SYNTHESIS AND CHARACTERISATION OF SUBSTITUTED -9-(3, 4, 5-TRIMETHOXYPHENYL) TETRALONE-TRIAZOLES BY CHALCONE PATH AND THEIR BIOLOGICAL ACTIVITY

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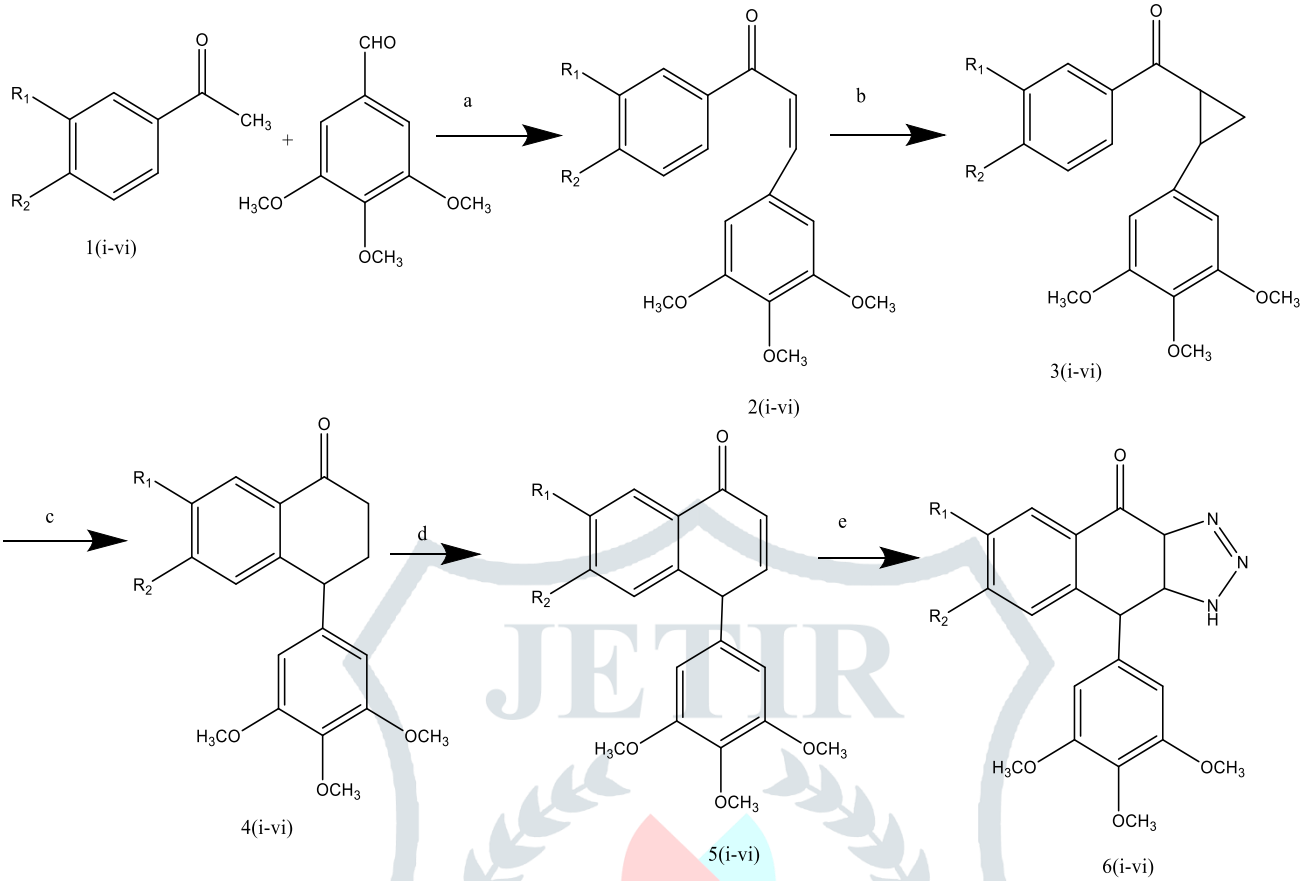
Abstract: Lignans are naturally occurring class of secondary metabolites in plant kingdom that have numerous biological effects in mammals. These compounds contains tetralone moiety, besides of this, the triazoles are the special class of heterocyclic compounds with a broad spectrum of biological activities. Therefore we synthesized triazole derivatives of substituted -9-(3, 4, 5-trimethoxyphenyl) tetralone in presence of Zn catalyst in THF in good yields by chalcone method. All synthesized compounds were characterized by spectral techniques. Further, the compounds were evaluated for microbial activity.

***Keywords*:** Lignans, tetralone, triazole, zinc, azide, Click, Simmon-smith, azide

I.INTRODUCTION

There is well known pharmaceutical application of synthetic drugs is based on the nucleus of the compound such that important nucleus containing compounds are lignans. Lignans are naturally occurring class of secondary metabolites in plant kingdom[1-6]. These compounds contain analogues of tetralone moiety. The tetralone [naphthalene-1(4H) - one] is α, β-unsaturated ketones containing a benzene ring with different substituent's and a cyclohexenone ring like alkene which increase the reactivity[8-11]. Hence modifications in tetralone structure required to reduce its toxicity and enhance its biological activity. besides of this, the triazoles are a special class of heterocyclic compounds with a broad spectrum of biological activities such as antimicrobial, cytotoxic, antihistaminic, anticonvulsant, analgesic, anti-inflammatory, insecticidal, antimycotic, antimycobacterial, anticancer, antiprotozoal, antimalarial and anti-ulcer activity[3,4,12-15]. Therefore the medicinally active and less cytotoxic new nitrogen heterocyclic intermediates of tetralone have been synthesized. The modification of the tetralone structure might enhance the biological activity with favorable solubility and reduced toxicity [16-19].Some synthesized analogs of tetralone showed better antibacterial antifungal activity. The structures of the synthesized new tetralone-triazole compounds were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral data. They have been screened for biological activities.

