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Synthesis And Characterization Of Triazolo [3,4-B][1,3,4]Thiadiazoles Derivatives.

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Abstract: Synthesis of a series of 5,6-Dihydro-6-aryl-3-(4-isopropylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazoles for obtaining biologically potent agents. Thiadiazoles have been synthesized by cyclo condensation of 1-amino-3-[4-(propan-2-yl)phenyl]-1*H*-1,2,4-triazole-5-thiol with different aromatic aldehydes in presence of p-TsOH (p-toluene sulphonic acid) as a catalyst. The constitution of newly synthesized compounds has been supported by using elemental analysis, infrared, ^{1}H NMR and ^{13}C NMR spectroscopy and further supported by mass spectrometry. The purity of all the compounds has been checked by thin-layer chromatography.

Keywords: 1,3,4- Thiadiazole; p-TsOH; antimicrobial activity; Antibacterial and Anti-fungal activity

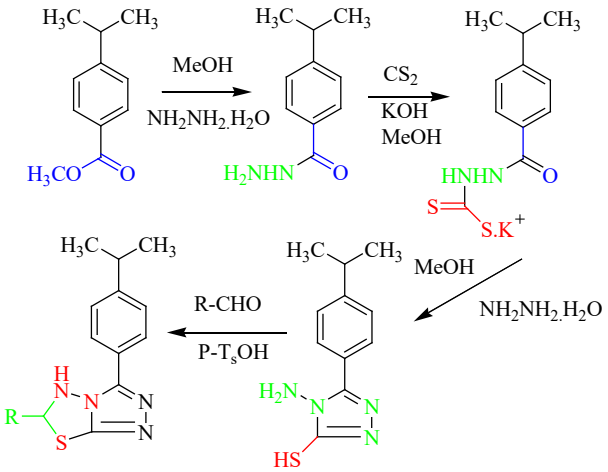
Introduction

The bibliographical review has publicized the importance of 1,2,4-triazoles as antimicrobial agents[1–9] such as Fluconazole, Ravuconazole, Voriconazole, Itraconazole and Posaconazole Several potent drug compounds possessing the triazole ring have been used in medicine. These are alprazolam, estazolam, nefazodone, and triazolam. Thiadiazole derivatives have played a significant part in pharmaceutical industries and exhibited different biological activities due to the existence of –N=C-S group. The genetic contour of 1, 3, 4-Thiadiazole derivatives is very broad. Thiadiazole derivatives are endowed with a range of biological activities. The enhancement of the reaction selectivity, product purity, reaction rate, reaction yield, and extravagance minimization are desired goals of parallel green approach.

Our research studies brief about the synthesis of biologically and fluorescently active heterocyclic systems using obtainable reagents, and simple microwave approach.[10-11] In this work, the annulation

of new N-bridged thiadiazine and thiazole rings to the-triazole.

Scheme



Where R
4a = 4-OCH_3-C_6H_4-
4b = 3,4-$(OCH_3)_2$-C_6H_3-
4c = 4-NO_2-C_6H_4-
4d = 2-NO_2-C_6H_4-

Material and Methods

Melting points of all the synthesized compounds were taken in open capillary tubes with an electrothermal-9200 melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FTIR-8400 spectrophotometer in KBr. ^{1}H NMR spectra were recorded on a bruker Avance II spectrometer(33 MHz) using TMS as an internal standard, Chemical shifts are given in δ ppm. Mass spectra were determined using a direct inlet probe on a GCMS-QP2010 Mass spectrometer, elemental analysis was performed on a Carlo Earba Ea 1108 elemental analyzer. The result on the Elemental analyser.

1. Preparation of 4-isopropylbenzohydrazide.

When we react methyl 4-isopropylbenzoate (16gm, 0.1mol) in the presence of hydrazine hydrate (3.2gm, 0.1mol) in methanol as a solvent and if the mixture is refluxed and stirred for 2 hours and then solid obtained was filtered and washed with ether and dried. So 4-isopropylbenzohydrazide is formed There is no need to purify the salt for further reaction.

