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Synthesis and antimicrobial activity of some new Imidazo[1,2-a]pyridine derivatives

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ABSTRACT

Some new 1,2,4-triazolo[3,4-b][1,3,4]thiadiazoles and 1,2,4-triazoles derived from 7-methyl-2-(p-methylphenyl)imidazo[1,2-a]pyridine-3-ethylcarboxylate (3), The newly synthesized compounds were characterized by elemental analysis, IR, ^{1}H NMR and mass spectra. All the synthesized compounds were tested for their antibacterial activities against Gram positive and Gram negative bacteria.

Key Words: Imidazo[1,2-a]pyridine, 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles, 1,2,4-triazolo, Arylamides, antimicrobial activity

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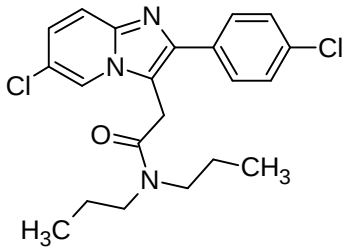
INTRODUCTION

Imidazo[1,2-a]pyridine has significant importance in the pharmaceutical industry owing to the interesting biological activities displayed over a broad range of therapeutic classes, exhibiting like anti-inflammatory[1], antiulcer[2], antibacterial[3], properties. Imidazo[1,2-a]pyridine also act as selective cyclin-dependant kinase inhibitors[4], GABA and benzodiazepine receptor agonists[5], and cardiotonic agents[6]. Drug formulation containing imidazo[1,2-a]pyridine currently available on the market include alpidem (anxiolytic)[7], zolpidem (hypnotic)[8], zolimidine (antiulcer)[9] and olprinone (PDE-3 inhibitor)[10] Figure 1.

Recently, it was reported that the 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles possess cytotoxic activity[11]. The 1,2,4-triazoles and 1,3,4-thiadiazoles are known for their broad-spectrum of biological activities and many other uses[12-15]. Moreover, the triazolothiadiazoles substituted in the 3 and 6 positions by aryl, alkyl or heterocyclic moiety possess pharmacological activity such as antibacterial[16], anti-inflammatory[17], herbicidal[18] and anti-HIV-1 effects[19]. On the other hand, it has been reported that certain compounds bearing a thiadiazole and 1,2,4-triazole nucleus possess significant anti-inflammatory activity[20-23]. In addition, it was mentioned that [1,3,4]thiadiazoles exhibit various biological activities possibly due to the presence of the =N-C-S moiety[24]. The synthesis of triazoles fused to another heterocyclic ring has attracted particular attention due to their diverse applications as antibacterial, antidepressant,

antiviral, antitumor and anti-inflammatory agents, pesticides, herbicides, lubricant and analytical reagents[25]. It is common observation that combination of two or more biologically active heterocyclic rings, either in condensed form or coupled form results in enhancement of biological profile of such compounds by many folds. Guided by this fact, it was contemplated to synthesize new heterocyclic systems involving imidazo[1,2-a]pyrimidine, 1,2,4-triazole and 1,3,4-thiadiazole (Scheme 1), and evaluate them for antimicrobial activity.

Figure 1 :



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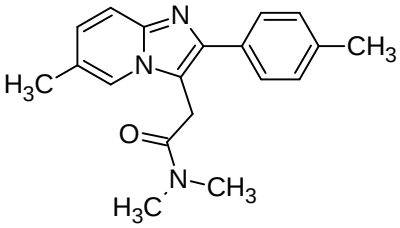
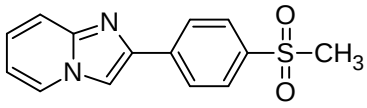
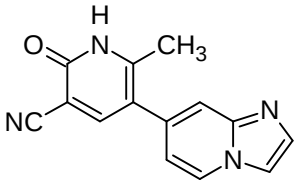


Zolpidem



Zolimidine



Olprinone

MATERIALS AND METHODS

Chemistry

All chemicals and reagents were obtained from Merck or BDH. All melting points are uncorrected and were taken in open capillaries. TLC analysis was carried out on silica gel-G pre-coated aluminum sheet (Merck) and detected under U.V. light. Infrared spectra were determined in KBr on a FT-IR-8400 tensor spectrometer. ^{1}H NMR spectra were measured in BRUKER-300 MHz spectrometer using TMS as an internal standard and $CDCl_3$ & DMSO-d_6 as solvent.