SCHEME



Compound	R_1	R_2
1-6(i)	OCH_3	OCH_3
1-6(ii)	CH_3	CH_3
1-6(iii)	Cl	OCH_3
1-6(iv)	OH	OH
1-6(v)	NH_2	H
1-6(vi)	NO_2	H

a = KOH/EtOH(aq)
b = CH_2Cl_2, Zn-Cu couple/ diethylether
c = Anhy. $SnCl_2$ / Ac_2O , Dry CH_2Cl_2
d = NBS, MeCN, /PTSA, Ter-potassium butoxide/THF
e = NaN_3 /Zn -metal /THF

EXPERIMENTAL

Material and Methods

All the reagents and chemicals were purchased from Merck chemicals used without further purification. Melting points were taken in open capillary tubes and are uncorrected. TLC is performed with E. Merck precoated silica gel plates (60F-254) with iodine as a spot developing agent. Acme, India silica gel, 60–120 mesh is used for column chromatography. IR spectra in KBr were recorded on Perkin-Elmer model 683 spectrometers. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded $CDCl_3$ solvent containing tetra methyl silane (TMS) as internal references were recorded on Bruker spectrometer;

Elemental analyses were performed on a PerkinElmer 2400. Mass spectra were obtained by Water-QTOF ultima spectrometer. Micro analytical data were obtained by elemental-Vario EL-III

General procedure for synthesis of substituted –[2-(3, 4, 5-trimethoxyphenyl) cyclopropyl] methanone 3(i-vi): A mixture of substituted acetophenone 1(i-vi) 0.02 mole and 3, 4, 5-trimethoxybenzaldehyde 0.02 mole was stirred using magnetic stirrer at room temperature in an ethanolic solution of potassium hydroxide for 2-3 hours. The formed yellowish crystals were filtered off washed with distilled water, dried and recrystallized from ethanol to give the chalcone 2(i-vi). Freshly prepared zinc-copper couple 0.4 mole using Simmons and Smith reaction was taken in a round-bottomed flask which was fitted with a condenser, dropping funnel and magnetic stirrer. 40 cm^3 of ether was added to the dry Zn-Cu couple followed by 10 cm^3 of the dichloromethane. The reaction was started immediately which was indicated by bubbles rising from the couple while the stirred suspension was kept at gentle reflux for three minutes. A mixture of chalcone 2(i-vi), 0.2 mole and the dichloromethane 0.3 mole was added drop wise for 2 hours. The reaction mixture was refluxed for 15-20 hours. After completion of the reaction, the ether solution was decanted slowly and the remaining mixture was poured in water and extracted with ethyl acetate, washed with Na_2CO_3 solution, dried in anhydrous Na_2SO_4, Then, the solvent evaporated to dryness, to give crude product 3(i-vi). The products were recrystallized from ethanol.

(3, 4-dimethoxyphenyl)[2-(3,4,5-trimethoxyphenyl)cyclopropyl]methanone(3i): Colour: Yellow solid. M. P. 92-94^{0}C, Yield 81.3%. IR (KBr): 1723cm^{-1}(C=O), 1387cm^{-1}(Ar-OCH_3).^{1}H- NMR ($CDCl_3$); δ (ppm):1.58-1.83(bt, 2H, CH_2); 2.77(q, 2H, CH_2); 3.24(q, 2H, CH_2); 3.71-3.85 (bs, 15H, OCH_3), 6.79 – 7.62 (m, 5H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ (ppm):14.7, 25.8, 27.1, 56.1, 60.8, 102.4, 110.3, 111.7, 122.1, 130.0, 135.6, 137.6, 149.7, 152.3, 154.2, 192.4. Mass (*m/z*): 372.16, Elemental Analysis (%): For $C_{21}H_{24}O_6$, Calculated: C, 67.73; H, 6.50; O, 25.78. Found: C, 67.85; H, 6.61; O, 25.54.

(3,4-dimethylphenyl)[2-(3,4,5-trimethoxyphenyl)cyclopropyl]methanone(3ii): Colour: Pale yellow solid. M. P. 86-87^{0}C, Yield 79.7%. IR (KBr): 1735cm^{-1}(C=O),1381cm^{-1}(Ar-OCH_3).^{1}H- NMR ($CDCl_3$); δ (ppm):1.58-1.83(bt, 2H, CH_2); 2.77(q, 2H, CH_2); 3.24(q, 2H, CH_2); 2.31-2.34 (bs, 6H, Ar-CH_3), 3.71-3.72 (bs, 9H, OCH_3), 6.65 – 7.70 (m, 5H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ (ppm):14.7, 18.8, 25.8, 27.1, 56.1, 60.8, 102.4, 125.7, 128.9, 130.0, 133.6, 135.6, 137.6, 141.2, 152.3, 192.4. Mass (*m/z*): 341.17, Elemental Analysis (%): For $C_{21}H_{24}O_4$, Calculated: C, 74.09; H, 7.11; O, 18.80. Found: C, 74.14; H, 7.15; O, 18.71.

