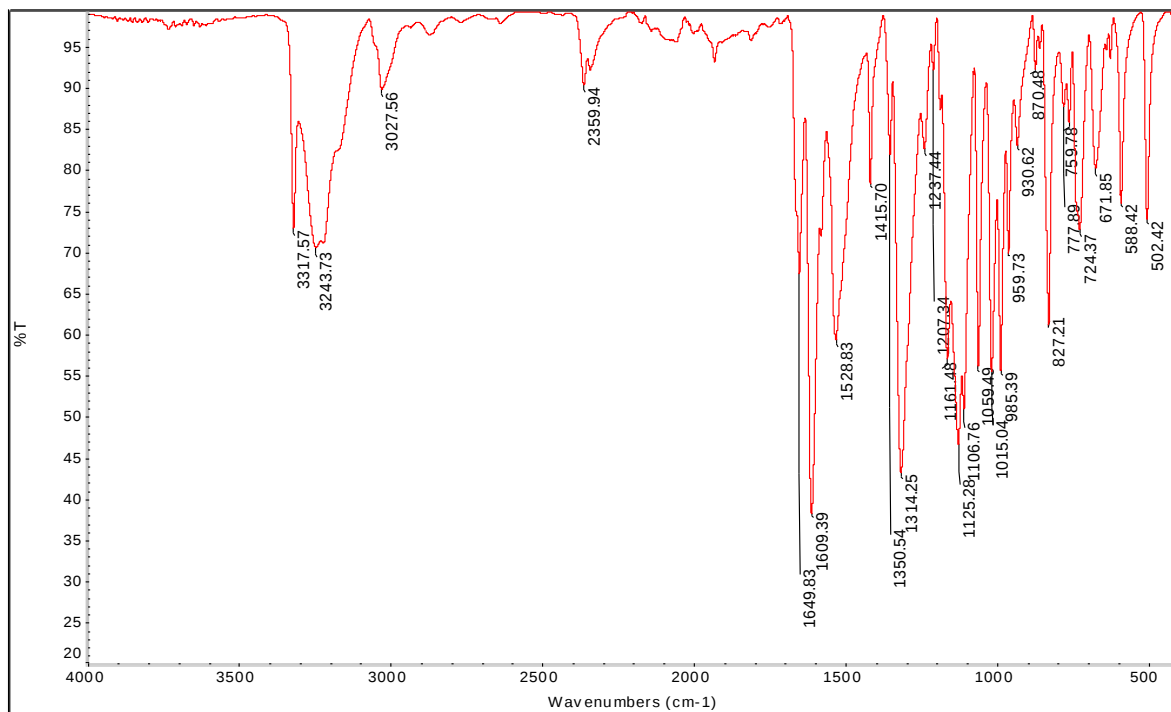


Figure 19. Absorption spectra in the infrared region of (*E*)-3-(4-(trifluoromethyl)phenyl)acrylohydrazide (**6g**) (ATR).

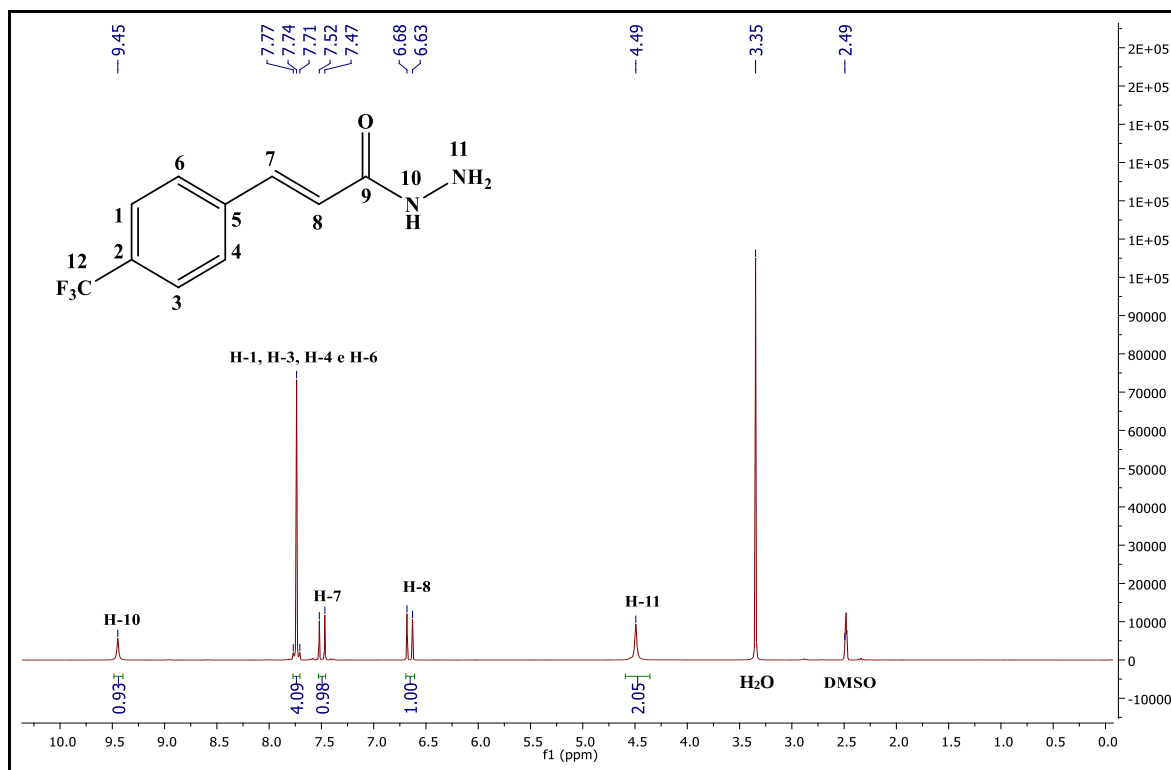


Figure 20. ¹H NMR spectra of (*E*)-3-(4-(trifluoromethyl)phenyl)acrylohydrazide (**6g**) (300 MHz, DMSO-d₆).

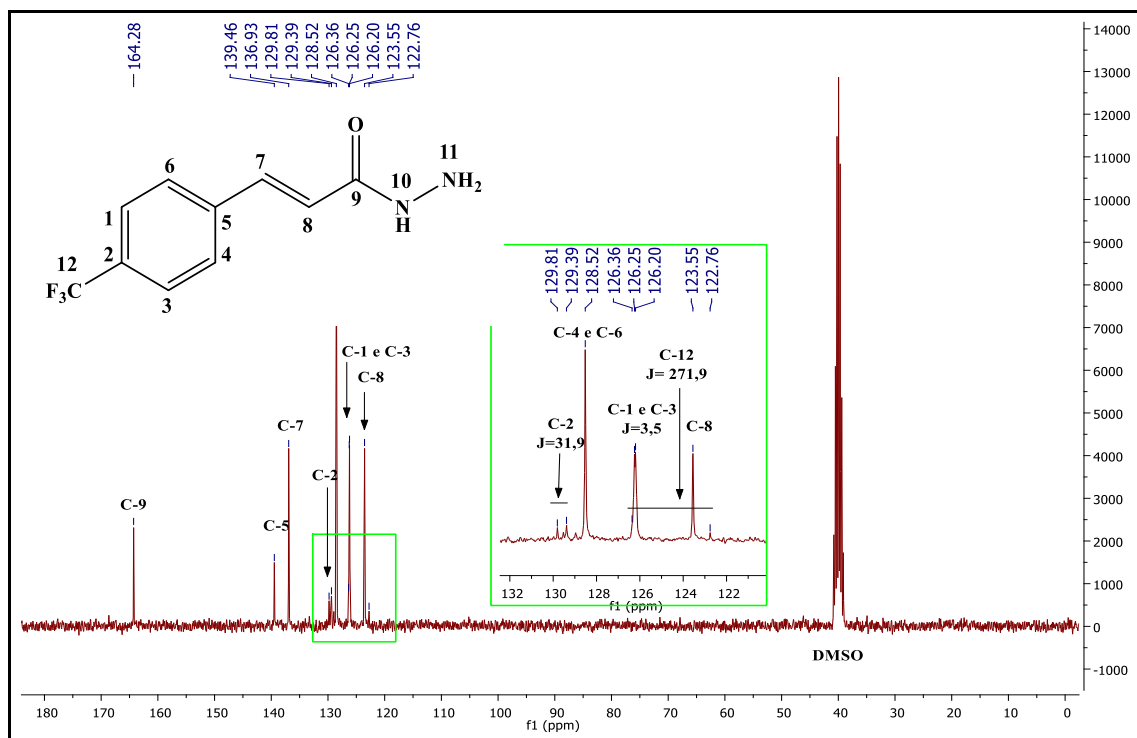


Figure 21. ¹³C NMR spectra of (*E*)-3-(4-(trifluoromethyl)phenyl)acrylohydrazide (**6g**) (75 MHz, DMSO-d₆).

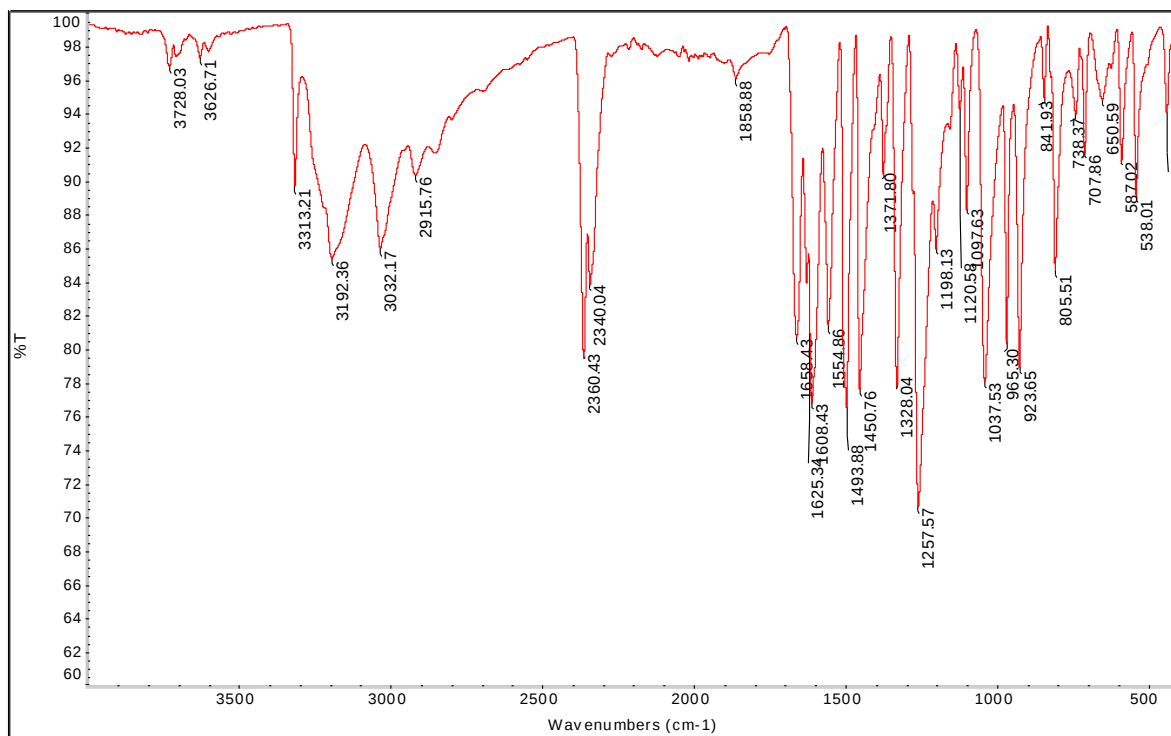


Figure 22. Absorption spectra in the infrared region of (*E*)-3-(benzo[d][1,3]dioxol-5-yl)acrylohydrazide (**6h**) (ATR).

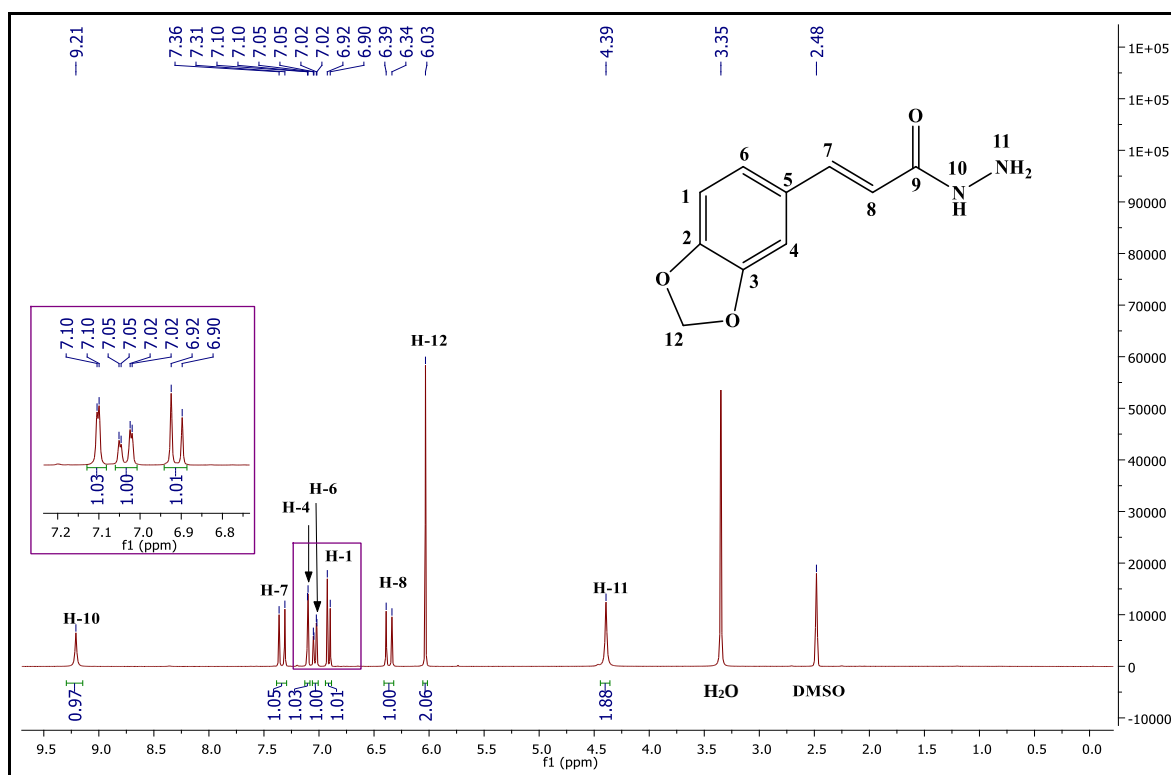


Figure 23. ¹H NMR spectra of (*E*)-3-(benzo[d][1,3]dioxol-5-yl)acrylohydrazide (**6h**) (300 MHz, DMSO-*d*₆).

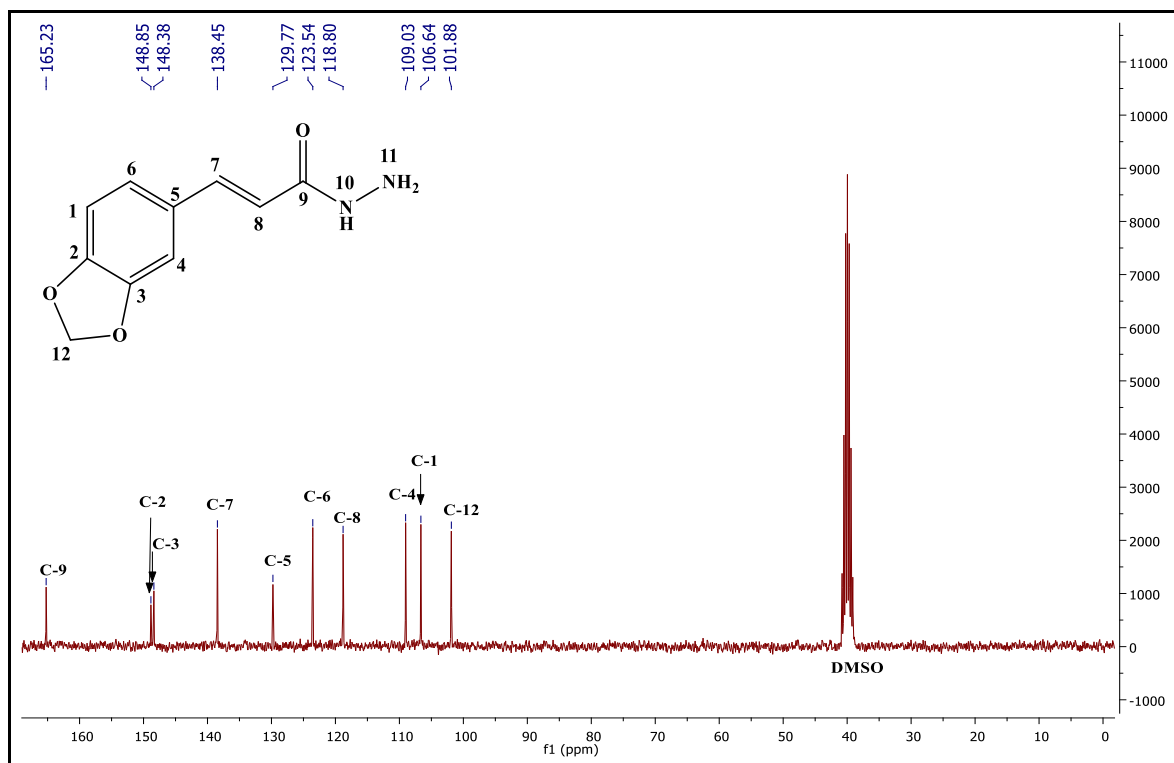


Figure 24. ^{13}C NMR spectra of (*E*)-3-(benzo[d][1,3]dioxol-5-yl)acrylohydrazide (**6h**) (75 MHz, DMSO- d_6).

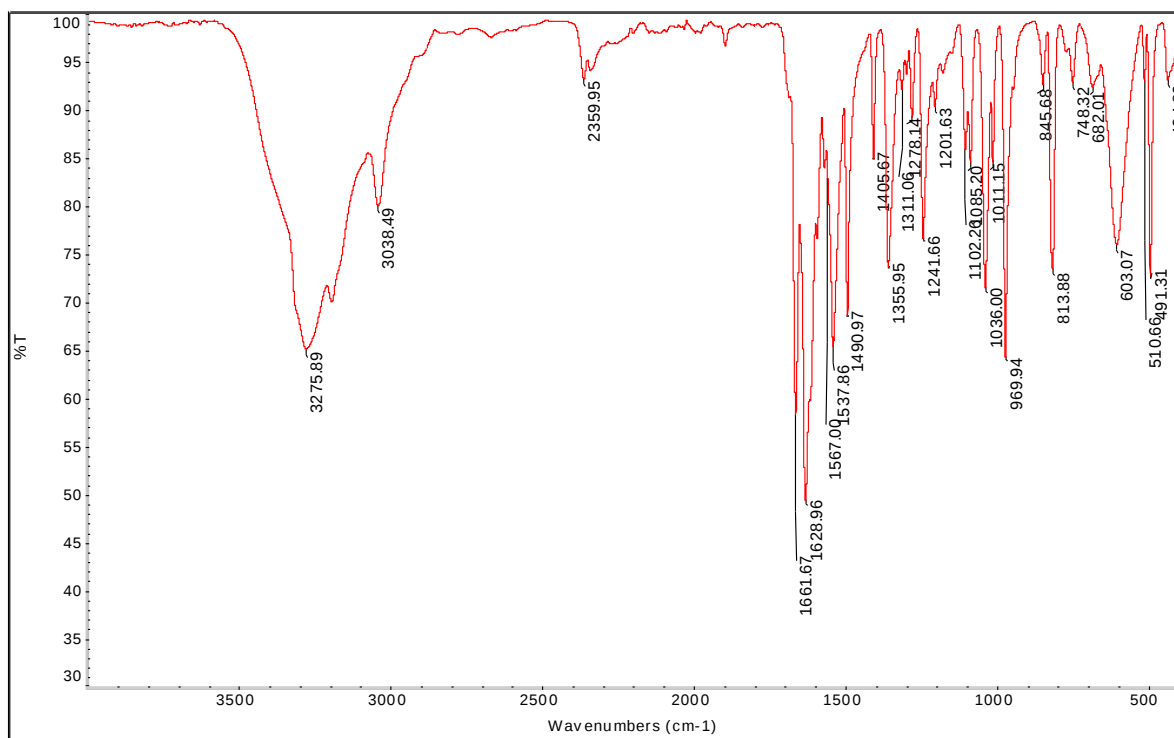


Figure 25. Absorption spectra in the infrared region of (*E*)-3-(4-chlorophenyl)acrylohydrazide (**6i**) (ATR).

