International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 617-625 www.ijprajournal.com ISSN: 2456-4494

Synthesis, Characterization of Substituted tert-butyl 4-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)piperazine-1-carboxylate and Evaluation of their Anti-Microbial Activity

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Date of Submission: 10-11-2023 Date of Acceptance: 25-11-2023

ABSTRACT: In an attempt to find potential anti-microbial medications (anti-bacterial, anti-fungal), a series of novel tert-butyl 4-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)piperazine-1-carboxylate (5a-I) were produced in good yields utilizing suitable reaction procedures. Using mass spectrum analysis, ^{1}H NMR, ^{13}C NMR, and infrared spectra, their chemical structures were characterised. Anti-microbial (anti-bacterial, anti-fungal) activity of all the compounds 5a-l have been evaluated and found **5b**, **5c**, **5h**, and **5i** have exhibited good anti-microbial effect in compared to the popular medications streptomycin and Amphotericin I, whereas the remaining compounds shown moderate activity.

KEYWORDS: 1, 2, 3 triazole linked indole hybrids, anti-cancer activity, and Anti-microbial Activity.

I. INTRODUCTION

Benzotriazole (BTA) is a heterocyclic compound with the chemical formula C6H5N3. The ring's five members are successively composed of three nitrogen atoms. This bicyclic molecule is conceptualized as the linked rings of the aromatic compounds triazole and benzene. Its numerous applications include the inhibition of copper corrosion, a solid that ranges from white to light brown[1]. It is a bicyclic heterocyclic chemical compound made up of two rings: benzene and 1,2,3-triazole. It has nitrogen in it. An inhibitor that is frequently used in the multilayer copper interconnect CMP process is BTA. It can greatly reduce the amount of copper surface corrosion and help to smooth the wafer surface after CMP[1-5].

Benzotriazole is slightly water soluble, has a restricted sorption tendency, and is not readily degraded. As a result, only a small percentage of it is removed in wastewater treatment plants, and a large amount ends up in surface waterways like rivers and lakes. Though it exhibits some antiestrogenic properties, there are believed to be few health hazards and low toxicity for humans[6,7].

Considered a physiologically preferable scaffold, the most prominent bicyclic heterocyclic molecule has a pyridine ring connected to a triazole ring. It is found in many natural products, including plants, animals, alkaloids, and microbial hormones [8,9,10].

It exhibits a wide range of pharmacological properties, such as anti–inflammatory, anti–diabetic, antioxidant, antiviral, antifungal, antibacterial, anticholinesterase, and anti–inflammatory [10–12].

Examples of natural anticancer drugs with pyridine and triazole ring as their backbones include vincristine and vinblastine, which are extracted from Catharanthus roseus and used as antimitotic medicines to treat breast cancer, Kaposi's sarcoma, Hodgkin's disease, and non-Hodgkin's lymphoma [13-16]. The marine alkaloid eudistomin K (1) inhibits the P-388 tumor cell line with an IC50 range of 0.01 µg/mL[17-20].

II. RESULTS AND DISCUSSION

The synthetic route for the compounds substituted tert-butyl 4-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)piperazine-1-carboxylate (5a-I) was outlined **scheme-1**. The benzonitrile conjugate

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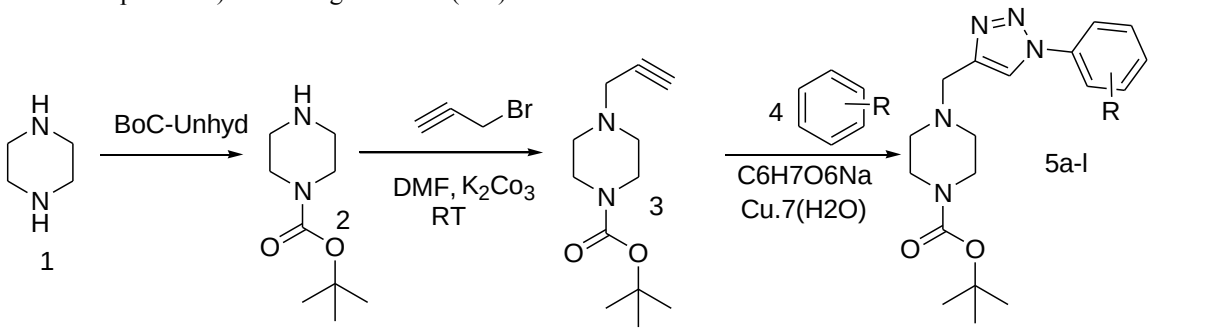
1,2,3-triazole derivatives were synthesized from commercially available moieties. The synthesis of starting compounds was carried out piperazine **(1)** in the vicinity of dichloro methane (DCM) as a solvent. Stirr the reaction mixture in cool condition at 0^0C. Add TEA of 1 equivalence, DMAP of 0.01 equivalence then add BoC unhydride of 1.2 equivalence dropwise and product **(2)** confirmed by TLC. After that compound-2 and DMF as a solvent, add K_2CO_3 (2.5 eq) as a base, and Propargyl Bromide(PBr) 1.2eq as a reactant stir the reaction mixture for about 4-5 hours in room temperature. Check the TLC (20% EtOAc) if starting material (SM) was completed than quinch with ice, liquid is formed extract with DCM, Distil the organic layer, liquid is formed (3). (Yield 78%). Now compound-3 in DMF as a solvent, add $CuSO_4.7H_2O$ (2 ml) Colour changed can be observed, add sodium Ascorbate ($Na_2S_2O_3$) (2ml) solid appearance is observed, than add different substituted aromatic azides 1.2eq, stir reaction mixture for about 16-18 hours at room temperature, Check the TLC (50% EtOAc in pet ether) if starting material (SM) was completed than quinch with ice, and filter with reaction filtrate and wash with PET ether solid is formed substituted 4-(1-Phenyl-1H-[1,2,3]triazol-4-ylmethyl)-piperazine-1-carboxylic acid tert-butyl ester derivatives (5 a-l) (Yeild 76-86%).

