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ORIGINAL RESEARCH ARTICLE

Synthesis and Characterization of Some New Drug Derivatives containing thiadiazole, oxadiazole, and triazole rings, and studying their antibacterial activity

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ABSTRACT

A series of new drug derivatives containing thiadiazole, oxadiazole, and triazole rings were successfully synthesized. In this study, the terminal carboxylic acid groups of cephalexin and 4-aminobenzoic acid were reacted with thiosemicarbazide and semicarbazide, respectively, in the presence of phosphorus oxychloride to create the thiadiazole and oxadiazole derivatives. Cephalexin and 4-aminobenzoic acid's terminal carboxylic acid group reacted with thiosemicarbazide to create triazole derivatives, which were then treated with sodium hydroxide.The structures of the newly synthesized compounds were confirmed using IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. The antibacterial activity of these compounds was evaluated against Escherichia coli and Staphylococcus aureus

Keywords: Cephalexin; 4-aminobenzoic acid; thiadiazole; oxadiazole, triazole

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1. Introduction

Cephalexin is a first-generation cephalosporin antibiotic that is widely prescribed on a global scale. It is used to treat a range of illnesses[1]. It is a semi-synthetic antibiotic that belongs to the class of β-lactam antibiotics[2]. The prevalence of Cephalexin in pharmaceutical effluents is due to its recognized effectiveness[3]. Unfortunately, in recent decades, the overuse and misuse of antibiotics, coupled with social and economic factors, have increased the rise of antibiotic-resistant bacteria, rendering drug treatment ineffective. The World Health Organization (WHO) has identified antimicrobial resistance (AMR) as one of the top ten threats to global health[4]. Similarly, 4-Aminobenzoic acid has attracted considerable attention within the biomedical field. It has been shown to play a role in various biological processes, including the synthesis of neurotransmitters and antioxidant activity[5]. 4-aminobenzoic acid-containing medications are considered well-tolerated [6]. Heterocyclic compounds contain at least one heteroatom. The most frequent of these atoms are oxygen, nitrogen, and sulfur, which may be found in many compounds(7-9). Heteroatoms and heterocyclic frameworks make up the majority of biologically active chemicals and are regarded as some of the most significant organic molecules. They are commonly present in medicinal chemistry-related compounds[10]. Because of their complicated structure, these compounds have several distinguishing qualities and traits compared to homocyclic rings[11]. The fusing of heteroatoms gives them importance in reactions that function within

the scope of biological targeting and a connection to build desired structural forms. Chemists are interested in heterocyclic chemistry to synthesize novel, powerful derivatives of five-membered heterocyclic rings, wherein both nitrogen atoms are attached to one or two heterocyclic or substituted aryl groups[12-14]. They exhibit several biological activities, such as anti-cancer[15-16] , anti-inflammatory[17] , anti-bacterial[18] , and anti-oxidant[19].The pharmaceutical industry uses heterocyclic chemicals because of their biological activity. Atoms of nitrogen and oxygen contribute to the enhancement of the physical characteristics of substances with biological activity[20]. The biological substances found in living things, such as hormones, vitamins, and antibiotics, are made up of heterocyclic molecules. These compounds, which contain a sulfur atom, have been proven effective by FAD on medicines. Heterocyclic compounds containing nitrogen are found in many physiologically active agents utilized in patient treatment or approved pharmaceuticals[21]. Despite the individual significance of cephalexin, PABA, and heterocyclic scaffolds, limited research has focused on hybrid molecules combining these pharmacophores. Therefore, this study aims to synthesize and characterize a novel series of cephalexin–PABA derivatives incorporating thiadiazole and oxadiazole rings, and to evaluate their biological activity compared to the parent drug and standard antibiotics.

2. Materials and methods

The chemicals used were provided by BDH, Sigma Aldrich, CDH, and Merck. To determine melting points, an open capillary approach was used along with an SMP30 melting point device. The findings were published without any further corrections. A Shimadzu spectrometer with the model number IRAFFINITY-1CE was used to compose the FT-IR spectra (KBr-discs). When it came to the recording of NMR spectra, a Jeol-400Hz-NMR- NMR spectrophotometer running at 400 MHz was used for the 1H measurements.

Synthesis of: (S)-2-amino-N-((6R,7S)-2-(5-amino-1,3,4-thiadiazol-2-yl)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl)-2-phenylacetamide (M1) [22]

3.036 grams (33.3 mmol) of thiosemicarbazide and 11.579 grams (33.3 mmol) of cephalexin were placed into a 250 ml round-bottom flask containing an excess of POCl3, and the reacted mixture was heated for thirty minutes. After ten minutes, 90 mL of water was added, and the reaction was refluxed for three hours. Upon cooling the entire mixture to room temperature, it was poured into ice-cold water, neutralized with a saturated potassium hydroxide solution, filtered, dried, and recrystallized from absolute ethanol. As shown in scheme [1]

Color: Dark Brown; Yield: 53%; melting point: 203-205°C; Infrared spectrum (v, cm- 1): 3406 (NH2), 3088 (C-H Ar),1649 (C=N),1572(C-S); 1HNMR (400MHz, DMSO-d6) δ (ppm): 7.4 (t ,5H, CH-Ar), 1.2 (S, 3H, CH-aliph), 8.5 (S, 1H, NH-Sec) 13CNMR (400MHz, DMSO-d6) δ (ppm): 60 ppm (C-aliph), 165 ppm (C-amide), 135 ppm (C-Ar).

Synthesis of: (S)-2-amino-N-((6R,7S)-2-(5-amino-1,3,4-oxadiazol-2-yl)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl)-2-phenylacetamide (M2) [22]

3.71 grams (33.3 mmol) of semicarbazide and 11.579 grams (33.3 mmol) of cephalexin were mixed in excess POCl3 in a 250 ml round-bottom flask. The reaction mixture was heated for thirty minutes. After ten minutes, 90 mL of water was added, and the reaction was refluxed for three hours. Upon cooling the entire mixture to room temperature, it was poured into ice-cold water, neutralized with a saturated potassium hydroxide solution, filtered, dried, and recrystallized from absolute ethanol. As shown in scheme [1]

Color: Dark Brown; Yield: 63%; melting point: 253-255°C; Infrared spectrum (v, cm- 1): 3363 (NH2), 2972 (C-H aliph), 1670 (C=N); 1HNMR (400 MHz, DMSO-d6) δ (ppm): 8.6 (S, 2H, NH2), 1.9 (S, 3H, CH-Aliph), 8.2 (S, 1H, NH). 13CNMR (400MHz, DMSO-d6) δ (ppm): 167 ppm (C-amide), 131 ppm and 135 ppm for C-aromatic group.

Synthesis of : (S)-2-amino-N-((6R,7S)-2-(5-mercapto-4H-1,2,4-triazol-3-yl)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-yl)-2-phenylacetamide (M3) [23][24]

1.39 grams (4mmol) of cephalexin was added to 0.36 grams (4mmol) of thiosemicarbazide and 1.64 ml (12 mmol) of triethylamine (Et3N) in DMF solvent, followed by adding 0.28 ml (4 mmol) of SOCl2 at ambient temperature. The reaction mixture was stirred for five to twenty minutes at ambient temperature. The recovery of the reaction product entailed the evaporation of the solvent under reduced pressure. The residue was solubilized in DMF and then washed with 1N HCl and 1N NaOH. To produce the appropriate carboxylic amide, the organic phase was dried with Na2SO4. The product was reacted in 20 ml of 4% NaOH and refluxed for 4 hours. Then it was acidified with 10% HCl, and the precipitate was obtained and recrystallized from absolute ethanol. As shown in scheme [2]

Color: yellow; Yield: 66 %; melting point: 299-301°C; Infrared spectrum (v, cm- 1): 3404 (NH2), 1633(C=N)); 1HNMR (400 MHz, DMSO-d6) δ (ppm): 8.5 (S, 2H, NH2), 1.2 (S, 3H, CH-Aliph), 7.3 (t, 5H, C-Ar). 13CNMR (400MHz, DMSO-d6) δ (ppm): 156 ppm (C-imine), 129 ppm (C-aromatic).

Synthesis of: (2S,2'S)-N,N'-((6R,6'R,7S,7'S)-((ethane-1,2-diylbis(sulfanediyl))bis(4H-1,2,4-triazole-5,3-diyl))bis(3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2,7-diyl))bis(2-amino-2-phenylacetamide (M4)[25]

1.0 gram (2.6 mmol) of compound M3 was taken and dissolved in ethanol. 0.1 ml (1.3 mmol) of dichloroethane was added, and the mixture was refluxed for seven hours. After that, the precipitate was collected, and the product was recrystallized from ethyl acetate. As shown in scheme [3]

Color: pale-yellow; Yield: 53%; melting point: 206-204 °C; Infrared spectrum (v, cm- 1): 3415 (NH2), 692 (C-S); 1HNMR (400 MHz, DMSO-d6) δ (ppm): 7.3 (t, 5H, CH-Ar), 3.7 (t, 2H, S-CH2), 8.1 (S, 2H, NH2). 13CNMR (400MHz, DMSO-d6) δ (ppm): 166 ppm (C-amide), 159 ppm (C-imine), 137 ppm (C-aromatic).

Synthesis of: 5-(4-aminophenyl)-1,3,4-thiadiazol-2-amine (M5) [22]

3.036 grams (33.3 mmol) of thiosemicarbazide and 4.571 grams (33.3 mmol) of 4-aminobenzoic acid in POCl3 (excess) were mixed in a round-bottomed flask with a capacity of 250 ml. After heating the reacted mixture for half an hour, 90 ml of water was added after ten minutes, and the reaction was refluxed for three hours. The mixture was cooled to room temperature, split into ice-cold water, neutralized with a saturated potassium hydroxide solution, filtered, dried, and finally recrystallized from absolute ethanol. As shown in scheme [1]

Color: off-white ; Yield: 65%; melting point: 227-229 °C ; Infrared spectrum (v, cm- 1) :) 3415(NH2) , 1608(C=N ring) ; H1-NMR (400 MHz, DMSO-d6) δ (ppm): 6.5 (d, 4H, CH-Ar), 7.2 (S, 2H, NH2) . 13C-NMR (400MHz, DMSO-d6) δ (ppm): 118 and 128 ppm (C-aromatic), 158 ppm (C-imine).

Synthesis of : 5-(4-aminophenyl)-1,3,4-oxadiazol-2-amine (M6) [22]

5.78 grams (51.85 mmol) of semicarbazide and 6.857 grams (49.97 mmol) of 4-aminobenzoic acid in POCl3 (excess) in a round-bottomed flask with a capacity of 250 ml. The reaction mixture was heated for half an hour. After ten minutes, 90 ml of water was added, and the reaction was refluxed for three hours. The entire mixture was cooled down to room temperature, then poured into ice-cold water, neutralized with a saturated KOH solution, filtered, dried, and finally recrystallized from absolute ethanol. As shown in scheme [1]

Color: off-white; Yield: 60%; melting point: 353-355°C; Infrared spectrum (v, cm- 1): 3338 (NH2), 1608 (C=N ring); H1-NMR (400 MHz, DMSO-d6) δ (ppm): 7.4 (d, 4H, CH- Ar), 7.2 (S, 2H, NH2). 13CNMR (400MHz, DMSO-d6) δ (ppm): 125 and 129 ppm (C-aromatic), 165 ppm for C-imine group.

Synthesis of : 5-(4-aminophenyl)-4H-1,2,4-triazole-3-thiol (M7) [23][24]

1.3 grams (9.48mmol) of 4-aminobenzoic acid was added to 0.91 grams (10 mmol) of thiosemicarbazide and 4.0 ml (28.7 mmol) of triethylamine (Et3N) in DMF, followed by adding 0.7 ml (10 mmol) of SOCl2

at ambient temperature. The reaction was stirred at room temperature for 5 to 20 minutes. Using a rotary evaporator, the solvent was evaporated as part of the reaction product recovery. To make the right carboxylic amide, the residue was dissolved in DMF and then washed with 1.0 N HCl and 1.0 N NaOH. Na2SO4 dried the organic phase, and then the product was mixed with 20 ml of 4% NaOH and refluxed for four hours. After that, it was acidified with 10% HCl, and then the precipitate was collected. The product was recrystallized from absolute ethanol. As shown in scheme [2]

Color: off- white; Yield: 70 %; melting point: 256-258 °C; Infrared spectrum (v, cm- 1): 3346 (NH2), 1672 (C=N); 1HNMR (400 MHz, DMSO-d6) δ (ppm): 6.7 (d, 4H, CH-Ar), 5.8 (S, 2H, NH2). 13CNMR (400MHz, DMSO-d6) δ (ppm): 112 and 128 ppm (C-aromatic), 165 and 167 ppm (C-imine).

Synthesis of: 4,4'-((ethane-1,2-diylbis(sulfanediyl)) bis(4H-1,2,4-triazole-5,3-diyl)) dianiline (M8)[25]

0.56 grams (3mmol) of compound M7 was taken and dissolved in ethanol. 0.11 ml (1.5 mmol) of dichloroethane was added, and the mixture was refluxed for seven hours. Then, the precipitate was collected, and the product was recrystallized in absolute ethanol. As shown in scheme [3].