2. Preparation of potassium 4-isopropylbenzyl carbamodithiote.

To a mixture of potassium hydroxide (8.40g, 0.15mol) and 4-isopropyl benzohydrazide (17.8g, 0.1mol) in methanol (25ml), carbon disulphide (11.4g, 0.15mol) was added. This mixture was stirred for 12-14 hours. It was then diluted with dry ether (200 ml) and thus the solid obtained was filtered and washed with ether and dried. There is no need to purify the salt for further reaction.

3. Preparation of 1-Amino-3-[4-(propan-2-yl)phenyl]-1H-1,2,4-triazole-5-thiol.

A suspension of the potassium salt (29.2g, 0.1 mol), hydrazine hydrate (10 ml, 0.2 mol) and water (2 ml) was refluxed with stirring for 3 hours. The color of the reaction mixture changed to green, hydrogen sulfide was evolved (lead acetate paper and odor) and a homogeneous solution resulted. Dilute the solution with cold water (100 ml) and neutralize with glacial acetic acid, precipitating a white solid. The product was filtered, washed with cold water and crystallized from dioxane yield 60%, m.p. 190 ^{o}C. It is confirmed by ^{1}H NMR and its multiplicity shown in δ ppm. ^{1}H NMR: 7.40 (s,2H), 7.19(s,2H), 3.12(m,1H), 3.0(s,1H), 2.0(s,2H), 1.29(d,6H).

4. Preparation of 5,6-dihydro-3-(4-isopropylphenyl)-6(4-Nitrophenyl)-[1,2,4] triazolo[3,4-b][1,3,4]thiadiazoles

A mixture of 1-amino-3-[4-(propan-2-yl) phenyl]-1H-1,2,4-triazole-5-thiol (2.34g, 0.01mol), p-nitrobenzaldehyde (1.65g, 0.01mol) and p-Ts-OH (50 mg) in dry DMF (50 ml) was refluxed with stirring for 10 hrs. The reaction mixture was poured on to crushed ice and thus solid separated was filtered, washed with water and crystallized from methanol yield 60%, m.p. 265^{O}c Anal. Calcd. For $C_{18}H_{17}N_5O_2S$; C, 58.84; H,4.66; N,19.06 %; Found: C,58.53; H,4.93; N,19.32 %. ^{1}H NMR: 7.41 (s,2H), 7.19(s,2H), 3.12(m,1H), 3.0(s,1H), 2.0(s,2H), 1.28(d,6H). IR (KBr Disc.) cm^{-1}: 3055 (Aromatic symmetrical stretch of C-H), 2880 (C-H asymmetrical stretch of isopropyl group), 1591 (C=N stretch of triazole ring), 1520 (Aromatic ring C=C asymmetrical stretch), 1341 (C-N stretch of triazole ring), 1280 (C-O-C asy stretch),1018 (N-N stretch of triazole ring), 1014 (Aromatic ring, C-H in plane deformation), 760 (C-H out of plane deformation of mono substituted benzene ring), 680(C-S-C stretch of thiadiazole) [Table 1 near here]