Data from infrared spectroscopy (IR), ^{13}C NMR, ESI-MS, and ^{1}H NMR were used to characterize each and every structure of the newly synthesized compounds. The Proton nuclear magnetic resonance (^{1}H NMR) spectrum of descriptive compound 5**a-l** (dissolved in $CDCl_3$) exhibited the characteristic singlet appearance of the triazole proton at 8.18-9.28 ppm, a singlet appearance of the oxygen-attached methylene proton (O–CH_2) at 5.39-5.78 ppm. The carbon of the triazole ring showed up in the ^{13}C NMR spectra at a frequency of 121.74 ppm, whereas the carbonyl carbon appeared at a frequency of 180.01 to 200.00 ppm, and all of the other protons and carbons resonated in the expected region.

Scheme1.



a=H, b=p-NO2, c=o-Cl, d=p-Cl, e=p-Br, f=o-OCH3, g=p-OCH3, h=m-COCH3, i=m-F, j=o-CH3, k=p-CH3, l=p-OH

Scheme 1: The synthetic route of substituted piperadine attached benzotriazole hybrids

III. BIOLOGICAL EVALUATION:

III.I. ANTI-MICROBIAL ACTIVITY:

III.I.I. ANTIBACTERIAL ACTIVITY OF COMPOUNDS 5(A-L)

By using the disc diffusion method, the antibacterial activity of all five newly synthesized compounds (a–l) was evaluated against three representative Gram-positive bacteria (Bacillus Subtilis, MTCC 441, Bacillus Sphaericus, MTCC 11, and Staphylococcus Aureus, MTCC 96), as well as three representative Gram-negative bacteria (Pseudomonas Aeruginosa, MTCC 741, Klobsinella Aerogenes, MTCC 39, and Chromobacterium Violaceum, MTCC 2656). Standard inoculums (1-2×107 c.f.u/mL 0.5 Mc Farland standards) were applied to the surface of sterile agar plates for the antibacterial assay, and a sterile glass spreader was utilized to ensure uniform dispersion of the inoculums. The discs, which had a diameter of 6.26 mm, were made using Whatman No. 1 filter paper and dried at 140 °C for one hour. Nutrient agar medium was added to the sterile discs that had previously been soaked in a known concentration of the test chemicals. After being inverted, the plates were incubated at 37 °C for 24 hours. Table 1 displays the results of measuring and comparing the

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mean inhibition zones with the common medication streptomycin.

