

Preparation, Categorization and Anticancer Study of Novel Bicyclic Compounds from Various Types for (Five and Six)- Membered Ring

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Abstract

The Compounds that contain only carbon and hydrogen are called homogeneous rings, while those that contain other elements are called heterogeneous rings, and the atom substituted in place of the carbon atom is called a heterogeneous atom. Generally, the heterocyclic atom is an oxygen, nitrogen, or sulfur atom, but it is often nitrogen, and heterocyclic rings in living organisms are composed of nitrogen. Existing examples of heterocyclic rings include the aniline dye, most compounds discussed in biochemistry such as alkaloids, several vitamins, nucleic acids and many medicinal compounds. These structural compounds include (Five-cyclic), (Six-cyclic) and seven membered ring. This study included the preparation of cyclic and bicyclic compounds from starting material (Oxadiazole and Triazole) to formation Bicyclic compounds as (five, six, seven)-membered ring as a novel compounds .,All instrumental analysis gave clear evidences of their chemical structures via many technical instruments like (FT IR-Spectra, ¹H.NMR-Spectra, ¹³C.NMR-Spectra, melting points, also following by TLC with anticancer evaluation against breast cells .

Keywords: heterocyclic, Oxadiazole, Triazole, bicyclic, five ring, six ring, seven ring

INTRODUCTION

The cyclic compounds are credited to A. Kekulé in 1854 for stating that the main difference in the structure and in the characteristics and interactive capabilities of carbon compounds is due to the unique characteristics of the carbon atom that allow the formation of a huge number of compounds [1-4], due to the possibility of carbon atoms bonding with each other[5-9]. The other to form chains containing thousands of atoms or rings of different sizes, which is not possible for atoms of other elements. These chains can twist or branch [10-13] and attach to other atoms, such as mainly hydrogen atoms, halogens, oxygen [14-18], nitrogen [19-20], sulfur, phosphorus and many others. An example is chlorophyll and hemoglobin. These hetero atoms are within a system of chains or heterocyclic compounds, as in the two-ring system of sulfur and nitrogen. Therefore, it is not surprising that the number of known carbon compounds is more than ten million compounds, and that this number increases to about half a million compounds annually.

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EXPERIMENTAL

Methodology

Methods and Devices

The study deliberately excluded the synthesis of all bicyclic compounds using unverified methods, relying instead on well-established and credible literature procedures. The successful formation of the target bicyclic compounds was confirmed by the appearance of distinct spectral signals and the disappearance of others, indicating the structural transformation into new cyclic systems. Spectral characterization was carried out using key analytical techniques, including infrared (IR)

spectroscopy and nuclear magnetic resonance (NMR) spectroscopy—specifically, both proton (^1H NMR) and carbon (^{13}C NMR) analyses. The preparation of these novel bicyclic compounds was further validated by consistent data on melting points, FT-IR spectral ranges, ^1H NMR chemical shifts, and ^{13}C NMR chemical shift ranges.

Experimental Approaches

Synthesis of Cyclic Compound{1}

2-Methyl-3-acetobenzoic acid (0.001 mol) refluxed in (50 ml) absolute ethanol and sulfuric acid for esterification reaction for 2 hrs, then refluxed with (0.001 mol) of semicarbazide for (27 hrs) in absolute ethanol (30 ml $\text{C}_2\text{H}_5\text{OH}$), the product filtered, desiccated, purified to yield cyclic derivative {1} of oxadiazole according to procedures [13-15].

Synthesis of Cyclic Compound{2}

Cyclic compound {1} as oxadiazole (0.001 mol) refluxed with (0.001 mol) of hydrazine for (5-6 hrs) with acetone (50 ml), the product filtered, desiccated, purified to yield cyclic compound {2} as Triazole according to procedures [13-15].

Synthesis of Bicyclic Compound [3]

Cyclic compound {2} as Triazole (0.001 mol) refluxed with (0.001 mol) of formaldehyde for (9 hrs) with (5 ml) of sulfuric acid and absolute ethanol (50 ml $\text{C}_2\text{H}_5\text{OH}$), the product filtered, desiccated, purified to yield bicyclic compound {3} as five-membered ring according to procedures [13-15].

Synthesis of Bicyclic Compound{4}

Cyclic compound {2} as Triazole (0.001 mol) refluxed with (0.001 mol) of chloroacetyl chloride for (10 hrs) with (0.0005) of potassium carbonate and absolute ethanol (50 ml $\text{C}_2\text{H}_5\text{OH}$), the product filtered, desiccated, purified to yield bicyclic compound {4} as six-membered ring according to procedures [13-15].

Synthesis of Bicyclic Compound{5}

Cyclic compound {2} as Triazole (0.001 mol) refluxed with (0.001 mol) of diethyl oxalate for (4 hrs) with absolute ethanol (50 ml $\text{C}_2\text{H}_5\text{OH}$), the product filtered, desiccated, purified to yield bicyclic compound {5} as six-membered ring according to procedures [13-15]., Pattern (1)

RESULTS AND DISCUSSION

Series of Spectral procedures were carried out to be indications for synthesized cyclic and bicyclic compounds by followed many chemical methods from references [1-7].

Evidences of Cyclic and Bicyclic Compounds via Spectral Identification

FT-IR- Spectra: Indication for formation of Oxadiazole-Derivatives in compound{1} appeared band at 1170 cm^{-1} due to (C-O-C-) ether for oxadiazole and bands ($3398, 3338$) cm^{-1} for amine group (NH_2)

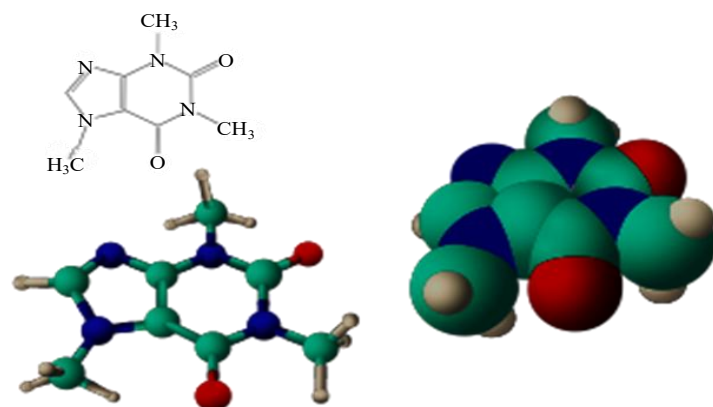


Figure 1. Bicyclic System.

compound {1} as a starting material, in addition to other essential functional groups in this compound which appeared in spectral figures of FT.IR. But all amine bands (two bands) disappeared and one band appeared instead of them due to (NH-CO) amine of amide and secondary amine (NH) at about {(3305 to 3172) cm^{-1} } as a result to formation new compounds (cyclic and bicyclic) besides to appearance of other essential bands in cyclic compounds. All frequencies identified and explained according to reference [15], and other functional groups in some Figures (1-5):

