

Antioxidant Activity Of Some Triazoles Synthesized By Click Chemistry

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Abstract: *In this research, eight new compounds were created from the interaction of a number of aromatic and aliphatic compounds with propargyl bromide to prepare the alkynes after that; alkynes is reacted with the organic azide to form eight new compounds of 1,2,3-triazole by click reaction Using copper as a catalyst After that an antioxidant was done For prepared triazole , DPPH radical scavenging activity and It was the best result values 76.54+-1.9 for compound 9 Compared to the standard model ascorbic acid values 86.03+-4.02 at 200 mg/ml concentration .*

Key words: *1, 2, 3-triazole, Click chemistry, Antioxidant.*

1. INTRODUCTION

Triazoles are cyclic aromatic compounds that contain three nitrogen atoms; there are two types of Triazoles 1, 2, 3-triazoles or 1, 2, 4-triazoles {1} 1,2,3-Triazoles is one of the most important cyclic aromatic compounds Because of its wide range of biological activity, such as antibacterial and antifungal agents {2} anti- HIV , and anti-viral {3} Copper-catalyzed azide-alkyne cycloaddition reaction, It is used in organic synthesis and in medical chemistry, surface chemistry and polymer in 2001 by Sharpless, He invented a new reaction is called click chemistry Where the terminal alkynes interacts with the organic azide Where it produces 1,4-disubstituted 1,2,3-triazoles,{4,5}click chemistry reaction is the copper(I)-catalyzed [3+2] cycloaddition is regioselective 1,4-disubstitued-1,2,3-triazole It consists by adding copper(II) sulphate pentahydrate and sodium ascorbate {6,7}1,2,3-triazole This group includes the formation of a number of important drugs such as β -lactam antibiotic tazobactam and cephalosporin cefatrizine {8}There are many important applications of 1,4-disubstituted 1H-1,2,3-triazoles , for example recyclable catalysts, Cu nanoparticles, complex catalytic systems , solid phase supports and microwave heating {9,10,11,12} The CuAAC triazole have green solvents or no solvent,The reaction is also characterized by safety and low energy with presence catalyst{13,14}

2. MATERIALS AND METHODS

All solvents and chemicals are pure and reliable sources, Diagnosed by a device Bruker FTIR spectrophotometer and HNMR, The type of device and solvent used Varian 500 spectrometer, DMSO-d₆, the melting point and thin-layer chromatography (TLC) technique was also used to confirm the prepared compounds.

Synthesis of organic azide derivatives

Sodium azide (5gm) was added to the stirred solution of benzyl bromide (5 mL) in DMSO (150 mL) and distilled water (50 ml) the suspension was stirred at room temperature for 24h, and then the reaction mixture was diluted with distilled water (200 mL), extracted with diethyl ether (3×100 mL). The combined organic layer was washed with water (50 mL), dried with MgSO₄ and evaporated to give a colorless liquid 90%) {15}

Synthesis of terminal alkynes derivatives

(20 mmol) from organic compounds was dissolved in DMF (60 mL) in a dry beaker and treated with K₂CO₃ (4 g). The beaker was cooled in an ice salt bath and stirred for 20 min then add propargyl bromide (2 mL). The mixture was then allowed to stir for 24 h, at room temperature. Then add H₂O (120 mL) and extracted with di ethyl ether (3 × 70 mL). The organic layers were washed with 10% aqueous HCl , dried over MgSO₄ and filtered. The solvent was evaporated to yield yellow oil.

Synthesis of Triazoles derivatives

Sodium ascorbate (0.0954 g) and CuSO₄.5H₂O (0.0583 g) in DMSO (5 mL) was added to a solution of terminal alkyne (5.3 mmol) in the mixture stirred for 10 min. then organic azide was added and the mixture heated at 60°C with stirring for 48 h. The mixture was diluted with H₂O (80 mL), extracted with EtOAc (3 × 60 mL), the organic layers washed with water (2 × 40 mL), dried with MgSO₄ and evaporated {16}

Antioxidant test

Antioxidant action was used for triazoles products (9, 10, 11, 12, 13, 14, 15, and 16) using DPPH radical scavenging assay, by Rajesh and Natvar, About 150 µl of methanol was added to 20 µl of prepared samples and vitamin C, after which the samples were diluted ten times, Then the reagent was added to the solutions From 50 µl of DPPH radical , Then, place the samples for one hour in a dark place at 37 ° C ,then Radical scavenging activity against the stable DPPH Measurement is done by a spectrophotometer , The color change appears from dark purple to light yellow with a reading of 517 nm, The inhibition ratio of radical. {17}.

$$\% \text{ inhibition} = \frac{\text{Absorbance of -ve control} - \text{Absorbance of sample}}{\text{Absorbance of -ve control}} \times 100$$

3. RESULTS AND DISCUSSION

In this research, a number of alkynes (1,2,3,4,5,6,7,8) were prepared by the interaction of a number of aromatic and aliphatic compounds with propargyl bromide, and then obtaining triazoles (9,10,11,12,13,14,15,16) from the interaction of alkynes with organic azide by Click chemistry, The prepared compounds were examined and diagnosed by the IR and NMR spectrum and the results were as follows , IR spectrum of the terminal alkynes appears at 2250 cm⁻¹ for Triple bond and 3300 cm⁻¹ for CH-Strech of alkyne and HNMR spectrum of the terminal alkynes appears at 3.37 δ (ppm) for compound 1 , IR spectrum of the triazoles, The disappearance of the alkynes and azide absorption band from the spectrum is an important indication of the formation of triazoles , HNMR spectrum of the triazoles appears at 7.63 δ (ppm) for CH of tiazole ring for compound 9. After reading the results of the antioxidant test, it was found that compound 9 is the best antioxidant and the closest reading of vitamin C. Israa F. Ascar *etal* attended ginger extract by ethanol and the extract had a clear effect on free radicals and has anti-tumor and cancer properties. Ginger can be used as additives in the food and drug industries [18], Ahmet Cetin *etal* a number of triazole was

synthesized and the antioxidant examined by DPPH. The compounds showed strong activity as an antioxidant better than expected. {19}, Hany A. M. El-Sherief *etal* a number of triazoles were also prepared and the antioxidant tested. The results were medium, but compound No. 9 was better than the remaining compounds. {20}

Compound (1) (1, 2-bis (prop-2-yn-1-yloxy) benzene)

Brown liquid compound in 80 % yield, Chemical formula $C_{12}H_{10}O_2$, IR ν_{max} cm^{-1} 2250 (CH- Triple bond), 3300 (CH -Strech). 1H -NMR δ (ppm): 3.5 (2H, for alkyne), 4.6 (4H, O-CH₂), 7.0 (4H, for benzene ring).

Compound (2) (1-methyl-3, 5-bis (prop-2-yn-1-yloxy) benzene)

Yellow liquid compound in 85 % yield, Chemical formula $C_{13}H_{12}O_2$, IR ν_{max} cm^{-1} 2200 (CH- Triple bond), 3310 (CH -Strech). 1H -NMR δ (ppm): 3.5 (2H, for alkyne), 4.7 (4H, O-CH₂), 6.2, 6.4 (3H, for benzene ring), 2.4 (for CH₃).