Color: off- white; Yield: 55%; melting point: 355-353°C; Infrared spectrum (v, cm- 1): 3338 (NH2), 1608 (C=N ring); 1HNMR (400 MHz, DMSO-d6) δ (ppm): 7.9 (d, 4H, CH- Ar), 3.4 (t, 2H, S-CH2). 13CNMR (400MHz, DMSO-d6) δ (ppm): 119.3 and 129.9 ppm for C-aromatic, 156 ppm for C-imine, and 33.5 ppm for C-aliph group.

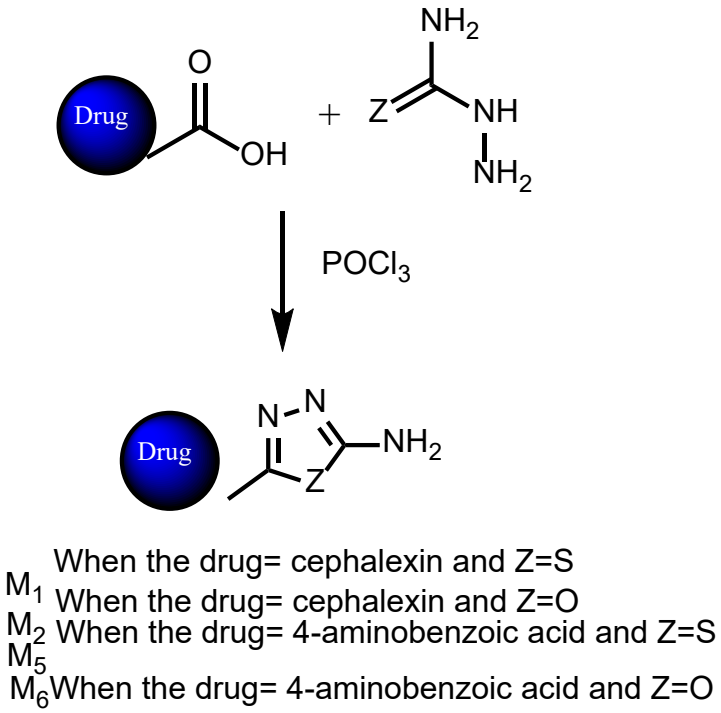
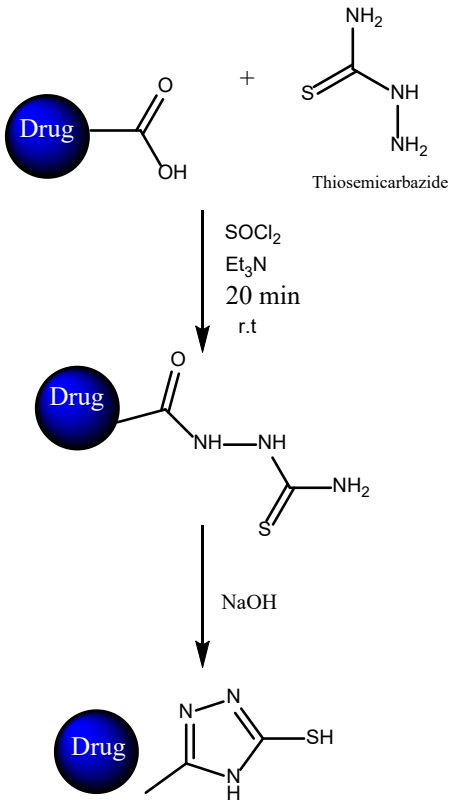
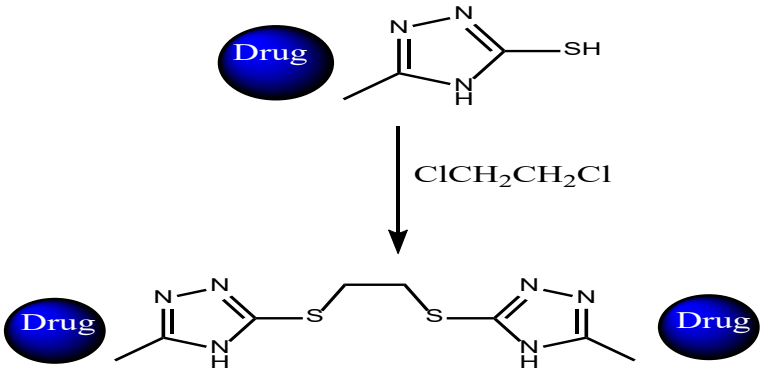


Figure 1. Synthesis of compounds M1, M2, M5 and M6



M3 When the drug =cephlexin
M7 When the drug = 4-aminobenzoic acid

Figure 2. Synthesis of compounds M3 and M7



M4 When the drug = cephalexin
M8 When the drug = 4-aminobenzoic acid

Figure 3. Synthesis of compounds M4 and M8

3. Results and discussion

Compound M1revealed IR absorbtion at 3406–3300 cm- 1 that was connected to the NH2 group. a band at 3086 cm- 1 that was related to the CH-Ar group, a band at 2980 cm- 1 associated with the CH-aliph group, and a band at 1649 cm- 1 that revealed to the existence of the imine C=N functional group (Figure 1). In the 1HNMR technique, there was a triplet peak at 7.4 ppm for CH-Ar, a singlet peak at 8.57 ppm for secondary amine NH, and a singlet peak at 1.2 ppm for CH-Aliph (Figure 2). The 13CNMR spectra of compound M1 showed an aliphatic carbon signal peak at 60 ppm. A C-amide signal was found at 165 (ppm), and a C-Ar signal peak was seen at 135 (ppm)(Figure 3) .

Compound M2 exhibited IR absorption bands at 3363 and 3240 cm^{-1}, consistent with NH_2 stretching vibrations, and a band at 3066 cm^{-1} corresponding to aromatic C–H. A strong band at 1670 cm^{-1} confirmed the presence of an imine (C=N) group, while the band at 2972 cm^{-1} was attributed to aliphatic C–H (Figure 4).1HNMR showed that a singlet peak at 8.6 ppm belongs to NH2, a singlet peak at 8.27 ppm corresponds to the NH of a secondary amine, and a singlet peak at 1.9 ppm is linked to CH-Aliph(Figure 5). The 13CNMR spectra of compound M2 showed a signal at 167 ppm that was linked to carbonyl carbon (C=O) of an amide and signals at 131 and 135 ppm that were linked to C-Ar(Figure 6).

Compound M3 showed no wide range in the area of 2600–3200 cm- 1, confirming the disappearance of the carboxylic group. a band at 1633 cm- 1, confirmed the successful formation of the imine C=N group during the reaction, and a band at 3404 cm- 1 was linked to NH2 (Figure 7).The 1HNMR spectrum had a singlet peak at 8.5 ppm that corresponded to the NH2 group, a singlet peak at 1.2 ppm that was linked to the CH–aliph group, a triplet peak at 7.3 ppm that corresponded to the CH-aromatic group, and no peak above 10 ppm, indicating the absence of a carboxylic acid proton(Figure 8). The 13CNMR spectra of the compound M3 showed two peaks: one at 156 ppm, which was linked to C-imine, and another at 129 ppm, which was linked to the C-Ar group (Figure 9).

The infrared spectra of compound M4 showed a band at 3415 cm- 1 connected to the NH2 group. a band at 692 cm- 1 confirmed the formation of the C-S group (Figure 10). In the 1HNMR spectra, a singlet peak at 8.1 ppm for NH2, a triplet peak at 7.3 ppm belongs to CH-Ar, and a triplet peak at 3.7 ppm is related to the S-CH2 group (Figure 11). In the 13CNMR spectra of organic compound M4, a signal at 159 ppm matched C-imine. Also, a signal at 137 ppm that related to the C-Ar group and another at 166 ppm that linked to the C-amide group (Figure 12).

Compound M5 have a band at 3415 cm- 1 that was connected to the NH2 group and a band at 1608 cm-1 that confirmed the presence of the C=N group of thiadiazole(Fig13). The 1HNMR spectra showed a doublet peak at 6.5 ppm related to the CH-Ar group, a singlet peak at 7.2 ppm related to the NH2 group, no peak above 10 ppm related to the carboxylic group (Figure 14). In the 13CNMR spectra for the compound M5, we found the C-imine group appeared at 158 ppm and the C-aromatic group at 128 and 118 ppm (Figure 15).

Compound M6 exhibited IR absorption bands at 3338 cm- 1 for the NH2 group and another at 3005 cm-1 for the CH-Ar group. At 1608 cm- 1, a band for the C=N group appeared during the reaction (Fig16). The NH2 signal in the 1HNMR spectra was a singlet peak at 7.2 ppm, whereas a doublet peak at 7.4 ppm belongs to the CH-Ar group (Figure 17). The 13CNMR spectra for M6 showed a C-imine group at 165 ppm and a C-aromatic at 129 and 125 ppm (Figre 18).

The infrared spectra of M7 indicated that the NH2 group made a band appear at 3346 cm- 1, and the imine band appeared at 1672 cm- 1 (Figure 19). The 1HNMR spectra indicated two peaks: a singlet peak at 5.8 ppm for NH2 and a doublet peak at 6.7 ppm for CH-Ar (Figure 20). The 13CNMR spectra of compound M7 revealed a C-imine group at 165 and 167 ppm and a C-Ar group at 128 and 112 ppm (Figure 21).

Compound M8 revealed a band at 3473 cm- 1 for NH2, the band at 3049 cm- 1 was connected to the CH-Ar group, while the band at 2920 cm- 1 was related to the CH-Aliphatic group (Figure 22). In the 1H-NMR spectra, a doublet peak at 7.9 ppm matched to the CH-Ar group and a triplet peak at 3.4 ppm that matched the S-CH2 group (Figure 23). The 13C-NMR spectra indicated that there was a C-imine group, a C-Ar group, and a C-aliph group at 156 ppm, 129 ppm, and 33 ppm, respectively (Figure 24).