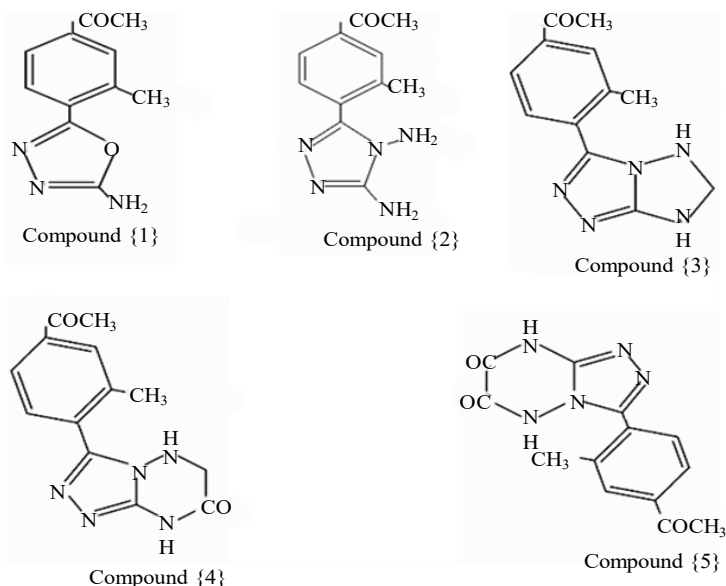


Figure 2. Synthesized Cyclic and Bicyclic Compounds [1-5]

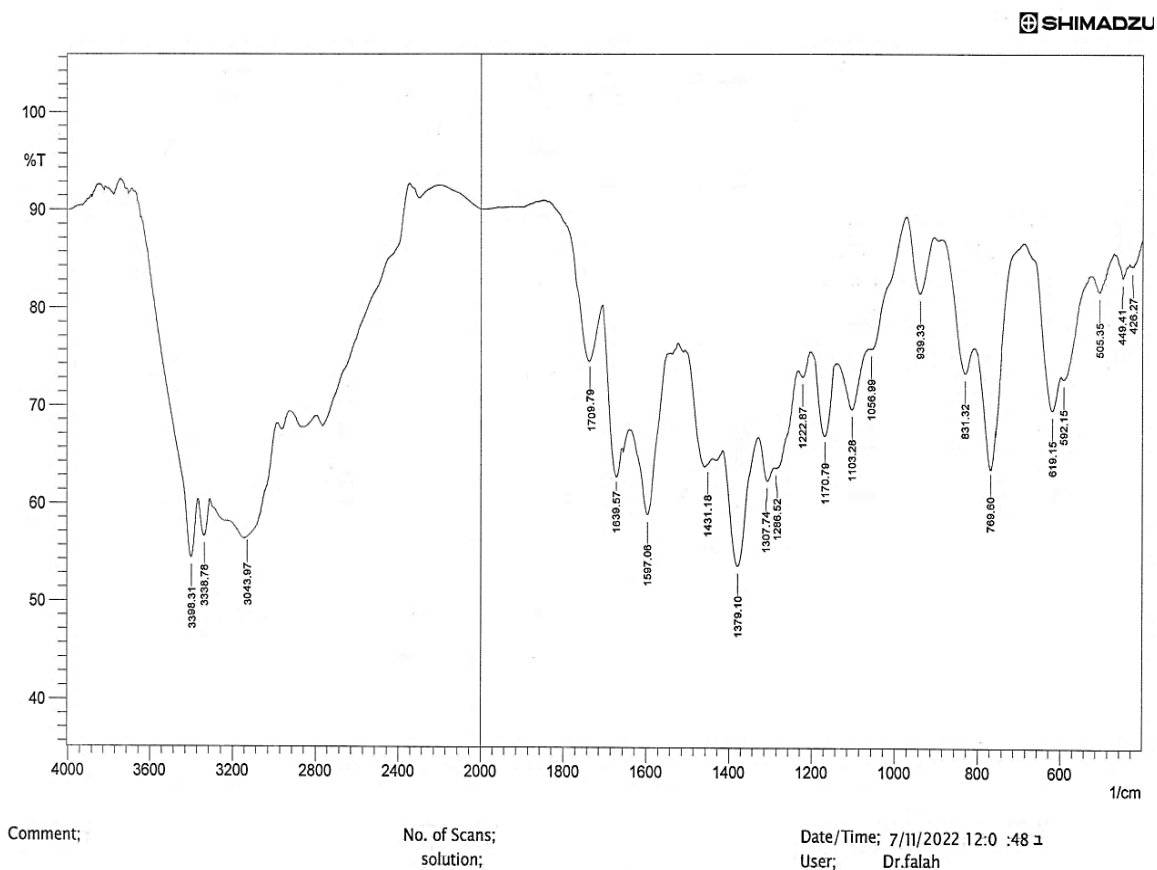


Figure 3. I.R of Compound [1]

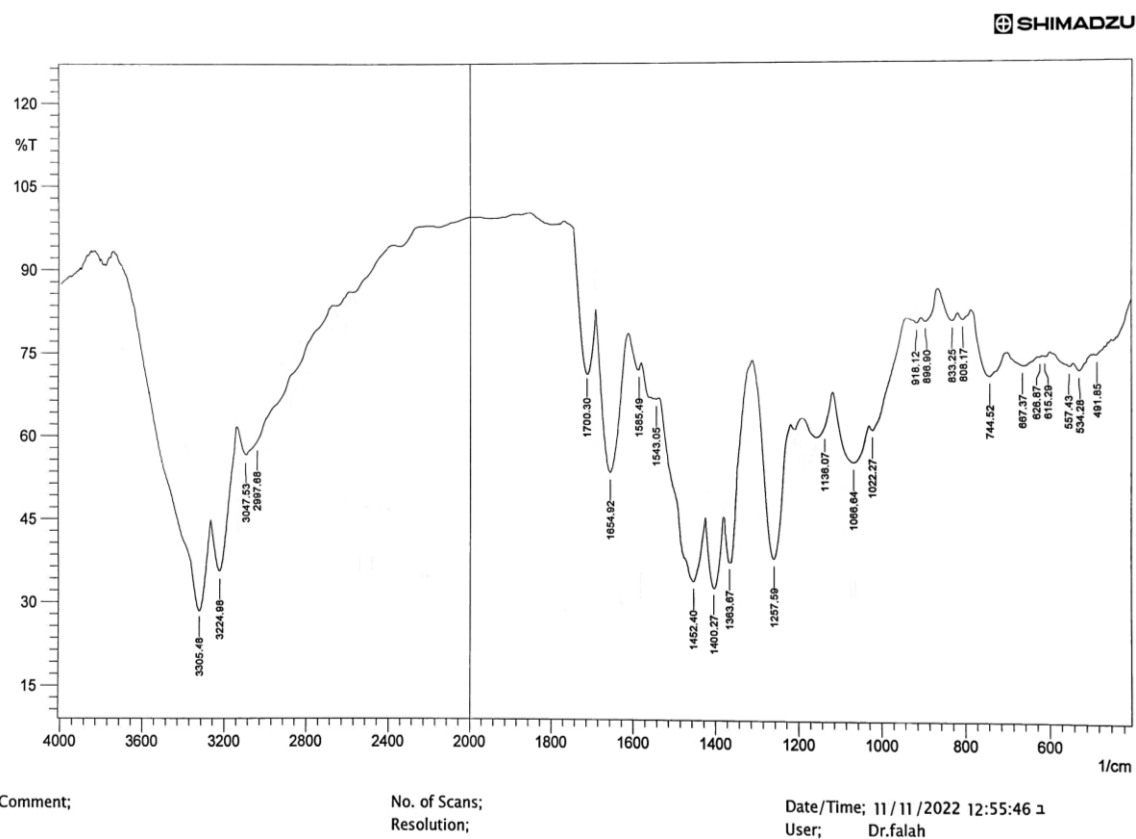


Figure 4. I.R of Compound [2]