Compound (3) (1-isopropyl-4-methyl-2-(prop-2-yn-1-yloxy) cyclohexane)

Yellow liquid compound in 88 % yield, Chemical formula $C_{13}H_{22}O$, IR ν_{max} cm^{-1} 2230 (CH- Triple bond), 3300 (CH -Strech). 1H -NMR δ (ppm): 3.3 (1H, for alkyne), 4.1 (2H, O-CH₂), 1.0 (9H, for CH₃).

Compound (4) (3-methoxy-4-(prop-2-yn-1-yloxy)benzaldehyde)

White solid compound in 77 % yield, Chemical formula $C_{11}H_{10}O_3$, IR ν_{max} cm^{-1} 2100 (CH- Triple bond), 3300 (CH -Strech). 1H -NMR δ (ppm): 3.5 (1H, for alkyne), 4.1(2H, O-CH₂), 7.1, 7.3, 7.5 (3H, for benzene ring), 9.6 (for CHO).

Compound (5) (1, 3-bis (prop-2-yn-1-yloxy) benzene)

Yellow liquid compound in 85 % yield, Chemical formula $C_{12}H_{10}O_2$, IR ν_{max} cm^{-1} 2220 (CH- Triple bond), 3300 (CH -Strech). 1H -NMR δ (ppm): 3.5 (2H, for alkyne), 4.7 (4H, O-CH₂), 6.3, 6.6, 7.5 (4H, for benzene ring).

Compound (6) (1, 4-bis (prop-2-yn-1-yloxy) benzene)

White solid compound in 90 % yield, Chemical formula $C_{12}H_{10}O_2$, IR ν_{max} cm^{-1} 2150 (CH- Triple bond), 3320 (CH -Strech). 1H -NMR δ (ppm): 3.4 (2H, for alkyne), 4.6 (4H, O-CH₂), 6.99 (4H, for benzene ring).

Compound (7) (4-methoxy-N-(prop-2-yn-1-yl) aniline)

Black solid compound in 70 % yield, Chemical formula $C_{10}H_{11}NO$, IR ν_{max} cm^{-1} 2200 (CH- Triple bond), 3300 (CH -Strech). 1H -NMR δ (ppm): 3.1 (1H, for alkyne), 3.8 (2H, N-CH₂), 6.77, 7.30 (4H, for benzene ring).

Compound (8) (1-isopropyl-4-methyl-2-(prop-2-yn-1-yloxy) benzene)

Yellow liquid compound in 90 % yield, Chemical formula $C_{13}H_{16}O$, IR ν_{max} cm^{-1} 2250 (CH- Triple bond), 3300 (CH -Strech). 1H -NMR δ (ppm): 3.1 (1H, for alkyne), 4.6 (2H, O-CH₂), 6.8, 6.9, 7.4 (3H, for benzene ring).

Compound (9) (1-benzyl-4-(((2-isopropyl-5-methylcyclohexyl) oxy) methyl)-1H-1, 2, 3-triazole)

Yellow solid compound in 70 % yield, Chemical formula $C_{20}H_{29}N_3O$, IR ν_{max} cm^{-1} 3140 (CH- triazole), 2999 (CH -CH₃).1550(C=C) 1H -NMR δ (ppm): 7.6 (1H, for triazole), 1.0 (9H, CH₃), 7.2, 7.3 (5H, for benzene ring). ^{13}C -NMR δ (ppm): 128,136 (C, of triazole), 60.1(C, O-CH₂), 20(C, CH₃), 39, 40 (DMSO)

Compound (10) (1-benzyl-4-(((2-isopropyl-5-methylphenoxy)methyl)-1H-1,2,3-triazole)

Yellow liquid compound in 90% yield, Chemical formula $C_{20}H_{23}N_3O$, IR ν_{max} cm^{-1} 3100 (CH- triazole), 2900 (CH -CH₃).1600(C=C) 1H -NMR δ (ppm): 7.6 (1H, for triazole), 1.1,2.1 (9H, CH₃), 6.5, 6.9,7.3 (3H, for benzene ring). ^{13}C -NMR δ (ppm): 121,143 (C, Triazole),23 (C, CH₃),54 (CH₂),122,126,128 (benzene ring), 39, 40 (DMSO)

Compound (11) (N-(((1-benzyl-1H-1, 2, 3-triazol-4-yl)methyl)-4-methoxyaniline)

Yellow liquid compound in 90% yield, Chemical formula $C_{17}H_{18}N_4O$, IR ν_{max} cm^{-1} 3150 (CH- triazole), 2950 (CH -CH₃).1570(C=C) 1H -NMR δ (ppm): 7.66 (1H, for triazole), 6.3

(1H, NH), 6.70, 6.77, 7.2, 7.3 (8H, for benzene ring). 13C-NMR δ (ppm): 121, 129 (C, Triazole), 55 (C, CH₃), 40 (CH₂), 114, 128, 136 (benzene ring), 39, 40 (DMSO)

Compound (12) (1, 4-bis ((1-benzyl-1H-1, 2, 3-triazol-4-yl)methoxy)benzene)

Brown liquid compound in 90% yield, Chemical formula C₂₆H₂₄N₆O₂, IR ν_{\max} cm⁻¹ 3100 (CH- triazole), **2980** (CH –CH₃).1600(C=C) ¹H-NMR δ (ppm): 7.63 (2H, for triazole), 5.3 (4H, O-CH₂), 7.1, 7.2, 7.3 (14 H, for benzene ring). 13C-NMR δ (ppm): 124, 136 (C, Triazole), 56 (CH₂), 115, 128, 129 (benzene ring), 39, 40 (DMSO)

Compound (13) (4-((1-benzyl-1H-1, 2, 3-triazol-4-yl)methoxy)-3-methoxybenzaldehyde)

Black solid compound in 70% yield, Chemical formula C₁₈H₁₇N₃O₃, IR ν_{\max} cm⁻¹ 3130 (CH- triazole), **2990** (CH –CH₃).1610(C=C) ¹H-NMR δ (ppm): 7.60 (1H, for triazole), 5.2 (4H, O-CH₂), 7.2, 7.3, 7.5 (8 H, for benzene ring) 9.6(1H, CHO). 13C-NMR δ (ppm): 129, 142 (C, Triazole), 55 (CH₂), 113, 125, 130 (benzene ring), 191 (C, carbonyl compound), 39, 40 (DMSO)

Compound (14) (4,4'-(((5-methyl-1,3-phenylene)bis(oxy))bis(methylene))bis(1-benzyl-1H-1,2,3-triazole))

Black Liquid compound in 70% yield, Chemical formula C₂₇H₂₆N₆O₂, IR ν_{\max} cm⁻¹ 3100 (CH- triazole), **2999** (CH –CH₃).1600(C=C) ¹H-NMR δ (ppm): 7.60 (2H, for triazole), 5.2 (4H, O-CH₂), 7.2, 7.3, 6.4 (13 H, for benzene ring). 13C-NMR δ (ppm): 124, 143 (C, Triazole), 54 (CH₂), 105, 125, 129 (benzene ring), 39, 40 (DMSO).