Ethyl 3-(p-methylphenyl)-3-oxopropanoate (1)

To a mixture of 3-ethoxy-3-oxopropanoic acid (1.32gm, 0.01m) and 2,2'-bipyridyle (0.01gm) in tetrahydrofuran(30ml) was added a solution of 1.6M bulyle Lithium(12.8ml) at -40^{o}C, followed by a solution of p-methylbenzoyl chloride (1.2gm, 0.008m) in tetrahydrofuran (10ml). The reaction mixture was heated under reflux for 3 hr. Then it was concentrated, acidified with dilute hydrochloric acid and the separated product was filtered off and crystallized from chloroform/petroleum ether to give compound **1**. Yield 66% (1.07 gm); m.p. 93°C; ($C_{12}H_{14}O_3$; Found: C, 69.61%; H, 6.16%; N, 9.52%; Required: C, 69.88%; H, 6.84%).
TLC solvent system: Ethyl acetate : Hexane (3 : 7).

2-bromo-3-(p-methylphenyl)-ethyl-3-oxopropanoate (2)

A solution of bromine(3.5 gm, 0.022m) in acetic acid(10ml) was added drop wise to a solution of 3-(4-methylphenyl)-ethyl-3-oxopropanoate(2.06 gm, 0.01m) in acetic acid(10ml). The mixture was stirred at room temperature for 24 hrs. The solvent was removed in vacuum and the residue was poured in to crush ice by addition of 1N NaOH solution. The compound was extracted with dichloromethane. The organic layer was dried over Na_2SO_4 and the solvent was removed in

vacuum to afford the oily liquid. Yield 79% (2.25 gm); b.p. 148°C; ($C_{12}H_{13}BrO_3$; Found: C, 50.28%; H, 4.16%; Required: C, 50.55%; H, 4.60%).
TLC solvent system: Ethyl acetate : Hexane (2 : 8).

7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridine-3-ethylcarboxylate (3)
A mixture of 2-amino-4-methyl pyridine(1.08 gm, 0.01m) and 2-bromo-3-(p-methylphenyl)-ethyl-3-oxopropanoate (2.85 gm, 0.01m) in ethanol(10ml.) was refluxed for about 8 hrs. The red oil obtained after evaporate excess ethanol was partitioned between ether-water. The ether extract was allowed to dry and the oil crystallized to get the targeted compound 7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridine-3-ethylcarboxylate. Yield 73% (2.14 gm); m.p. 74°C; ($C_{18}H_{18}N_2O_2$; Found: C, 73.45%; H, 6.16%; N, 9.52%; Required: C, 73.20%; H, 6.24%; N,9.41%).
TLC solvent system: Ethyl acetate : Hexane (4 : 6).

7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridine-3-carbohydrazide (4)
A mixture of 7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridine-3-ethylcarboxylate (2.94 gm, 0.01m) was heated under reflux with hydrazine hydrate (1.00 gm, 0.02m) in ethanol (10 ml) for about 5 hrs. Excess ethanol was evaporated in vacuum. The obtained residue was poured in to crushed ice. Solid product crystallized in ethanol. Yield 84%(2.35 gm); m.p. 132°C. ($C_{16}H_{16}N_4O$; Found: C, 68.61%; H, 5.82%; N, 19.87 %; Required: C, 68.55%; H, 5.75%; N, 19.99 %).
TLC solvent system: Ethyl acetate : Hexane (5 : 5).

3-Mercapto-4-amino-5-[7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4*H*-1,2,4-triazole (5)
A mixture of potassium hydroxide (0.56g, 0.01m) in absolute ethanol (25 ml), 7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridine-3-carbohydrazide(2.80gm, 0.01m) and carbon disulfide (1ml, 0.015 m) was stirred for 15 hrs. The solid product was filtered and wash with diethyl ether (150 ml). A suspension of solid salt, hydrazine hydrate (95%, 1ml, 0.02m) and water(3 ml) was refluxed with stirring for 5 hrs. The contents were diluted with water and acidified with glacial acetic acid to get the product. The isolated product was crystallised from ethanol. yield, 62%; m.p. 207°C. ($C_{17}H_{16}N_6S$; Found: C, 60.51%; H, 4.67%; N, 24.86%; Required: C, 60.69%; H, 4.79%; N, 24.98%).
TLC solvent system : Methanol : Chloroform (1 : 9).

General preparation of *N*-{3-mercapto-5-[7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*] pyridin-3-yl]-4*H*-1,2,4-triazol-4-yl}arylamide (6a-j)
A mixture of 3-Mercapto-4-amino-5-[7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*] pyridin-3-yl]-4*H*-1,2,4-triazole(3.36g, 0.01M) and aromatic acid chloride (0.01m) in dry pyridine (20 ml) was refluxed for 6-10 hrs. The resulting mixture was poured onto crushed ice and neutralized with dilute hydrochloric acid. The product was filtered, washed with cold water and crystallised from ethanol. The progress of reaction was monitored by TLC.