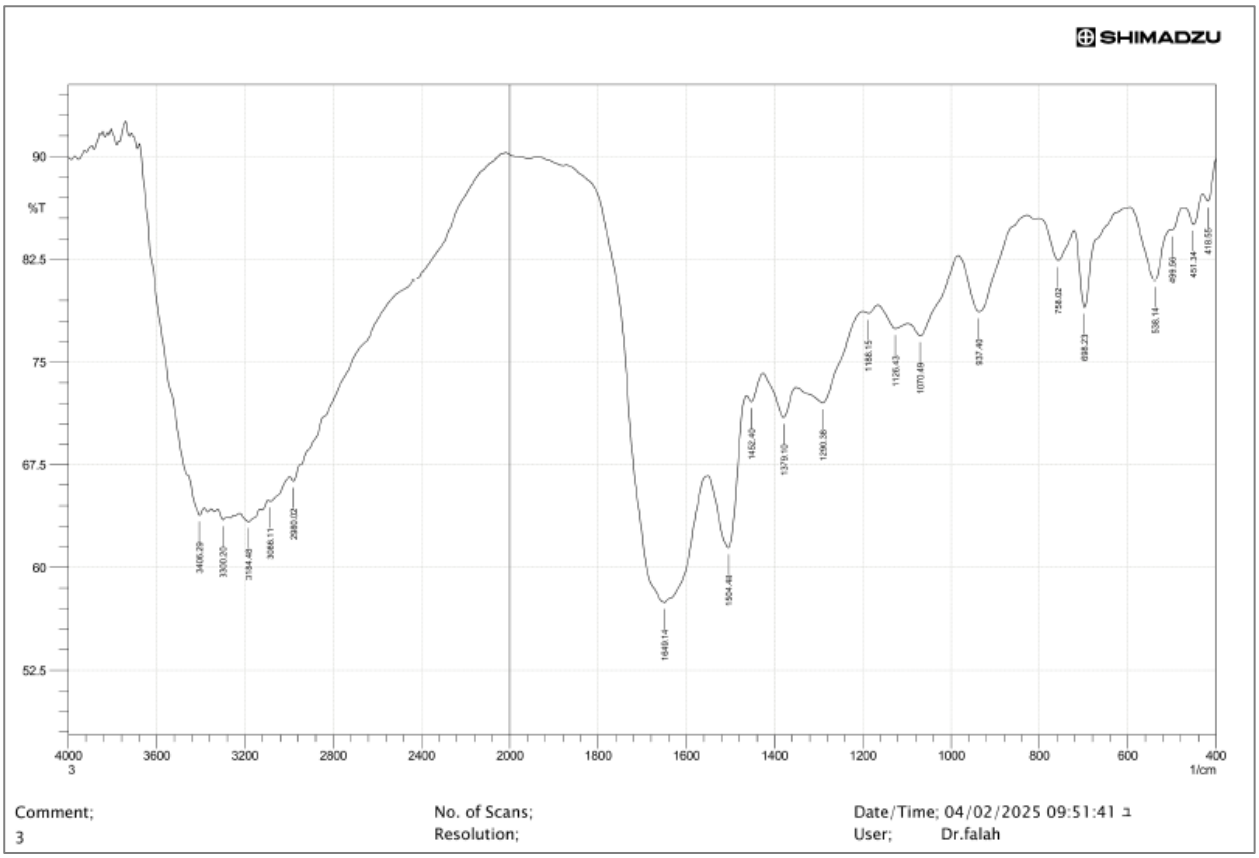


Figure 4. IR of compound M1

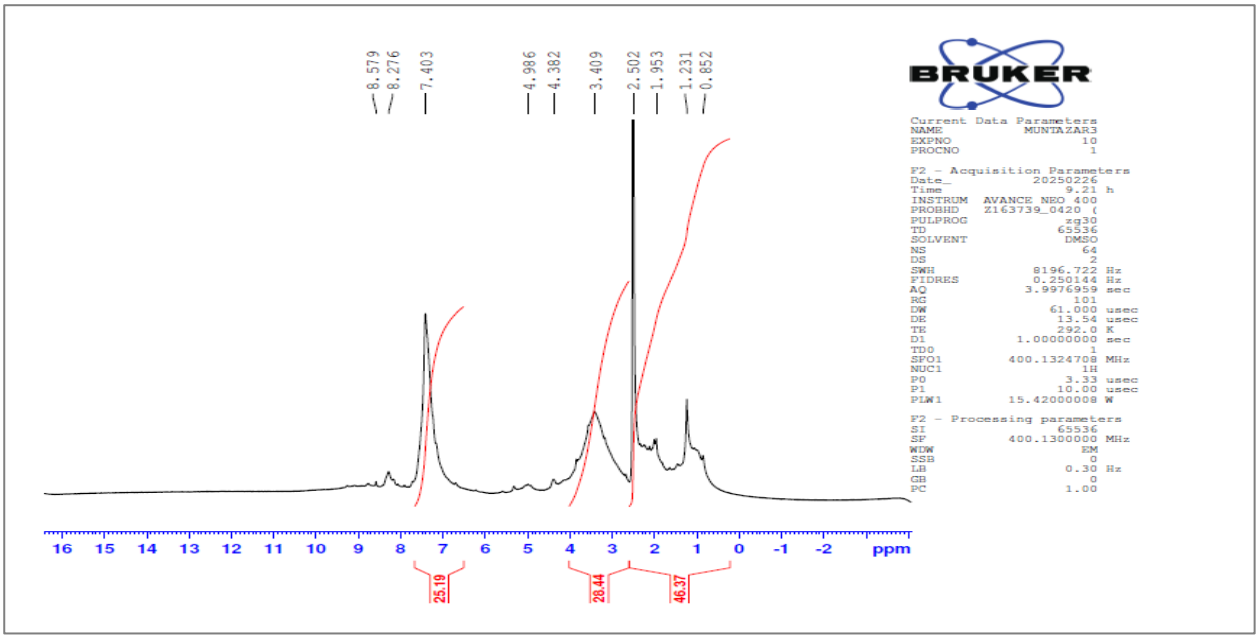


Figure 5. [1]HNMR of compound M1

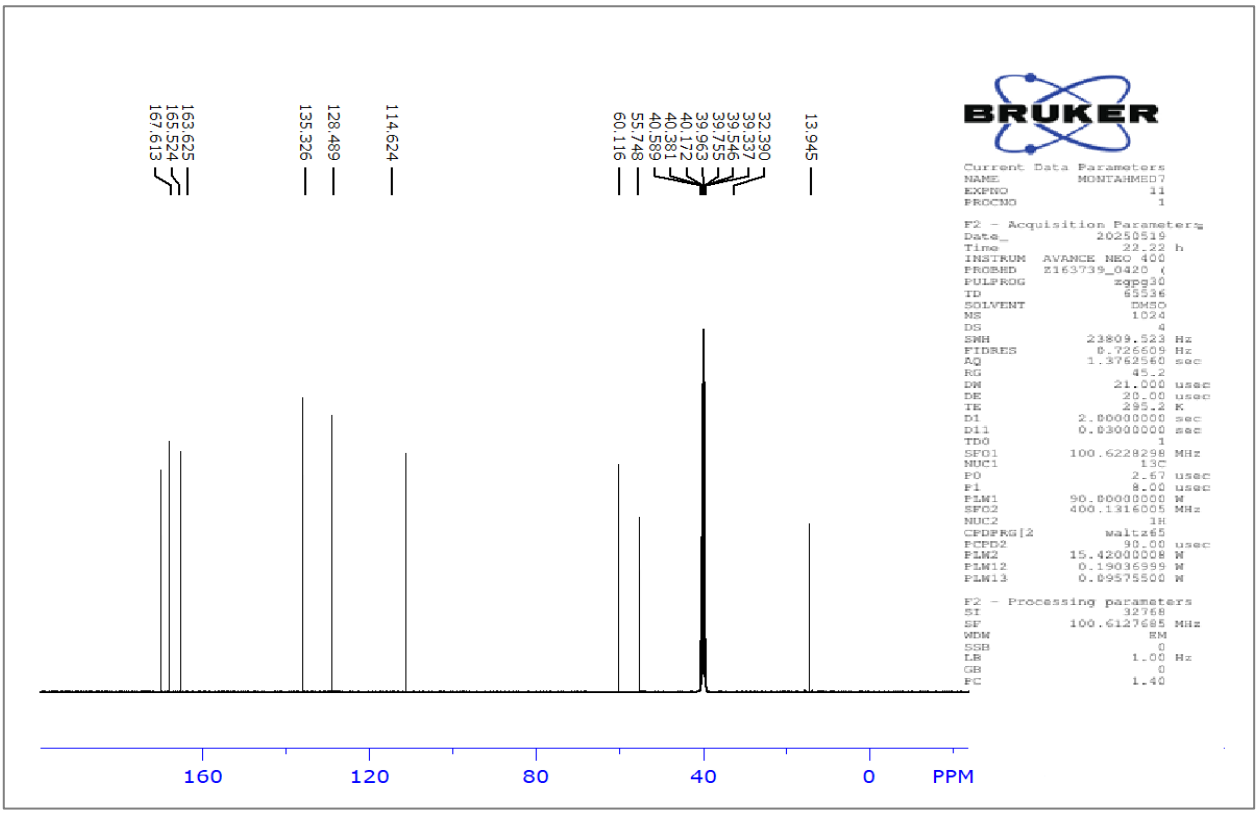


Figure 6. ^{13}CNMR of compound M1

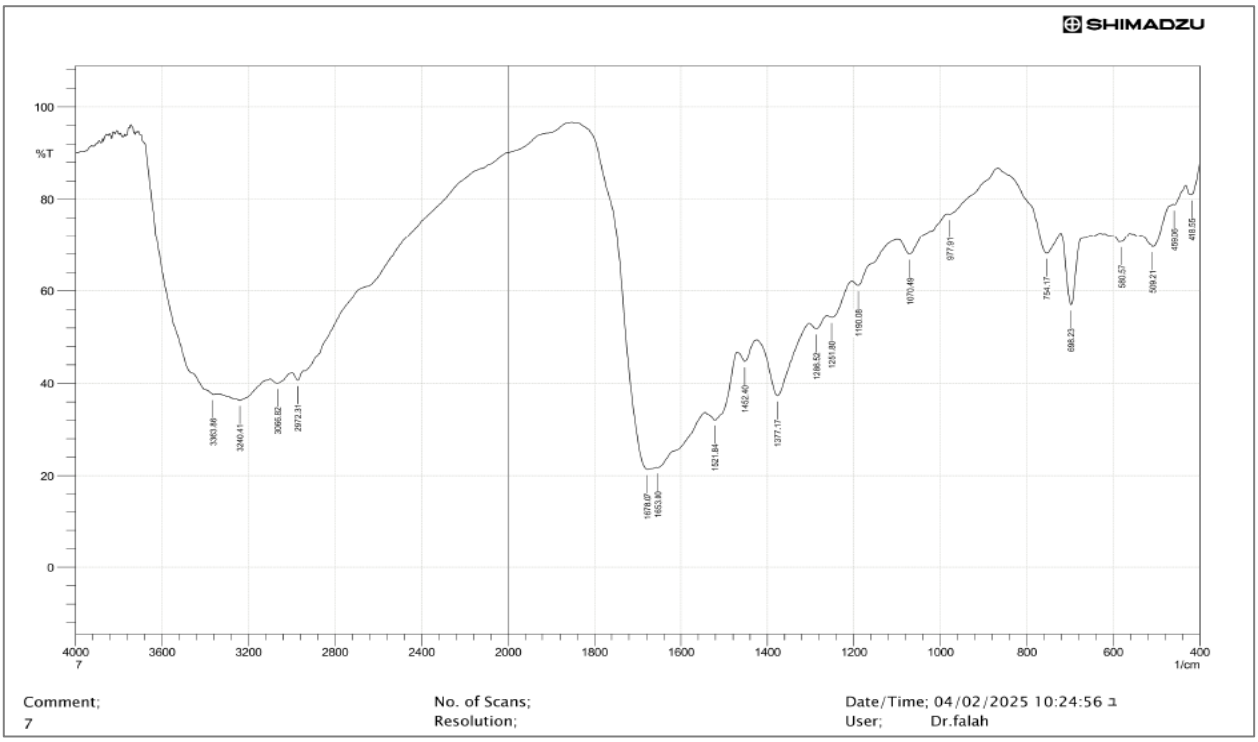


Figure 7. IR of compound M2

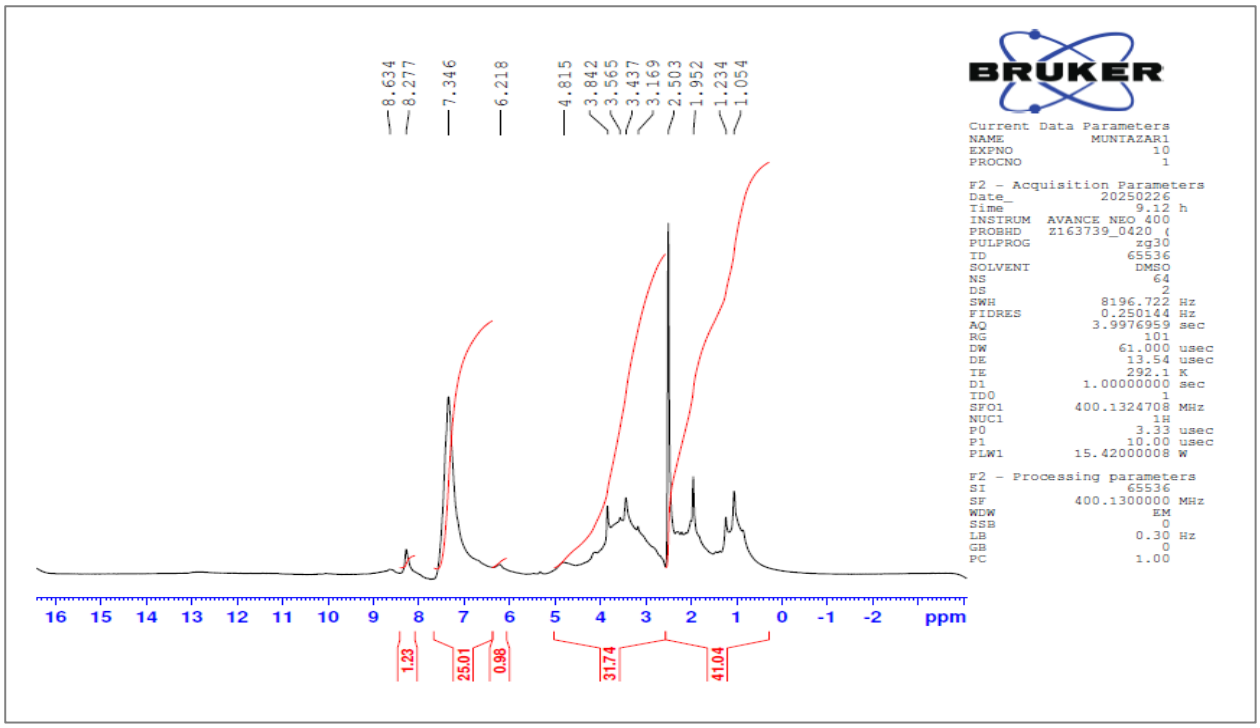


Figure 8. [1]HNMR of compound M2

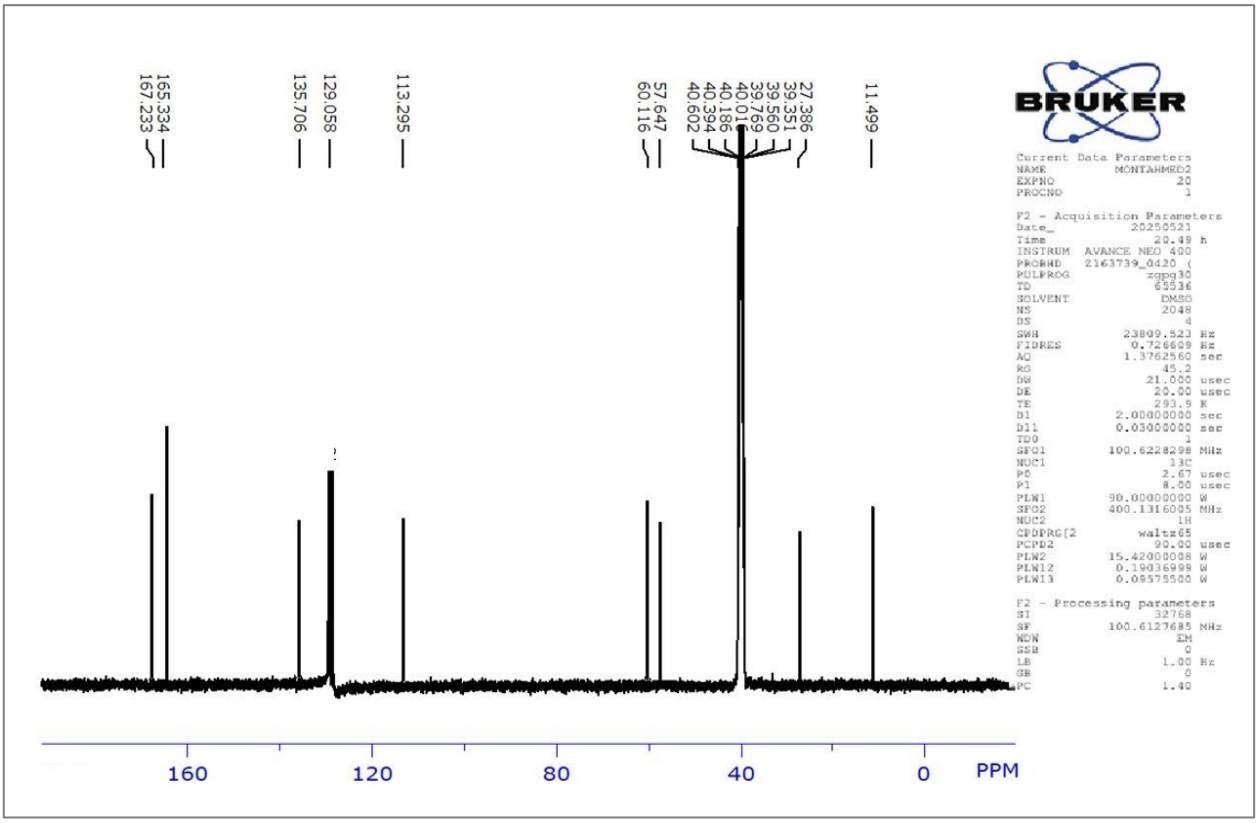


Figure 9. [13]CNMR of compound M2

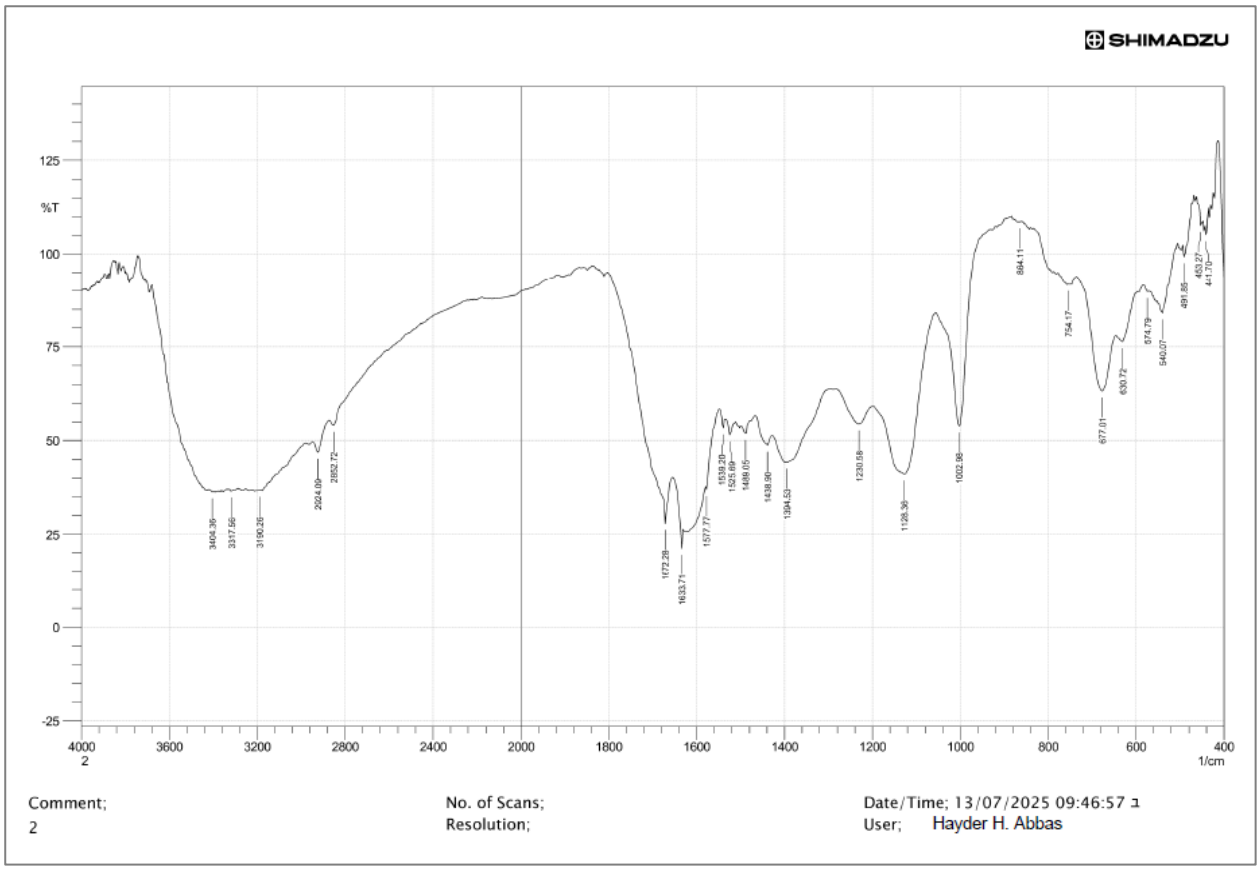


Figure 10. IR of compound M3

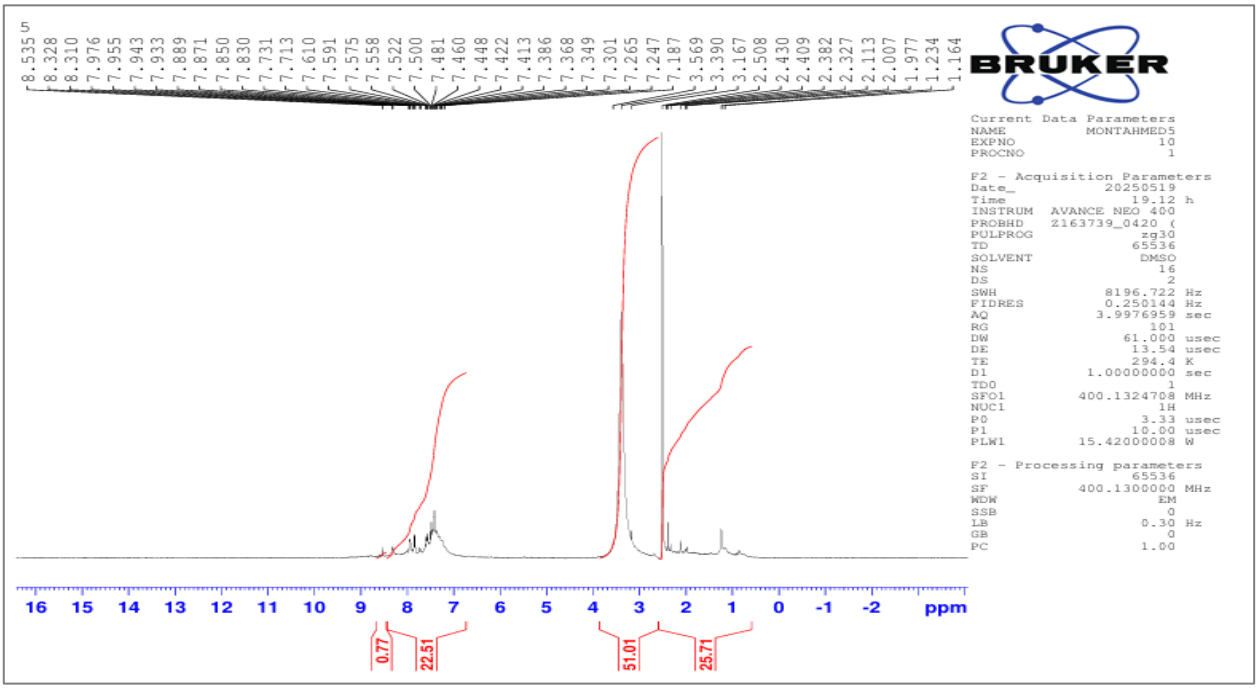


Figure 11. [1]HNMR of compound M3

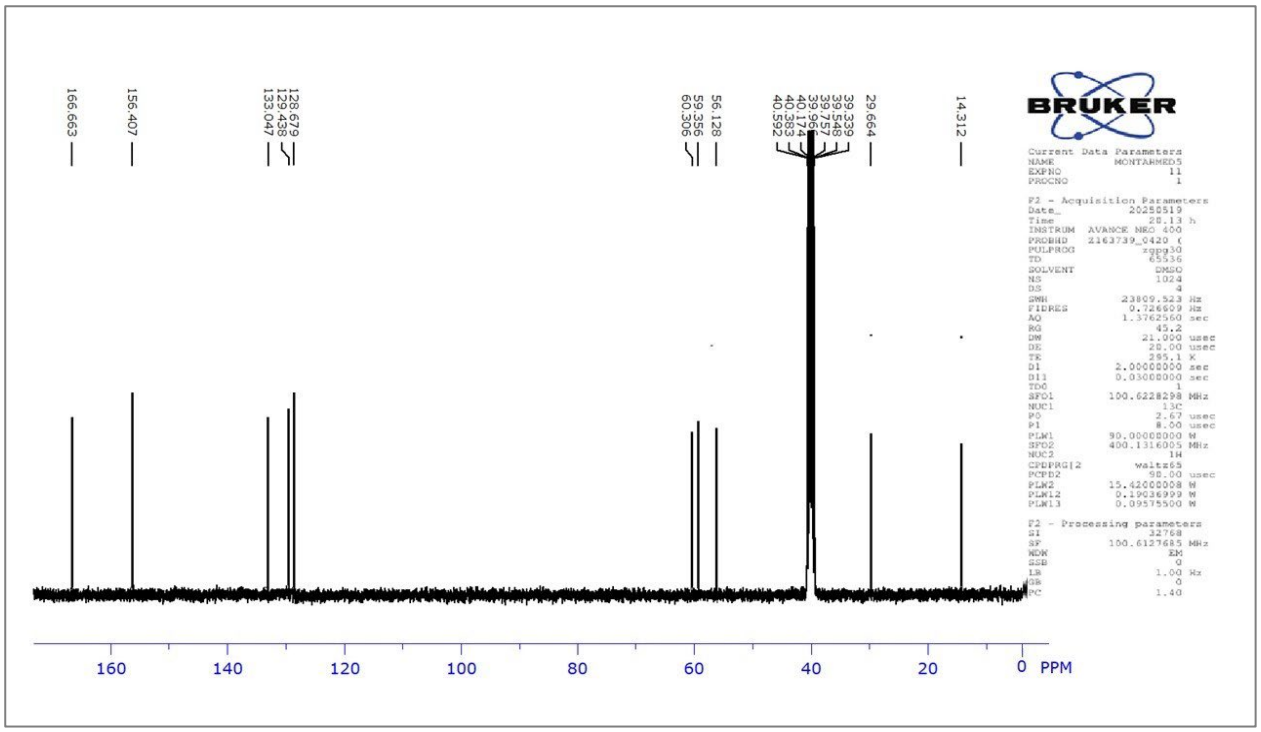


Figure 12. ^{13}CNMR of compound M3

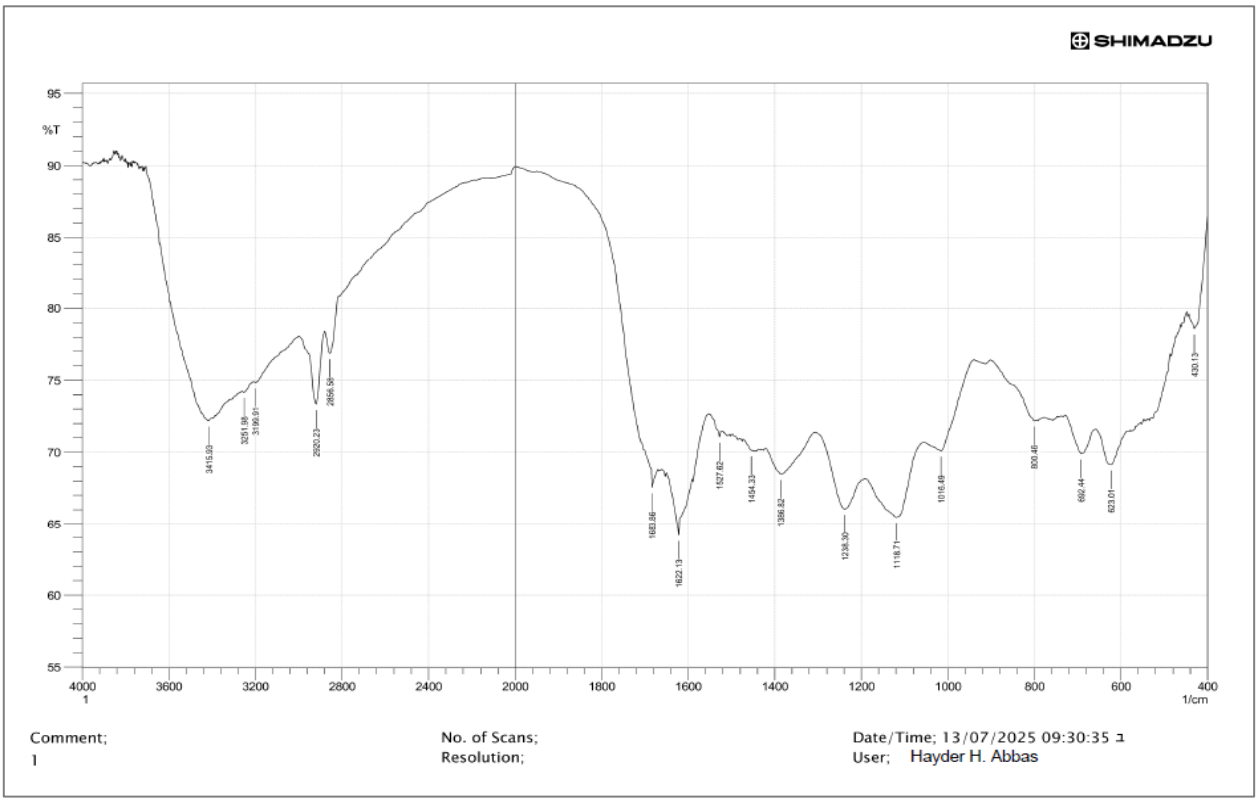


Figure 13. IR of compound M4

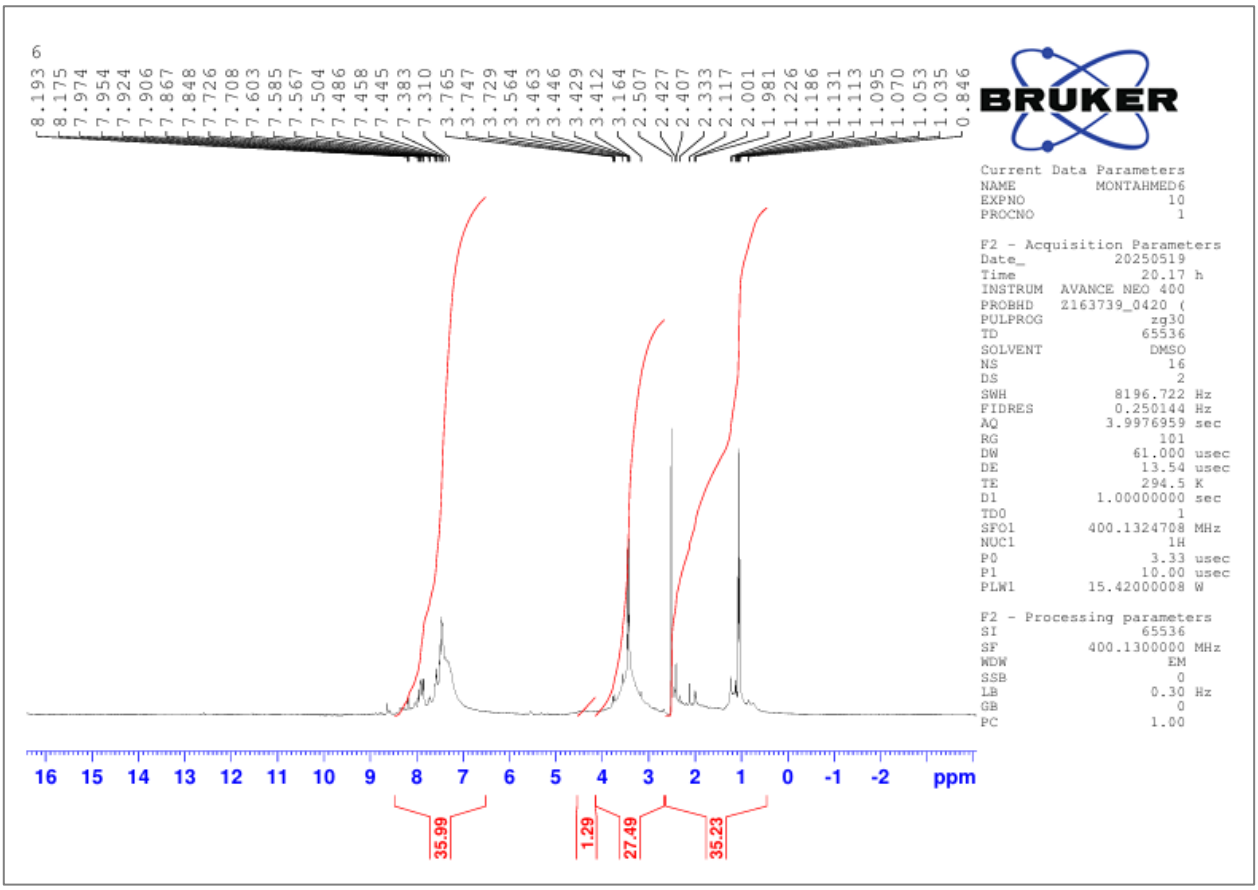


Figure 14. [1]HNMR of compound M4

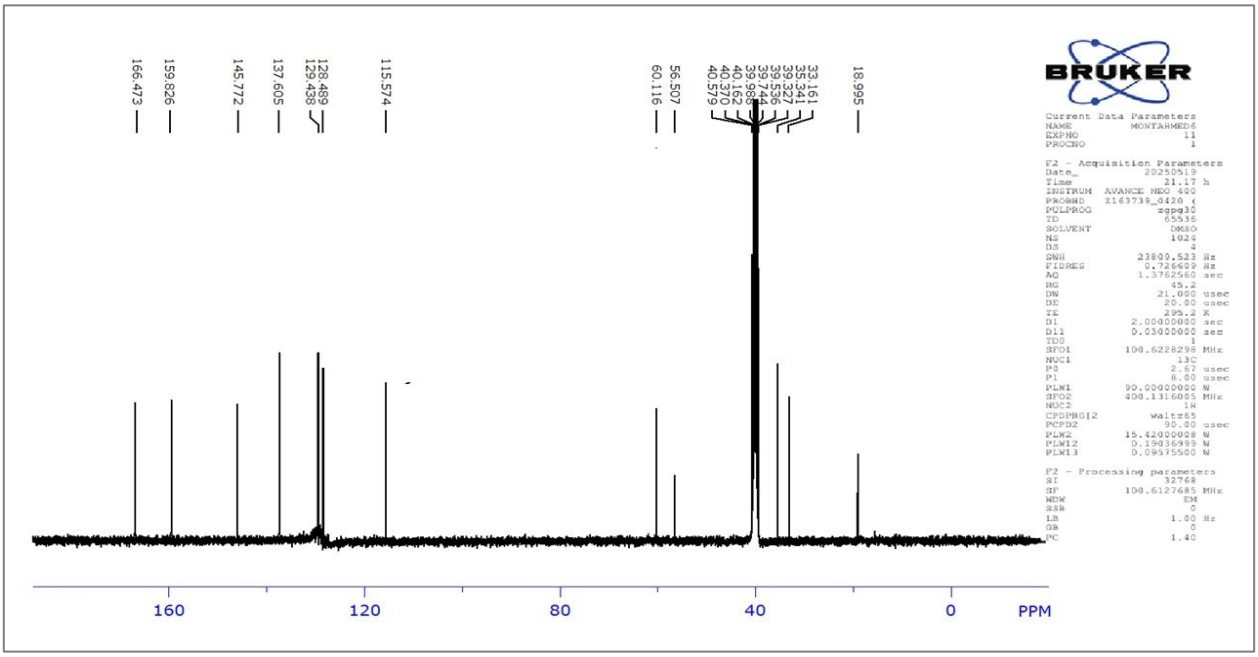


Figure 15. [13]CNMR of compound M4

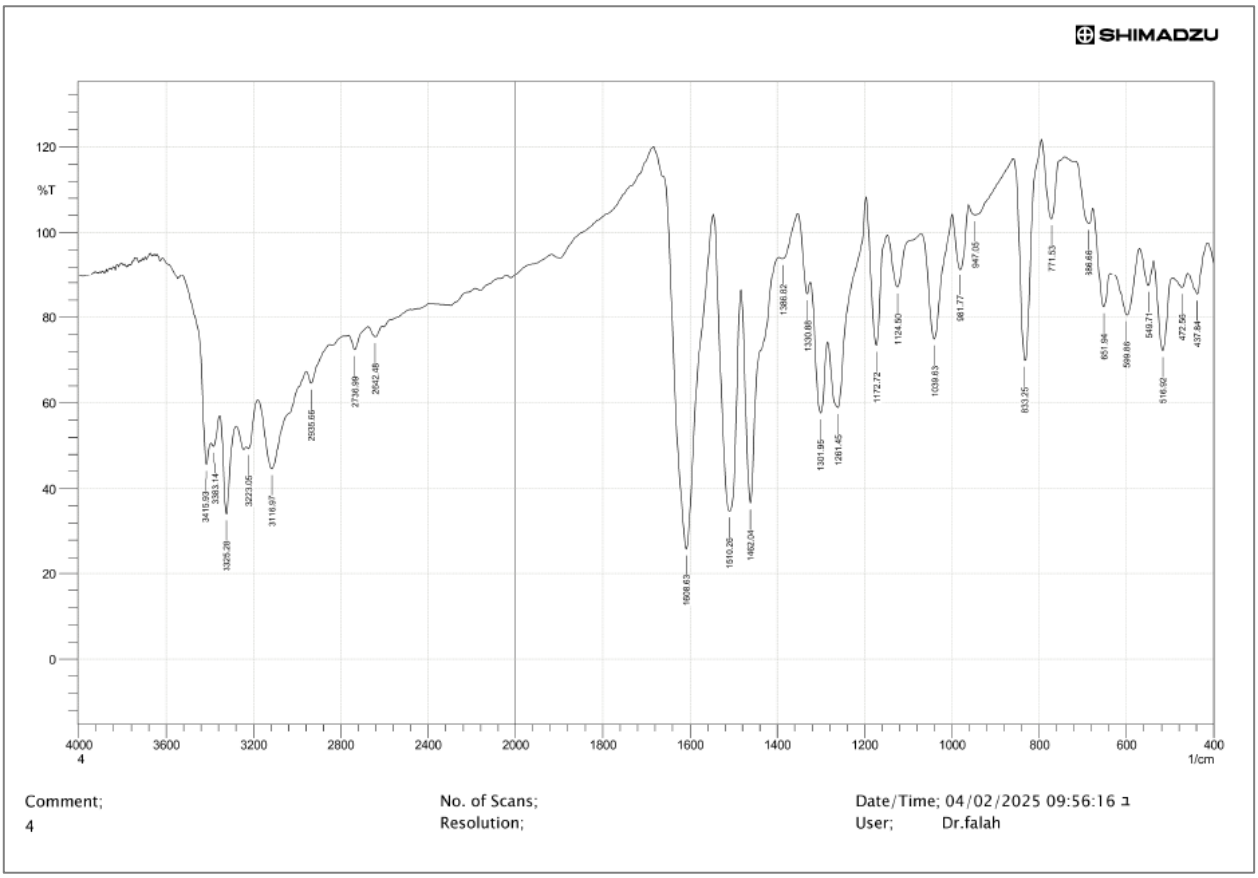


Figure 16. IR of compound M5