Table 1. The % yield and the elemental analysis of the synthesized compounds

Sr. No.	Substitution R	Molecular Formula/ Molecular Weight	M.P. °C	Yield %	% Composition Calcd./Found		
					C	H	N
4a	4-OCH_3-C_6H_4-	$C_{19}H_{20}N_4OS$ 352.45	231	58	64.75 (65.19)	5.72 (5.36)	15.90(16.26)
4b	3,4-$(OCH_3)_2$-C_6H_3-	$C_{20}H_{22}N_4O_2S$ 382.47	196	54	62.80 (62.16)	5.80 (5.46)	14.65 (14.32)
4c	4-NO_2-C_6H_4-	$C_{18}H_{17}N_5O_2S$ 367.42	180	60	58.84 (58.79)	4.66 (4.83)	19.06 (19.35)
4d	2-NO_2-C_6H_4-	$C_{18}H_{17}N_5O_2S$ 367.42	185	61	58.84 (58.53)	4.66 (4.97)	19.06 (19.32)
4e	4-OH-C_6H_4-	$C_{18}H_{18}N_4OS$ 338.42	221	64	63.88 (63.75)	5.36 (5.49)	16.56 (16.63)
4f	C_6H_5-	$C_{18}H_{18}N_4S$ 322.42	195	53	67.05 (67.34)	5.63 (5.34)	17.38 (17.09)
4g	3-Cl-C_6H_4-	$C_{18}H_{17}ClN_4S$ 356.87	180	49	60.58 (60.66)	4.80 (4.98)	15.70 (15.83)
4h	4-CH_3-C_6H_4-	$C_{19}H_{20}N_4S$ 336.45	154	45	67.83 (67.64)	5.99 (6.15)	16.65 (16.91)
4i	4-F-C_6H_4-	$C_{18}H_{17}FN_4S$ 340.41	184	58	63.51 (63.87)	5.03 (5.12)	16.46 (16.29)
4j	2-OH-C_6H_4-	$C_{18}H_{18}N_4OS$ 338.42	193	45	63.88 (63.98)	5.36 (5.11)	16.56 (16.23)

4a. 3-(4-isopropylphenyl)-6-(4-methoxyphenyl)-5,6-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole IR (KBr Disc.) cm^{-1}: 3059 (Aromatic symmetrical stretch of C-H), 2887 (C-H asymmetrical stretch of isopropyl group), 1595 (C=N stretch of triazole ring), 1525 (Aromatic ring C=C asymmetrical stretch), 1343 (C-N stretch of triazole ring), 1288 (C-O-C asy stretch)1014 (N-N stretch of triazole ring), 1014 (Aromatic ring, C-H in plane deformation), 765 (C-H out of plane deformation of mono substituted benzene ring), 682(C-S-C stretch of thiadiazole)) ^{1}H NMR: δ 8.71 (s, 1H) δ 8.33 (d, 2H); δ 7.95 (d,2H) δ 7.76 (d,2H); δ 7.29 (d,2H) ; δ 3.70 (s,3H) δ 2.93(m,1H); δ 2.18(s,1H); δ 1.26(d, 6H) ^{13}C NMR δ 159.6, 159.0, 151.1, 148.4, 134.2, 128.7, 128.1,127.8, ,125.5, 114.5, 64.5,55.3,33.2,23.3.

4b. 6-(2,4-dimethoxyphenyl)-3-(4-isopropylphenyl)-5,6-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole : IR (KBr Disc.) cm^{-1}: 3054 (Aromatic symmetrical stretch of C-H), 2879 (C-H asymmetrical stretch of isopropyl group), 1590 (C=N stretch of triazole ring), 1528 (Aromatic ring C=C asymmetrical stretch), 1348 (C-N stretch of triazole ring), 1282 (C-O-C asy stretch)1014 (N-N stretch of triazole ring), 1020 (Aromatic ring, C-H in plane deformation), 760 (C-H out of plane deformation of mono substituted benzene ring), 680(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.73 (s, 1H) δ 8.31 (d, 2H); δ 7.99 (d,2H) δ 7.71 (d,2H); δ 7.34 (d,1H) ; δ 4.84(m,1H); δ 3.76 (s,6H) ; δ 2.24(s,1H); δ 1.19(d, 6H) ^{13}C NMR δ 159.3, 159.1, 151.3, 148.8, 134.1, 128.6 , 128.2,127.5, ,125.5, 114.3, 64.5,55.3,33.2,23.3.

