Article

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Synthesis,Characterization biological activity and molecular docking of triazole derivatives from the medication sulphadoxin

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Abstract

In this study, click chemistry is used to synthesize heterocyclic derivatives from the medication sulphadoxine. To create the (S) derivative, sulphadoxine initially interacted with sodium nitrate, sodium hydrochloric acid, and sodium azide (1).,then *P*-hydroxy benzaldehyde and 3-bromo-1-propyne reacted in the second stage to form the (A) derivative, which then reacted with various aromatic ketones to create many additional chalcons derivatives (A_3-A_5). These chalcons then reacted with the (S) derivative to create the triazole derivatives (E_3-E_5). These structures were found using TLC, FT-IR,^{1}H-NMR,^{13}C-NMR and the study of Molecular docking of some derivatives.

Key words: Sulfonamides, Chalcones, Triazoles, molecular docking

Introduction

Sulfonamides

This functional group, known as a sulfa medicine, serves as the foundation for additional pharmacological groupings. These compounds were the first to be used

to treat and prevent human bacterial illnesses. Sulfonamides are frequently used to treat a variety of infections brought on by specific fungi, protozoa, and gram-positive and gram-negative bacteria. These medications are also used to treat specific types of pneumonia and malaria in HIV/AIDS patients, prevent burns, and treat urinary tract infections. Sulfa medications held a significant position in the medical professionals' and veterinarians' therapeutic toolkits. [1, 2]. A notable class of synthetic antimicrobial drugs, sulfonamides (SN) or sulfanilamides, are used pharmacologically to treat a range of bacterial diseases in both people and animals [3].

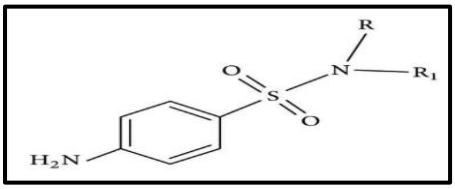


Figure (1) The general structure of sulfonamides.[4]

The presence of a sulfanilamide group4 and a recognizable 6- or 5-membered heterocyclic ring define SN structures, which are organo-sulfur compounds with the -SO2NH2 and/or -SO2NH-group. SNs can have a number of negative side effects, such as digestive problems, in addition to being difficult to biodegrade[5] and respiratory problems. Several SN medications are linked to non-allergic symptoms, such as headaches, candidiasis, nausea, vomiting, dizziness, diarrhea, and folate deficiency5. This study focused on sulfonamides, sulfadimethoxine (SDM), and sulfa guanidine (SGD), which are commonly used in veterinary medicine. The main reason SDM[6] was chosen was because it recently showed the highest phytotoxic potential of any sulfonamide that had ever been investigated.

Heterocyclic substances

The most prevalent heteroatoms are nitrogen, oxygen, and sulfur, while heterocyclic rings with additional heteroatoms are also well-known.. Cyclic organic molecules with at least one heteroatom[7] are known as heterocyclic compounds. Organic chemical compounds with a ring-like structure and one or more heteroatoms are referred to as heterocyclic compounds, or heterocycles. Both cyclic and acyclic heterocycles are possible [8-12]. The compound's activity (or toxicity), interactions with various target inhibitors and target medications, target skeleton responsiveness, and capacity to alter pharmacokinetics and metabolism are all directly impacted by these heteroatoms [13-15].

Chalcones

Chalcones are either edible or medicinal secondary metabolites of plants of the flavonoid family. An α,β-unsaturated carbonyl group bridges two aryl moieties to form chalcones, also called 1,3-diphenyl-2-propen-1-ones[16]. One The structure of these compounds has a –C=O−CH=CH− ketoethylenic moiety.

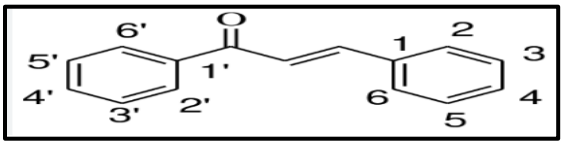


Figure (2) The general structure of Chalcone[17]

Their aromatic rings are arranged in an adelocalized π-electron configuration [17].

Licochalcone A (I), a chalcone derivative that was isolated from the roots of Glycyrrhiza inflata (licorice), is one of the medicinally significant chalcones Both in vitro and in vivo, it possesses antimalarial and antileishmanial qualities. However,, 3-methoxy-4-hydroxyloncocarpin (II), which was isolated from Lonchocarpusutilis roots, suppressed the activity of NADH-ubiquinone oxidoreductase[18] . Without endangering healthy cells, the coumarin chalcones (III) function as selective anticancer medicines that are used to treat and prevent brain tumors, lung, prostate, cervical, and oral squamous cancers [19].

Click chemistry

The fundamental click chemistry procedures, such as cycloaddition, acylation/sulfonylation, strained ring opening, conjugate addition, and aldehyde capture by α-effect nucleophiles, were well-known in the history of organic synthesis. A common omission is the copper-mediated azide–alkyne cycloaddition [20,21]. Cu(I)-catalyzed azide–alkyne cycloaddition (CuAAC) is the name of the click reaction that Huisgen and colleagues demonstrated. K. Barry Sharpless introduced the sophisticated application of this reaction and click chemistry in 2001. In addition to rapid reactions, "click chemistry" also includes reactions that apply the twelve green chemistry principles [22]. Click Chemistry's numerous

features make it an effective tool that may be applied to a range of scientific fields, including as the identification of lead and drug structures [23].

Triazoles

The biological activities of azoles, a noteworthy class of nitrogen-containing heterocycles, have been demonstrated to include antibacterial, antimalarial, antifungal, anti-HIV, anti-inflammatory, and anti-TB properties. Triazoles, namely the 1,2,3-triazole moiety, are the basis for some currently prescribed drugs, including the anti-HIV drug TSAO, the antibiotic Cefatrizine, the anti-bacterial drug Tazobactum, and the anti-cancer drug. Medicinal chemistry has continuously been interested in triazoles, namely 1,2,3-triazole, triazolopyrimidine, benzotriazole, 1,2,4-triazole, and as well as its derivatives [24]. Triazole heterocyclic compounds have received particular attention because of their prospective uses as biomimetic catalysts, supramolecular ligands, agrochemicals, and pharmaceuticals, among other things. [25].

Chemistry

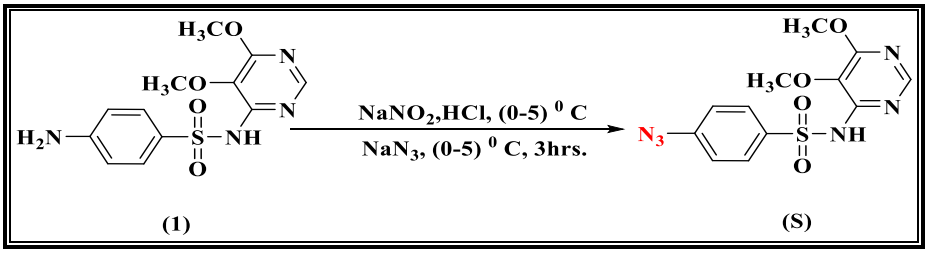
Materials and Methods:

The chemicals utilized in this study were purchased from Fluka and Merck and were of the greatest purity possible. Using an electro-thermal 9300 melting point apparatus (United Kingdom), melting points were determined. Silica gel plates were used for TLC (thin-layer chromatography), and compound spots were found by exposing them to iodine vapor. Until the produced compounds were examined using the infrared spectrum FTIR Shimadzu model (8400) was also measured utilizing the range 600-4000 cm^{-1}. NMR spectra were recorded using (Bruker NMR) spectrophotometer system using((DMSO-$\mathbf{d_6}$ solvent)) , (Iran) .

Synthesis of 4-azido-N-(5,6-dimethoxypyrimidin-4-yl)benzenesulfonamide[26,27] (S)

A salt-ice bath is used to chill the mixture to 0 °C after (1gm, 0.003 mol) of sulphadoxine (1) reacts with 1 mL of distilled water and 1 mL of hydrochloric acid.This involved making an aqueous solution of sodium nitrite (0.23 gm,0.003 mol) and cooling it to zero degrees Celsius. Next, A solution of nitrite was included, drop by drop, as an the sulphadoxine solution where. After several additions, the solution's color turned slightly yellow. The solution was then

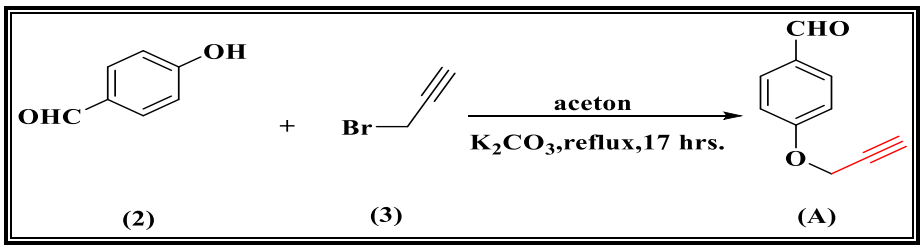
permitted to swirl for 45 minutes while an aqueous solution of sodium azide (2eq , 0.2gm , 0.003 mol)) was made. Then, Bubbles were observed when the sodium azide solution was applied in batches. as it was being added. Following the addition of the solution, it is left to For two hours, whisk The resultant silt is filtered and repeatedly washed with distilled water.as a white crystalline.



Equation (1) synthesis of derivative (S)

4-(prop-2-yn-1-yloxy)benzaldehyde synthesis [28,29] (A)

After adding (2 eq., 1.104gm , 0.001 mol) of anhydrous potassium carbonate K_2CO_3 to (0.5gm, 0.001 mol) of the 4-hydroxy benzyldehyde dissolved in acetone and chilling the reaction below 15° C, ,(0.487gm, 0.001 mole) of batches of 3-bromo-1-propyne (2) solution are added in small amounts , and The response was then allowed to reflux. TLC was used to track the reaction's conclusion . TLC was used to track the reaction's conclusion (benzene:ethanol,3:2), Rf =0.85 Reduced pressure is used to extract the solvent. After dissolving the residue in distilled water, ethyl acetate is added twice to complete the extraction process. It was prepared as a yellow solid.