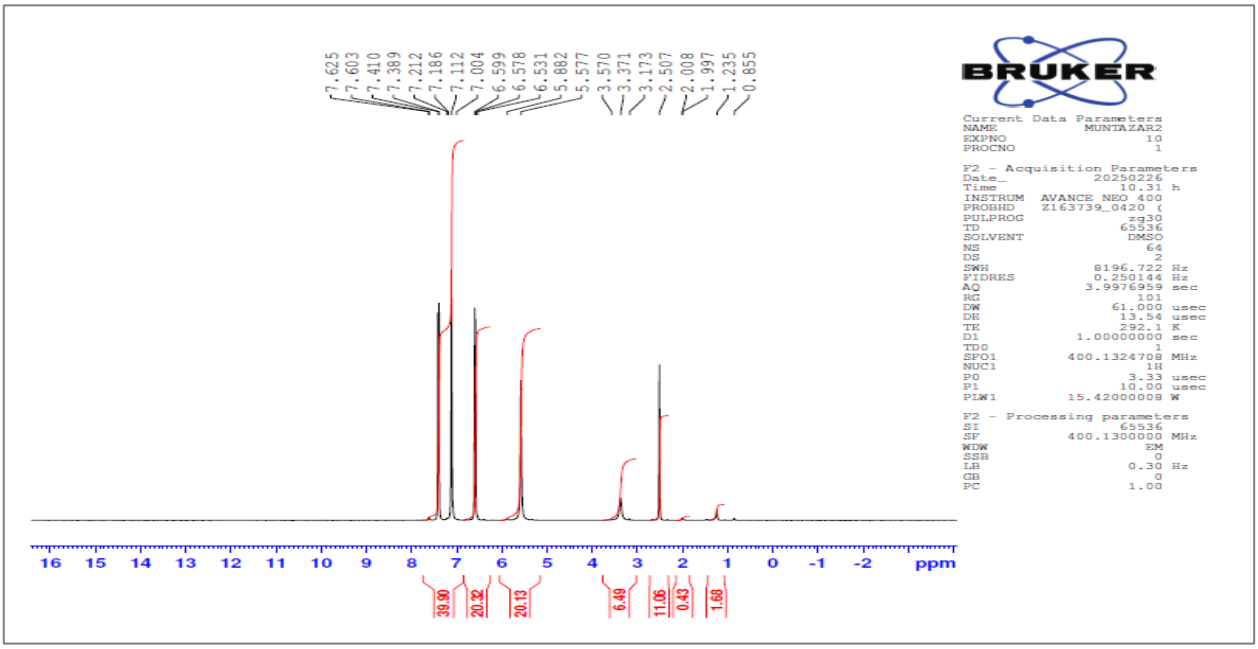


Figure 17. [1]HNMR of compound M5

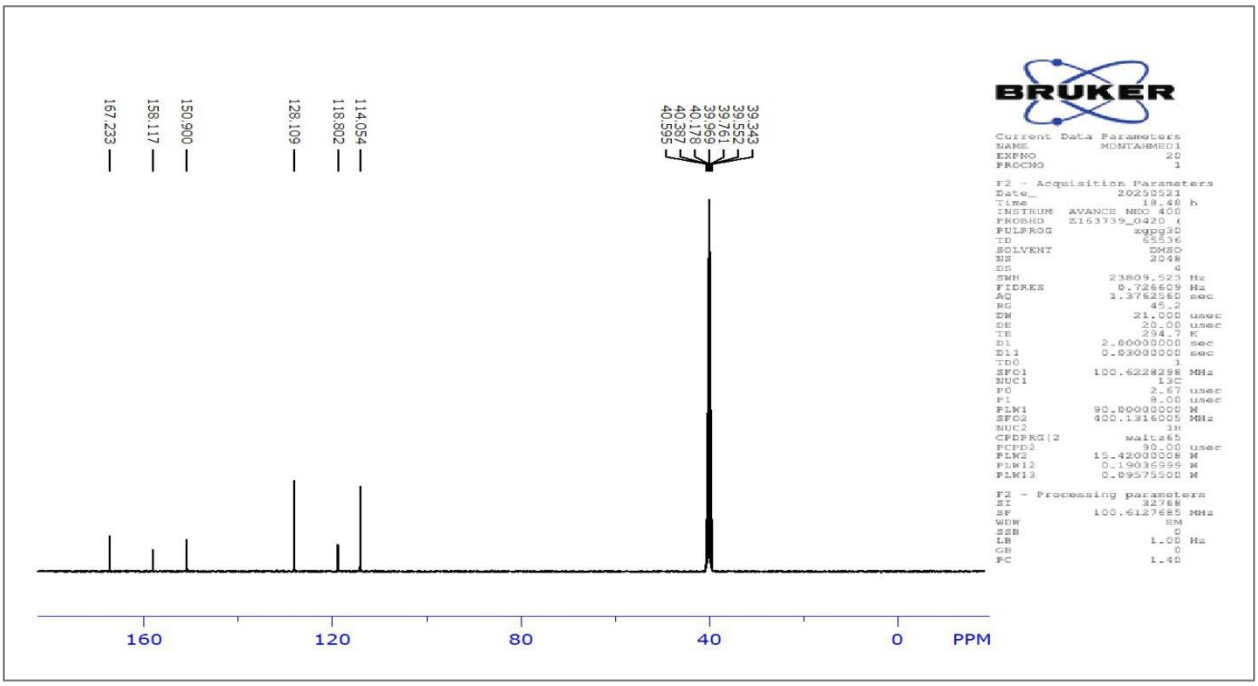


Figure 18. ^{13}CNMR of compound M5

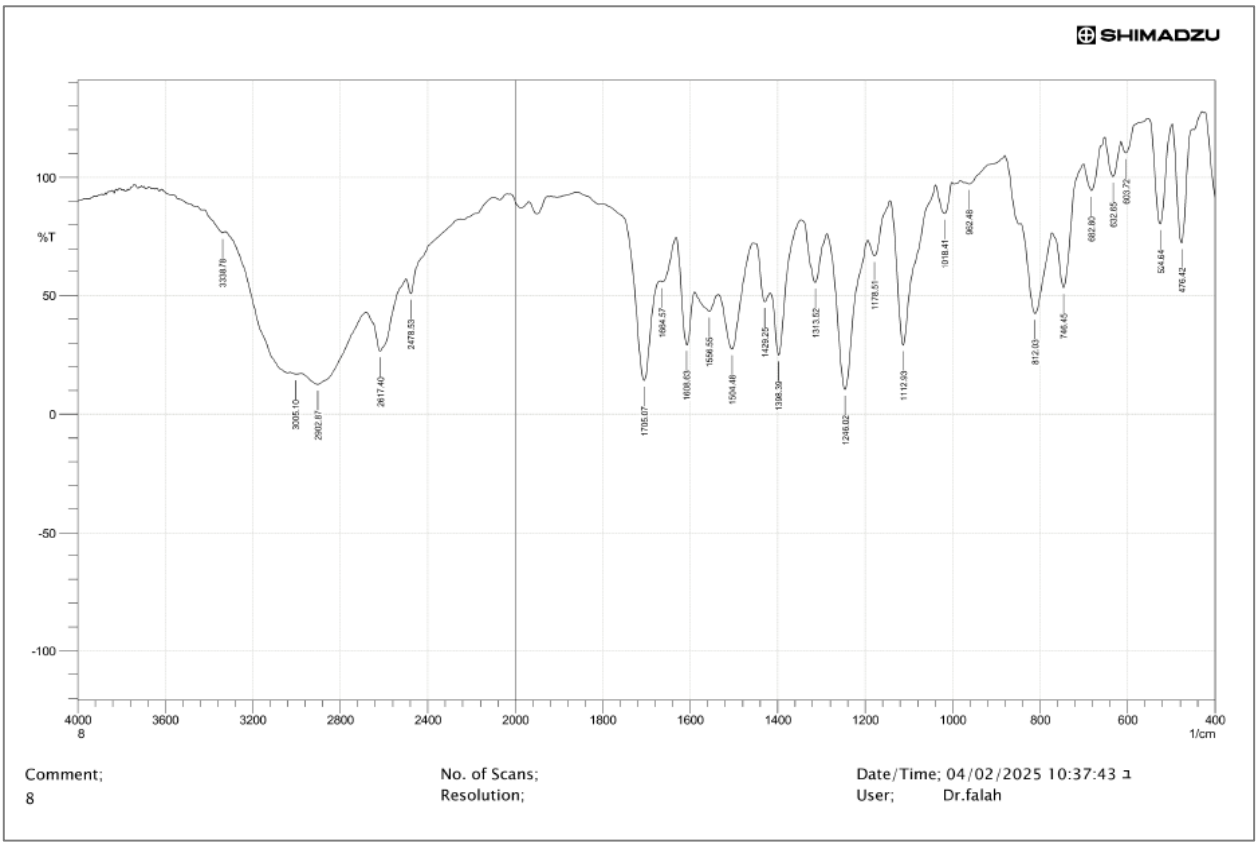


Figure 19. IR of compound M6

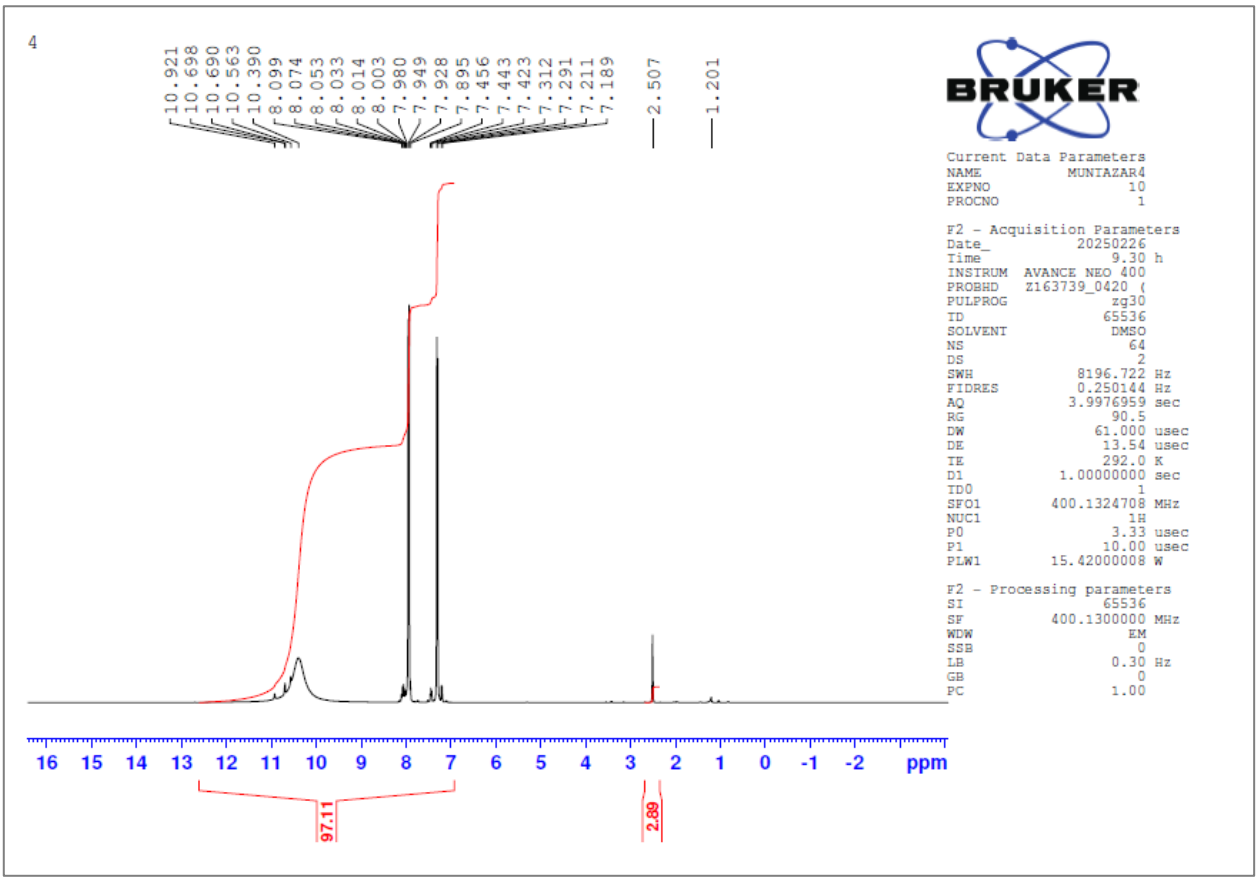


Figure 20. [1]HNMR of compound M6

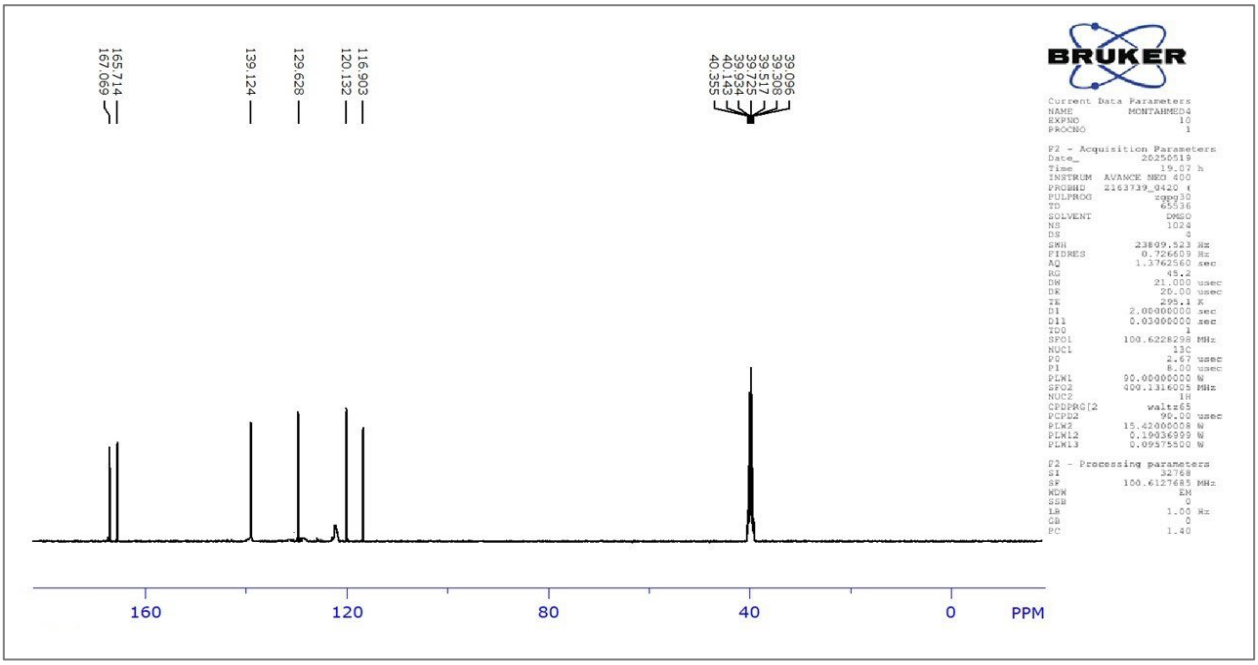


Figure 21. [13]CNMR of compound M6

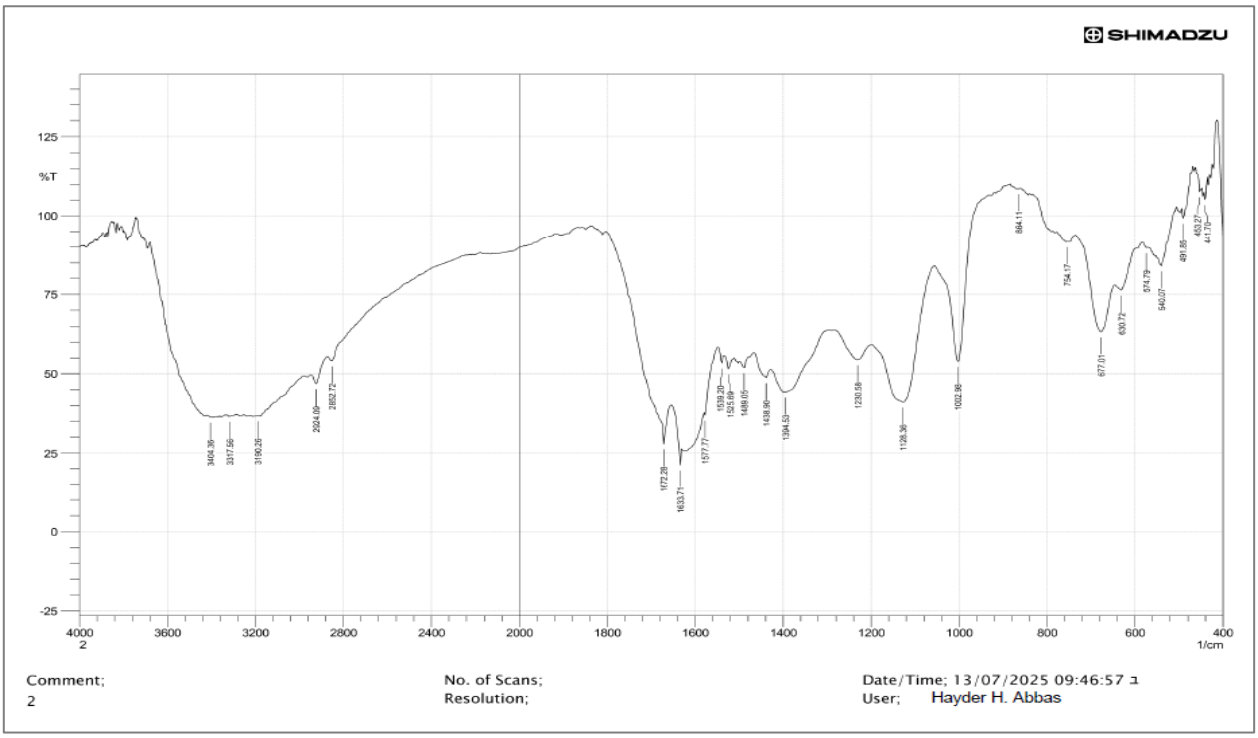


Figure 22. IR of compound M7

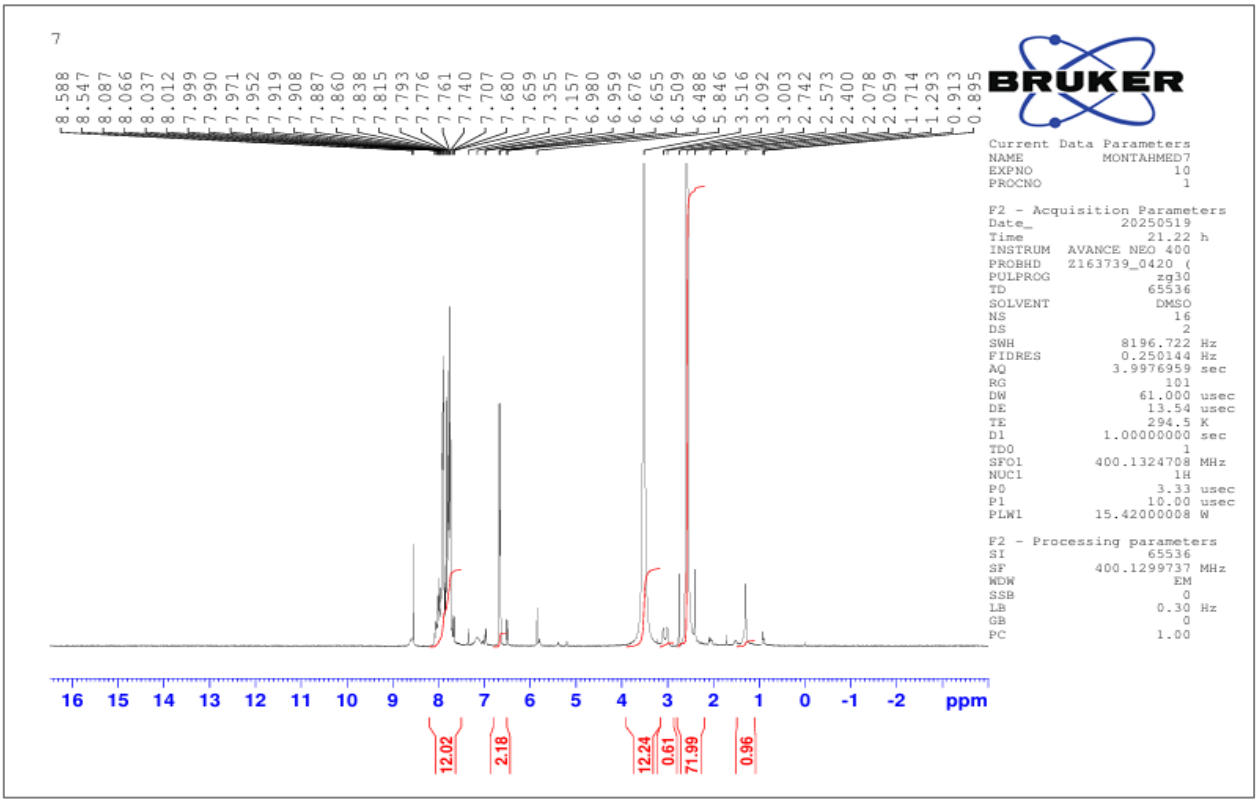


Figure 23. [1]HNMR of compound M7

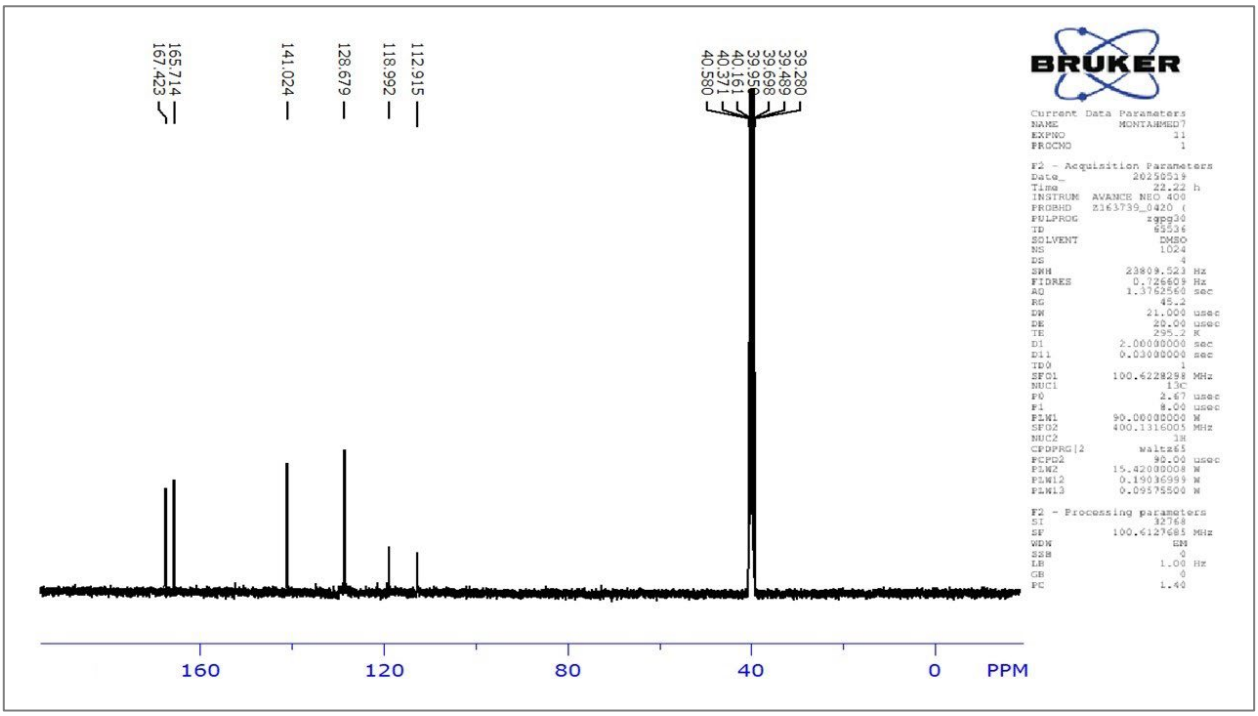


Figure 24. ^{13}CNMR of compound M7

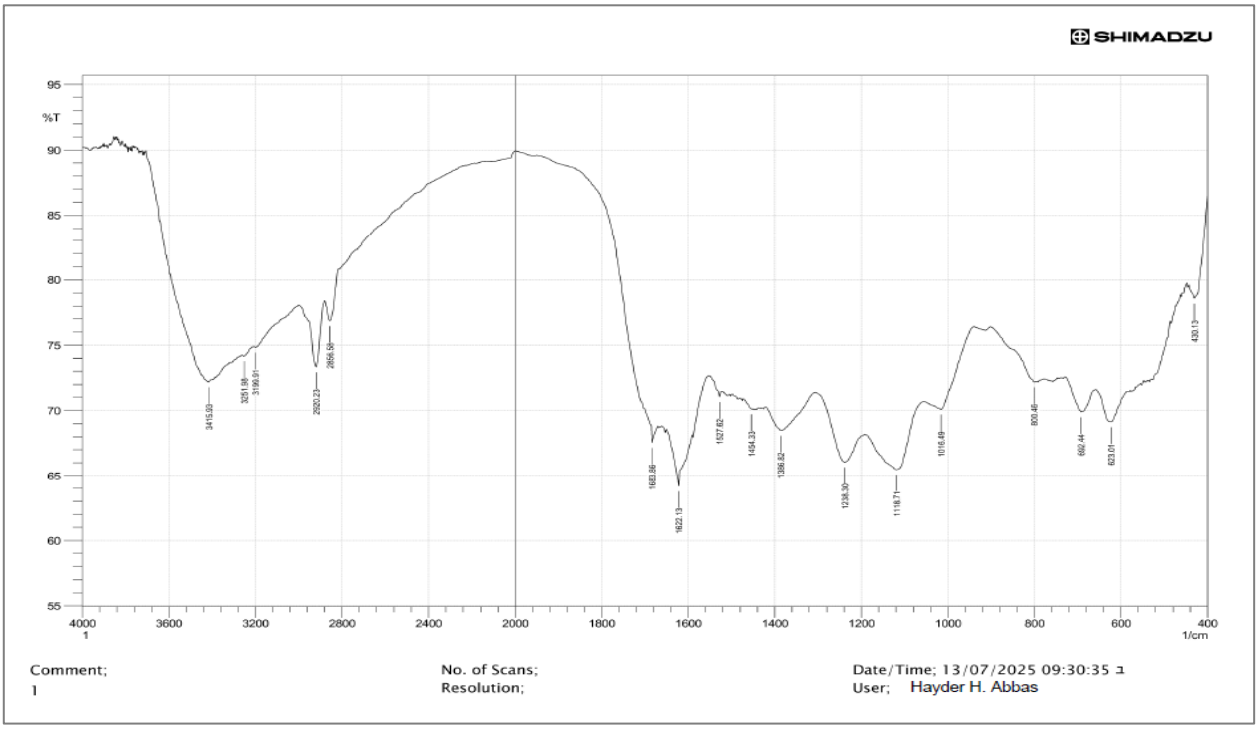


Figure 25. IR of compound M8

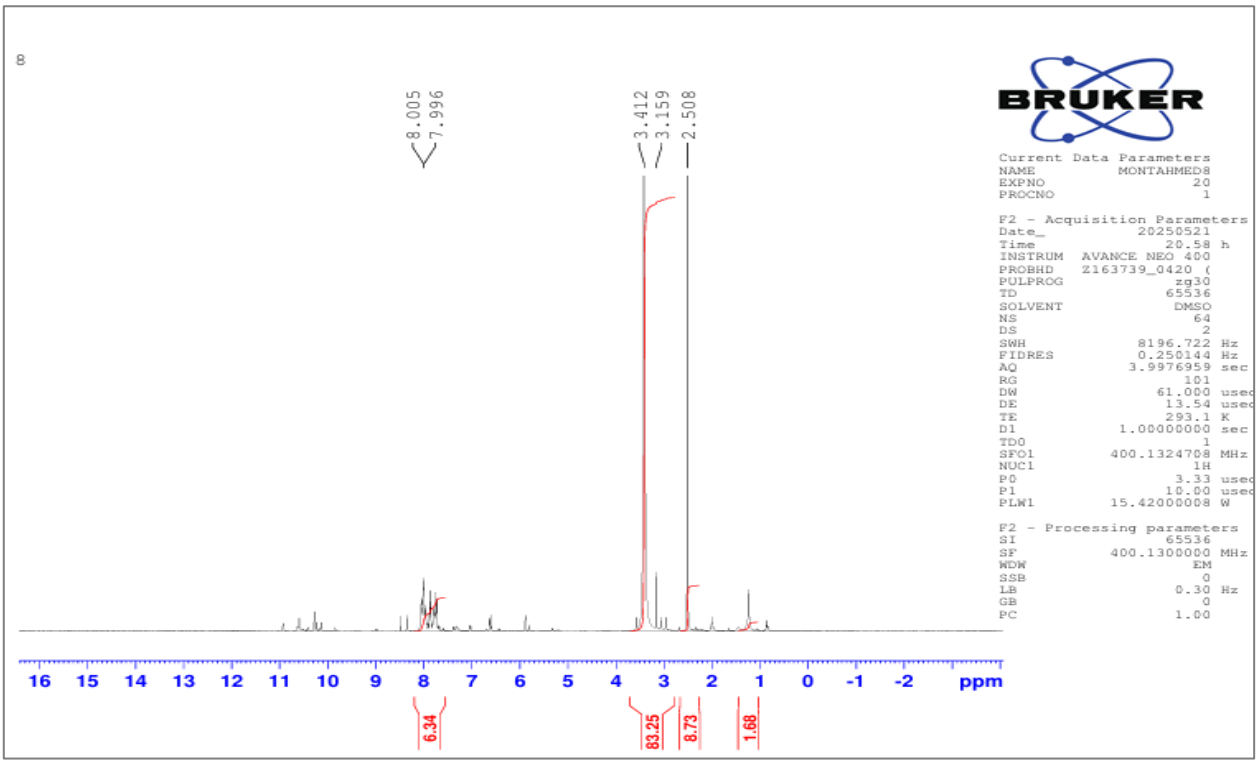


Figure 26. [1]HNMR of compound M8

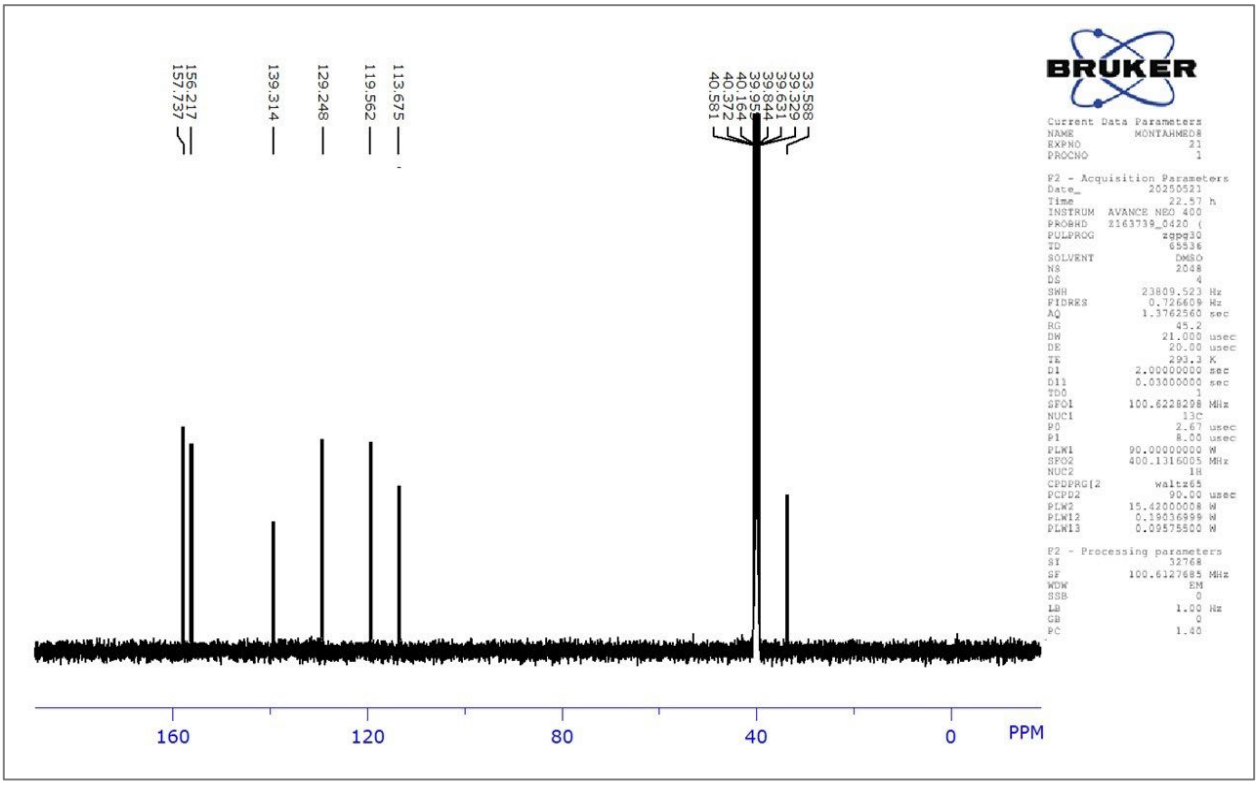


Figure 27. [13]CNMR of compound M8

4. Biological activity [26]