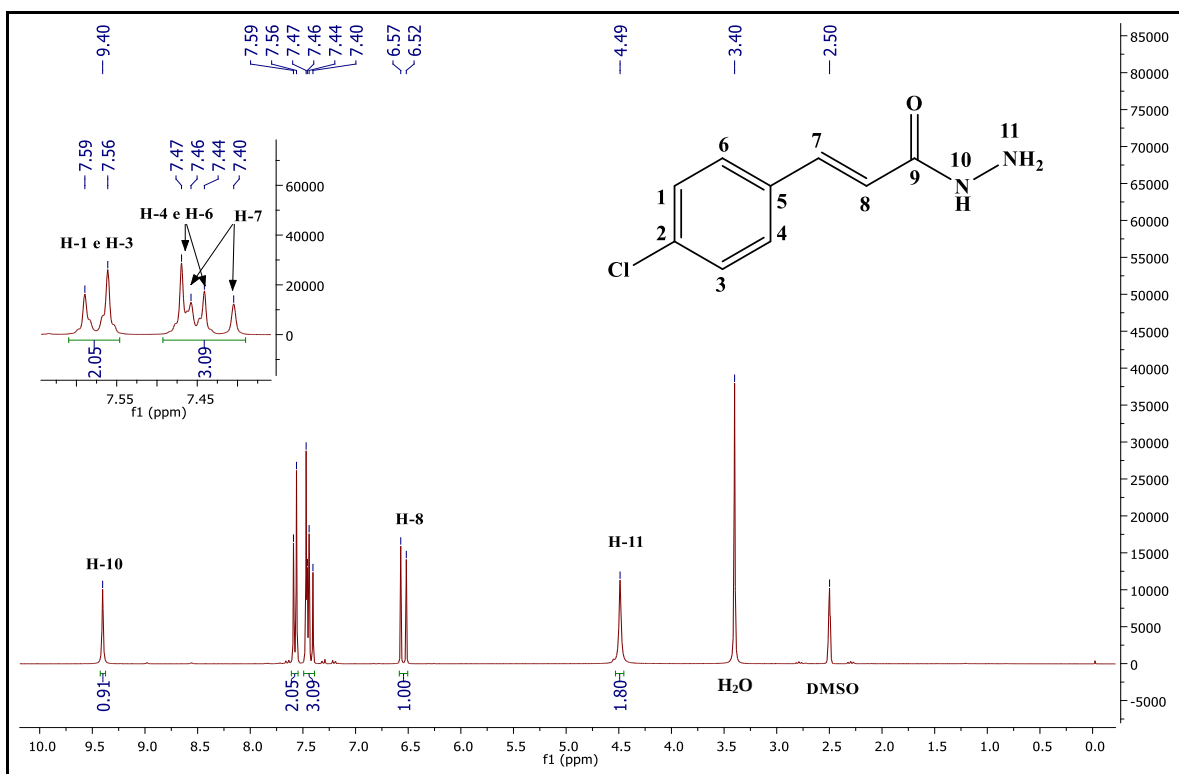


Figure 26. ¹H NMR spectra of (*E*)-3-(4-chlorophenyl)acrylohydrazide (**6i**) (300 MHz, DMSO-*d*₆).

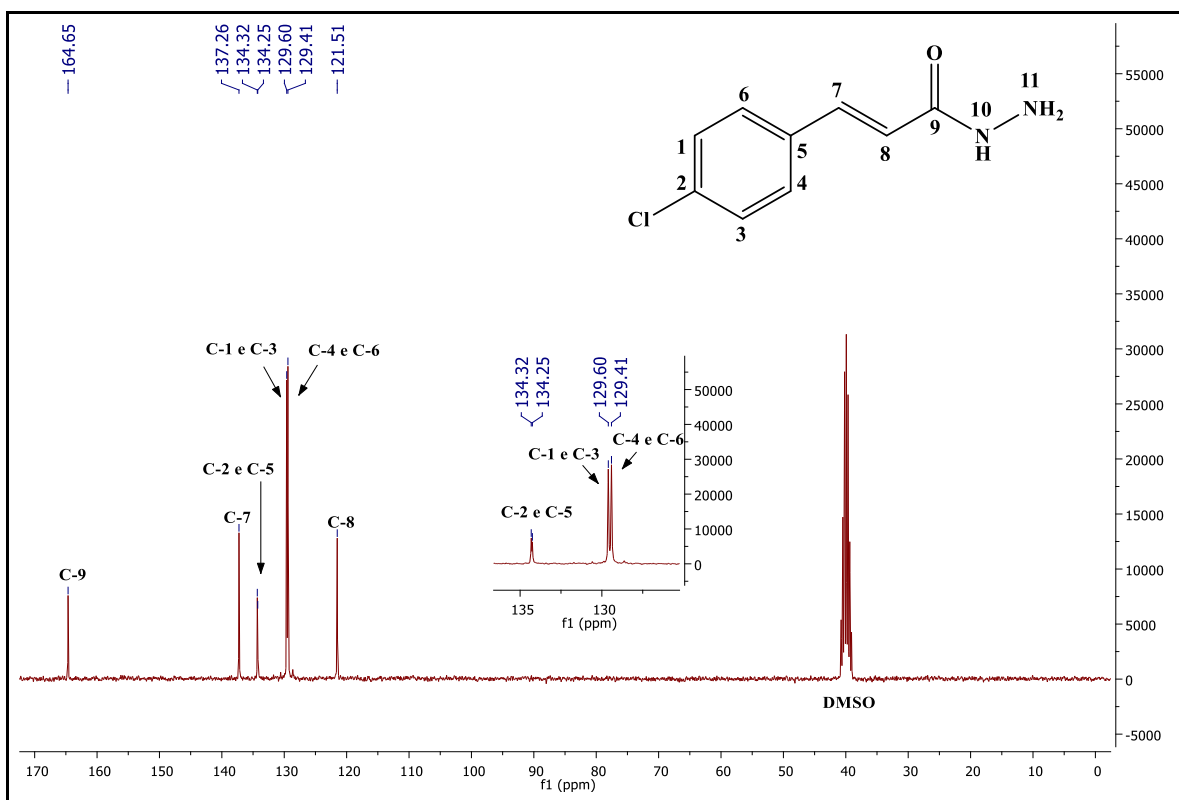


Figure 27. ¹³C NMR spectra of (*E*)-3-(4-chlorophenyl)acrylohydrazide (**6i**) (75 MHz, DMSO-*d*₆).

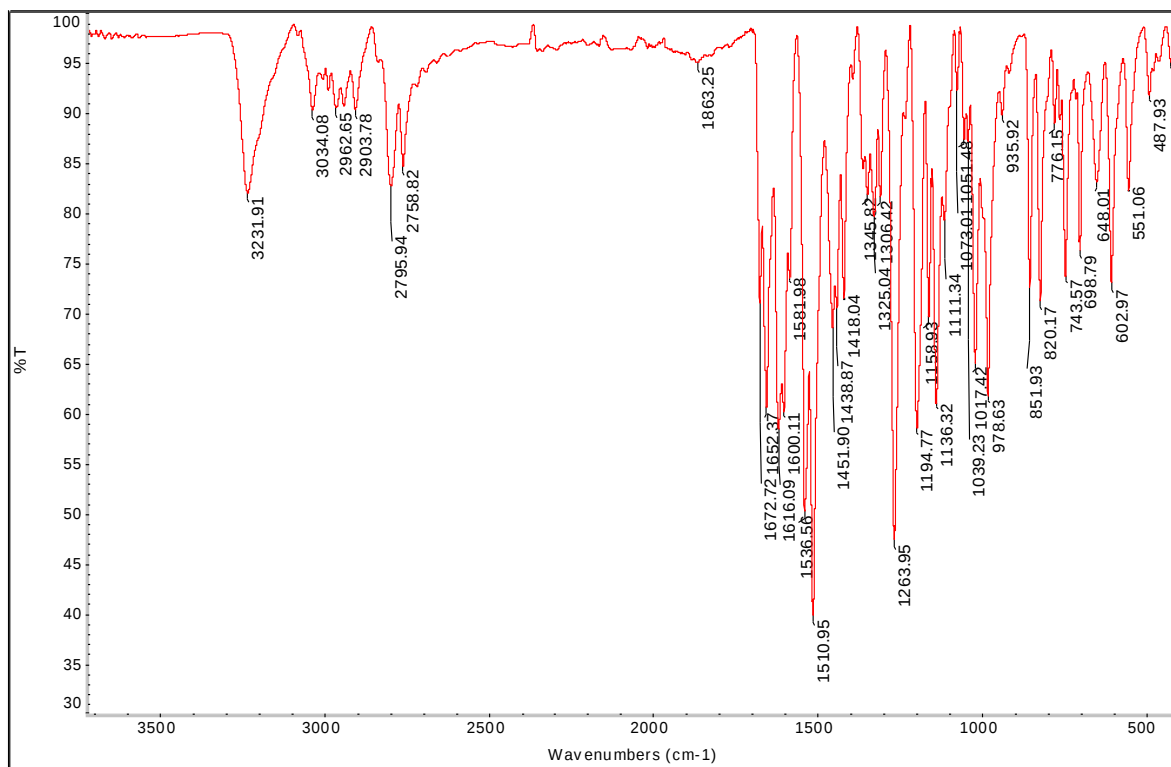


Figure 28. Absorption spectra in the infrared region of Cinnamoylhydrazide (6j) (ATR).

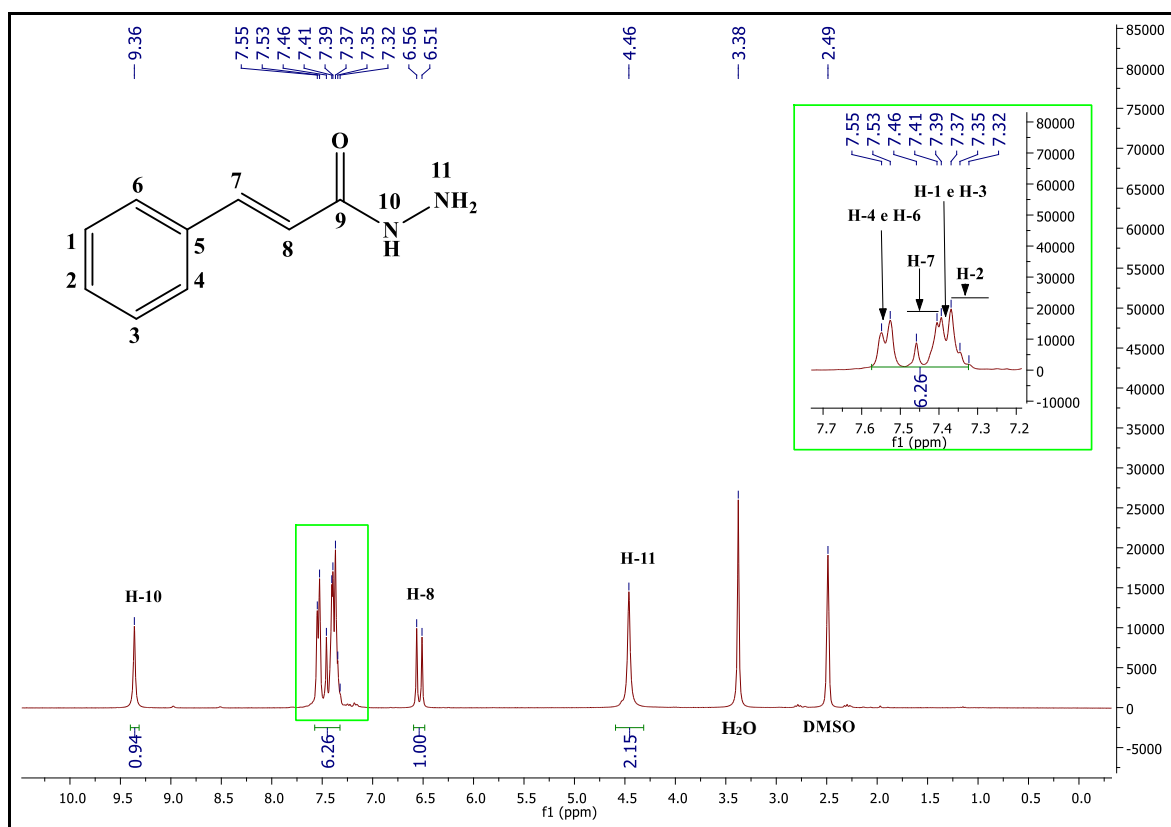


Figure 29. ¹H NMR spectra of Cinnamoylhydrazide (6j) (300 MHz, DMSO-*d*₆).

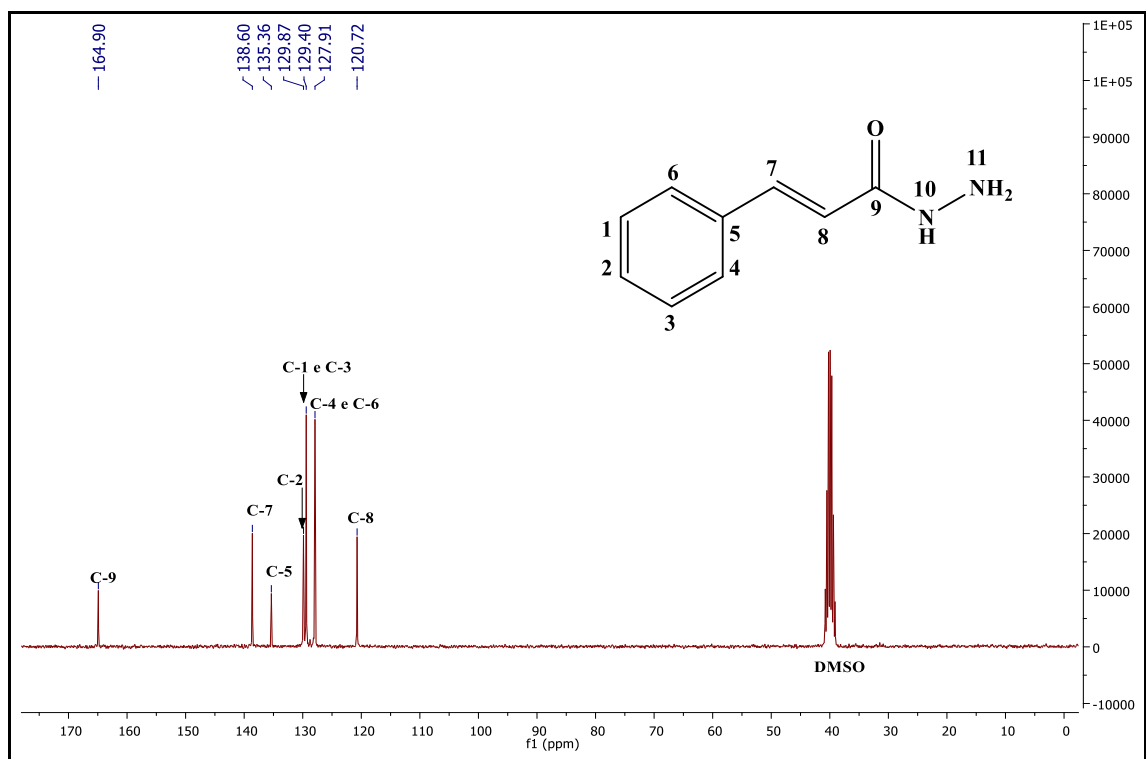


Figure 30. ^{13}C NMR spectra of Cinnamoylhydrazide (**6j**) (75 MHz, $\text{DMSO-}d_6$).

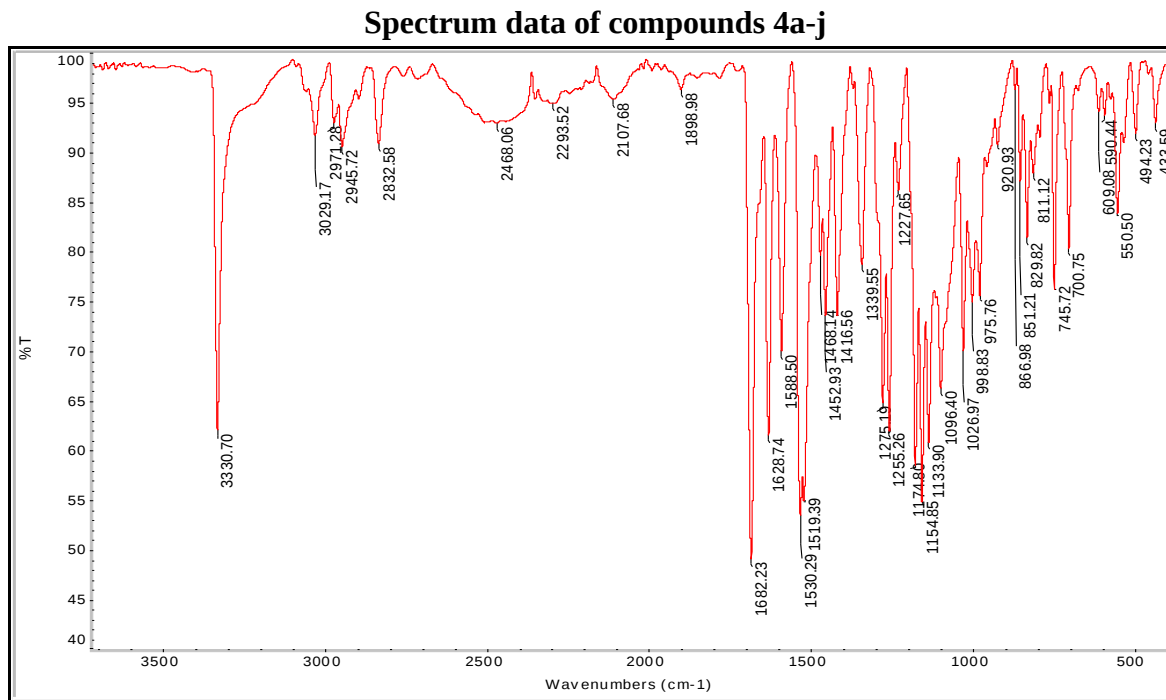


Figure 31. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxy-3-methoxyphenyl) acrylohydrazide (**4a**) (ATR).

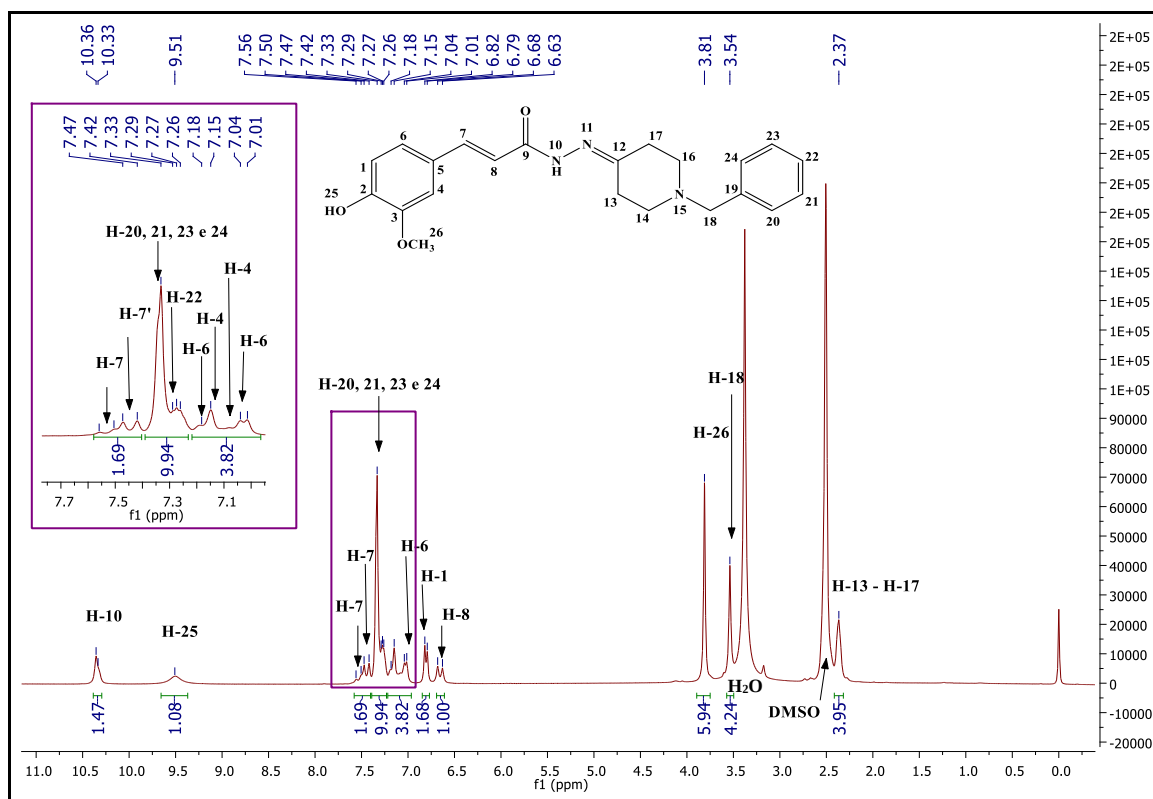


Figure 32. ^1H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxy-3-methoxyphenyl) acrylohydrazide (**4a**) (300 MHz, $\text{DMSO}-d_6$).

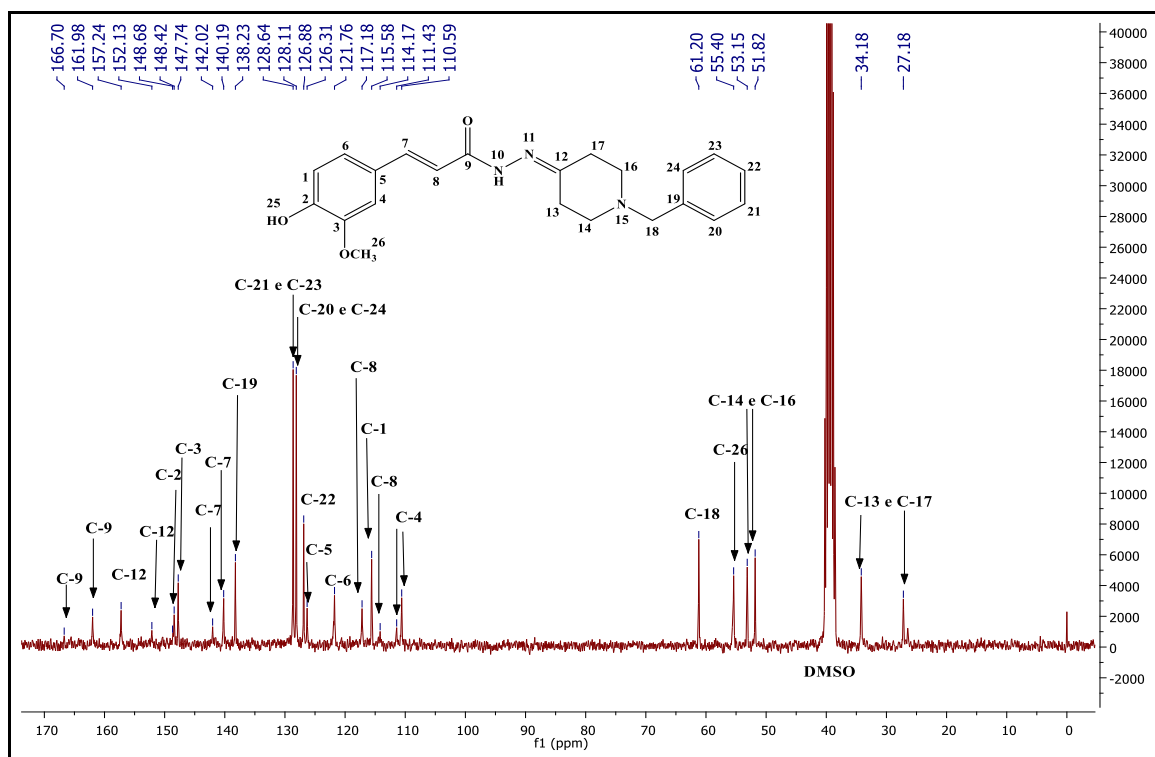


Figure 33. ^{13}C NMR spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxy-3-methoxyphenyl) acrylohydrazide (**4a**) (75 MHz, $\text{DMSO}-d_6$).