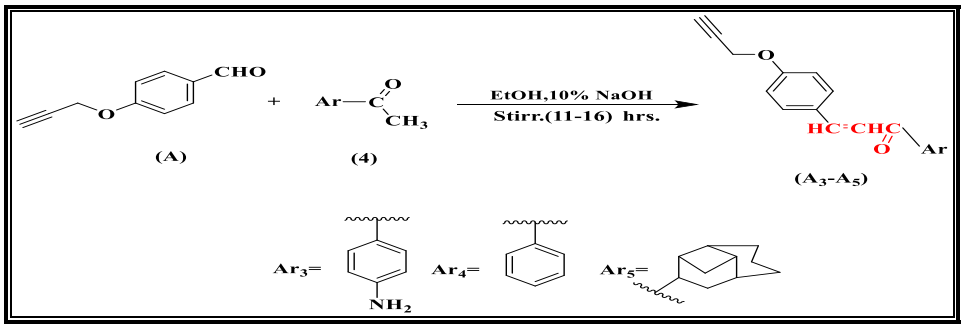


Equation (2) synthesis of derivative (A)

Synthesis of derivatives of chalcones [30](A_3-A_5)

In round flask dissolve 0.001 mol from (A) derivative in 30 ml absolute ethanol with shaking, then add 5 ml of 10% NaOH solution then add 0.001 mol from (5) compound: (4-amino acetophenone ,4-amino acetophenon and admantyl -1-

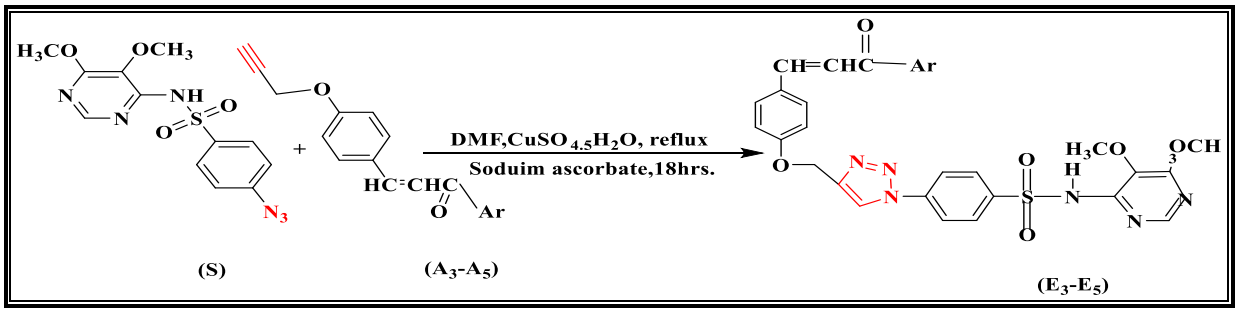
methyl ketone) respectively for 16 hrs,at the room temperature , verified using TLC employing a 2:3 ethanol to benzene combination.



Scheme (1) preparation of derivatives of chalcones (A_3-A_5)

Synthesis of triazoles derivatives [31,32] (E_3-E_5) .

From 0.0006mole (A_3-A_5) derivatives to 0.0006 mol, from (S) derivative, dissolved in 20 mL DMF after the mixture remained on stirring for 10 minutes , added 0.0006 mole from $CuSO_4.5H_2O$ and 0.0006 mole sodium ascorbate, which the reaction is left for(18 h) stirring at (75˚c), following the reaction's completion (as verified by TLC using a mixture of ethylacetate:n-hexane:ethanol 3:1.5:0.5), After removing the solvent with a rotary evaporator, glacial acetic acid and ethanol (1:3) were used to wash and recrystallize the sediment.



Scheme (4) synthesis of derivative (A)

Table (1) physical properties of preparation derivatives

No.	Molecular formula	M.Wt	M.P	Yield%	R_f	Color
S	$C_{12}H_{12}N_6O_4S$	304	197-199	80%	0.84	Yellow
A	$C_{10}H_8O_2$	160	100-102	86%	0.85	Yellow
A_3	$C_{18}H_{15}NO_2$	277	140-142	60%	0.74	Brown
A_4	$C_{18}H_{14}O_2$	262	154-156	60%	0.86	Yellow
A_5	$C_{22}H_{24}O_2$	320	155-157	89%	0.87	Brown
E_3	$C_{30}H_{28}O_8N_7S$	689	204-206	89%	0.61	Brown
E_4	$C_{30}H_{27}O_6N_6S$	660	202-204	76%	0.51	Brown
E_5	$C_{33}H_{38}O_6N_6S$	718	206-208	86%	0.57	Brown

Result and discussion:

4-azido-N-(5,6-dimethoxypyrimidin-4-yl)benzenesulfonamide (S) identification

FT-IR / υ (cm−1) : Disappearance 3466 ν str. (N-H) 1° amine, appearance 2102, ν str. (-N3),3267 ν str. (N-H) 2° amine 2951,2862 ν str.aliphatic1581 ν str. (C=N) endocyclic and (C=N)Imine1485,1450,νstr.(C=C) aromatic,1384 asy.1166 sy.ν str. (SO2) 1336 ν str. (C-N) Amine,1085 ν str. (O-CH3)Methoxy,848 ν str. (C-S) ,1450 ,1384 ν bend.(C-H) –CH3 ,1085 ν str.(S-N),711 ν bend. (C-H Aromatic out –of- plane bend).

1H-NMR / δ:3.74,4.33(S,6H , -OCH3),7.90-7.61 (m, 4H, Ar-H),8.34 (S, 3H, C-H-Pyrimidine ring), 11.97 (S,1H, N-H sulphonyl).

13C-NMR /ppm :53.41 (C-N) pyrimidine,57.46 (OCH3)methoxy,156.66 (C=N)pyrimidine,131.31-115.41(C=C)Aromatic.

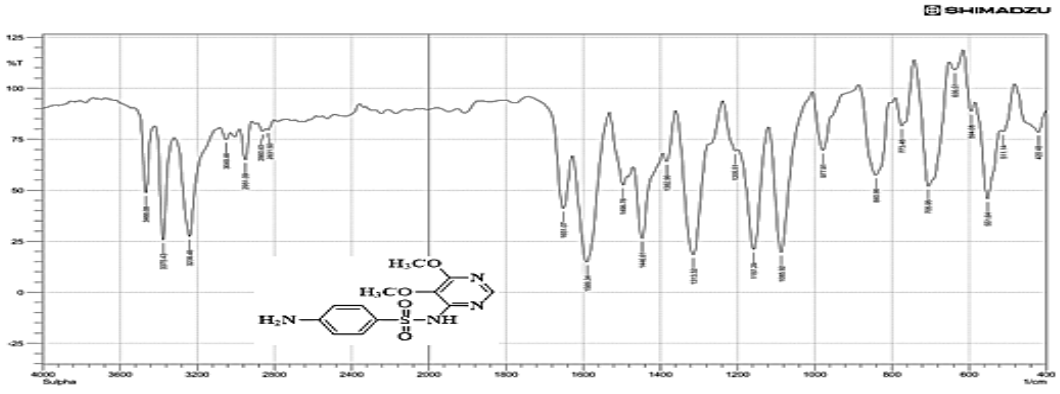


Figure (3) FTIR spectrum of sulphadoxin drug

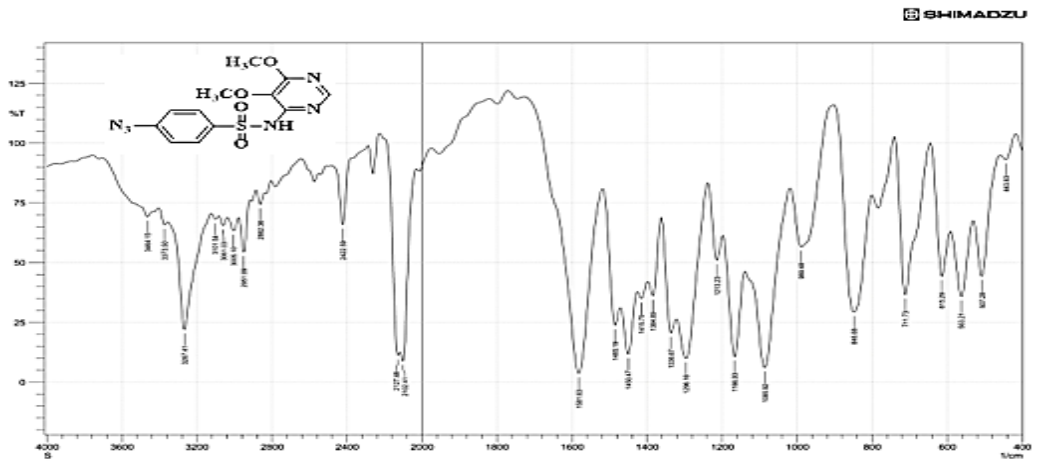


Figure (4) FTIR spectrum of (S) derivative

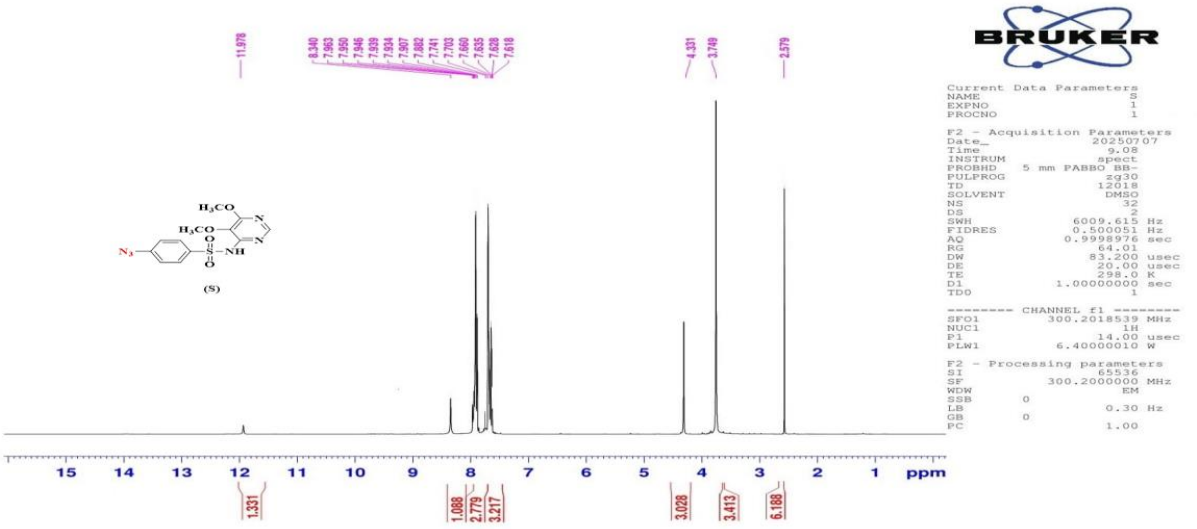


Figure (5) [1] HNMR spectrum of derivative (S)