Both Escherichia coli and Staphylococcus aureus were used as the kinds of bacteria that were examined over this period of the research. The relevance of this specific strain of bacteria in the realm of medicine was the primary factor that led to be selection. For the purpose of determining the inhibitory effect of compounds

that have been generated on these specific kinds of bacteria, the methodology that was used is known as the agar diffusion method. The following are the parts that make up this method:

1-Many holes took place in the dishes that were planted with bacteria.

2- (0.1 milliliters) of various derivatives that were created in the excavation of cultivars were planted with bacteria of (0.1mg.ml-1).

3-Incubate the dishes for a period of twenty-four hours at a temperature of 37 degrees Celsius in an incubator.

4-The area of inhibition was measured, and the findings are shown in (Table 1)

Table 1. Antibacterial activity for compounds (M1-M8)

Compound. No	Inhibition zone (mm)	
	Escherichia coli	***Staphylococcus aureus***
Cephalexin (antibiotics) standard	18	15
M1	17	18
M2	20	22
M3	8	8
M4	11	11
4-Aminobenzoic acid (Bx) standard	12	8
M5	12	13
M6	10	14
M7	13	13
M8	15	15

The selected bacteria include one that is positive for the Gram stain (Staphylococcus aureus) and another that is negative for the stain (Escherichia coli). The degree of bacterial growth inhibition was examined using the agar diffusion technique, revealing that the majority of the synthesized compounds exhibit biological effectiveness as growth inhibitors for these two bacterial strains. The trend concerning Staphylococcus aureus indicates that compounds M1 and M2 exhibit higher inhibiting growth than the Cephalexin standard. Furthermore, Compounds M5, M6, M7, and M8 demonstrate higher inhibiting growth of Staphylococcus aureus than 4-aminobenzoic acid standard. While the trend regarding Escherichia coli demonstrates that compounds M2 display greater growth inhibition compared to the Cephalexin standard. Furthermore, compounds M7 and M8 have higher inhibitory effects on the growth of Escherichia coli compared to the 4-aminobenzoic acid standard.(Table1) and (Figure 5)