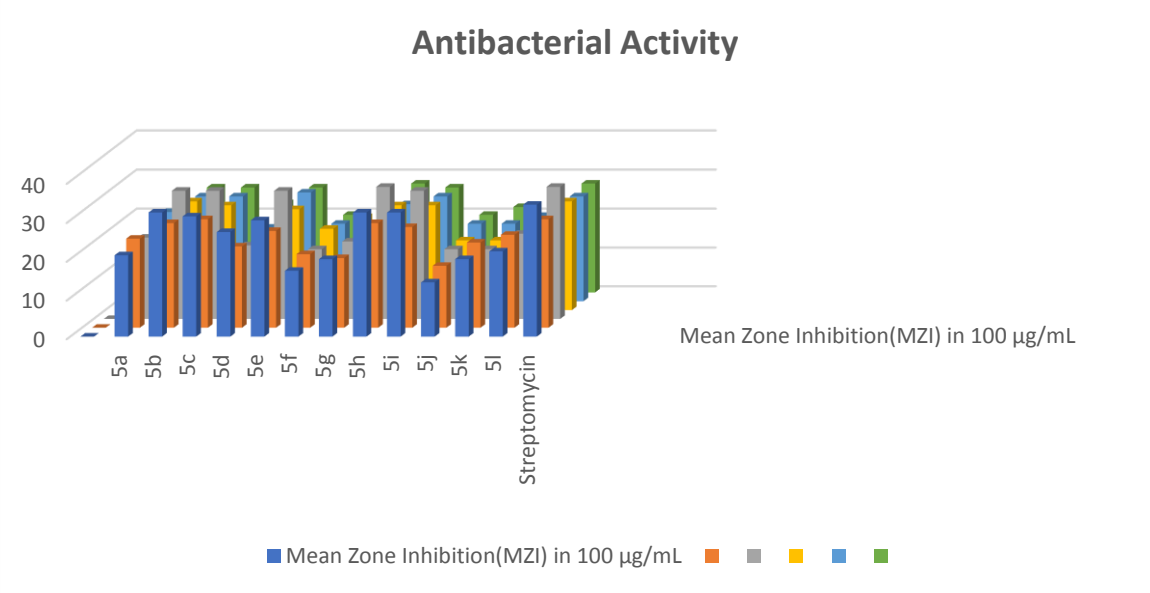
Nearly all of the compounds **5(a-l)** are active and exhibit moderate to good antibacterial activity, according to an analysis of antibacterial screening data. Those with good activity were **5b, 5e, 5f,** and **5l** (Table 1). The activity of the remaining chemicals ranged from good to moderate.

Table-1:ANTIBACTERIAL ACTIVITY OF COMPOUNDS 5(a-l)

Compound	Mean Zone Inhibition(MZI) in 100 µg/mL					
	B. Subtilis	***B. Sphaericus***	***S. Aureus***	***P. aeruginosa***	***K. aerogenes***	***C. violaceum***
5a	21	23	21	21	23	21
5b	**32**	**27**	**33**	**28**	**27**	**27**
5c	**31**	**28**	**33**	**27**	**27**	**27**
5d	27	21	19	17	19	23
5e	**30**	**25**	**33**	**26**	**28**	**27**
5f	17	19	18	21	20	20
5g	20	18	20	24	20	18
5h	**32**	**27**	**34**	**27**	**25**	**28**
5i	**32**	**26**	**33**	**27**	**27**	**27**
5j	14	16	18	18	20	20
5k	20	22	18	18	20	22
5l	22	24	22	21	22	23
Streptomycin	**34**	**28**	**34**	**28**	**27**	**28**

Streptomycin (50 µg/disc) was used as positive reference and compounds **5(a-l)** (50 µg/disc).[a] Values are mean (n=3)

GRAPHICAL FLOW CHAT ANTIBACTERIAL ACTIVITY OF COMPOUNDS 5(a-l)