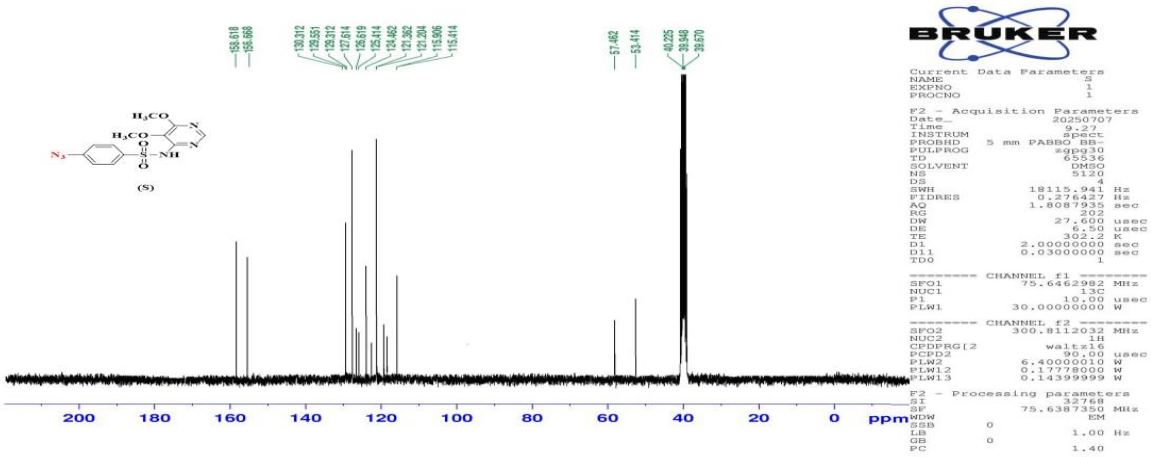


Figure (6) ^{13} CNMR spectrum of derivative (S)

4-(prop-2-yn-1-yloxy)benzaldehyde identification (A)

FT-IR / υ (cm−1):3209 ν str. (C≡C) Alkyne,3072 ν str. (C-H) Aromatic 2929 ν str.(C-H)Aliphatic,2837 ν str.(C-HO) Aldehyde 2119 ν str. (C-H)Acetylenic 1683 ν str. (C=O) Aldehyde,1600 ν str. (C=C Aromatic) 1427 (ν bend.) aliphatic, 1170 (ν str. (O-C) ether,860 ν bend. (C-H Aromatic out –of- plane bend).

1H-NMR / δ:13,81 (S, 1H, -CHO),7.96-7.70 (m, 4H, Aromatic),4.73, 3.74 (s, 2H, O-CH2-C≡C).

13C-NMR /ppm :178.14 (H-C=O)aldehyde,131.42-118.63(C=C)aromatic ,76.85 (HC≡C-)Acteylene,74.88 (O-C) ether.

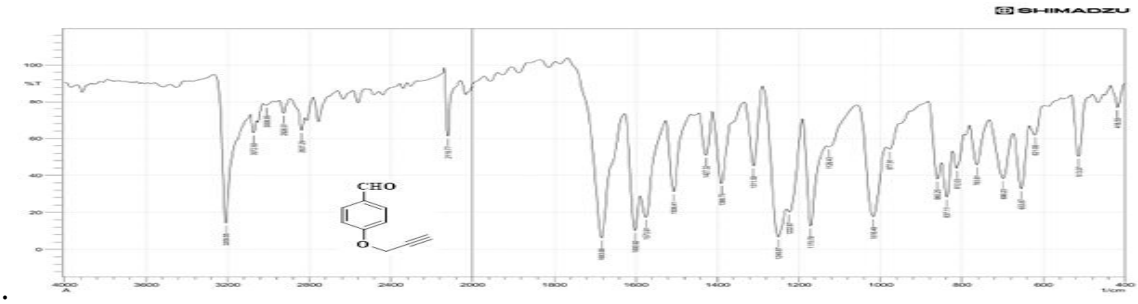


Figure (7) FTIR of (A) derivative

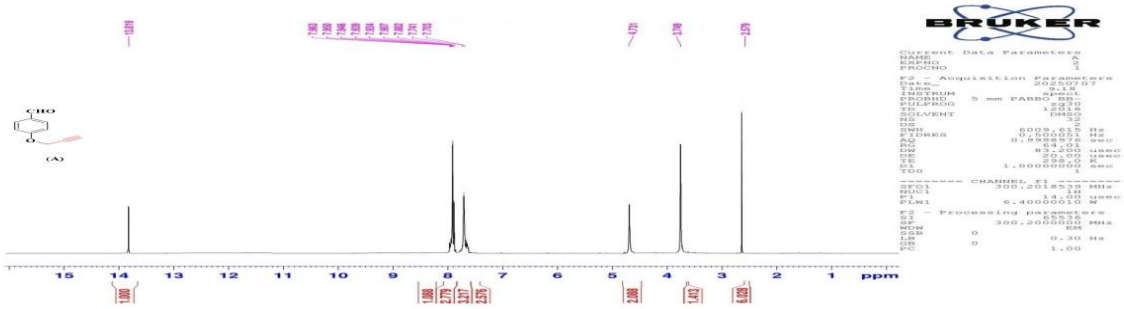


Figure (8) [1] HNMR spectrum of derivative (A)

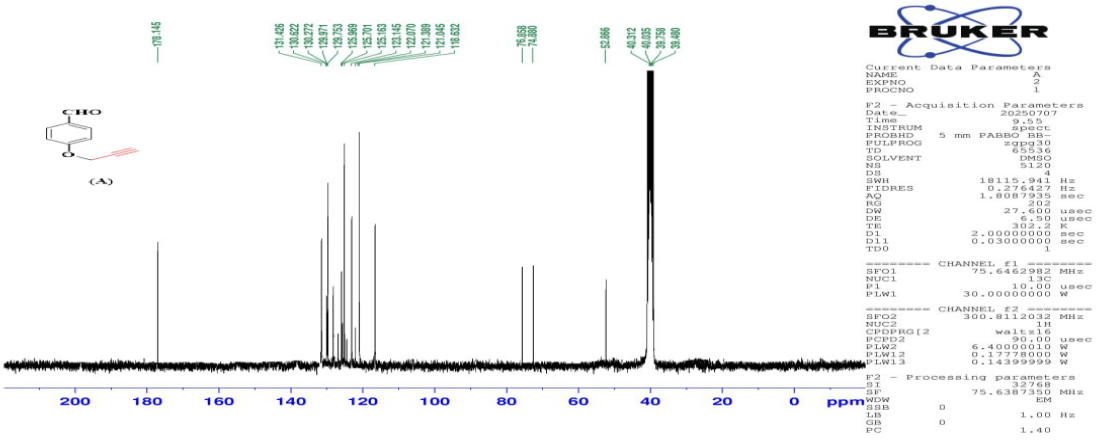


Figure (9) [13]CNMR spectrum of derivative (A)

Identification of (E)-1-(4-aminophenyl)-4-(4-(prop-2-yn-1-yloxy)phenyl)but-3-en-2-one (A_3)

FT-IR / υ (cm−1):3419 ν str. (N-H 1° amine , 3215 (C-H Acetylenic), 3290 ν str. (C-H Alkyne) , 3078,2929, ν str. (C-H Alkene) 2833 ν str. (C-H) -CH2- ,2121 ν str. (C≡ C Alkyne) ,1683 (ν str.C=O ketone) , 1602,1577 ν str. (C=C Aromatic),1170 ν str. (O-C) Ether, 1317 ν str. C-N (1° amine ,929,860 ν bend. (C-H Aromatic out –of- plane bend).

1H-NMR / δ: 7.37-7.02 (m, 8H, Ar-H),6.56,6.16,4.72 (s, 2H, CH=CH),3.73(S, 2H, O-CH2-C≡C) ,2.52(S, 1H, C≡C-H).

13C-NMR /ppm : 180.74 (H-C=O)aldehyde,130.27-121.03 (C=C) aromatic ,126.22 (C=C) alkene ,75.71 (HC≡C-) acetylene,57.27(O-C) ether.

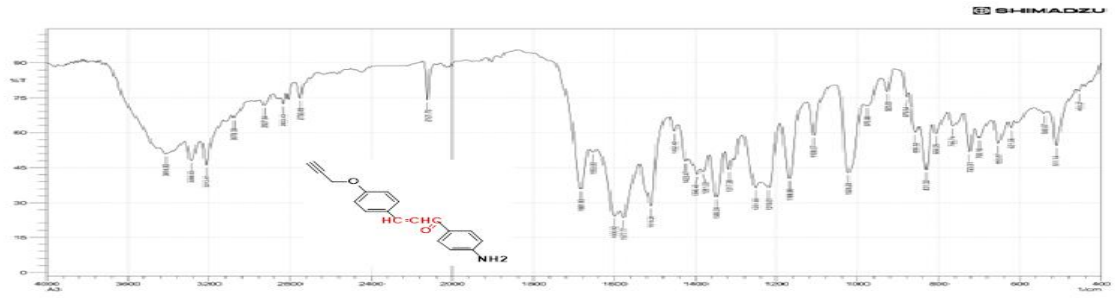


Figure (10) FTIR of (A_3) derivative

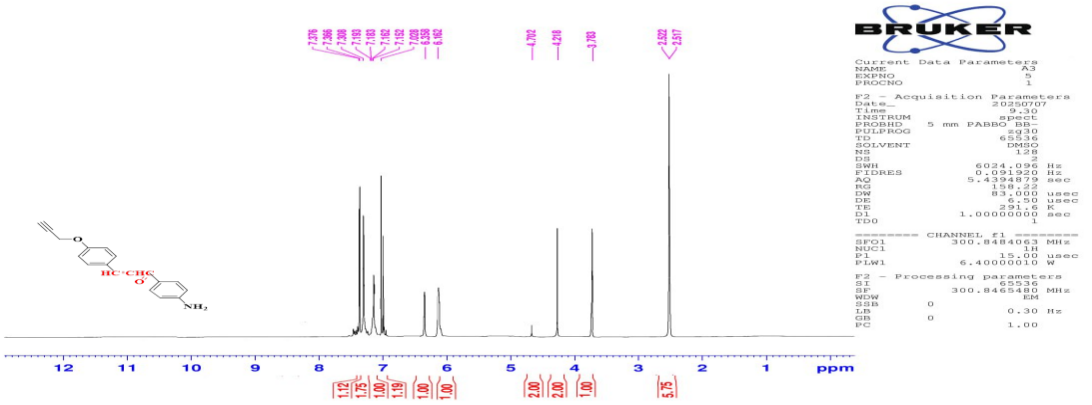


Figure (11) ^{1}HNMR spectrum of derivative (A_3)