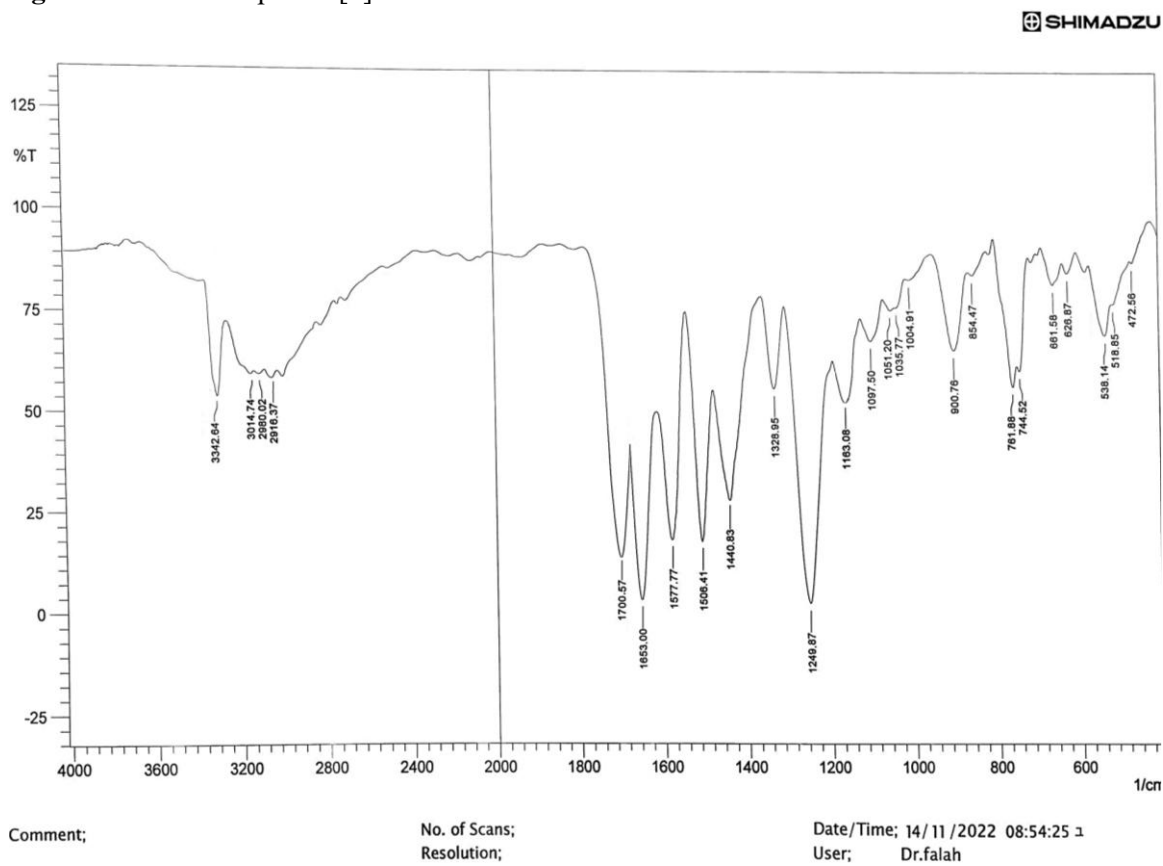


Figure 5. I.R of Compound [3].

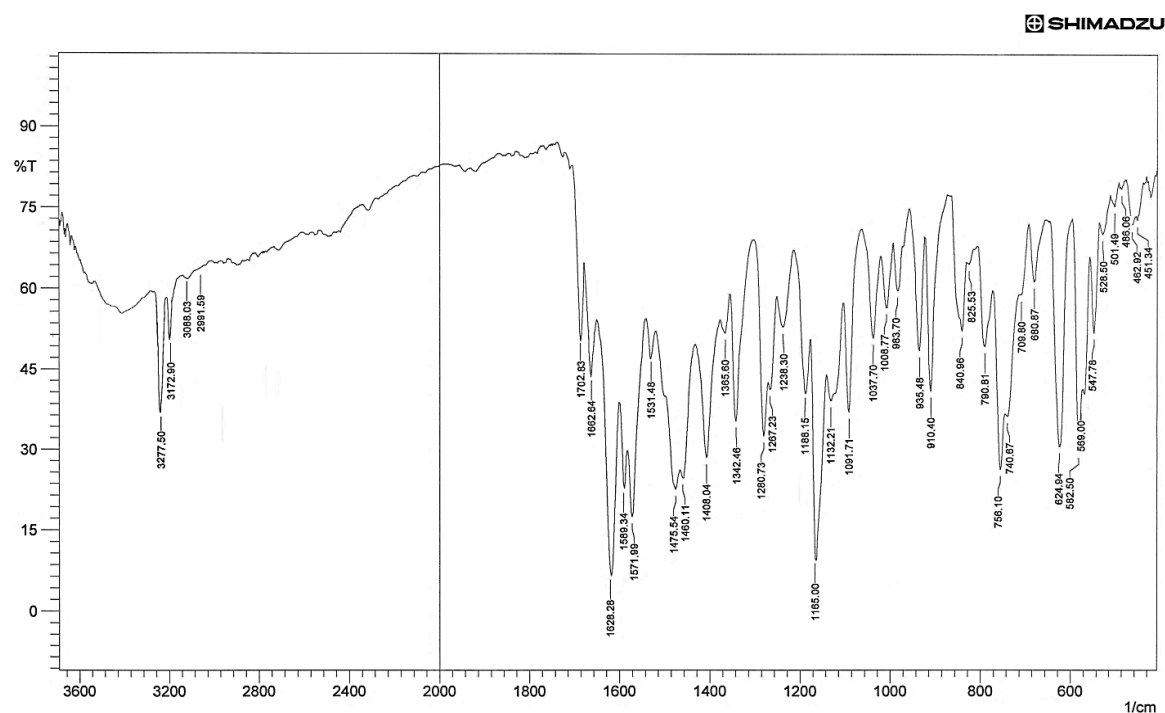


Figure 6. I.R of Compound [4]