4c. 3-(4-isopropylphenyl)-6-(4-nitrophenyl)-5,6-dihydro-[1,2,4]triazolo[3,4 b][1,3,4] thiadiazole IR (KBr Disc.) cm^{-1}: 3056 (Aromatic symmetrical stretch of C-H), 2885 (C-H asymmetrical stretch of isopropyl group), 1592 (C=N stretch of triazole ring), 1525 (Aromatic ring C=C asymmetrical stretch), 1530 (N–O asymmetric stretch), 1345 (N–O asymmetric stretch) 1343 (C-N stretch of triazole ring), 1280 (C-O-C asy stretch)1014 (N-N stretch of triazole ring), 1021 (Aromatic ring, C-H in plane deformation), 768 (C-H out of plane deformation of mono substituted benzene ring), 685(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.71 (s, 1H) δ 8.33 (d, 2H); δ 7.95 (d,2H) δ 7.76 (d,2H); δ 7.29 (d,2H) ; δ 2.93(m,1H); δ 2.18(s,1H); δ 1.26(d, 6H) 13C NMR δ 159.2, 159.6, 151.1, 148.9, 134.5, 128.6 , 128.1,127.7, ,125.5, 114.3, 64.4,55.5,33.4,23.2.

4d. 3-(4-isopropylphenyl)-6-(2-nitrophenyl)-5,6-dihydro-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazole IR (KBr Disc.) cm^{-1}: 3055 (Aromatic symmetrical stretch of C-H), 2884 (C-H asymmetrical stretch of isopropyl group), 1595 (C=N stretch of triazole ring), 1520 (Aromatic ring C=C asymmetrical stretch), 1525 (N–O asymmetric stretch), 1340 (N–O asymmetric stretch) 1340 (C-N stretch of triazole ring), 1282 (C-O-C asy stretch)1015 (N-N stretch of triazole ring), 1022 (Aromatic ring, C-H in plane deformation), 785 (C-H out of plane deformation of mono substituted benzene ring), 685(C-S-C stretch of thiadiazole)) ^{1}H NMR: δ 8.72 (s, 1H) δ 8.32 (d, 2H); δ 7.95 (d,2H) δ 7.75 (d,2H); δ 7.30 (d,2H) ; δ 2.91(m,1H); δ 2.19(s,1H); δ 1.27(d, 6H) ^{13}C NMR δ 159.5, 159.3, 151.2, 148.8, 134.4, 128.6 , 128.2,127.4, ,125.4, 114.2, 64.8,55.6,33.4,23.3.

4e. 4-(3-(4-isopropylphenyl)-5,6-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-6-yl)phenol IR (KBr Disc.) cm^{-1}: 3501(-OH stretch), 3058 (Aromatic symmetrical stretch of C-H), 2881 (C-H asymmetrical stretch of isopropyl group), 1590 (C=N stretch of triazole ring), 1525 (Aromatic ring C=C asymmetrical stretch), 1345 (C-N stretch of triazole ring), 1286 (C-O-C asy stretch),1016 (N-N stretch of triazole ring), 1015 (Aromatic ring, C-H in plane deformation), 765 (C-H out of plane deformation of mono substituted benzene ring),

682(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.69 (s, 1H) δ 8.36 (d, 2H); δ 7.93 (d,2H) δ 7.71 (d,2H); δ 7.32 (d,2H) ; δ 4.91(s,1H); δ 2.96(m,1H); δ 2.16(s,1H); δ 1.21(d, 6H) ^{13}C NMR δ 159.5, 159.1, 151.4, 148.8, 134.4, 128.6 , 128.2,127.6, 125.5, 114.2, 64.5,55.8,33.5,23.5.

4f.3-(4-isopropylphenyl)-6-phenyl-5,6-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole IR (KBr Disc.) cm^{-1}: 3058 (Aromatic symmetrical stretch of C-H), 2881 (C-H asymmetrical stretch of isopropyl group), 1590 (C=N stretch of triazole ring), 1525 (Aromatic ring C=C asymmetrical stretch), 1345 (C-N stretch of triazole ring), 1286 (C-O-C asy stretch),1015 (N-N stretch of triazole ring), 1015 (Aromatic ring, C-H in plane deformation), 765 (C-H out of plane deformation of mono substituted benzene ring), 682(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.71 (s, 1H) δ 8.31 (d, 2H); δ 7.94 (d,2H) δ 7.78 (d,2H); δ 7.27 (d,2H) ; δ 7.09 (d,1H) ; δ 2.91(m,1H); δ 2.18(s,1H); δ 1.26(d, 6H) ^{13}C NMR δ 174.5, 159.1, 151.4, 148.8, 134.4, 128.6 , 128.2,127.6, 125.5, 114.2, 64.5,55.8,33.5,23.5.