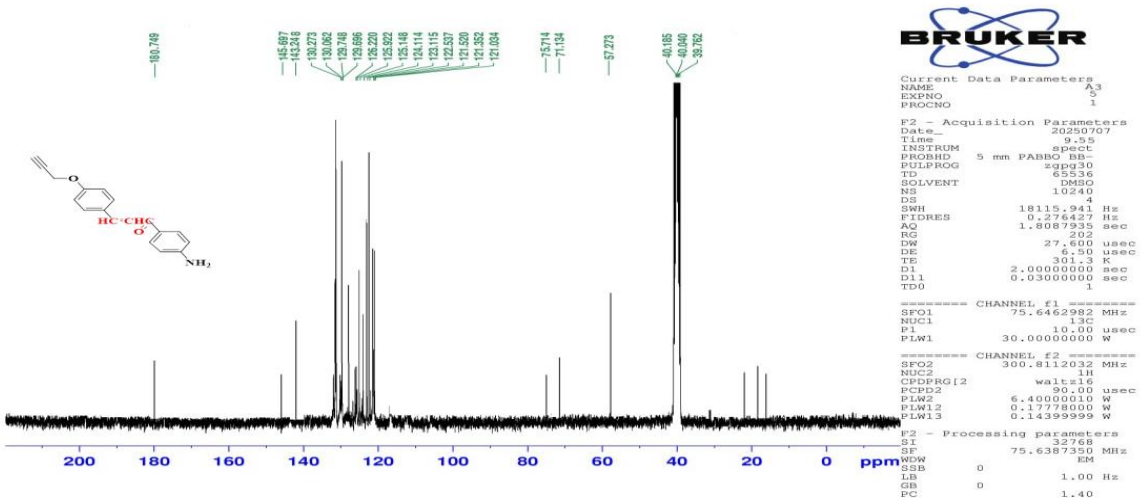


Figure (12) ^{13}CNMR spectrum of derivative (A_3)

(E)-1-phenyl-4-(4-(prop-2-yn-1-yloxy)phenyl)but-3-en-2-one identification (A_4).

FT-IR / υ (cm−1):3290 ν str.(C-H Aromatic),3219 ν str. (C-H Acetylenic) 3062 ν str. (C-H Alkene),2935,2875,2806 ν str. (C-H) -CH2- 2112 ν str. (C≡ C) Alkyne),1683 (ν str.C=O ketone) ,1660 ν str. (C=C Aromatic, 1168 ν str. (O-C) ether,860 ν bend. (C-H Aromatic out –of- plane bend).

1H-NMR / δ: 7.52-7.54, (m, 11H, Ar-H) ,7.18(S, 2H, CH=CH),4.41 (S, 2H, O-CH2-C≡C)

13C-NMR /ppm : 3.71(s, 1H, C≡C-H). 181.74 (H-C=O)aldehyde, 130.61-115.80 (C=C) aromatic 129.74(C=C) alkene,77.51(HC≡C-) acetylene, 56.52 (O-C) ether

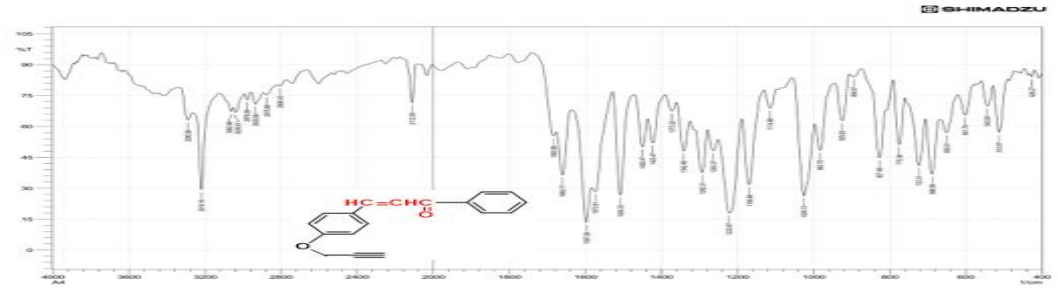


Figure (13) FTIR of (A_4) derivative

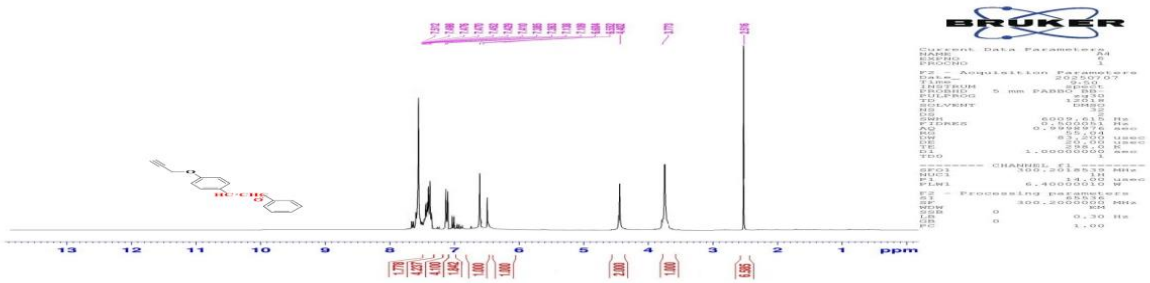


Figure (14) ^{1}HNMR spectrum of derivative (A_4)

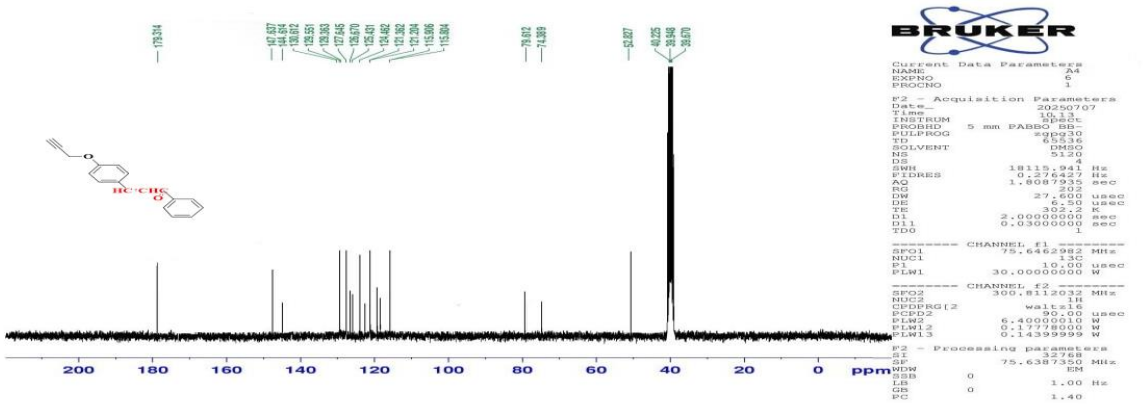


Figure (15) ^{13}CNMR spectrum of derivative (A_4)

Finding 1-((3ar,4R,7aS)) -octahydro 2-yl-2H-2,4-methanoinden (prop-2-yn-1-yloxy)phenyl-2-(4-) -1l5-ethen-1-one (A_5)

FT-IR / υ (cm−1):3061 ν str. (C-H Acetylenic) ,2906 ν str. (C-H Alkene), 2850 ν str. C-H aromatic,2750, ν str. aliphatic ,2119 ν str. (C≡ C Alkyne),1683 (ν str.C=O ketone) 1600 ν str. (C=C Aromatic),1166 ν str. (O-C) ether,860 ν bend.
1H-NMR / δ: (C-H) 7.95-7.64 (m, 4H, aromatic),6.74(S, 2H, CH=CH),4.34 (S, 2H, O-CH2-C≡C),3.63(S, 1H, C≡C-H),1.74(m,19 H,CH2).

13C-NMR /ppm:181.74 (H-C=O) aldehyde,,130.27-117.65 (C=C)aromatic,129.74(C=C) alkene 77.51 (HC≡C-) Acetylenic,56.52 (O-C)ether .

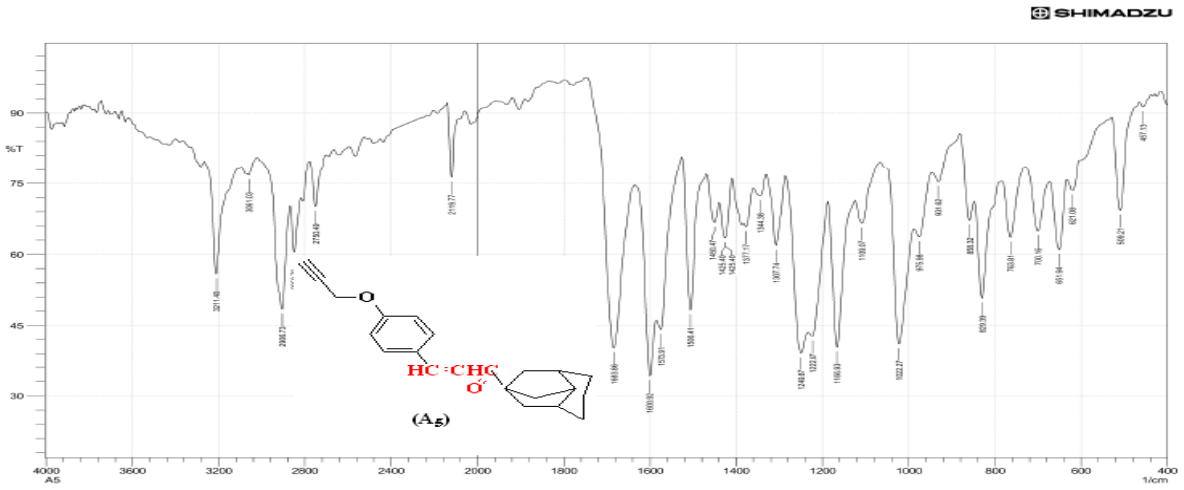


Figure (16) FTIR of (A_5) derivative

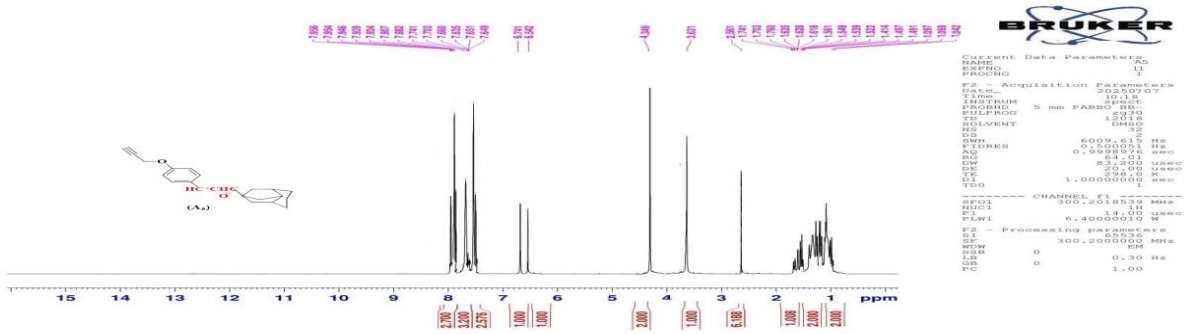


Figure (17) ^{1}HNMR spectrum of derivative (A_5)

