

Supplementary Information

Design, synthesis, characterization and biological evaluation of some
azetidinone derivatives containing pyrimidine moiety

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Materials and methods

“All of the initial materials and reagents were proffered by Sigma-Aldrich, Merck, and Loba Chemical. Thin layer chromatography (TLC) on silica gel plates was used to check the purity and monitor the reaction (Merck, 60, F254). Melting points were measured in open capillaries on an electrical melting point apparatus and are uncorrected. The elemental analysis (% C, H, N) was performed using a Perkin-Elmer 2400 CHN analyzer. All synthesized compounds' IR spectra were recorded in KBr using a Perkin-Elmer FT-IR spectrophotometer. Tetramethyl silane (TMS) was used as an internal standard, and ^1H and ^{13}C were recorded using a Varian Gemini 500 MHz NMR instrument. Chemical shifts are reported in parts per million (δ in ppm). To scan the mass spectra of synthesized compounds, a Shimadzu LC-MS 2010 spectrometer was employed”.

Antimicrobial activity

The antimicrobial activity of recently created compounds (**4a-o**) was examined against a representative panel of bacteria, including *Escherichia coli* (gram-negative, ATCC 25922), *Serratia marcescens* (gram-negative, ATCC 14756), *Staphylococcus epidermis* (gram-positive, ATCC 12228), and *Streptococcus pyogens* (gram-positive, ATCC 19615), using chloramphenicol as the standard antibacterial drug. Nystatin was employed as the standard antifungal drug throughout the screening of antifungal activity against the two fungus species *Aspergillus Niger* (ATCC 16404) and *Fusarium Javanicum* (ATCC 22403). Chloramphenicol (100 μg susceptibility disc) was used as a standard drug. The concentration of the tested hybrids, as well as Chloramphenicol used in the study, ranged from 2500 to 10 $\mu\text{g}/\text{mL}$. The sterile Muller-Hinton broth (MHB) was enriched with 2% NaCl before the tested antimicrobial agents were inserted into the well at concentration gradient in a serial dilution.

Then the diluted bacterial suspension at final inoculum of 10^6 CFU/mL was added. The tested compound in MHB was used as negative control to ensure medium sterility, while the inoculum in MHB served as positive control to ensure the adequacy of the broth for bacterial growth. To facilitate the observation of the growth of bacteria in each well, 20 μ L of 2,3,5-triphenyltetrazolium chloride (TTC) at 2 mg/mL was added into each well. Each of the tested strains was cultured in sterile broth medium for 24 h at 37 °C. The assay was performed in 2 mL microcentrifuge tubes with concentrations ranging from 2500 to 10 μ g/mL of the tested derivatives. To each concentration of the tested derivatives, 0.1 mL of the cultured bacterial strain was added and then, allowed to incubate for 24 h at 37 °C. All the results were carried out in duplicate and the average values were determined. ^[1-3]

References

1. Mekky, A. E. M.; Sanad, S. M. H. Novel bis(pyrazole-benzofuran) hybrids possessing piperazine linker: Synthesis of potent bacterial biofilm and MurB inhibitors. *Bioorg. Chem.* **2020**, *102*, 104094. DOI: 10.1016/j.bioorg.2020.104094.
2. Mohammad, H.; Reddy, P. N.; Monteleone, D.; Mayhoub, A. S.; Cushman, M.; Seleem, M. N. Synthesis and antibacterial evaluation of a novel series of synthetic phenylthiazole compounds against methicillin-resistant *Staphylococcus aureus* (MRSA). *Eur. J. Med. Chem.* **2015**, *94*, 306-316. DOI: 10.1016/j.ejmech.2015.03.015.
3. Kamal, A.; Rahim, A.; Riyaz, S.; Poornachandra, Y.; Balakrishna, M.; Kumar, C. G.; Hussaini, S. M. A.; Sridhar, B.; Machiraju, P. K. Regioselective synthesis, antimicrobial evaluation and theoretical studies of 2-styryl quinolines. *Org. Biomol. Chem.* **2015**, *13*, 1347-1357. DOI: 10.1039/c4ob02277g.