Compound (15) (1, 3-bis ((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)benzene)

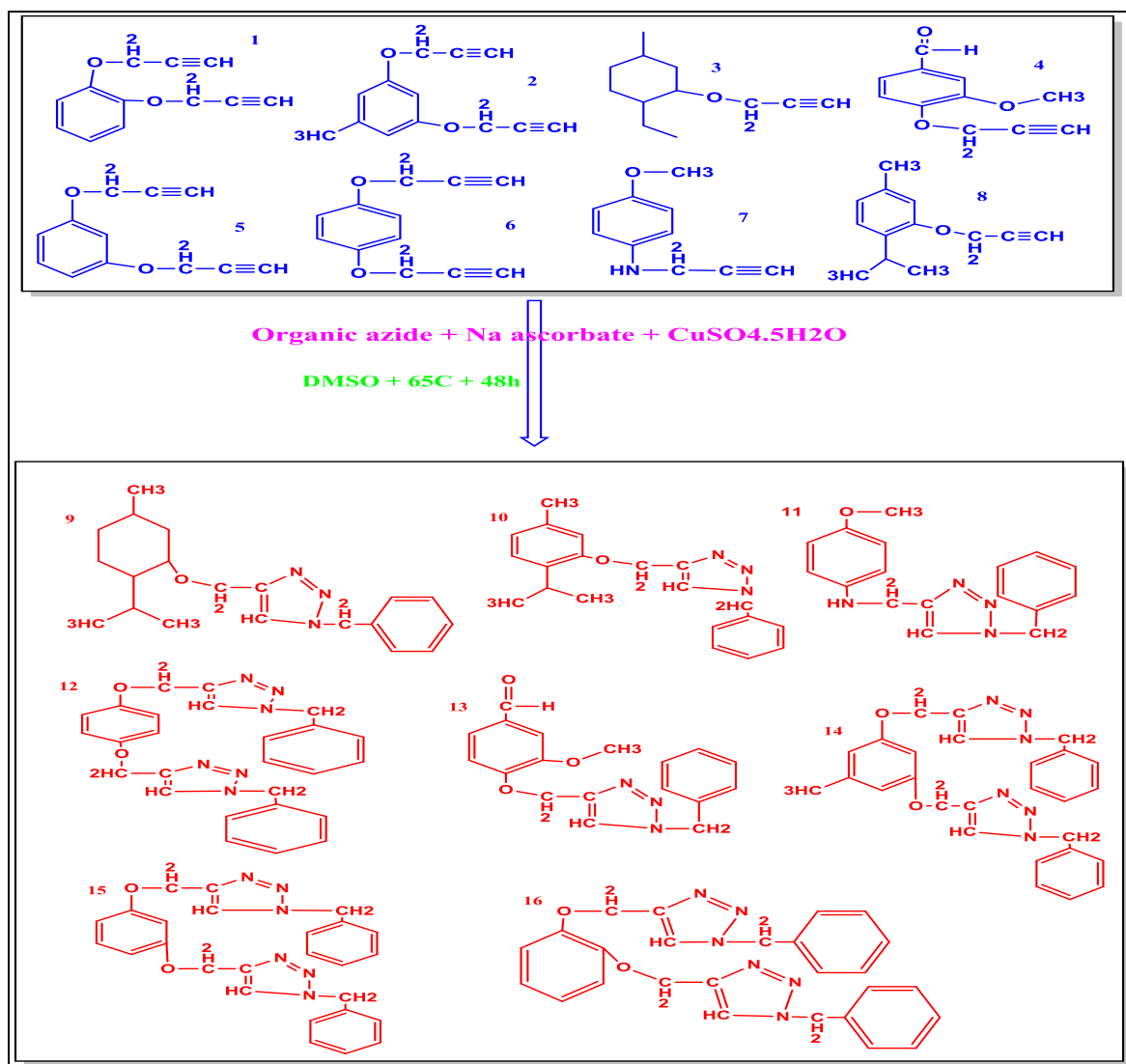
Yellow Liquid compound in 75% yield, Chemical formula C₂₆H₂₄N₆O₂, IR ν_{\max} cm⁻¹ 3150 (CH- triazole), **2950** (CH –CH₃).1620(C=C) ¹H-NMR δ (ppm): 7.60 (2H, for triazole), 5.2 (4H, O-CH₂), 7.2, 7.3, 6.7 (14 H, for benzene ring). 13C-NMR δ (ppm): 124, 136 (C, Triazole), 54 (CH₂), 106, 125, 128 (benzene ring) 39, 40 (DMSO),

Compound (16) (1, 2-bis ((1-benzyl-1H-1, 2, 3-triazol-4-yl)methoxy)benzene)

Black Liquid compound in 75% yield, Chemical formula C₂₆H₂₄N₆O₂, IR ν_{\max} cm⁻¹ 3100 (CH- triazole), **2940** (CH –CH₃).1600(C=C) ¹H-NMR δ (ppm): 7.60 (2H, for triazole), 5.2 (4H, O-CH₂), 7.2, 7.3, 6.8, 6.9 (14 H, for benzene ring). 13C-NMR δ (ppm): 122, 143 (C, Triazole), 54 (CH₂), 124, 127, 129 (benzene ring), 39, 40 (DMSO).



Scheme 1: The alkyne and triazole synthesis equation



Scheme 2: Click chemistry equation

Sample	Concentration				
	200	100	50	25	12.5
Ascorbic acid	86.03±4.02	74.07±1.0	57.60±2.2	39.00±1.7	22.90±1.8
15	73.57±1.0	63.70±1.2	54.48±1.3	40.43±4.0	17.63±4.1
14	54.59±1.1	43.79±0.9	21.34±4.0	17.40±2.4	20.60±3.7
16	74.92±1.1	62.15±3.3	51.16±1.7	28.70±4.2	14.93±0.5
11	41.05±1.5	27.24±0.7	25.42±1.6	16.90±3.0	15.78±0.5
10	50.50±5.2	40.28±2.0	35.19±4.6	17.67±3.0	17.40±2.4
12	65.20±2.3	52.43±2.9	44.10±0.8	30.56±2.7	17.63±2.0
9	76.54±1.9	62.08±0.5	52.74±1.8	39.62±2.3	27.70±0.7
13	44.02±1.8	34.92±1.1	20.10±2.2	17.21±1.7	14.54±1.5