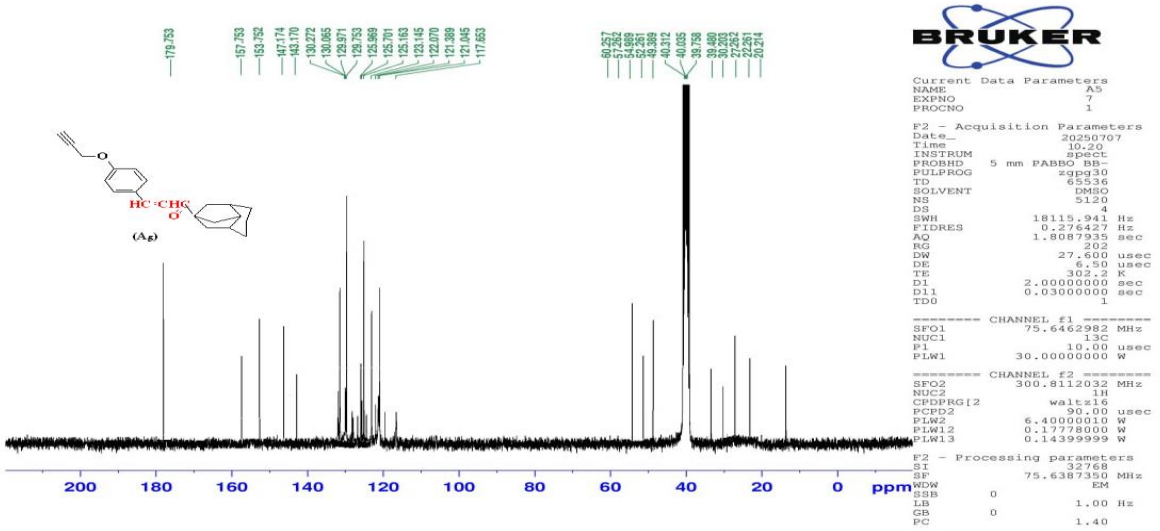


Figure (14) ^{13}CNMR spectrum of derivative (A_5)

(E)-4-(4-(4-(4-(4-aminophenyl) identification 1-en-1-yl)phenoxy)methyl-3-oxobut-1-en 1-yl-1H-1,2,3-triazol Sulfonamide of N-(5,6-dimethoxypyrimidin-4-yl) (E_3)

FT-IR / υ (cm−1): Disappearance 3290 ν str. (C-H Acetylenic) ,2121 ν str. (C≡ C Alkyne) appearance 3415 ν str.1º amine ,3145 ν str.2º amine,3080 ν str. (C-,H aromatic),3080 ν str.(C-H triazole), 2945 ν str. C-H aromatic,2854 ν str. Aliphatic,1710 (ν str.C=O ketone) 1598 ν str. (C=C Aromatic ,1165 ν str. (O-C) methoxy,860 ν bend. (C-H Aromatic out –of- plane bend),1622 ν str. (C=N),1085 ,1342 ν str. (SO2) 1018 (S-N) ν str. 1408 ν str.(N=N), 839 ν str. (C-S).

1H-NMR / δ:11.31 (s, 1H, NH-) sulphonamide,7.63 (s, 1H, (-CH=N-) Pyrimidine ring, 7.62 (s,1H, triazole ring),7.49-7.12 (m, 7H, Aromatic),6.26 (s, 1H, C-H-Pyrimidine ring) 4.51(S,CH-C=C),3.86 (S, 2H, O-CH2-,triazole ring), 3.35 (S, 6H, -O-CH3)

13C-NMR /ppm:180.28(C=N)Pyrimidine ring,159.96 (C-N) Pyrimidine ring ,156.70 (C-H)Pyrimidine ring,149.96(C-H triazole ring), 130.07-117.54 (C=C Aromatic),122.07(C-N triazole ring),57.86 (O-CH3)methoxy,129.97(C=C alkene)

53.86 (O-C ether).

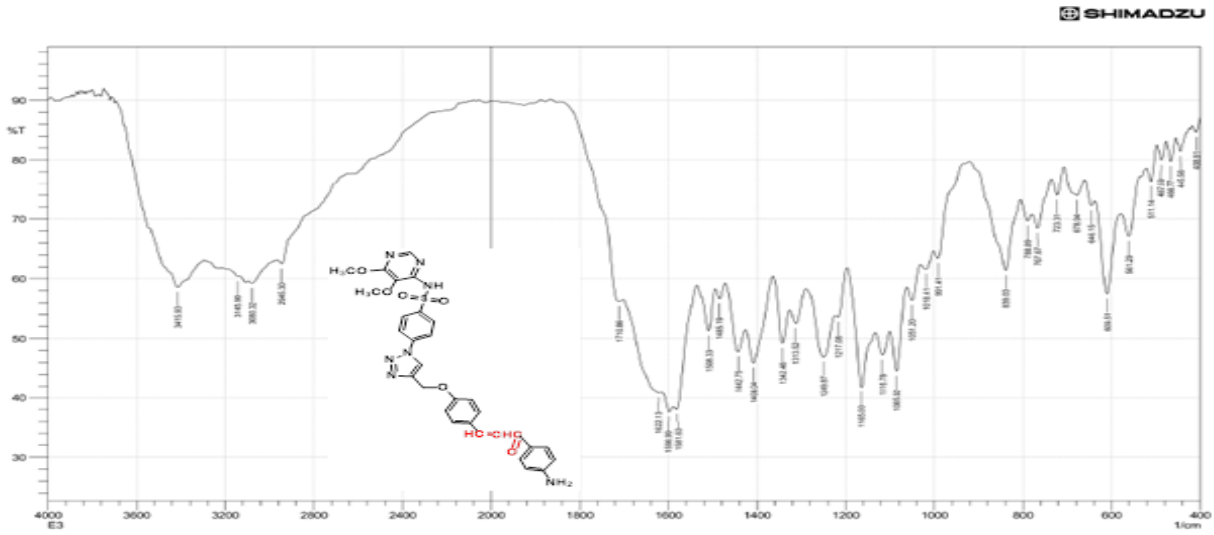


Figure (15) FTIR of (E_3) derivative

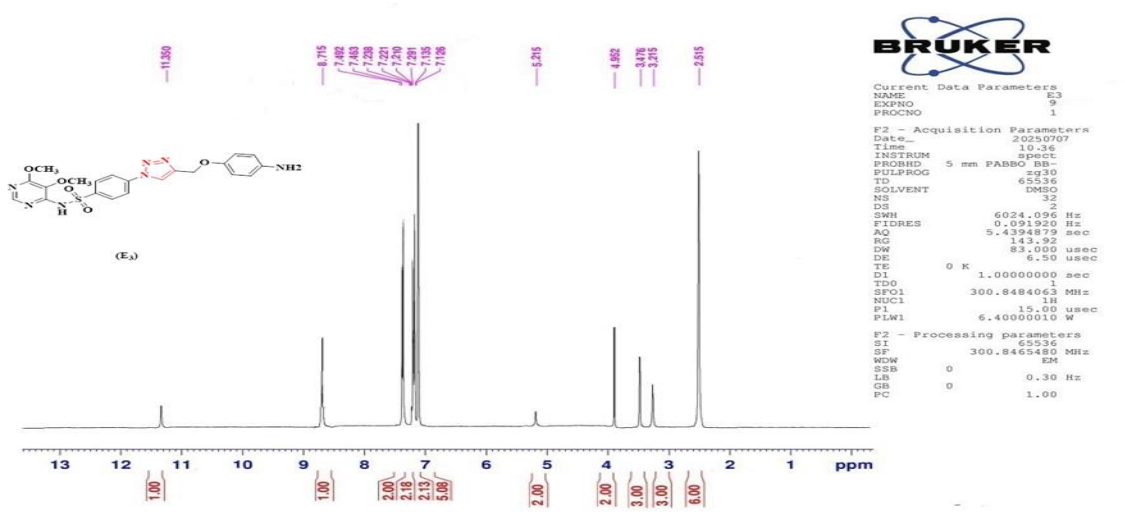


Figure (16) HNMR spectrum of derivative (E_3)

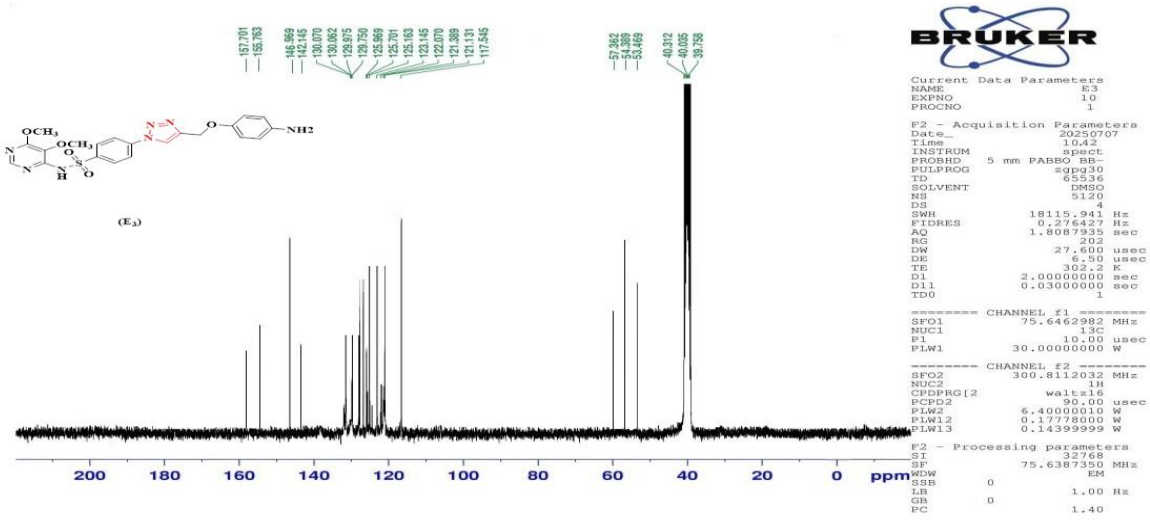


Figure (17) ^{13}CNMR spectrum of derivative (E_3)

(E)-N-(5,6-dimethoxypyrimidin-4-yl)-4-(4-(3-oxo-4-phenylbut-1-en-1-yl)phenoxy)methyl) identification Triazol-1-yl)benzenesulfonamide -1H-1,2,3-(E_4)

E4:FT-IR / υ (cm−1): Disappearance 3219 ν str. (C-H Acetylenic), 2112 ν str. (C≡ C) Alkyne) , appearance 3414 ν str .2º amine ,3149 ν str.(C-H triazole), 3082 ν str. C-H aromatic ,2949 ν str. (C-H) -CH2- ,1714 (ν str.C=O ketone) ,1587 ν str. (C=C Aromatic),1168 ν str. (O-C) Ether ,929,860 ν bend. (C-H Aromatic out –of-

plane bend), 3078 ν str. (C-,H aromatic), 1620 ν str. (C,=N, 1085 ,1336 ν str. (SO2) , ν str. 1045 (S-N) , ν str. 1402 ν str.(N=N), 837ν str. (C-S).