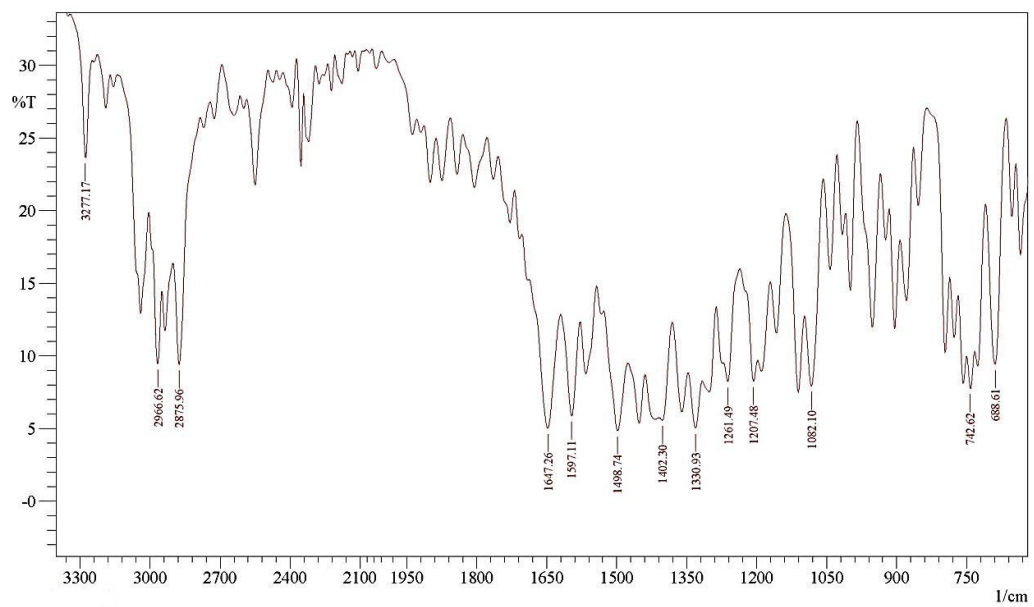


Figure 1: IR spectrum of compound 3a

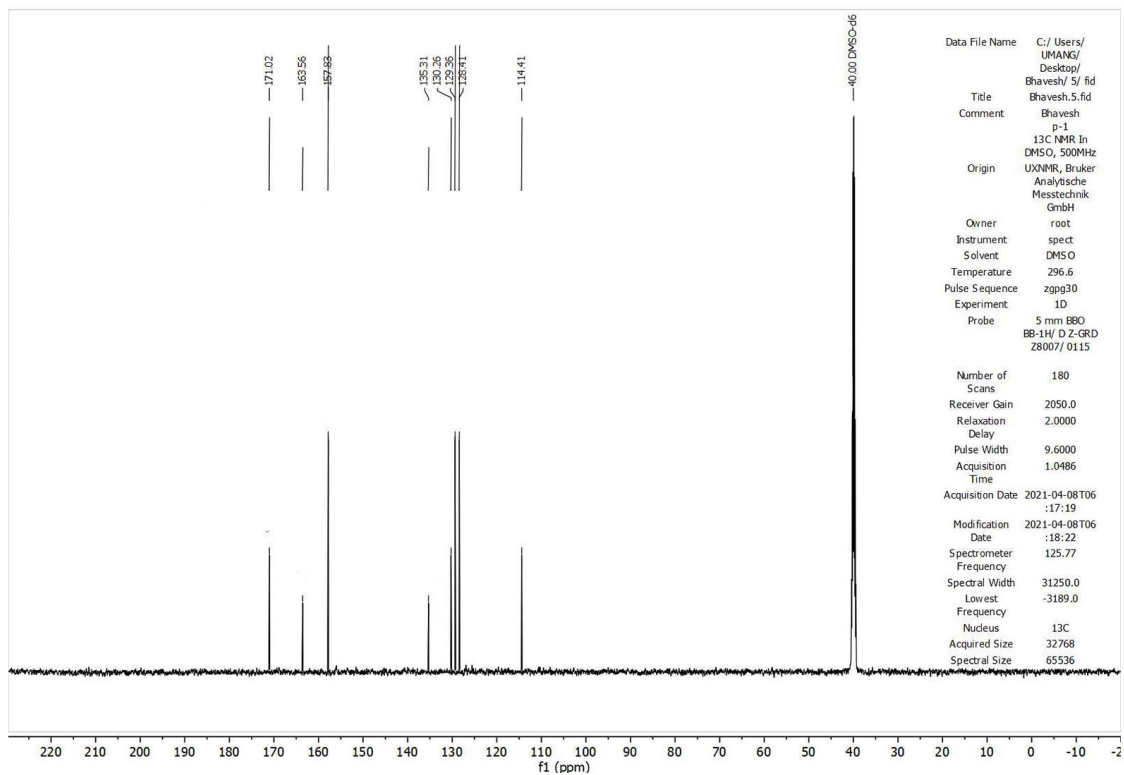


Figure 3: ^{13}C NMR spectrum of compound 3a

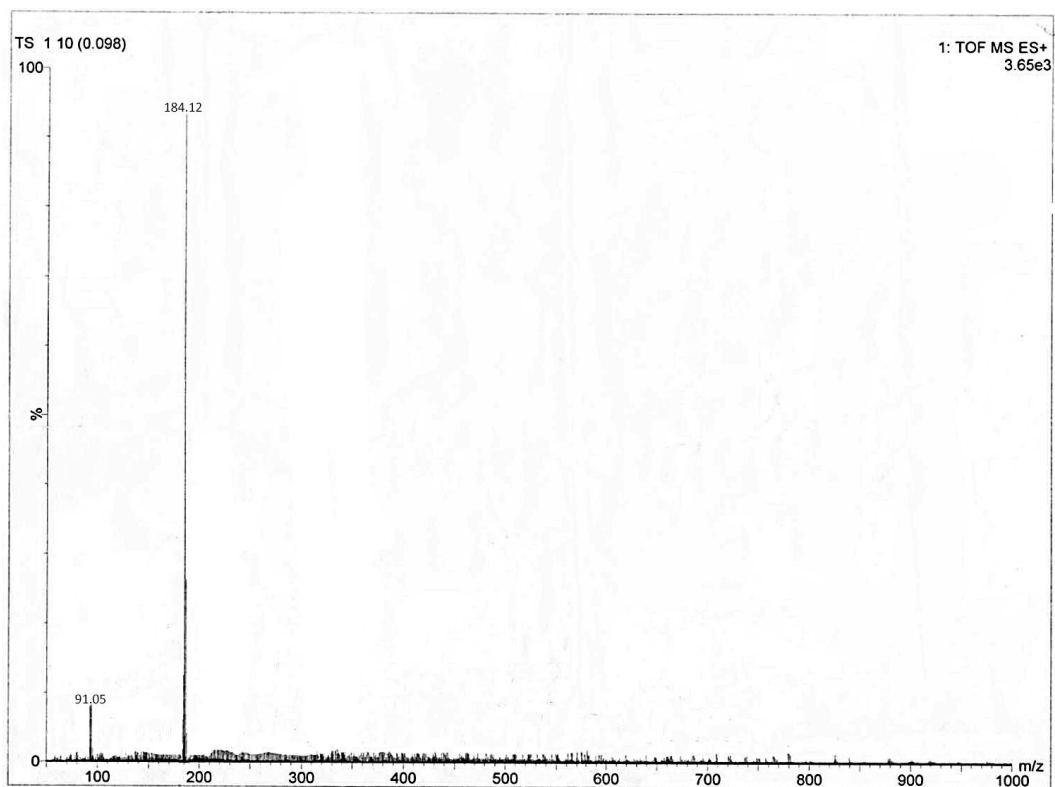


Figure 4: Mass spectrum of compound 3a

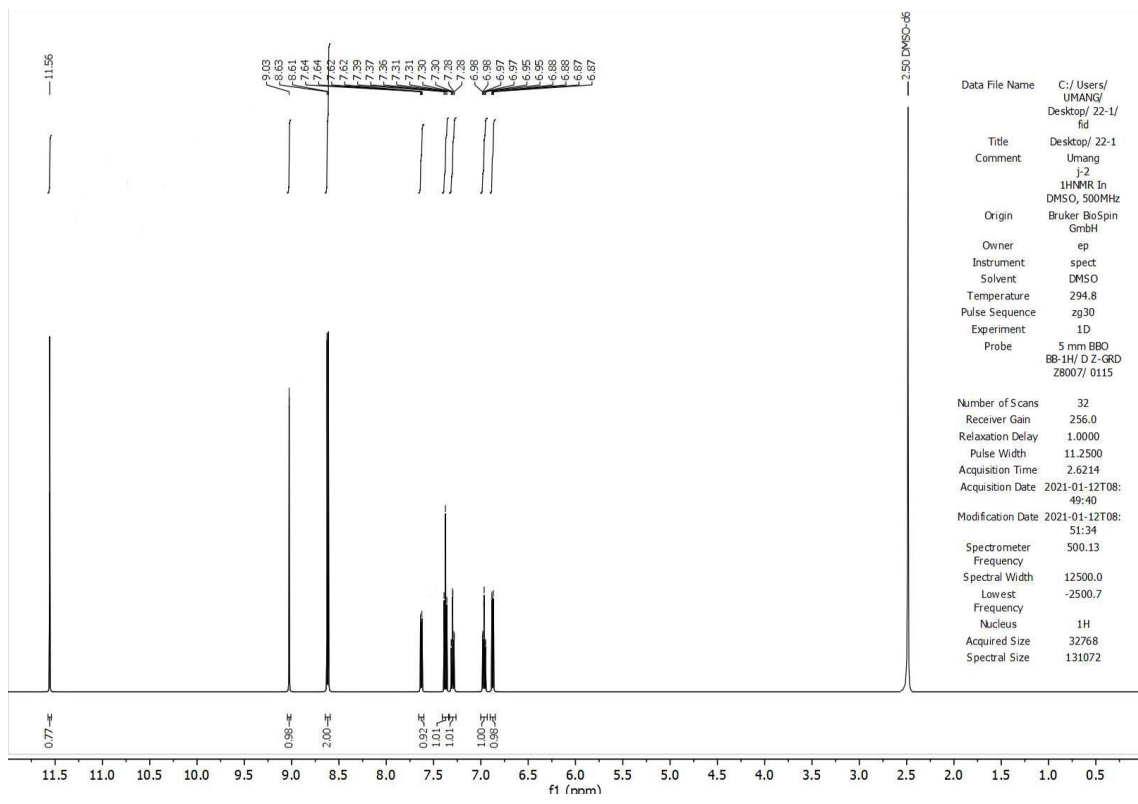


Figure 5: ¹H NMR spectrum of compound 3b

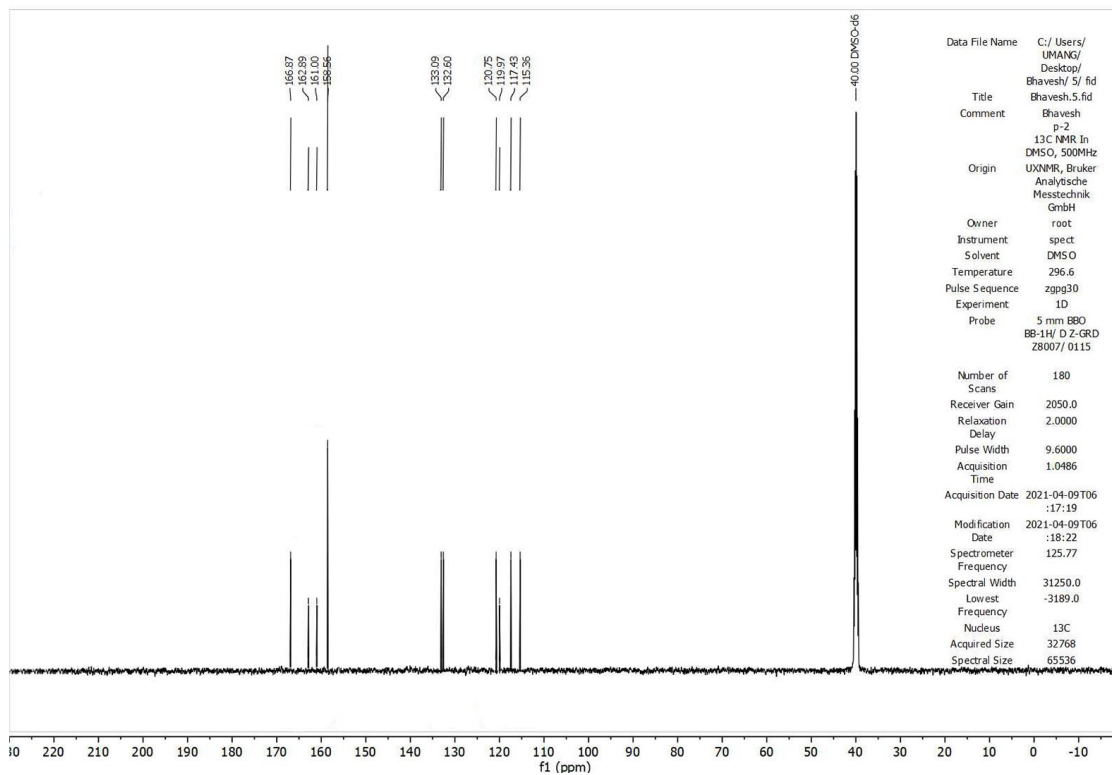


Figure 6: ^{13}C NMR spectrum of compound 3b

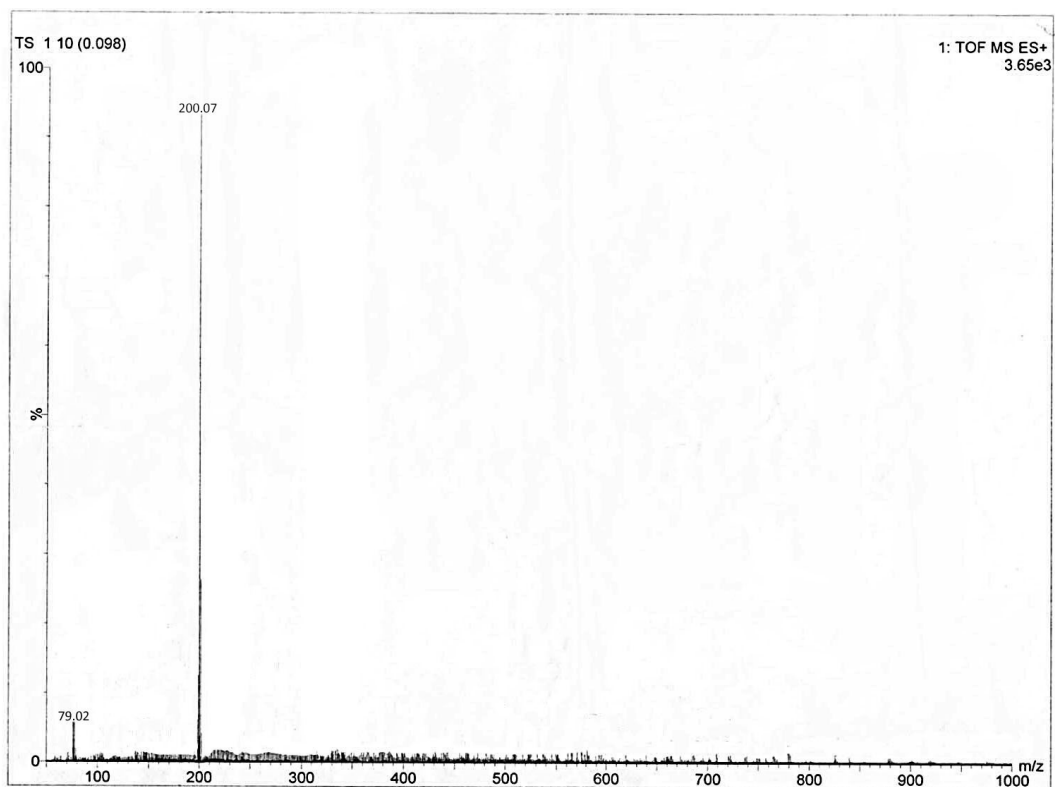


Figure 7: Mass spectrum of compound 3b

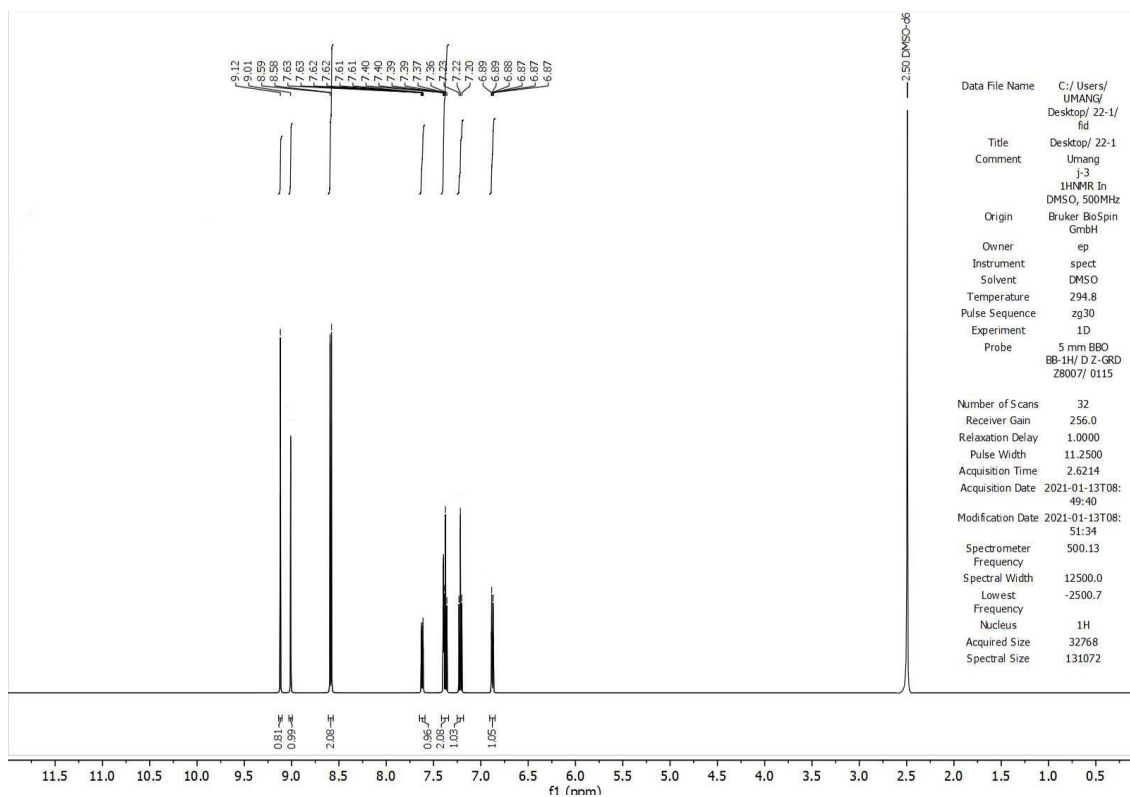


Figure 8: ¹H NMR spectrum of compound 3c

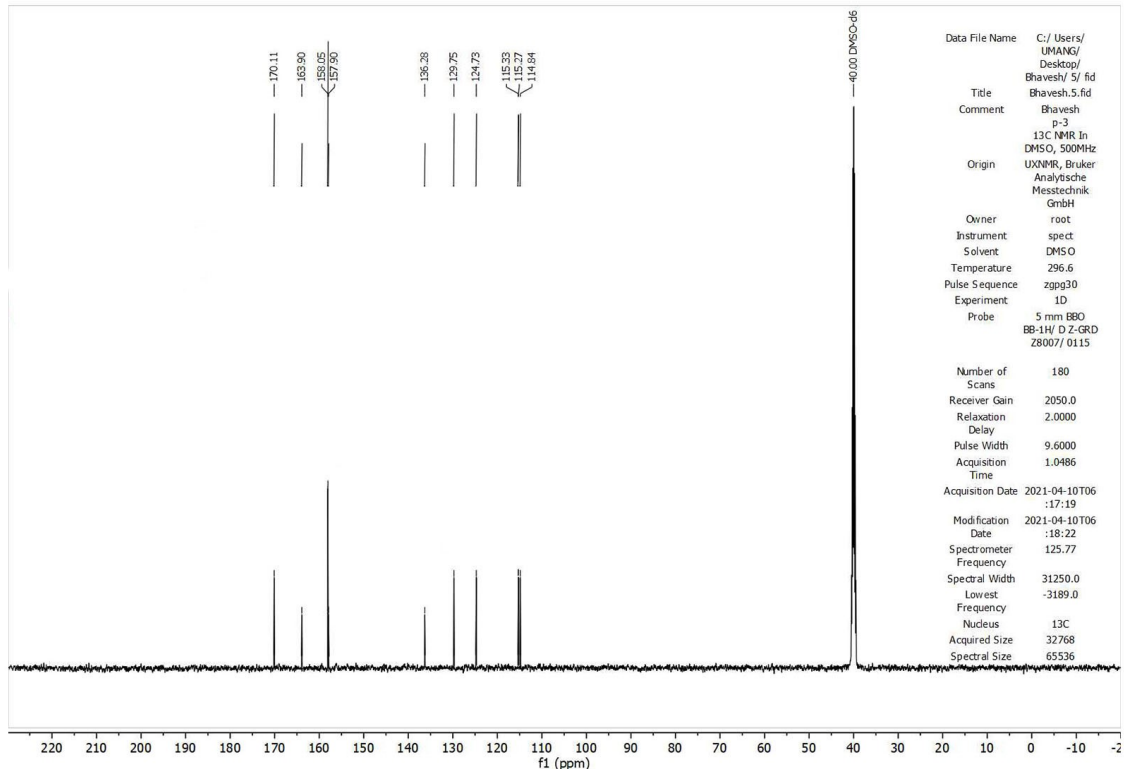


Figure 9: ^{13}C NMR spectrum of compound **3c**

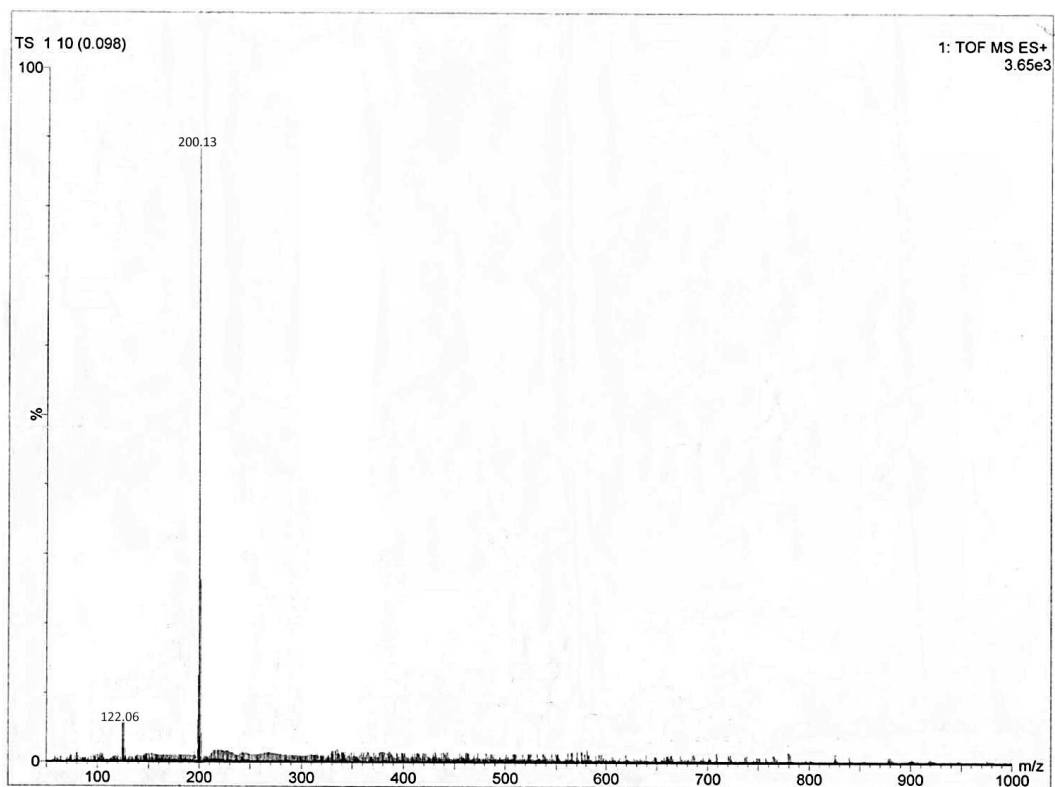


Figure 10: Mass spectrum of compound 3c

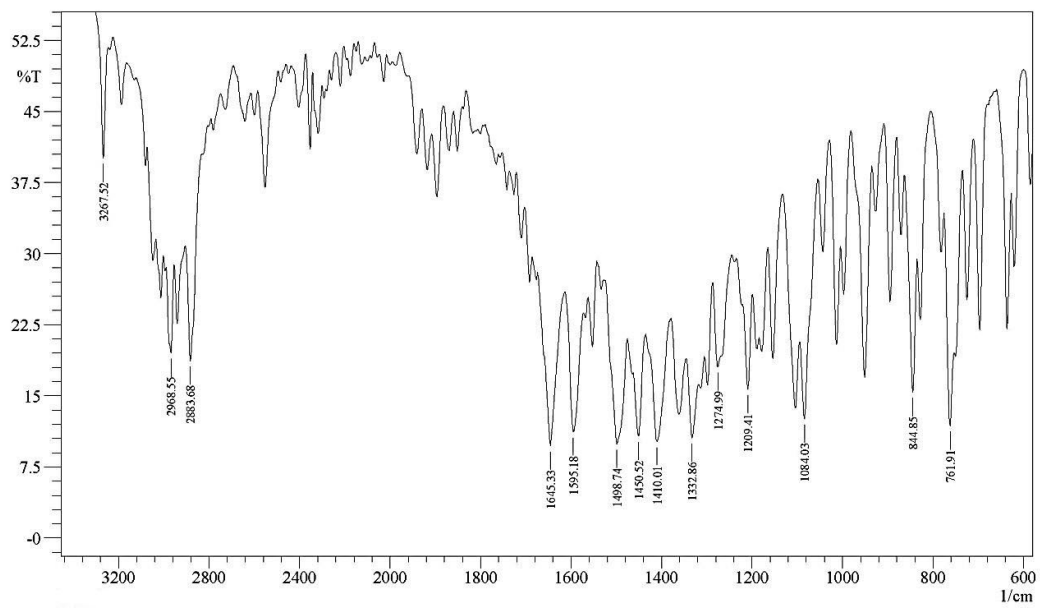


Figure 11: IR spectrum of compound 3d

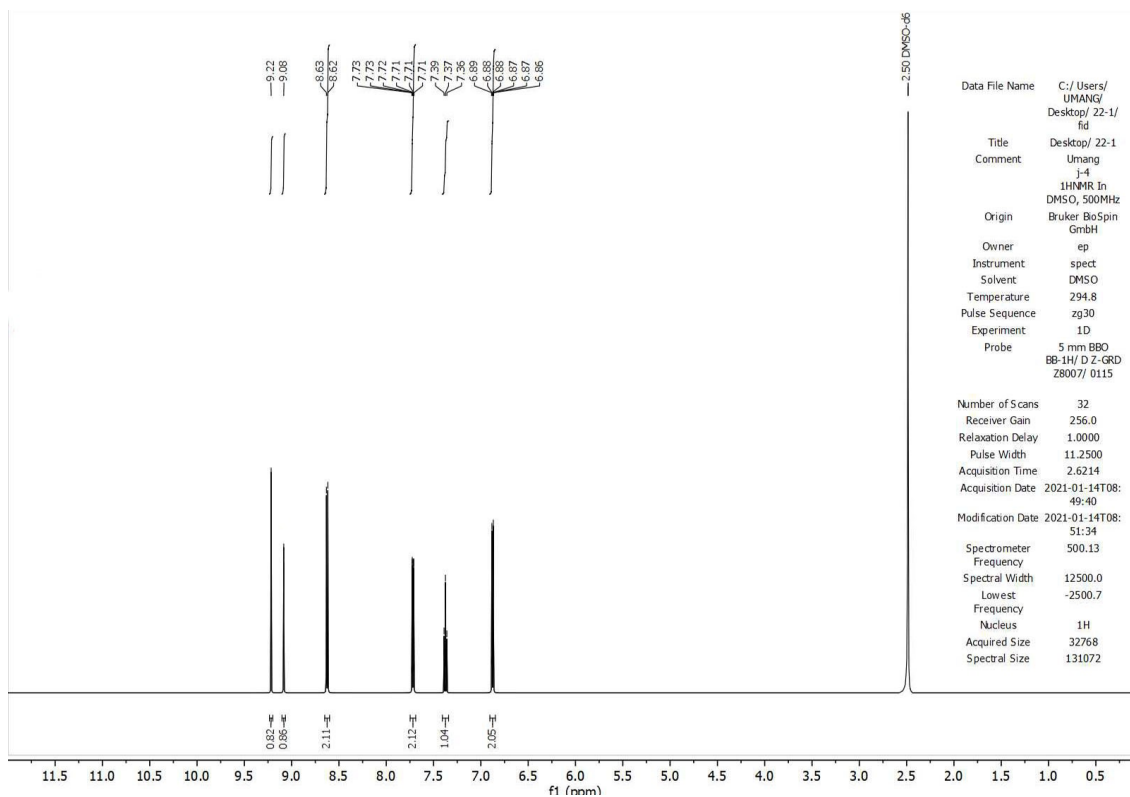


Figure 12: ¹H NMR spectrum of compound 3d

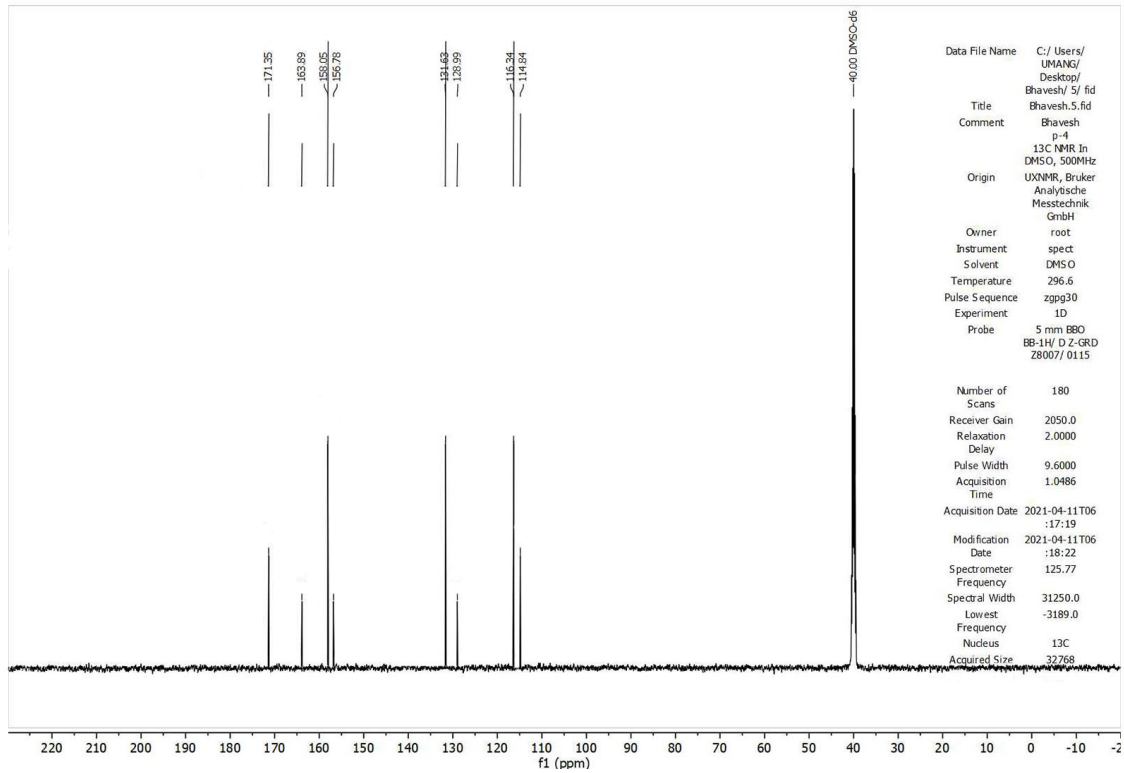


Figure 13: ^{13}C NMR spectrum of compound 3d

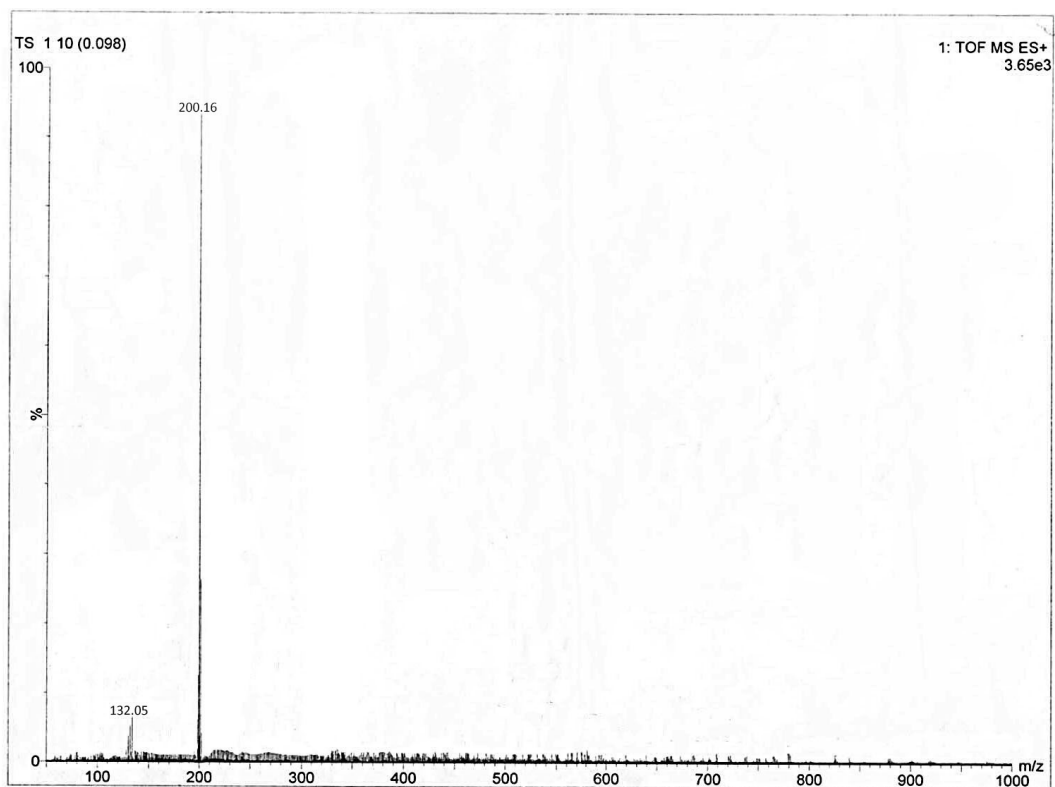


Figure 14: Mass spectrum of compound 3d

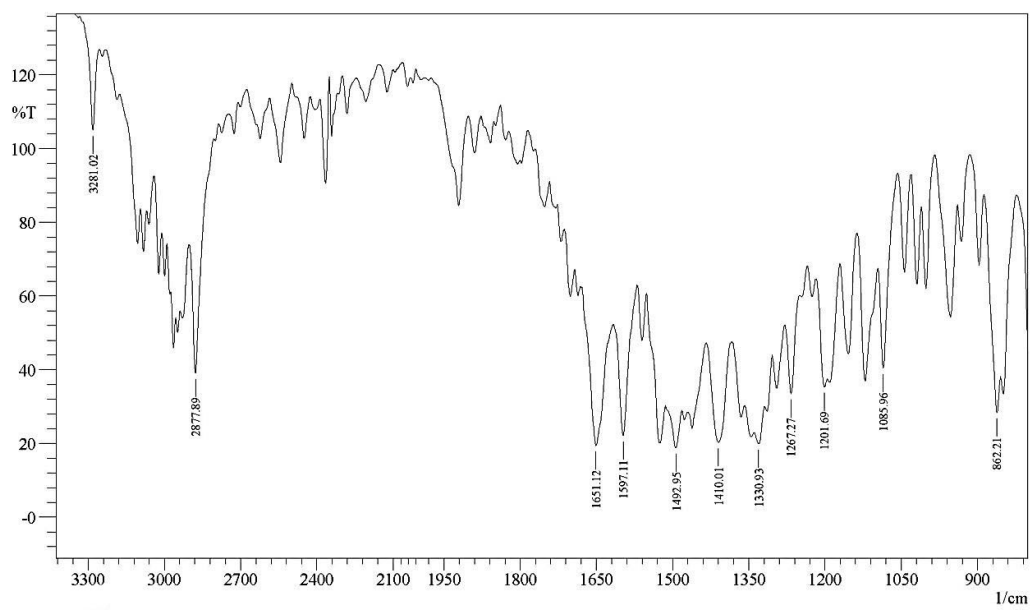


Figure 15: IR spectrum of compound 3e

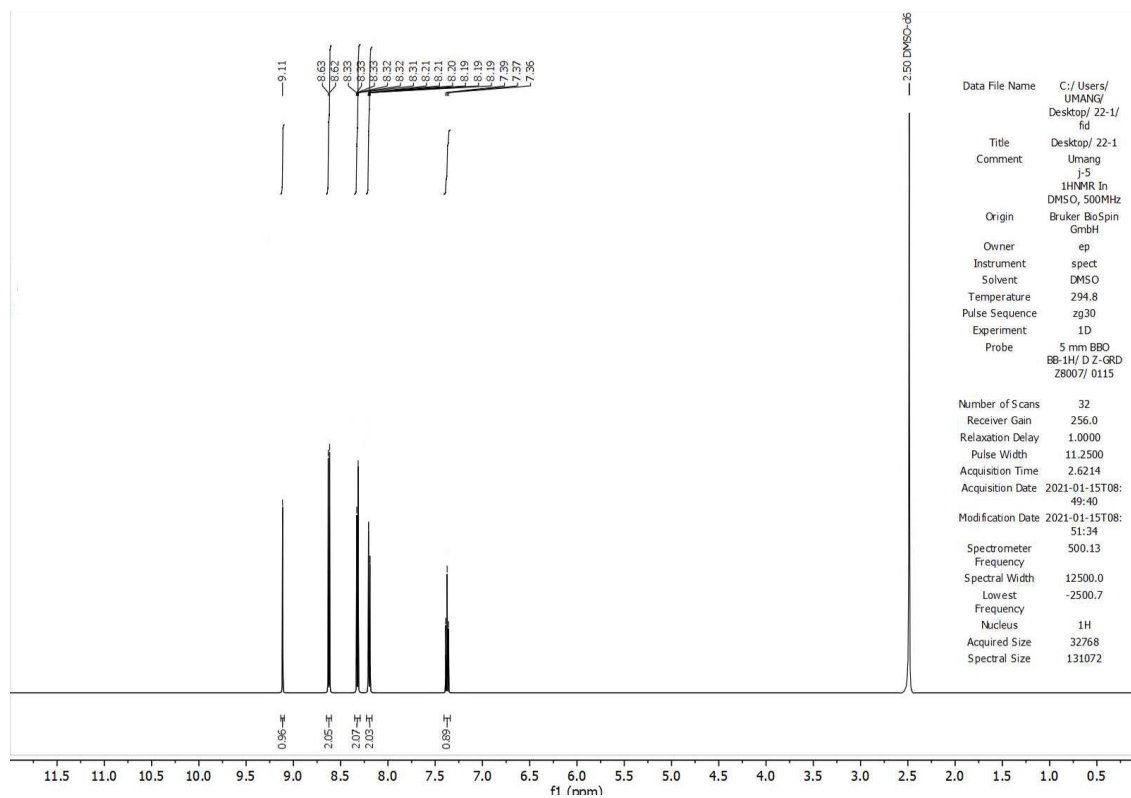