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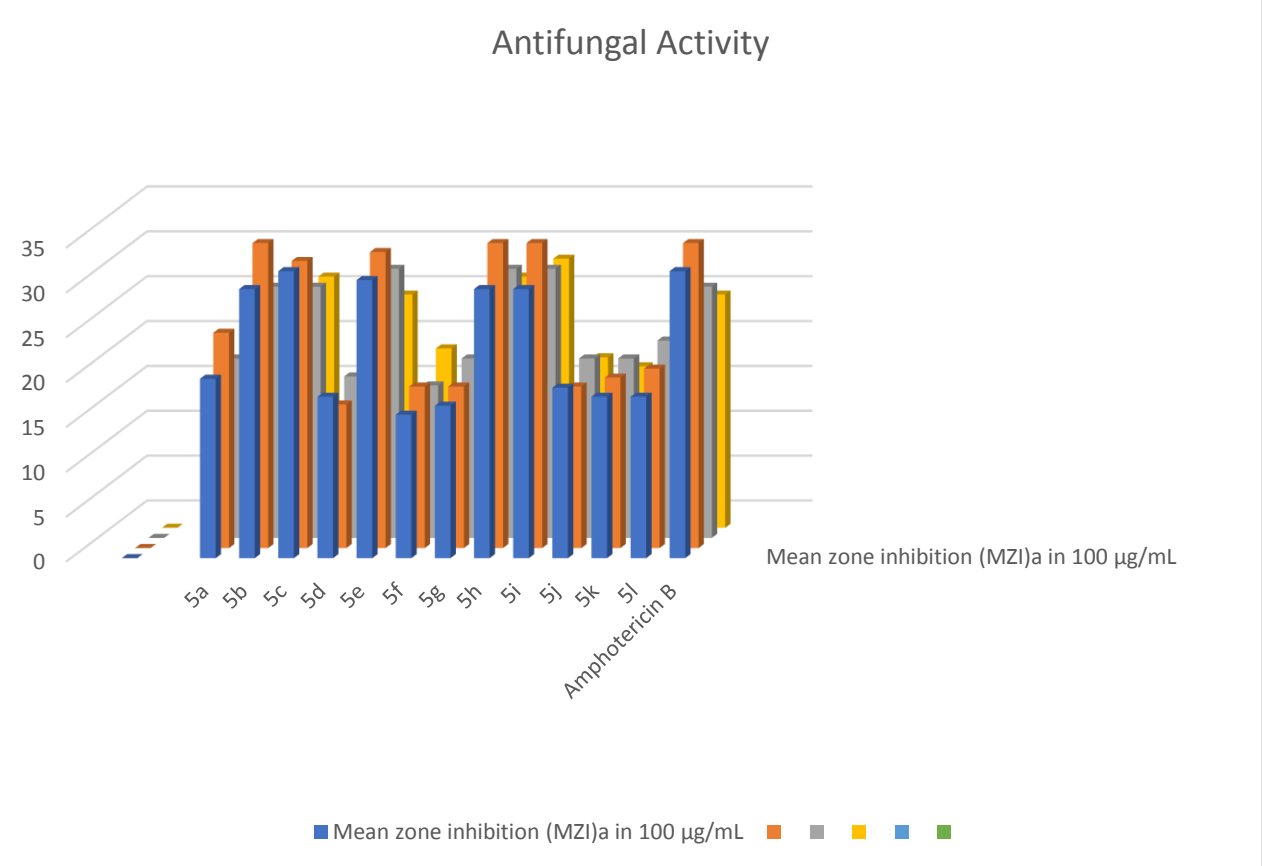
III.I.I. II. ANTIFUNGAL ACTIVITY OF COMPONDS 5(a-l)

Compound	Mean zone inhibition (MZI)[a] in 100 µg/mL			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagrophytes*
5a	20	24	20	18
5b	**30**	**34**	**28**	**26**
5c	**32**	**32**	**28**	**28**
5d	18	16	18	20
5e	**31**	**33**	**30**	**26**
5f	16	18	17	20
5g	17	18	20	19
5h	**30**	**34**	**30**	**28**
5i	**30**	**34**	**30**	**30**
5j	19	18	20	19
5k	18	19	20	18
5l	18	20	22	20
Amphotericin B	**32**	**34**	**28**	**26**

Amphotericin B (100 µg/disc) was used as positive reference and compounds 5**(a-l)** (100 µg/disc).

GRAPHICAL FLOW CHAT OF ANTI FUNGAL ACTIVITY (5 A-L)



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IV.CONCLUSION

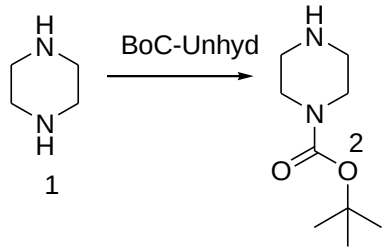
To sum up, we have created a range of unique derivatives of Substituted 4-(1-Phenyl-1H-[1,2,3]triazol-4-ylmethyl)-piperazine-1-carboxylic acid tert-butyl ester derivatives **(5a–l)** and evaluated their anti-microbial activity (anti-bacterial, anti-fungal activity) using IR, 13C NMR, ESI-MS, and 1H NMR. The inclusion of **(5b)** 4-Nitrophenyl, **(5c)** 2-Chlorophenyl, **(5h)** 2-acetophenyl, and (**5i**) 3-Flourophenyl on the triazole moiety may be the cause of the notable inhibitory effect, even though several of the compounds show comparable activity.

V. RESULT AND DISCUSSION

V.I. GENERAL EXPERIMENTAL METHODS

All of the chemicals, including the organic reagents and solvents, were obtained from TCI, and Merck was used directly without further purification. With the aid of spectrometers operating at 500 and 125 MHz (device Bruker Avance II 400 MHz), 13C NMR and 1H NMR spectra were obtained in CDCl3. The spin multiplicities are designated as follows: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), and multiplets (m), and the values of the coupling constants are shown in hertz. The values of chemical shift are expressed in parts per million (ppm). The chromatography procedure made use of a silica gel column with a mesh size range of 60–120 using distilled hexane and ethyl acetate as solvents. The mass and infrared spectra were captured using the QSTAR XL GCMS and the Shimadzu FT-IR-8400s mass spectrometer, respectively. Melting points were measured on a DbkProg melting point equipment in an exposed glass capillary tube, and the data were shown uncorrected.