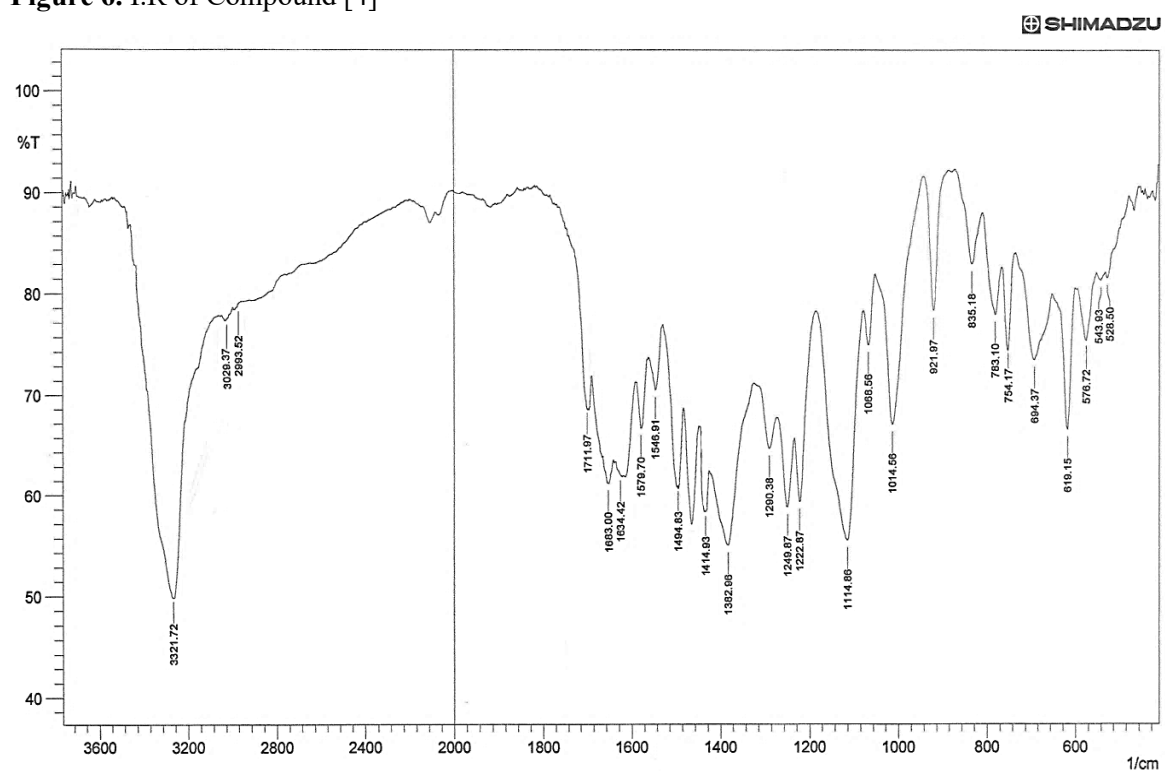
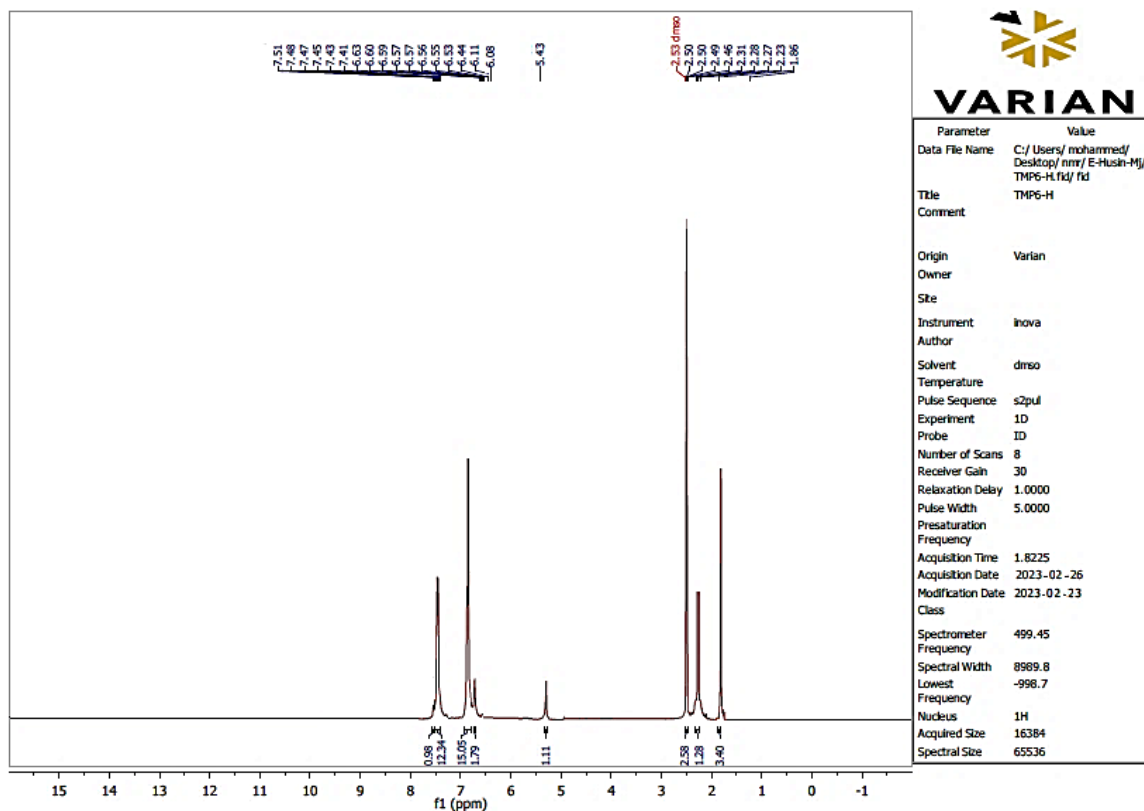
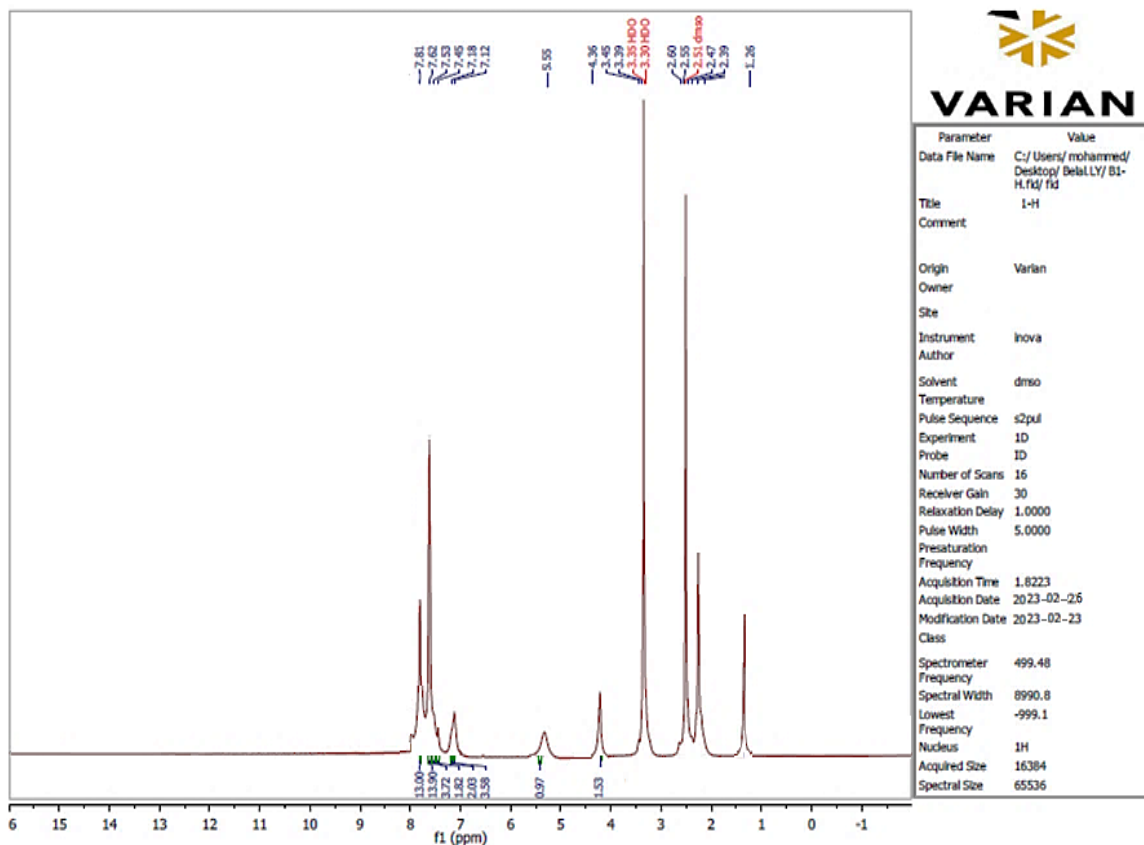


Figure 7. I.R of Compound [5].