Figure 16: ^1H NMR spectrum of compound 3e

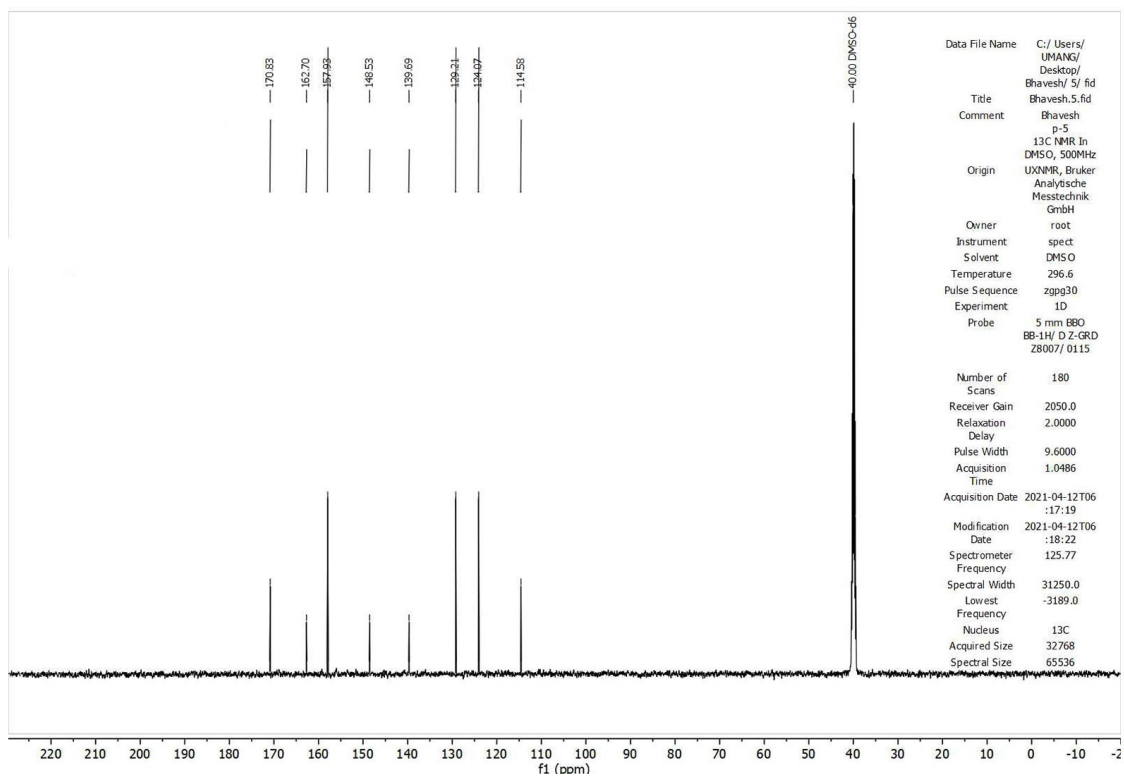


Figure 17: ^{13}C NMR spectrum of compound 3e

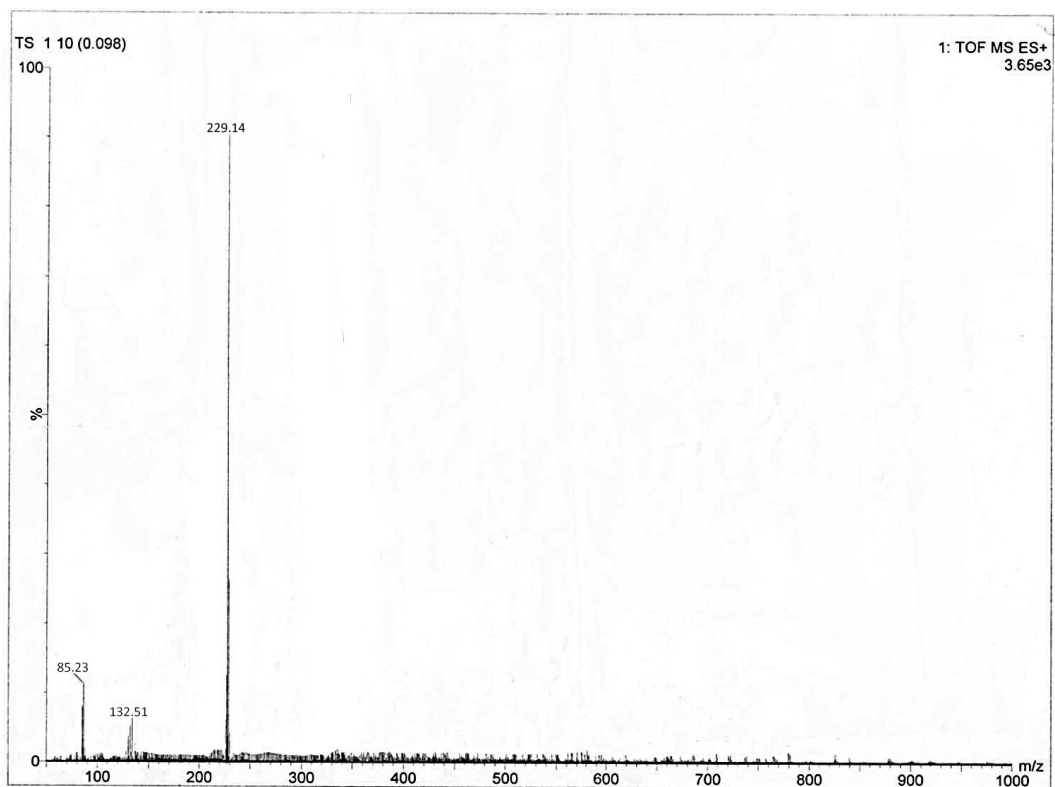


Figure 18: Mass spectrum of compound 3e

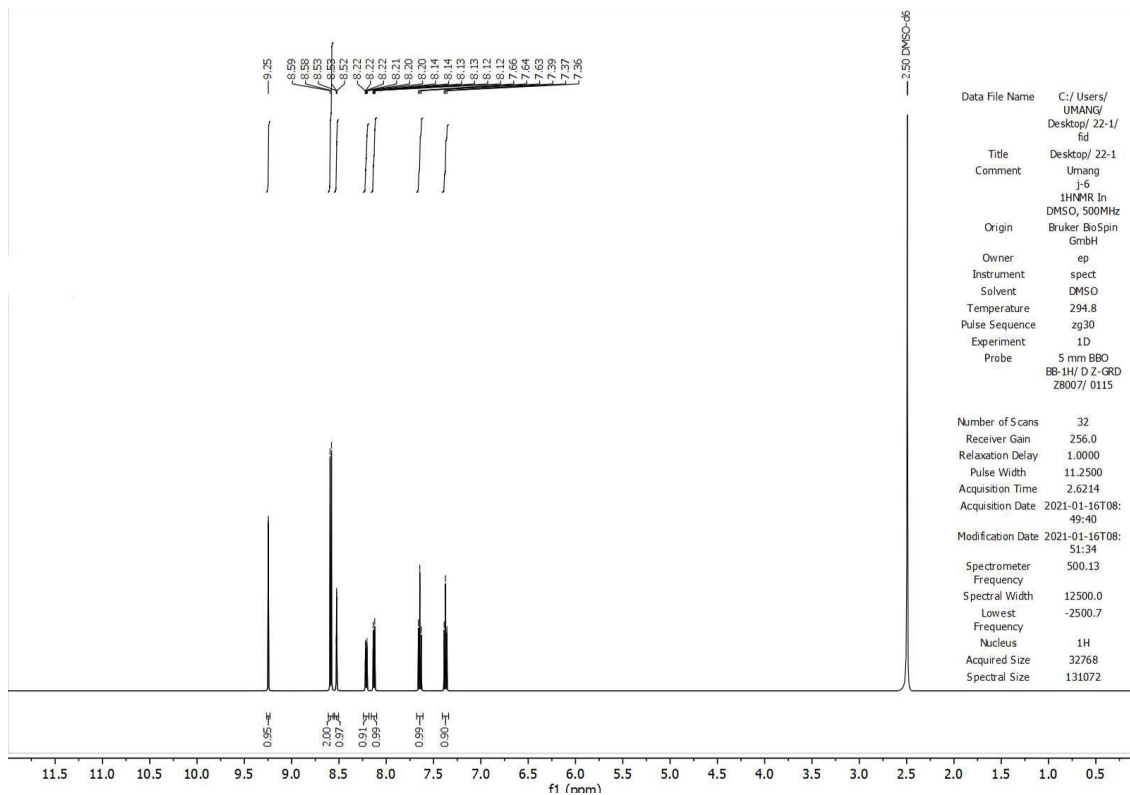


Figure 19: ¹H NMR spectrum of compound 3f

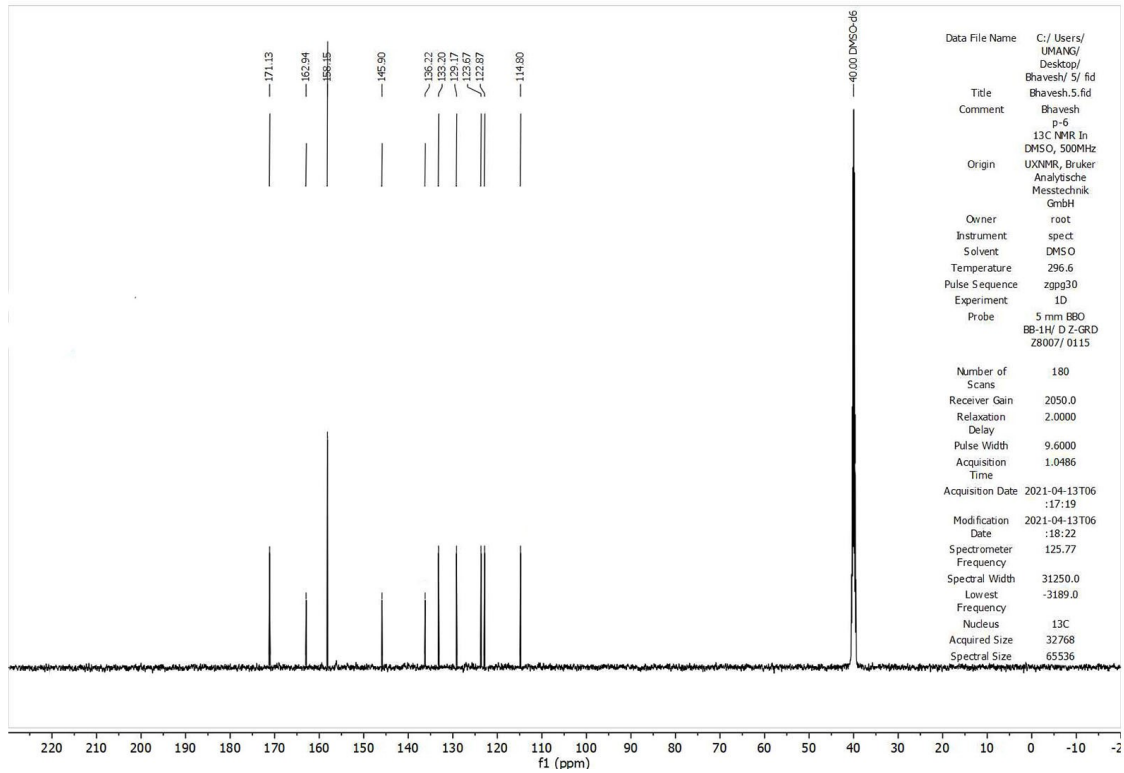


Figure 20: ^{13}C NMR spectrum of compound 3f

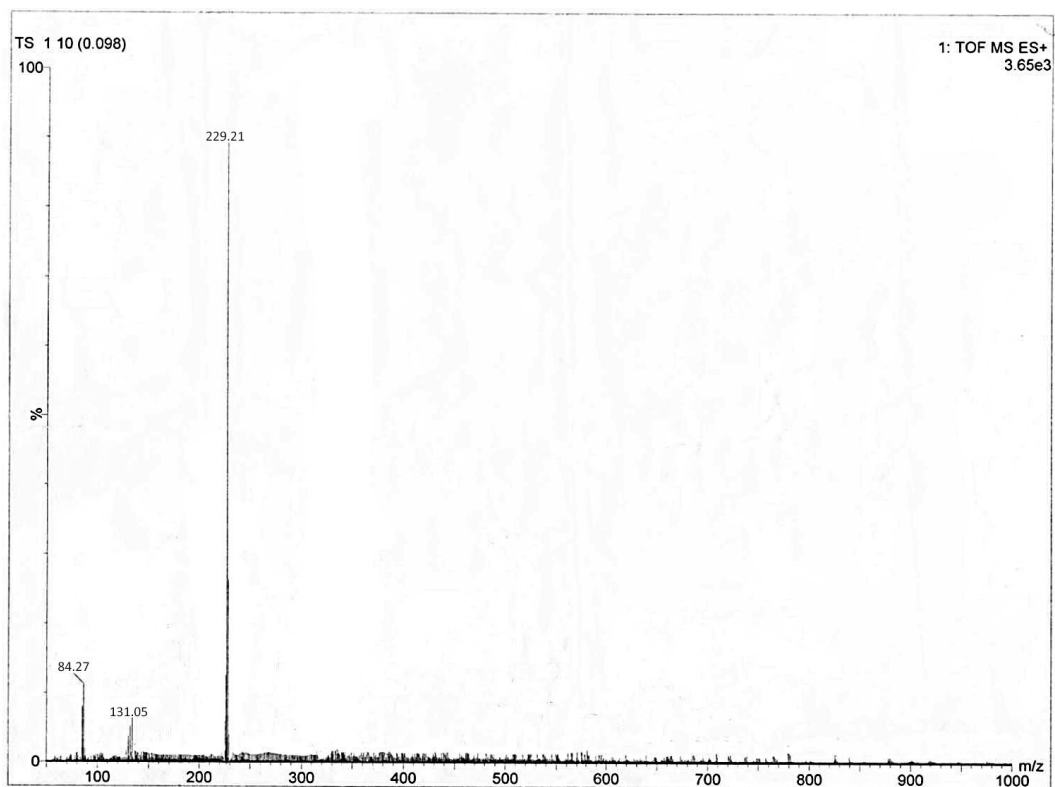


Figure 21: Mass spectrum of compound 3f

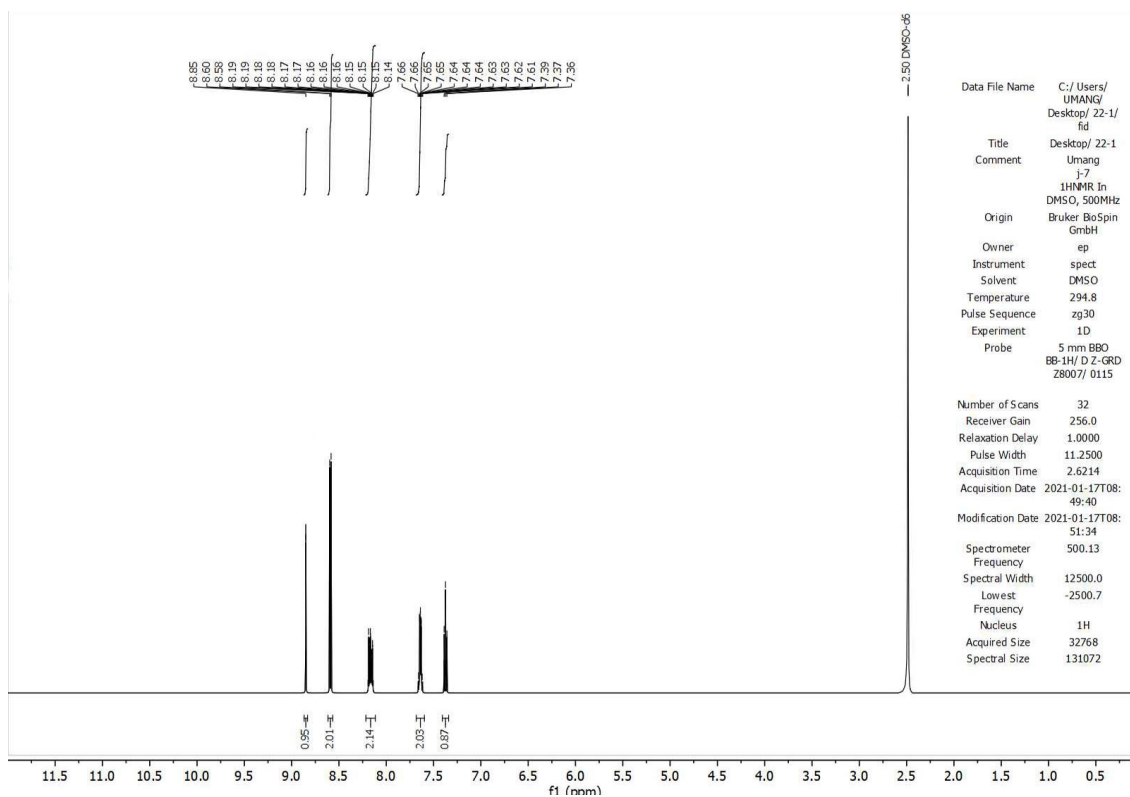


Figure 22: ^1H NMR spectrum of compound 3g

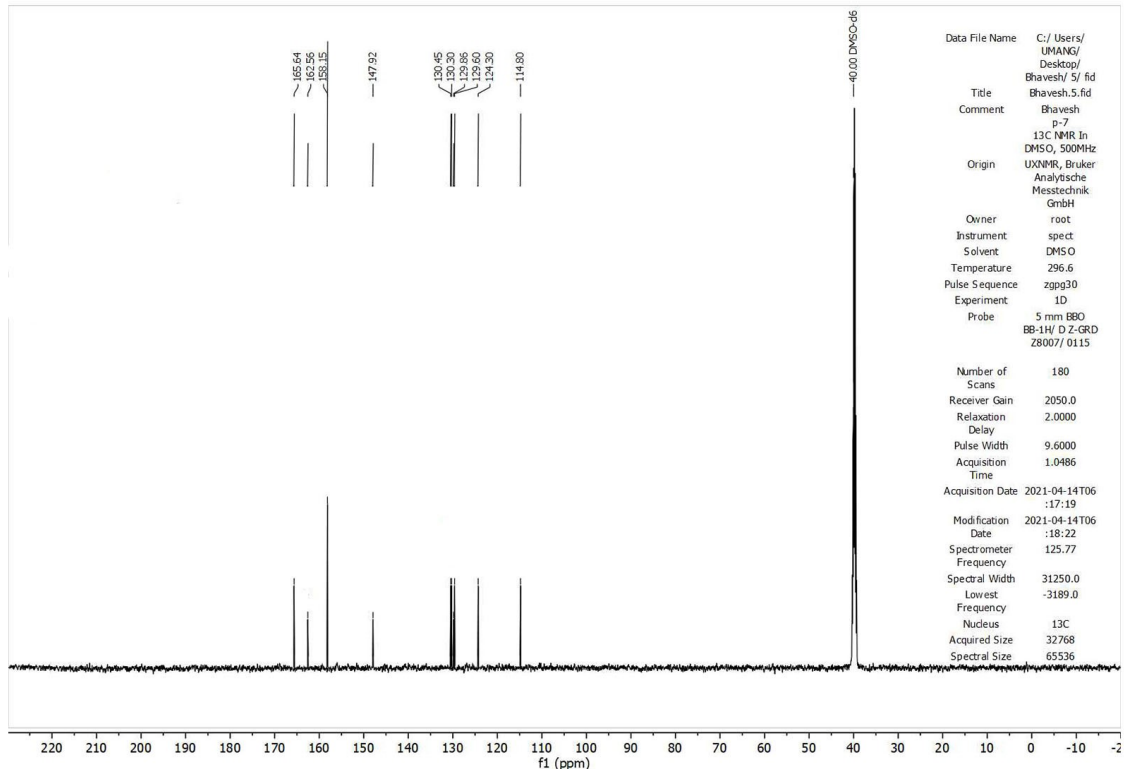


Figure 23: ^{13}C NMR spectrum of compound **3g**

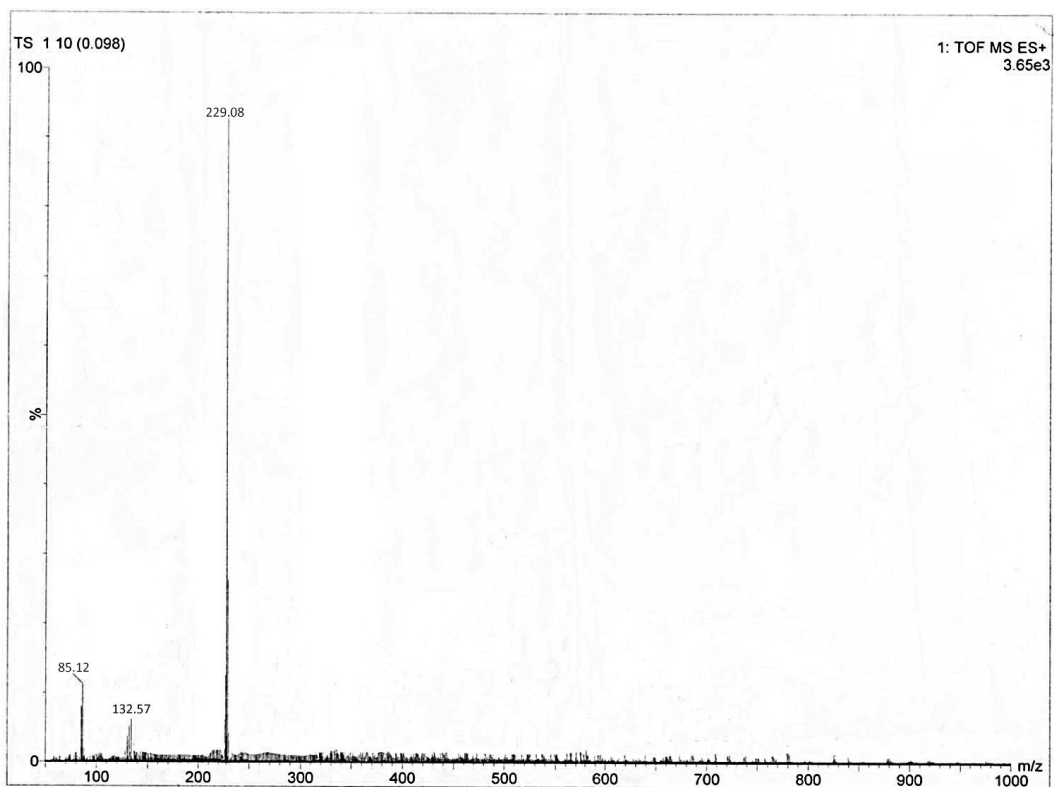


Figure 24: Mass spectrum of compound :3g

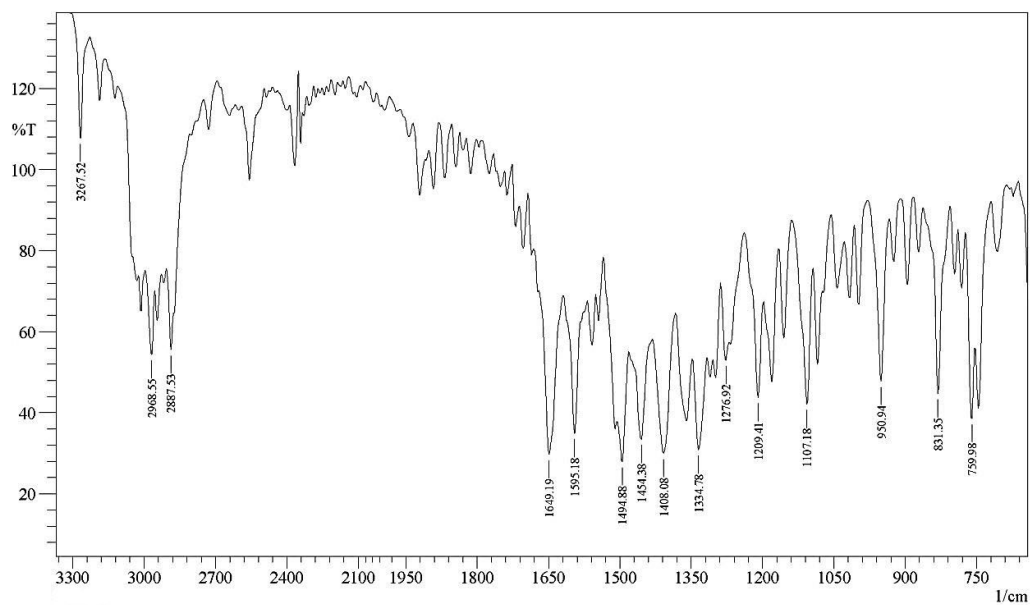


Figure 25: IR spectrum of compound 3h

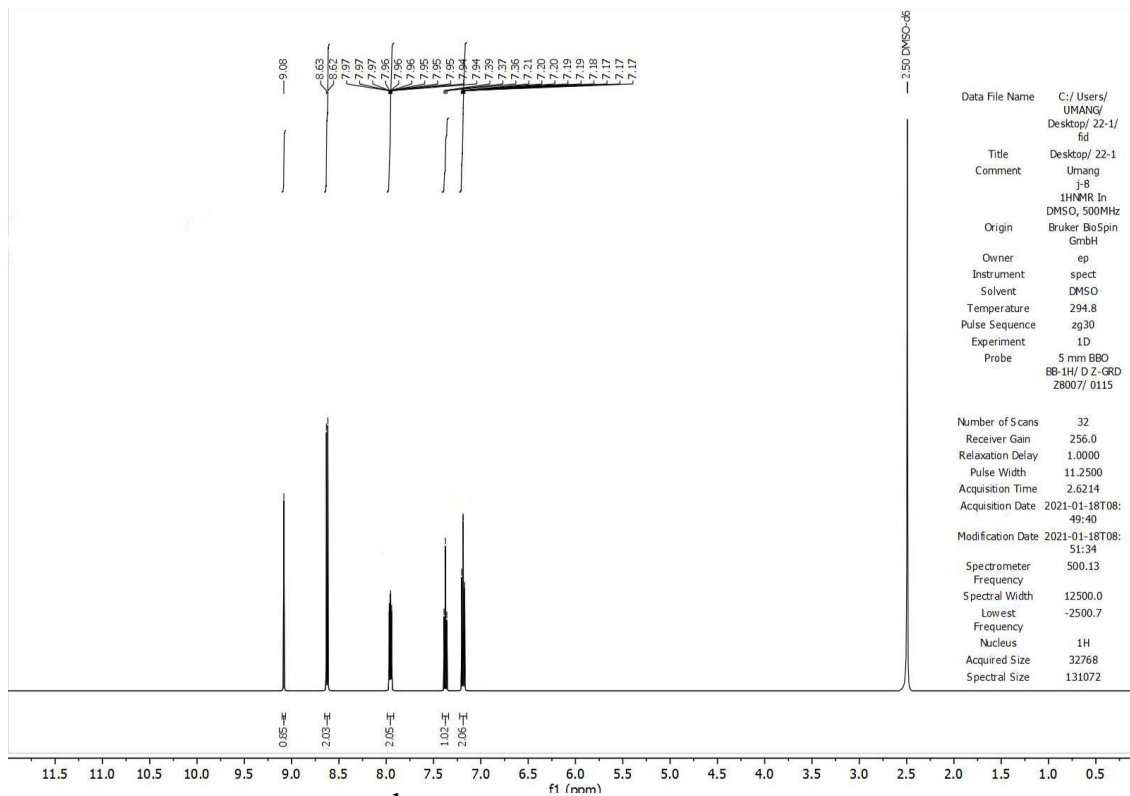


Figure 26: ¹H NMR spectrum of compound 3h

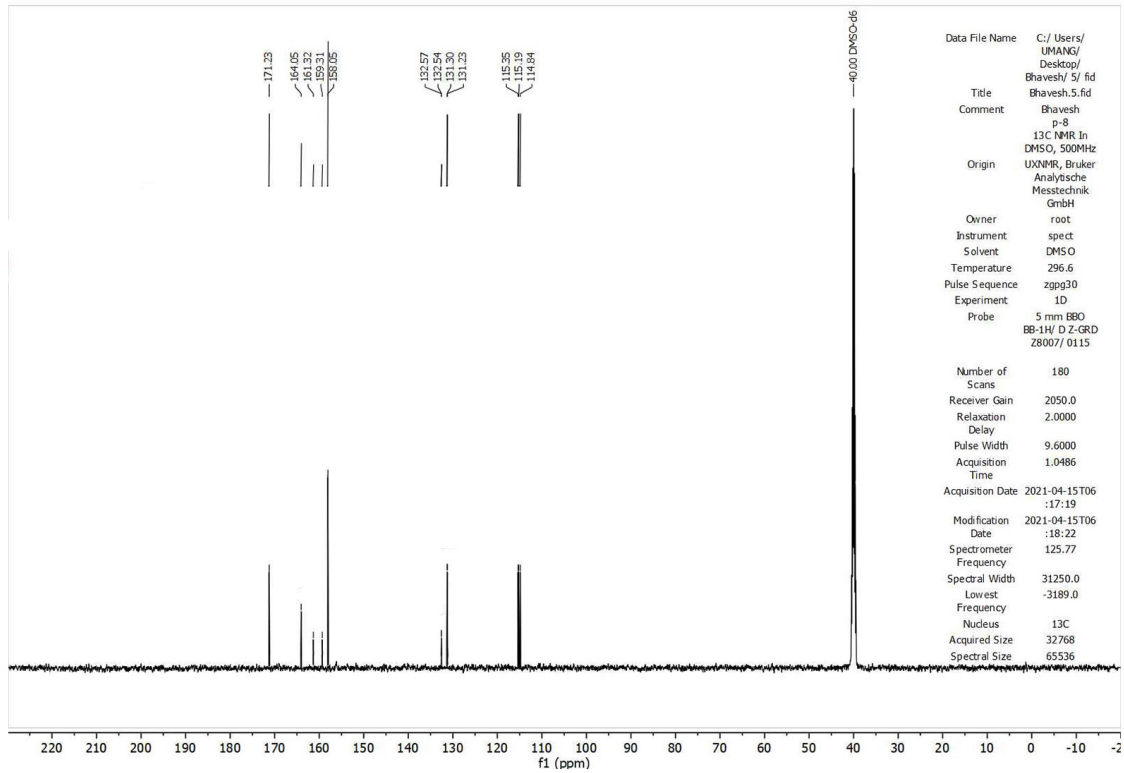


Figure 27: ^{13}C NMR spectrum of compound 3h

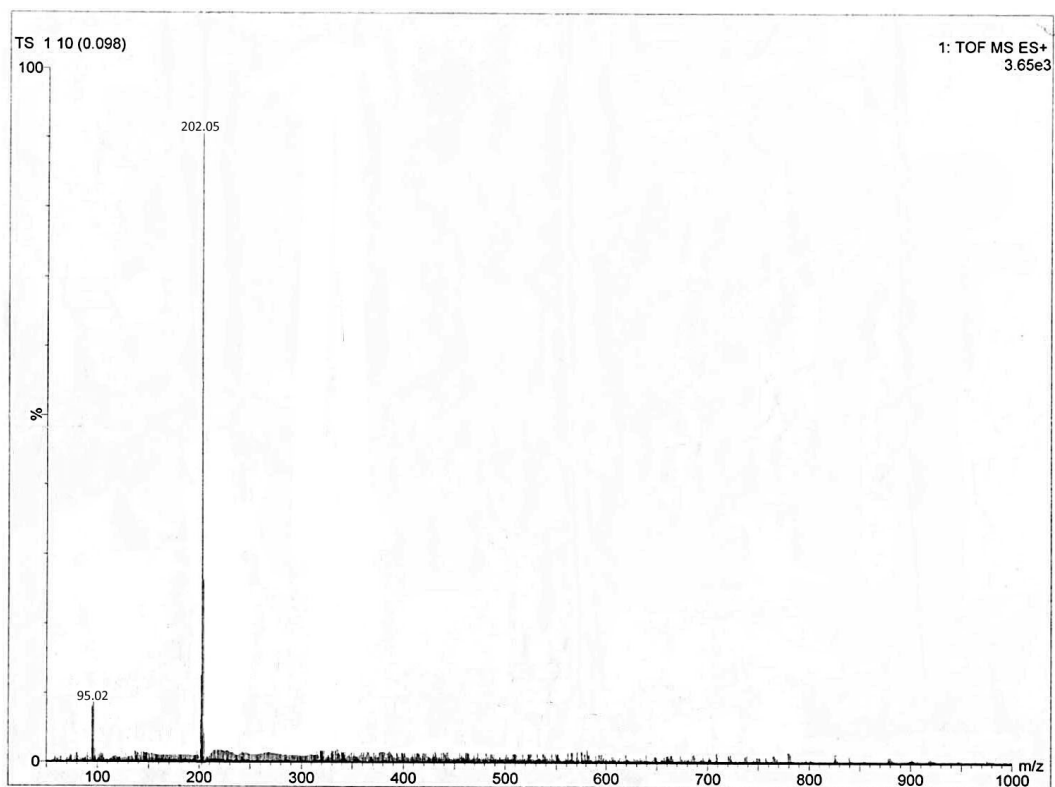


Figure 28: Mass spectrum of compound 3h

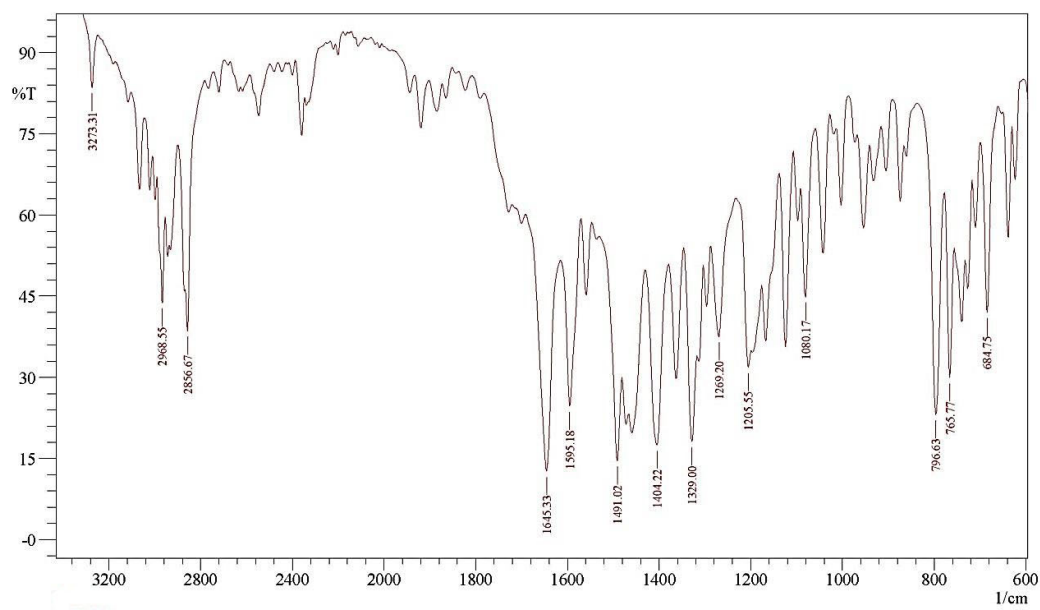


Figure 29: IR spectrum of compound 3i

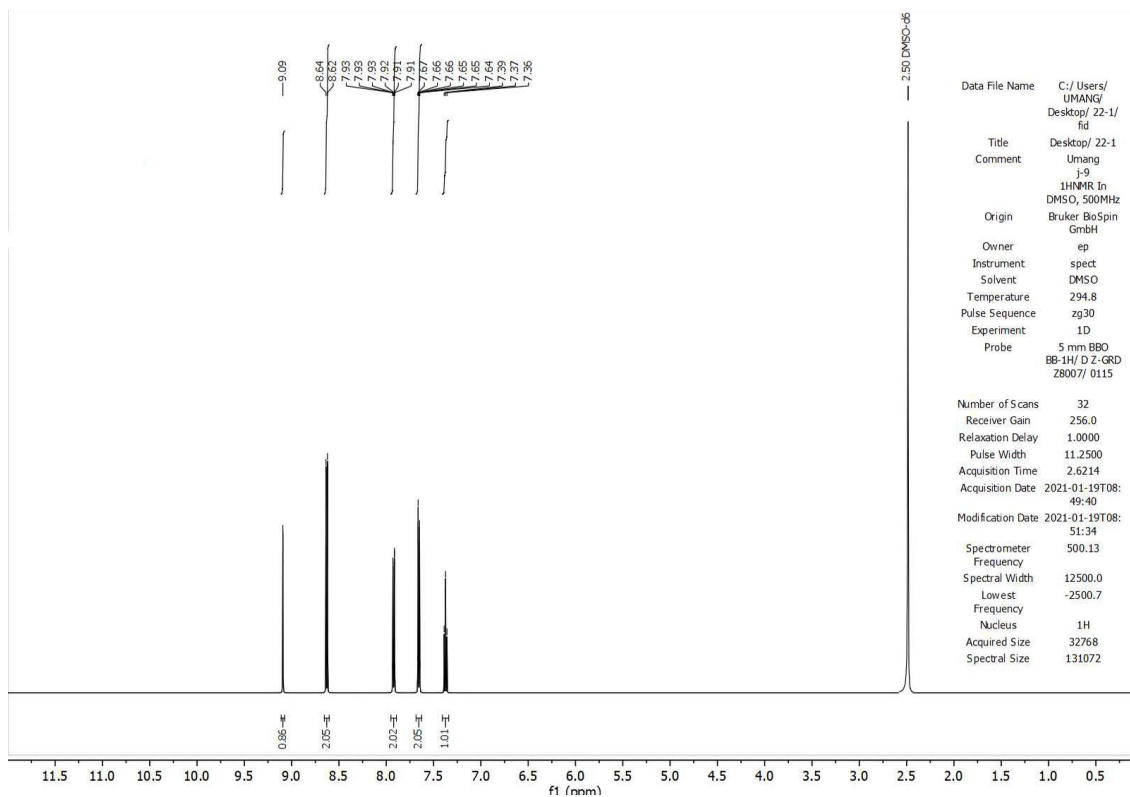


Figure 30: ^1H NMR spectrum of compound 3i