V.I.I. GENERAL PROCEDURE FOR SYNTHESIS OF TERT-BUTYL PIPERAZINE-1-CARBOXYLATE (2)



tert-butyl piperazine-1-carboxylate

In 50ml single neck round bottom Flask (RBF). piperazine (1) and dry Chloro Methane (DCM) as a solvent. Stirr the reaction mixture in cool condition at 0^0C. Add TEA of 1 equivalence, DMAP of 0.01 equivalence then add BoC unhydride of 1.2 equivalence dropwise. After addition of BoC unhydride stir the reaction mixture in room temperature for 30 Mints. Check the TLC (10% EtoAc in Pet Ether) if SM(Starting Material) was completed than quench with ice, liquid is formed,

Extract with DCM. Distil the organic Layer, Solid is formed (2) (Yeild 82%).

In a dry 50ml single neck RBF and charged compound-2 and DMF as a solvent, add K_2CO_3 (2.5 eq) as a base, and Propargyl Bromide(PBr) 1.2eq as a reactant stir the reaction mixture for about 4-5 hours in room temperature. Check the TLC (20% EtOAc) if starting material (SM) was completed than quinch with ice, liquid is formed extract with DCM, Distil the organic layer, liquid is formed.(Yeild 78%).

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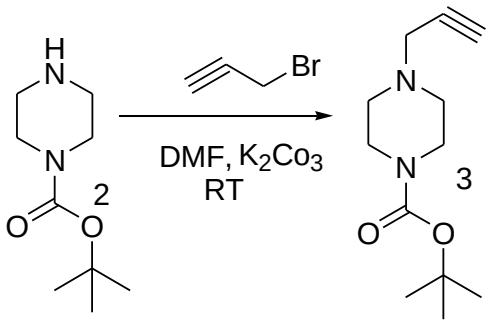
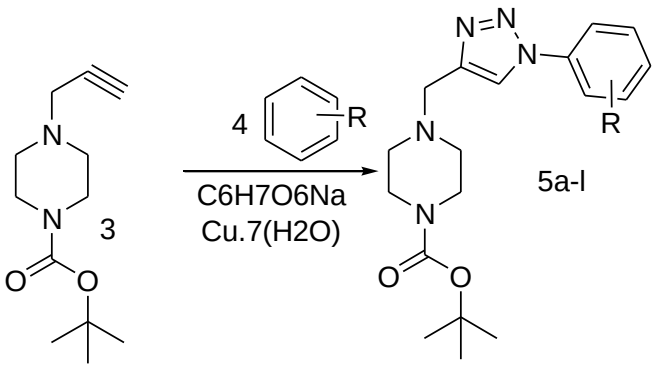


tert-butyl piperazine-1-carboxylate

tert-butyl 4-(prop-2-yn-1-yl)piperazine-1-carboxylate

V.I.II SYNTHESIS OF 4-(1-PHENYL-1H-[1,2,3]TRIAZOL-4-YLMETHYL)-PIPERAZINE-1-CARBOXYLIC ACID TERT-BUTYL ESTER DERIVATIVES, (5A-L)



tert-butyl 4-(prop-2-yn-1-yl)piperazine-1-carboxylate

tert-butyl 4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl)piperazine-1-carboxylate

Arrange a clean and dry 50ml single neck RBF and charged compound-3 and DMF as a solvent, add $CuSO_4.7H_2O$ (2 ml) Colour changed can be observed, add sodium Ascorbate ($Na_2S_2O_3$) (2ml) solid appearance is observed, than add different substituted aromatic azides 1.2eq, stir reaction mixture for about 16-18 hours at room temperature, Check the TLC (50% EtOAc in pet ether) if starting material (SM) was completed than quinch with ice, and filter with reaction filtrate and wash with PET ether solid is formed substituted (4-Chloro-pyridin-2-yl)-(1-phenyl-1H-[1,2,3]triazol-4-ylmethyl)-carbamic acid tert-butyl ester (5 a-l) (Yeild 76-86%).

V.I.III SYNTHESIS OF SUBSTITUTED AZIDOBENZENE (4.1A-L):

The aromatic substituted azidobenzene **(4.1a-l)** was made by adding 5N hydrochloric acid (HCl) solution to a mixture of corresponding amines (3.24a-l) in CH_2Cl_2 at 0°C, then gradually adding sodium nitrite solution ($NaNO_2$) while shaking at zero degrees Celsius for half an hour. After adding NaN_3 at zero degrees Celsius, the mixture was agitated for two hours at the ambient temperature. After that, it was left alone to let the organic and aqueous layers separate. To get the needed aryl azides **(4.1a-l)**, the organic layer was washed with $NaHCO_3$, then brine, and the solvent was evaporated in a vacuum. In the next step, these azides are used without any further purification.