¹H.NMR- Indication of Cyclic and Bicyclic derivatives: The additional characterization by appearance peaks at δ (5.43), (5.5)} respectively for proton of amine group (NH₂) in compounds {1, 2} respectively., which desertion in compounds {3-5} as a results to formation cyclic and bicyclic compounds and appearance new signals at {(9.81, 9.80, 10.0)} due to proton of amide in compounds {4,5}, also all signals of aromatic protons were at about (6.50- 7.99)., All signals clarified according to reference [15], and other functional groups in Figures (6-10):

Figure 8. ¹H.NMR of [1]Figure 9. ¹H.NMR- of [2].

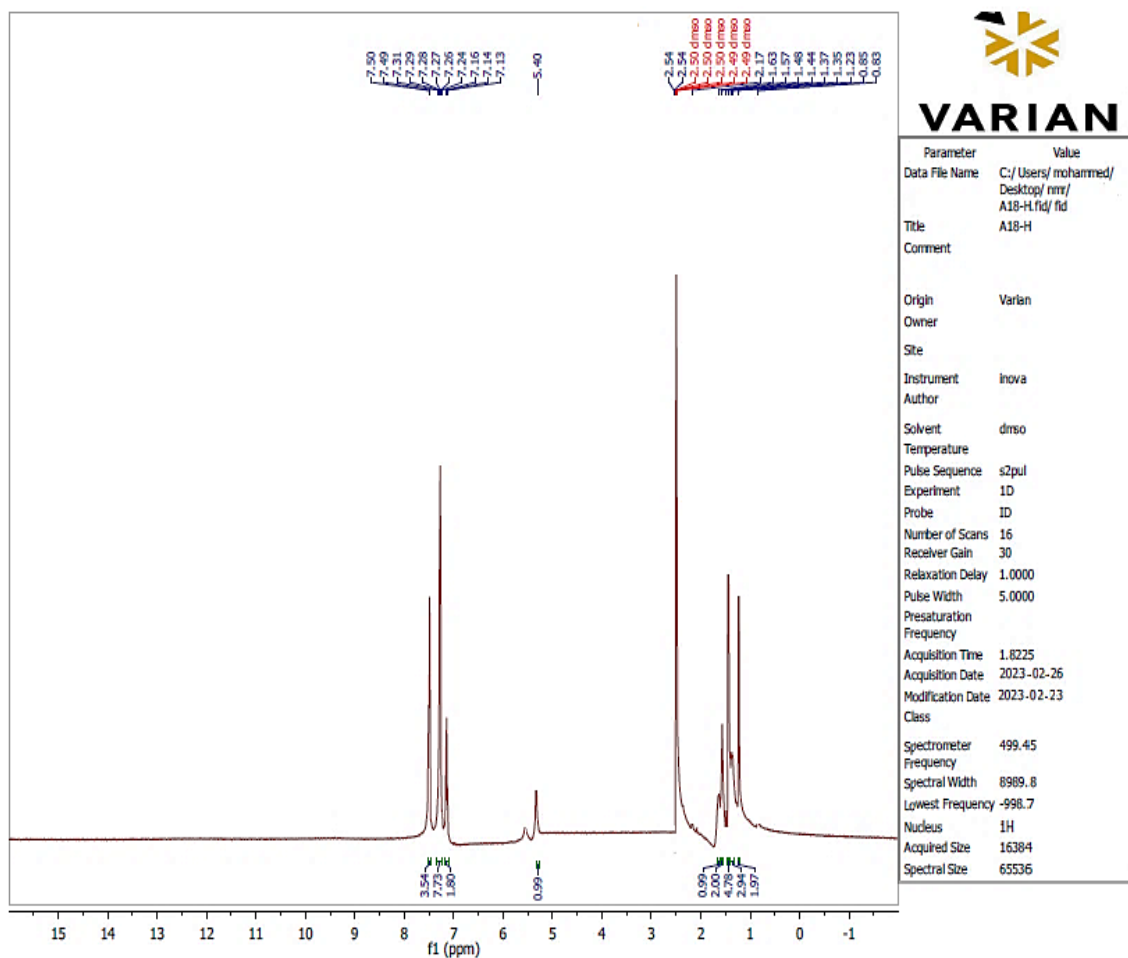


Figure 10. ¹H.NMR- of [3]

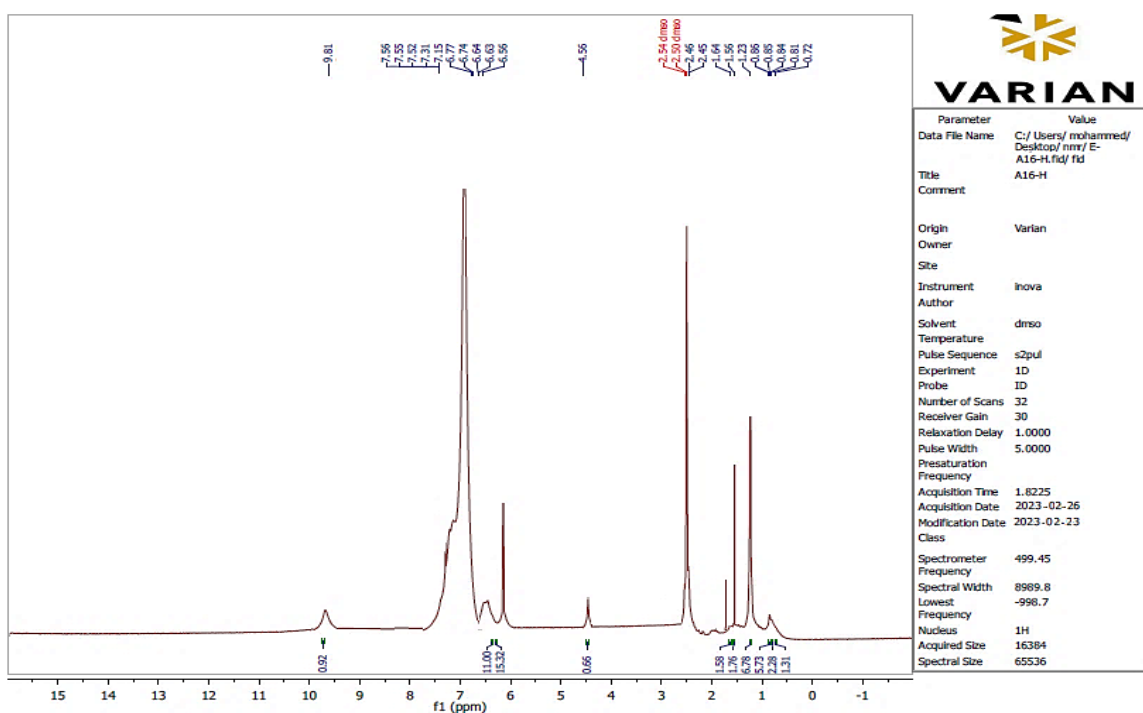


Figure 11. ¹H.NMR- of [4].