1H-NMR / δ:11.31 (S, 1H, -NH sulphonamide), 7.63 (S, 1H),(-CH=N- Pyrimidine ring), 7.62 (S,1H, triazole ring),7.37-7.02(m, 7H,Aromatic), 6.26 (s, 1H, C-H-Pyrimidine ring), 4.51(s,CH-C=C),3.86 (s, 2H, O-CH2- triazole ring),3.35 (s, 6H, -O-CH3).

13C-NMR /ppm:180.28(C=N) Pyrimidine ring,159.96(C-N)Pyrimidine ring,156.70 (C-H)Pyrimidine ring,149.96 (C-H triazole ring),132.21-121.16(C=C Aromatic) ,122.07(C-N triazole ring), 57.86 (OCH3)methoxy ,129.97(C=C alkene), 53.86(O-C ether).

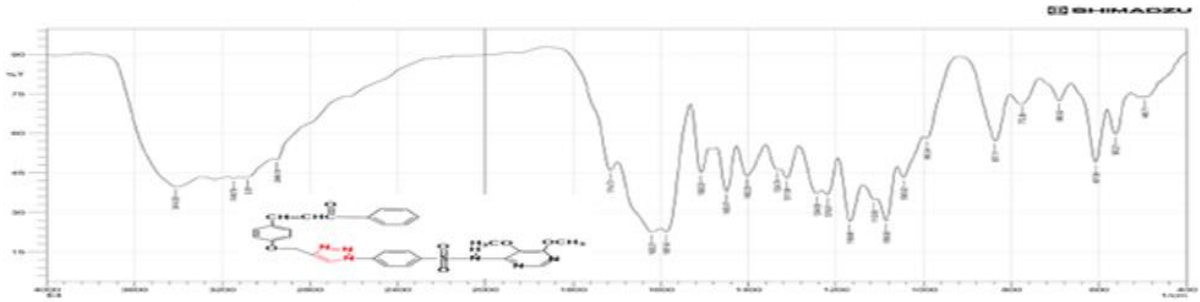


Figure (18) FTIR of (E_4) derivative

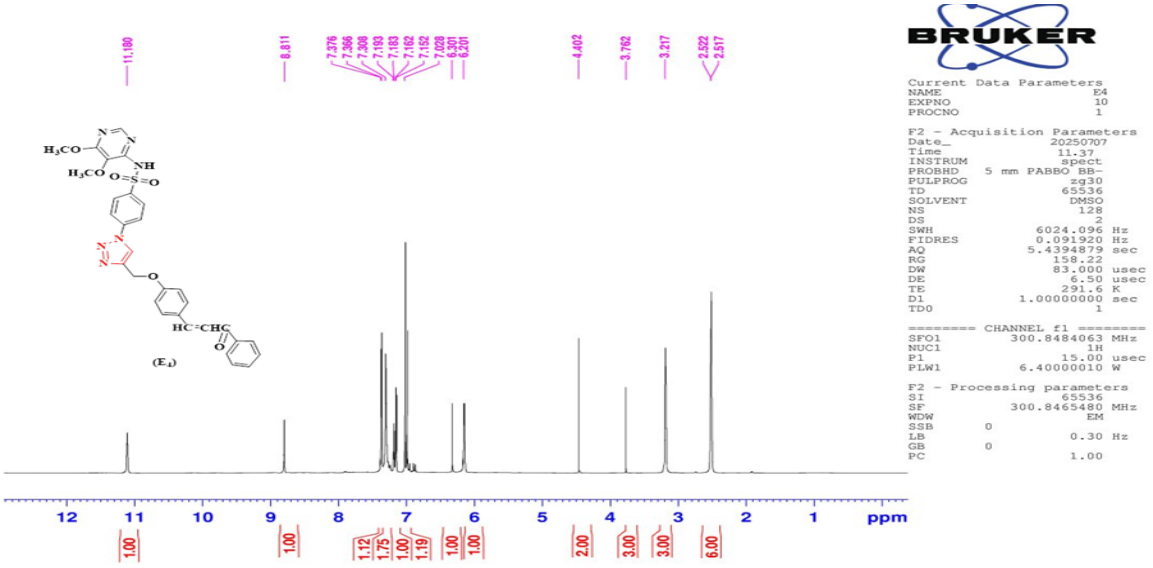


Figure (19) [1] HNMR spectrum of derivative (E_4)

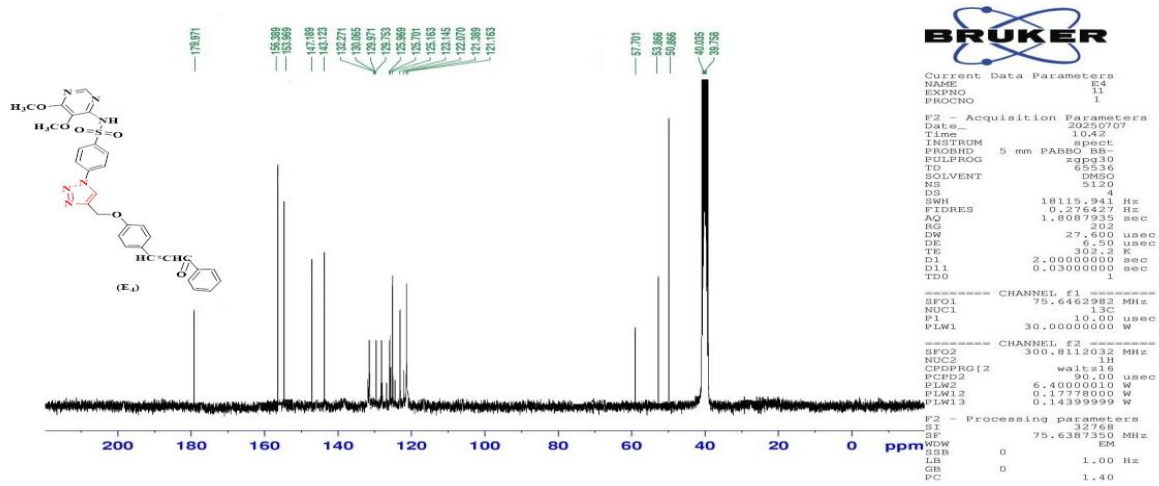


Figure (20) ^{13}CNMR spectrum of derivative (E_4)

Recognition of N The compound 5,6-dimethoxypyrimidin-4-yl Four-(four-((1S,2R,6R)) [4.4.0.02,9]decan-9-yl)phenoxy)methyl tricyclo Triazol-1-yl)benzenesulfonamide -1H-1,2,3- (E_5)

E5:FT-IR / υ (cm−1): Disappearance 3219 ν str. (C-H Acetylenic), 2119 ν str. (C≡ C Alkyne ,appearance 3439 ν str. 2º amine ,3105 ν str.(C-H triazole), 3082 ν str. C-H aromatic,2935 ν str. (C-H) -CH2- ,1714 (ν str.C=O ketone) ,1593 ν str. (C=C Aromatic),1168 ν str. (O-C) Ether ,929,860 ν bend. (C-H Aromatic out –of-plane bend), 3078 ν str. (C-,H aromatic), 1627 ν str. (C,=N, 1089 ,1336 ν str. (SO2) , ν str. 1055 (S-N) , ν str. 1408 ν str.(N=N), 839 ν str. (C-S).

1H-NMR / δ:11.37 (S, 1H, -NH sulphonamide), 9.88 (S, 1H, (-CH=N-) Pyrimidine ring,7.97 (S,1H, triazole ring),8.16 -7.13, (m, 20 H, aromatic),6.77 (S, 8H, C-H-Pyrimidine ring), 4.07 (S,1H,CH-C=C),3.58 (S, 2H, O-CH2-, triazole ring), 3.35 (S, 3H, -O-CH3),2.21(S, 20H, -CH2-).

13C-NMR /ppm:177.57 (C=N)Pyrimidine ring,153.72 (C-N) Pyrimidine ring,148.14(C-H) Pyrimidine ring),143.16(C-H)triazole ring,131.42-118.61(C=C Aromatic),122.07(C-N triazole ring), 60.83 (OCH3)methoxy, 129.97(C=C alkene), 54.86 (O-C)ether.