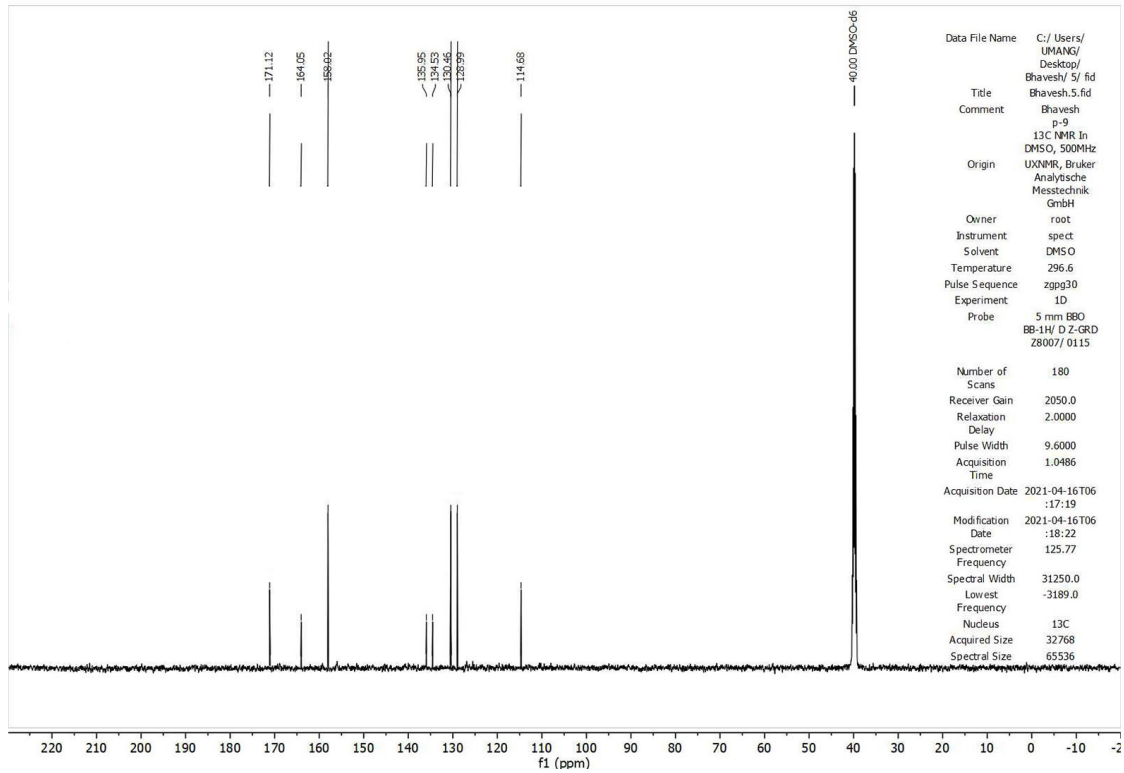


Figure 31: ^{13}C NMR spectrum of compound 3i

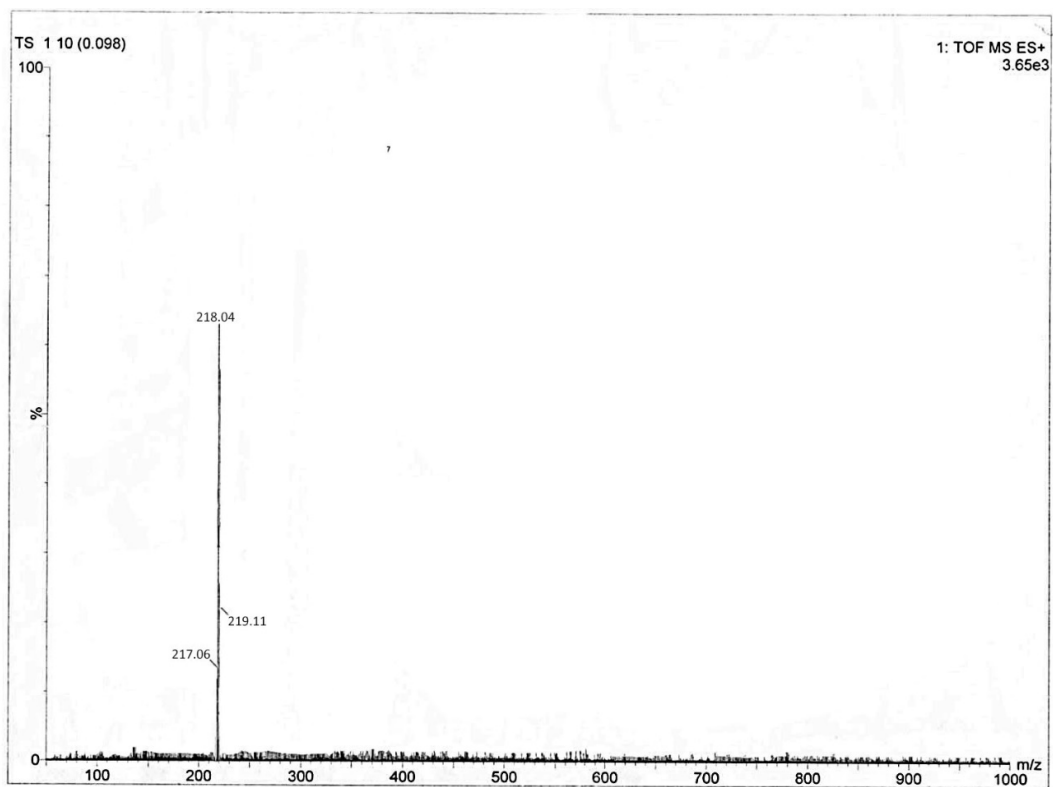


Figure 32: Mass spectrum of compound 3i

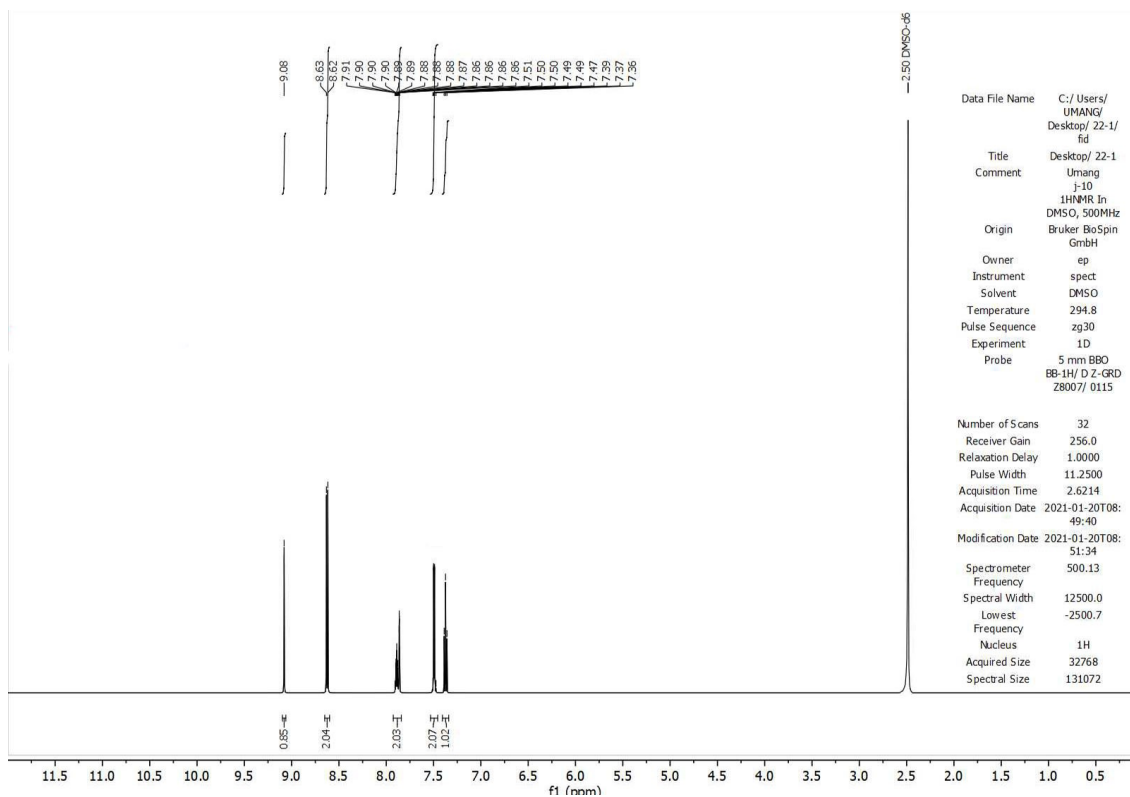


Figure 33: ^1H NMR spectrum of compound 3j

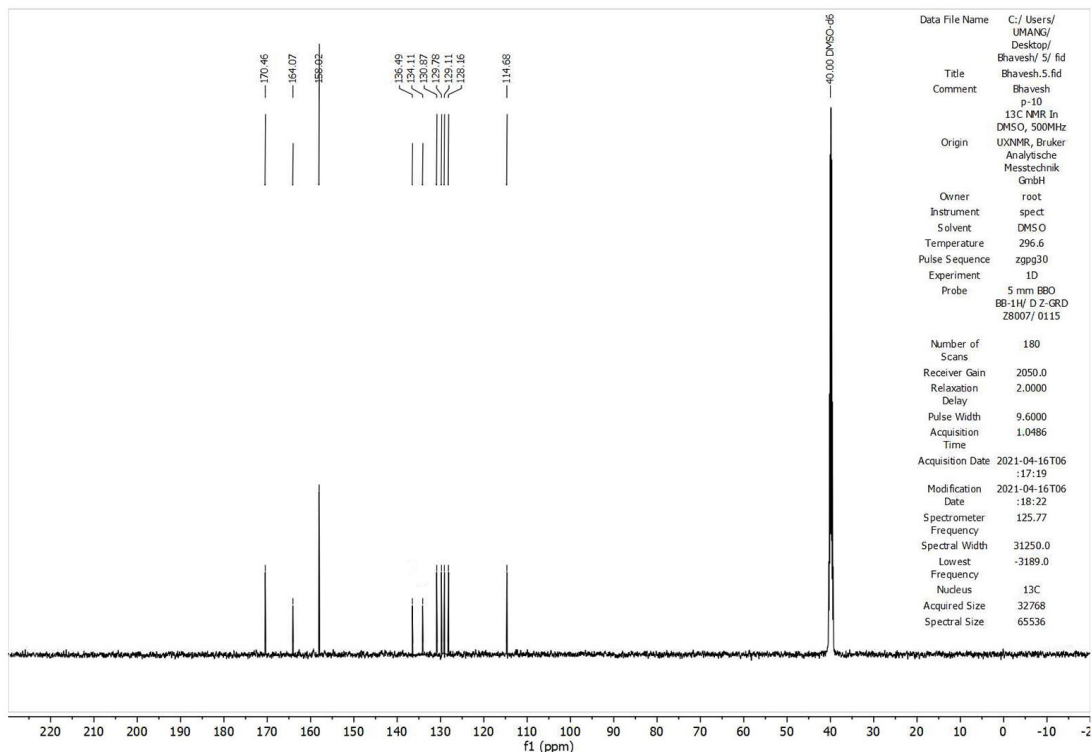


Figure 34: ^{13}C NMR spectrum of compound 3j

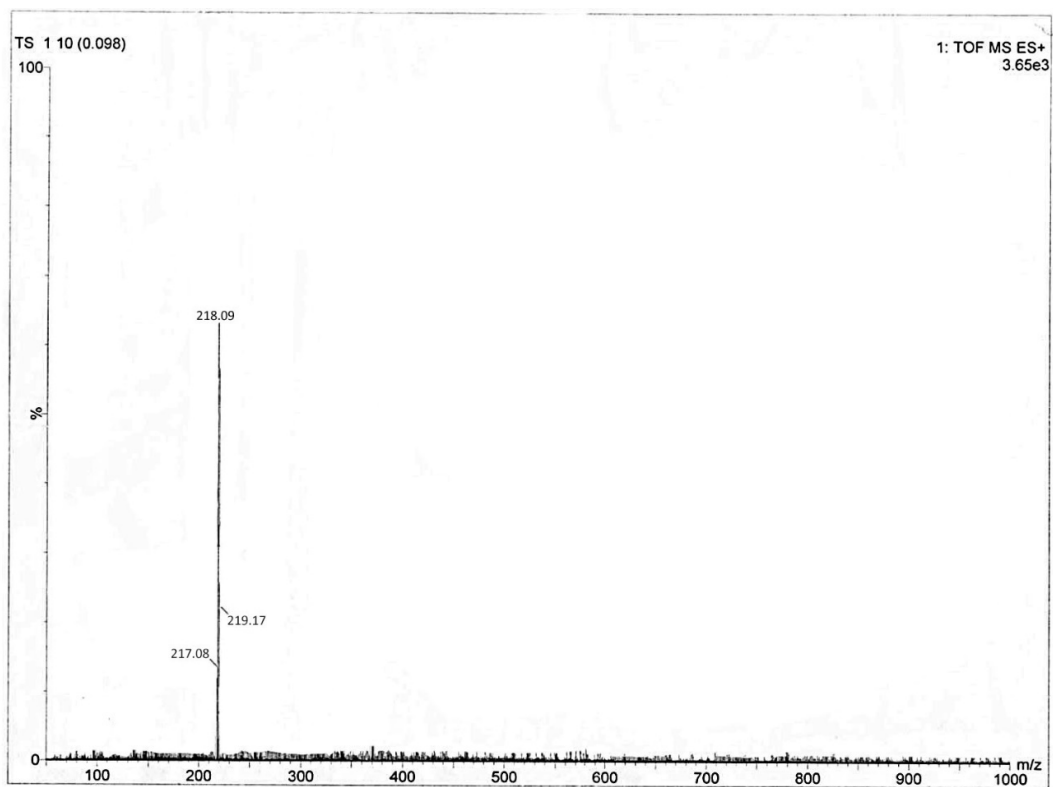


Figure 35: Mass spectrum of compound 3j

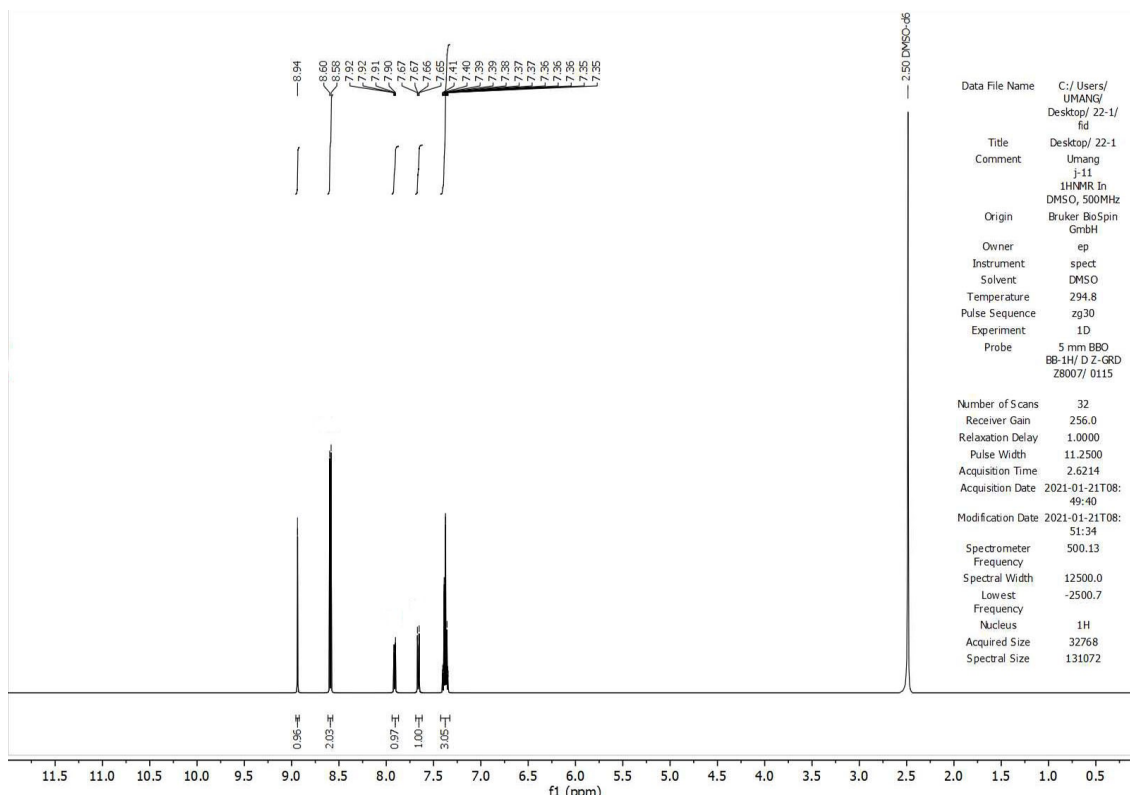


Figure 36: ^1H NMR spectrum of compound 3k

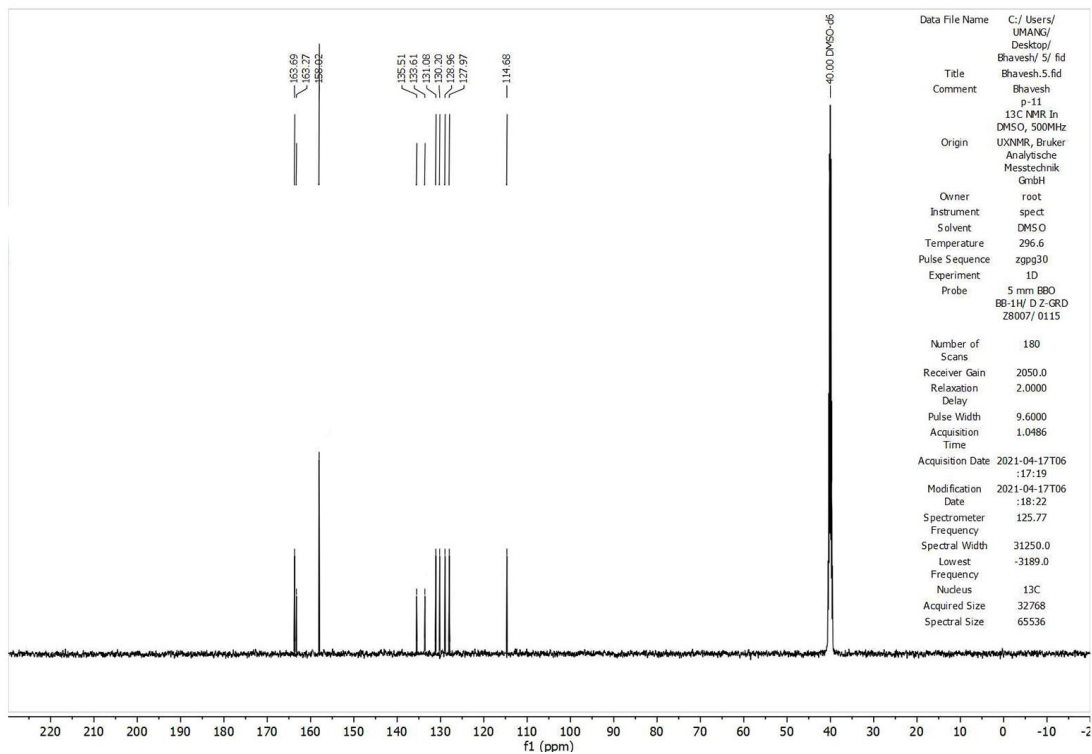


Figure 37: ^{13}C NMR spectrum of compound 3k

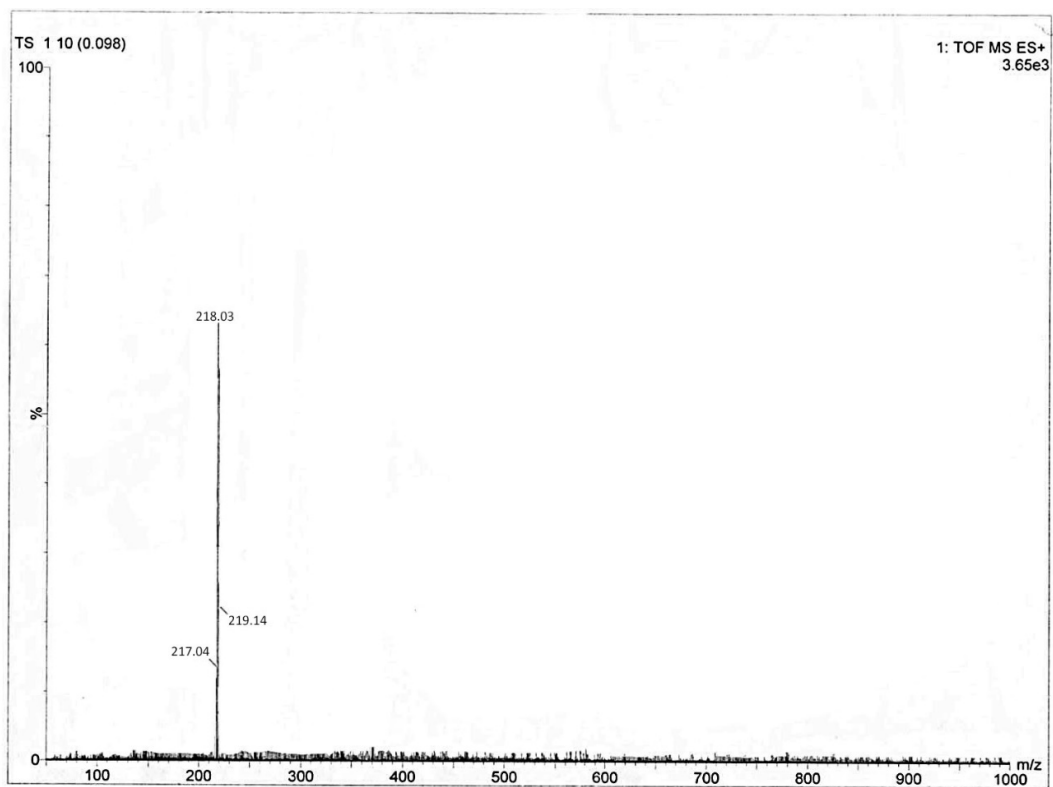


Figure 38: Mass spectrum of compound 3k

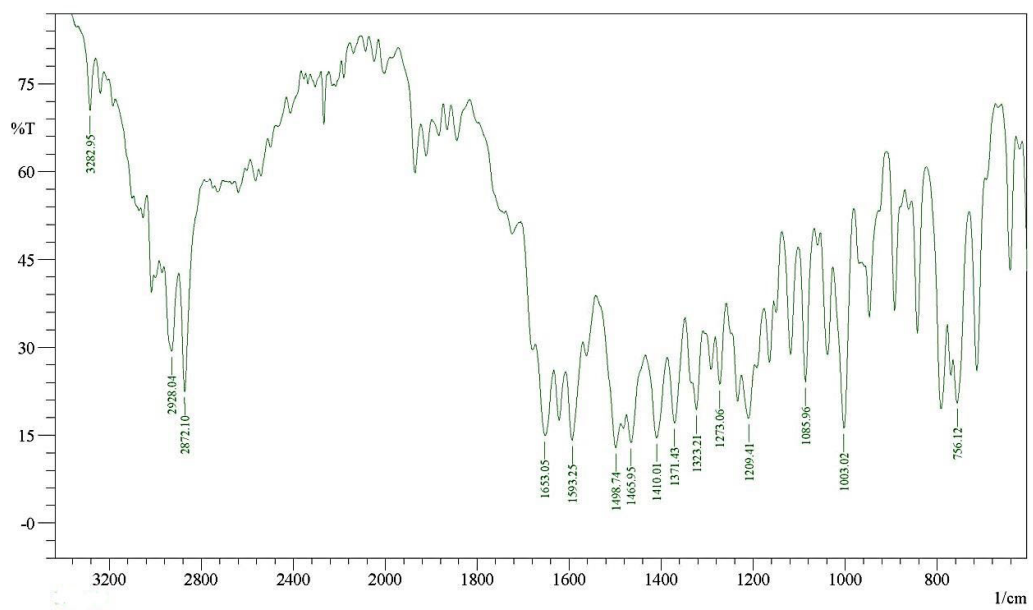


Figure 39: IR spectrum of compound 31

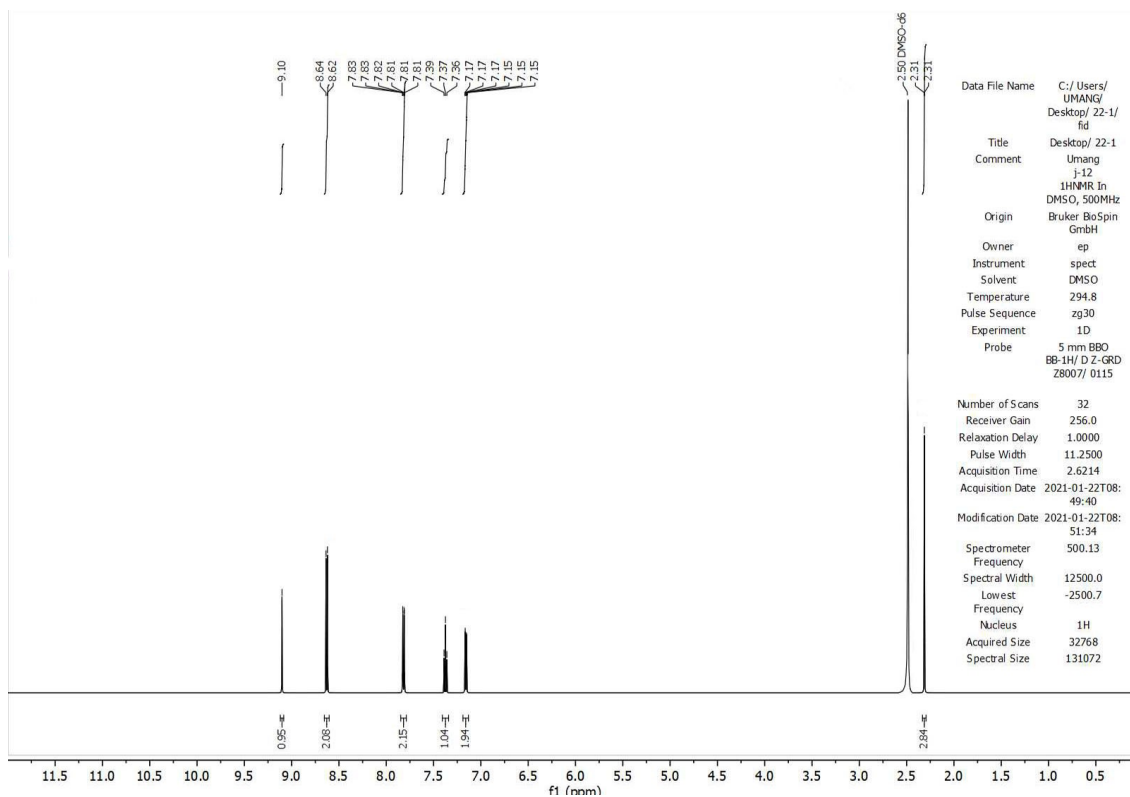


Figure 40: ^1H NMR spectrum of compound 31

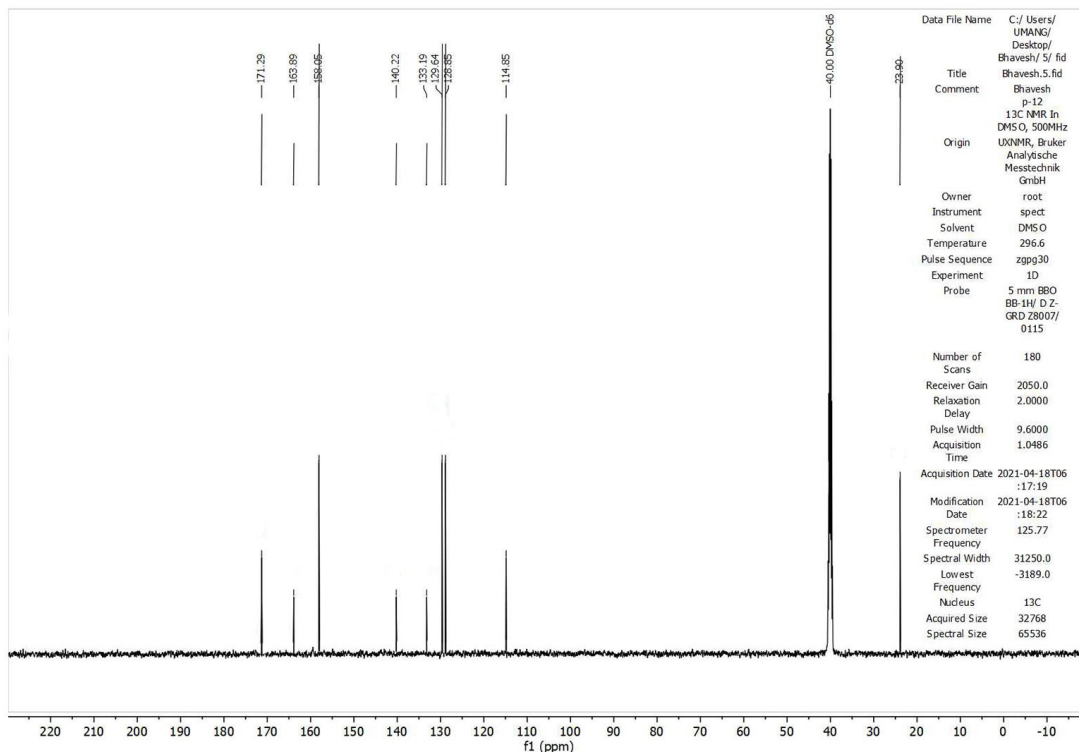


Figure 41: ¹³C NMR spectrum of compound 31

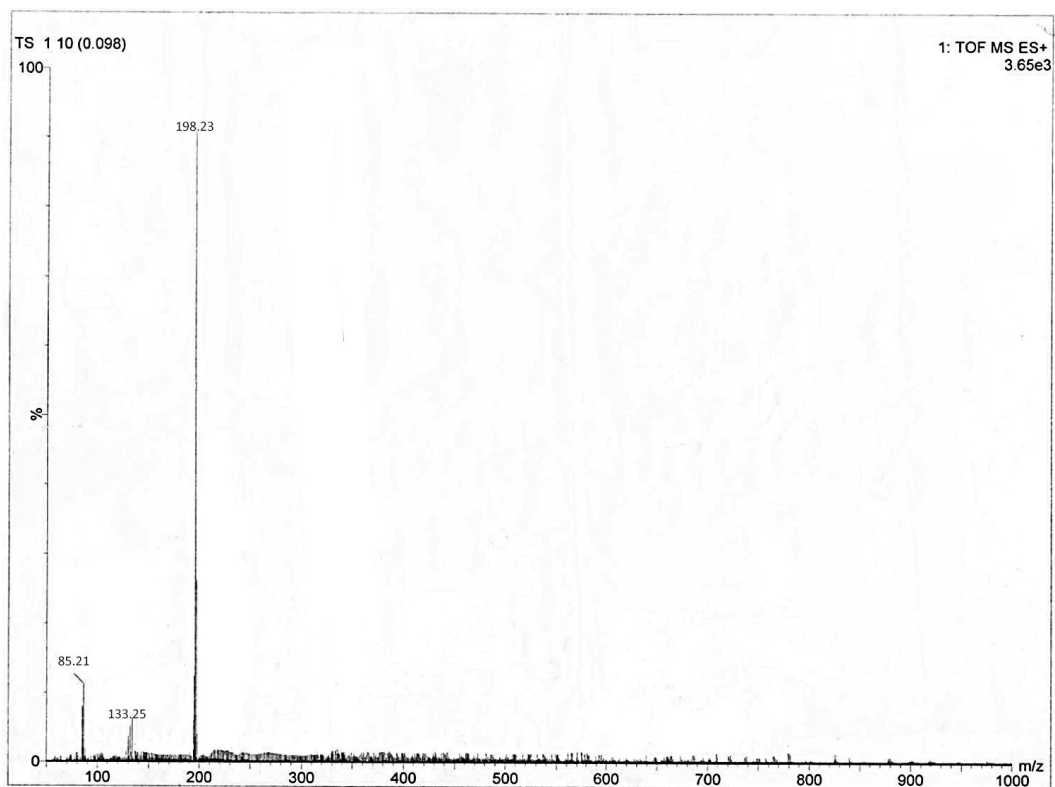


Figure 42: Mass spectrum of compound 31

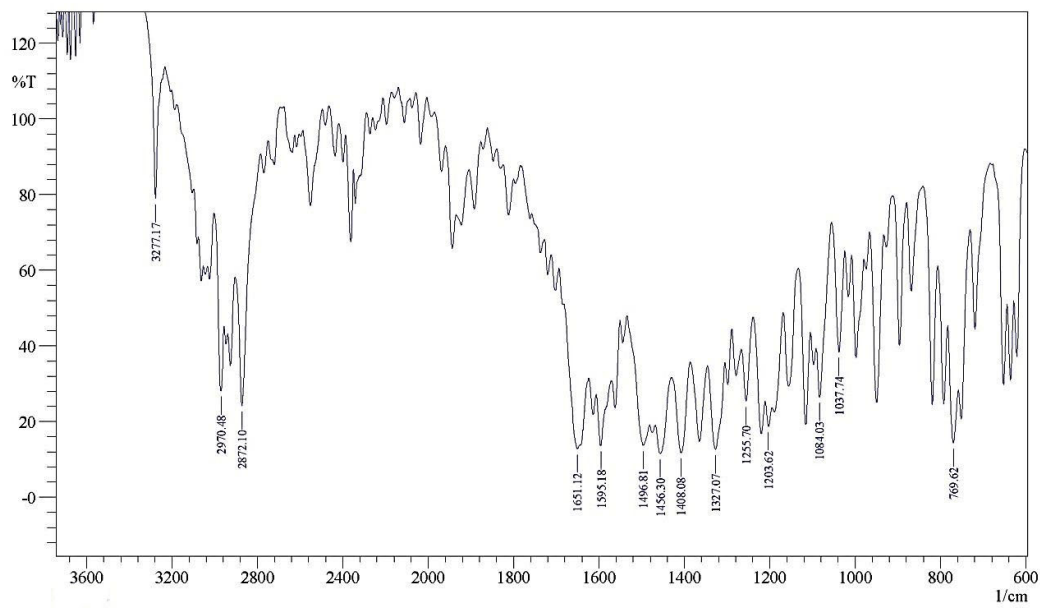


Figure 43: IR spectrum of compound 3m

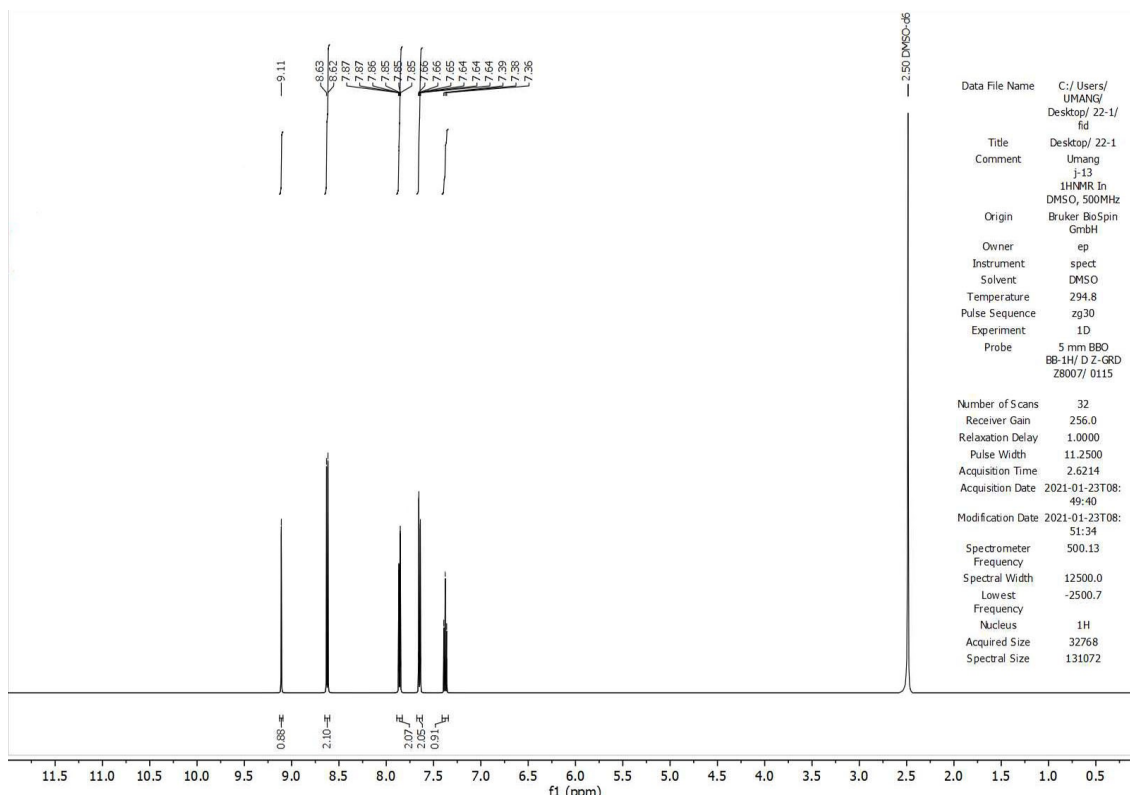


Figure 44: ¹H NMR spectrum of compound 3m

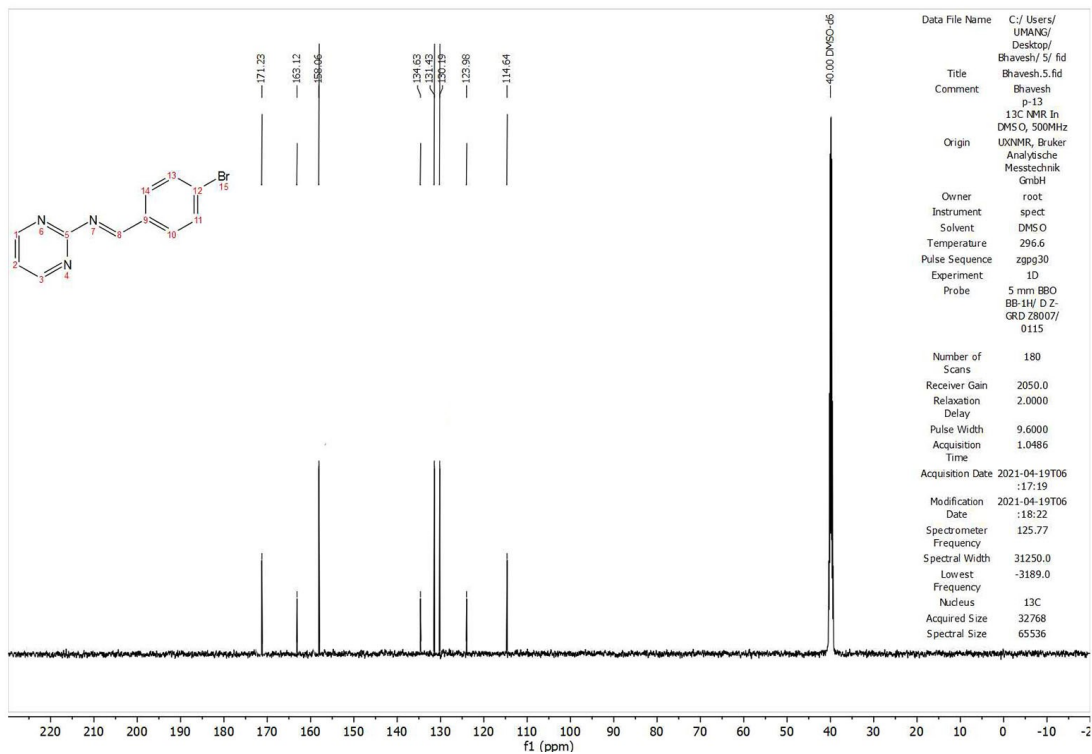


Figure 45: ¹³C NMR spectrum of compound 3m