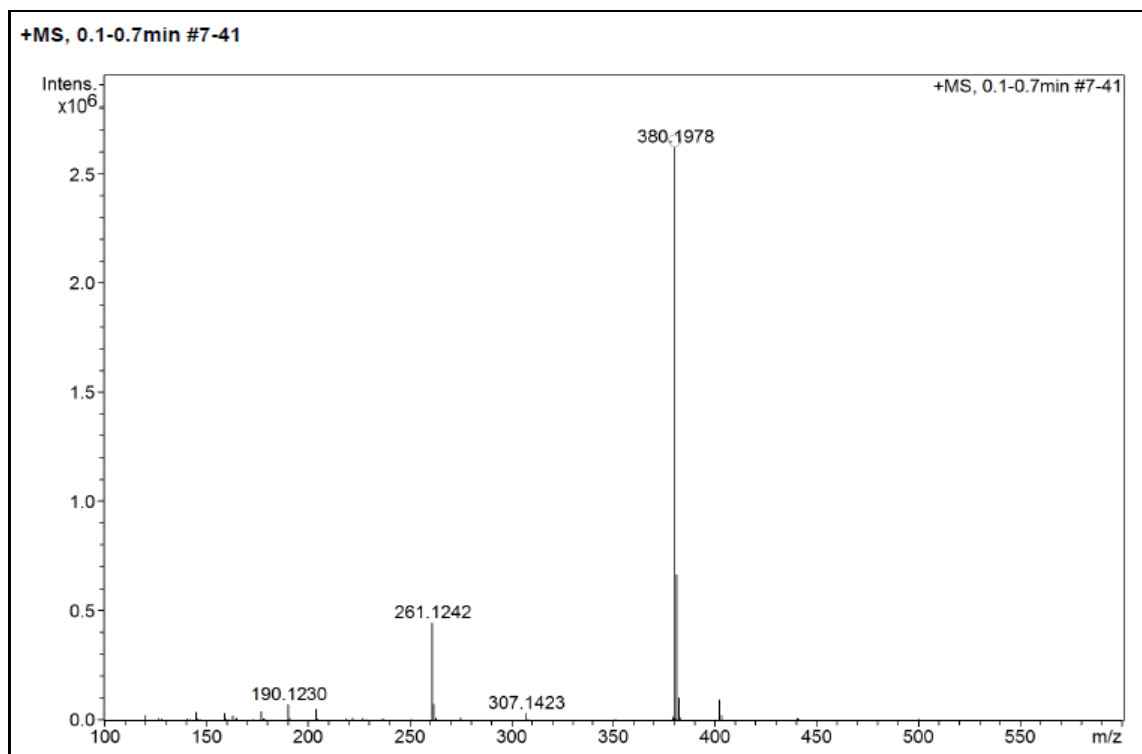


Figure 34. HR-MS spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxy-3-methoxyphenyl) acrylohydrazide (**4a**) (ESI-MS).

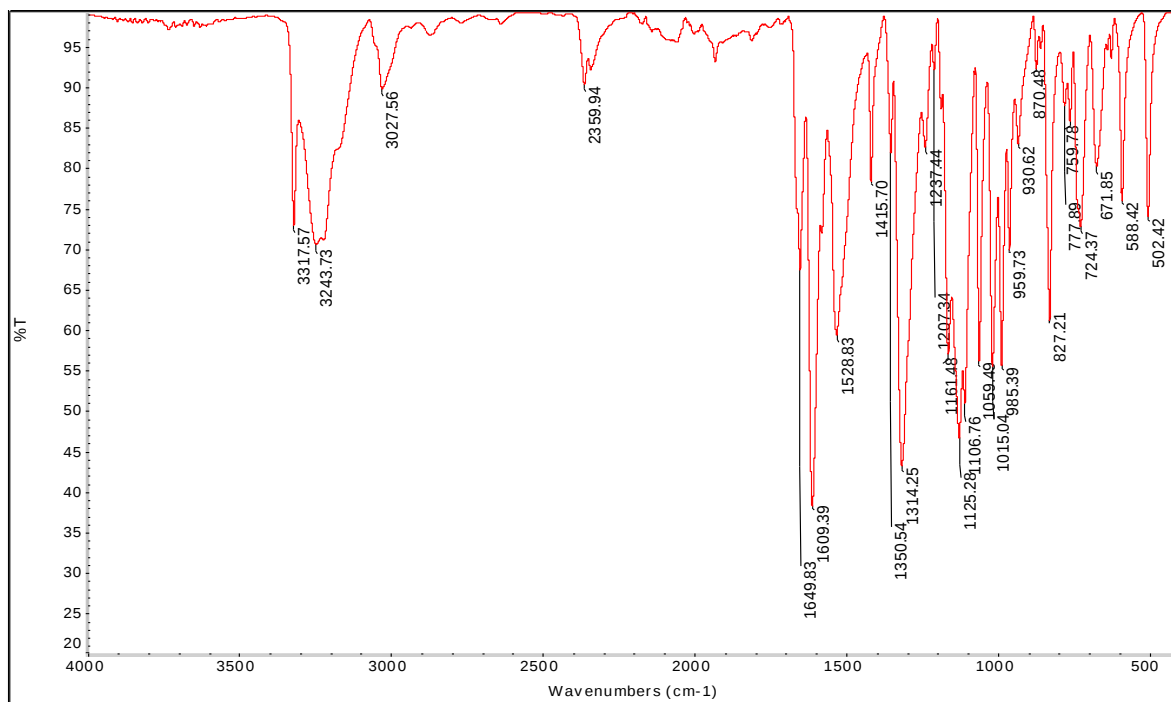


Figure 35. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3-hydroxy-4-methoxyphenyl) acrylohydrazide (**4b**) (ATR).

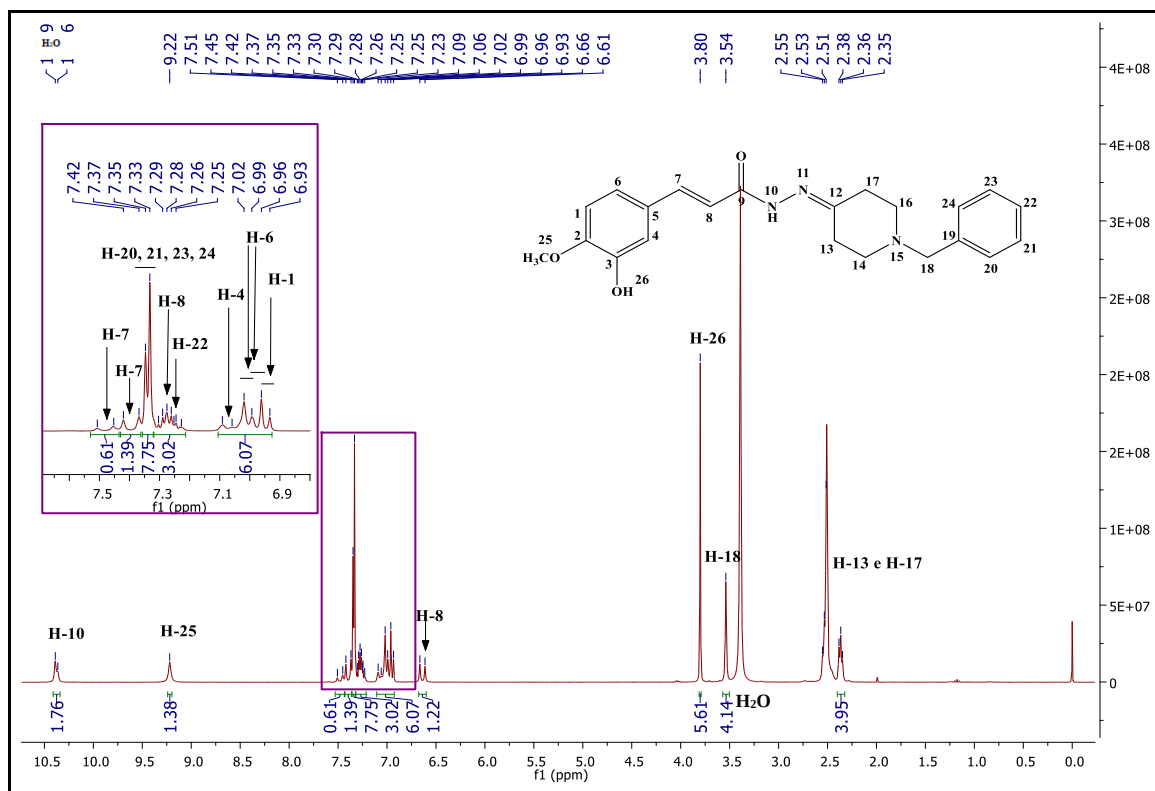


Figure 36. ¹H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3-hydroxy-4-methoxyphenyl) acrylohydrazide (**4b**) (300 MHz, DMSO-*d*₆).

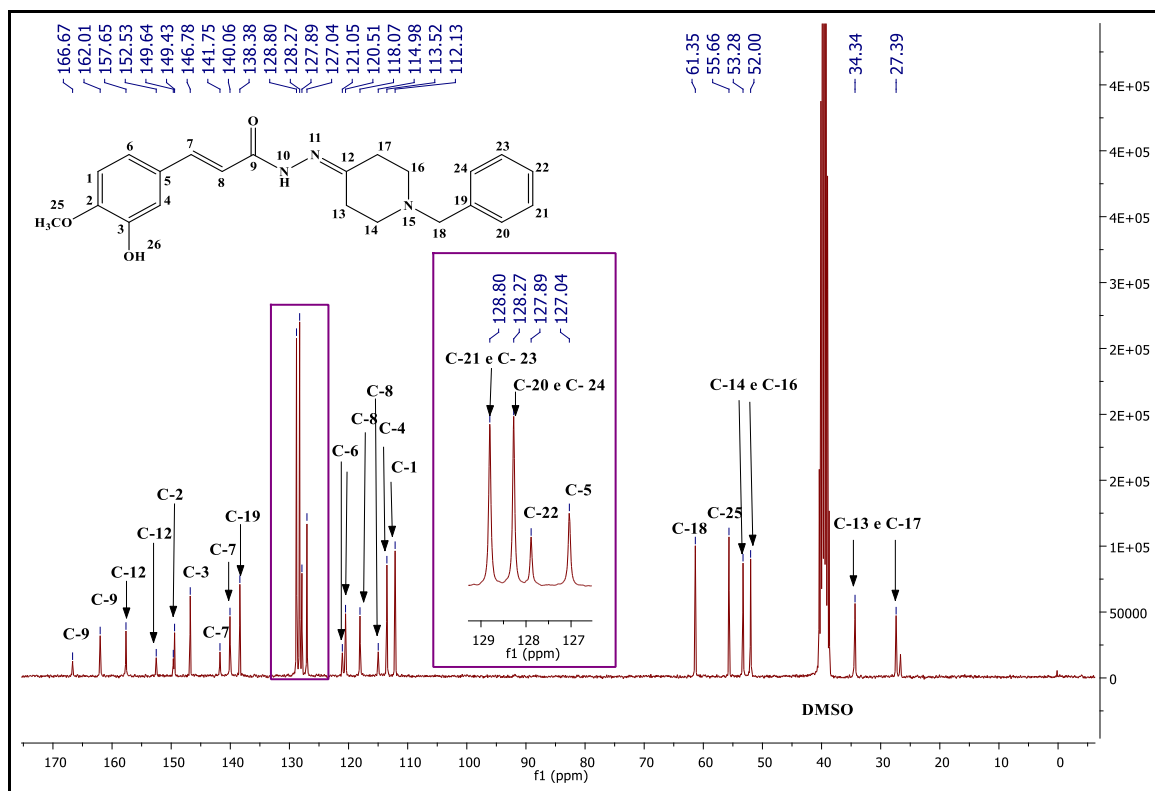


Figure 37. ^{13}C NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3-hydroxy-4-methoxyphenyl) acrylohydrazide (**4b**) (75 MHz, $\text{DMSO-}d_6$).

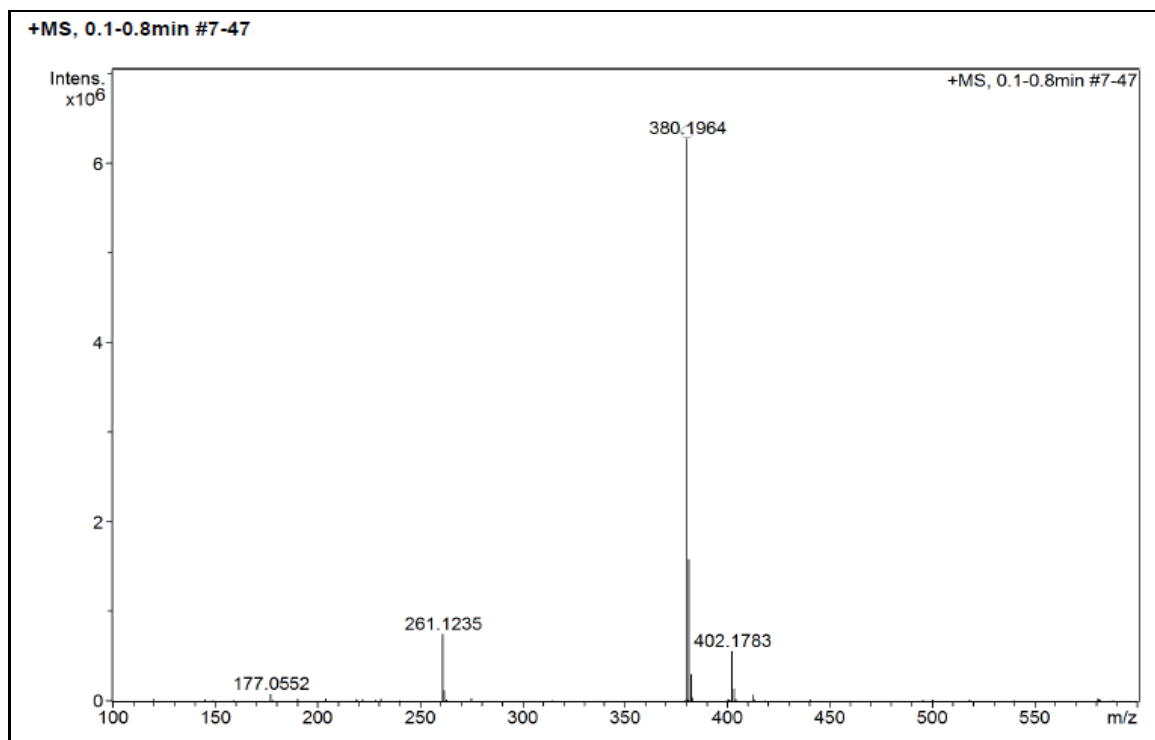


Figure 38. HR-MS spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3-hydroxy-4-methoxyphenyl) acrylohydrazide (**4b**) (ESI-MS).

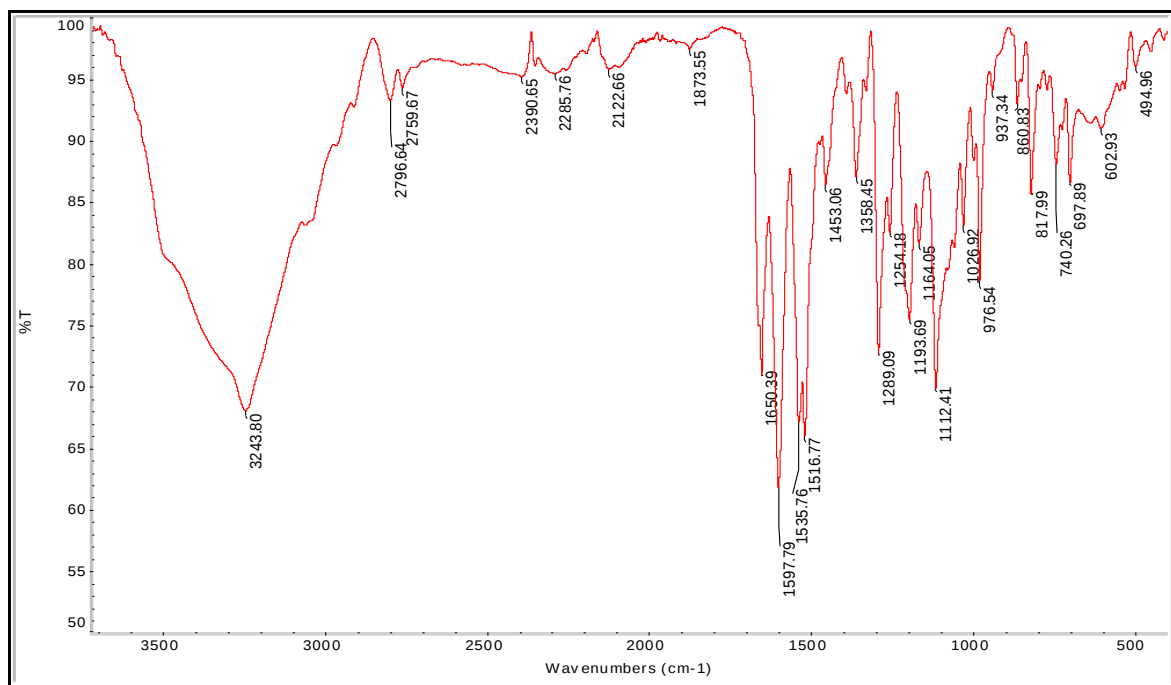


Figure 39. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dihydroxyphenyl) acrylohydrazide (**4c**) (ATR).

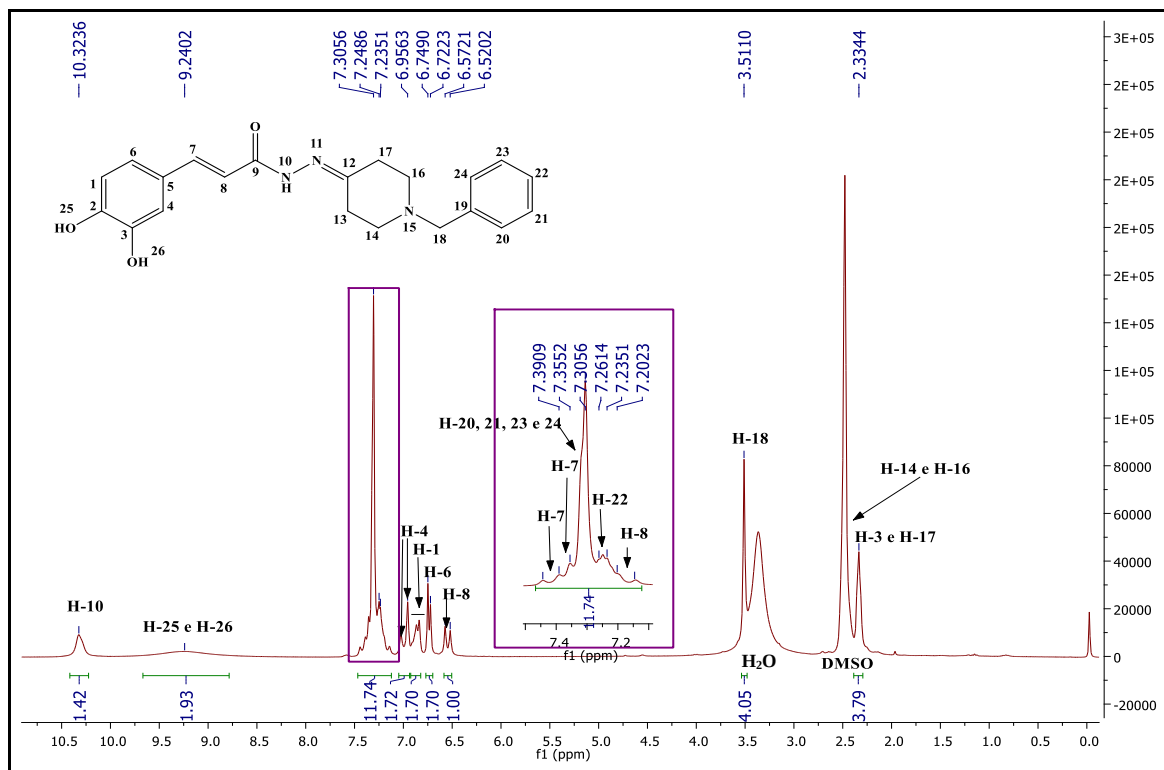


Figure 40. ¹H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dihydroxyphenyl) acrylohydrazide (**4c**) (300 MHz, DMSO-*d*₆).