Fig 1. Table of scavenging activity assay by DPPH of all compounds

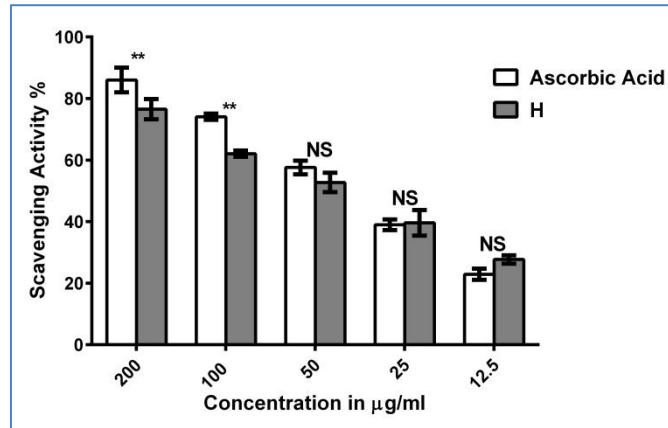


Fig 2 scavenging activity assay by DPPH of compound 9

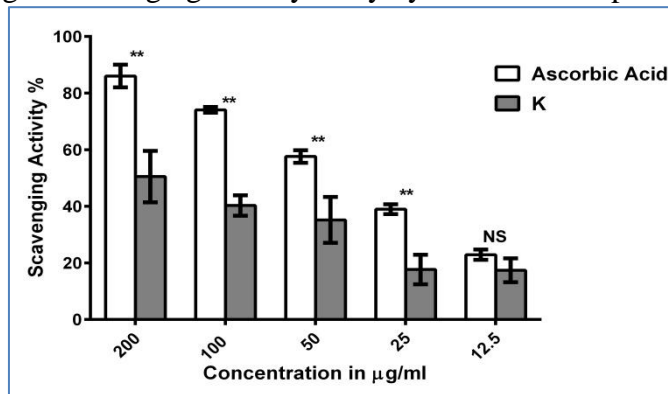


Fig 3 scavenging activity assay by DPPH of compound 10

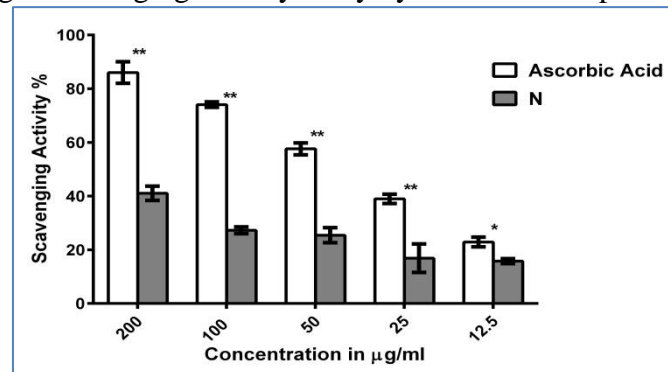


Fig 4 scavenging activity assay by DPPH of compound 11

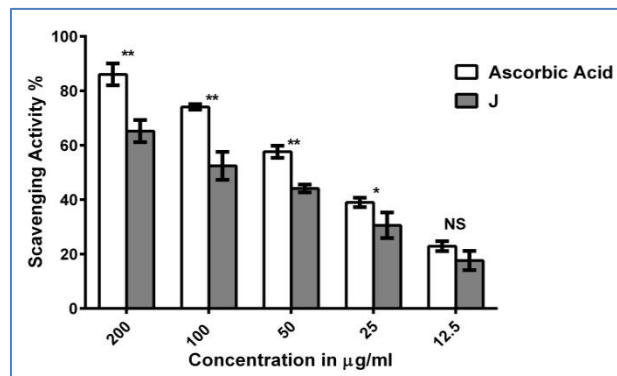


Fig 5 scavenging activity assay by DPPH of compound 12

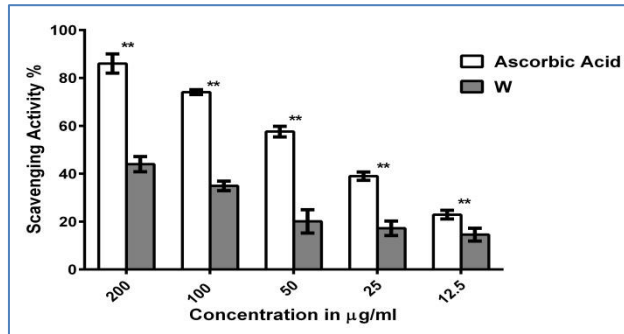


Fig 6 scavenging activity assay by DPPH of compound 13