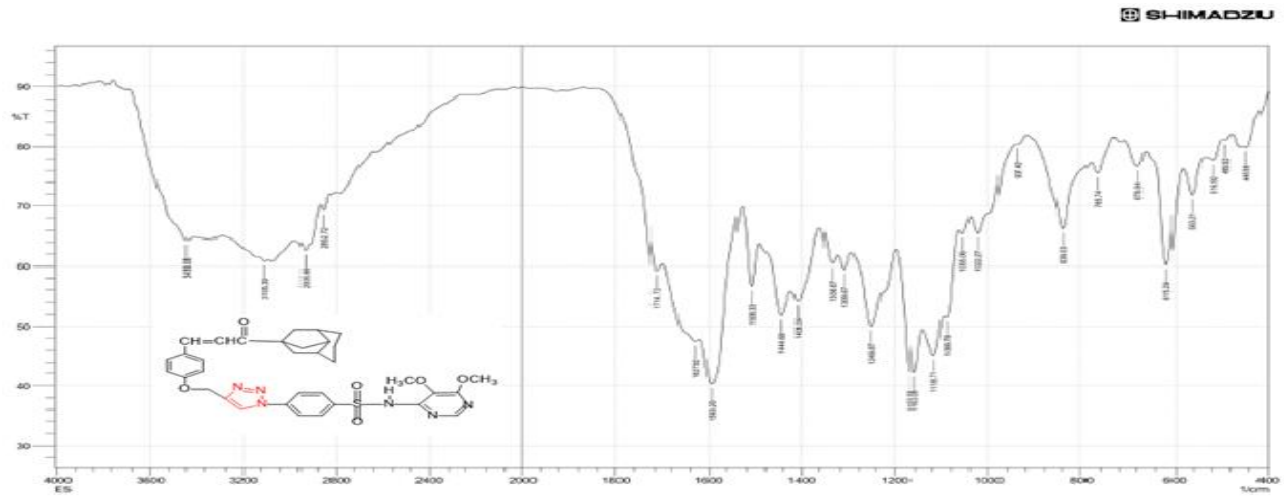


Figure (21) FTIR of (E_5) derivative

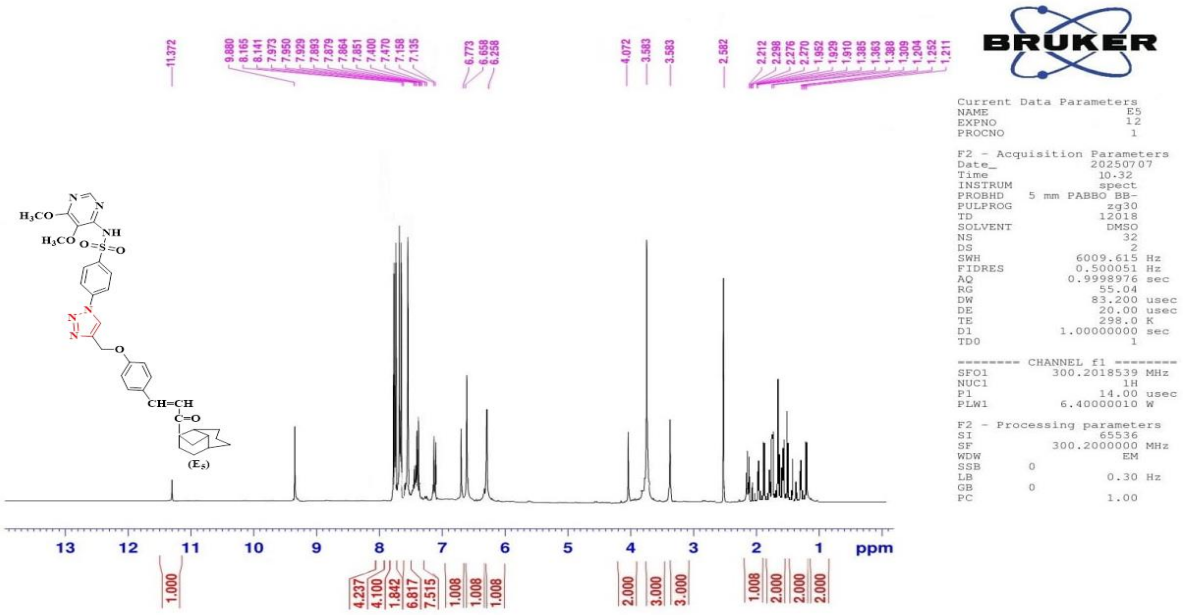


Figure (22) [1] HNMR spectrum of derivative (E_5)

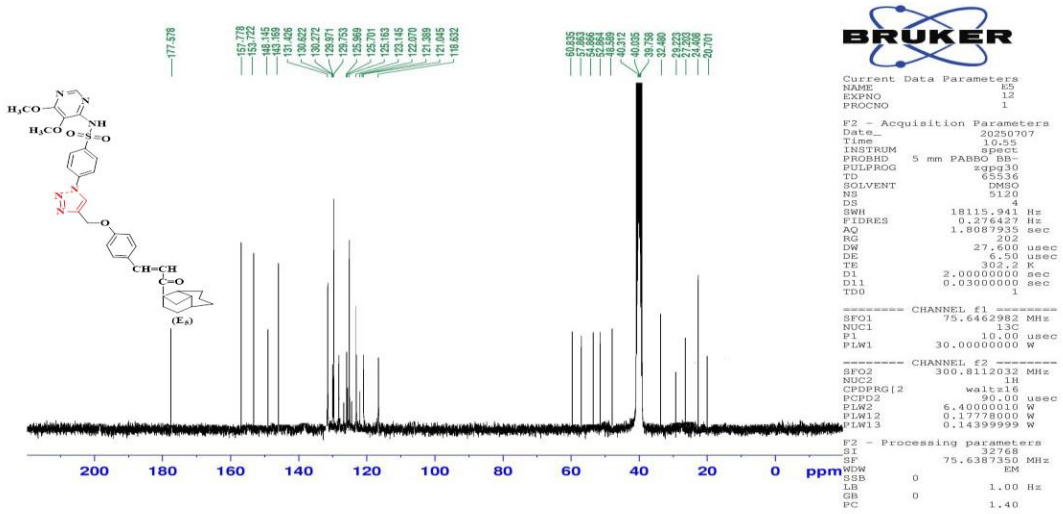


Figure (23) ^{13}CNMR spectrum of derivative (E_5)

Antioxidant [33]

Since they have a high inhibition rate at a concentration of 1 mg/ml, the findings of antioxidant studies demonstrate that the active groups of the produced compounds triazoles have antioxidant capabilities in comparison to ascorbic acid. Because they include groups rich in electrons that can attach to free radicals and prevent oxidation, compounds (S,,E3,E5) have also demonstrated the highest inhibition rate when compared to ascorbic acid.

The proportion of antioxidant activity of substance (S) for four samples is shown in graph (1) below. The maximum activity, 86.28%, is found in sample 1, and the lowest, 80.70 %, is found in sample 4. We can quickly compare the antioxidant efficacy of various samples thanks to this graphic representation.

Table (3) Shows the antioxidants of the prepared compounds, S

sample name	Concentration	absorbency	scavenging %
1	1 mg/ml	0.2036	86.2822
2	0.5 mg/ml	0.2566	82.5889
3	0.25 mg/ml	0.2773	81.2356
4	0.125 mg/ml	0.2851	80.7078
	Control	1.4778	

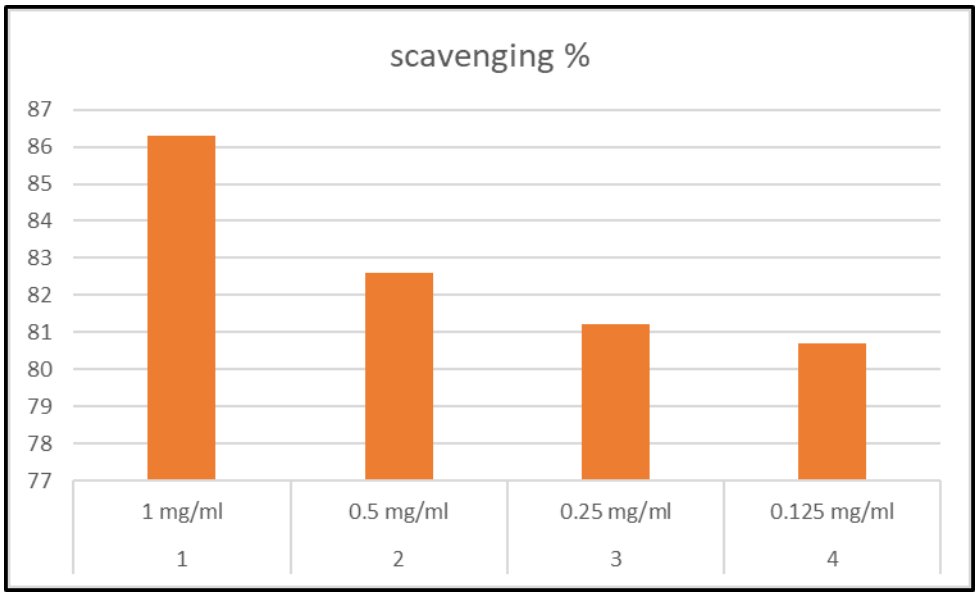


Diagram (3.1) Scavenging effect of compound [S]

The proportion of antioxidant activity of substance (E3) for four samples is shown in graph (2) below. The maximum activity, 70.55%, is found in sample 1, and the lowest, 64.11%, is found in sample 4. We can quickly compare the antioxidant efficacy of various samples thanks to this graphic representation.

Table (2) Shows the antioxidants of the prepared compounds, E3

sample name	concentration	absorbency	scavenging %
1	1 mg/ml	0.4204	70.5561
2	0.5 mg/ml	0.4349	69.5405
3	0.25 mg/ml	0.4701	68.189
4	0.125 mg/ml	0.51231	64.1189
	control	1.4278	

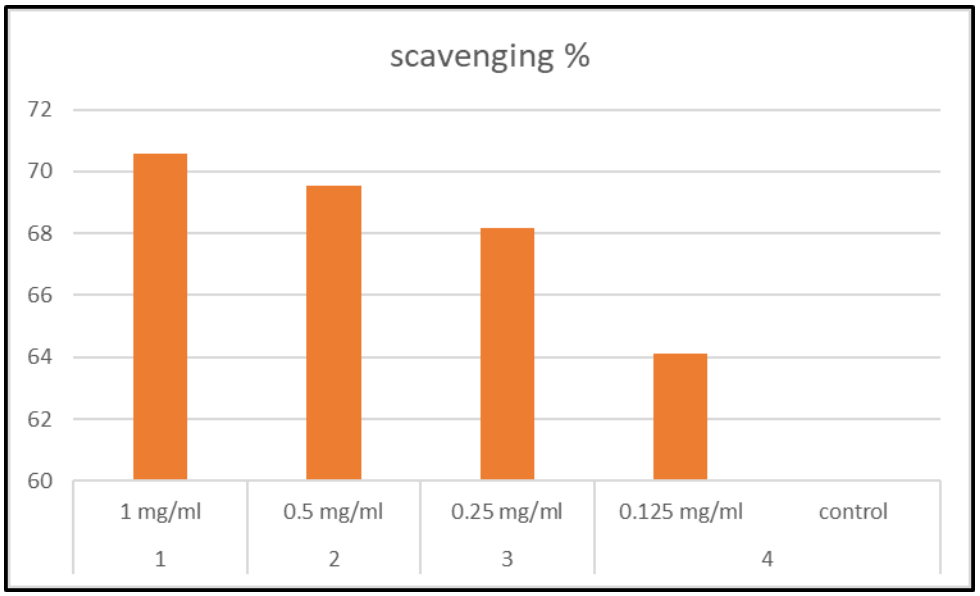


Diagram (2)Scavenging effect of compound [E3]

Table (3) Shows the antioxidants of the prepared compounds, E5

sample name	concentration	absorbency	scavenging %
1	1 mg/ml	0.3704	70.6590
2	0.5 mg/ml	0.4093	67.5756
3	0.25 mg/ml	0.4421	64.9794
4	0.125 mg/ml	0.4894	61.2325
	control	1.2624	