4g.6-(4-chlorophenyl)-3-(4-isopropylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole: IR (KBr Disc.) cm^{-1}: 3055 (Aromatic symmetrical stretch of C-H), 2885 (C-H asymmetrical stretch of isopropyl group), 1554 (C=N stretch of triazole ring), 1520 (Aromatic ring C=C asymmetrical stretch), 1346 (C-N stretch of triazole ring), 1289 (C-O-C asy stretch),1015 (N-N stretch of triazole ring), 1014 (Aromatic ring, C-H in plane deformation), 778 (C-H out of plane deformation of mono substituted benzene ring), 682(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.70 (s, 1H) δ 8.33 (d, 2H); δ 7.35 (d,2H) δ 7.26 (d,2H); δ 7.09 (d,2H) ; δ 2.91(m,1H); δ 2.09(s,1H); δ 1.20(d, 6H) ^{13}C NMR δ 175.0, 148.6, 148.0, 134.3, 131.6, 129.4, 128.9, 127.9, 127.2, 126.7, 36.3, 23.4.

4h.3-(4-isopropylphenyl)-6-(o-tolyl)-5,6-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole: IR (KBr Disc.) cm^{-1}: 3058 (Aromatic symmetrical stretch of C-H), 2890 (C-H asymmetrical stretch of isopropyl group), 1556 (C=N stretch of triazole ring), 1522 (Aromatic ring C=C asymmetrical stretch), 1342 (C-N stretch of triazole ring), 1280 (C-O-C asy stretch),1015 (N-N stretch of triazole ring), 1016 (Aromatic ring, C-H in plane deformation), 774 (C-H out of plane deformation of mono substituted benzene ring), 680(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.70 (s, 1H) δ 8.34 (d, 2H); δ 7.94 (d,2H) δ 7.72 (d,2H); δ 7.38 (d,2H) ; δ 2.85(m,1H); δ 2.34 (d, 3H) ; δ 2.19(s,1H); δ 1.17(d, 6H) ^{13}C NMR δ 175.0, 148.2, 148.0, 137.2, 136.8, 129.6, 128.7, 127.9, 127.4, 36.3, 23.4, 17.7

4i.6-(4-flourophenyl)-3-(4-isopropylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole: IR (KBr Disc.) cm^{-1}: 3056 (Aromatic symmetrical stretch of C-H), 2885 (C-H asymmetrical stretch of isopropyl group), 1560 (C=N stretch of triazole ring), 1528 (Aromatic ring C=C asymmetrical stretch), 1342 (C-N stretch of triazole ring), 1278 (C-O-C asy stretch),1017 (N-N stretch of triazole ring), 1016 (Aromatic ring, C-H in plane deformation), 774 (C-H out of plane deformation of mono substituted benzene ring), 689(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.65 (s, 1H) δ 8.28 (d, 2H); δ 7.31 (d,2H) δ 7.24 (d,2H); δ 7.11 (d,2H) ; δ 2.88(m,1H); δ 2.01(s,1H); δ 1.24(d, 6H) ^{13}C NMR δ 168.1, 148.0, 143.5, 131.4, 129.5, 127.2, 126.7, 125.4, 36.3, 23.4

4j.2-(3-(4-isopropylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-6-yl)phenol: IR (KBr Disc.) cm^{-1}: 3511(-OH stretch), 3058 (Aromatic symmetrical stretch of C-H), 2881 (C-H asymmetrical stretch of isopropyl group), 1590 (C=N stretch of triazole ring), 1525 (Aromatic ring C=C asymmetrical stretch), 1344 (C-N stretch of triazole ring), 12860(C-O-C asy stretch),1014 (N-N stretch of triazole ring), 101