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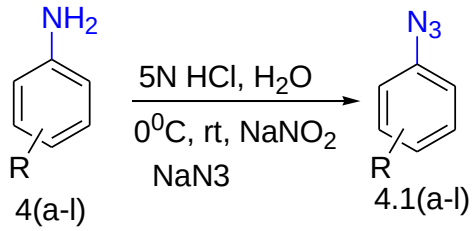

a=H, b=p-NO2, c=o-Cl, d=p-Cl, e=p-Br, f=o-OCH3, g=p-OCH3, h=m-COCH3, i=m-F, j=o-CH3, k=p-CH3, l=p-OH

Scheme-4: Synthesis of substituted azidobenzene (4.1a-l)

5.2. SPECTRAL DATA

5.2.1. Analytical data of 4-(1-Phenyl-1H-[1,2,3]triazol-4-ylmethyl)-piperazine-1-carboxylic acid tert-butyl ester (5a)

^{1}H NMR -400 MHz (DMSO-d6): 8.91 (s, 1H), 7.80 (d, J=6.9 Hz,2H), 7.59 (d, J=6.3 Hz, 2H), 7.51 (t, J=6.9 Hz, 3H), 5.43 (s, 2H), 2.48 (s, 8H), 1.41(s, 9H). ^{13}C NMR: 189.5, 134.9, 132.5, 129.5, 121.5, 31.6, 28.9, 21.7, 17.8 IR Data ν, cm^{-1}(KBr): 3105.57, 2992.91, 2872.43, 1765.62, 1405.21, 812.78, 706.48 ESI-MS: m/Z: 343.20 [M+1]+, Colour: Yellow solid, Yield: 83%, Mol. Formula: C18H25N5O2, M.P: 142-144º C, Elemental Analysis: CAL: C, 62.95; H, 7.34; N, 20.39; O, 9.32, EXP: C, 60.27; H, 5.09; N, 16.01; O, 7.05

5.2.2. Analytical data of 4-[1-(4-Nitro-phenyl)-1H-[1,2,3] triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5b):

^{1}H NMR -400 MHz (DMSO-d6): 8.98 (s, 1H), 7.82 (d, J=7.3 Hz,4H), 5.46 (s, 2H), 2.54 (s, 8H), 1.48(s, 9H). ^{13}C NMR: 192.5, 142.6, 132.5, 130.6, 126.5, 36.6, 32.9, 26.7, 16.8, IR Data ν, cm^{-1}(KBr): 3124.39, 2996.28, 2876.52, 1768.38, 1412.35, 810.36, 708.21, ESI-MS: m/Z: 388.19 [M+1]+ Colour: Pale yellow solid, Yield: 81%, Mol. Formula: C18H24N6O4, M.P: 132-134º C, Elemental Analysis: CAL: C, 64.66; H, 6.23; N, 12.64; O, 09.48

EXP: C, 63.29; H, 4.52; N, 10.25; O, 08.78

5.2.3.: Analytical data of 4-[1-(2-Chloro-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5c):

^{1}H NMR -400 MHz (DMSO-d6): 8.98 (s, 1H), 7.82 (d, J=7.3 Hz,1H), 7.21 (d, J=7.2 Hz,1H), 7.08 (t, J=6.9 Hz,1H), 6.78 (t, J=7.12 Hz,1H), 5.42 (s, 2H), 2.24 (s, 8H), 1.42(s, 9H). ^{13}C NMR: 191.8, 152.2, 150.3, 143.49, 140.3, 138.6, 134.5, 132.9, 126.2, 34.6, 31.9, 25.7, 15.2. IR Data ν, cm^{-1}(KBr): 3109.22, 2992.67, 2871.02, 1710.34, 1410.21, 809.12, 710.23, ESI-MS: m/Z: 377.16 [M+H]+. Colour: White solid, Yield: 82%, Mol. Formula: C15H12BrN5O3, M.P: 144-146º C, Elemental Analysis: CAL: C, 65.99; H, 6.76; N, 15.32; O, 14.38, EXP: C, 64.98; H, 5.04; N, 13.54; O, 13.95.