(3-chloro, 4-methoxyphenyl)[2-(3,4,5-trimethoxyphenyl)cyclopropyl]methanone(3iii): Colour: Brown solid. M. P. 111-113^{0}C, Yield 85.5%. IR (KBr): 1717cm^{-1}(C=O), 1393cm^{-1}(Ar-OCH_3). ^{1}H- NMR ($CDCl_3$); δ (ppm):1.58-1.83(bt, 2H, CH_2); 2.77(q, 2H, CH_2); 3.24(q, 2H, CH_2); 3.71-3.88 (bs, 12H, OCH_3), 6.79 – 7.88 (m, 5H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ (ppm):14.7, 25.8, 27.1, 55.3, 56.1, 60.8, 102.4, 112, 122.5, 127.9, 129.8, 130.4, 135.6, 137.6, 141.2, 152.3, 192.4. Mass (*m/z*): 376.11, Elemental Analysis (%): For $C_{20}H_{21}ClO_5$, Calculated: C, 63.75; H, 5.62; Cl, 9.41; O, 21.23. Found: C, 63.79; H, 5.66; Cl, 9.39; O, 21.16.

(3, 4-dihydroxyphenyl)[2-(3,4,5-trimethoxyphenyl)cyclopropyl]methanone(3iv): Colour: Colouless solid. M. P. 107-109^{0}C, Yield 75.9%. IR (KBr): 1735cm^{-1}(C=O),1399cm^{-1}(Ar-OCH_3), 3210 -3300cm^{-1}(Ar-OH); ^{1}H- NMR ($CDCl_3$); δ (ppm):1.58-1.83(bt, 2H, CH_2); 2.77(q, 2H, CH_2); 3.24(q, 2H, CH_2); 3.71-3.72 (bs, 9H, OCH_3), 6.79 – 7.33 (m, 5H, Ar.-H), 9.48 (s, 2H, Ar-OH), ^{13}C-NMR ($CDCl_3$); δ (ppm):14.7, 25.8, 27.1, 55.3, 56.1, 60.8, 102.4, 114.5, 115.9, 122.8, 130.7, 135.6, 137.6, 145.9, 151.7, 152.3, 192.4.
Mass (*m/z*): 344.13, Elemental Analysis (%): For $C_{19}H_{20}O_6$, Calculated: C, 66.27; H, 5.85; O, 27.88. Found: C, 66.35; H, 5.87; O, 27.78.

(3-aminophenyl)[2-(3,4,5-trimethoxyphenyl)cyclopropyl]methanone(3v): Colour: dark brown solid. M. P. 101-102^{0}C, Yield 77.6%. IR (KBr): 1710cm^{-1}(C=O), 1365cm^{-1}(Ar-OCH_3), 3149cm^{-1}(Ar-NH_2); ^{1}H- NMR ($CDCl_3$); δ (ppm):1.58-1.83(bt, 2H, CH_2); 2.77(q, 2H, CH_2); 3.24(q, 2H, CH_2); 3.71-3.72 (bs, 9H, OCH_3), 5.28 (s, 2H, Ar-NH_2), 6.79 – 7.49 (m, 6H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):14.7, 25.8, 27.1, 55.3, 56.1, 60.8, 102.4, 113.1, 118.8, 119.4, 129.1, 135.6, 137.5, 137.6, 148.3, 152.3, 192.4. Mass (*m/z*):

327.38,Elemental Analysis (%): For $C_{19}H_{20}O_6$, Calculated: C, 69.71; H, 6.47; N, 4.28; O, 19.55. Found: C, 69.77; H, 6.51; N, 4.25; O, 19.47.

(3-nitrophenyl)[2-(3,4,5-trimethoxyphenyl)cyclopropyl]methanone(3vi): Colour: Pale yellow solid. M. P. 126-127^{0}C, Yield 83.3%. IR (KBr):1741cm^{-1}(C=O), 1402cm^{-1}(Ar-OCH_3), 1349cm^{-1}(Ar-NO_2); ^{1}H- NMR ($CDCl_3$); δ (ppm):1.58-1.83(bt, 2H, CH_2); 2.77(q, 2H, CH_2); 3.24(q, 2H, CH_2); 3.71-3.72 (bs, 9H, OCH_3), 6.79 – 8.64 (m, 6H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):14.7, 25.8, 27.1, 56.1, 60.8, 102.4, 122.8, 128.3, 129.5, 134.9, 135.6, 137.6, 147.8, 152.3, 192.4.
Mass (*m/z*): 357.12, Elemental Analysis (%): For $C_{19}H_{19}NO_6$, Calculated: C, 63.86; H, 5.36; N, 3.92; O, 26.86. Found: C, 63.91; H, 5.39; N, 3.90; O, 26.80.

General procedure for synthesis of substituted –4-(3, 4, 5-trimethoxyphenyl) 3,4-dihydronaphthalen-1(2H)-one 4(i-vi): The substituted –[2-(3, 4, 5-trimethoxyphenyl) cyclopropyl] methanone 3(i-vi) (2.2 mmol) were dissolved in dry dichloromethane(25 cm^3) and the mixture of acetic anhydride (5 cm^3) and anhydrous stannic chloride (1 cm^3) was added. The resultant reaction mixture was stirred at 30^{0}C for 3 hours. The completion of reaction was known by TLC. The reaction mixture was poured into 5% HCl solution (20 cm^3), the product was extracted into chloroform. The organic layer was washed with 5% HCl solution followed by water, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give semi solid residue. The product was purified by column chromatography using silica gel (60-120 mesh) as adsorbent and benzene as eluent. The benzene solution was concentrated to a small volume (20 ml) and hexane (100 ml) was added drop wise to give solid compound 4(i-vi) in good yields. They were recrystallised from methanol.