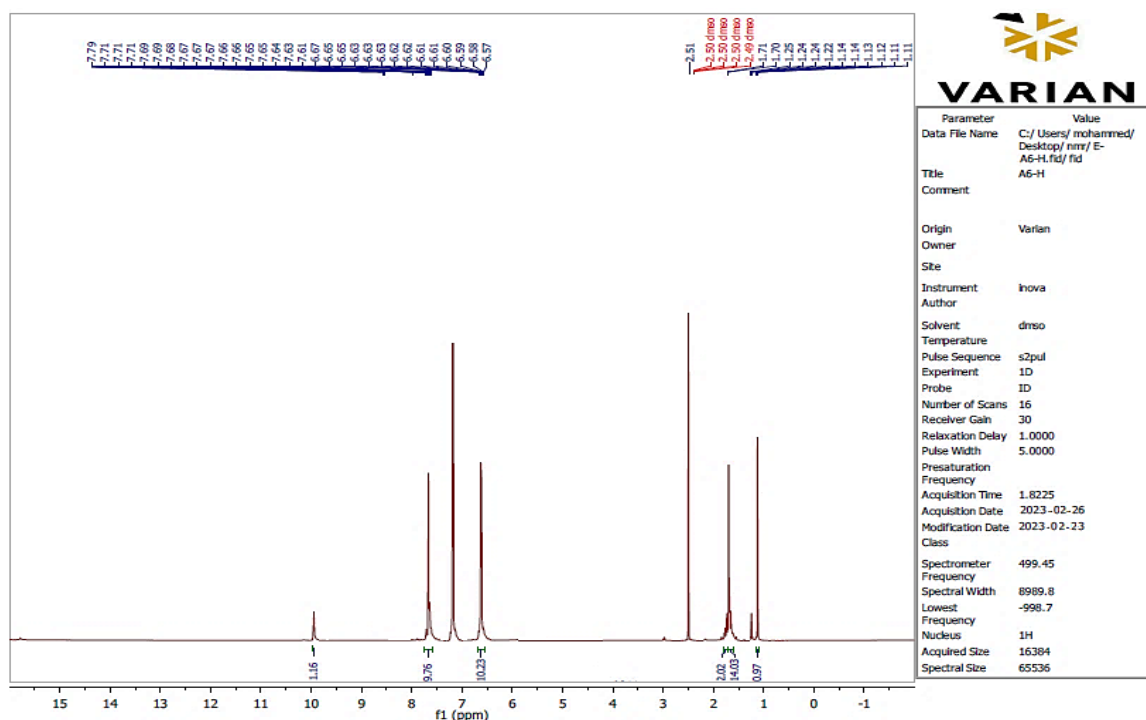


Figure 12. ¹H.NMR- of [5]

C.NMR- Indication of Cyclic and Bicyclic Compounds: By appearance peak about at δ {(170.0 – 175.0)} in all compounds {1 -5} respectively for carbon atom in carbonyl groups of ketone, while other peaks appeared at about {(160.0), (162.11), (161.62)} and like this in cyclic and bicyclic compounds {4, 5} respectively for carbon atom of carbonyl in amide as a result of formation cyclic and bicyclic compounds, Figures (11-15), all these peaks explained according to reference [15] Figures [11-19].

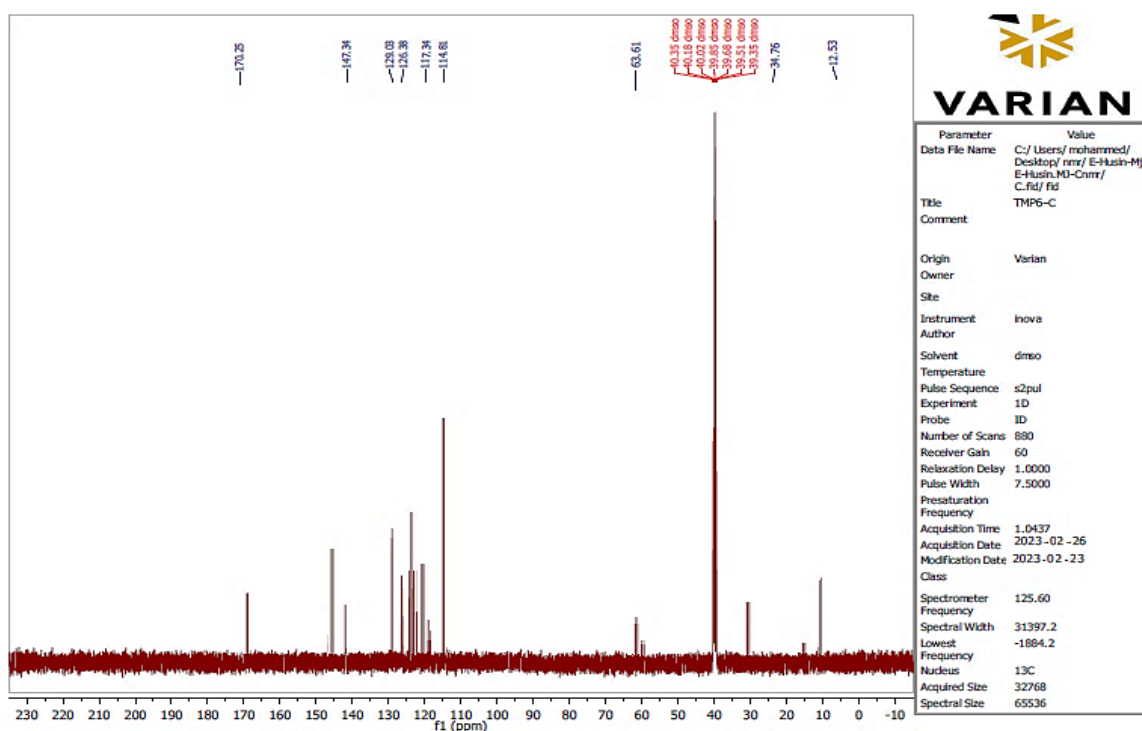


Figure 13. ¹³C.NMR of [1]