5.2.4.: Analytical data of 4-[1-(4-Chloro-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5d)

^{1}H NMR -400 MHz (DMSO-d6): 8.34 (s, 1H), 7.78 (d, J=7.3 Hz, 4H), 5.42 (s, 2H), 2.52 (s, 8H), 1.46(s, 9H). ^{13}C NMR: 190.8, 141.8, 133.2, 132.6, 127.5, 38.6, 31.9, 25.7, 17.8, IR Data ν, cm^{-1}(KBr): 3124.39, 2996.28, 2876.52, 1768.38, 1412.35, 810.36, 708.21, ESI-MS: m/Z: 377.16 (M+H)+. Colour: Yellow solid, Yield: 74%, Mol. Formula: C18H24ClN5O2, M.P: 138-140º C, Elemental Analysis: CAL: C, 67.21; H, 6.40; N, 14.53; O, 8.47, EXP: C, 63.09; H, 5.12; N,12.29; O, 7.24

5.2.5.: Analytical data of 4-[1-(4-Bromo-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5e)

^{1}H NMR -400 MHz (DMSO-d6): 8.21 (s, 1H), 7.71 (d, J=6.9 Hz, 4H), 5.12 (s, 2H), 2.41 (s, 8H), 1.41(s, 9H).^{13}C NMR: 192.8, 148.8, 134.2, 131.6, 126.5, 36.8, 32.9, 24.7, 18.8, IR Data ν, cm^{-1}(KBr): 3124.39, 2996.28, 2876.52, 1768.38, 1412.35, 810.36, 708.21, ESI-MS: m/Z: 421.11 (M+H)+. Colour: Yellow solid, Yield: 82%, Mol. Formula: C18H24BrN5O2, M.P: 142-144º C, Elemental Analysis: CAL: C, 51.19; H, 5.73; Br, 18.92; N, 16.58; O, 7.58, EXP: C, 70.93; H, 5.58; N, 12.78; O, 8.89.

5.2.6. : Analytical data of 4-[1-(2-Methoxy-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5f):

^{1}H NMR -400 MHz (DMSO-d6): 8.62 (s, 1H), 7.43 (d, J=7.1 Hz,1H), 7.37 (d, J=6.8 Hz,1H), 7.11 (t, J=6.7 Hz,1H), 6.92 (t, J=7.14 Hz,1H), 5.38 (s, 2H), 3.04 (s, 3H), 2.18 (s, 8H), 1.38(s, 9H). ^{13}C NMR:

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182.5, 151.2, 149.3, 146.8, 142.3, 136.6, 133.5, 131.9, 122.2, 56.7, 35.6, 32.4, 26.7, 14.2, IR Data ν, cm^{-1}(KBr): 3121.22, 2995.47, 2876.34, 1708.45, 1408.78, 811.10, 712.21, ESI-MS: m/Z: 373.21 (M+H)+. Colour: Pale Yellow solid, Yield: 80%, Mol. Formula: C19H27N5O3, M.P: 140-142° C, Elemental Analysis: CAL: C, 71.11; H, 7.29; N, 10.75; O, 09.85, EXP: C, 70.78; H, 4.32; N, 09.98; O, 08.52

5.2.7: Analytical data of 2-Bromo-3-[1-(4-methoxy-phenyl)-1H-[1,2,3]triazol-4-ylmethoxy]-pyridine (5g):

^{1}H NMR -400 MHz (DMSO-d6): 8.19 (s, 1H), 7.69 (d, J=6.8 Hz, 4H), 5.28 (s, 2H), 2.67 (s, 3H), 2.47 (s, 8H), 1.41(s, 9H).^{13}C NMR: 192.8, 148.8, 134.2, 131.6, 126.5, 36.8, 32.9, 24.7, 18.8. IR Data ν, cm^{-1}(KBr): 3124.39, 2996.28, 2876.52, 1768.38, 1412.35, 810.36, 708.21. ESI-MS: m/Z: 373.21 (M+H)+. Colour: White solid, Yield: 82%, Mol. Formula: C15H13BrN4O2, M.P: 138-140° C, Elemental Analysis: CAL: C, 69.88; H, 6.63; N, 15.51; O, 9.86, EXP: C, 68.23; H, 5.01; N, 14.12; O, 9.26

5.2.8: Analytical data of 4-[1-(2-Acetyl-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5h):

^{1}H NMR -400 MHz (DMSO-d6): 8.73 (s, 1H), 7.51 (d, J=7.1 Hz,1H), 7.42 (d, J=6.9 Hz,1H), 7.10 (t, J=7.1 Hz, 1H), 6.93 (t, J=7.12 Hz,1H), 5.41 (s, 2H), 3.21 (s, 3H), 2.43 (s, 8H), 1.32 (s, 9H). ^{13}C NMR: 187.3, 181.5, 150.2, 148.3, 145.8, 144.3, 134.6, 132.5, 130.9, 121.2, 57.7, 36.6, 33.4, 27.7, 15.2. IR Data ν, cm^{-1}(KBr): 3121.22, 2995.47, 2876.34, 1708.45, 1658.21, 1408.78, 811.10, 712.21. ESI-MS: m/Z: 385.21 (M+H)+. Colour: White solid, Yield: 84%, Mol. Formula: C15H12BrN5O3, M.P: 138-140^{0}C , Elemental Analysis: CAL: C, 67.32; H, 7.06; N, 12.17; O, 10.45, EXP: C, 66.28; H, 4.26; N, 10.99; O, 09.01