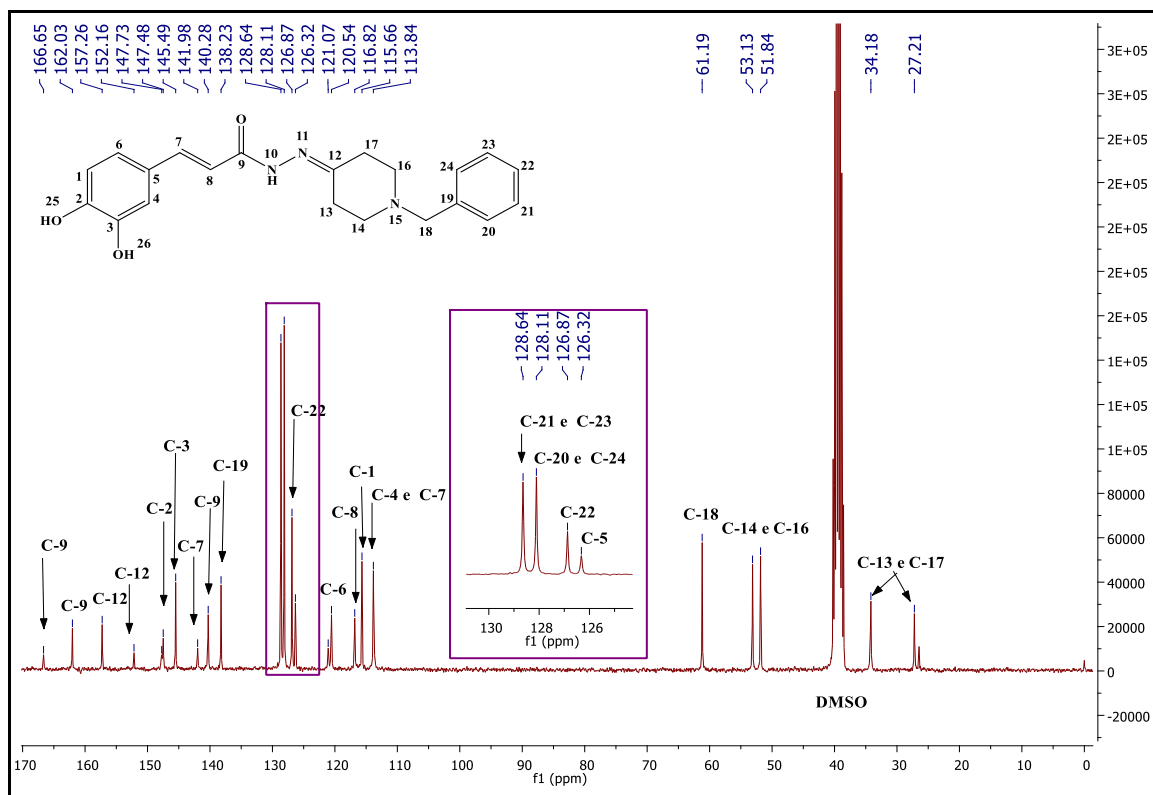


Figure 41. ^{13}C NMR spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dihydroxyphenyl)acrylohydrazide (**4c**) (75 MHz, $\text{DMSO-}d_6$).

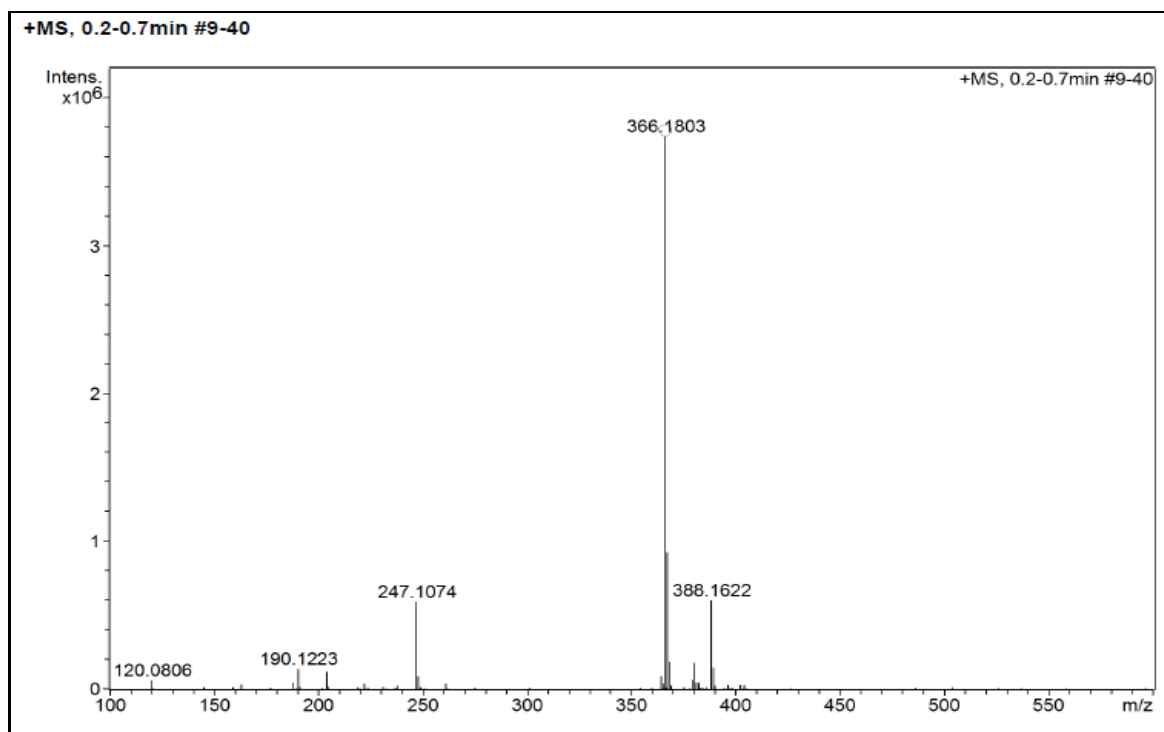


Figure 42. HR-MS spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dihydroxyphenyl)acrylohydrazide (**4c**) (ESI-MS).

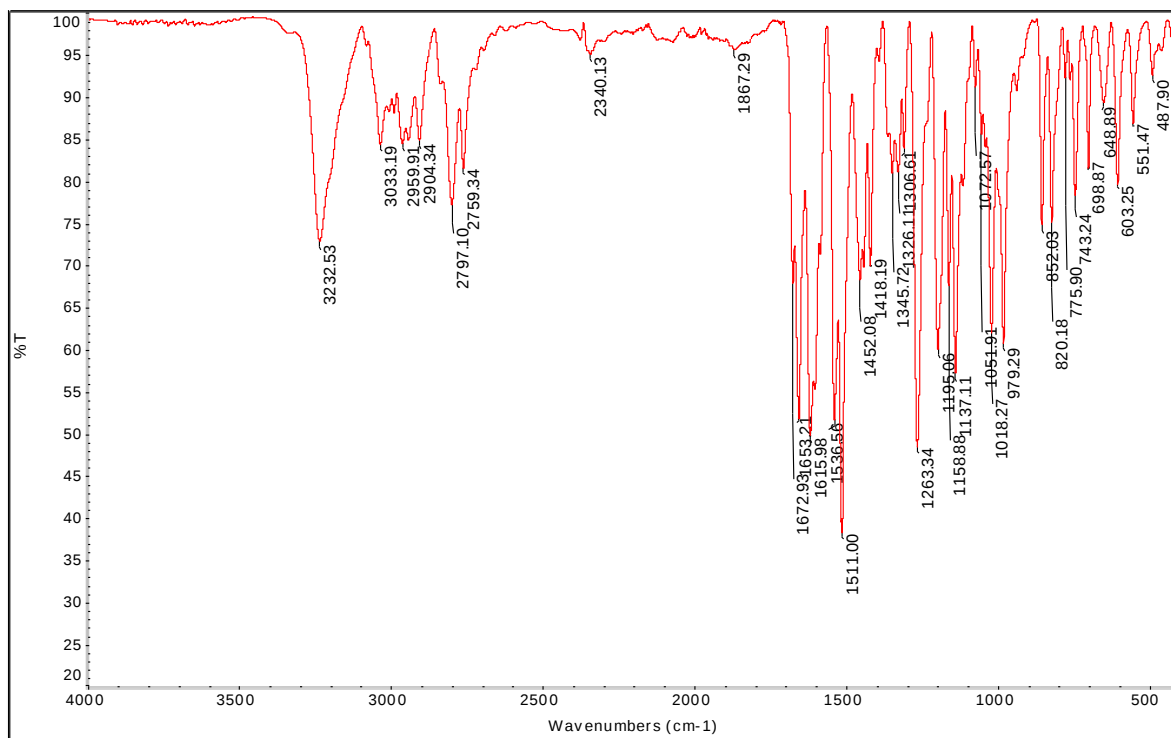


Figure 43. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dimethoxyphenyl) acryloylhydrazide (**4d**) (ATR).

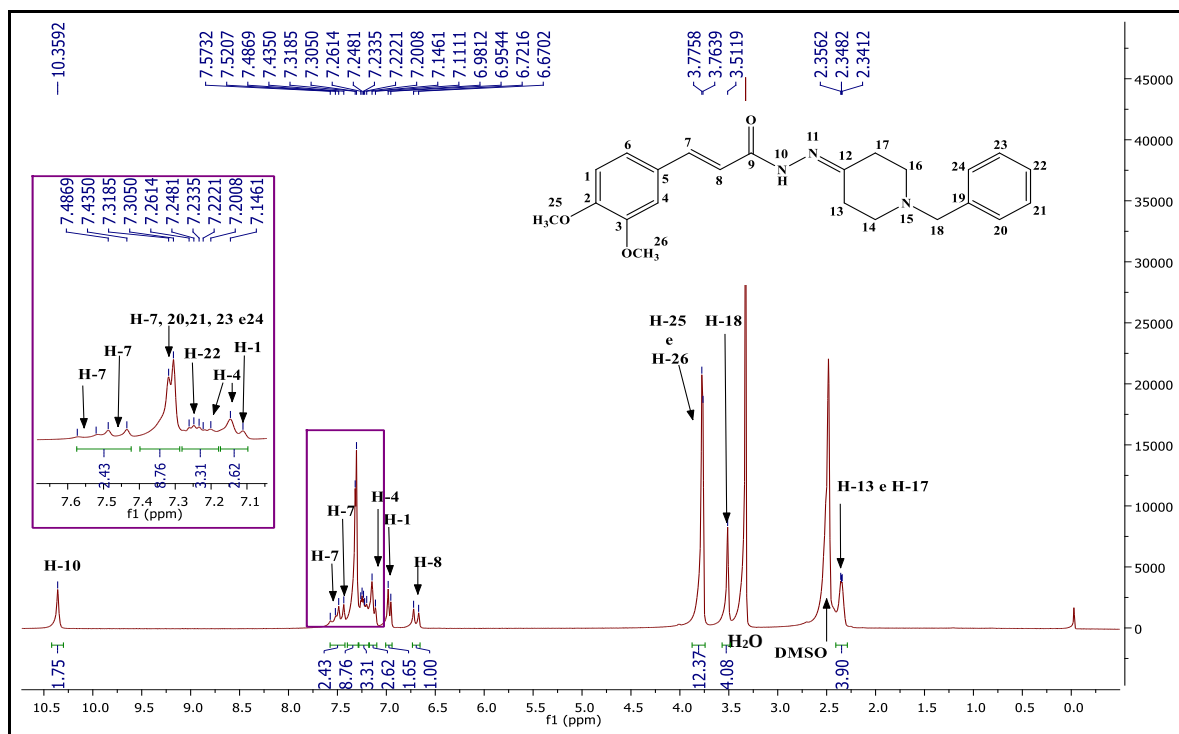


Figure 44. ^1H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dimethoxyphenyl) acryloylhydrazide (**4d**) (300 MHz, $\text{DMSO}-d_6$).

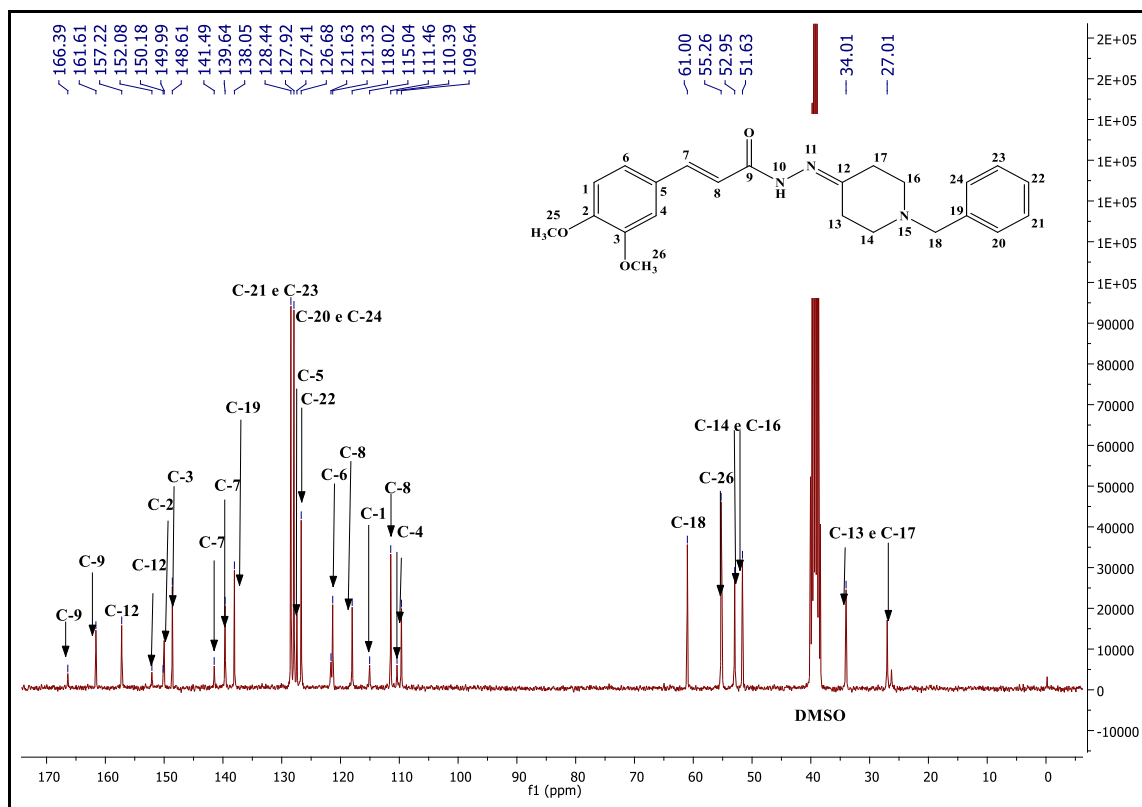


Figure 45. ¹³C NMR spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dimethoxyphenyl)acrylohydrazide (**4d**) (75 MHz, DMSO-*d*₆).

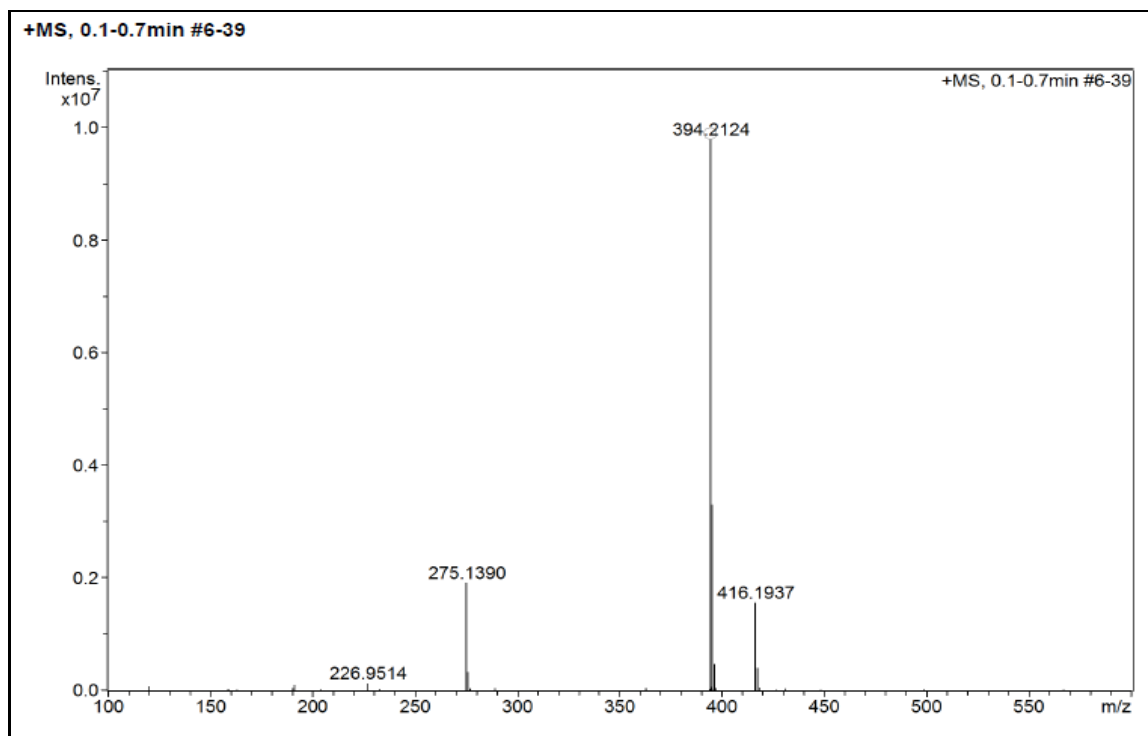


Figure 46. HR-MS spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dimethoxyphenyl)acrylohydrazide (**4d**) (ESI-MS).

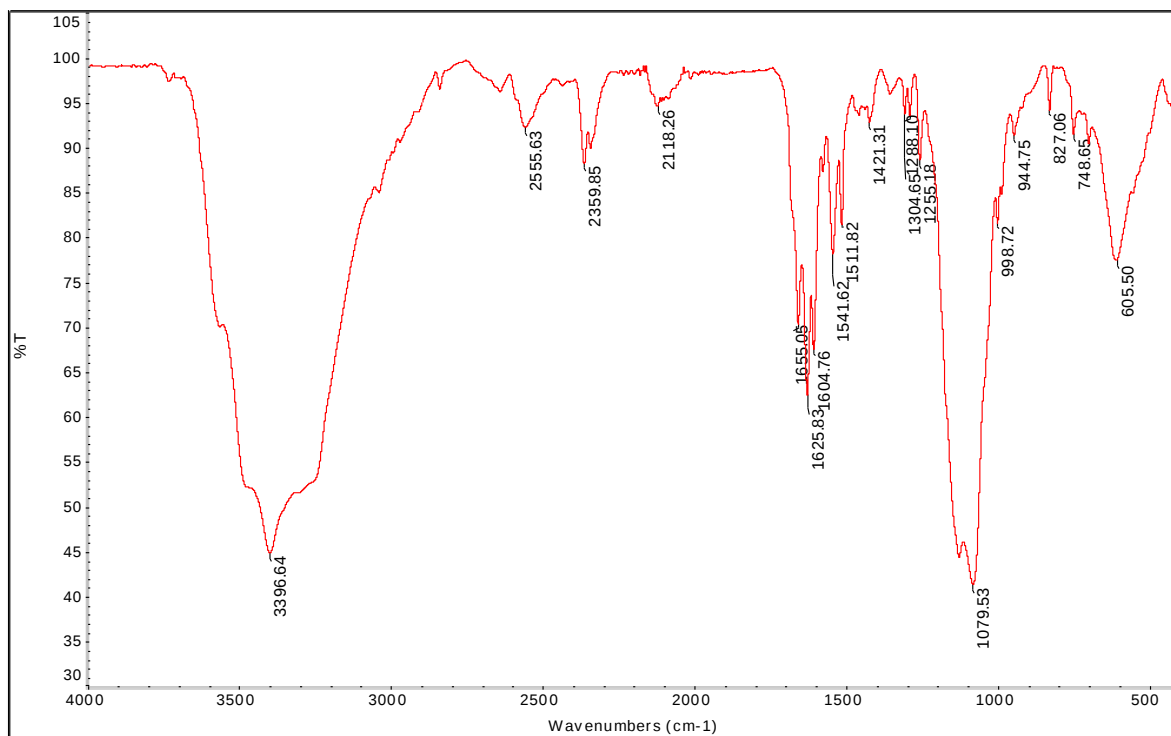


Figure 47. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-methoxyphenyl) acrylohydrazide (**4e**) (ATR).

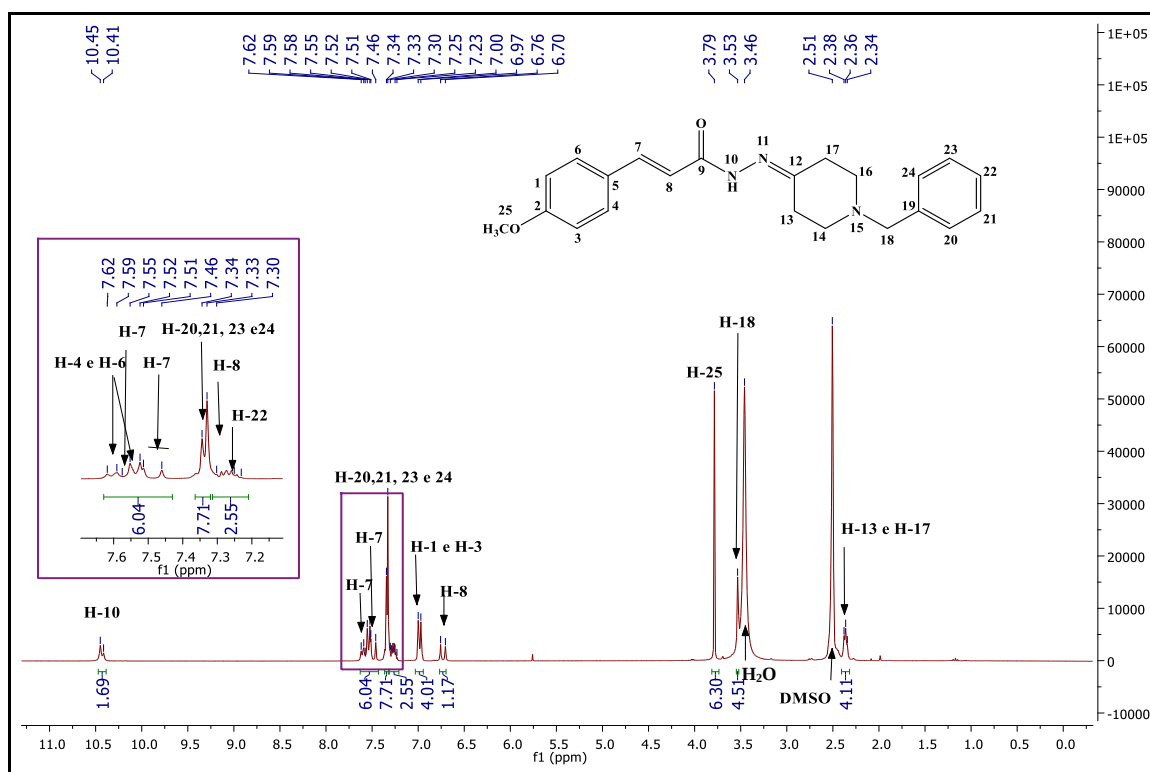


Figure 48. ¹H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-methoxyphenyl) acrylohydrazide (**4e**) (300 MHz, DMSO-*d*₆).