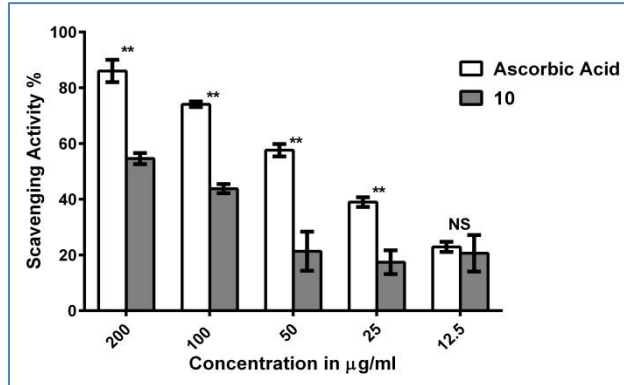


Fig 7 scavenging activity assay by DPPH of compound 14

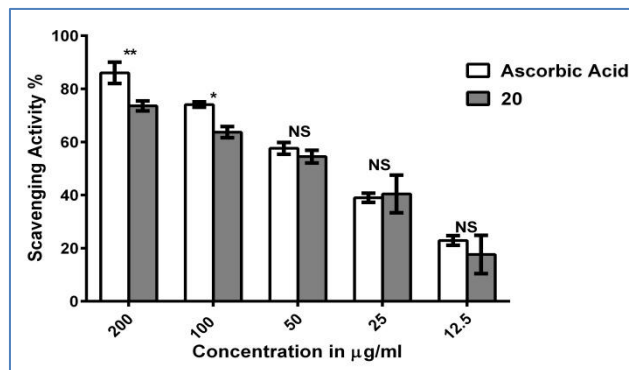


Fig 8 scavenging activity assay by DPPH of compound 15

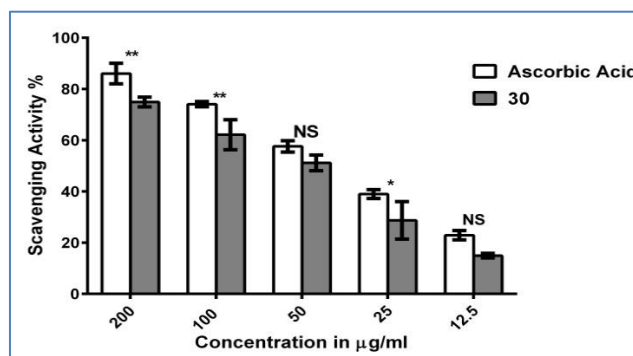


Fig 9 scavenging activity assay by DPPH of compound 16

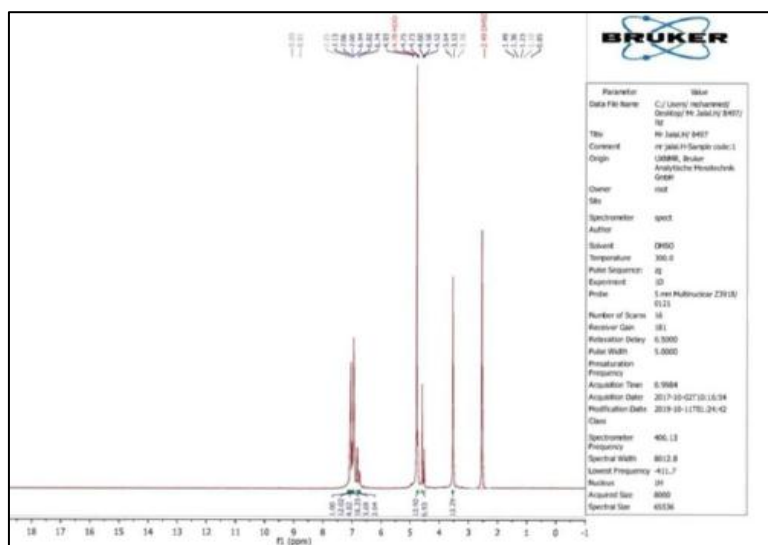


Fig: 10 .HNMR of compound 1

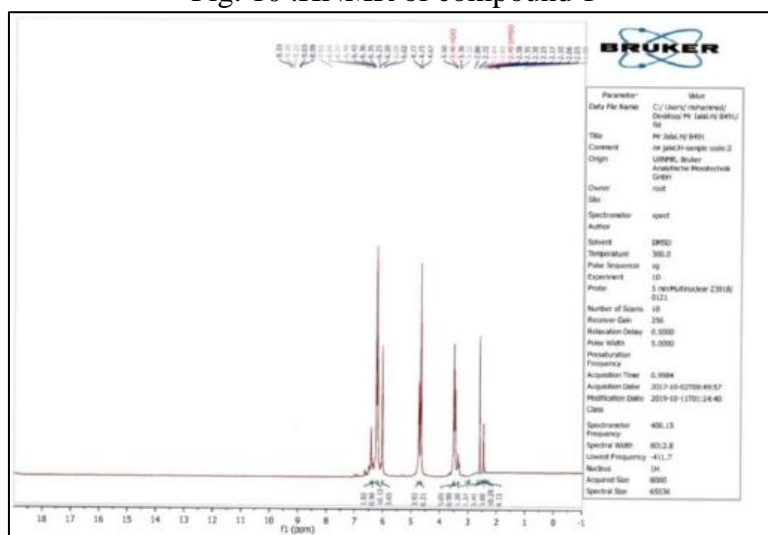


Fig: 11 .HNMR of compound 2

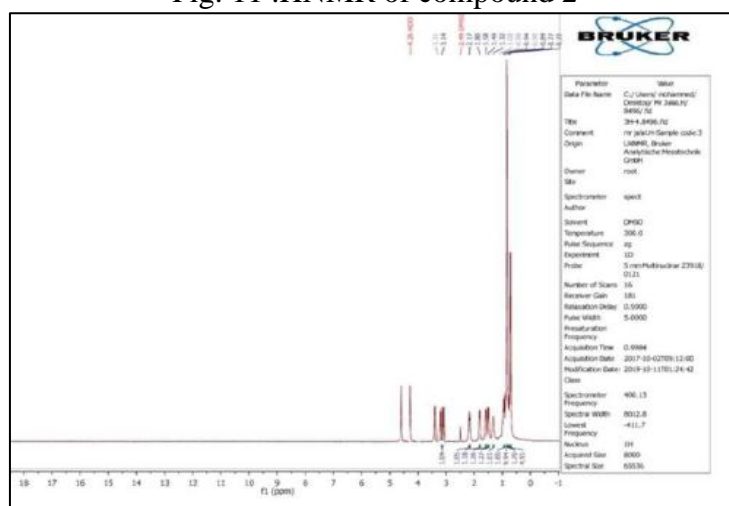


Fig: 12 .HNMR of compound 3