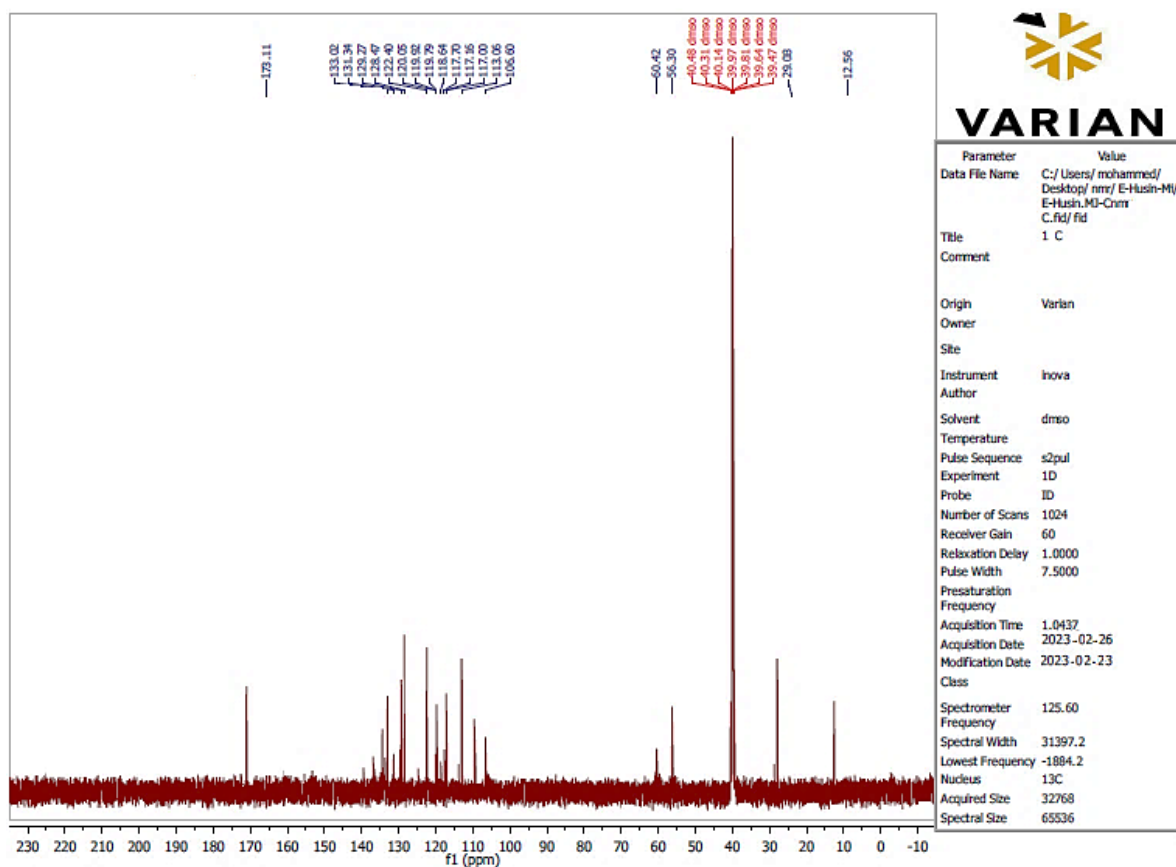


Figure 14. C.NMR of [2].

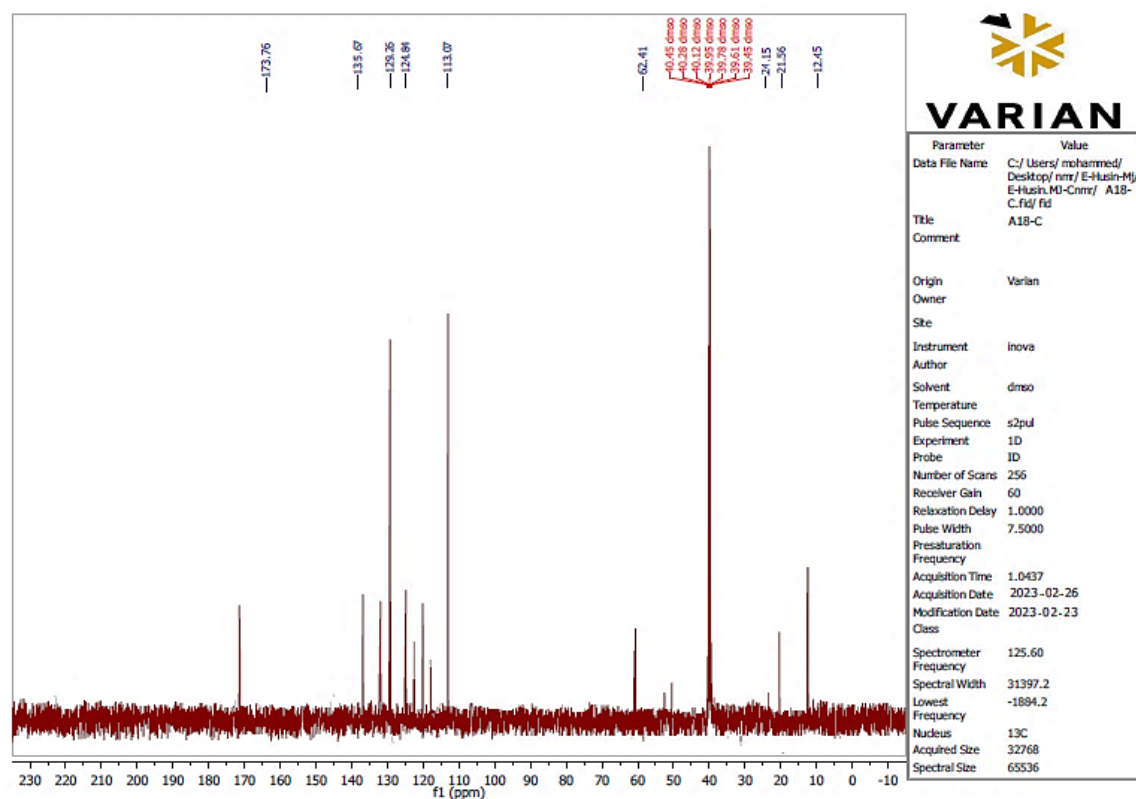


Figure 15. C.NMR of [3].

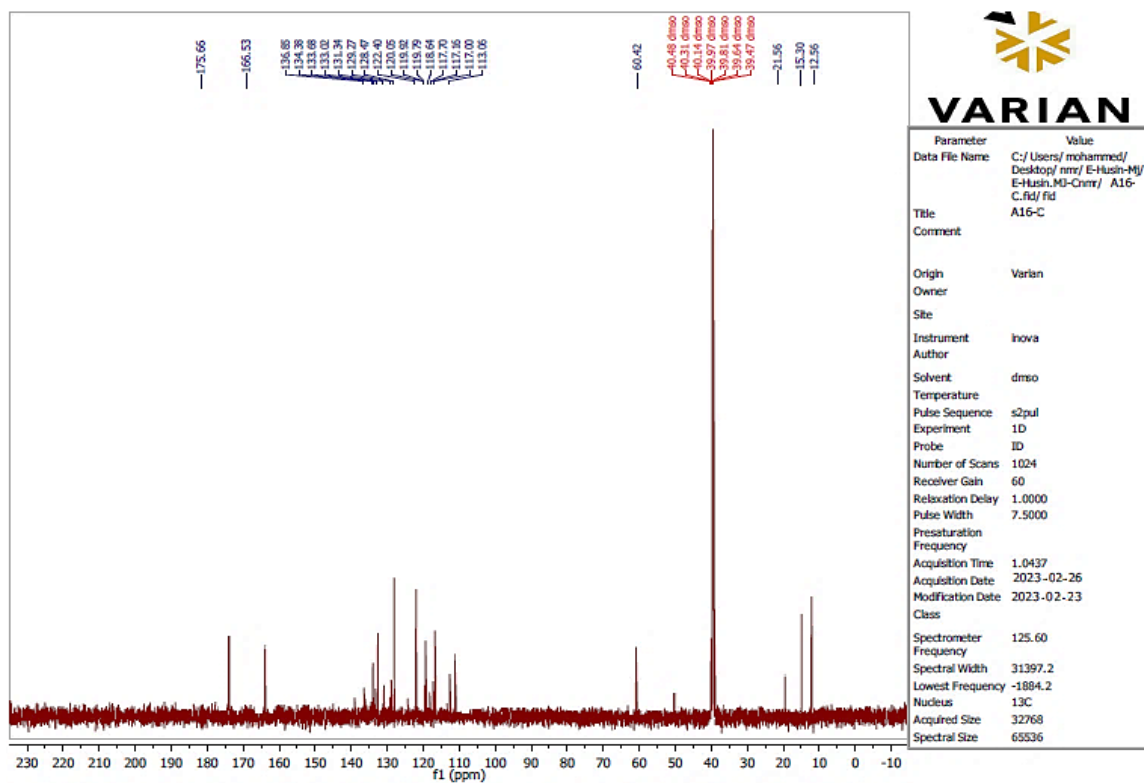


Figure 16. C.NMR of [4].