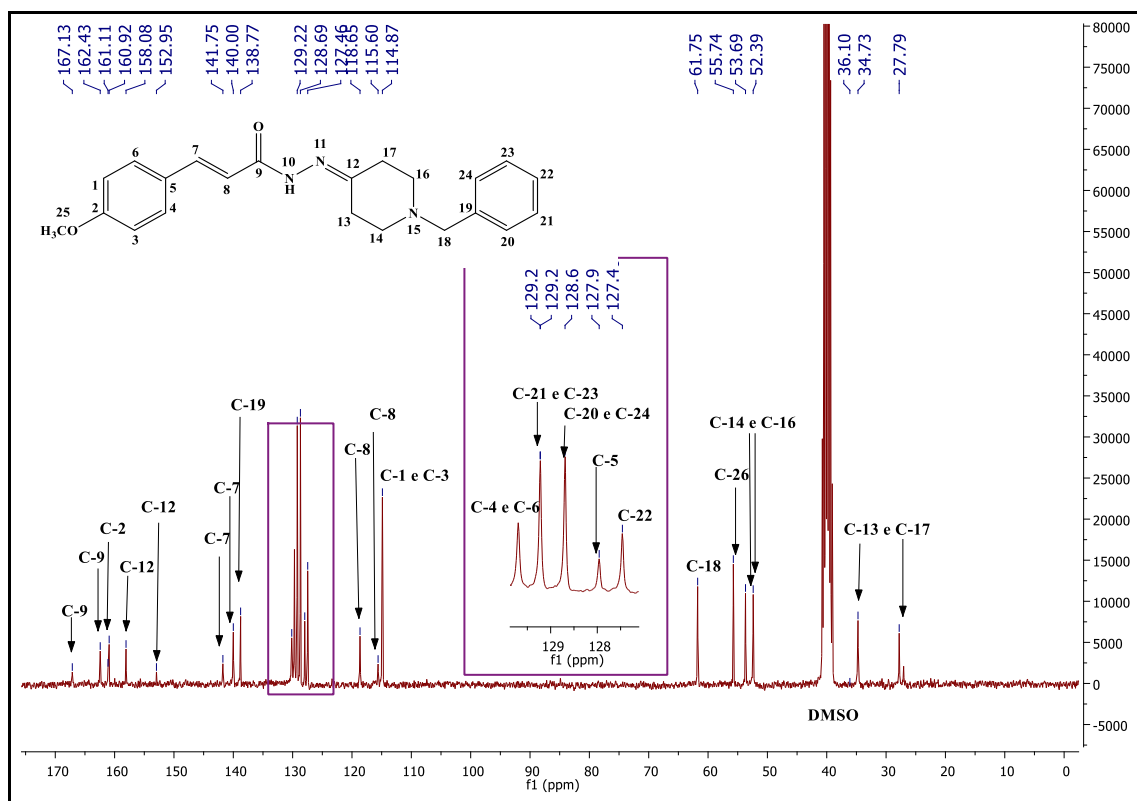


Figure 49. ^{13}C NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-methoxyphenyl)acrylohydrazide (**4e**) (75 MHz, $\text{DMSO-}d_6$).

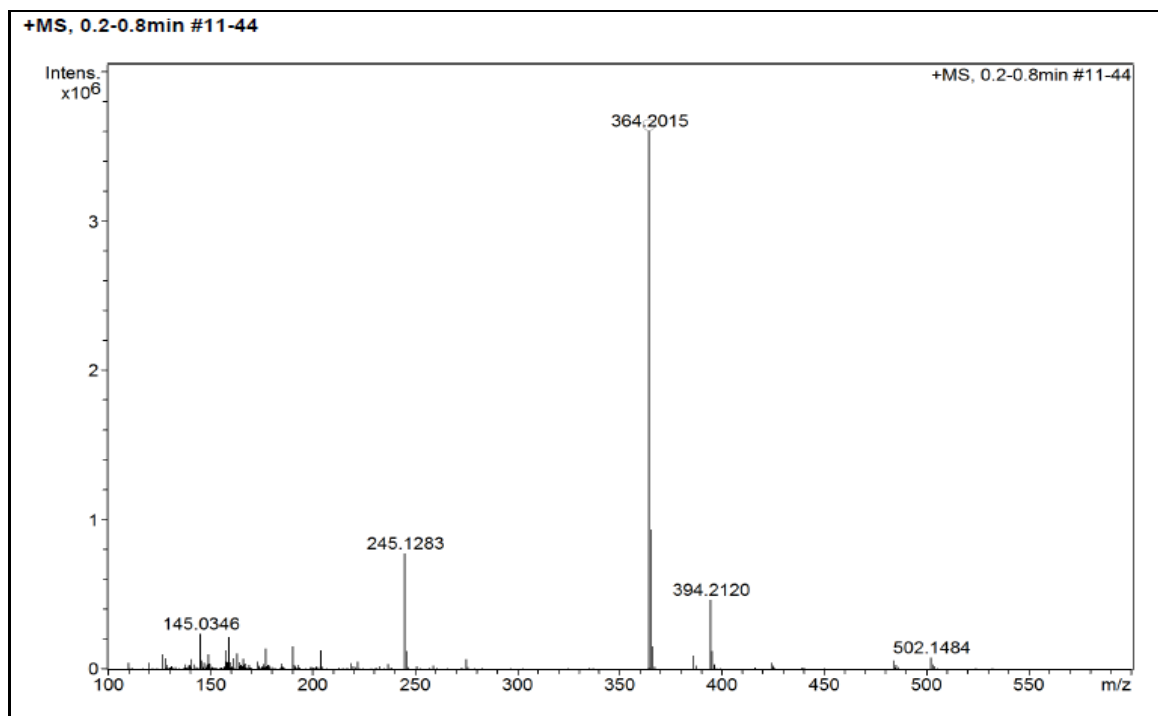


Figure 50. HR-MS spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-methoxyphenyl)acrylohydrazide (**4e**) (ESI-MS).

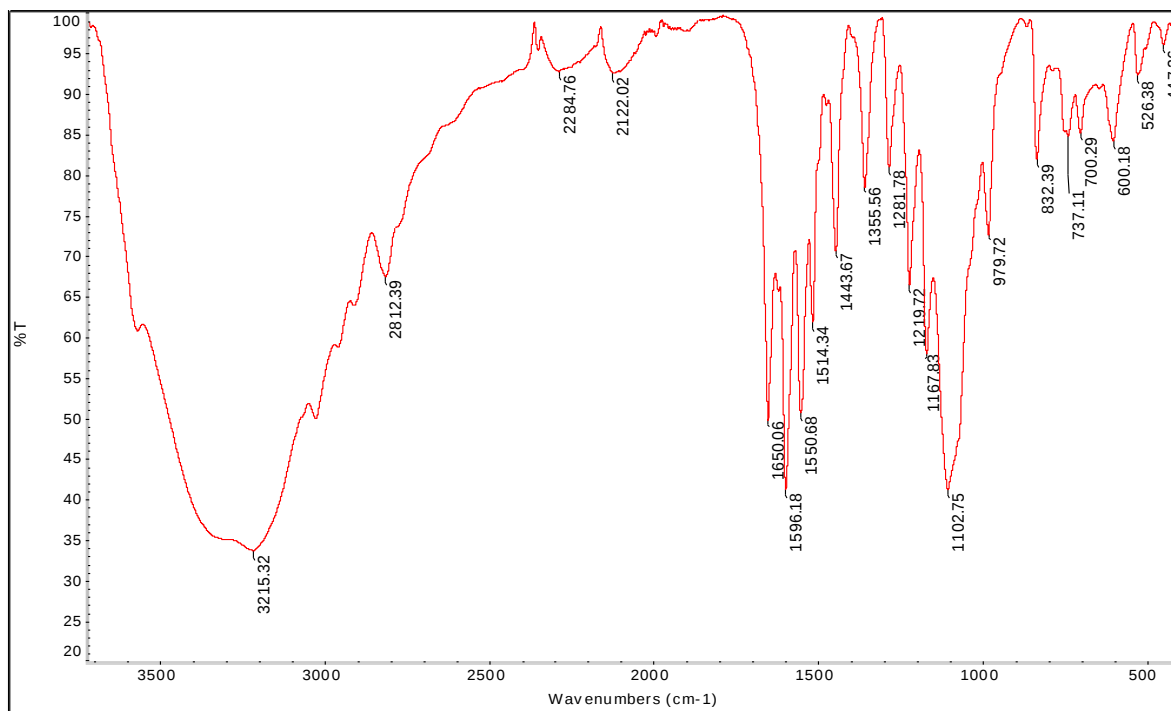


Figure 51. Absorption spectra in the infrared region of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxyphenyl) acryloylhydrazide (**4f**) (ATR).

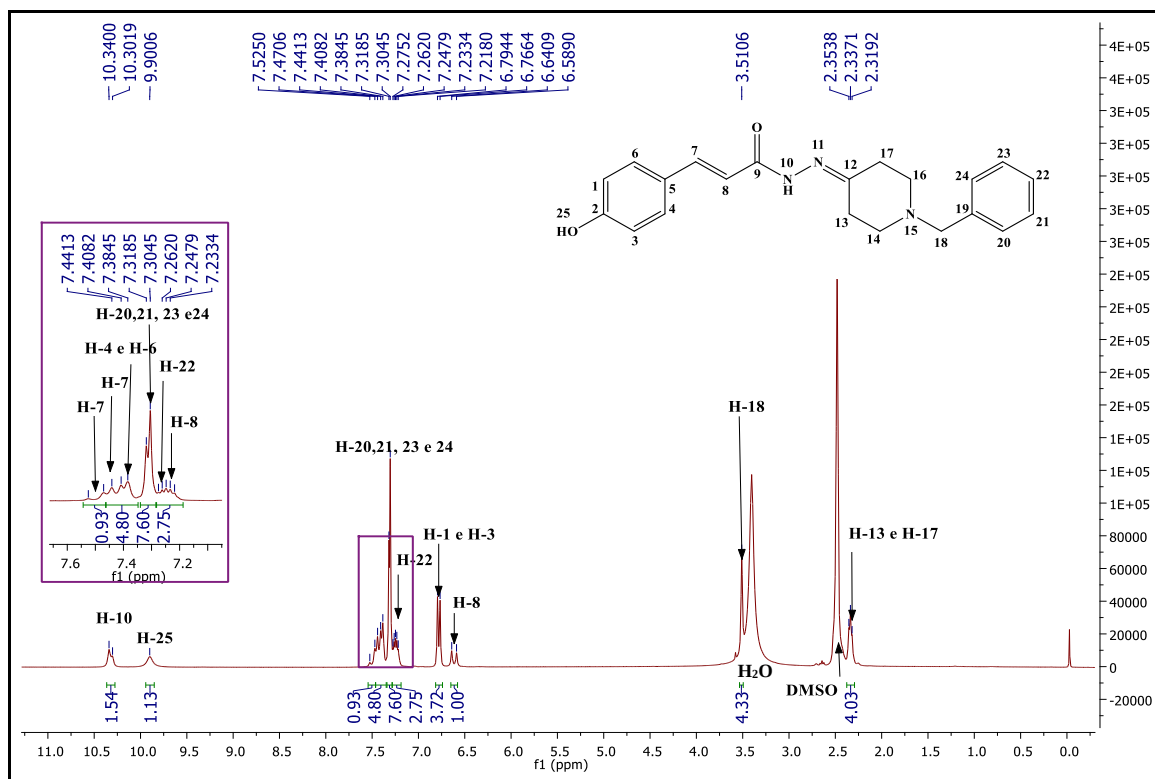


Figure 52. ¹H NMR spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxyphenyl) acryloylhydrazide (**4f**) (300 MHz, DMSO-*d*₆).

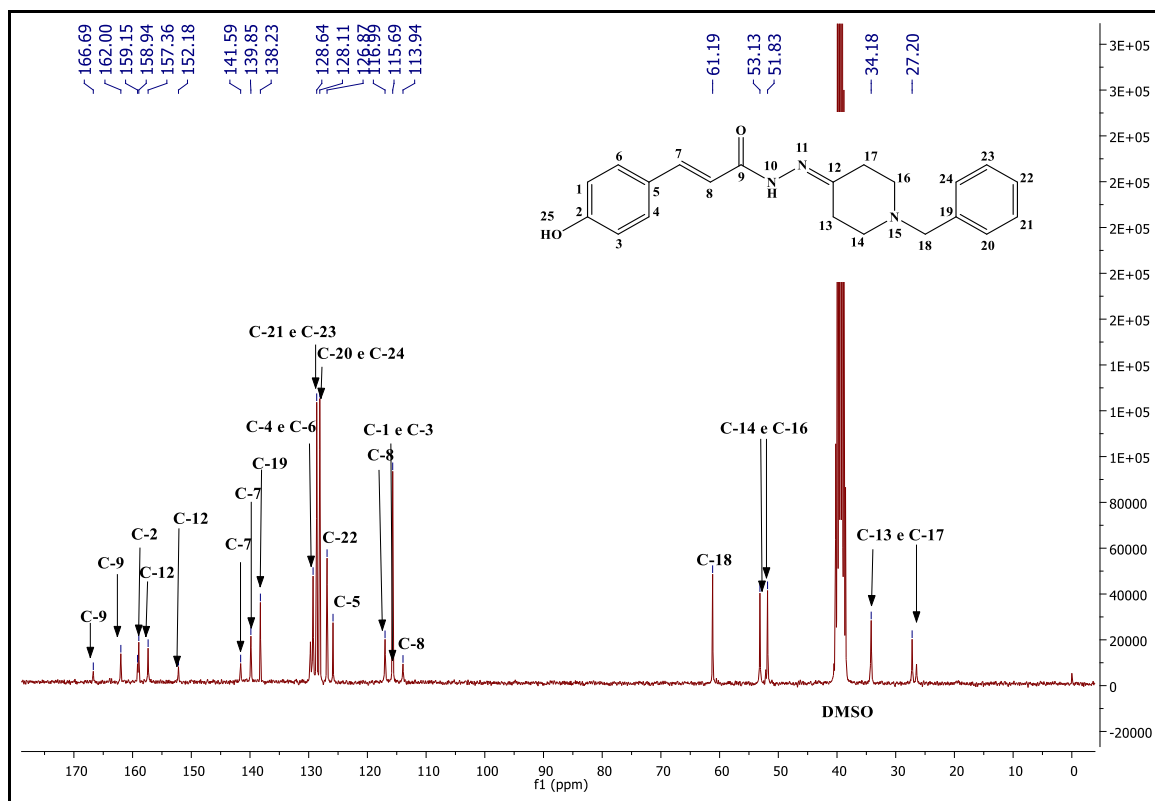


Figure 53. ^{13}C NMR spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxyphenyl)acryloylhydrazide (**4f**) (75 MHz, $\text{DMSO-}d_6$).

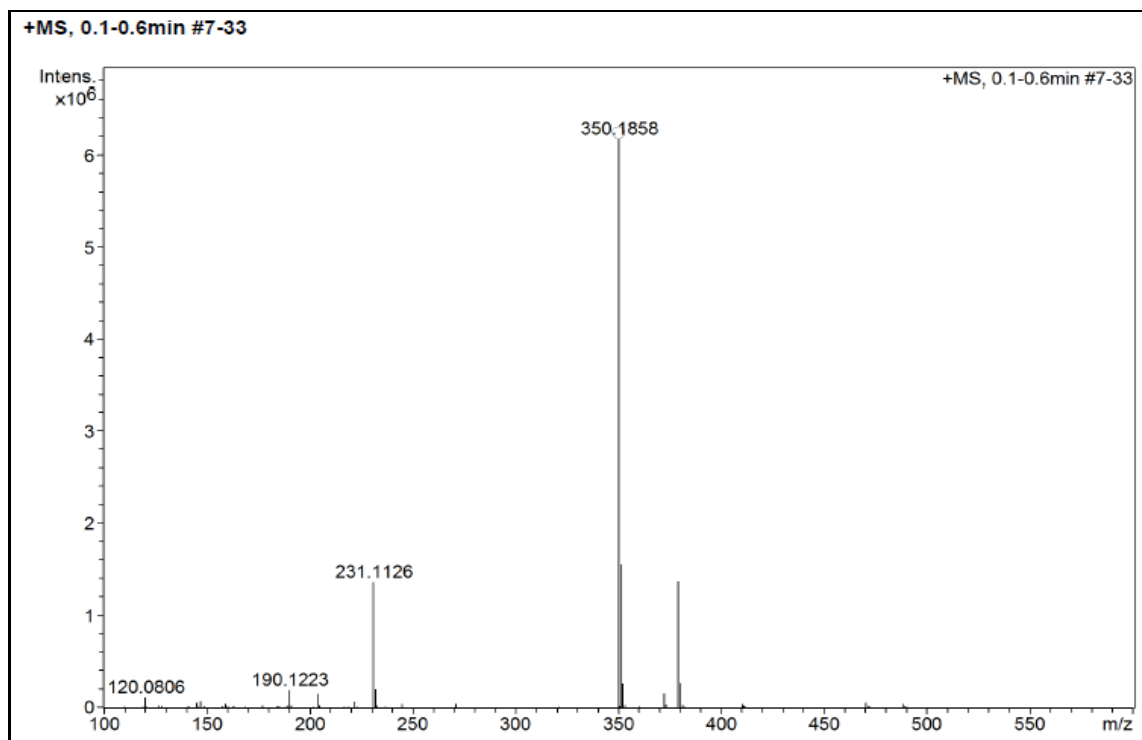


Figure 54. HR-MS spectra of *(E)*-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxyphenyl)acryloylhydrazide (**4f**) (ESI-MS).

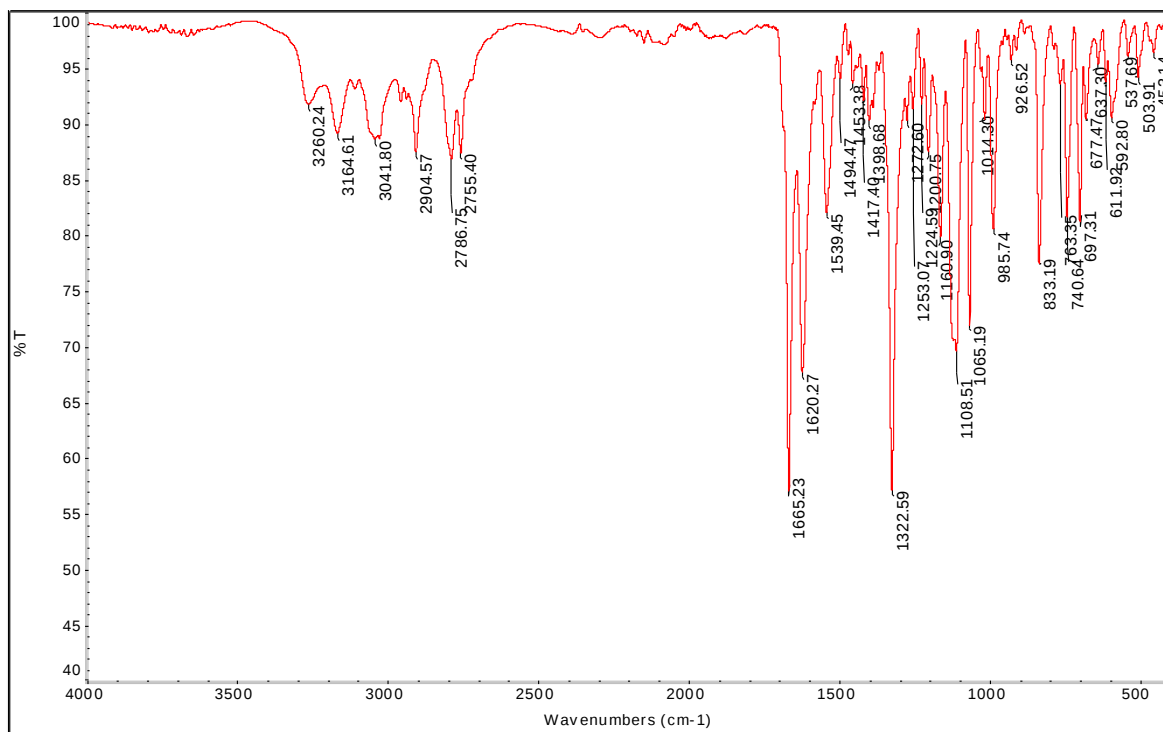


Figure 55. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-(trifluoromethyl)phenyl) acrylohydrazide (**4g**) (ATR).

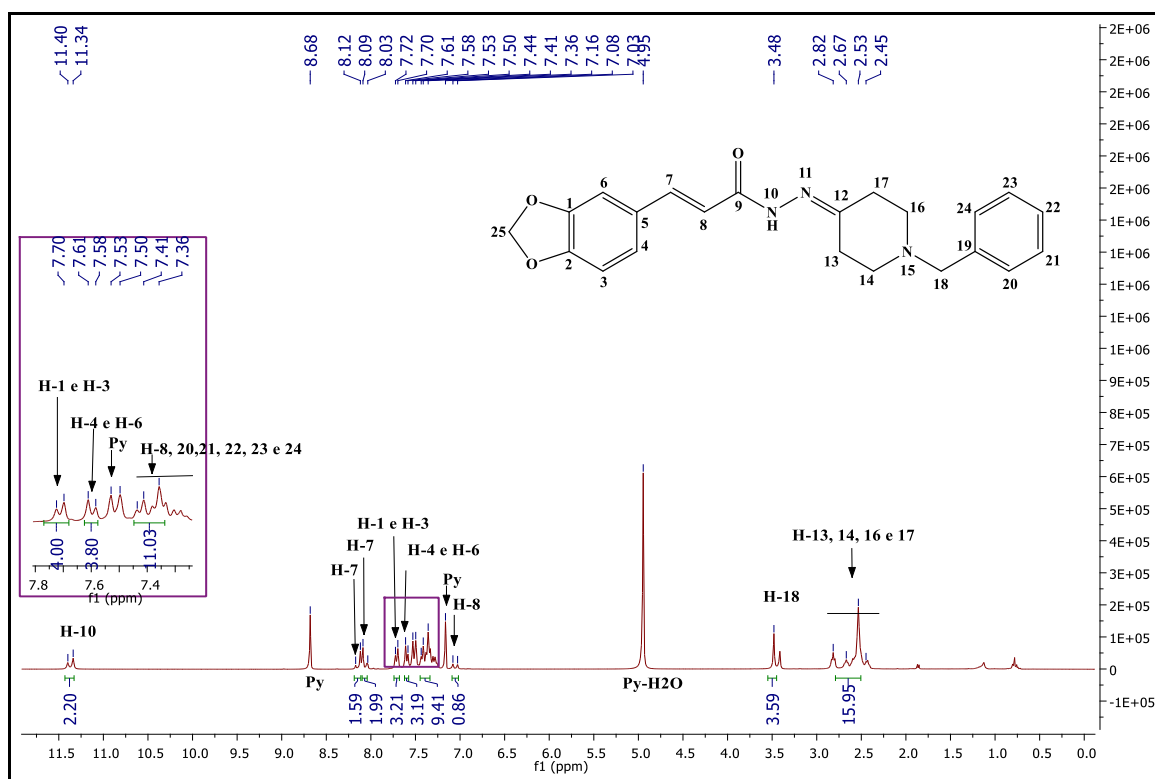


Figure 56. ¹H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-(trifluoromethyl)phenyl) acrylohydrazide (**4g**) (300 MHz, DMSO-*d*₆).