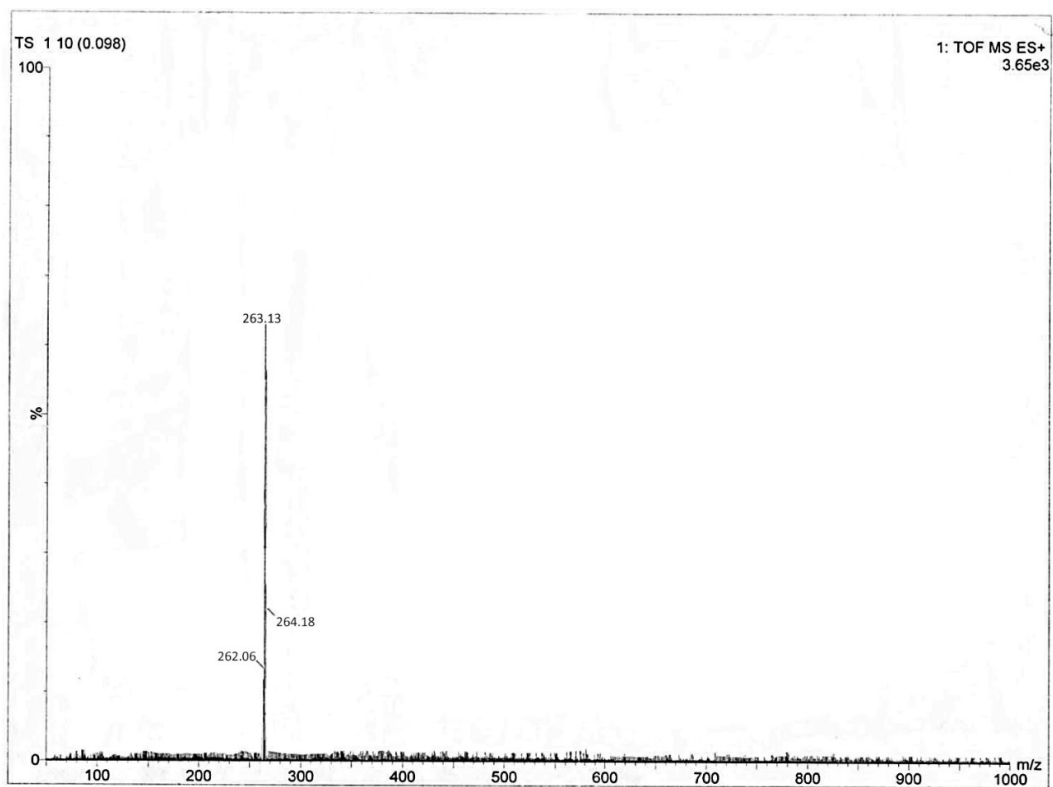


Figure 46: Mass spectrum of compound 3m

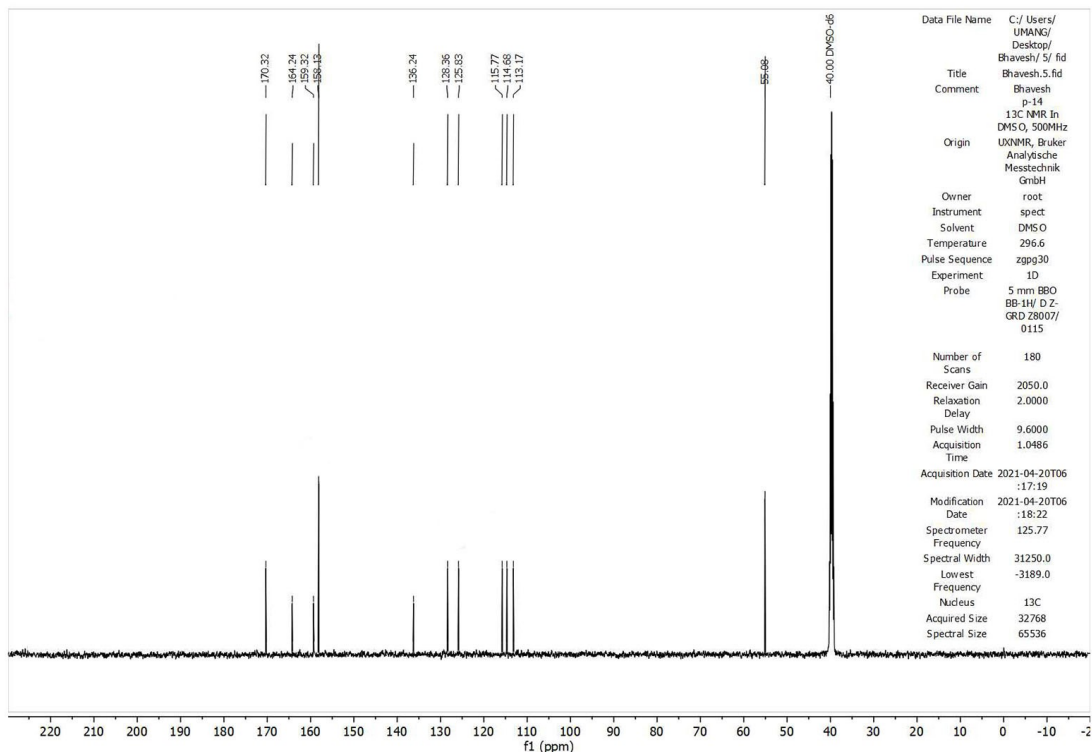


Figure 48: ^{13}C NMR spectrum of compound 3n

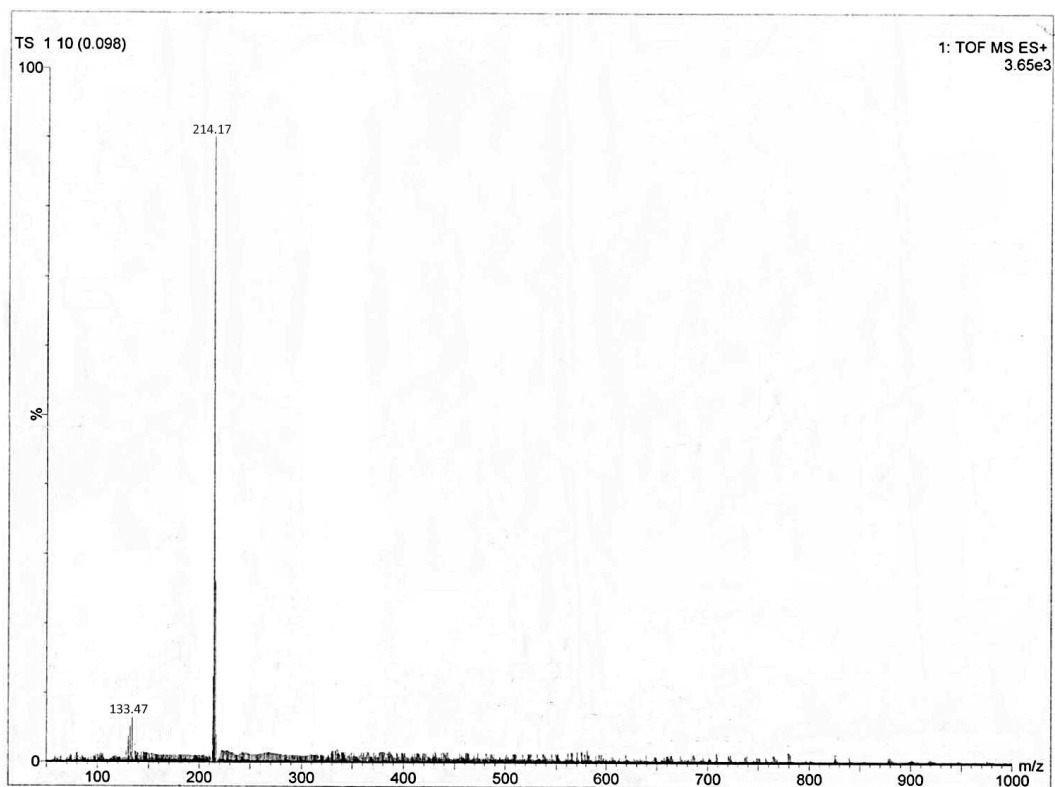


Figure 49: Mass spectrum of compound 3n

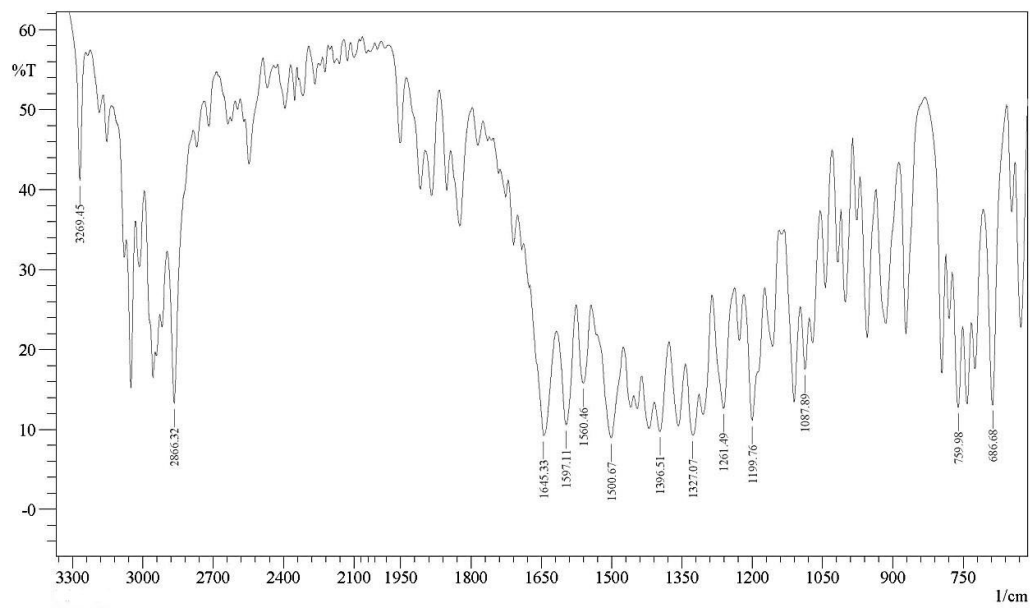


Figure 50: IR spectrum of compound 3o

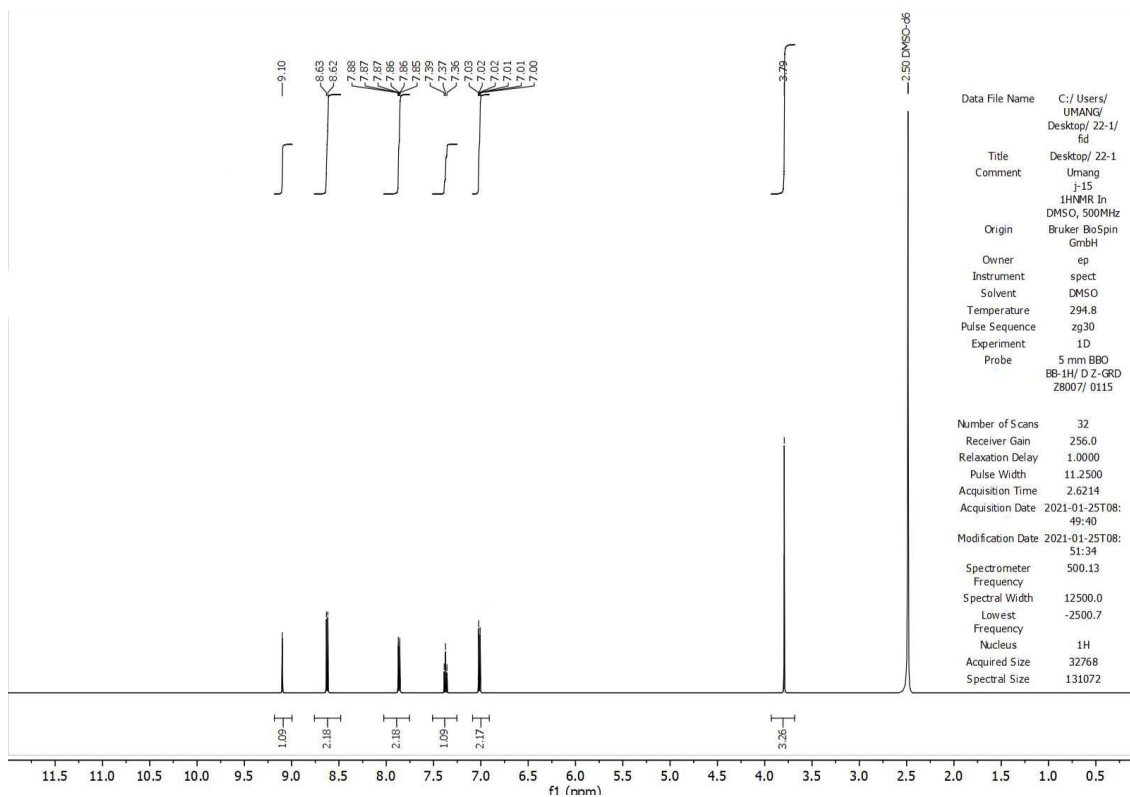


Figure 51: ¹H NMR spectrum of compound 3o

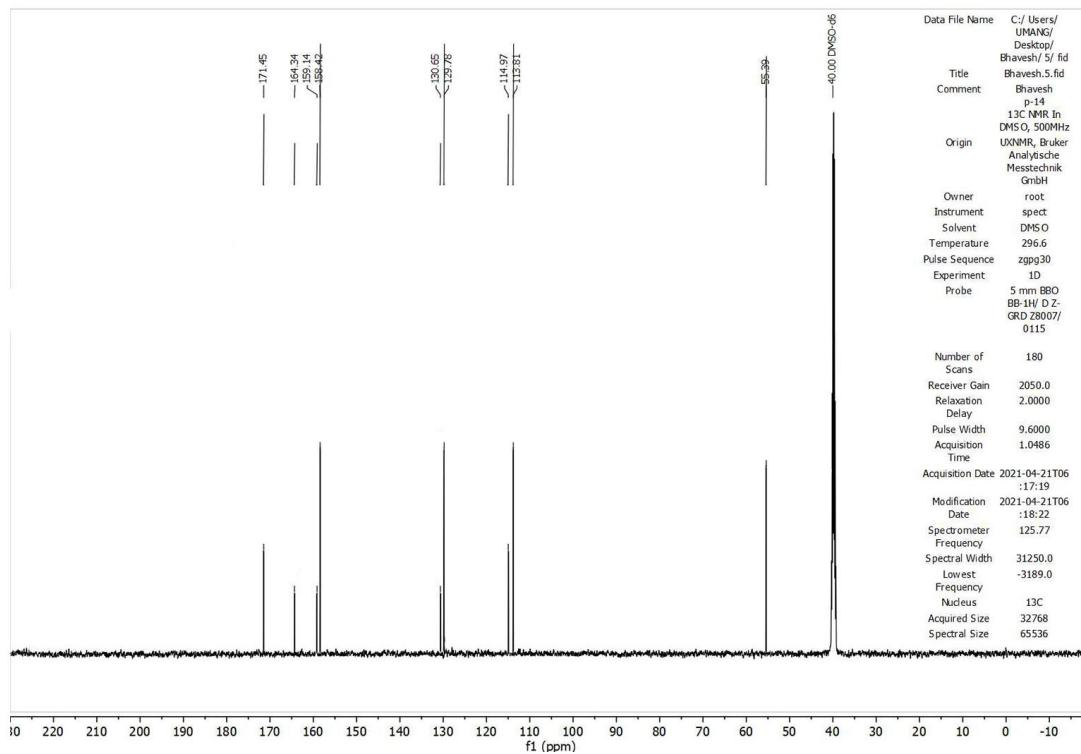


Figure 52: ¹³C NMR spectrum of compound 3o

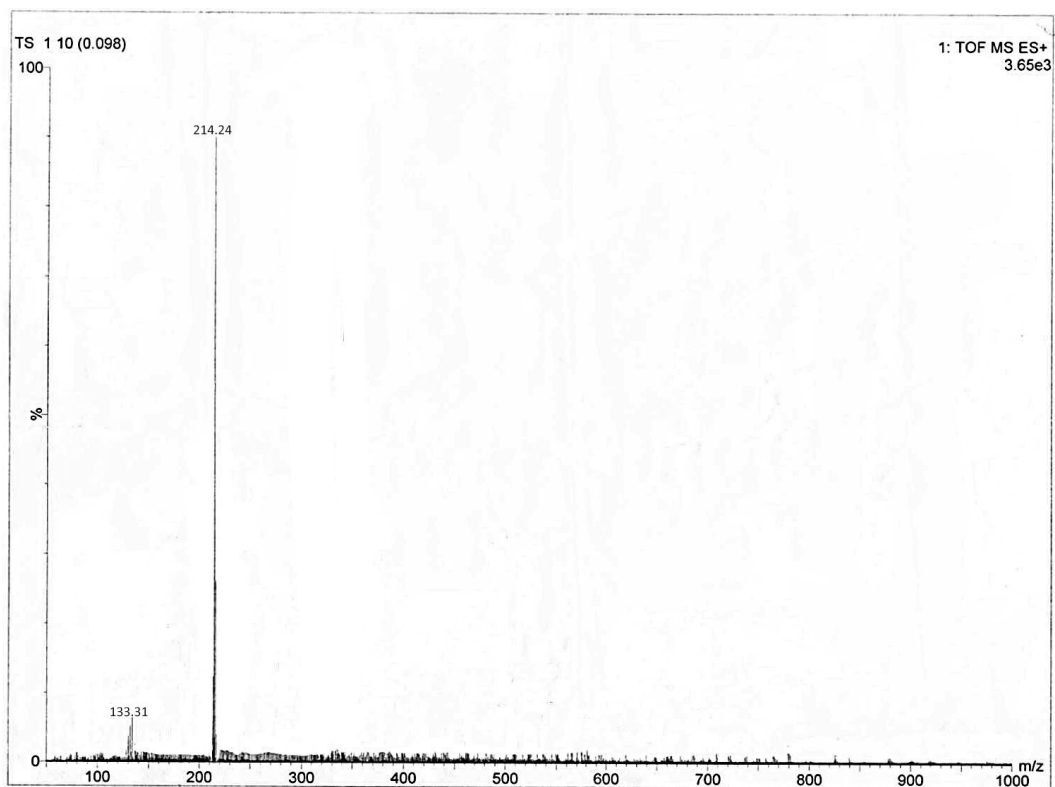


Figure 53: Mass spectrum of compound 3o

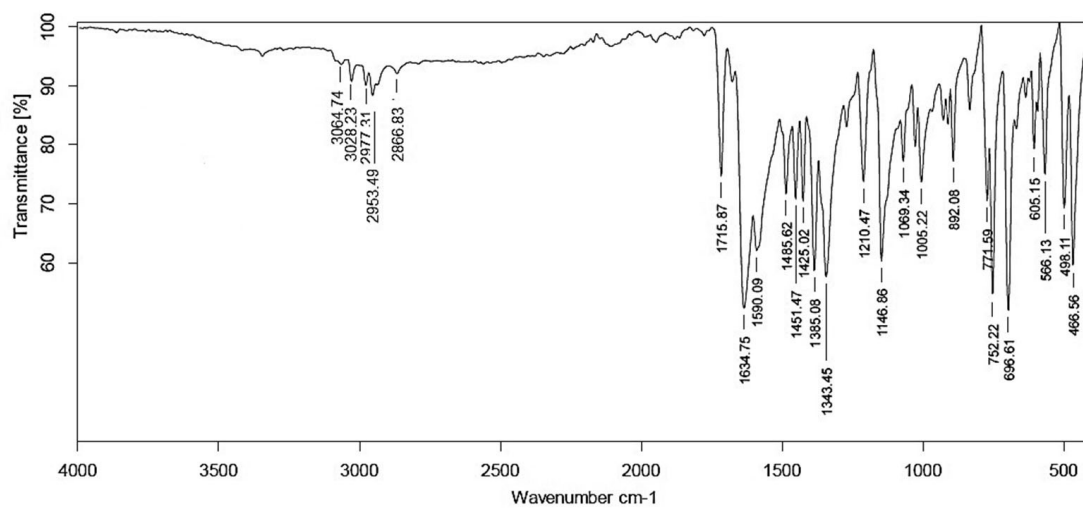


Figure 54: IR spectrum of compound 4a

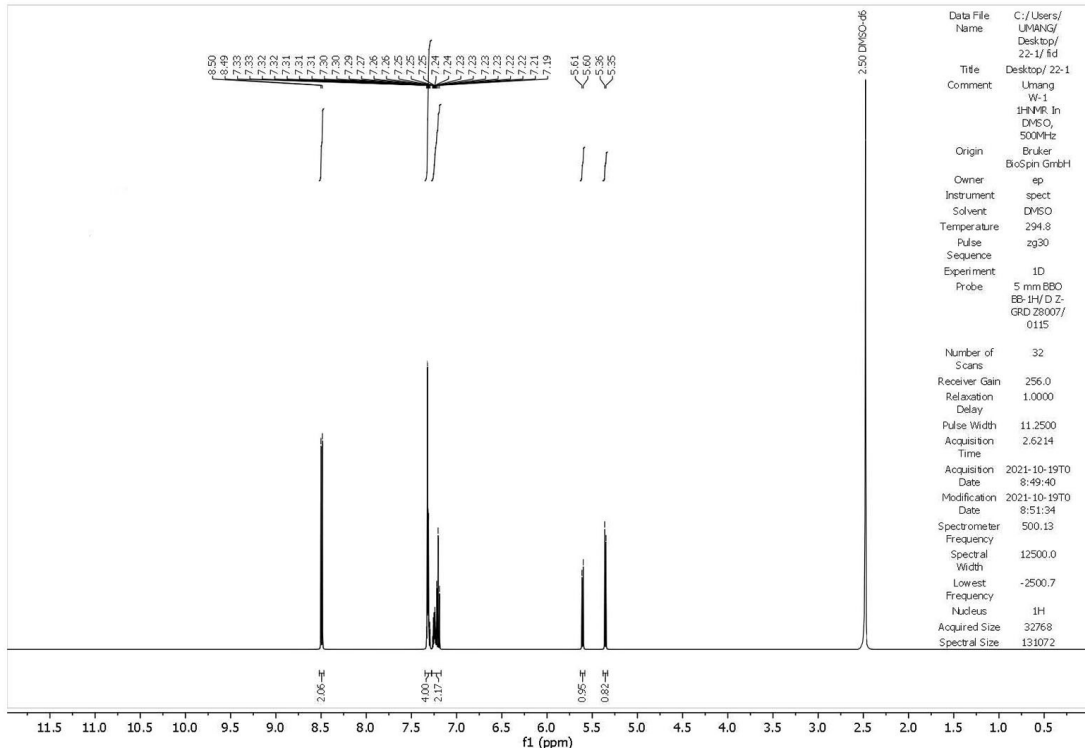


Figure 55: ¹H NMR spectrum of compound 4a

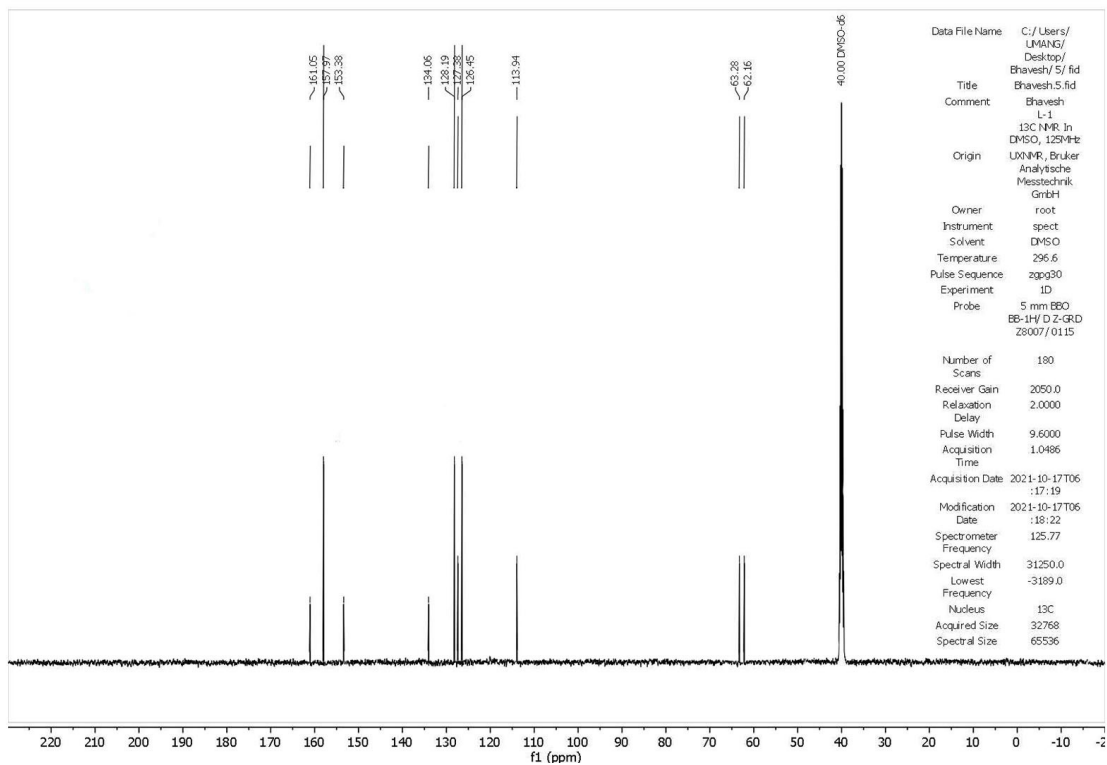


Figure 56: ^{13}C NMR spectrum of compound 4a

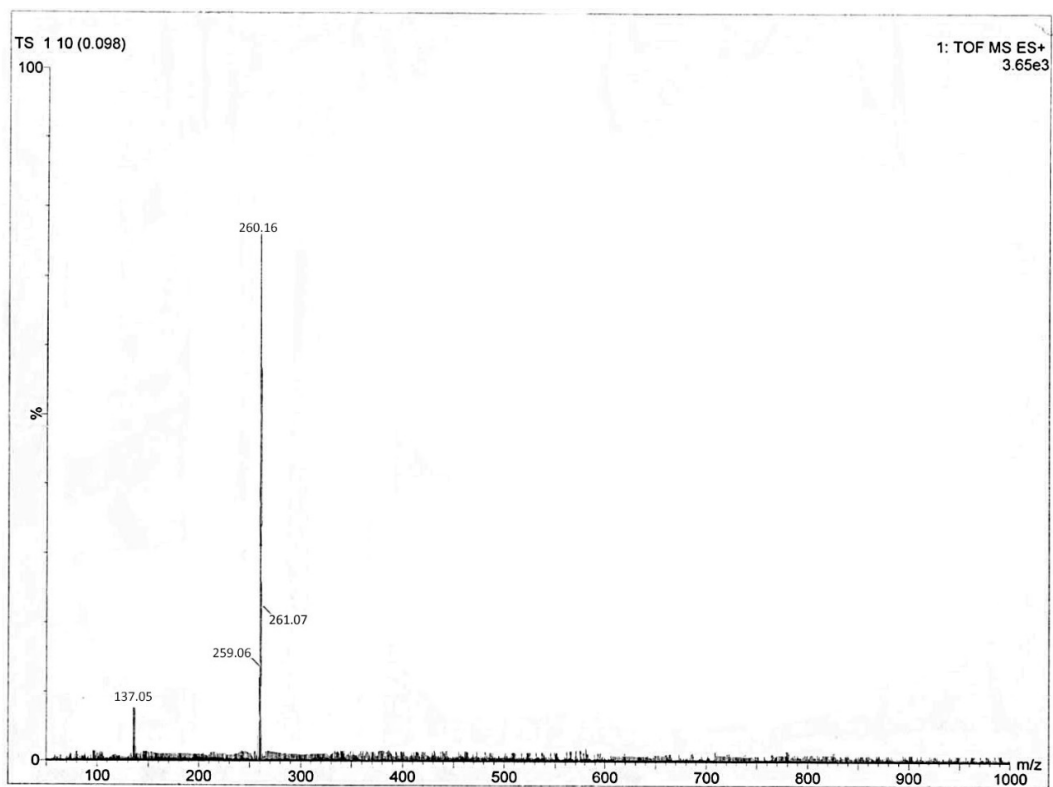


Figure 57: Mass spectrum of compound 4a

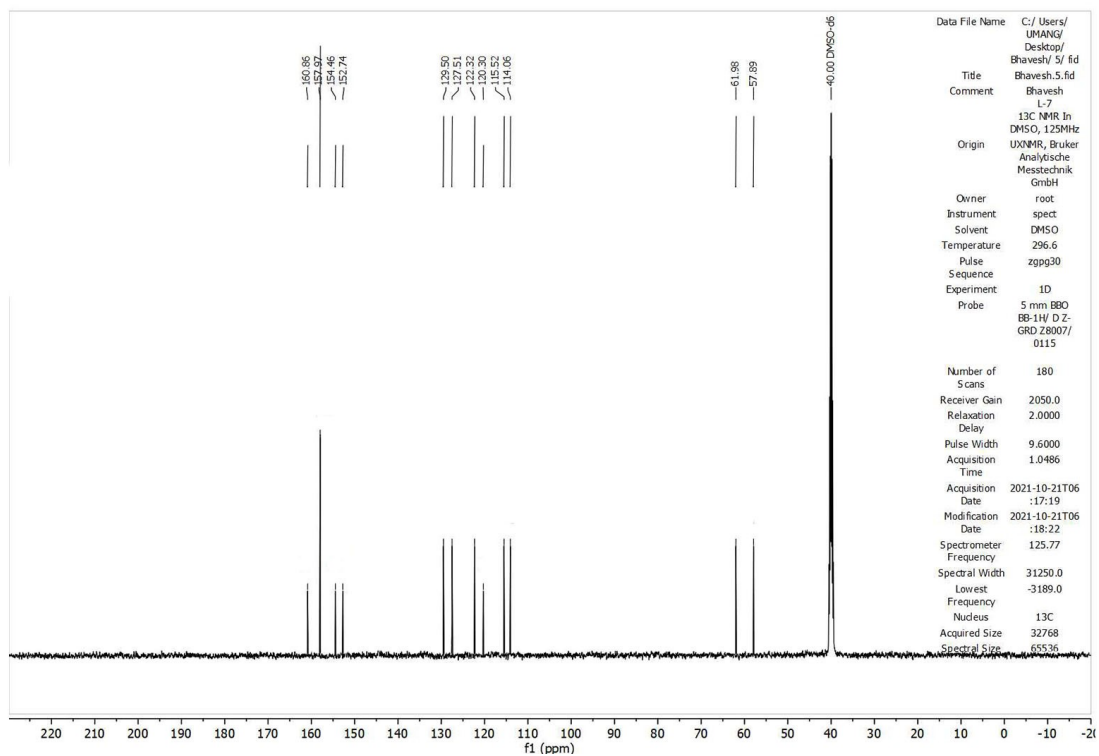


Figure 59: ^{13}C NMR spectrum of compound **4b**

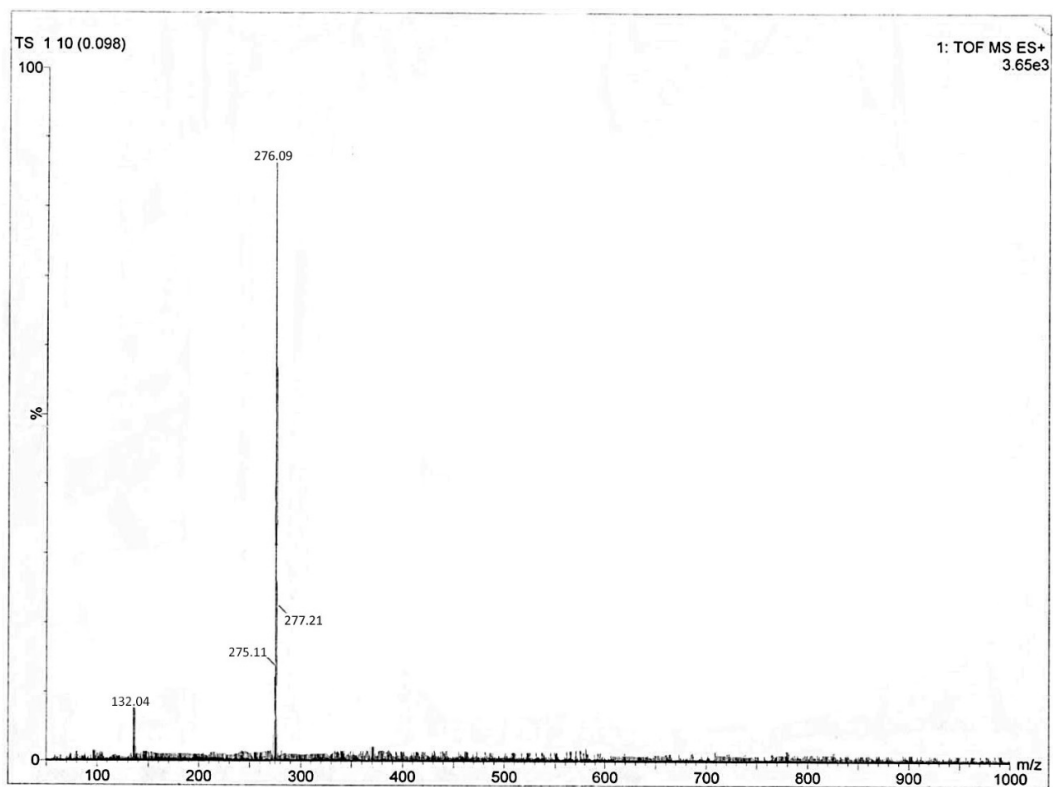


Figure 60: Mass spectrum of compound 4b

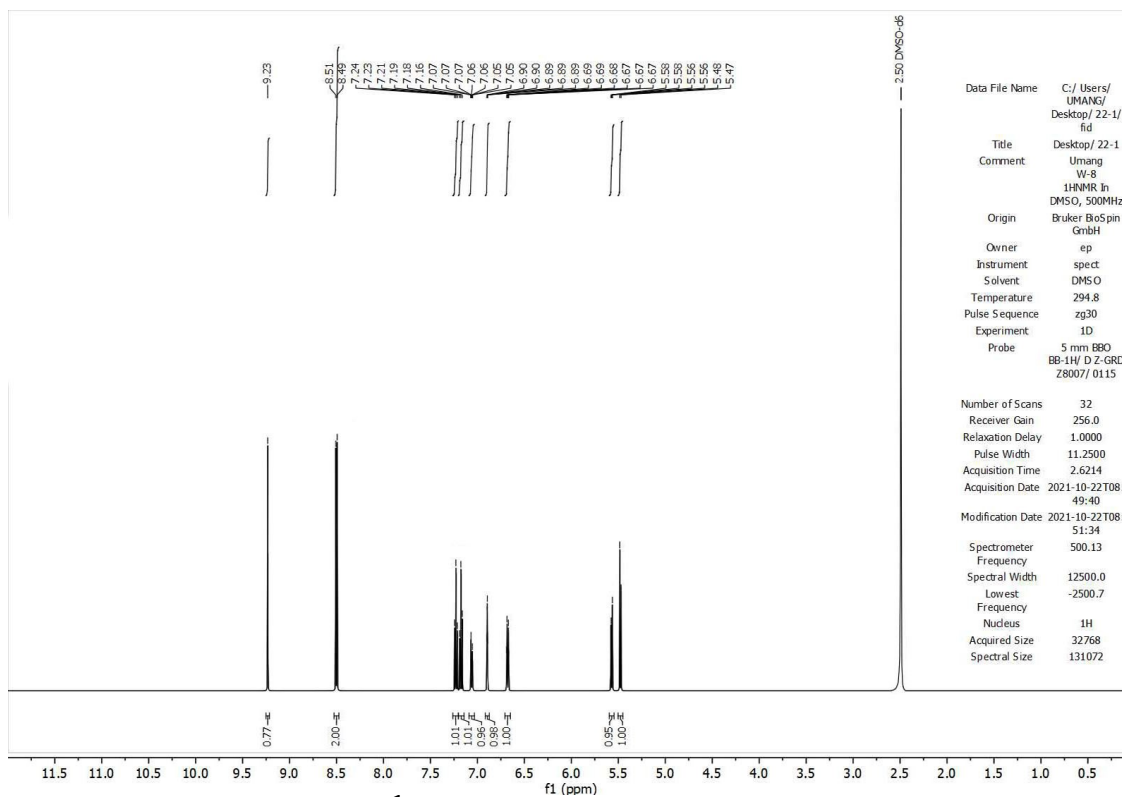


Figure 61: ^1H NMR spectrum of compound 4c

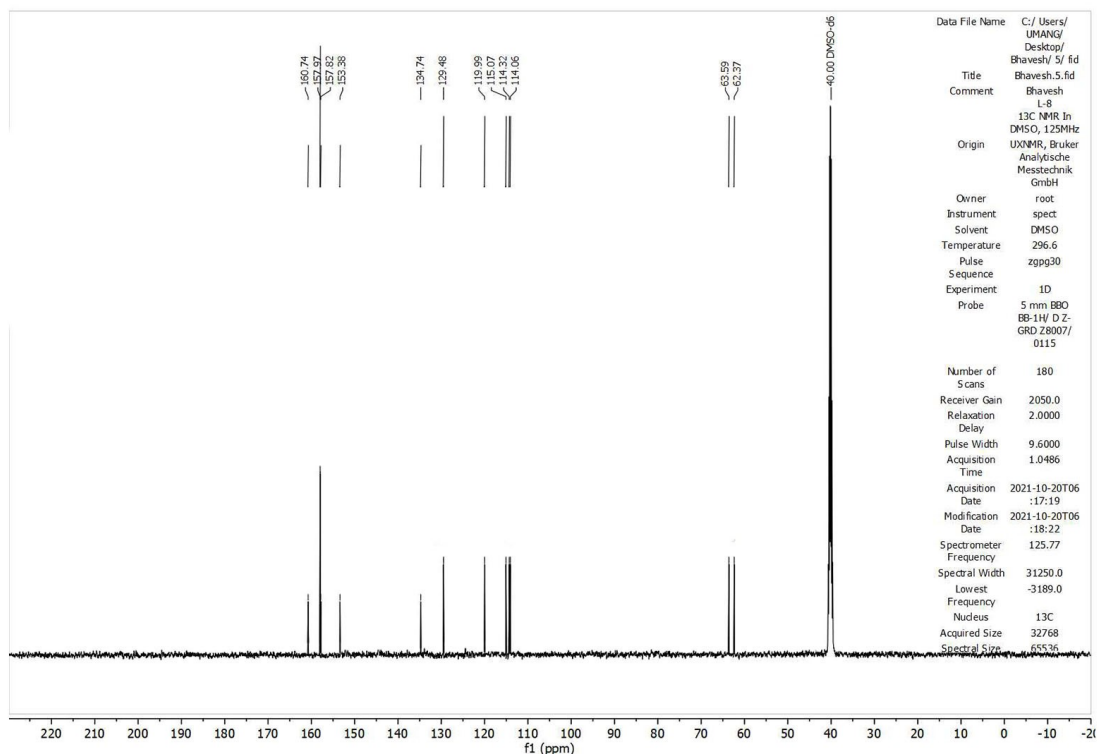