5.2.9. Analytical data of 4-[1-(4-Acetyl-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5i):

^{1}H NMR -400 MHz (DMSO-d6): 8.19 (s, 1H), 7.69 (d, J=6.8 Hz, 4H), 5.28 (s, 2H), 2.67 (s, 3H), 2.47 (s, 8H), 1.41(s, 9H). ^{13}C NMR: 193.4, 189.2, 151.2, 136.3, 134.5, 123.5, 39.1, 31.4, 26.2, 19.3 IR Data ν, cm^{-1}(KBr): 3124.39, 2996.28, 2876.52, 1768.38, 1668.38, 1412.35, 810.36, 708.21. ESI-MS: m/Z: 385.12 (M+H)+. Colour: Yellow solid, Yield: 80%, Mol. Formula: C16H13BrN4O2, M.P: 134-136^{0}C, Elemental Analysis: CAL: C, 71.49; H, 5.51; N, 12.01; O, 9.57, EXP: C, 70.32; H, 4.01; N, 11.09; O. 8.42

5.2.10. Analytical data of 4-(1-o-Tolyl-1H-[1,2,3]triazol-4-ylmethyl)-piperazine-1-carboxylic acid tert-butyl ester (5J):

^{1}H NMR -400 MHz (DMSO-d6): 8.78 (s, 1H), 7.41 (d, J=7.3 Hz,1H), 7.38 (d, J=6.9 Hz,1H), 7.21 (t, J=6.6 Hz,1H), 6.91 (t, J=7.21 Hz,1H), 5.42 (s, 2H), 3.21 (s, 3H), 2.26 (s, 8H), 1.42(s, 9H). ^{13}C NMR: 184.6, 150.6, 148.7, 145.2, 141.7, 137.2, 136.4, 132.2, 121.5, 36.8, 31.8, 28.3, 15.7, 12.9. IR Data ν, cm^{-1}(KBr): 3119.22, 2996.41, 2872.34, 1702.45, 1402.21, 810.10, 710.68. ESI-MS: m/Z: 357.22 (M+H)+. Colour: Pale Yellow solid, Yield: 84%, Mol. Formula: C16H15N5O4, M.P: 142-144° C, Elemental Analysis: CAL: C, 73.84; H, 7.61; N, 09.59; O, 8.95

EXP: C,70.01; H, 4.12; N, 08.68; O, 08.51

5.2.11. Analytical data of 4-[1-(4-Cyano-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5k):

^{1}H NMR -400 MHz (DMSO-d6): 8.71 (s, 1H), 7.34 (d, J=7.1 Hz, 4H), 5.36 (s, 2H), 2.42 (s, 8H), 1.32 (s, 9H). ^{13}C NMR: 187.5, 148.6, 136.2, 132.5, 128.2, 53.7, 33.5, 32.2, 25.2, 15.2, IR Data ν, cm^{-1}(KBr): 3119.25, 2992.38, 2868.36, 1752.38, 1410.29, 812.42, 702.78, ESI-MS: m/Z: 368.20 (M+H)+. Colour: Pale Yellow solid, Yield: 82%, Mol. Formula: C16H12N6O3, M.P: 146-148° C, Elemental Analysis: CAL: C, 71.94; H, 6.21; N, 10.81; O, 8.69, EXP: C, 69.54; H, 6.01; N, 09.25; O, 08.35

5.2.12. Analytical data of 4-[1-(4-Hydroxy-phenyl)-1H-[1,2,3]triazol-4-ylmethyl]-piperazine-1-carboxylic acid tert-butyl ester (5l):

^{1}H NMR -400 MHz (DMSO-d6): 10.01 (s, 1H), 8.76 (s, 1H), 7.32 (d, J=6.9 Hz, 4H), 5.32 (s, 2H), 2.38 (s, 8H), 1.28 (s, 9H). ^{13}C NMR: 181.2, 146.5, 137.5, 133.3, 126.1, 32.6, 31.5, 24.5, 18.2. IR Data ν, cm^{-1}(KBr): 3403.51, 3112.20, 2991.52, 2862.12, 1748.25, 1408.65, 808.35, 687.01. ESI-MS: m/Z: 359.20 (M+H)+. Colour: Pale Yellow solid, Yield: 81%, Mol. Formula: C18H25N5O3, M.P: 146-148° C, Elemental Analysis: CAL: C, 70.15; H, 7.01; N, 11.48; O, 09.35, EXP: C, 69.58; H, 4.12; N, 8.08; O, 09.01.

ACKNOWLEDGEMENT

The Authors are thankful to the Department of Chemistry, Telangana University, Telangana, India.

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