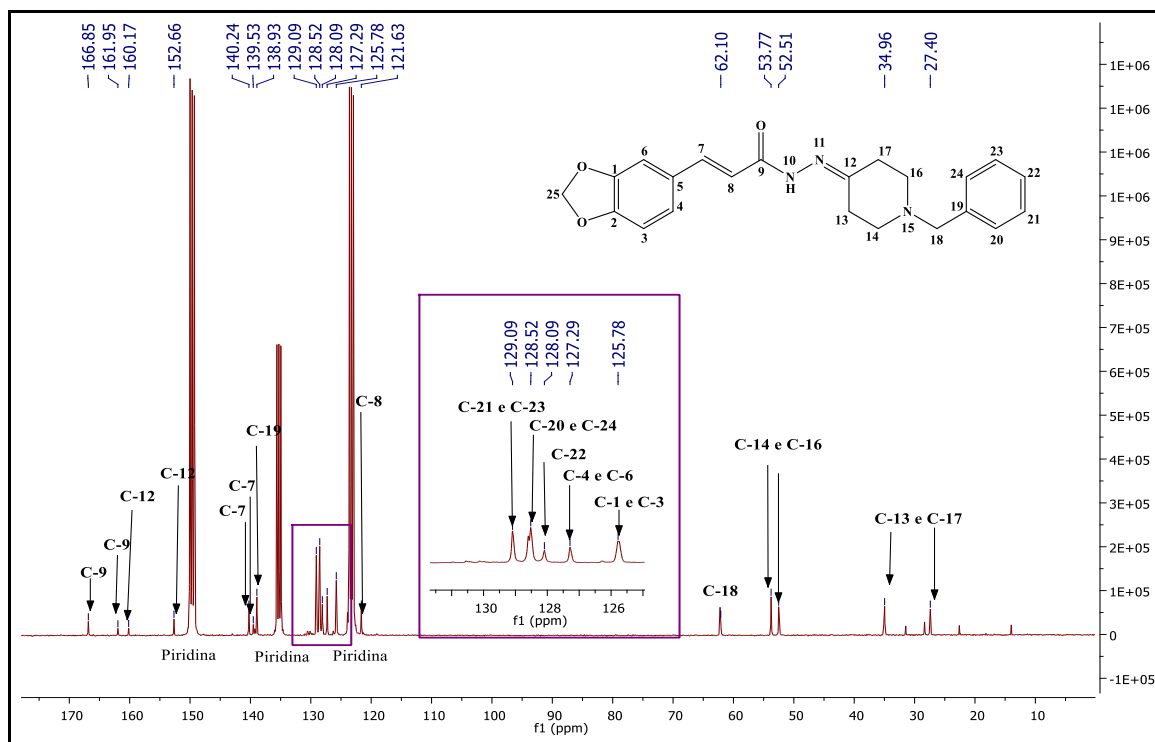


Figure 57. ^{13}C NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-(trifluoromethyl)phenyl)acrylohydrazide (**4g**) (75 MHz, $\text{DMSO}-d_6$).

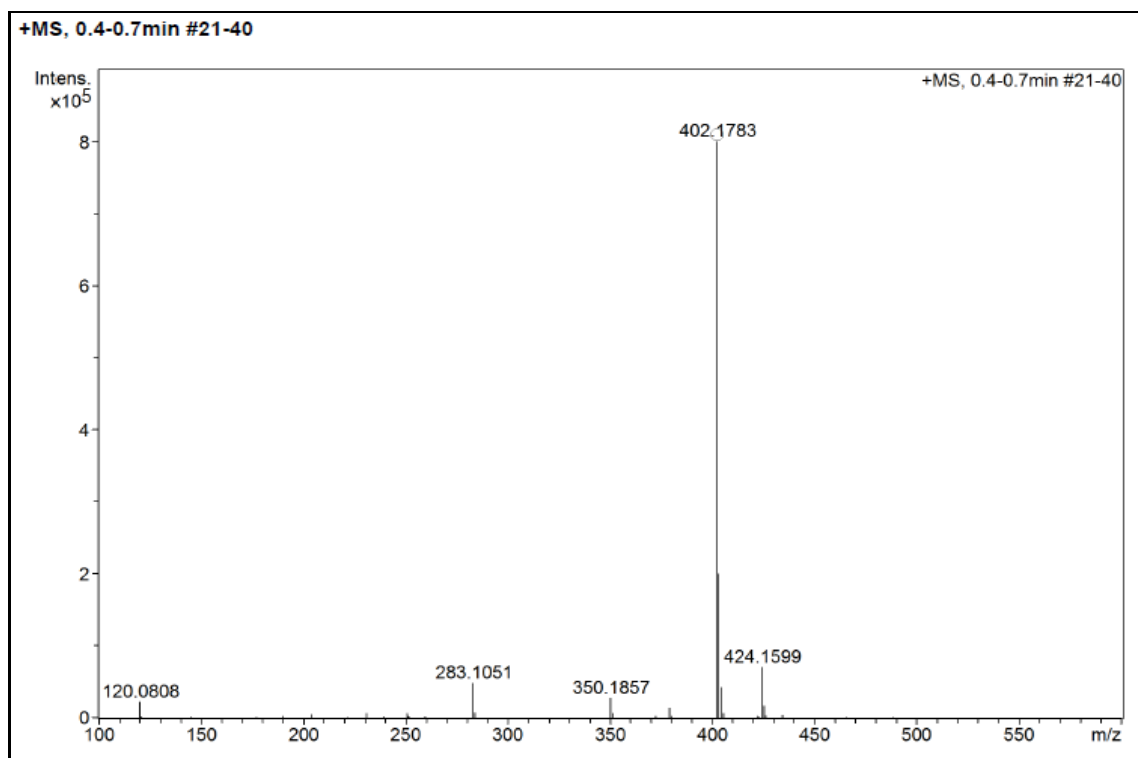


Figure 58. HR-MS spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-(trifluoromethyl)phenyl)acrylohydrazide (**4g**) (ESI-MS).

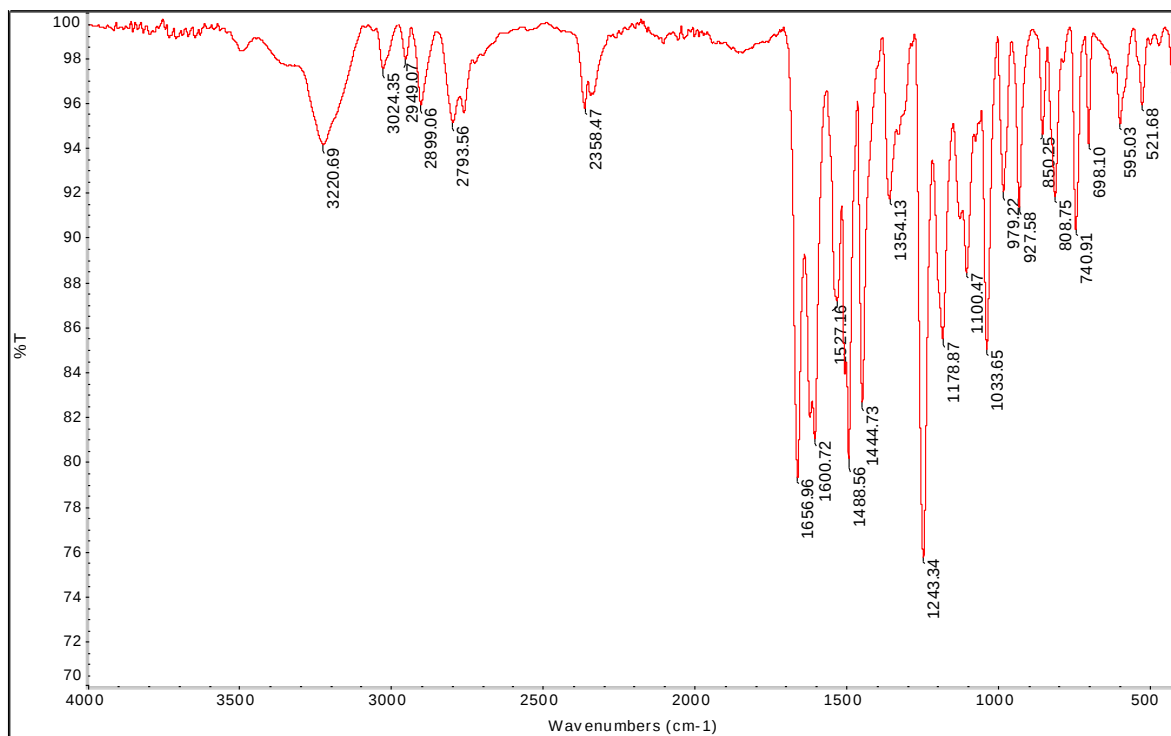


Figure 59. Absorption spectra in the infrared region of *(E)*-3-(benzo[d][1,3]dioxol-5-yl)-*N'*-(1-benzylpiperidin-4-ylidene)acrylohydrazide (**4h**) (ATR).

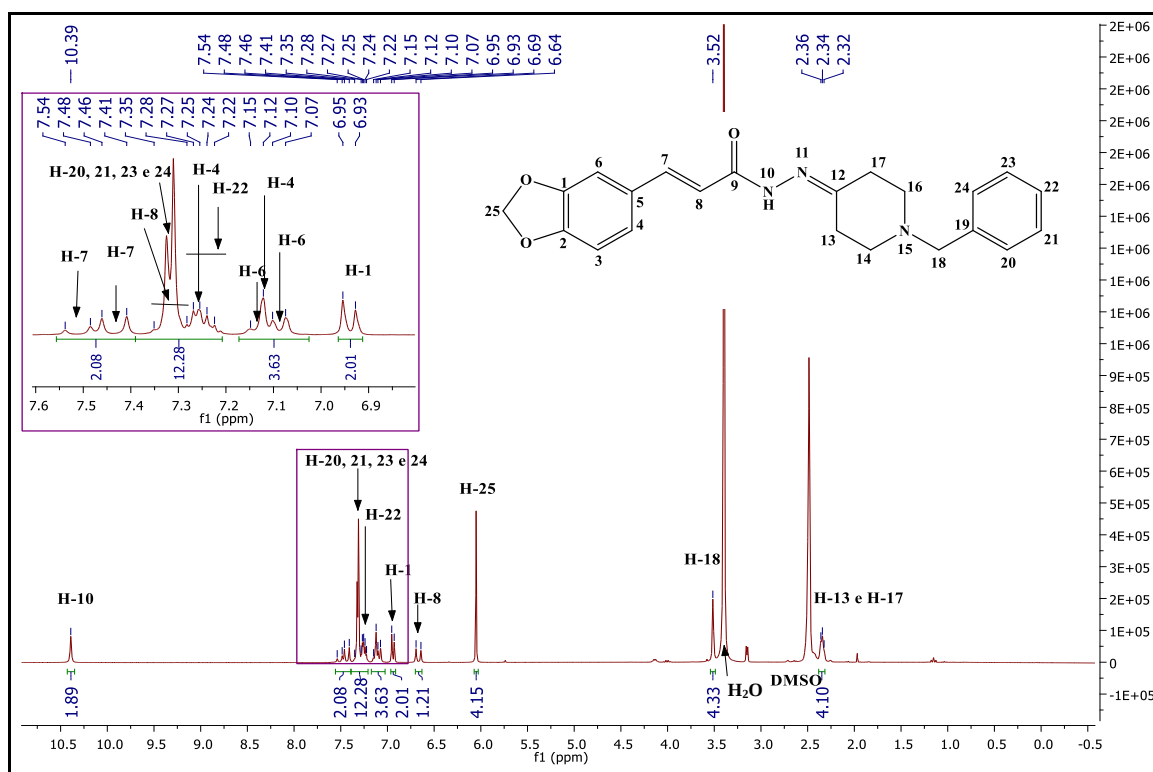


Figure 60. ¹H NMR spectra of *(E)*-3-(benzo[d][1,3]dioxol-5-yl)-*N'*-(1-benzylpiperidin-4-ylidene)acrylohydrazide (**4h**) (300 MHz, DMSO-*d*₆).

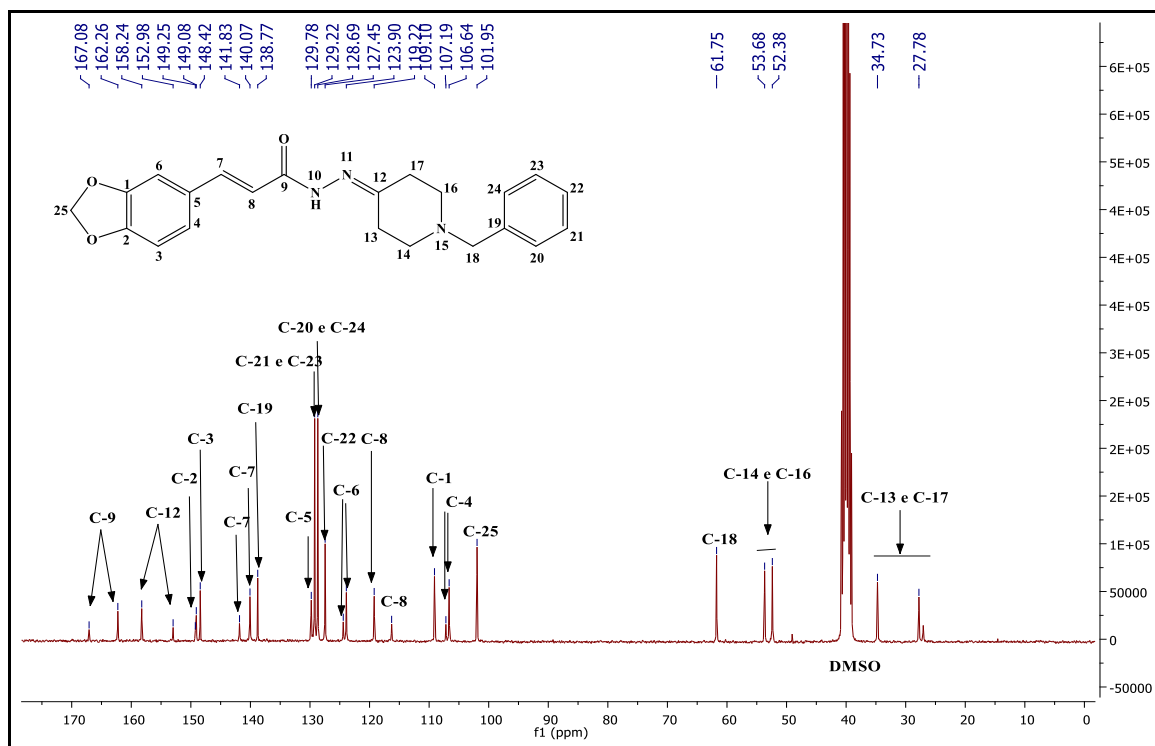


Figure 61. ¹³C NMR spectra of (*E*)-3-(benzo[d][1,3]dioxol-5-yl)-*N'*-(1-benzylpiperidin-4-ylidene)acrylohydrazide (**4h**) (75 MHz, DMSO-*d*₆).

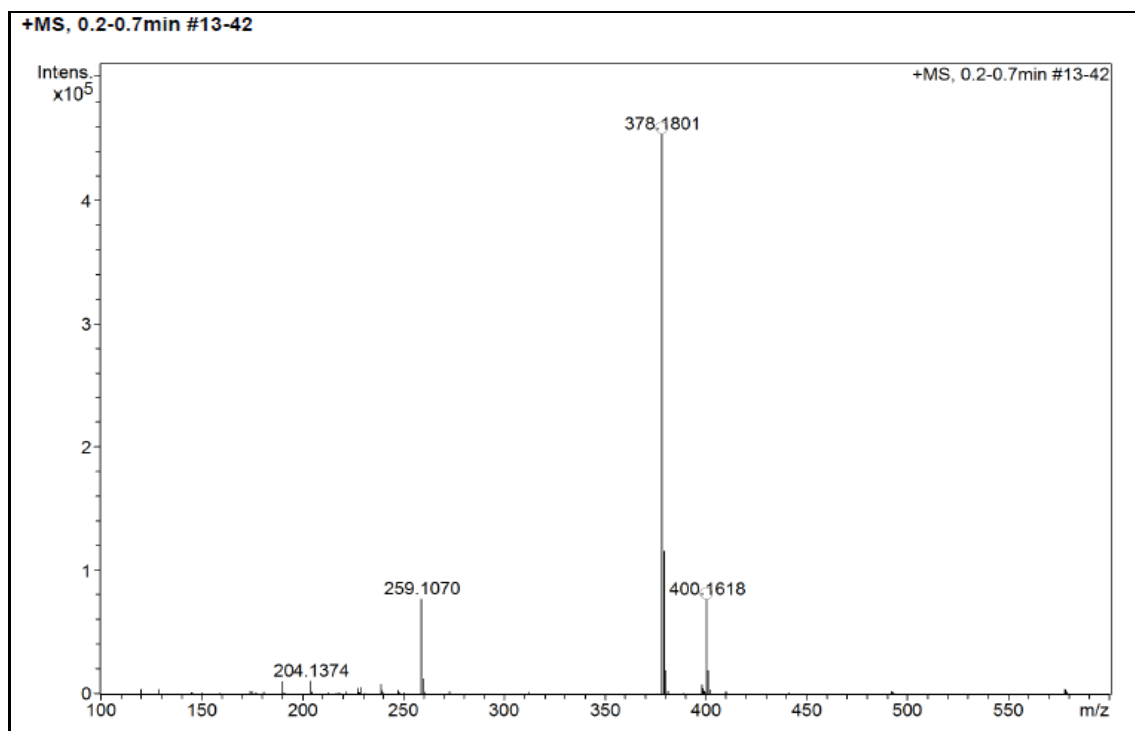


Figure 62. HR-MS spectra of (*E*)-3-(benzo[d][1,3]dioxol-5-yl)-*N'*-(1-benzylpiperidin-4-ylidene)acrylohydrazide (**4h**) (ESI-MS).

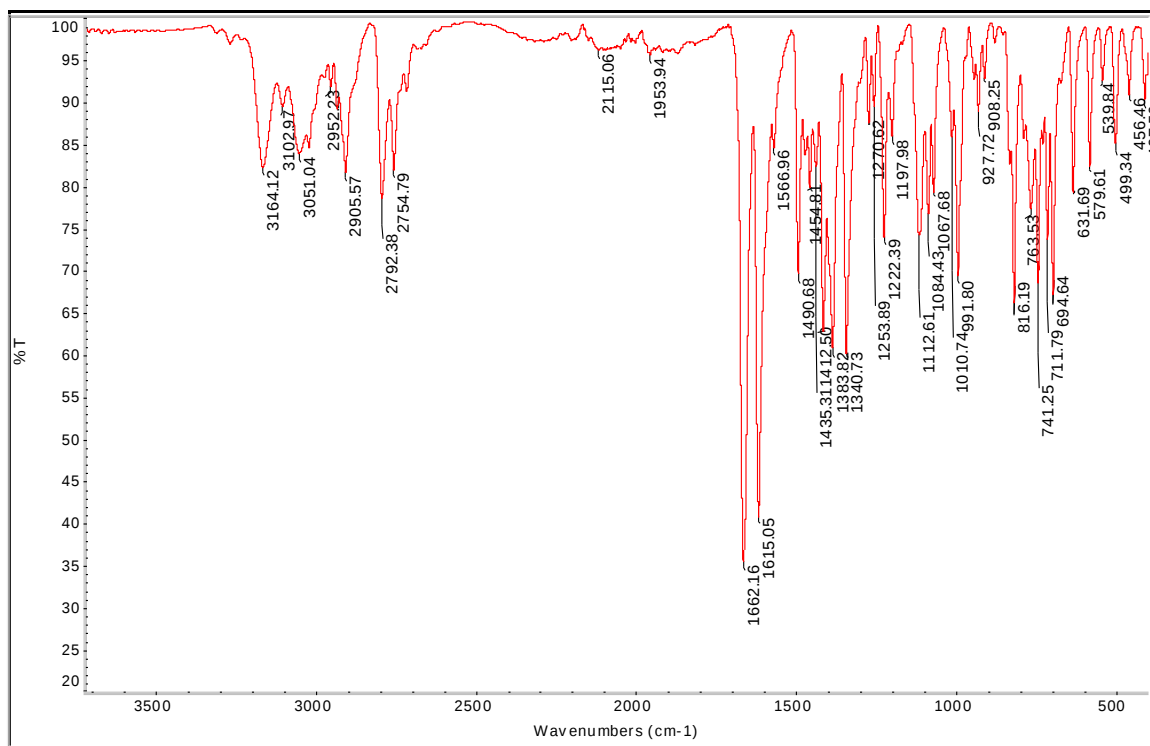


Figure 63. Absorption spectra in the infrared region of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-chlorophenyl) acrylohydrazide (**4i**) (ATR).