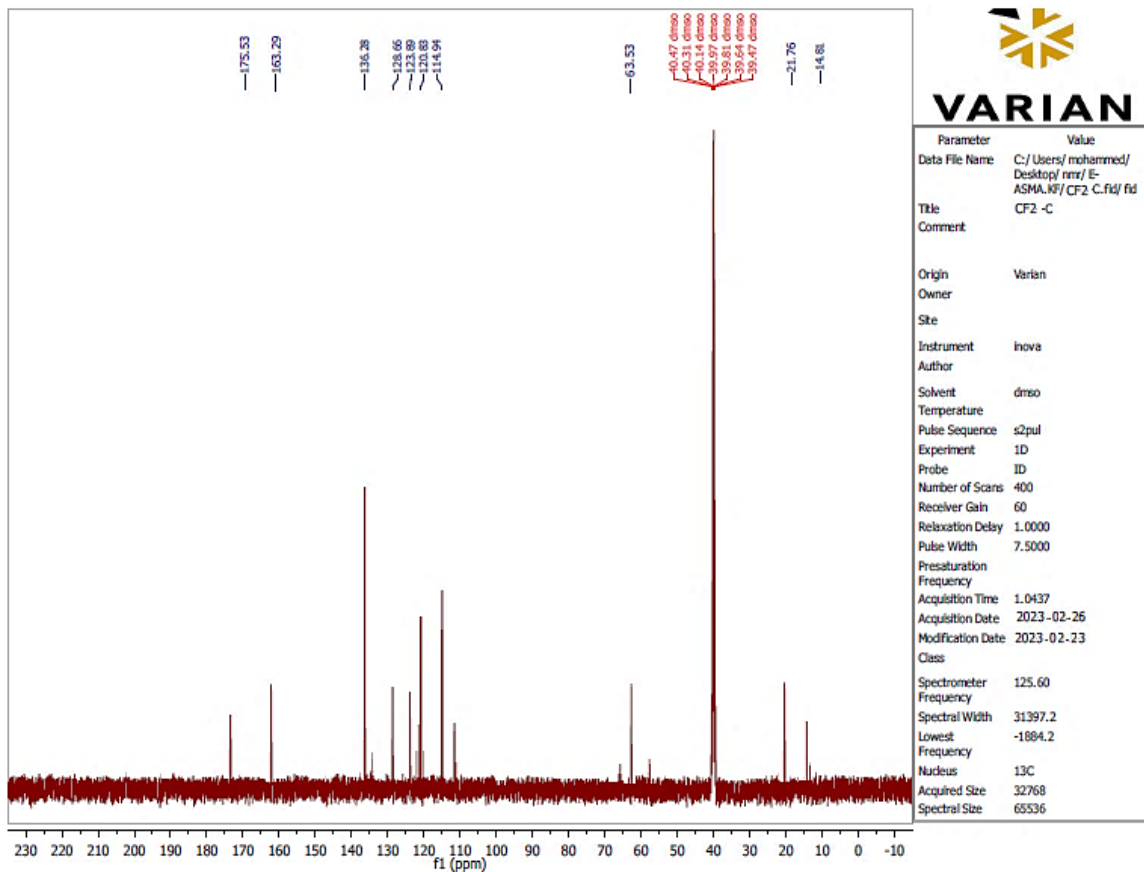


Figure 17. C.NMR of [5]

Table 1. Cytotoxic Commotion of Bicyclic Composite [5] continuously Breast Malignancy Cells (MCF-7) and Well Cells (MCF-10A) at the equivalent meditation exhausting 24 hrs., MTT trial 37°C.

Proportion (%) in place of every selected cells				Con. ($\mu\text{g.mL}^{-1}$)
<i>MCF-10A, IC₅₀ = 172.67</i>		<i>MCF-7, IC₅₀ = 32.74</i>		
<i>Common cells (MCF-10A)</i>		<i>Malignant cells (MCF-7)</i>		<i>Bicyclic Compound [5]</i>
<i>Cell -Inhibition</i>	<i>Cell -Viability</i>	<i>Cell -Inhibition</i>	<i>Cell -Viability</i>	
7.18	92.82	7.65	92.35	15.62
7.06	92.94	9.62	90.38	31.25
7.03	92.97	15.51	84.49	62.5
6.45	93.55	37.62	62.38	250
6.12	93.88	40.22	59.78	500
6.64	93.36	0.00	100	Control

Brief Interpretation OF Table 1

- The bicyclic compound [5] maintains low toxicity toward normal cells (MCF-10A) at all tested concentrations, with cell viability remaining above 92%.
- In contrast, it exhibits dose-dependent inhibition of malignant cells (MCF-7), with increasing inhibition from 7.65% to 40.22% as concentration increases from 15.62 to 500 $\mu\text{g/mL}$.
- The compound demonstrates selective cytotoxicity toward cancer cells, suggesting potential anticancer activity.



Figure 18. 2: Anti-malignancy commotion of Bicyclic {5} on (MCF-7) at 500 $\mu\text{g/ml}$.

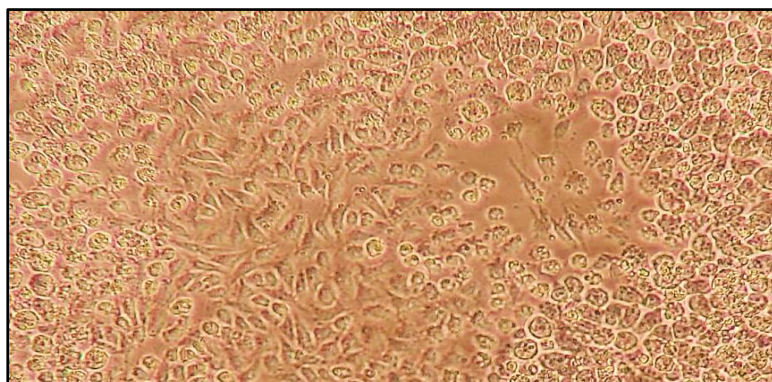


Figure 19. Anti-malignancy commotion of Bicyclic {5} on (MCF-A 10) at 500 $\mu\text{g/ml}$

CONCLUSIONS

Based on the results obtained from the current study, a comprehensive analysis using multiple spectral techniques provided strong and consistent evidence for the successful formation of both

monocyclic and bicyclic heterocyclic compounds. These findings were supported by the emergence of characteristic absorption bands and chemical shifts associated with newly formed functional groups, signifying structural transformations. The Fourier-transform infrared (FT-IR) spectroscopy analysis played a pivotal role in confirming the development of key functional groups during the cyclization process. The appearance of a sharp absorption band around 1650–1700 cm^{-1} was indicative of amide (C=O-NH) bond formation, a crucial marker of successful ring closure in several of the synthesized intermediates. Furthermore, bands observed in the region of 1450–1600 cm^{-1} were assigned to the C=N stretching vibration, specifically associated with the endocyclic nitrogen of the newly formed triazole ring. These bands serve as compelling evidence for the triazole ring formation through the insertion of a nitrogen atom into the oxadiazole framework. The presence of ether-like bands around 1100–1250 cm^{-1} , attributed to the C-O-C stretching of the oxadiazole ring, was another spectral marker confirming the formation of cyclic systems.

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