Figure 62: ^{13}C NMR spectrum of compound 4c

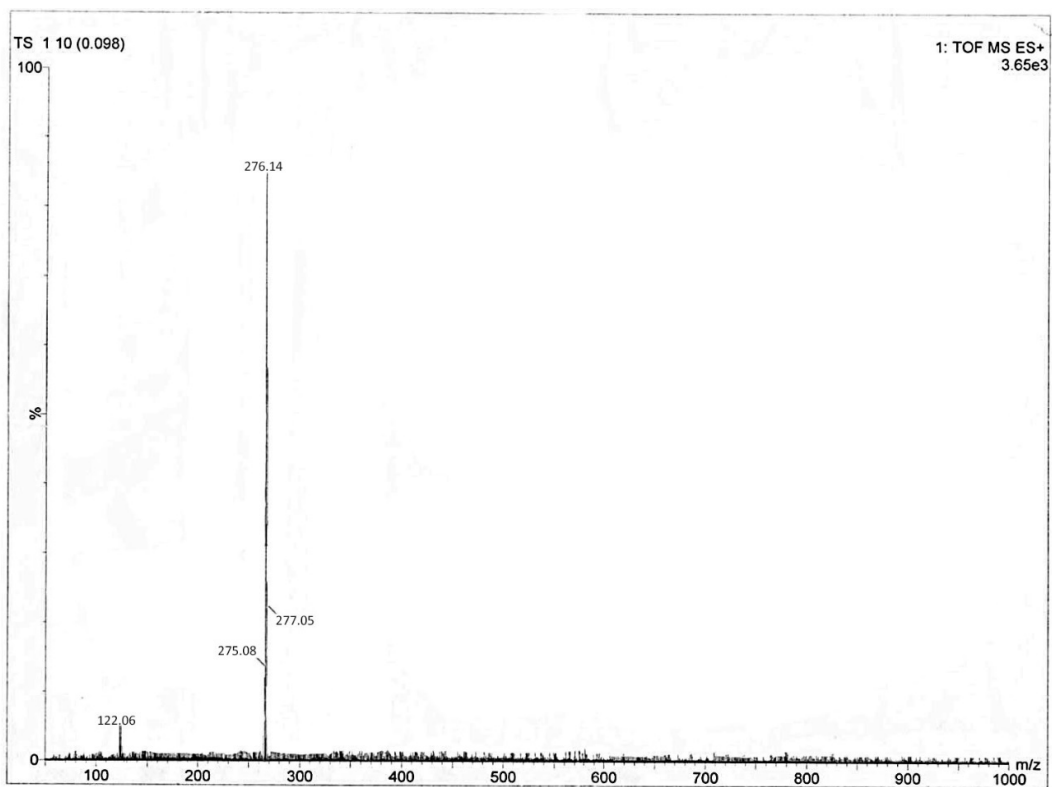


Figure 63: Mass spectrum of compound 4c

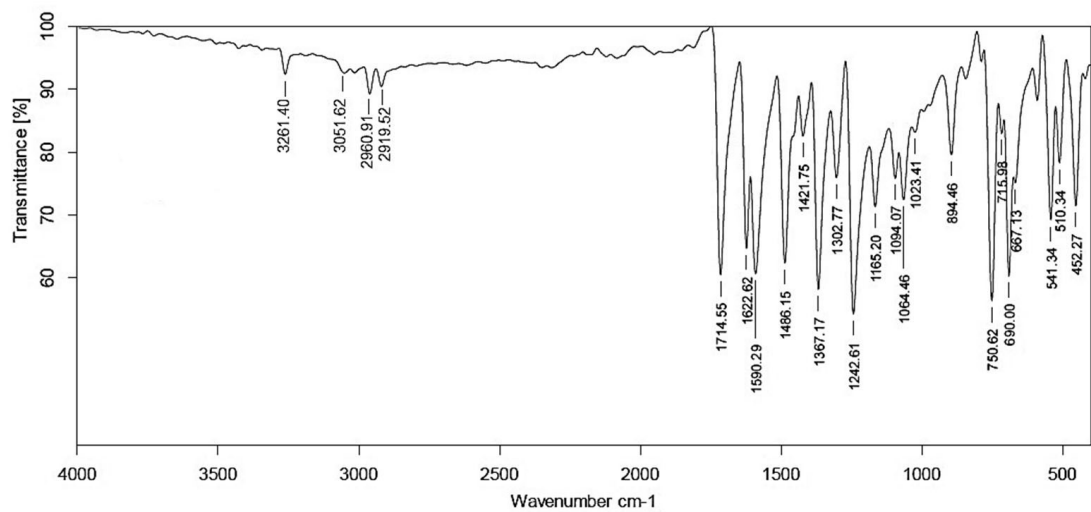


Figure 64: IR spectrum of compound 4d

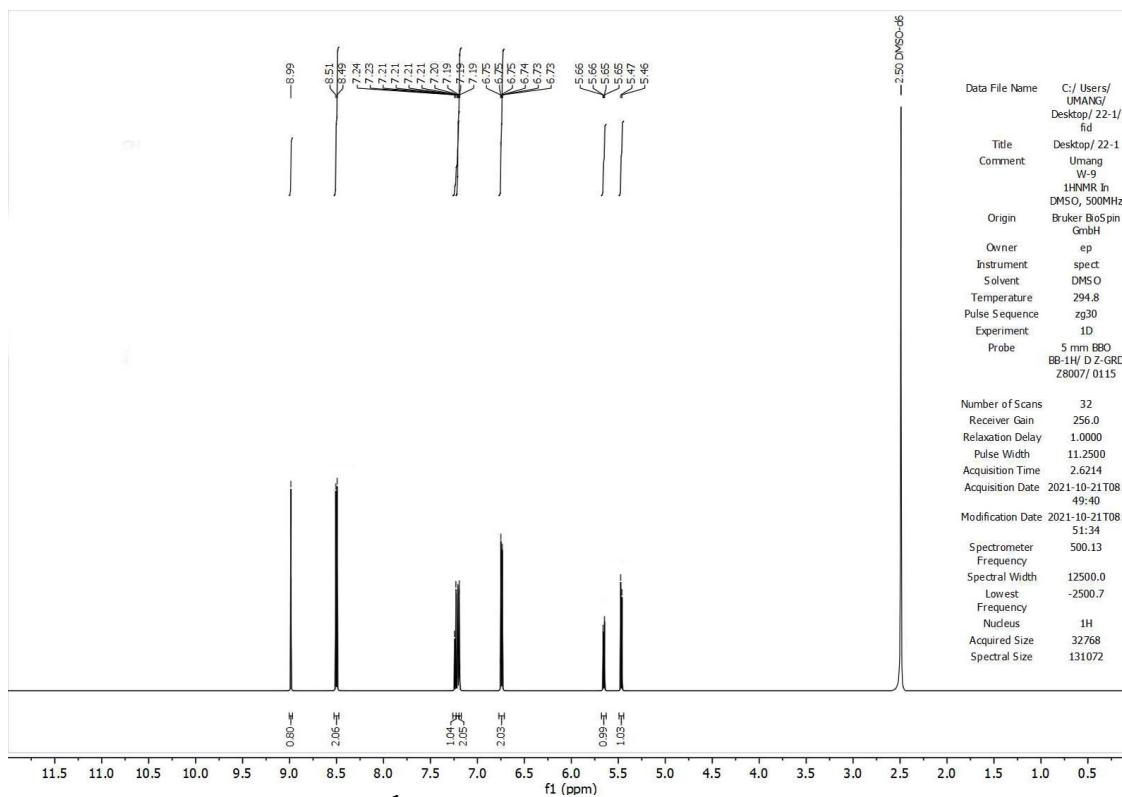


Figure 65: ^1H NMR spectrum of compound 4d

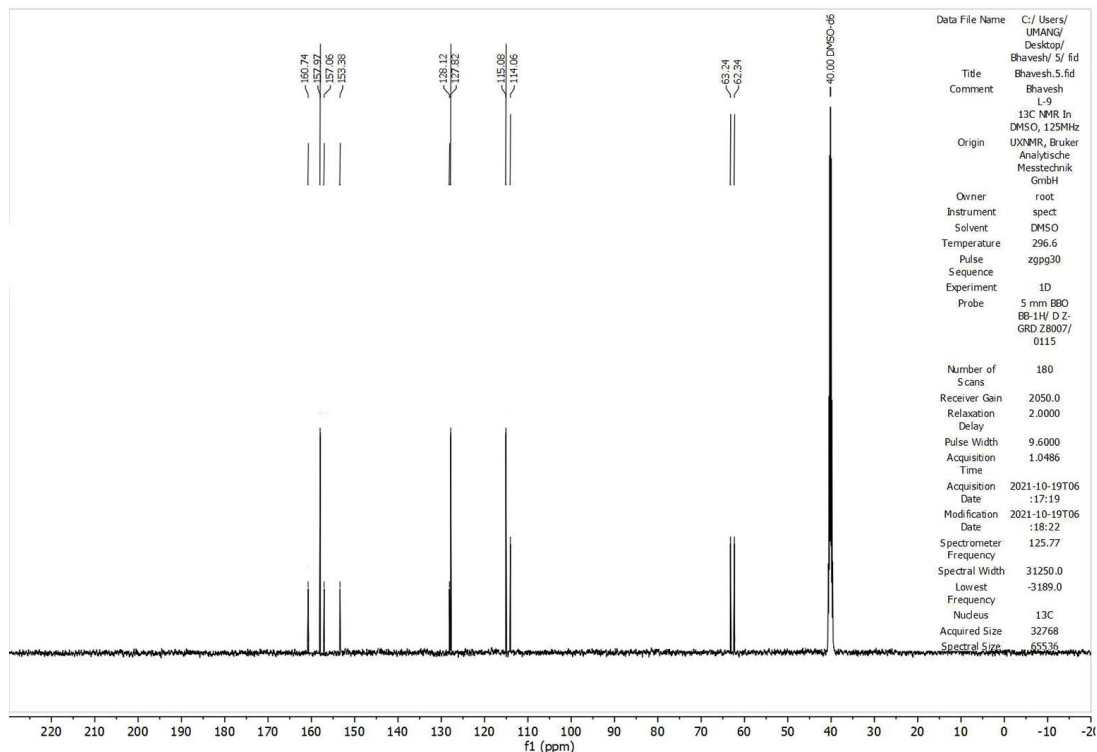


Figure 66: ^{13}C NMR spectrum of compound 4d

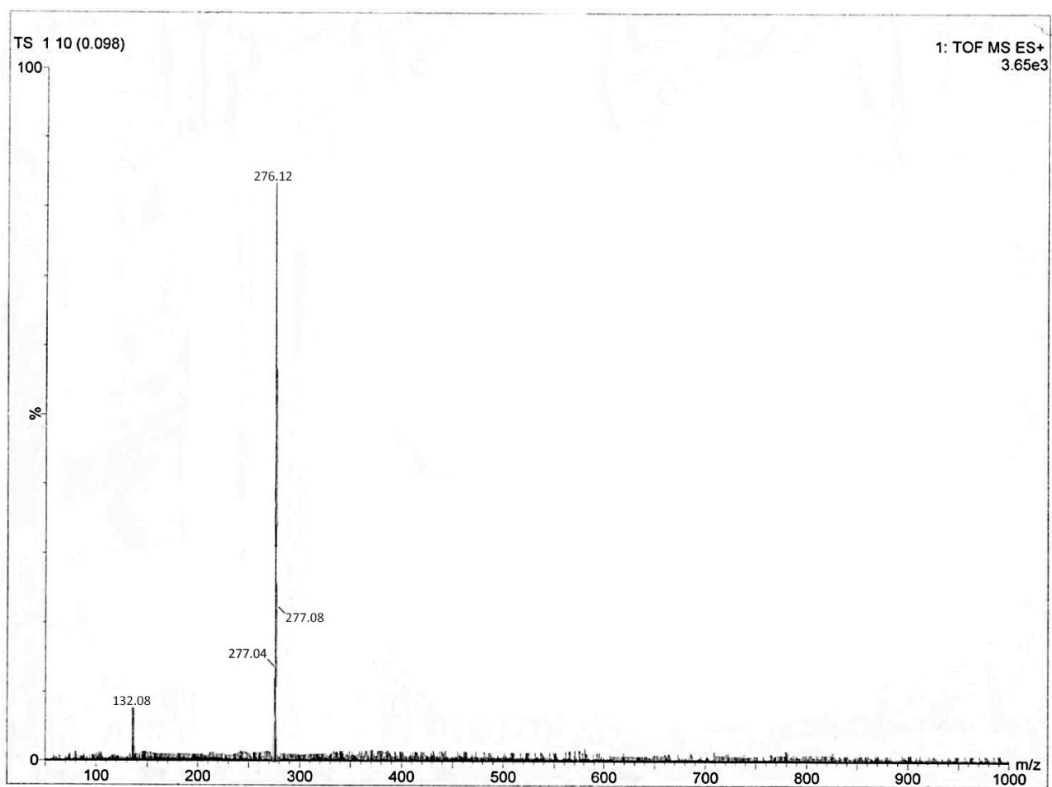


Figure 67: Mass spectrum of compound 4d

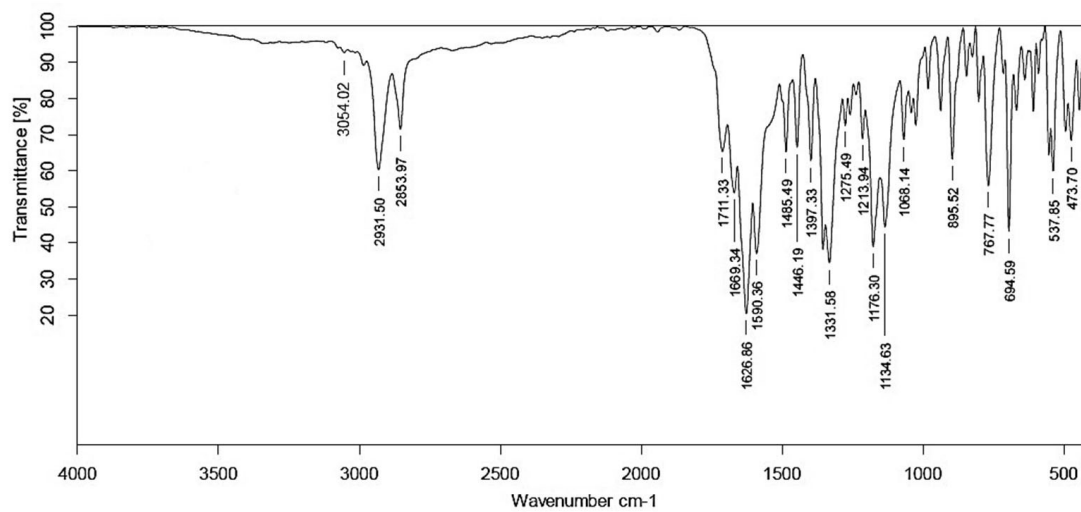


Figure 68: IR spectrum of compound 4e

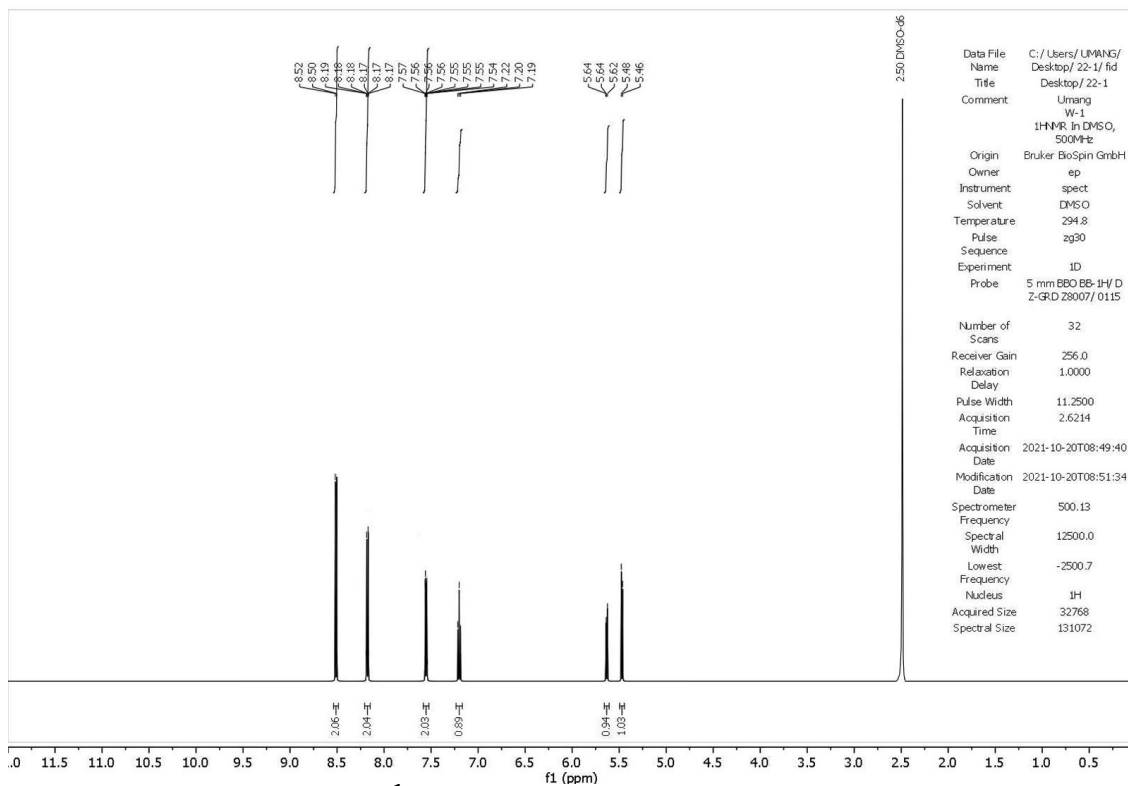


Figure 69: ¹H NMR spectrum of compound 4e

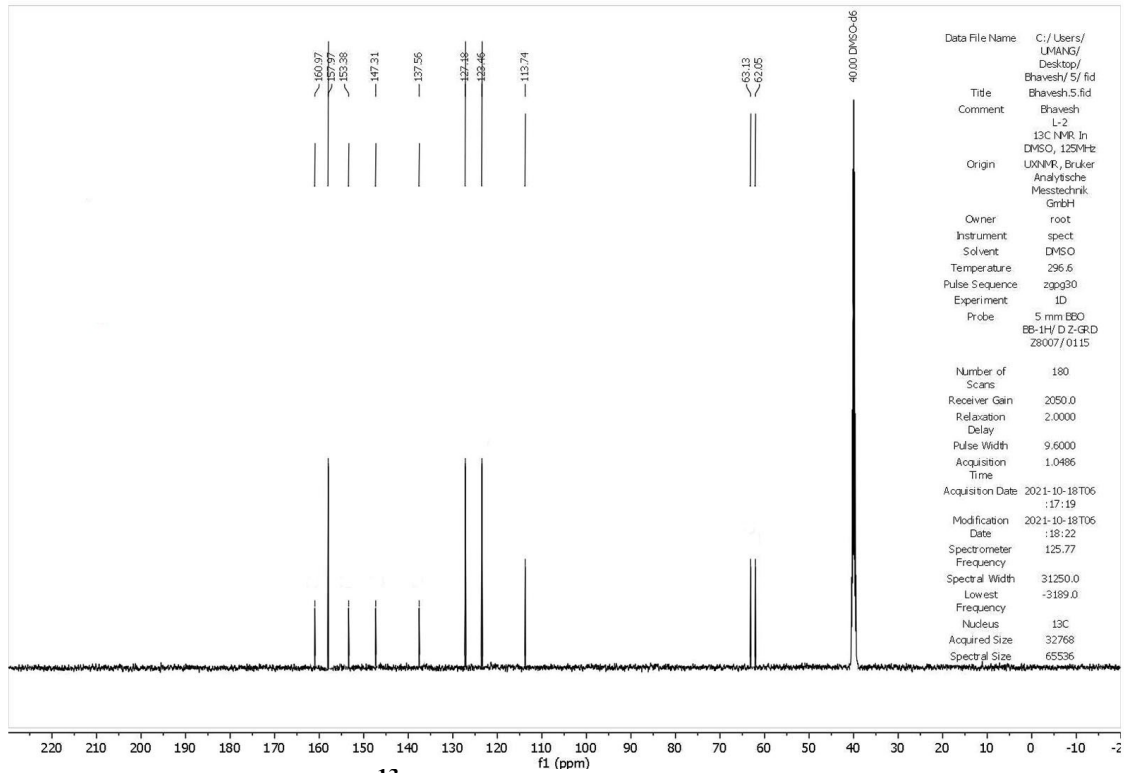


Figure 70: ^{13}C NMR spectrum of compound 4e

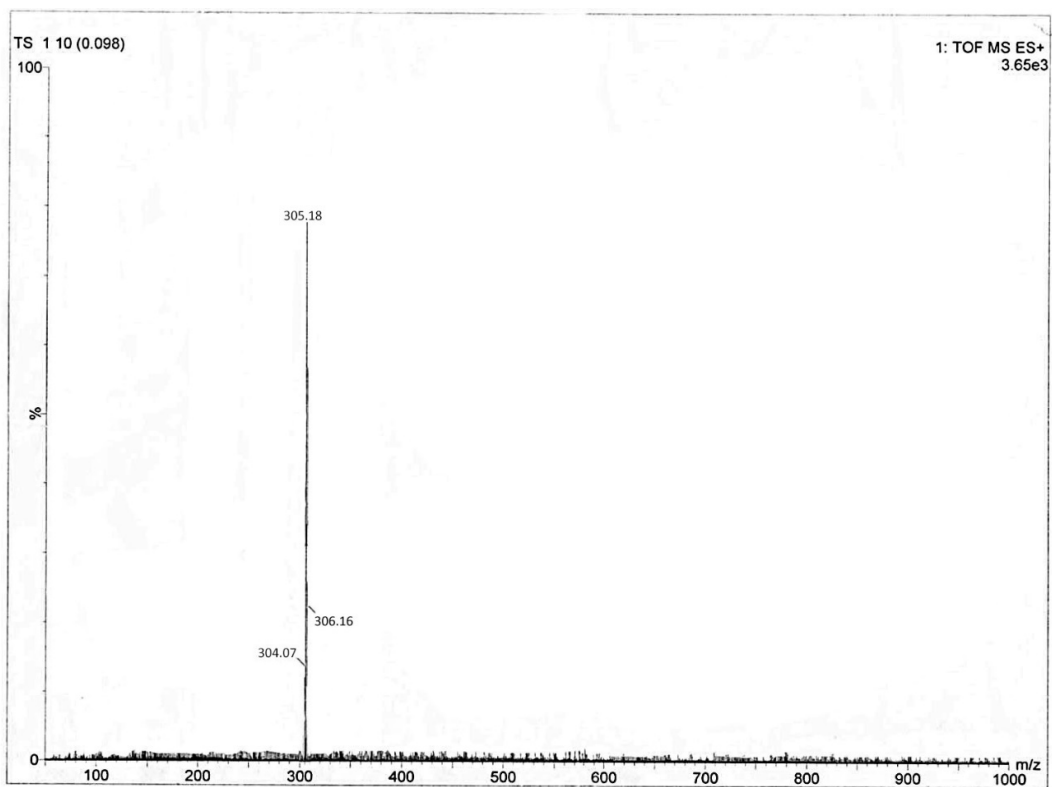


Figure 71: Mass spectrum of compound 4e

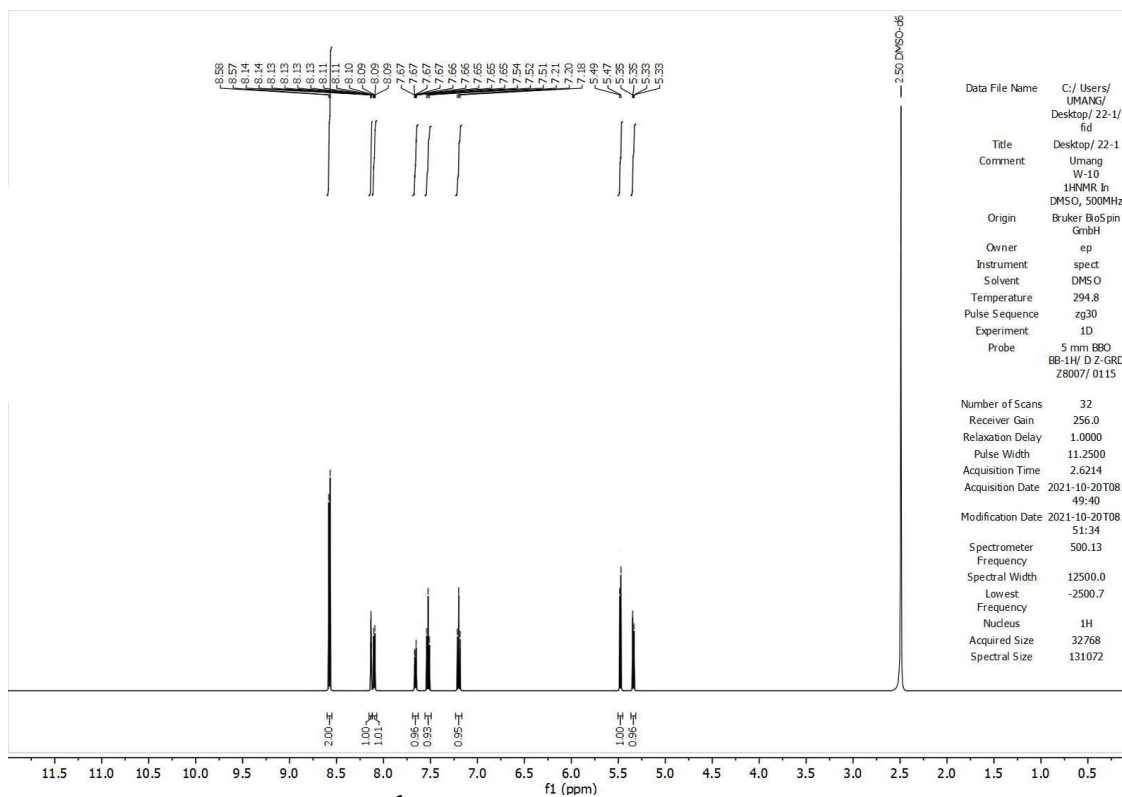


Figure 72: ^1H NMR spectrum of compound 4f

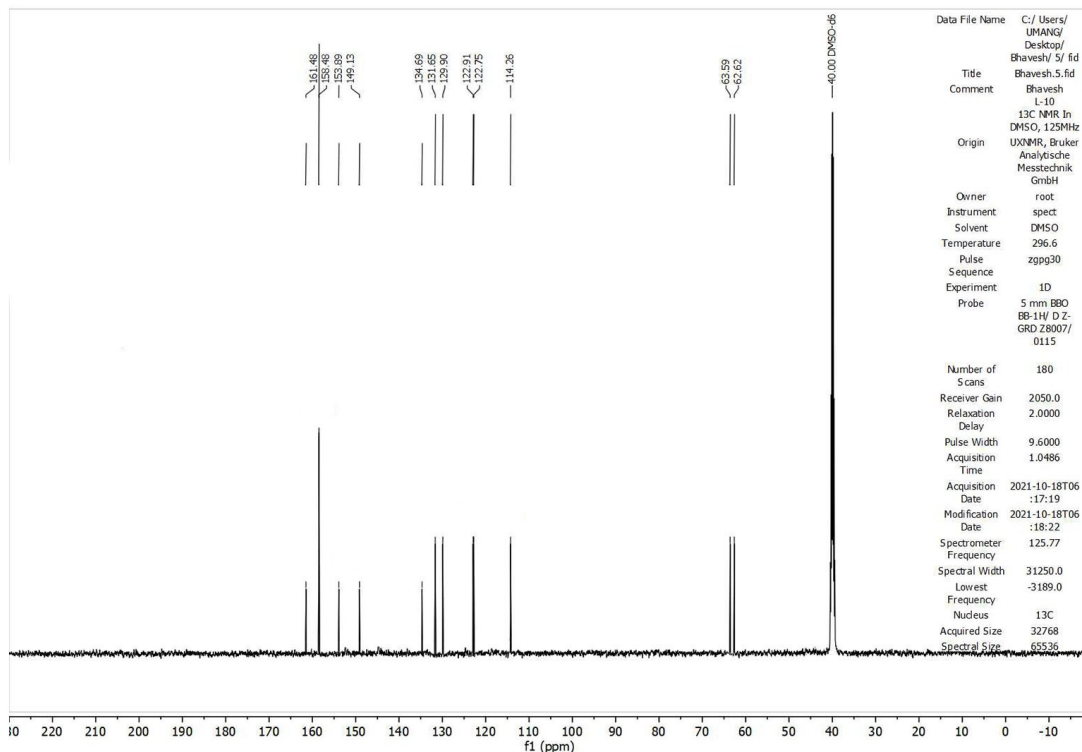


Figure 73: ^{13}C NMR spectrum of compound 4f

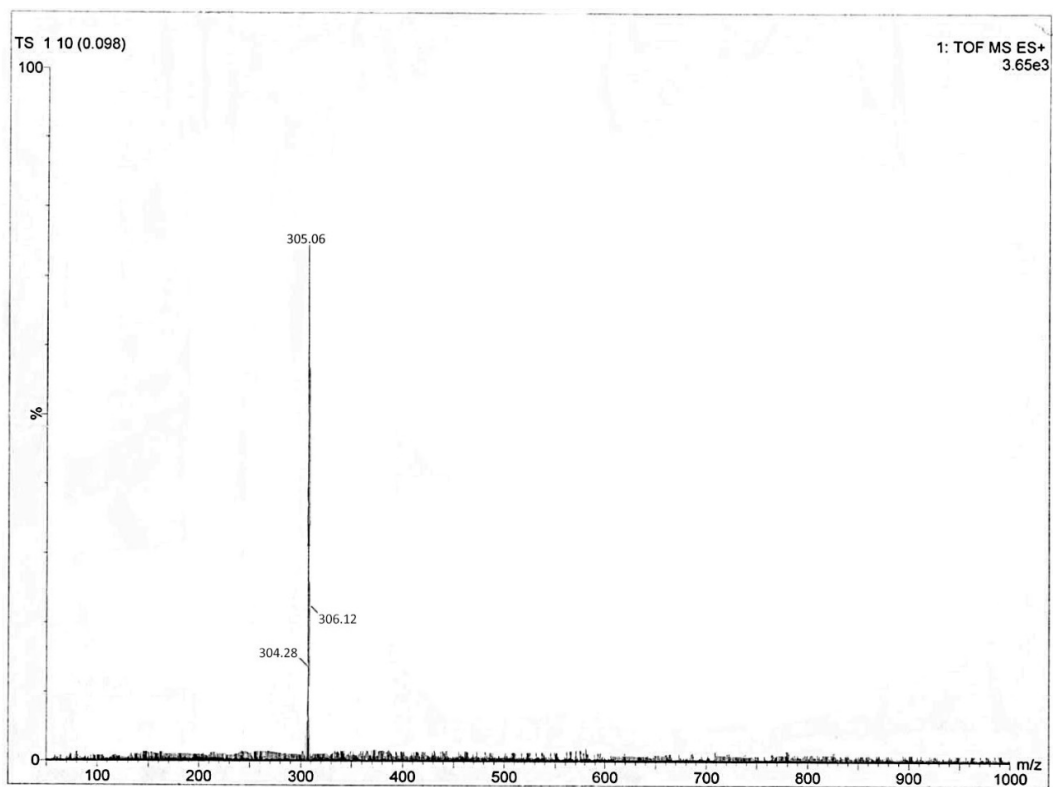


Figure 74: Mass spectrum of compound 4f

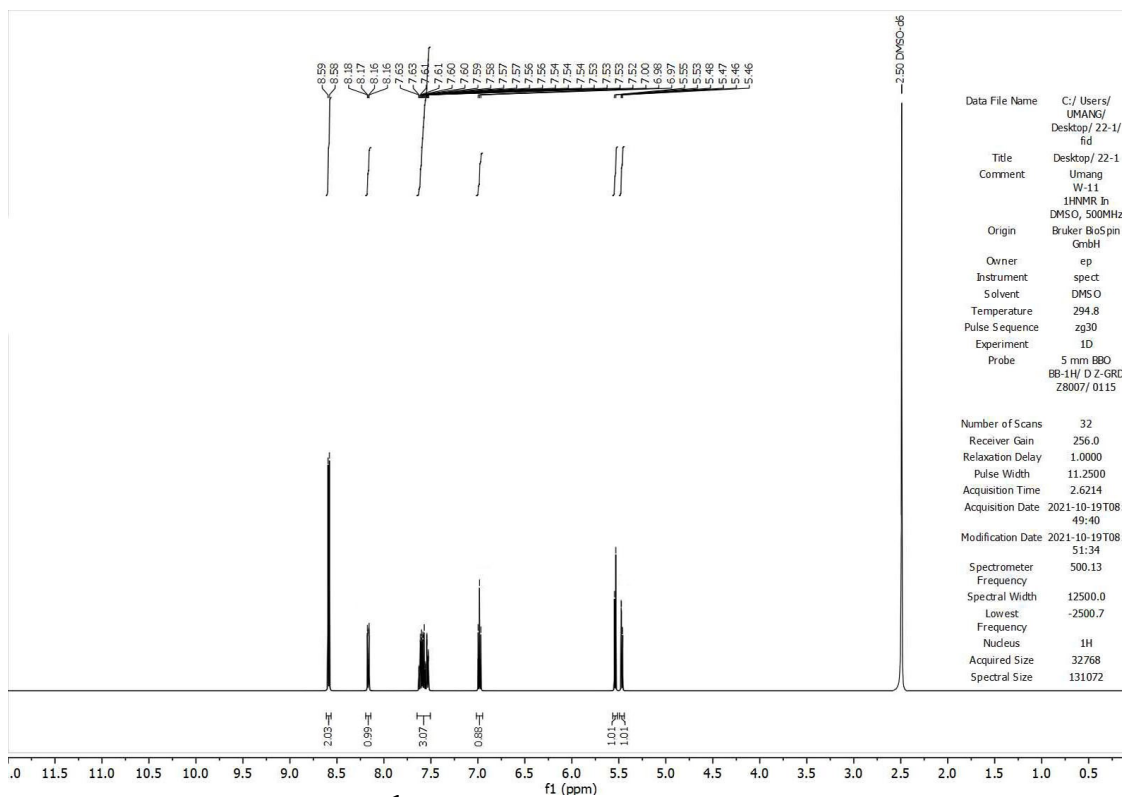


Figure 75: ¹H NMR spectrum of compound 4g

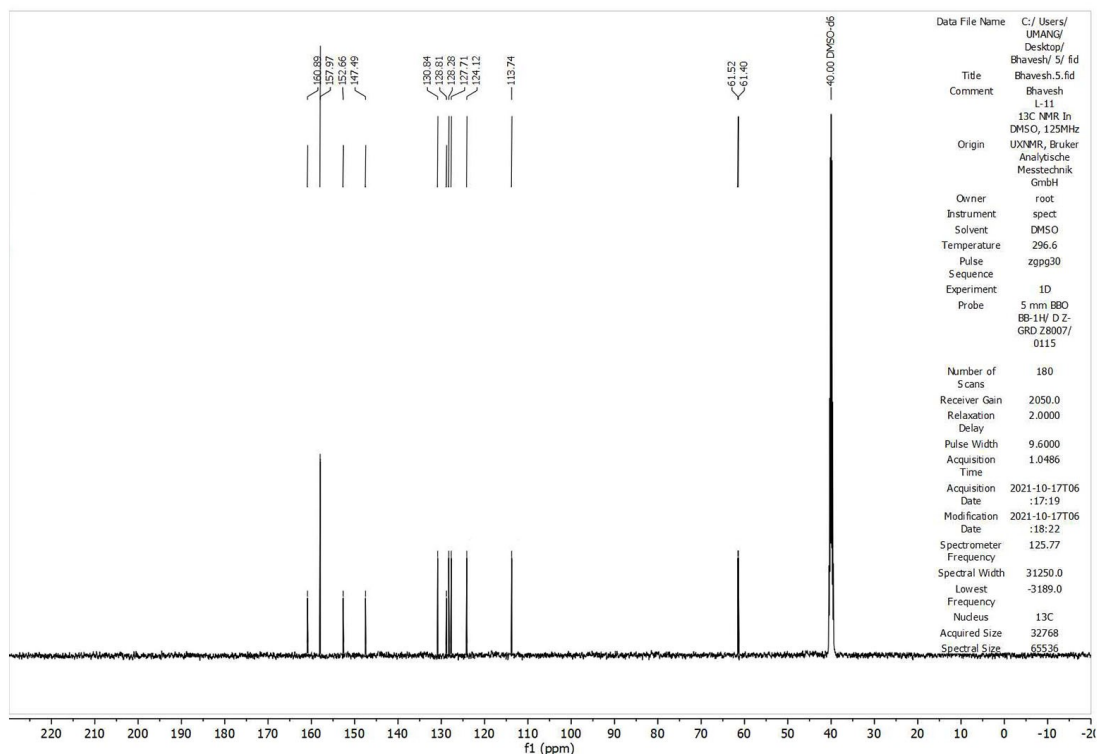


Figure 76: ^{13}C NMR spectrum of compound 4g