6,7-dimethoxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one (4i):
Colour: Yellow solid. M. P. 99 -100^{0}C, Yield 86.2%. IR (KBr): 1723cm^{-1}(C=O), 1387cm^{-1}(Ar-OCH_3).^{1}H-NMR ($CDCl_3$); δ (ppm):2.23-2.58(bq, 4H, CH_2); 3.71-3.85 (bs, 15H, OCH_3), 3.96(t, 1H, CH); 6.55 – 7.46 (m, 4H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ(ppm): 31.1, 37.5, 45.9, 56.1, 60.8, 106.6, 109.2, 110.6, 127.3, 133.8, 136.7, 137.3, 147.2, 153.4, 154.7, 198.0, Mass (*m/z*): 372.16,
Elemental Analysis (%): For $C_{21}H_{24}O_6$, Calculated: C, 67.73; H, 6.50; O, 25.78. Found: C, 67.77; H, 6.53; O, 25.70.

6,7-dimethyl-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one (4ii): Colour: Yellow solid. M. P. 90-91^{0}C, Yield 75.3%. IR (KBr): 1735cm^{-1}(C=O),1381cm^{-1}(Ar-OCH_3).
^{1}H- NMR ($CDCl_3$); δ (ppm):2.23-2.58(bq, 4H, CH_2); 2.29-2.31(bs, 6H, Ar-CH_3); 3.71-3.72 (bs, 9H, OCH_3), 3.96(t, 1H, CH); 6.55 – 7.69 (m, 4H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm): 18.8, 19.1, 31.1, 37.5, 45.9, 56.1,60.8, 106.6, 124.8, 129.9, 130.9, 134.2, 136.7, 137.3, 137.4, 141.7, 153.4, 198.0, Mass (*m/z*): 340.17, Elemental Analysis (%): For $C_{21}H_{24}O_4$, Calculated: C, 74.09; H, 7.11; O, 18.80. Found: C, 74.15; H, 7.13; O, 18.72.

7-chloro-6-methoxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one(4iii):
Colour: Pale brown solid. M. P. 111-113^{0}C, Yield 85.5%. IR (KBr): 1717cm^{-1}(C=O), 1393cm^{-1}(Ar-OCH_3). ^{1}H- NMR ($CDCl_3$); δ (ppm):2.23-2.58(bq, 4H, CH_2); 3.71-3.88 (bs, 12H, OCH_3), 3.96(t, 1H, CH); 6.55 – 7.87 (m, 4H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):31.1, 37.5,45.9, 55.3, 56.1, 60.8, 106.6, 113.6, 120.0, 127.7,130.8, 136.7, 137.3, 137.4,153.4, 159.5, 198.0, Mass (*m/z*): 376.11, Elemental Analysis (%): For $C_{21}H_{24}O_4$, Calculated: C, 63.75; H, 5.62; Cl, 9.41; O, 21.23. Found: C, 63.81; H, 5.65; Cl, 9.38; O, 21.16.

6, 7-dihydroxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one (4iv): Colour: Colouless solid. M. P. 115-116^{0}C, Yield 71.4%. IR (KBr): 1735cm^{-1}(C=O),1399cm^{-1}(Ar-OCH_3), 3210 -3300cm^{-1}(Ar-OH); ^{1}H- NMR ($CDCl_3$); δ (ppm):2.23-2.58(bq, 4H, CH_2); 3.71-3.72 (bs, 9H, OCH_3), 3.96(t, 1H, CH); 6.55 – 7.10 (m, 4H, Ar.-H), 9.48 (s, 2H, Ar.-OH), ^{13}C-NMR ($CDCl_3$); δ (ppm):31.1, 37.5,45.9, 56.1,60.8, 106.6, 113.4, 117.1, 128.0, 134.5,136.7, 137.3, 151.7,153.3, 153.4,198.0**,** Mass (*m/z*): 344.13, Elemental Analysis (%): For $C_{19}H_{20}O_6$, Calculated: C, 66.27; H, 5.85; O, 27.88. Found: C, 66.34; H, 5.87; O, 27.79.

7-amino-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one (4v): Colour: light brown solid. M. P. 107-108^{0}C, Yield 79.8%. IR (KBr): 1710cm^{-1}(C=O), 1365cm^{-1}(Ar-OCH_3), 3149cm^{-1}(Ar-NH_2); ^{1}H-NMR ($CDCl_3$); δ (ppm):2.23-2.58(bq, 4H, CH_2); 3.71-3.72 (bs, 9H, OCH_3), 3.96(t, 1H, CH); 5.28 (s, 2H, Ar.-NH_2), 6.55 – 7.25 (m, 5H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):31.1, 37.5,45.6, 56.1,60.8, 106.6, 113.6, 113.6, 120.1, 128.9, 130.5, 134.8, 136.7, 137.3, 145.8, 153.4, 198.0, Mass (*m/z*): 327.38, Elemental Analysis (%): For $C_{19}H_{20}O_6$, Calculated: C, 69.71; H, 6.47; N, 4.28; O, 19.55. Found: C, 69.75; H, 6.52; N, 4.26; O, 19.47.