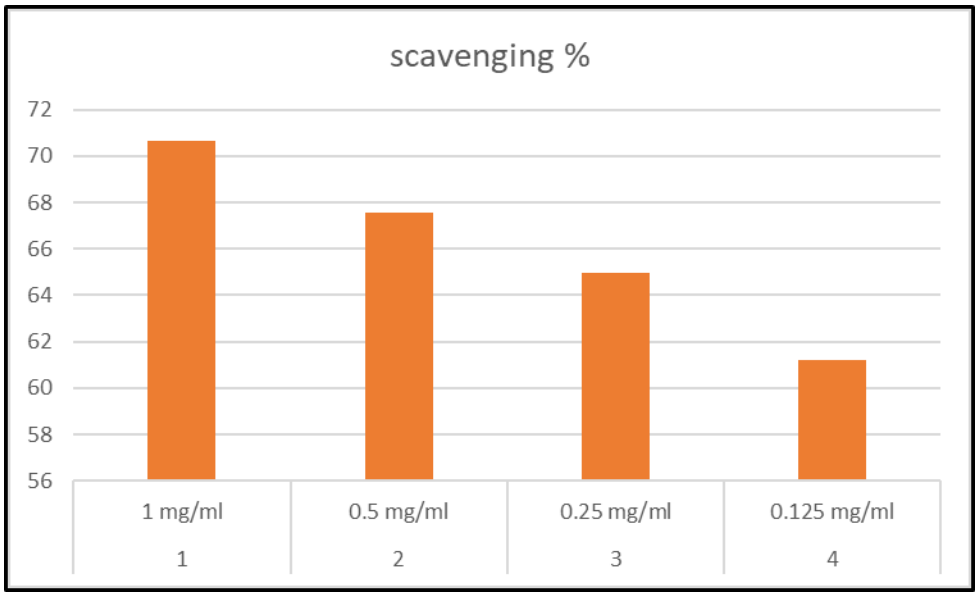
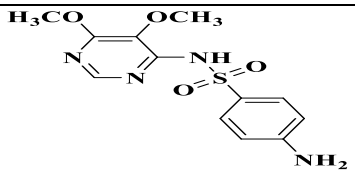
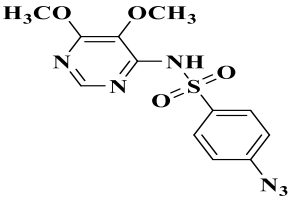
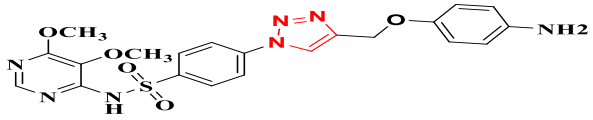
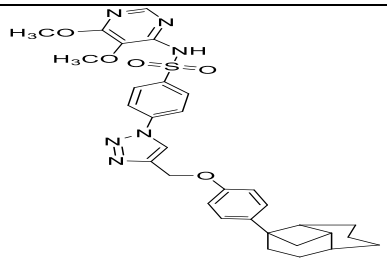


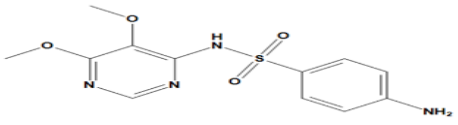
Diagram (3)Scavenging effect of compound [E5]

Molecular docking research [34,35]

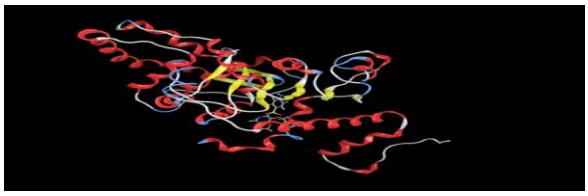
The molecular docking methodology is becoming a more important method in the drug creation process. Because it can be used to demonstrate how a protein and a small molecule interact at the nanoscale, it is essential to computer-based drug design. This enables us to describe the primary biochemical processes and the behavior of microscopic particles in the protein binding site.The free energy of binding (G) data indicated that most of these drugs had good binding affinities for the receptor, and the computed values demonstrated the overall trend.Part 1. DHPS protein-containing sulphadoxine medication (PDB code: 7A6S). where (Z) describes the two-dimensional picture of Sulphadoxine binding with an active site, (Y) describes the three-dimensional picture of Sulphadoxine binding with an active site, (Y) describes the three-dimensional picture of entrance and binding with the entire protein, and (X) describes the drug surface protein. Part 2: Dihydropteroate synthase (DHPS) protein-bound sulphadoxine derivatives (PDB code: 7A6S) explain the following: (Z) a 2D picture of sulphadoxine derivatives binding with an active site; (Y) a 3D picture of sulphadoxine derivatives binding with an active site; (X) a 3D picture of entrance and binding with whole protein; and (W) a surface protein with drug.The docking investigation's findings indicate that, as previously shown, sulphadoxine derivatives have a greater binding affinity for the target location than sulphadoxine. It will therefore be an excellent choice to act as a cytotoxic drug. The docking study revealed the target generated compounds' high affinity for the enzyme.in which the compounds [S, E_3,E_5] showed high docking scores (-5.38945389,-8.01673985,-9.5112524) comparison with Sulphadoxine)(-5.30702734) Kcal/mol.

Table (4) Results of the molecular docking study to compound [Sulphadoxine drug ,S, E_3,E_5]

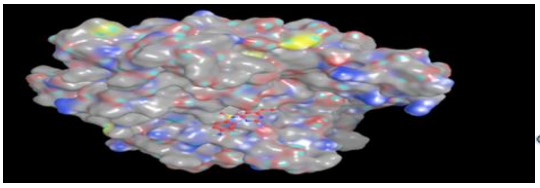
Compound NO.	Binding Energy Kcal/mol	RMSD
 4-amino-*N*-(5,6-dimethoxypyrimidin-4-yl)benzenesulfonamide	-5.30702734	2.25838041
 4-azido-*N*-(5,6-dimethoxypyrimidin-4-yl)benzenesulfonamide	-5.38945389	2.21673775
 4-(4-((4-aminophenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)-*N*-(5,6-dimethoxypyrimidin-4-yl)benzenesulfonamide	-8.01673985	1.86692798
 *N*-(5,6-dimethoxypyrimidin-4-yl)-4-(4-((4-((1*S*,2*R*,6*R*)-tricyclo[4.4.0.0^{2,9}]decan-9-yl)phenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide	-9.5112524	2.23385286

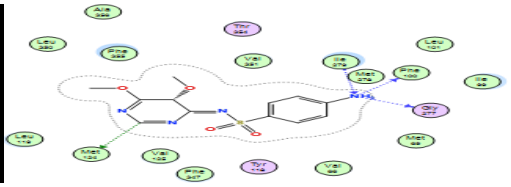


(Z)



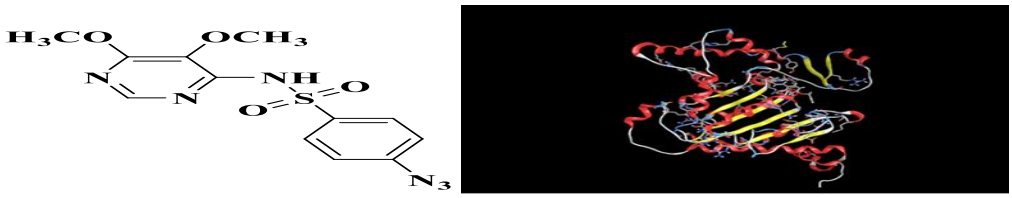
(Y)





(X) **(W)**

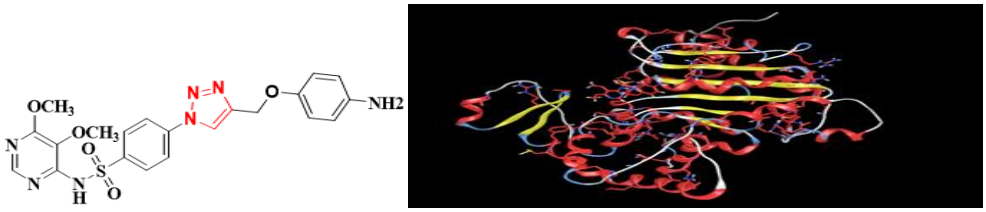
Figure (13) Docking result of compound (2D) &(3D) Sulphadoxine



(Z) (Y)

(X) (W)

Figure (14) Docking result of (S) derivative (2D) &(3D)



(Z) (Y)

(X) (W)

Figure (15) Docking result of (E3) derivative (2D) &(3D)

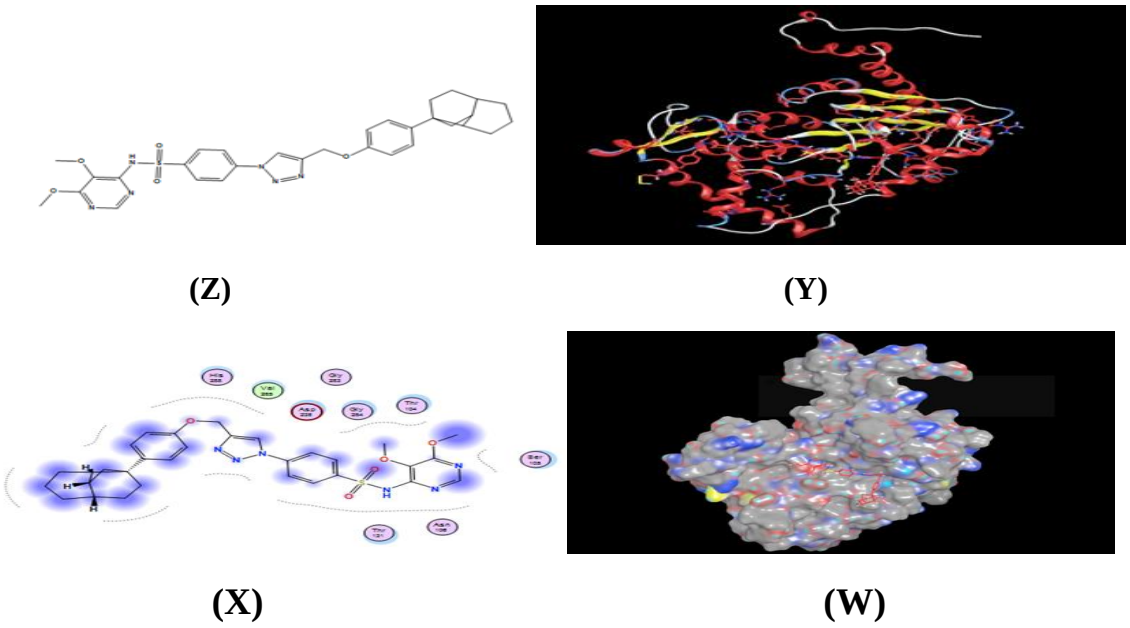


Figure (17) Docking result of (E_5) derivative (2D) &(3D)

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