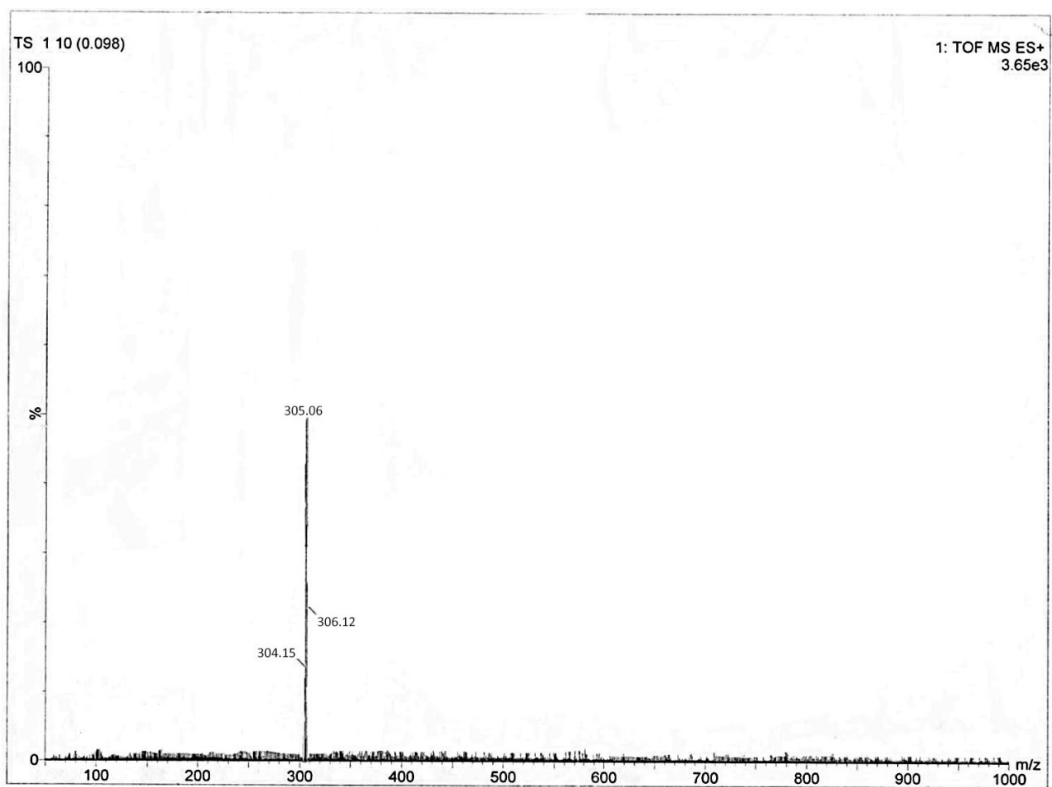


Figure 77: Mass spectrum of compound 4g

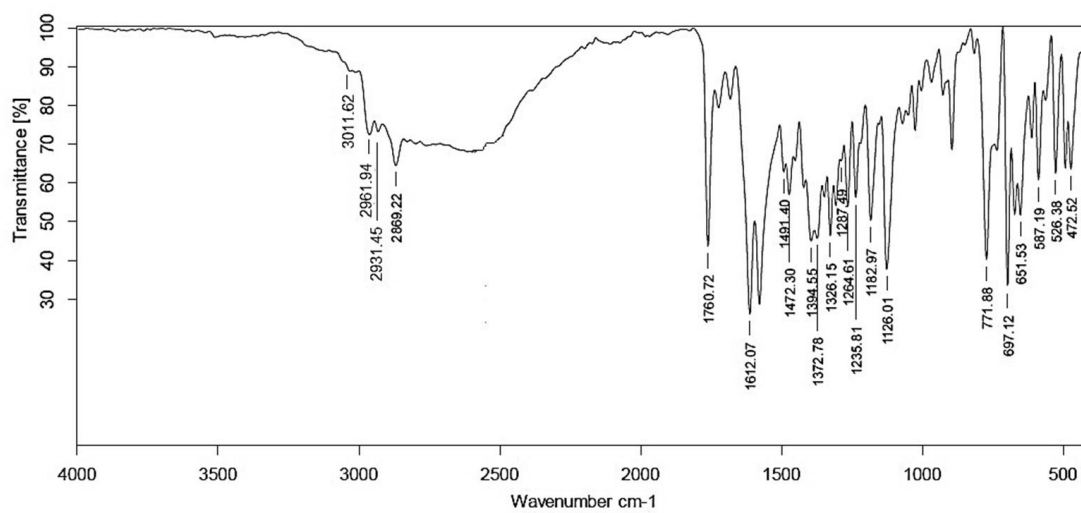


Figure 78: IR spectrum of compound 4h

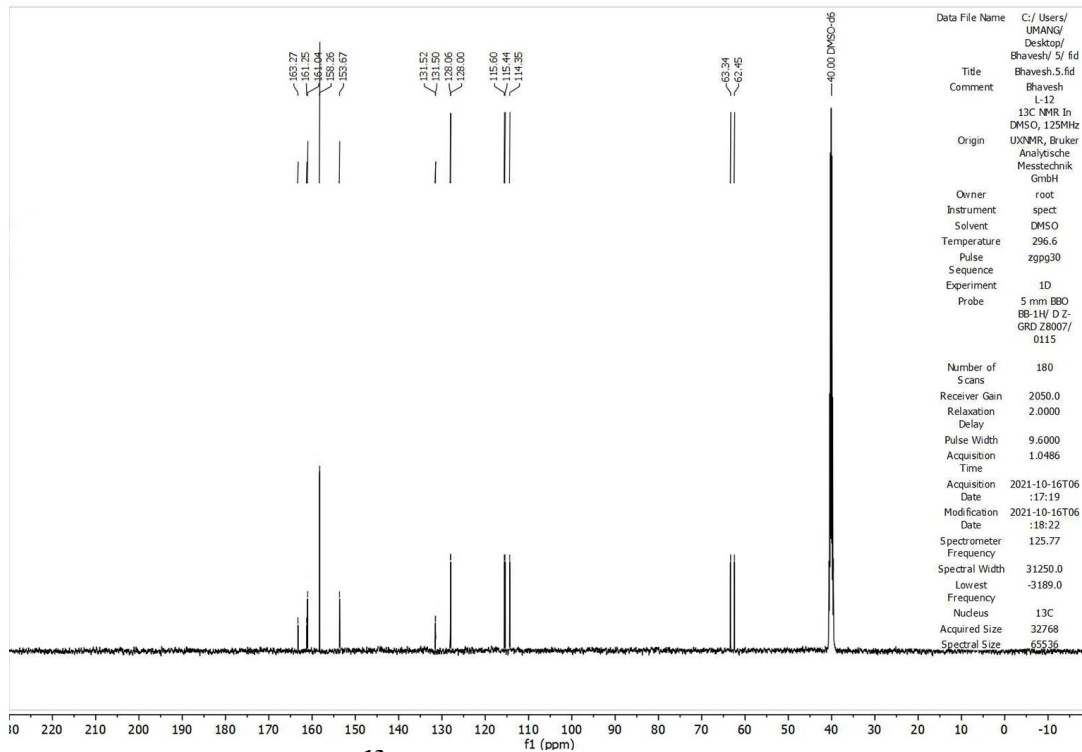


Figure 80: ^{13}C NMR spectrum of compound 4h

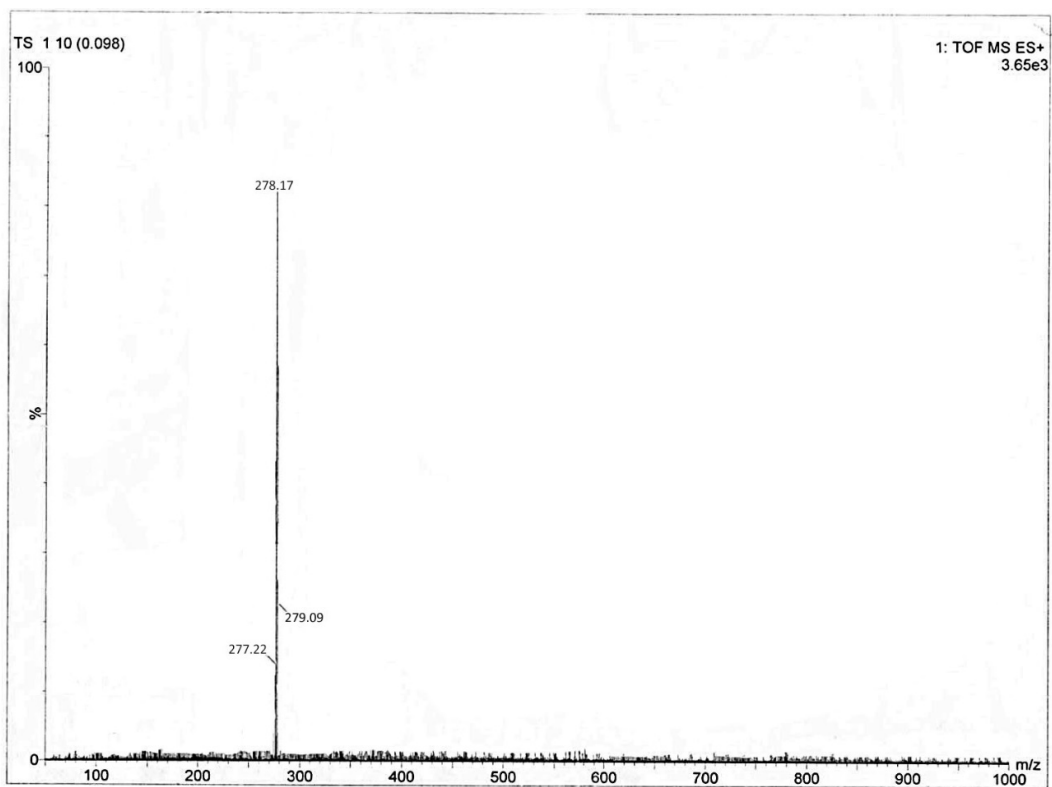


Figure 81: Mass spectrum of compound 4h

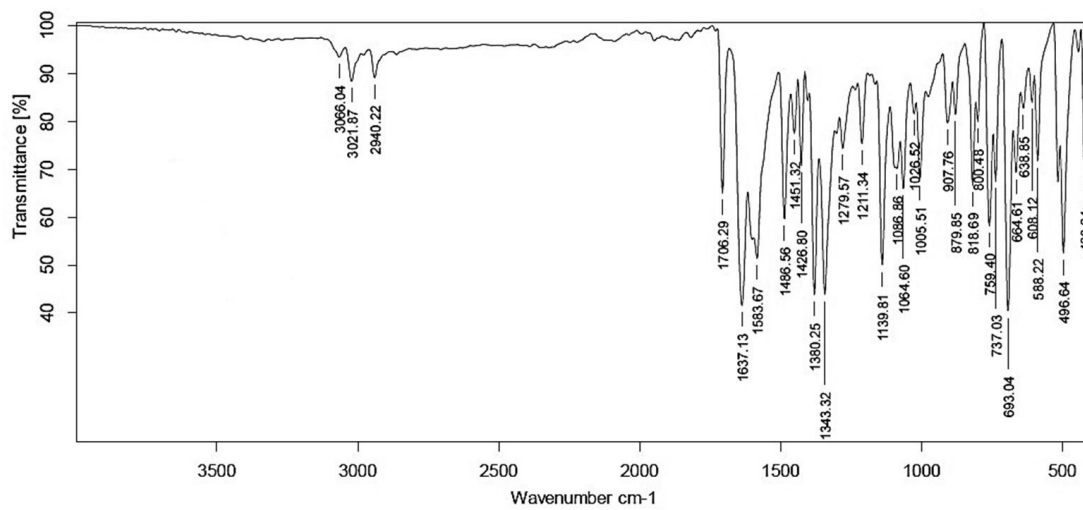


Figure 82: IR spectrum of compound 4i

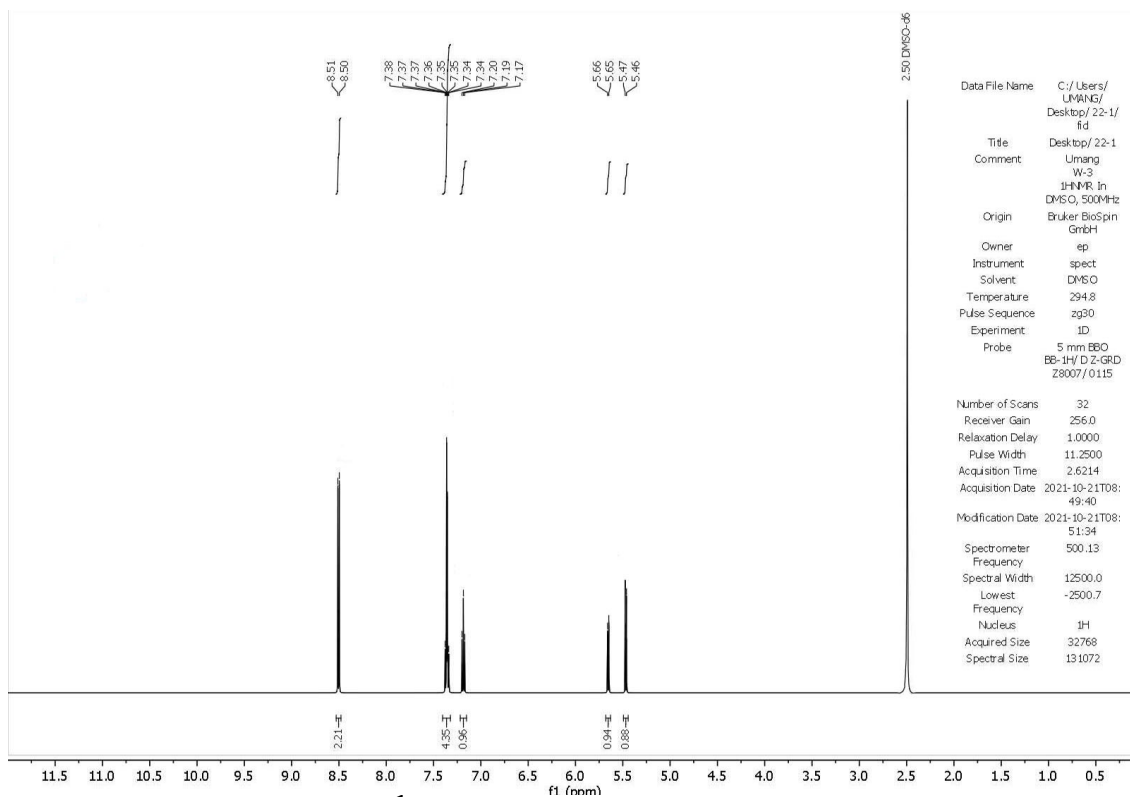


Figure 83: ^1H NMR spectrum of compound 4i

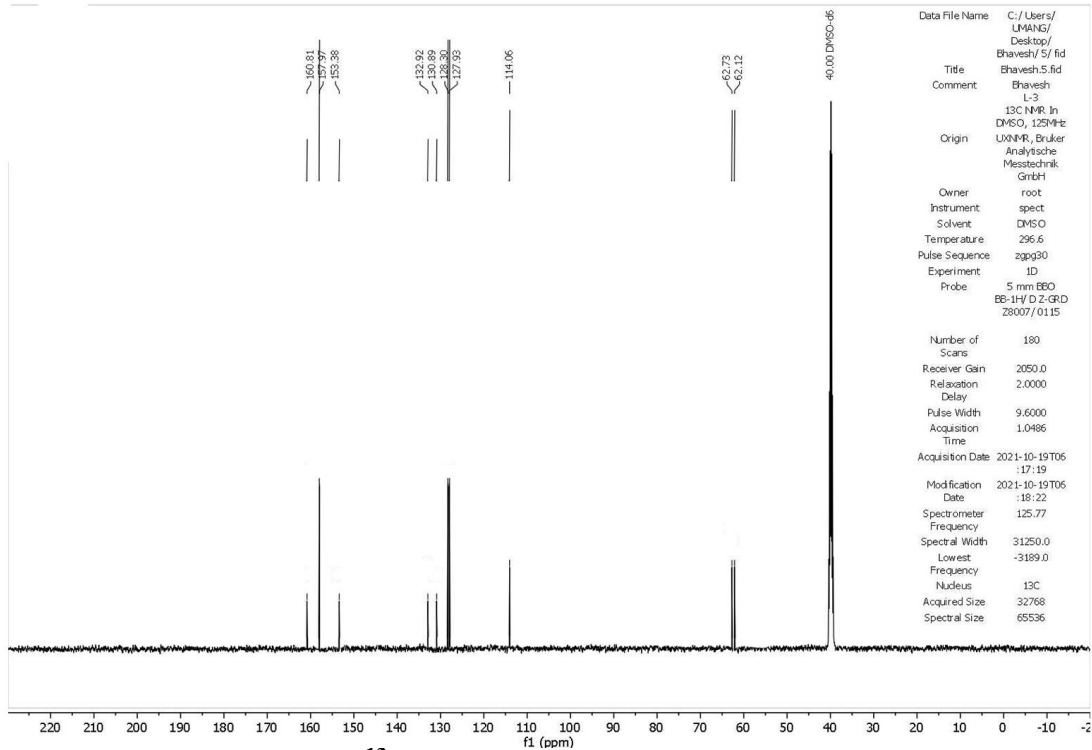


Figure 84: ^{13}C NMR spectrum of compound 4i

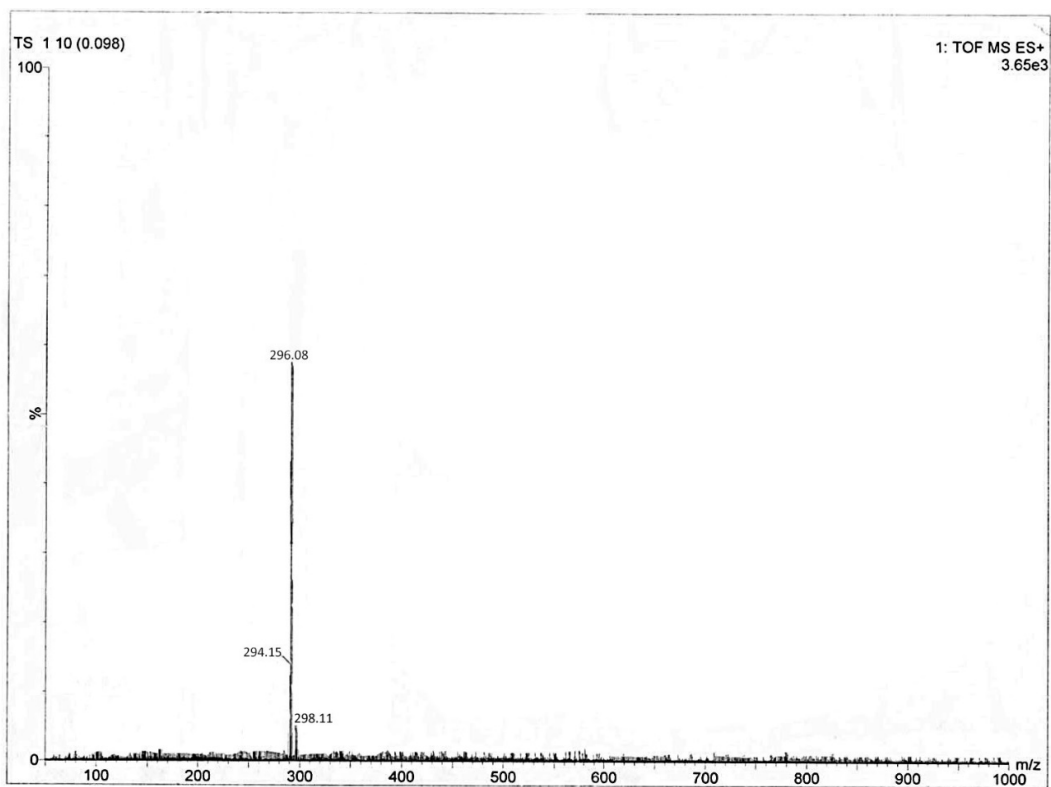


Figure 85: Mass spectrum of compound 4i

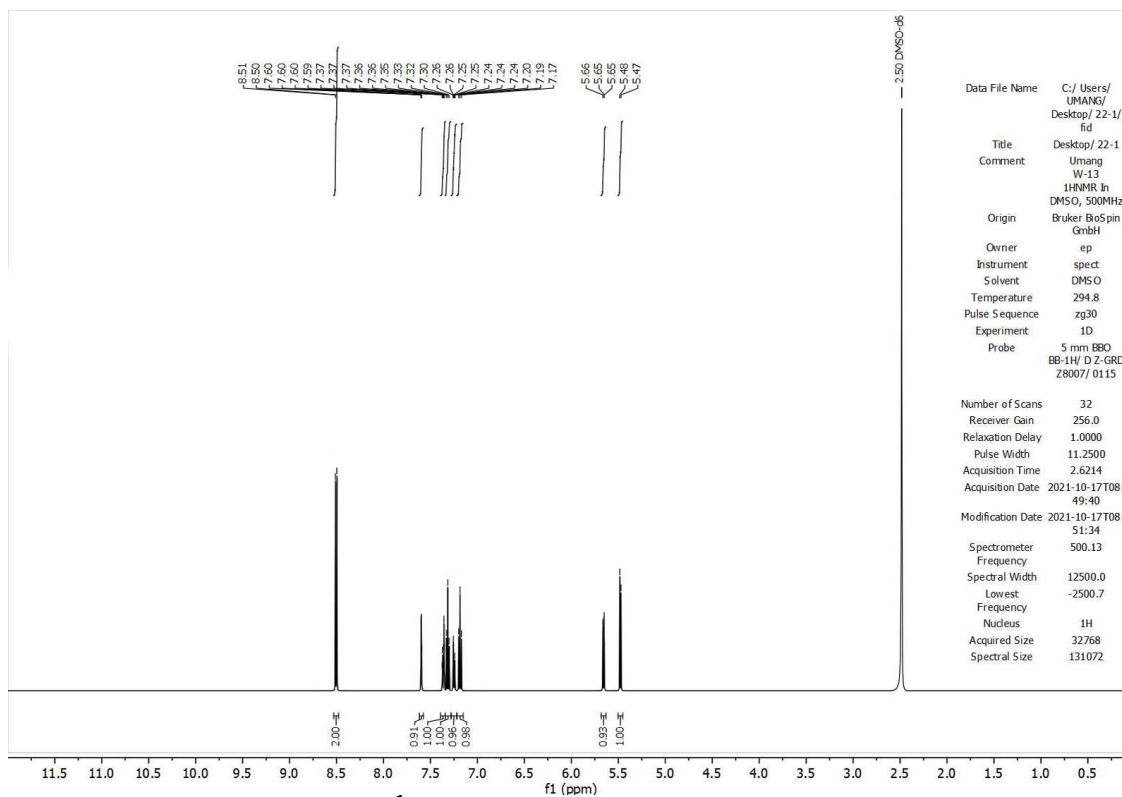


Figure 86: ^1H NMR spectrum of compound 4j

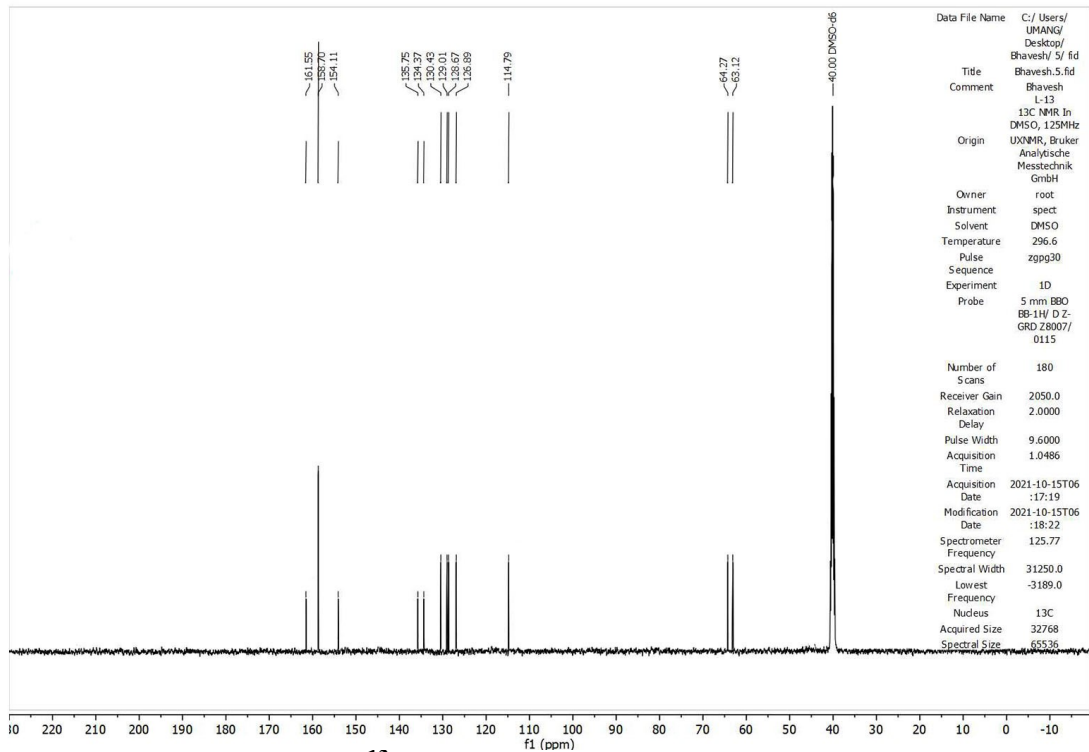


Figure 87: ^{13}C NMR spectrum of compound 4j

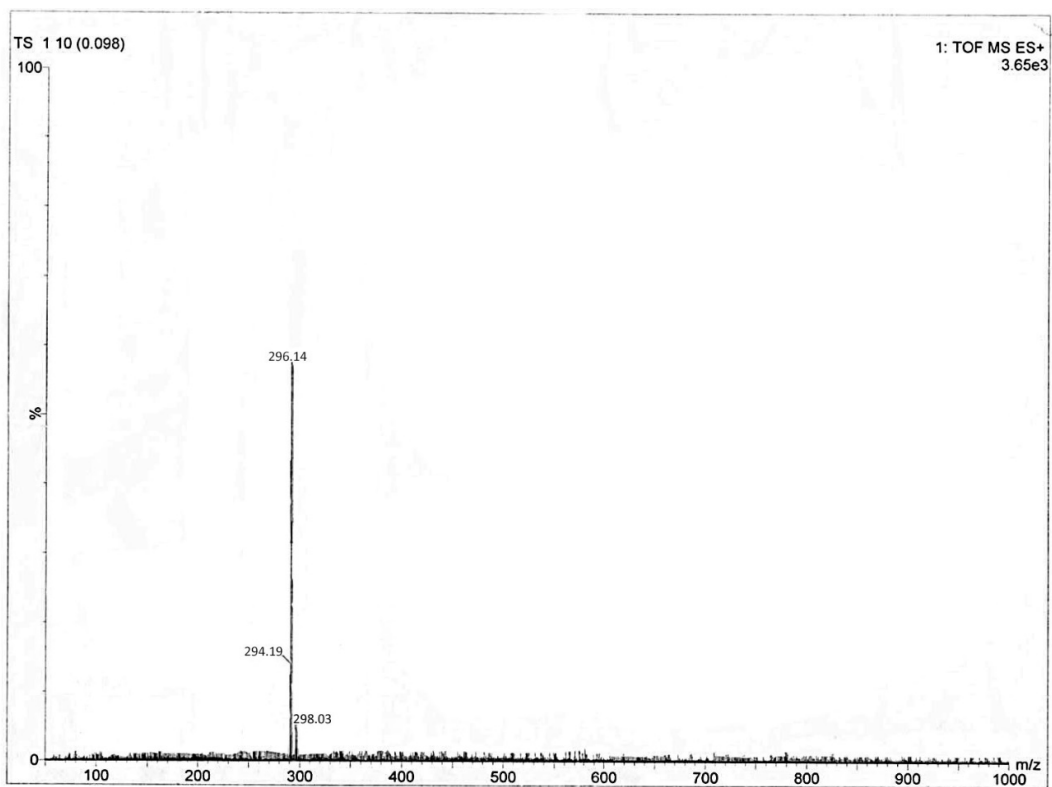


Figure 88: Mass spectrum of compound 4j

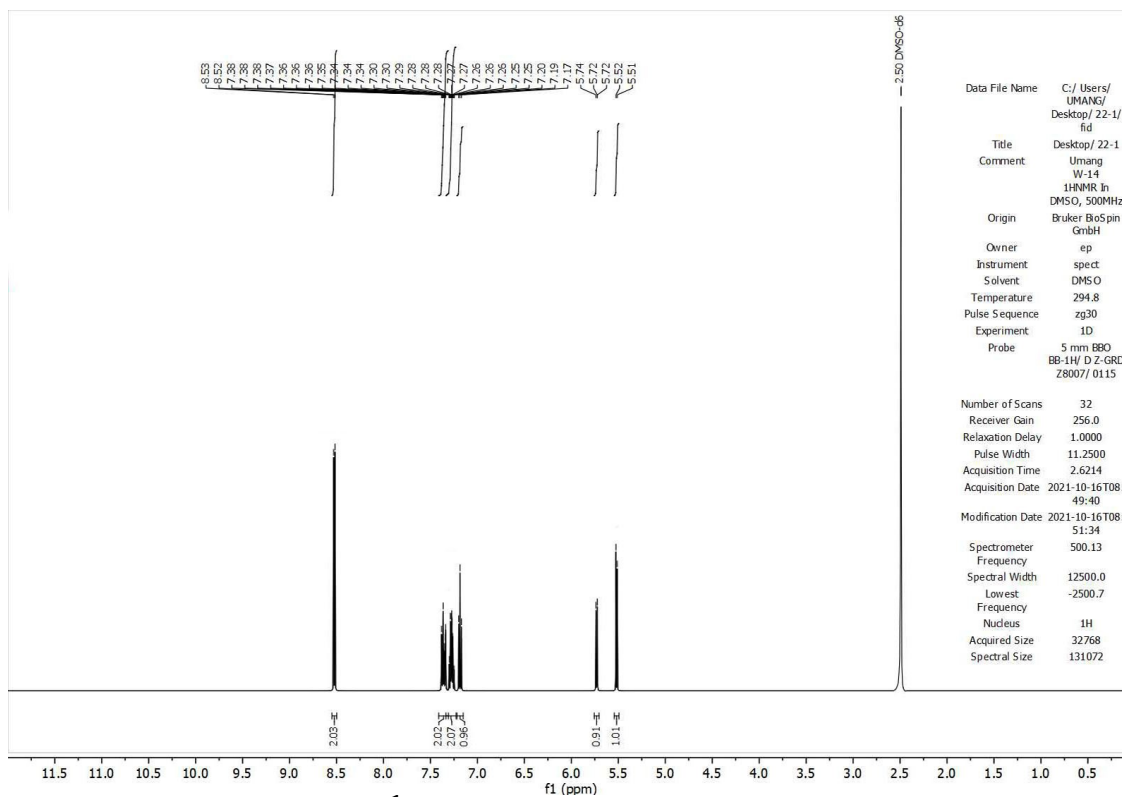


Figure 89: ¹H NMR spectrum of compound 4k

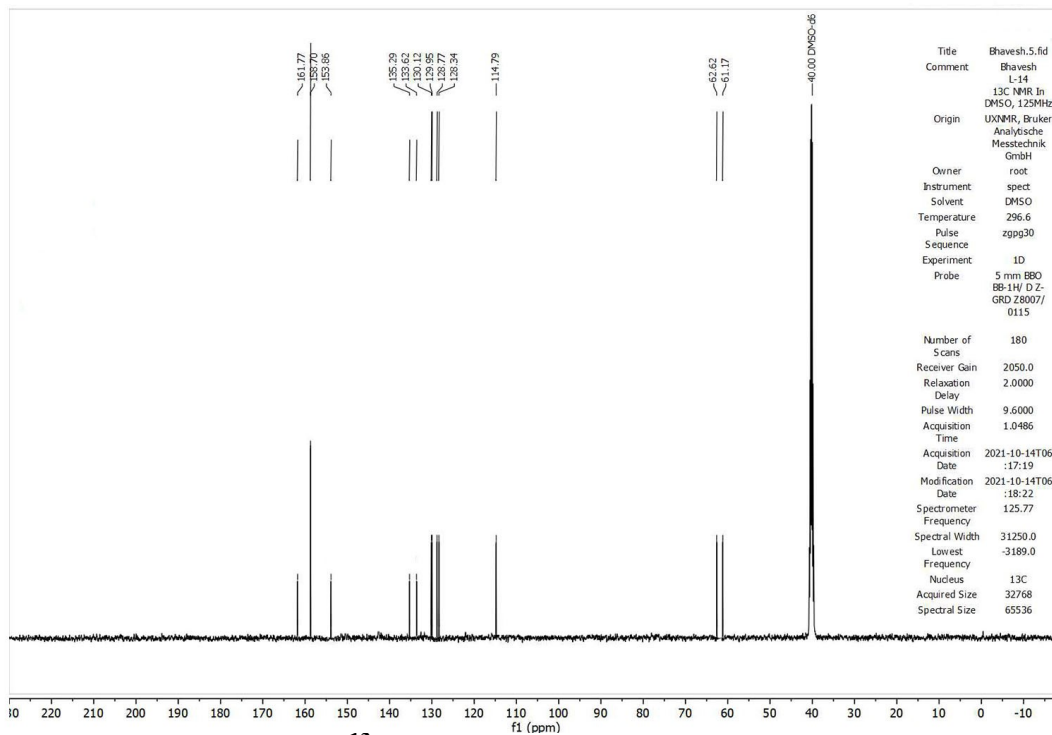


Figure 90: ^{13}C NMR spectrum of compound 4k

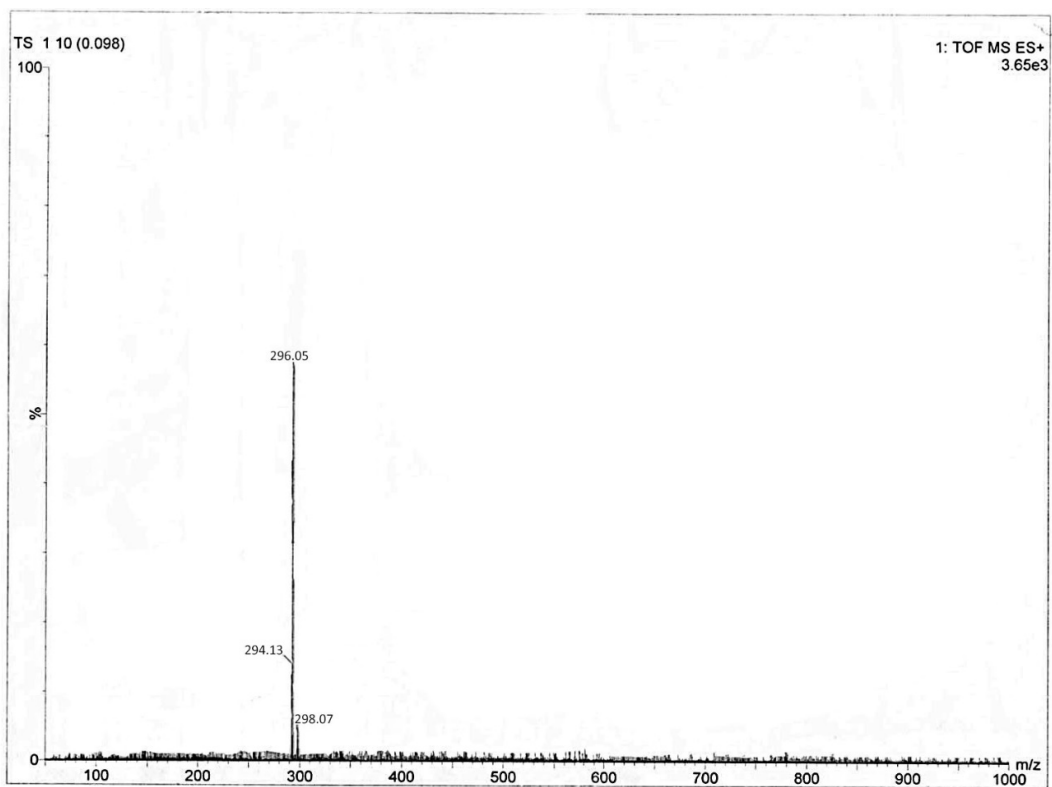


Figure 91: Mass spectrum of compound 4k

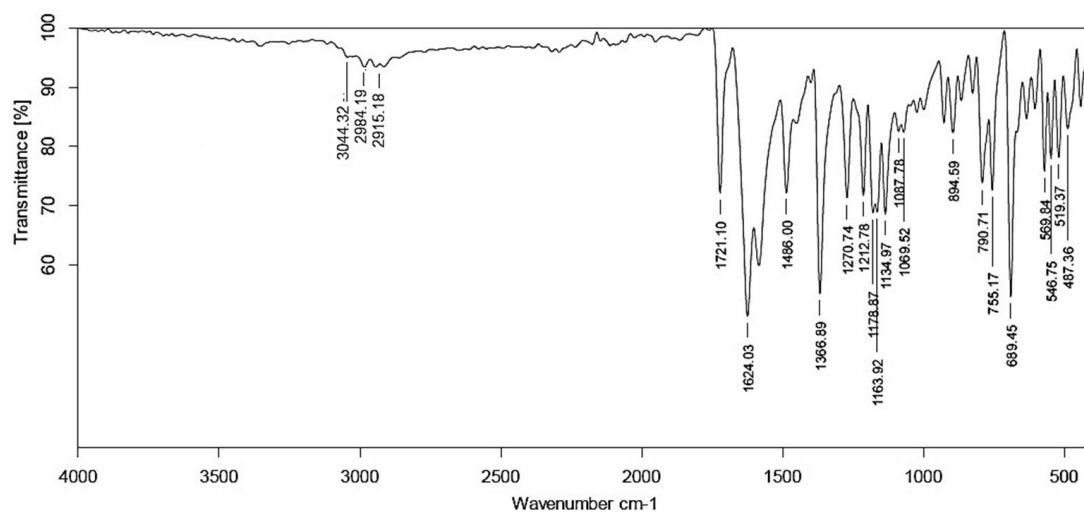