7-nitro-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one (4vi): Colour: Light yellow solid. M. P. 131-132^{0}C, Yield 80.1%. IR (KBr):1741cm^{-1}(C=O), 1402cm^{-1}(Ar-OCH_3), 1349cm^{-1}(Ar-NO_2);^{1}H-NMR ($CDCl_3$); δ (ppm):2.23-2.58(bq, 4H, CH_2); 3.71-3.72 (bs, 9H, OCH_3), 3.96(t, 1H, CH); 6.55 – 8.49 (m, 5H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):31.1, 37.5, 45.6, 56.1,60.8, 106.6, 1.6, 122.9, 128.8, 129.0, 134.9, 136.7, 137.3, 145.3, 146.6, 153.4, 198.0,
Mass (*m/z*): 357.36, Elemental Analysis (%): For $C_{19}H_{19}NO_6$, Calculated: C, 63.86; H, 5.36; N, 3.92; O, 26.86. Found: C, 63.91; H, 5.39; N, 3.90; O, 26.80.

General procedure for synthesis of substituted –4-(3, 4, 5-trimethoxyphenyl) naphthalen-1(4H)-one 5(i-vi): A solution of compound 4(i-vi) (1.3g, 4 mmol) in acetonitrile (50 cm^3) and p-toluene sulphonic acid(1.1g, 6mmol) was heated at 65^{0}C, N-bromosuccinimide (0.71g, 4mmol) was added slowly for 1 hour and the reaction mixture was stirred for 4-5 hours. After completion of reaction, reaction mixture was diluted with ethyl acetate (100 cm^3) and washed with water twice. The ethyl acetate layer was separated and evaporated to get solid compound. Further these compounds were mixed with potassium tertiary butoxide (0.317g, 3.3mmol) in THF (25 cm^3) and refluxed at room temperature under nitrogen atmosphere for 8 hrs. The completion of the reaction was monitored by TLC which showed the absence of starting material in the reaction mixture. After the completion of reaction, the mixture was poured into water and extracted with ethyl acetate, washed with Na_2CO_3 solution, dried with anhydrous Na_2SO_4, Then, the solvent evaporated to dryness, to gave crude product 6(i-vi). The products were recrystallized using ethanol.

6,7-dimethoxy-4-(3,4,5-trimethoxyphenyl)naphthalen-1(4H)-one (5i): Colour: Pale yellow solid. M. P. 117-119^{0}C, Yield 69.7%. IR (KBr): 1688cm^{-1}(C=O), 2940-3110cm^{-1}(Ar-CH), 3070-3078cm^{-1}(C=C). ^{1}H-NMR ($CDCl_3$); δ (ppm): 3.71-3.85 (bs, 15H, OCH_3), 4.74(d, 1H, CH); 6.81 – 7.35 (m, 6H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):47.4, 56.1, 60.8, 104.3, 106.7, 113.8, 126.3, 131.9, 134.6,136.2,136.7,139.7,147.8,153.4,156.1,183.7**,** Mass (*m/z*): 370.14, Elemental Analysis (%): For $C_{21}H_{22}O_6$, Calculated: C, 68.10; H, 5.99; O, 25.92. Found: C, 68.15; H, 6.03; O, 25.82.

6,7-dimethyl-4-(3,4,5-trimethoxyphenyl)naphthalen-1(4H)-one (5ii): Colour: Yellow solid. M. P. 77-78^{0}C, Yield 70.5%. IR (KBr): 1731cm^{-1}(C=O), 1379 cm^{-1}(Ar-OCH_3). ^{1}H- NMR ($CDCl_3$); δ (ppm): 2.29-2.31 (bs, 6H, Ar-CH_3),3.71-3.72 (bs, 9H, OCH_3), 4.74(d, 1H, CH); 6.81 – 7.62 (m, 6H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):18.8, 19.1, 47.4, 56.1, 60.8, 104.3, 129.9, 130.5, 134.6, 134.8, 135.5, 136.2, 139.7, 143.1, 153.4, 183.7, Mass (*m/z*): 338.15, Elemental Analysis (%): For $C_{21}H_{22}O_4$, Calculated: C, 74.54; H, 6.55; O, 18.91. Found: C, 74.61; H, 6.59; O, 18.80.

7-chloro-6-methoxy-4-(3,4,5-trimethoxyphenyl)naphthalen-1(4H)-one (5iii): Colour: brown solid. M. P. 121-123^{0}C, Yield 86.9%. IR (KBr): 1721cm^{-1}(C=O), 1387cm^{-1}(Ar-OCH_3). ^{1}H- NMR ($CDCl_3$); δ (ppm): 3.71-3.88 (bs, 12H, OCH_3), 4.74(d, 1H, CH); 6.81 – 7.80 (m, 6H, Ar.-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):47.4, 55.3, 56.1, 60.8, 104.3, 114.2, 120.6, 126.7, 131.4, 134.6, 136.2, 136.7, 137.7, 139.7, 153.4, 160.3, 183.7, Mass (*m/z*): 374.09, Elemental Analysis (%): For $C_{20}H_{19}ClO_5$, Calculated: C, 64.09; H, 5.11; Cl, 9.46; O, 21.34. Found: C, 64.14; H, 5.15; Cl, 9.43; O, 21.28.