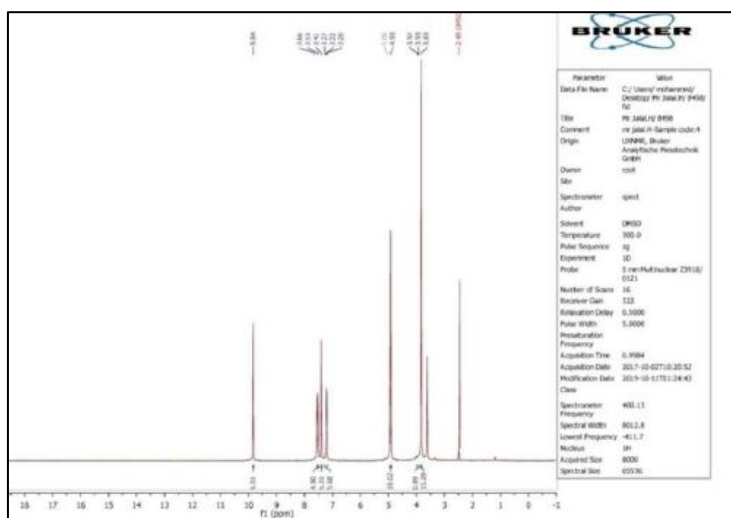


Fig: 13 .HNMR of compound 4

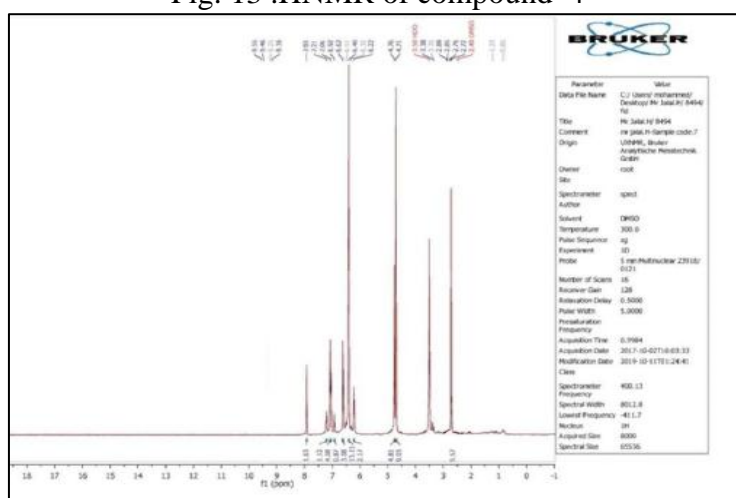


Fig: 14 .HNMR of compound 5

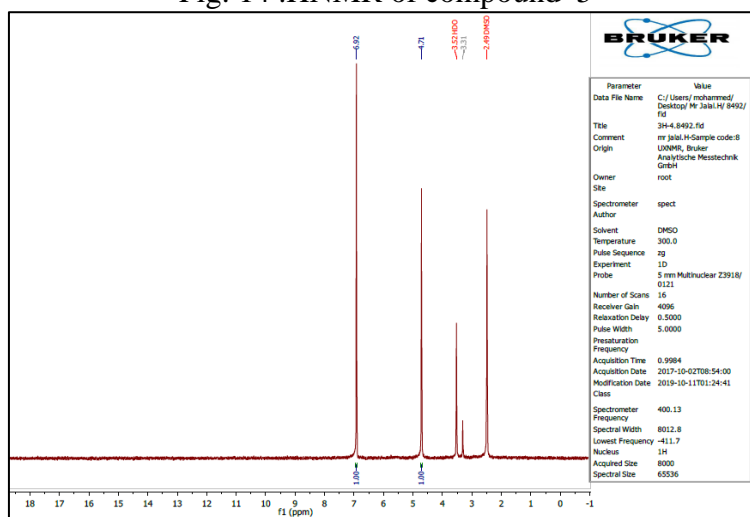


Fig: 15 .HNMR of compound 6

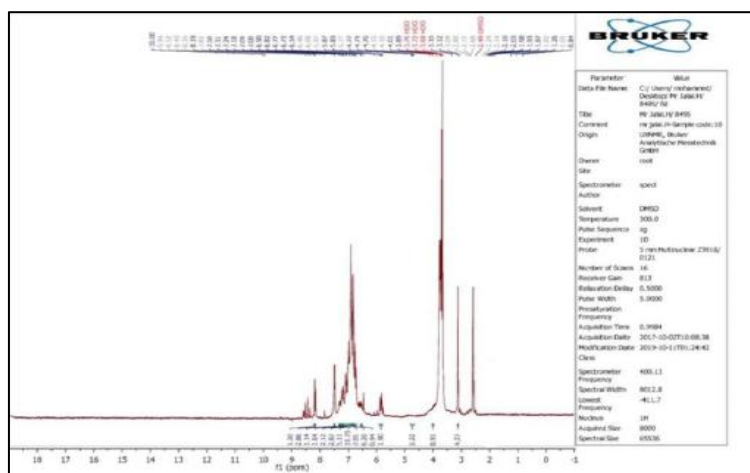


Fig: 16 .HNMR of compound 7

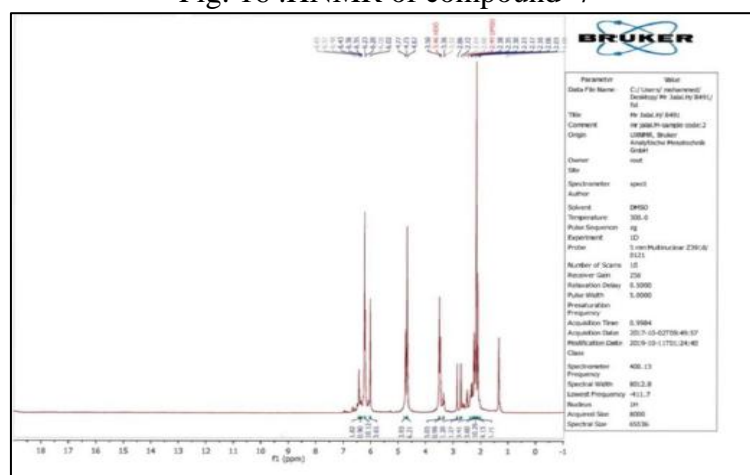


Fig: 17 .HNMR of compound 8

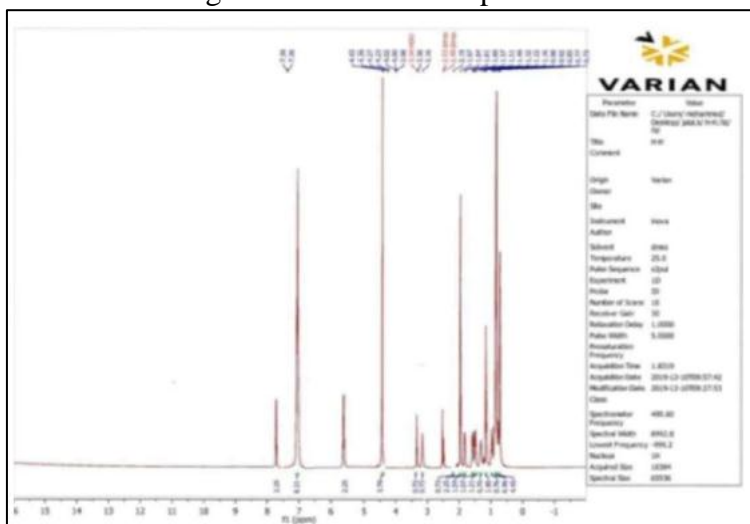


Fig: 18 .HNMR of compound 9

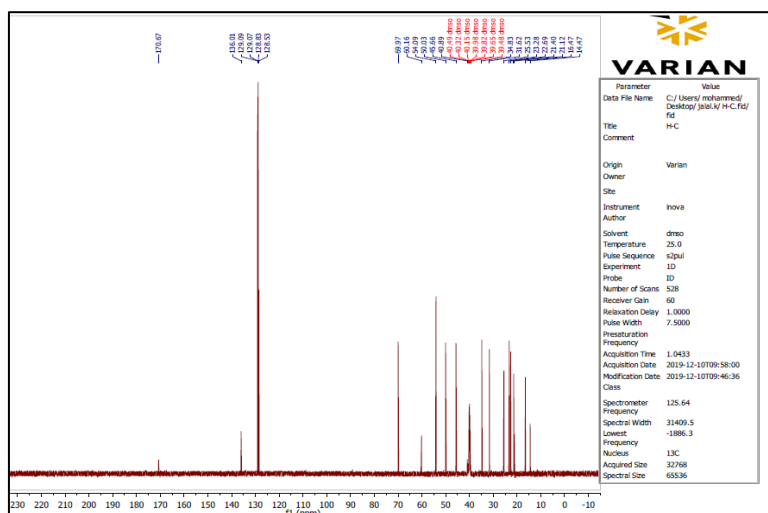


Fig: 19. ^{13}C NMR of compound 9

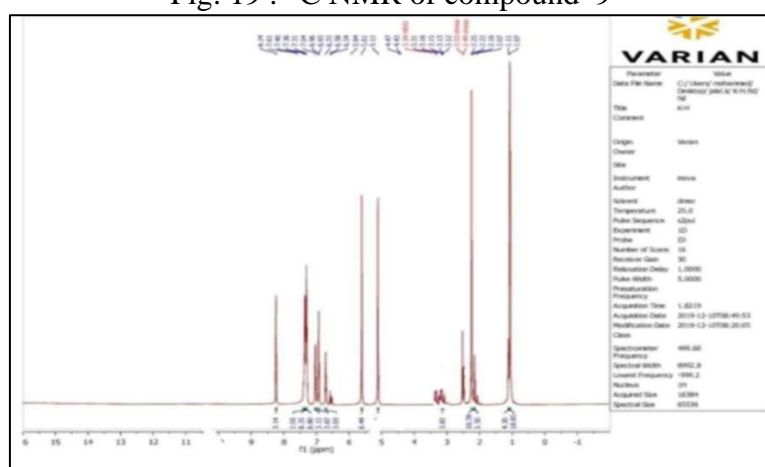