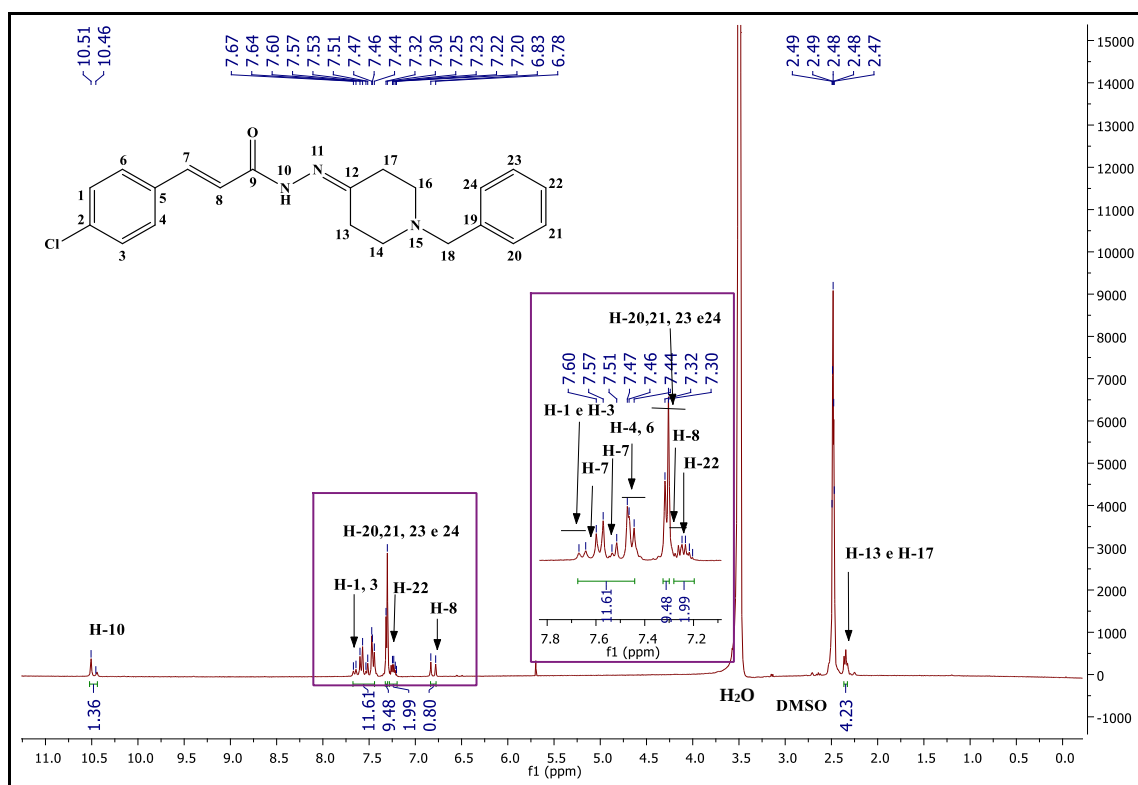


Figure 64. ¹H NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-chlorophenyl) acrylohydrazide (**4i**) (300 MHz, DMSO-d₆).

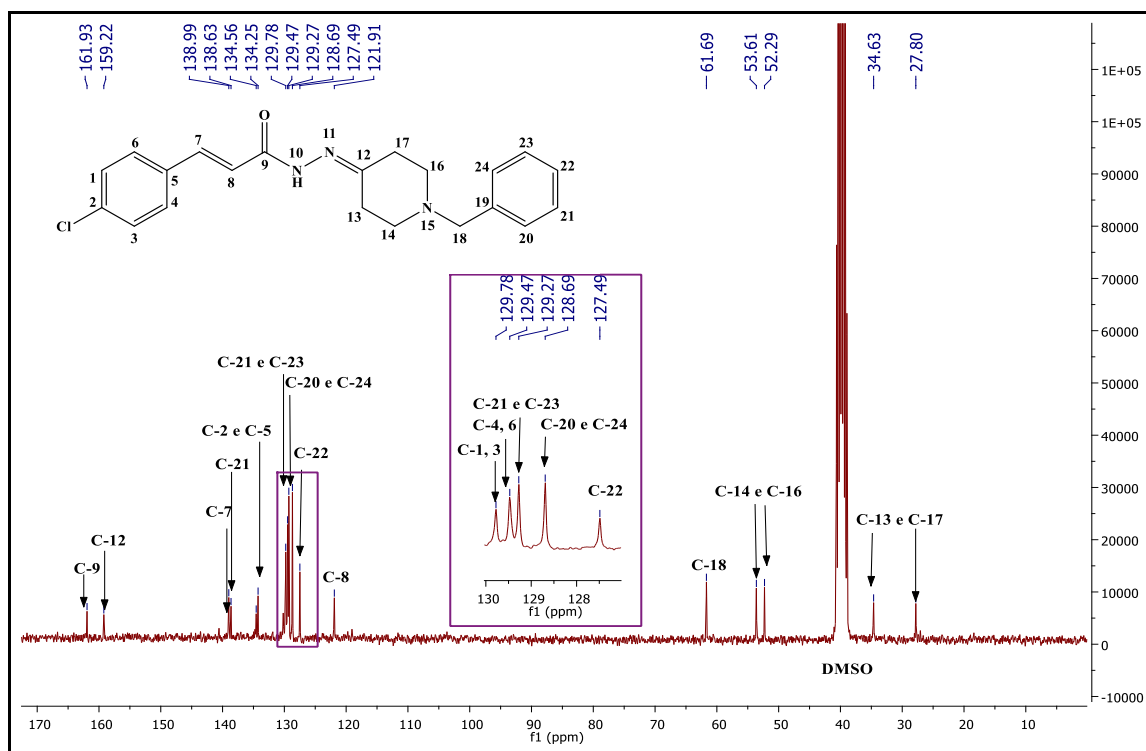


Figure 65. ^{13}C NMR spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-chlorophenyl)acrylohydrazide (**4i**) (75 MHz, $\text{DMSO-}d_6$).

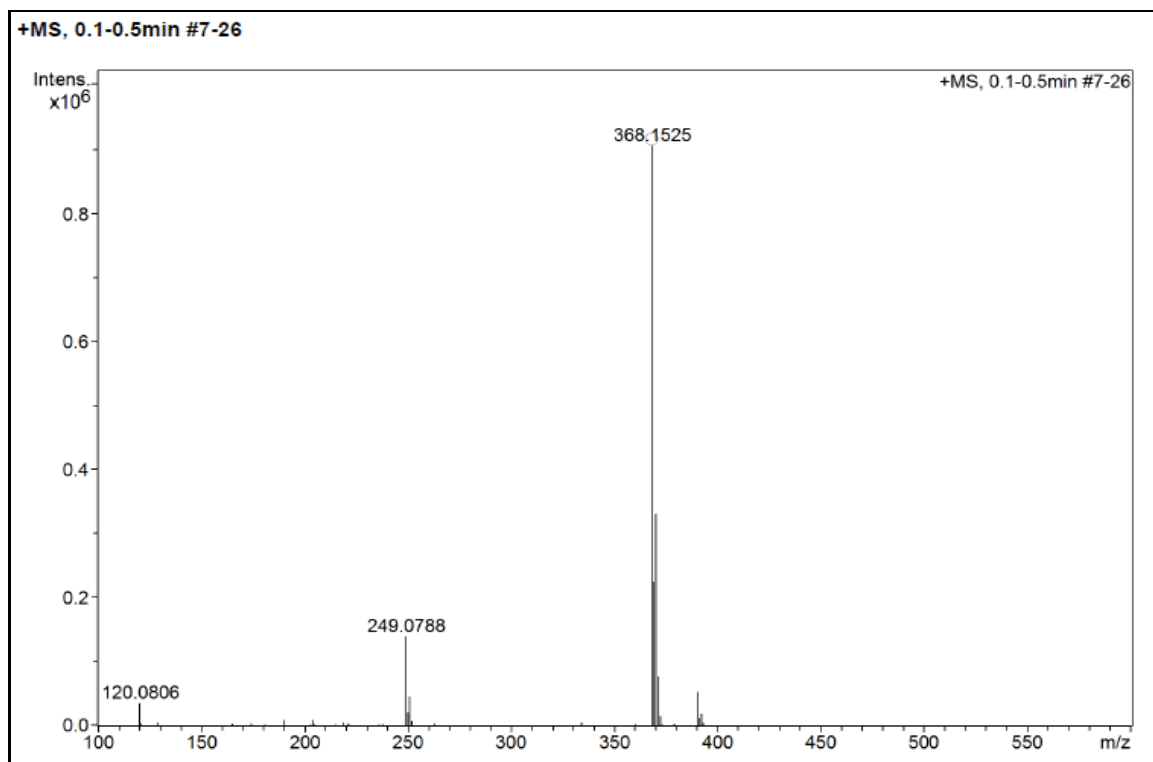


Figure 66. HR-MS spectra of (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-chlorophenyl)acrylohydrazide (**4i**) (ESI-MS).

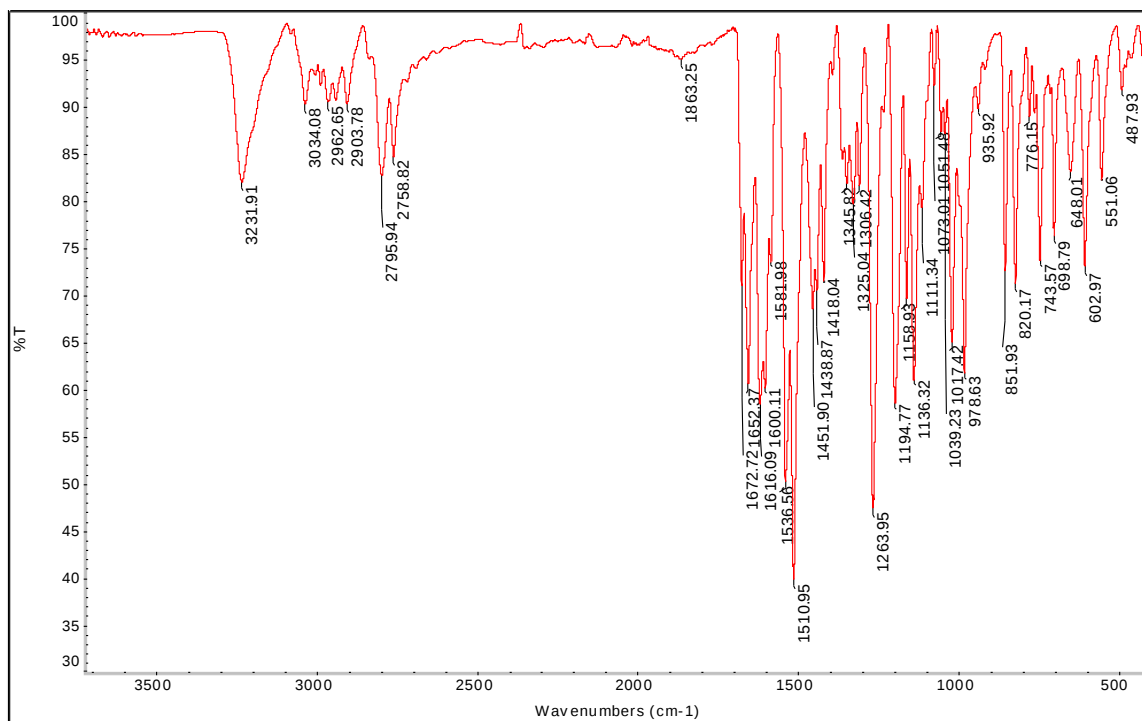


Figure 67. Absorption spectra in the infrared region of *N'*-(1-benzylpiperidin-4-ylidene)cinnamohydrazide (**4j**) (ATR).

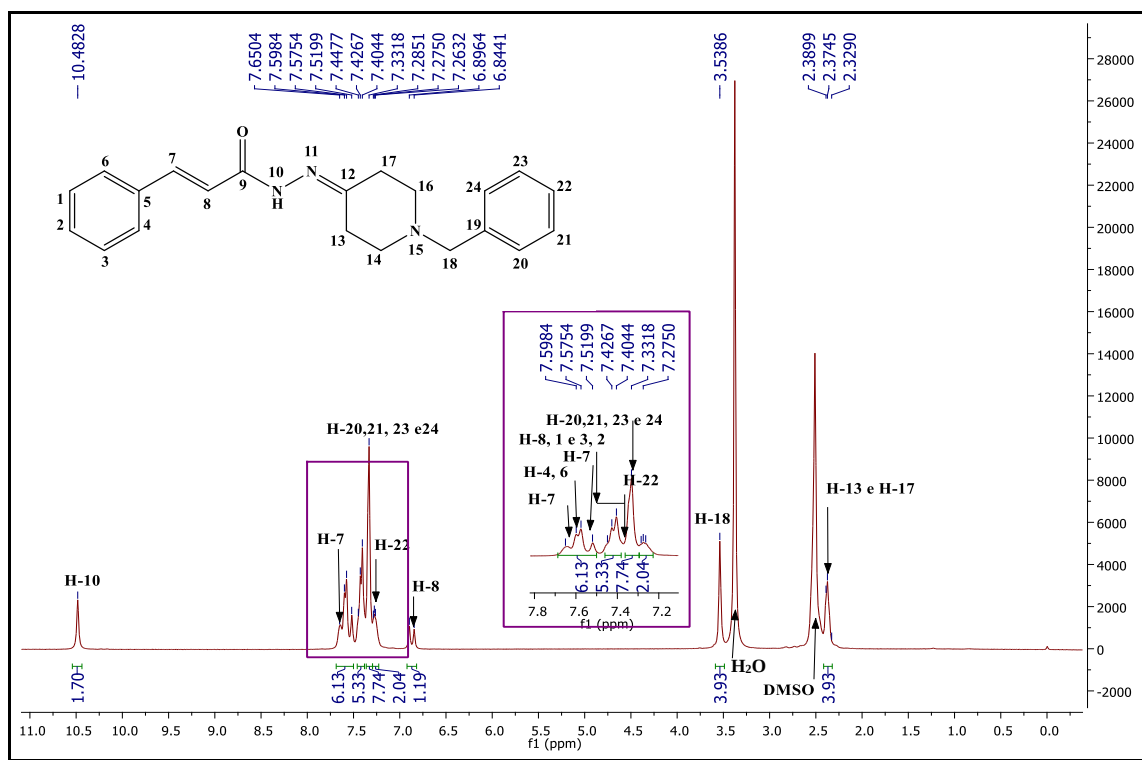


Figure 68. ¹H NMR spectra of *N'*-(1-benzylpiperidin-4-ylidene)cinnamohydrazide (**4j**) (300 MHz, DMSO-*d*₆).

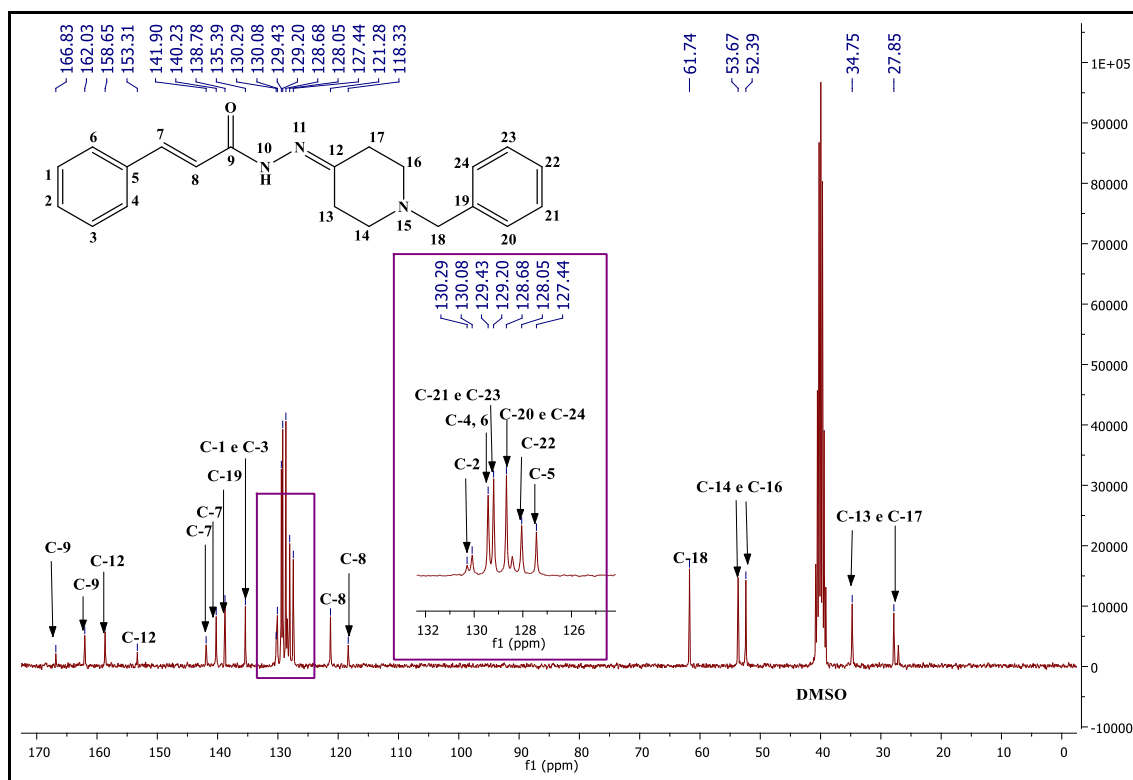


Figure 69. ¹³C NMR spectra of *N'*-(1-benzylpiperidin-4-ylidene)cinnamohydrazide (**4j**) (75 MHz, DMSO-*d*₆).

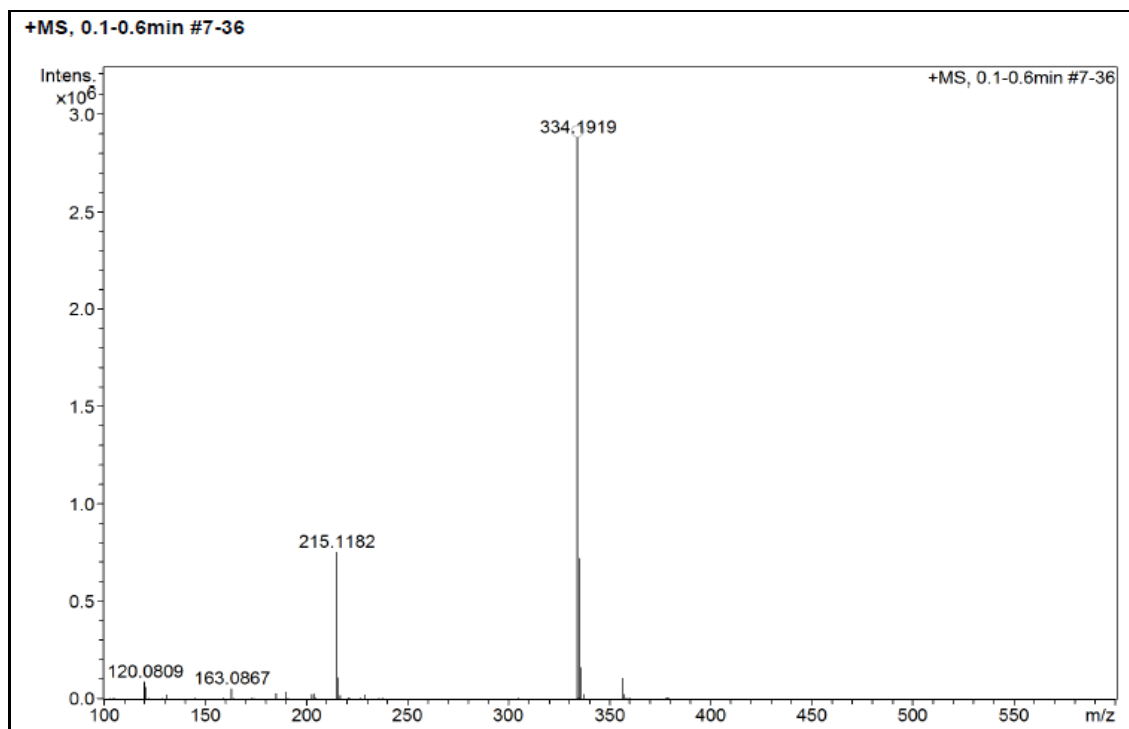


Figure 70. HR-MS spectra of *N'*-(1-benzylpiperidin-4-ylidene)cinnamohydrazide (**4j**) (ESI-MS).

HPLC Chromatograms of compounds 4a-j

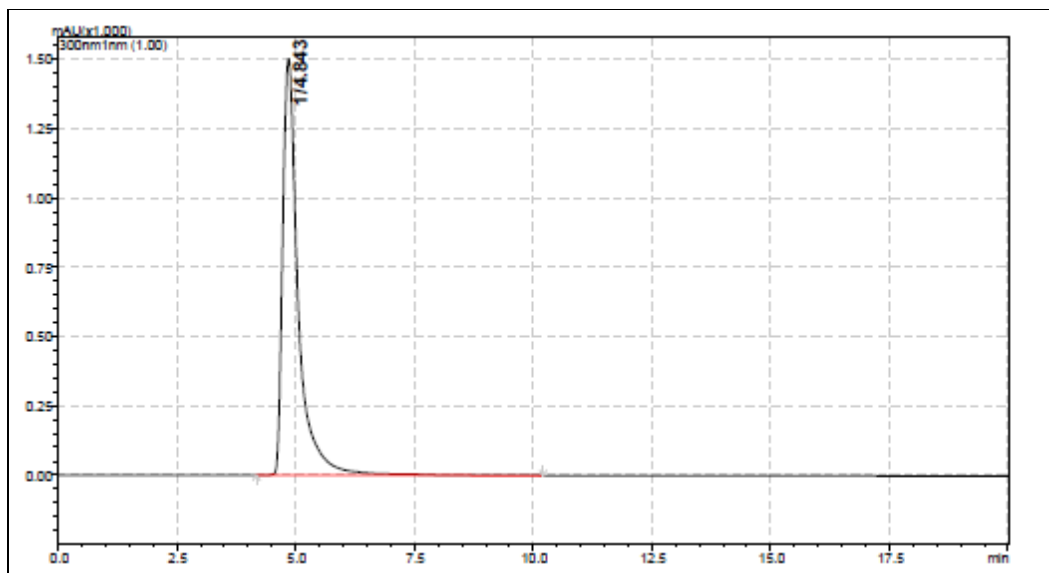


Figure 71. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxy-3-methoxyphenyl) acrylohydrazide (**4a**).