The structure-activity–activity relationship (SAR) analysis revealed that the presence of heterocyclic rings such as thiadiazole and oxadiazole played a crucial role in enhancing the biological activity of the Compounds. Compounds M1, M2, M7, and M8 showed superior activity compared to the standard due to the presence of thiadiazole and oxadiazole rings, which are well-known pharmacophores with a wide range of biological activities. These heterocyclic systems contribute to enhanced lipophilicity, electronic distribution, and hydrogen bonding potential, which may improve the compounds' ability to interact with biological targets such as enzymes or receptors. Furthermore, the electron-rich nitrogen and sulfur or oxygen atoms in these rings may facilitate stronger interactions (e.g., coordination or hydrogen bonding) with the active site residue, Compounds M1 and M2 showed the most promising biological activities among the synthesized derivatives, indicating that they could be the main candidates for additional pharmaceutical development.

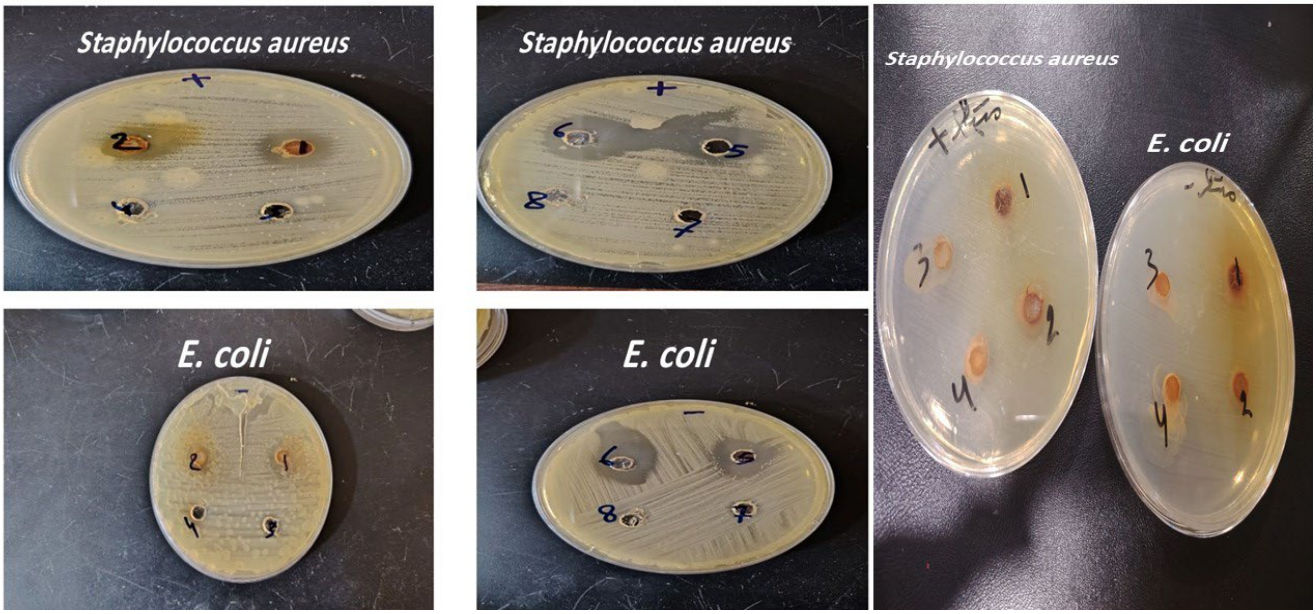


Figure 28. Staphylococcus aureus and E. coli activity test

5. Conclusion

To create heterocyclic compounds with thiadiazole, oxadiazole, and triazole rings, new pharmaceutical derivatives of cephalexin and 4-aminobenzoic acid were successfully synthesized in good yields. The majority of the derivatives showed modest antibacterial activity when these compounds were tested against Staphylococcus aureus and Escherichia coli. Compounds M1, M2, M7 and M8, on the other hand, showed notable inhibitory effects or even superior activity to the standard reference drug. According to these results, M1 and M2 have a great deal of promise as lead drug derivatives for the creation of novel antibacterial drug derivatives.

Conflict of interest

The authors declare no conflict of interest

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