6,7-dihydroxy-4-(3,4,5-trimethoxyphenyl)naphthalen-1(4H)-one (5iv): Colour: Colouless solid. M. P. 124-126^{0}C, Yield 77.4%. IR (KBr): 1730cm^{-1}(C=O),1395cm^{-1}(Ar-OCH_3), 3210 -3300cm^{-1}(Ar-OH); ^{1}H-NMR ($CDCl_3$); δ (ppm): 3.71-3.72 (bs, 9H, OCH_3), 4.74(d, 1H, CH); 6.81 – 7.03 (m, 6H, Ar-H), 9.48 (bs, 2H, Ar.-OH), ^{13}C-NMR ($CDCl_3$); δ (ppm):47.4, 56.1, 60.8, 104.3, 112.1. 115.8, 127.0, 132.6, 134.6, 136.2,

136.7, 139.7, 151.3, 152.0, 153.4, 183.7, Mass (*m/z*): 342.11, Elemental Analysis (%): For $C_{19}H_{18}O_6$, Calculated: C, 66.66; H, 5.30; O, 28.04. Found: C, 66.72; H, 5.33; O, 27.95.

7-amino-4-(3,4,5-trimethoxyphenyl)naphthalen-1(4H)-one (5v): Colour: Brown solid. M. P. 111-113^{0}C, Yield 76.9%. IR (KBr): 1715cm^{-1}(C=O), 1361cm^{-1}(Ar-OCH_3), 3142cm^{-1}(Ar-NH_2);
1H- NMR ($CDCl_3$); δ (ppm): 3.71-3.72 (bs, 9H, OCH_3), 4.74(d, 1H, CH); 5.28 (s, 2H, Ar-NH_2), 6.81 – 7.48 (m, 7H, Ar-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):47.1, 56.1, 60.8, 104.3, 114.7, 121.5, 128.6, 129.5, 133.8, 134.6, 136.2, 136.7, 139.7, 146.4, 153.4, 183.7, Mass (*m/z*): 325.13,
Elemental Analysis (%): For $C_{19}H_{19}NO_4$, Calculated: C, 70.14; H, 5.89; N, 4.31; O, 19.67. Found: C, 70.18; H, 5.91; N, 4.29; O, 19.62.

7-nitro-4-(3,4,5-trimethoxyphenyl)naphthalen-1(4H)-one (5vi): Colour: Yellowish solid. M. P. 143-145^{0}C, Yield 83.4%. IR (KBr):1737cm^{-1}(C=O), 1400cm^{-1}(Ar-OCH_3), 1344cm^{-1}(Ar-NO_2); ^{1}H- NMR ($CDCl_3$); δ (ppm): 3.71-3.72 (bs, 9H, OCH_3), 4.74(d, 1H, CH); 6.81 – 8.45 (m, 7H, Ar-H), ^{13}C-NMR ($CDCl_3$); δ (ppm):47.1, 56.1, 60.8, 104.3, 124.0, 129.6, 130.2, 133.9, 134.6, 136.2, 136.7, 139.7, 144.7, 145.9, 153.4, 183.7**,** Mass (*m/z*): 355.11, Elemental Analysis (%): For $C_{19}H_{17}NO_6$, Calculated: C, 64.22; H, 4.82; N, 3.94; O, 27.01. Found: C, 64.29; H, 4.86; N, 3.93; O, 26.92.

General procedure for synthesis of substituted –9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d][1,2,3] triazol-4-one 6(i-vi): A solution of compound 5(i-vi) (0.9g, 3 mmol) in THF (25 cm^3) and sodium azide(1.0 g, 3mmol) was refluxed at 75^{0}C, in presence of powder zinc metal for 11-12 hours. The completion of the reaction was monitored by TLC. After Completion of the reaction, the reaction mixture was poured into water (100 cm^3) and extracted with ethyl acetate (50 cm^3). The evaporation of the ethyl acetate layer gave products 6(i-vi) in moderate percentage of yield.

6,7-Dimethoxy-9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d][1,2,3] triazol-4-one (6i): Colour: Yellow solid. M. P. 122-123^{0}C, Yield 68.5%. IR (KBr): 1721cm^{-1}(C=O), 1617cm^{-1}(N=N), 1388cm^{-1}(Ar-OCH_3).^{1}H- NMR ($CDCl_3$); δ (ppm):1.5(s, 1H, NH); 2.9(d, 1H, CH, adj. N=N); 3.71-3.85 (bs, 15H,OCH_3), 3.9-3.91 (d, 2H, CH_2, adj NH); 6.55 – 7.46 (m, 4H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ (ppm): 38.6, 56.1, 60.8, 70.8, 78.6, 106.6, 109.2, 110.5, 127.3, 133.8, 136.7, 137.3, 147.2, 153.4, 154.7, 197.6, Mass (*m/z*): 413.16, Elemental Analysis (%): For $C_{21}H_{23}N_3O_6$, Calculated: C, 61.01; H, 5.61; N, 10.16; O, 23.22. Found: C, 60.88; H, 5.66; N, 10.18; O, 23.28.