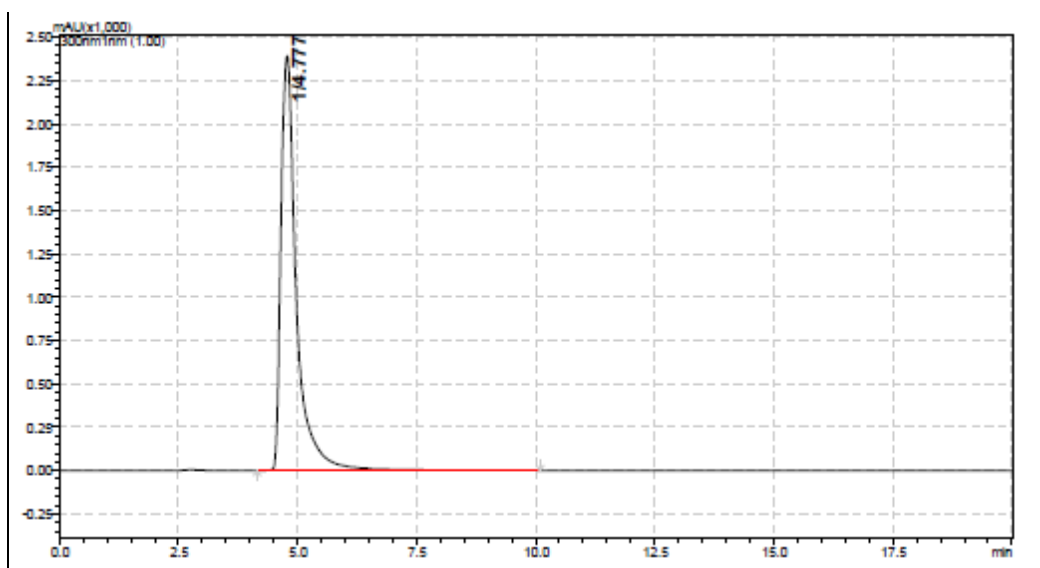


Figure 72. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3-hydroxy-4-methoxyphenyl) acrylohydrazide (**4b**).

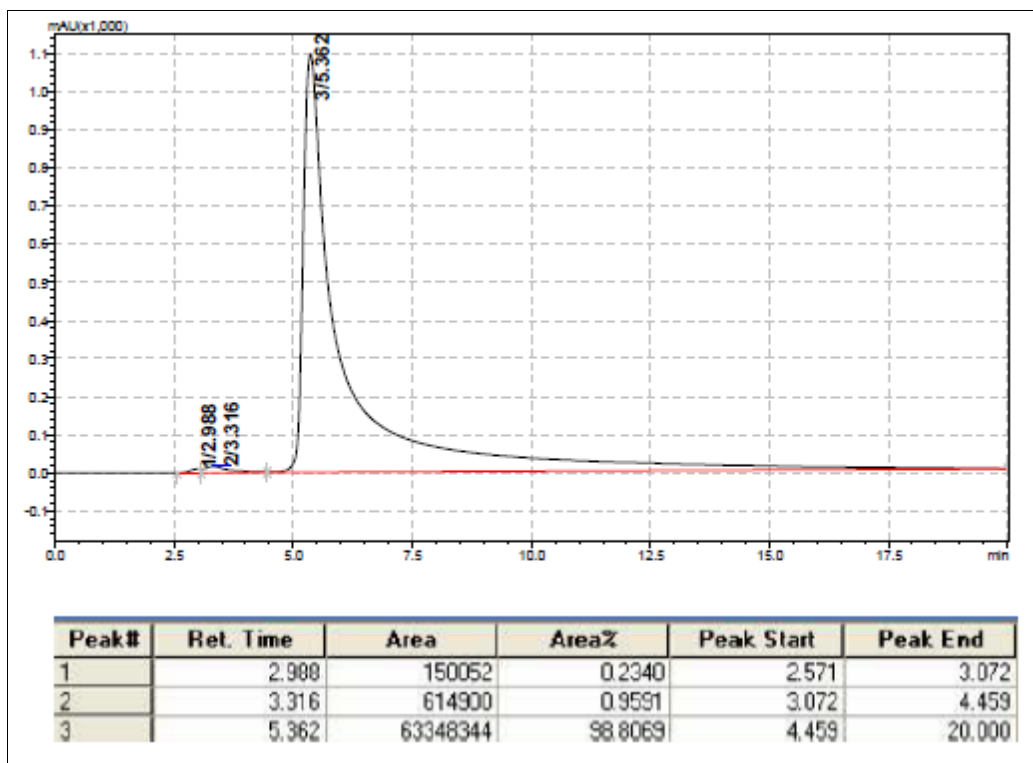


Figure 73. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dihydroxyphenyl) acrylohydrazide (**4c**).

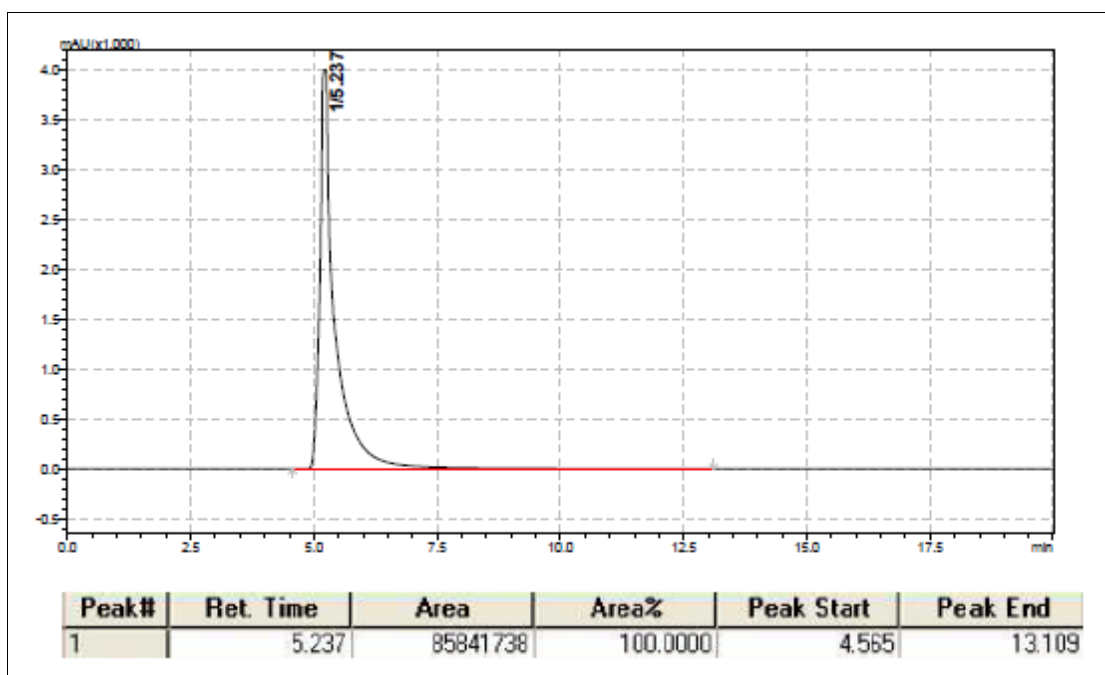


Figure 74. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(3,4-dimethoxyphenyl) acrylohydrazide (**4d**).

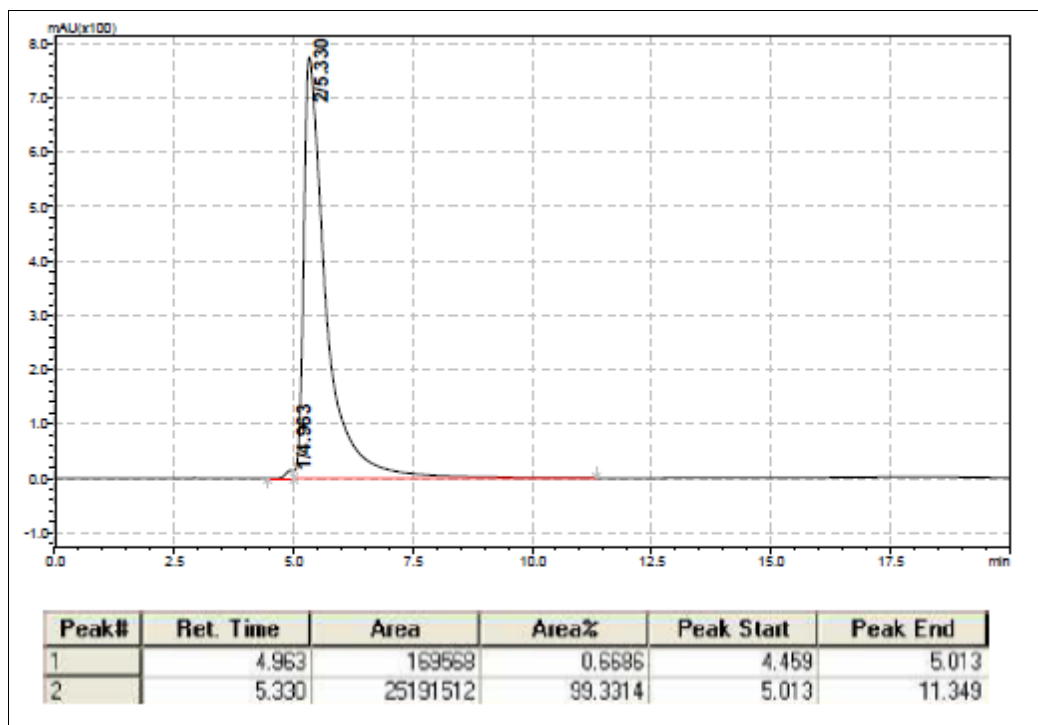


Figure 75. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-methoxyphenyl) acrylohydrazide (**4e**).

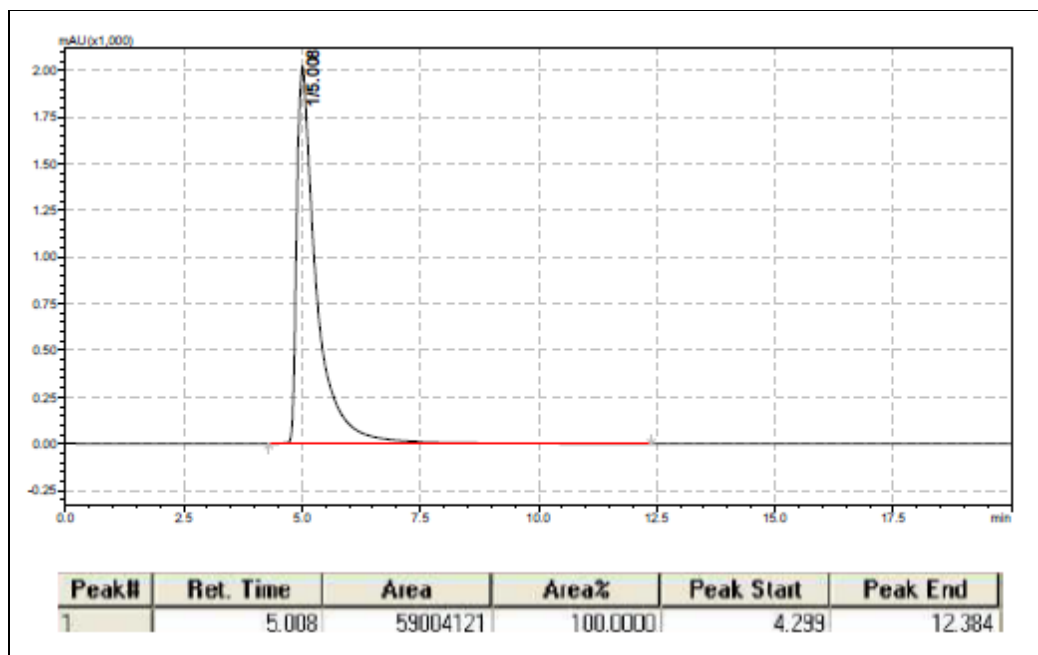


Figure 76. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-hydroxyphenyl) acrylohydrazide (**4f**).

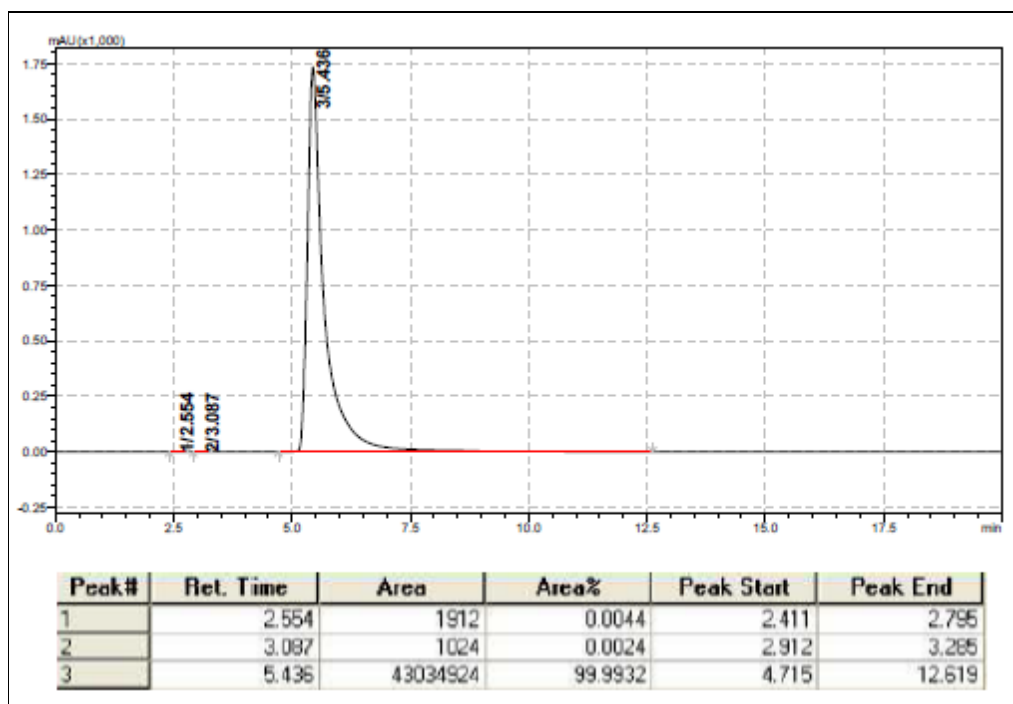


Figure 77. HPLC chromatogram of compound (*E*)-*N'*-(1-benzylpiperidin-4-ylidene)-3-(4-(trifluoromethyl)phenyl) acrylohydrazide (**4g**).

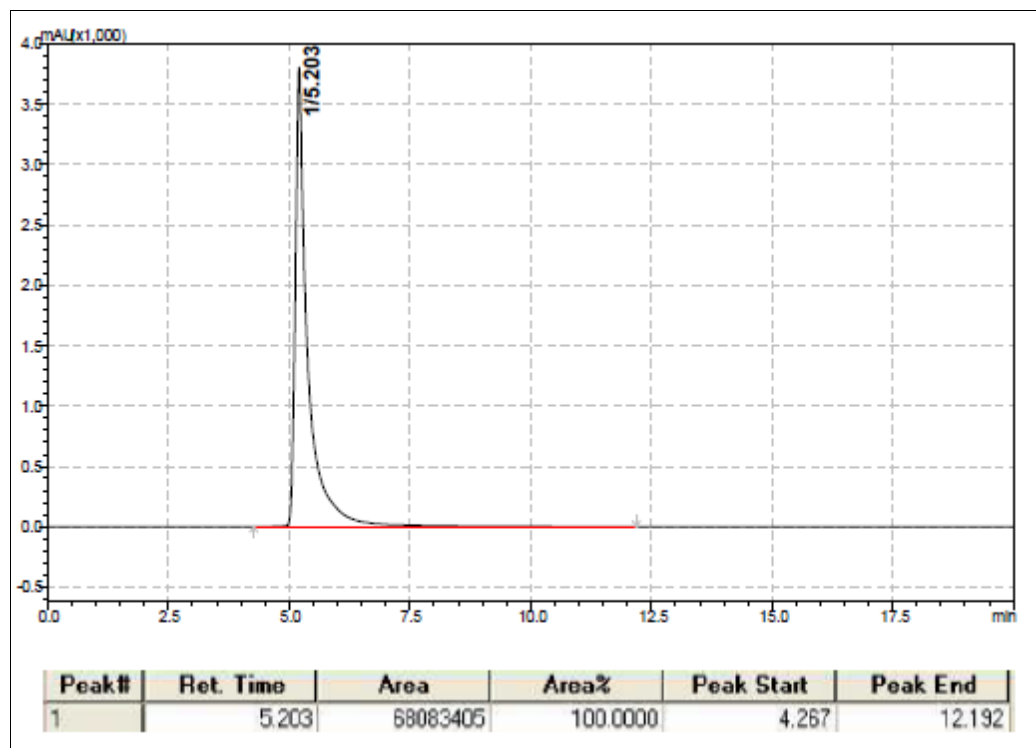


Figure 78. HPLC chromatogram of compound (*E*)-3-(benzo[d][1,3]dioxol-5-yl)-*N'*-(1-benzylpiperidin-4-ylidene) acrylohydrazide (**4h**).

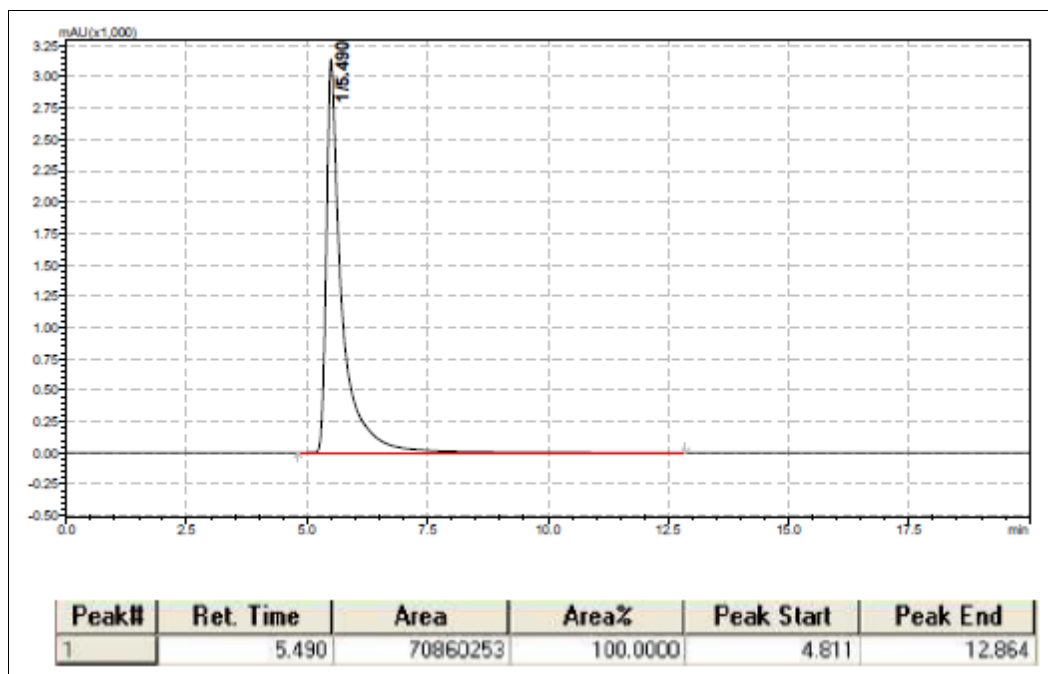


Figure 79. HPLC chromatogram of compound (*E*)-*N*-(1-benzylpiperidin-4-ylidene)-3-(4-chlorophenyl) acrylohydrazide (**4i**).

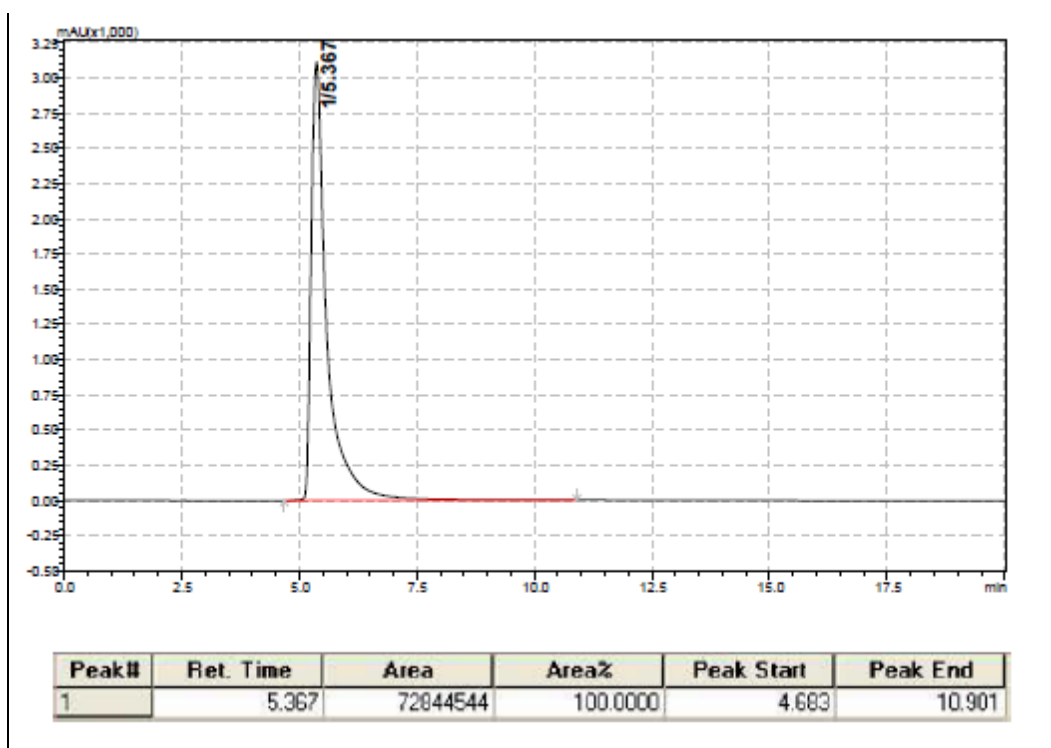


Figure 80. HPLC chromatogram of compound *N*-(1-benzylpiperidin-4-ylidene)cinnamohydrazide (**4j**).