(Aromatic ring, C-H in plane deformation), 765 (C-H out of plane deformation of mono substituted benzene ring), 685(C-S-C stretch of thiadiazole) ^{1}H NMR: δ 8.71 (s, 1H) δ 8.37 (d, 2H); δ 7.94 (d,2H) δ 7.71 (d,2H); δ 7.34 (d,2H) ; δ 4.94(s,1H); δ 2.94(m,1H); δ 2.18(s,1H); δ 1.24(d, 6H) ^{13}C NMR δ 175.1, 155.3, 148.5, 148.0, 130.2, 128.9, 127.9, 127.2, 126.7, 123.7, 121.9, 116.4, 36.3, 23.4.

Antibacterial Activity Determination:

Organic compounds may be bacteriostatic or bacteriocidal for microbial cultures. To check this, from the Mueller Hinton Agar plates (showing no visible growth of bacteria), sub-culturing was carried out on Nutrient Agar plates (Collins, 1967). After streaking, Nutrient Agar plates were incubated for 24 h at 37°C. Then after an observation was made to see the colonies formed. If colonies were found, the dilution was considered bacteriostatic and if no colonies were observed, it was considered bactericidal.

Antifungal Activity Determination:

For fungal cultures, the fungal media Yeast Nitrogen base agar plate (YNBG) (Difco Make) 6.7 g and Glucose 10 g, dissolved in 100 ml of distilled water and filter sterilized was used. The inoculum was prepared from 3-4 days old sabouraud's Dextrose agar slants. The growth was uniformly mixed with Distilled water. The Size of inoculum prepared for inoculating YNBG agar plates was 102 –103 cfu/ml, adjusted with McFarland solution. After inoculation of the properly diluted fungal solution, the plates were incubated at 37 °C for 48 hours.

Antimicrobial activity of 6-Aryl-3-(4-isopropylphenyl)-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazoles.

All the compounds have been evaluated for antimicrobial and antibacterial activity as described below.

Preparing Agar Dilution plates

Appropriate dilutions i.e. 1 ml quantity of antimicrobial solution are added to Mueller Hinton agar (19 ml quantity) (Hi Media) that have been allowed to equilibrate in a water bath to 45 to 50 °C. One part of the antimicrobial solution is added to nine parts of liquid agar. The agar and antimicrobial solution were mixed thoroughly and the mixture is poured into Borocil glass Petri dishes having 9 cm diameter on a level surface to result in an agar depth of 3 to 4 mm.

The plates should be poured as quickly after mixing as possible to prevent cooling and partial solidification in the mixing container, avoiding bubbles. The Agar was allowed to solidify at room temperature, and the plates were either used immediately or stored in sealed plastic bags at 2 to 8 °C for up to five days for reference work, or longer for routine tests. Plates stored at 2-8 °C were allowed to equilibrate at room temperature before use, assuring that the agar surface was dry before inoculating the plates. If necessary, plates were placed in an incubator or laminar flow hood for approximately 30 minutes with their lids. It helps agar to hasten the drying of the agar surface.

Source of Antimicrobial agent: It was stored in an airtight container or under desiccation at 4 °C if in powder form. All synthetic organic compounds were obtained from Chemistry Department, Saurashtra University. The Antibacterial, anti-fungal and Antimicrobial activities are shown in the form of the table below. [Table 2 near here]

Table 2. Results of the antibacterial and antimicrobial activity of synthesized compounds