6,7-Dimethyl-9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d][1,2,3] triazol-4-one (6ii): Colour: White solid. M. P. 117-119^{0}C, Yield 63.3%. IR (KBr): 1735cm^{-1}(C=O), 1645cm^{-1}(N=N), ^{1}H-NMR ($CDCl_3$); δ (ppm): 1.5(s, 1H, NH); 2.29-2.31(bs, 6H, CH_3); 2.9(d, 1H, CH, adj. N=N); 3.71-3.72 (bs, 9H, OCH_3), 3.9-3.91 (d, 2H, CH_2, adj NH) and 6.55 – 7.69 (m, 4H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ (ppm): 18.8, 19.1, 38.6, 56.1, 60.8, 70.8, 78.6, 106.6, 124.8, 129.9, 130.9, 134.2, 136.7, 137.3, 137.4, 141.7, 153.4, 197.6, Mass (*m/z*): 381.17, Elemental Analysis (%): For $C_{21}H_{23}N_3O_4$, Calculated: C, 66.13; H, 6.08; N, 11.02; O, 16.78. Found: C, 66.29; H, 6.14; N, 11.10; O, 16.47.

6-chloro-7-methoxy-9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d] [1,2,3]triazol-4-one (6iii): Colour: Yellowish solid. M. P. 113-115^{0}C, Yield 69.1%. IR (KBr): 1685cm^{-1}(C=O), 1631cm^{-1}(N=N), 1040cm^{-1}(Ar-Cl), 1388cm^{-1}(Ar-OCH_3), ^{1}H- NMR ($CDCl_3$); δ (ppm): 1.5(s, 1H, NH); 2.9(d, 1H, CH, adj. N=N); 3.71-3.88 (bs, 12H, OCH_3), 3.9-3.91 (d, 2H, CH_2, adj NH) and 6.55 – 7.87 (m, 4H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ (ppm):38.6,55.3,56.1,60.8,70.8,78.6,106.6,113.6,120,127.7,130.3,136.7,137.3,139.6,153.4,159.5,197.5.
Mass (*m/z*): 417.11, Elemental Analysis (%): For $C_{20}H_{20}ClN_3O_5$, Calculated: C, 57.49; H, 4.82; Cl, 8.48; N, 10.06; O, 19.14. Found: C, 57.58; H, 4.85; Cl, 8.43; N, 10.11; O, 19.03.

6,7-dihydroxy-9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d][1,2,3] triazol-4-one (6iv): Colour: colourless solid. M. P. 85-86^{0}C, Yield 81.4%. IR (KBr): 1392cm^{-1}(Ar-OCH_3), 1679cm^{-1}(C=O), 1637cm^{-1}(N=N), 3482-3590cm^{-1}(Ar-OH), ^{1}H- NMR ($CDCl_3$); δ (ppm): 1.5(s, 1H, NH); 2.9(d, 1H, CH, adj. N=N); 3.71-3.72 (bs, 9H, OCH_3), 3.9-3.91 (d, 2H, CH_2, adj NH) and 6.55 – 7.10 (m, 4H, Ar.-H); 9.48 (bs, 3H, Ar-OH). ^{13}C-NMR ($CDCl_3$); δ (ppm):38.6, 56.1, 60.8, 70.8, 78.6, 106.6, 113.4, 117.1, 128.0,

134.5, 136.7, 137.3, 151.7, 153.3, 153.4, 197.6, Mass (*m/z*): 385.3, Elemental Analysis (%): For $C_{19}H_{19}N_3O_6$, Calculated: C, 59.22; H, 4.97; N, 10.90; O, 24.91. Found: C, 59.31; H, 4.95; N, 10.97; O, 24.77.

6-amino-9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d][1,2,3]triazol-4-one (6v): Colour: Brown solid, M. P. 105-106^{0}C, Yield 59.1%. IR (KBr): 1396 cm^{-1}(Ar-OCH_3), 1681cm^{-1}(C=O), 1635cm^{-1}(N=N), 3470-3500cm^{-1}(Ar-NH_2), ^{1}H- NMR ($CDCl_3$); δ (ppm): 1.5(s, 1H, NH); 2.9(d, 1H, CH, adj. N=N); 3.71-3.72 (bs, 9H, OCH_3), 3.90-3.91 (d, 2H, CH_2, adj NH); 5.28(s, 2H, Ar-NH_2); 6.55 – 7.25 (m, 5H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ(ppm): 38.3, 56.1, 60.8, 70.8, 78.6, 106.6, 113.6, 120.1, 128.9, 130.5, 134.8, 136.7, 137.3, 145.8, 153.4, 197.6, Mass (*m/z*): 368.15, Elemental Analysis (%): For $C_{19}H_{20}N_4O_4$, Calculated: C, 61.95; H, 4.45; N, 15.21; O, 17.37. Found: C, 61.91; H, 4.39; N, 15.26; O, 17.44.

6-amino-9-(3,4,5-trimethoxyphenyl)-1,3a,9,9a-tetrahydro-4H-naphtho[2,3-d][1,2,3]triazol-4-one (6vi): Colour: Yellowish solid, M. P. 110-112^{0}C, Yield 65.9%. IR (KBr): 1389 cm^{-1}(Ar-OCH_3), 1679cm^{-1}(C=O), 1631cm^{-1}(N=N), 1465cm^{-1}(Ar-NO_2), ^{1}H- NMR ($CDCl_3$); δ (ppm): 1.5(s, 1H, NH); 2.9(d, 1H, CH, adj. N=N); 3.71-3.72 (bs, 9H, OCH_3), 3.90-3.91 (d, 2H, CH_2, adj NH); 6.55 – 7.49 (m, 5H, Ar.-H). ^{13}C-NMR ($CDCl_3$); δ(ppm): 38.3, 56.1, 60.8, 70.8, 78.6, 106.6, 122.9, 128.8, 129.0, 134.9, 136.7, 137.3, 145.3, 146.6, 153.4, 197.6, Mass (*m/z*): 398.12,
Elemental Analysis (%): For $C_{19}H_{18}N_4O_6$, Calculated: C, 57.28; H, 4.55; N, 14.06; O, 24.10. Found: C, 57.37; H, 4.59; N, 14.01; O, 24.03.