Fig: 20. ^1H NMR of compound 10

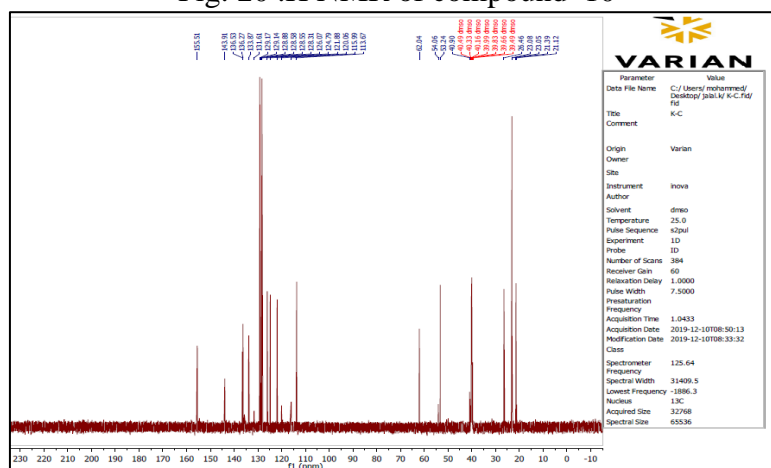


Fig: 21. ^{13}C NMR of compound 10

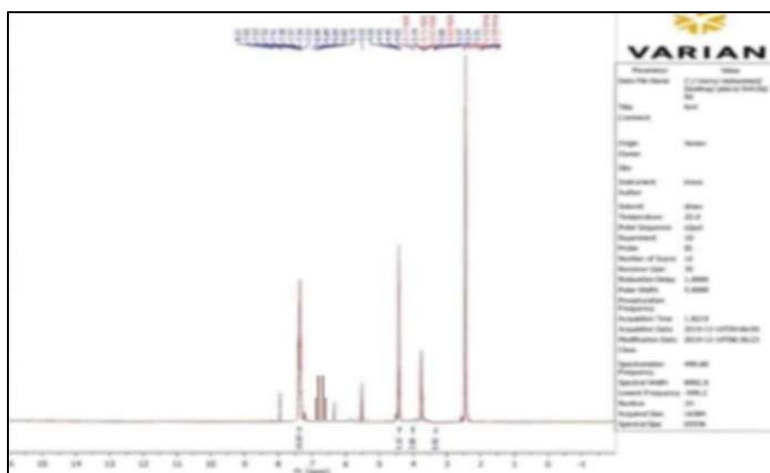


Fig: 22 .H NMR of compound 11

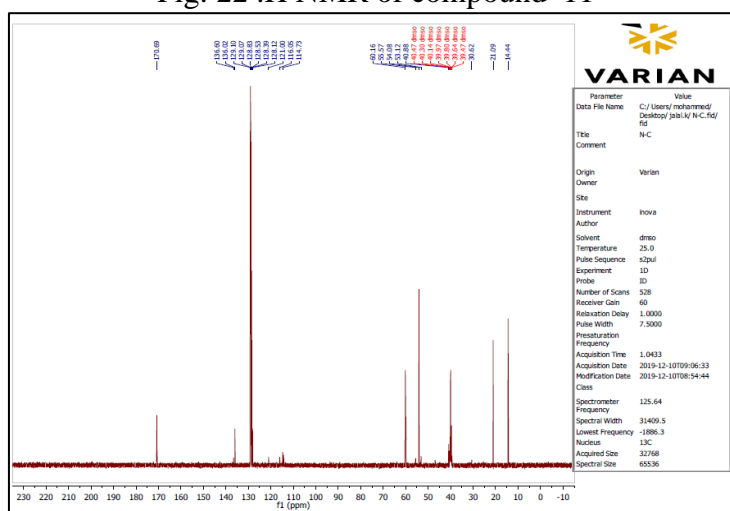


Fig: 23 .¹³C NMR of compound 11

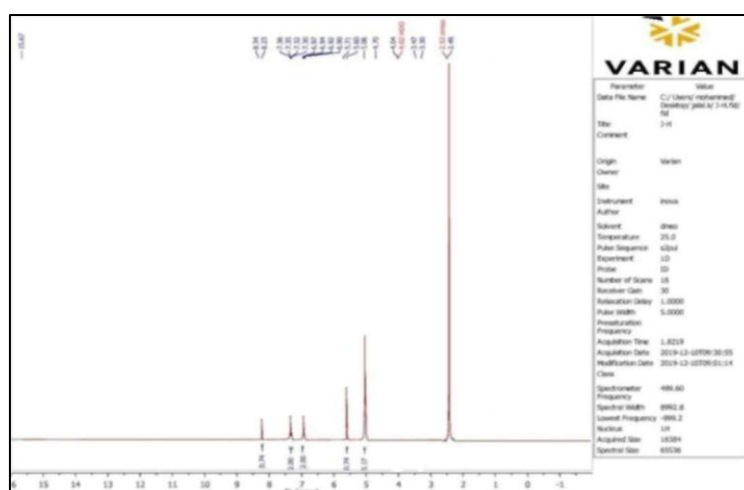


Fig: 24 .H NMR of compound 12

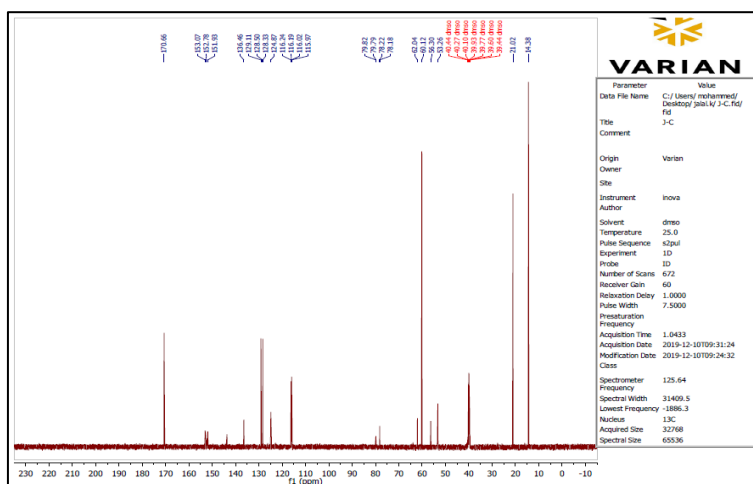


Fig: 25 . ¹³C NMR of compound 12

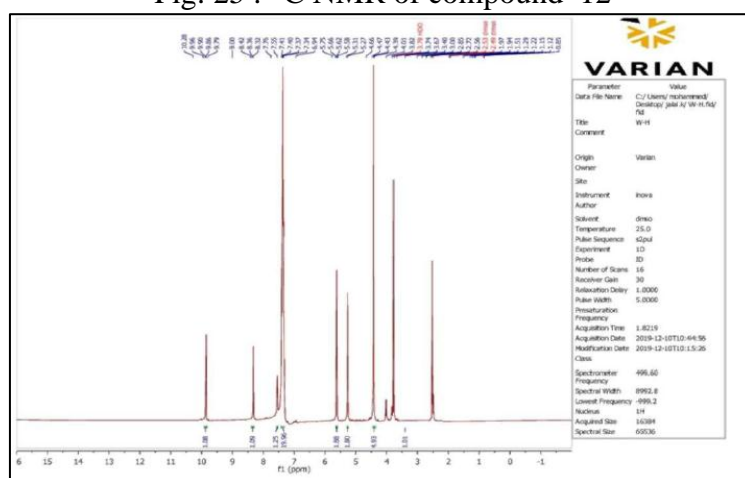


Fig: 26 .H NMR of compound 13

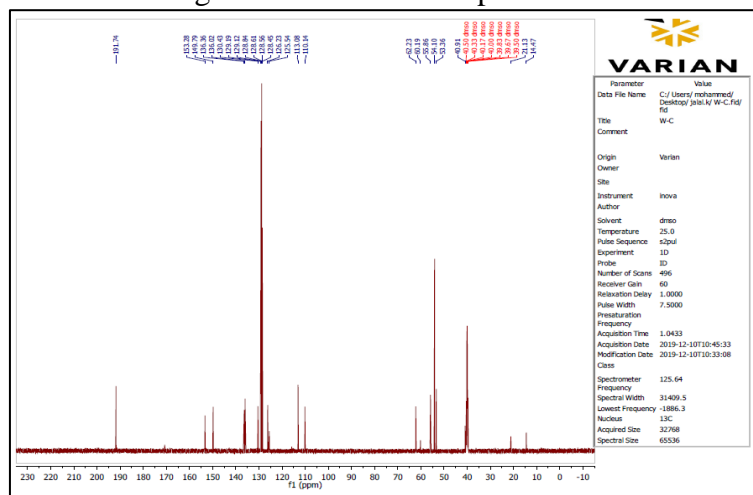