Figure 92: IR spectrum of compound 41

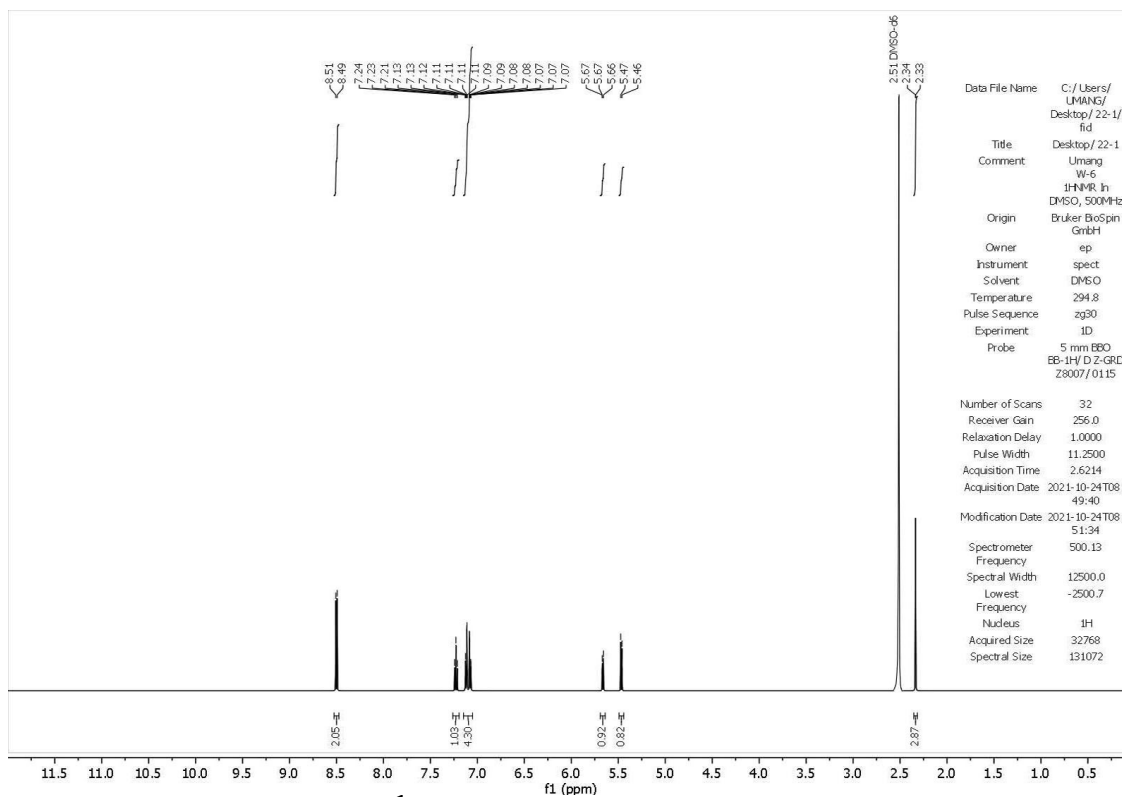


Figure 93: ¹H NMR spectrum of compound 4l

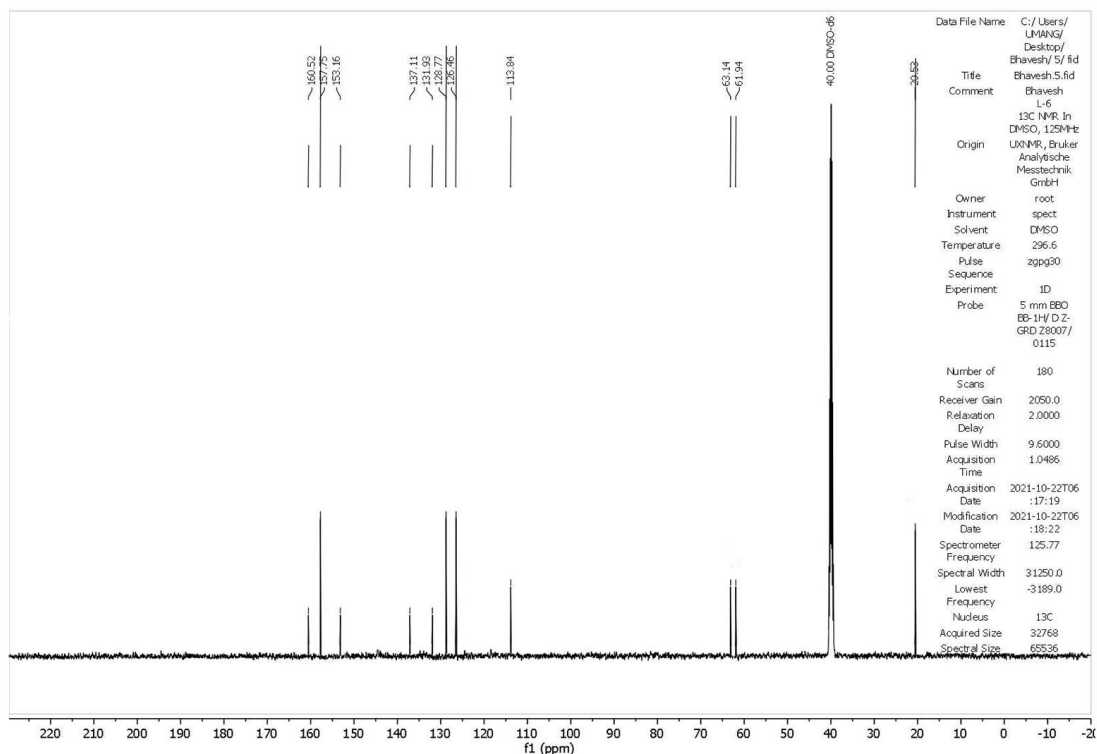


Figure 94: ^{13}C NMR spectrum of compound 4l

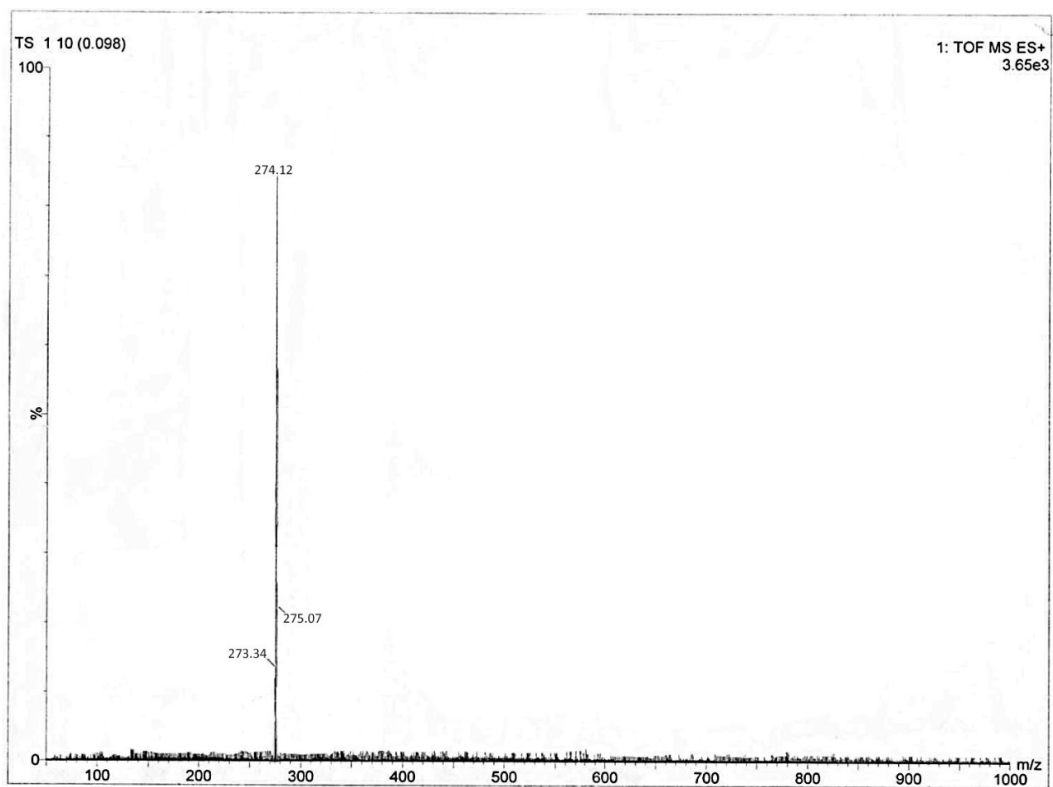


Figure 95: Mass spectrum of compound 4l

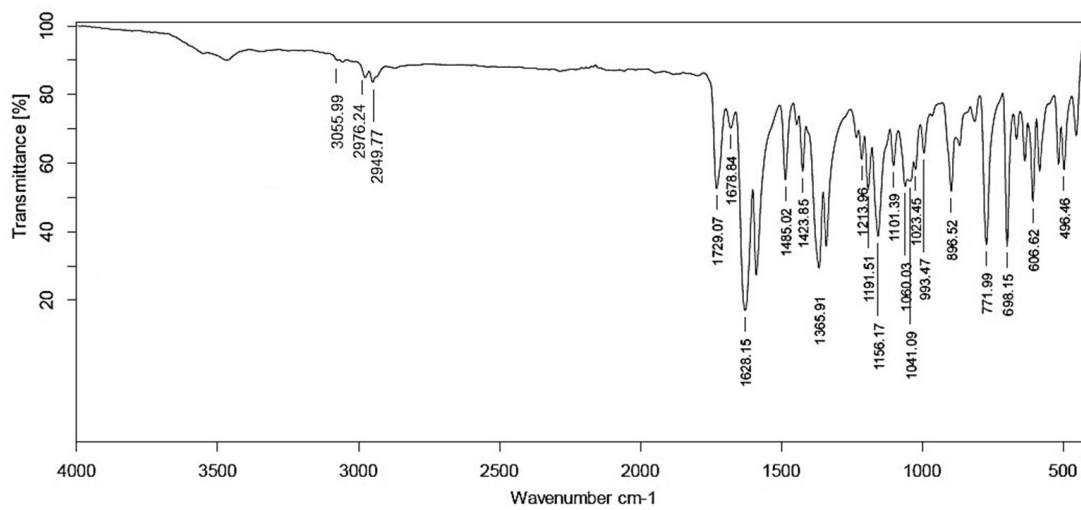


Figure 96: IR spectrum of compound 4m

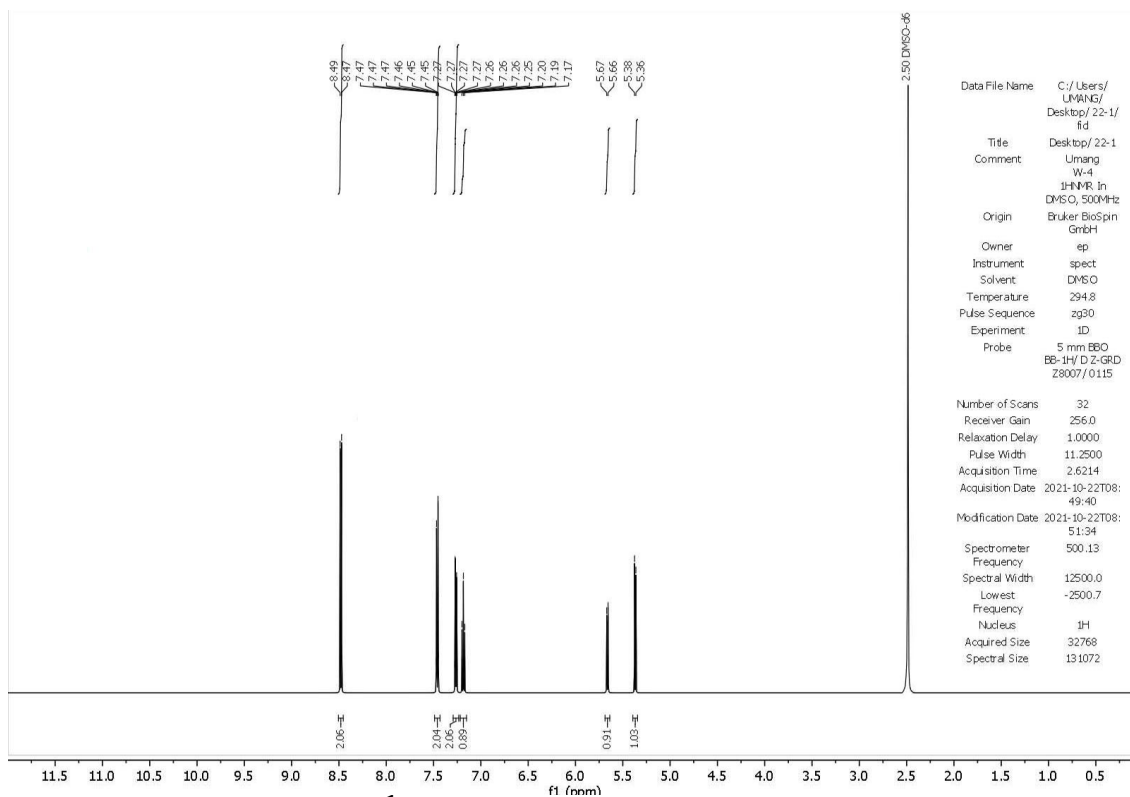


Figure 97: ¹H NMR spectrum of compound 4m

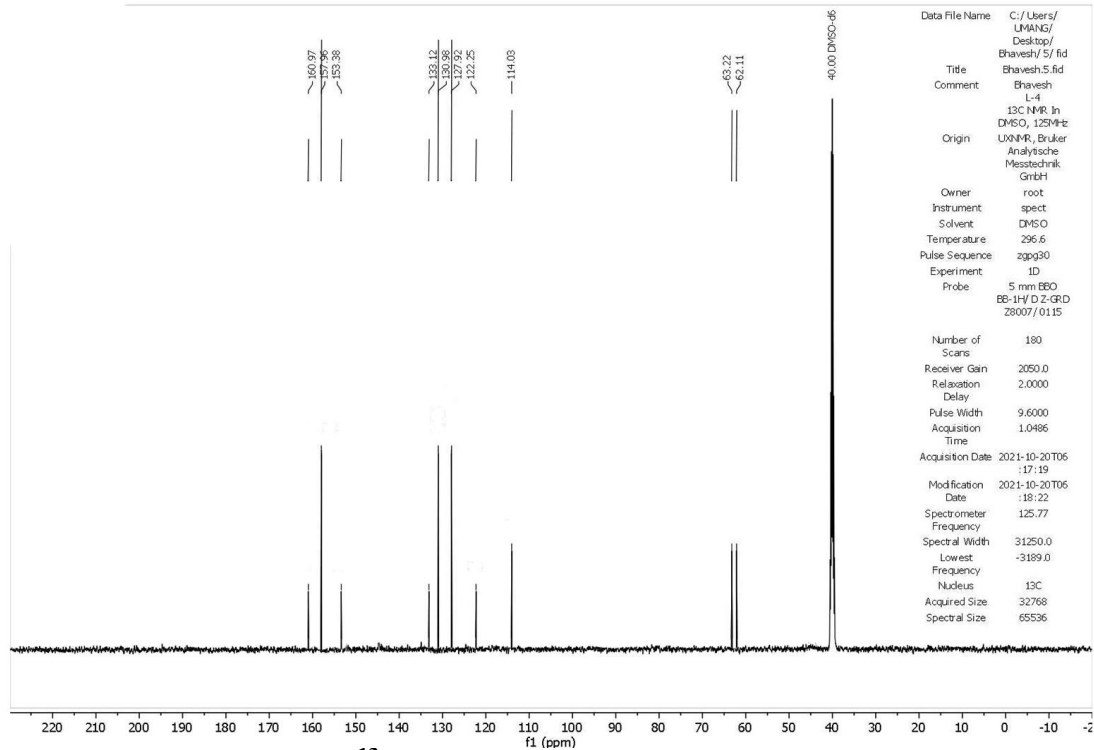


Figure 98: ^{13}C NMR spectrum of compound 4m

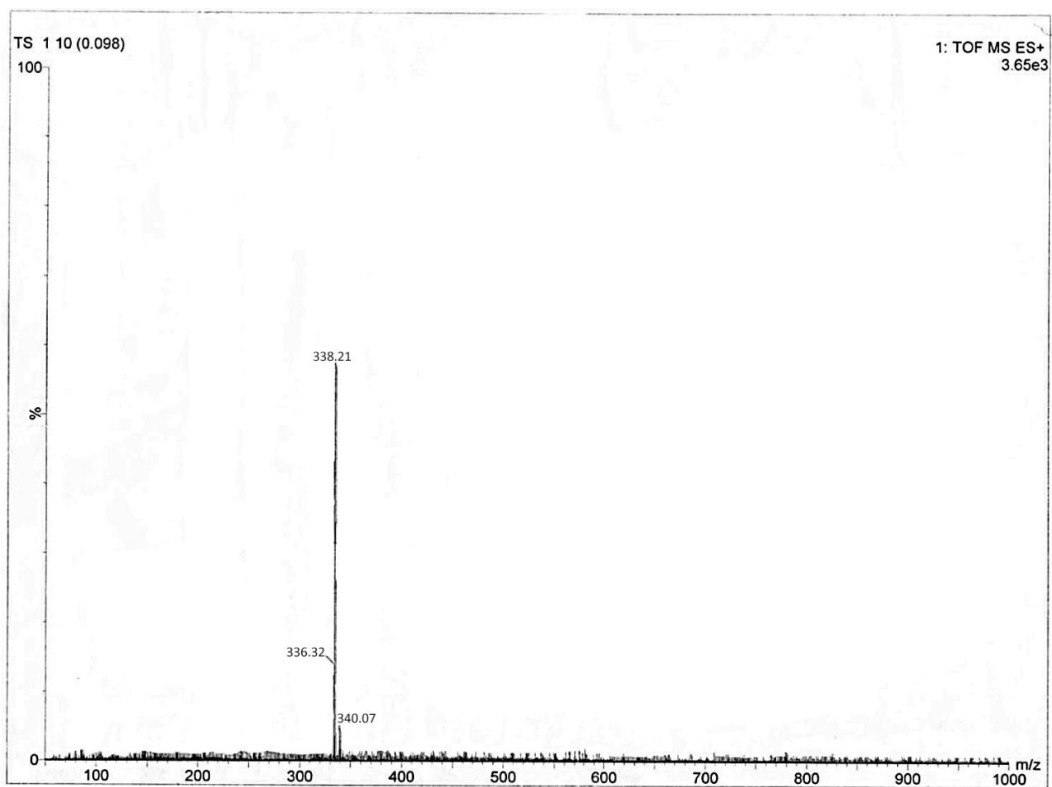


Figure 99: Mass spectrum of compound 4m

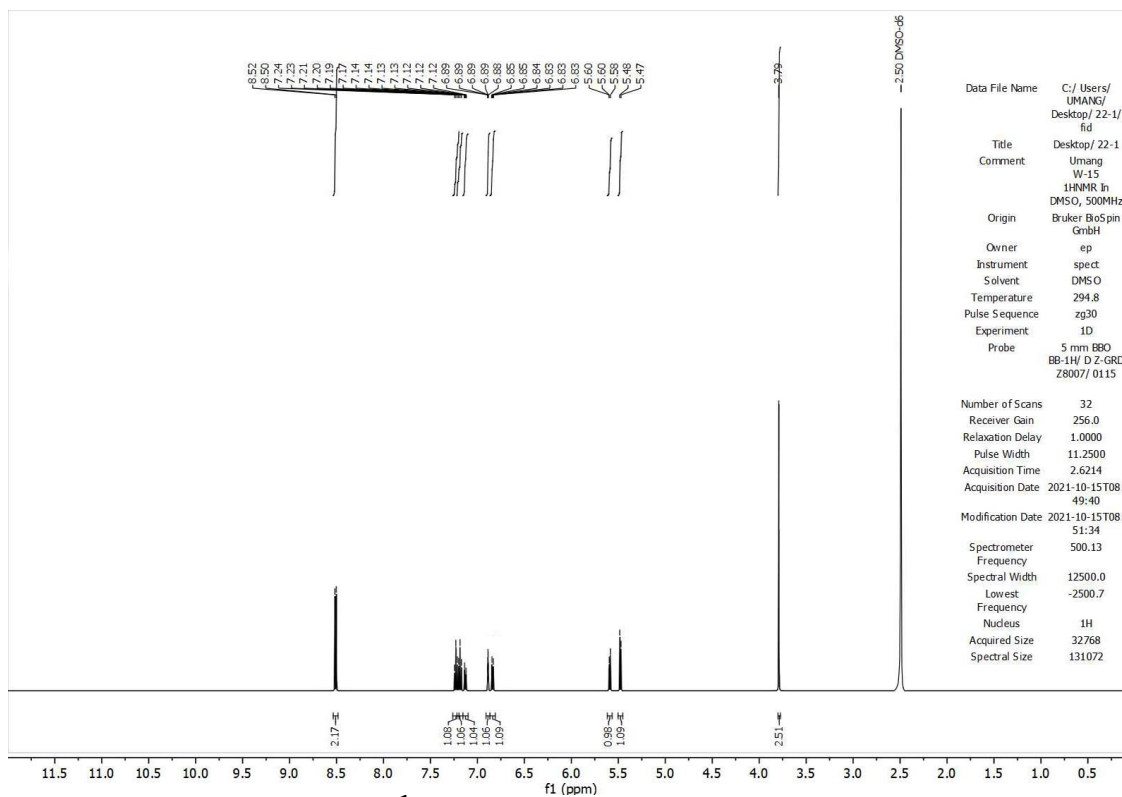


Figure 100: ^1H NMR spectrum of compound 4n

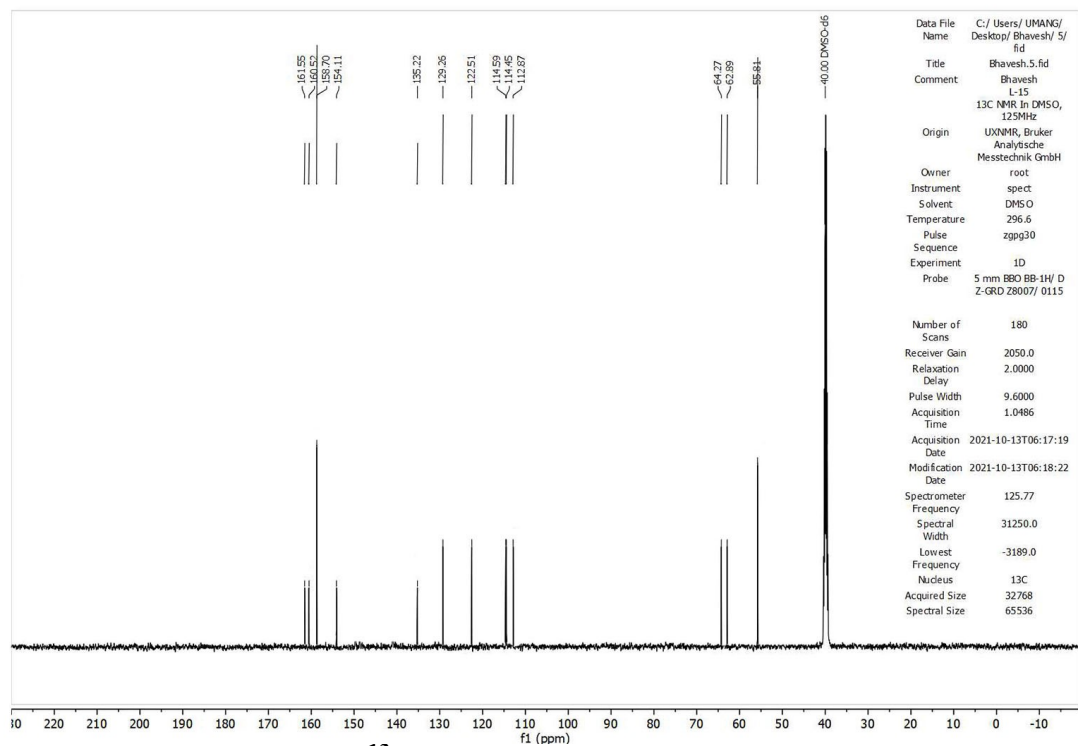


Figure 101: ^{13}C NMR spectrum of compound 4n

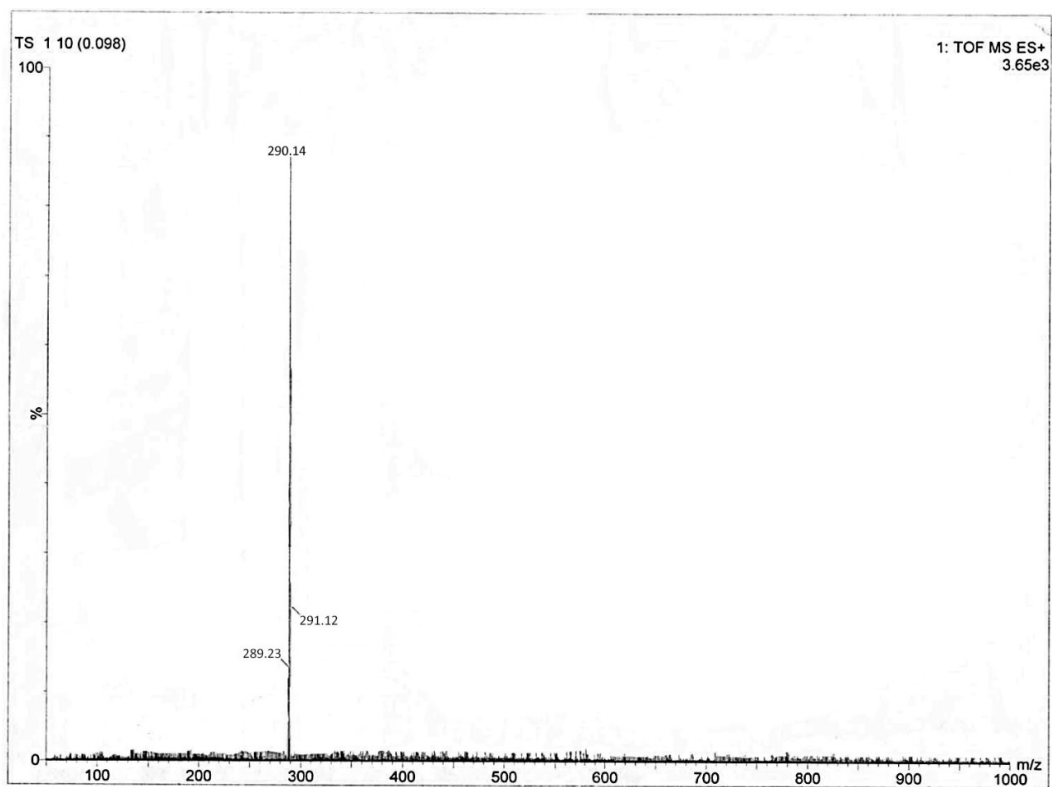


Figure 102: Mass spectrum of compound 4n

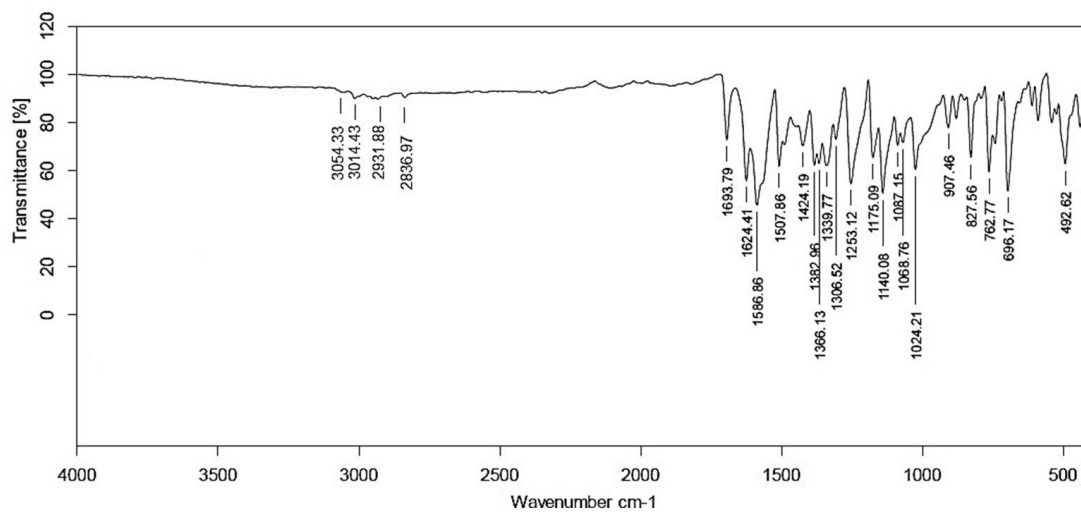


Figure 103: IR spectrum of compound 4o

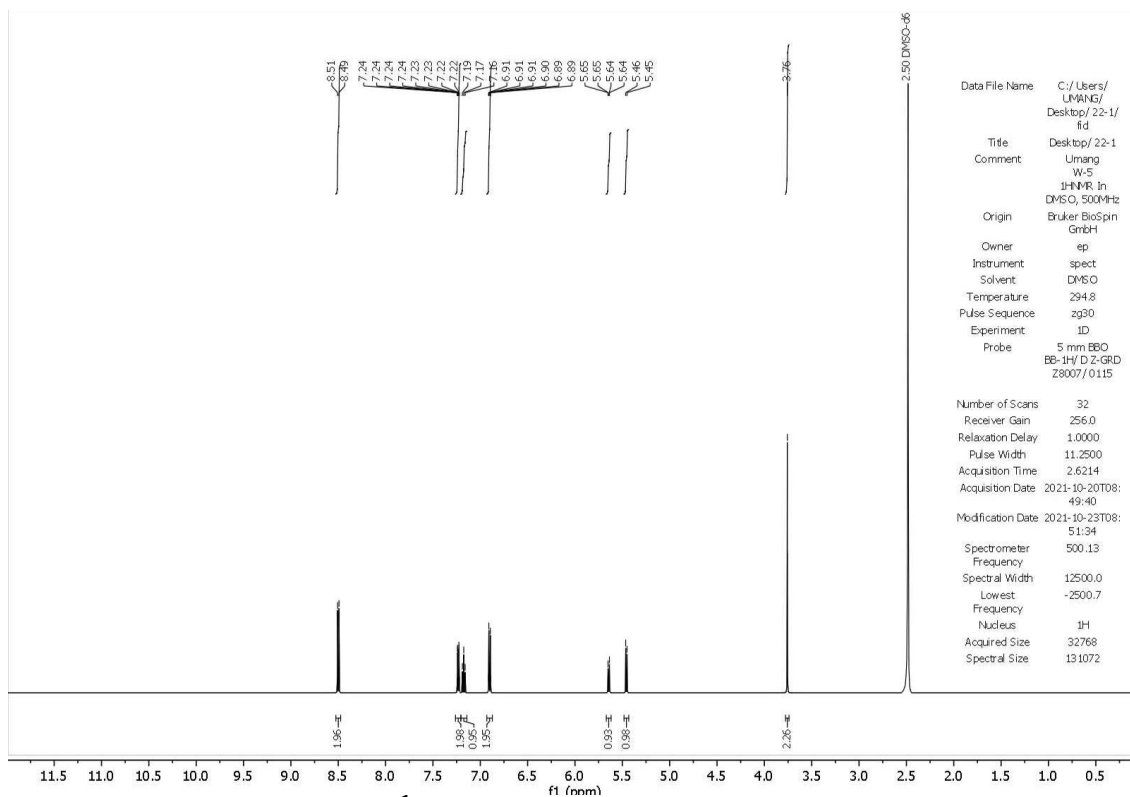


Figure 104: ¹H NMR spectrum of compound 4o

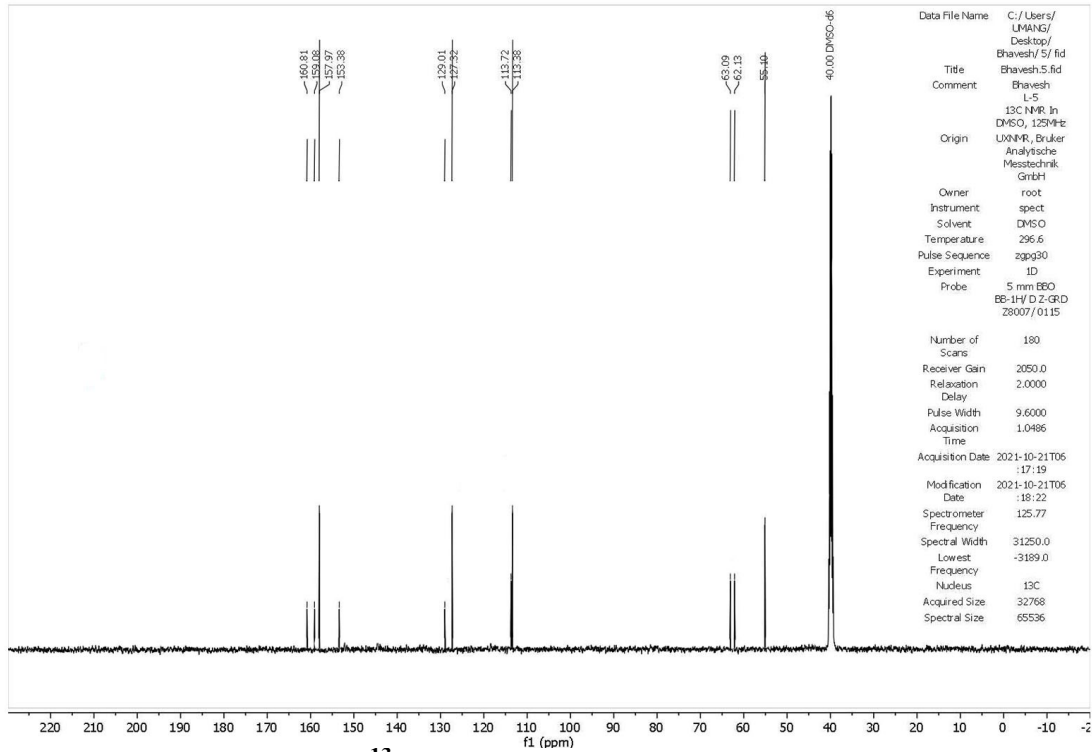


Figure 105: ^{13}C NMR spectrum of compound 40

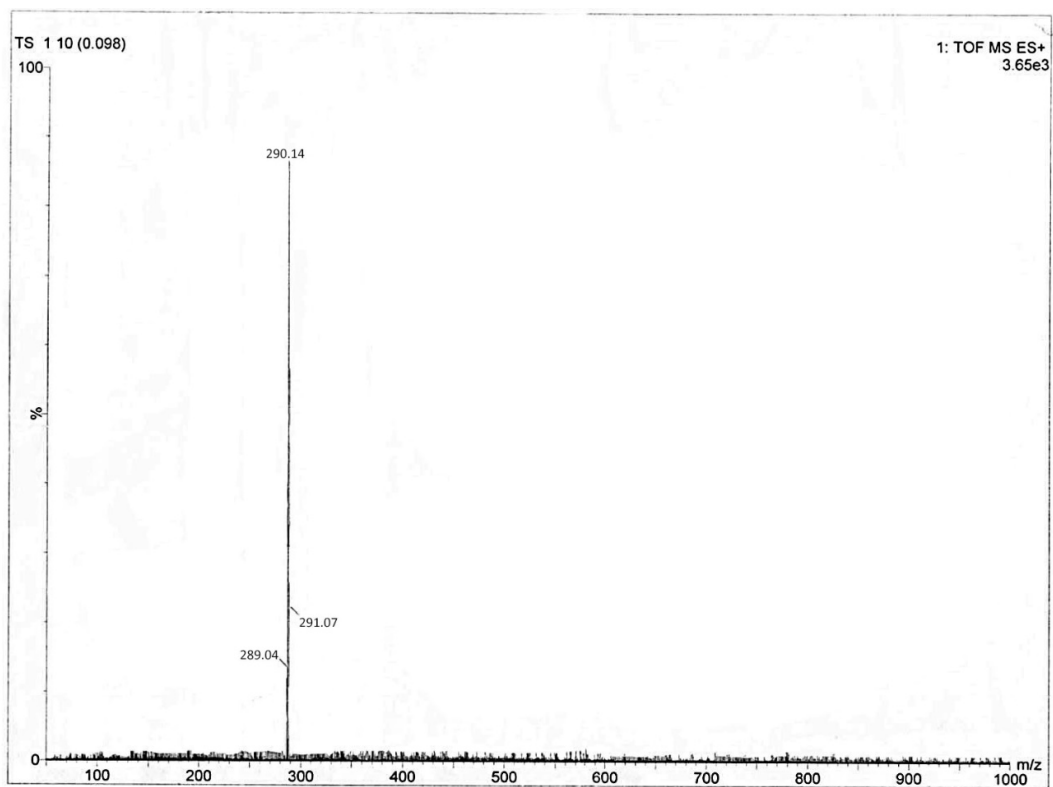


Figure 106: Mass spectrum of compound 40