Antibacterial Activity

The purified compounds 6(i-vi) were screened for their antibacterial activity by using disc diffusion method. The nutrient agar broth prepared by the usual method, was inoculated aseptically with 0.5 cm^3 of 24 hours old subculture of Staphylococcus aureus and Escherichia coli in separate conical flask at 35^0 - 45^{0}C and mixed well by gentle shaking. About 25 cm^3 of the contents of the flask were poured and evenly spread in Petridis (90 mm in diameter) and allowed to set for two hrs. The cups (8mm in diameter) were formed by the help of borer in agar medium and filled with 0.1 ml (1mg/ml) solution of sample in acetone.

Antifungal Activity

Trichoderma harzianum, Aspergillus niger, Colletotrichum capsici, Aspergillus tamari, Aspergillus flavus, Alternaria solani, and Penicillium oxalicum were employed for testing antifungal activity by disc diffusion method. The culture was maintained on sabouraud dextrose agar slants. Sterilized Sabouraud dextrose agar medium was inoculated with 72 hr old 0.5 cm^3 suspension of fungal spores in a separate flask. About 25 cm^3 of the inoculated medium was evenly spreader in a sterilized Petridis and allowed to set for 4 hr. The cups (8 mm in diameter) were punched in Petridis and loaded with 0.1 ml (2 mg/cm^3) of solution of sample in acetone. The plates were incubated at 25-27^{0}C for 7 days. After the completion of incubation period, the zones of inhibition growth is in the form of diameter in mm was measured. Along the test solution in each Petridis one cup was filled up with nystatin as standard and another cup was filled up with distilled water which acts as negative control.

Table 1: Antimicrobial activity of the synthesized compounds 6(i-vi)

Sl. No.	Name of the microorganism	Zone of inhibition in mm							
		6i	6ii	6iii	6iv	6v	6vi	Std.	Negative control
1	Staphylococcus aureus	18	20	17	26	22	24	22	15
2	Escherichia coli	33	23	25	29	31	30	28	15

3	Trichoderma harzianum	13	10	15	18	16	14	12	10
4	Aspergillus niger	17	20	21	16	22	24	11	10
5	Collectotrichum capsici	19	18	20	19	23	22	13	10
6	Aspergillus tammari	20	18	13	19	24	22	16	10
7	Aspergillus flavus	13	22	20	18	17	18	15	10
8	Alternria solani	16	19	12	15	14	17	21	10
9	Penicillium oxalicum	19	14	18	21	13	19	22	10

Standard – Ciprofloxacin 5µg /dics for bacteria; Nystatin100 units /disc for fungi.

RESULTS AND DISCUSSION:

Substituted 2(i-vi) were prepared in good yields by Claisen-Smidth condensation reaction of substituted acetophenone 1(i-vi) with 3, 4, 5-trimethoxybenzaldehyde in the presence of potassium hydroxide as base and water-ethanol mixture as solvent. Substituted chalcone containing α, β-unsaturated compounds 2(i-vi) were prepared in good yields. Cyclopropyl ketones 3(i-vi) was prepared in good yields by simmon smith reaction of chalcone. Tetralone ester intermediates 4(i-vi) was prepared in good yields by the intra-molecular Freidel-Crafts alkylation reaction of cyclopropyl ketones 3(i-vi) in the presence of anhydrous Stannic chloride and acetic anhydride in dry dichloromethane. The intermediate compound 5(i-vi) was obtained in good yield by heating compound 4(i-vi) in p-toluene sulphonic acid in presence of acetonitrile at 65^0C and the mixture was stirred with N-bromosuccinamide for 4-5 hrs. Further this mixture was mixed with tertiary potassium butoxide in tetrahydrofuran and reflux for 8 hours. We considered these substituted tetralone as intermediate compounds for our target compounds, triazole substituted tetralone 6(i-vi). These compounds were prepared in moderate yield by Click reaction method using sodium azide in THF with zinc metal as catalyst and the mixture was stirred at 85^0C (under air atmosphere) then followed by acid hydrolysis. The formation of product was checked by TLC. After the completion of reaction, the mixture was poured into water and extracted with ethyl acetate, washed with Na_2CO_3 solution, dried with anhydrous Na_2SO_4, Then, the solvent evaporated to dryness, to gave crude product 6(i-vi). The products were recrystallized using ethanol. The structure of tetralone triazole was confirmed by IR, ^{1}H NMR and mass spectral data. The synthesized compounds were conducted for microbial activity. The results were summarized in **table 1**.

CONCLUSION

We succeeded in the synthesis of triazole derivatives of substituted tetralone and their microbial activities. All synthesized compounds were very active against fungi trichoderma harzianum and aspergillus flavus , others are remains inactive compared to the standard nystatin and some of the compounds were active against bacteria Staphylococcus aureus and Escherichia coli compared to the standard Ciprofloxacin which is already available in the market.

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