Fig: 27 . ¹³C NMR of compound 13

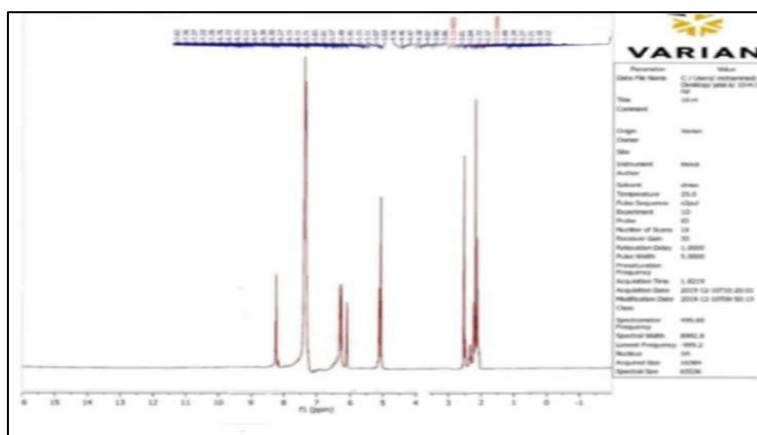


Fig: 28 .¹H NMR of compound 14

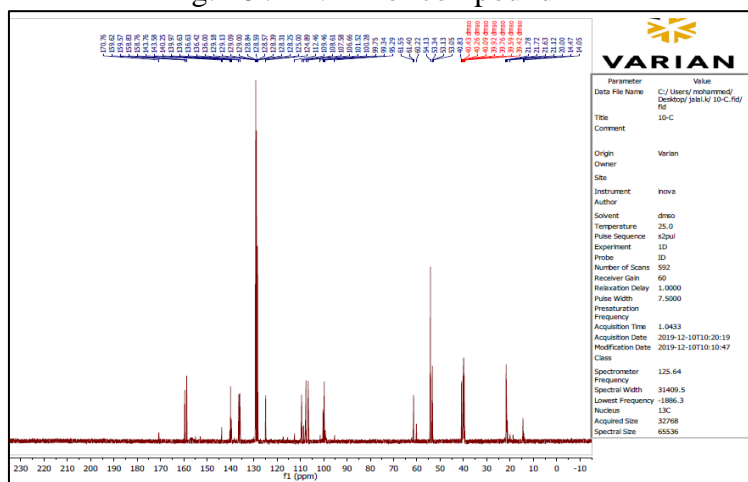


Fig: 29 .¹³C NMR of compound 14

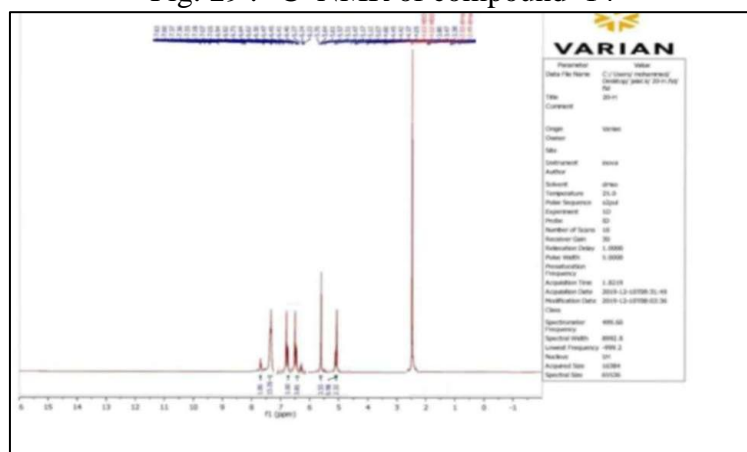


Fig: 30 .¹H NMR of compound 15

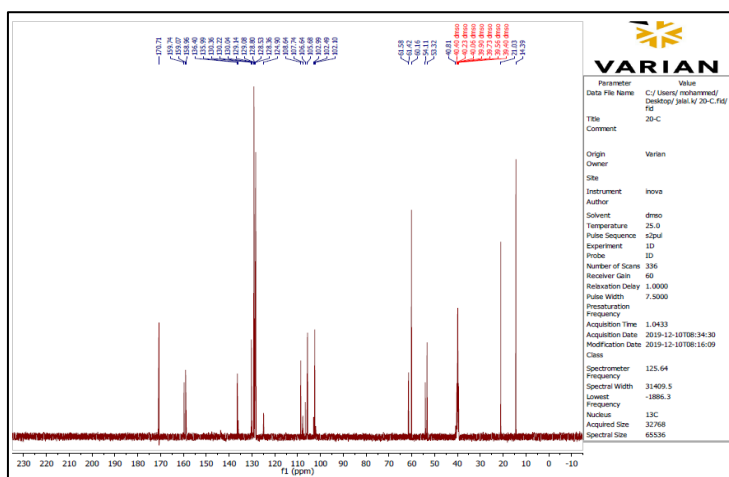


Fig: 31 . ^{13}C NMR of compound 15

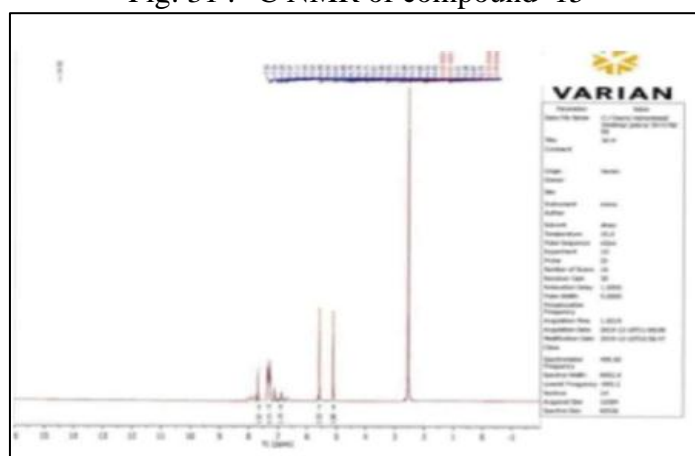


Fig: 32 . ^1H NMR of compound 16

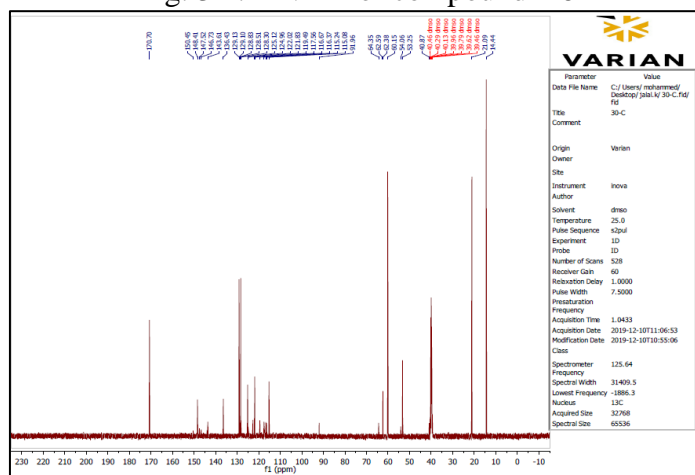


Fig: 33 . ^{13}C NMR of compound 16

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