NO	CODE	Antibacterial activity												Antifungal activity					
		Gram +ve Bacteria						Gram -ve Bacteria						Uni/Multicellular Fungi					
		Staphylococcus aureus			Bacillus subtilis			Escherichia coli			Salmonella paratyphi B			Aspergillus niger			Candida albicans		
		2000µg/ml	1000 µg/ml	500 µg/ml	2000µg/ml	1000 µg/ml	500 µg/ml	2000 µg/ml	1000 µg/ml	500 µg/ml	2000µg/ml	1000 µg/ml	500 µg/ml	2000µg/ml	1000 µg/ml	500 µg/ml	2000µg/ml	1000 µg/ml	500 µg/ml
1.	4a	+	+	-	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-
2.	4b	+	+	-	+	+	+	-	-	-	+	+	-	+	+	+	-	-	-
3.	4c	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
4.	4d	+	+	-	+	+	-	+	+	-	+	+	-	+	+	-	+	+	-
5.	4e	-	-	-	+	+	-	+	+	-	+	+	-	-	-	-	-	-	-
6.	4f	+	+	-	+	+	+	-	-	-	-	-	-	+	+	-	+	+	-
7.	4g	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-
8.	4h	+	+	+	+	+	+	-	-	-	-	-	-	+	+	-	+	+	-
9.	4i	+	+	-	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-
10	4j	+	+	-	+	+	+	-	-	-	+	+	-	+	+	+	-	-	-

Result and discussion

We include the synthesis of the compounds 6-aryl-3-(4-isopropylphenyl)- [1,2,4] triazolo[3,4-b][1,3,4]thiadiazoles has been done using a good method (which is described in the steps). This process produces good yields and simple workup. From which Compound 4a(4-OCH_3-C_6H_4-) shows considerably good anti-microbial activity and shows the yield of 68% and it is a pale yellow color substance. The other compounds having good % yields are, 4b(3,4-$(OCH_3)_2$-C_6H_3-) has to yield 62%, 4e(4-OH-C_6H_4-) and 4j(2-OH-C_6H_4-) has a yield of 65%. The purified products are very clean. This study gives a valuable synthesis of potentially biologically active compounds.

Here in manufacture compound (4a-4j) were checked for their antibacterial and anti-fungal activity MIC by the Mueller Hinton Agar plates (showing no visible growth of bacteria), subculturing was carried out on Nutrient Agar plates (Collins, 1967) by 2 Gram +Ve bacteria i.e. staphylococcus aureas, bacillus subtilis 2 Gram -Ve bacteria i.e. Escherichia coli and salmonella paratyphi B and 2 fungal strains Aspergillus niger Candida albicans. Detailed Methodology and interpretation of results for antimicrobial evaluation. The compounds 4b(3,4-$(OCH_3)_2$-C_6H_3-), 4c (4-NO_2-C_6H_4-),4i(4-F-C_6H_4-) and 4j(2-OH-C_6H_4-) shows good activity against these bacterial species. Specially The compound 4b, 6-(2,4-dimethoxyphenyl)-3-(4-isopropylphenyl)-5,6-dihydro-[1,2,4] triazolo[3,4 b][1,3,4]thiadiazole shows good antibacterial activity against gram –Ve bacteria Escherichia coli and salmonella paratyphi B also gram +Ve bacteria staphylococcus aureus and bacillus subtilis.

Conclusion

In conclusion, we can say that we have developed

a new and simple route for the synthesis of triazolo [3,4-b][1,3,4]thiadiazoles and their derivatives under mild reaction conditions. All the synthesized compounds were tested for their impact on above-mentioned microbes. Broth dilution methods have been used to determine the minimal concentration of antimicrobial agent that inhibits the growth or kill the microorganism.

The newly synthesized amino Thiadiazole compounds are giving good yield using commercial grade raw materials. The structures of all the compounds were confirmed by, ^1H NMR mass and FT-IR. The manufactured compounds were tested for potential biological activities. All the compounds were found to possess reasonably good antifungal activity and especially the compounds 4a(4-OCH_3-C_6H_4-), 4c(4-NO_2-C_6H_4-), 4h(4-CH_3-C_6H_4-), 4i(4-F-C_6H_4-) were found to be the most potent antimicrobial agent.

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