Different aromatic acid chlorides (a-j) condensed with 3-Mercapto-4-amino-5-[7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4*H*-1,2,4-triazole **5**. The physical data are recorded in Table-1.

Table-1: Physical constants of synthesized compounds

Sr. No.	R	Molecular Formula	M.W.	M.P. ° C	Rf Val	Yield %	% of Nitrogen Calcd.	% of Nitrogen Found	Solvent System
6a	C_6H_5-	$C_{24}H_{20}N_6OS$	440.5	186	0.50	51	19.08	18.87	S2
6b	3-OCH_3-C_6H_4-	$C_{25}H_{22}N_6O_2S$	470.5	179	0.58	54	17.86	17.61	S1
6c	2,3-$(OCH_3)_2$-C_6H_3-	$C_{26}H_{24}N_6O_3S$	500.5	177	0.47	63	16.79	16.52	S1
6d	3,5-$(NO_2)_2$-C_6H_3-	$C_{24}H_{18}N_8O_5S$	530.5	191	0.53	48	21.12	20.91	S1
6e	2-C_5H_4N-	$C_{23}H_{19}N_7OS$	441.5	160	0.59	61	22.21	20.96	S2
6f	3-C_5H_4N-	$C_{23}H_{19}N_7OS$	441.5	175	0.51	53	22.21	21.01	S2
6g	4-C_5H_4N-	$C_{23}H_{19}N_7OS$	441.5	189	0.54	52	22.21	20.98	S2
6h	2,4,5-$(F)_3$-C_6H_2-	$C_{24}H_{17}F_3N_6OS$	494.5	204	0.49	51	17.00	16.73	S1
6i	4-Cl-2,5-$(F)_2$-C_6H_2-	$C_{24}H_{17}ClF_2N_6OS$	510.9	208*	0.50	50	16.45	16.21	S1
6j	3-Cl-2,4,5-$(F)_3$-C_6H-	$C_{24}H_{16}ClF_3N_6OS$	528.9	193	0.53	51	15.89	15.63	S1
7a	C_6H_5-	$C_{24}H_{18}N_6S$	422.5	198	0.55	52	19.86	19.61	S1
7b	3-OCH_3-C_6H_4-	$C_{25}H_{20}N_6OS$	452.5	183	0.48	56	18.57	18.33	S3
7c	2,3-$(OCH_3)_2$-C_6H_3-	$C_{26}H_{22}N_6O_2S$	482.5	186	0.51	58	17.42	17.21	S3
7d	3,5-$(NO_2)_2$-C_6H_3-	$C_{24}H_{16}N_8O_4S$	512.5	196	0.49	50	21.86	21.60	S1
7e	2-C_5H_4N-	$C_{23}H_{17}N_7S$	423.5	180	0.51	59	23.15	22.94	S3
7f	3-C_5H_4N-	$C_{23}H_{17}N_7S$	423.5	190	0.47	55	23.15	22.91	S3
7g	4-C_5H_4N-	$C_{23}H_{17}N_7S$	423.5	187	0.48	54	23.15	22.89	S1
7h	2,4,5-$(F)_3$-C_6H_2-	$C_{24}H_{15}F_3N_6S$	476.5	183	0.51	57	17.64	17.41	S3
7i	4-Cl-2,5-$(F)_2$-C_6H_2-	$C_{24}H_{15}ClF_2N_6S$	492.9	194	0.53	53	17.05	16.83	S1
7j	3-Cl-2,4,5-$(F)_3$-C_6H-	$C_{24}H_{14}ClF_3N_6S$	510.9	188	0.52	54	16.45	16.19	S1
S1 Hexane:Ethyl acetate (3:7), S2 Hexane:Ethyl acetate (5:5), S3 Chloroform:Methanol (7:3)									
* : Compound decompose									

General preparation of 3-[7-methyl-2-(p-methylphenyl)imidazo[1,2-a]pyridin-3-yl]-6-phenyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol (7a-j)

A mixture of 3-Mercapto-4-amino-5-[7-methyl-2-(p-methylphenyl)imidazo [1,2-*a*]pyridin-3-yl]-4*H*-1,2,4-triazole (3.36gm, 0.01M) and aromatic acid (0.01M) in phosphorous oxychloride (20 ml) was refluxed for 10 hrs. The resulting mixture was poured onto crushed ice and neutralized with sodium bicarbonate. The product was filtered, washed with cold water and crystallised from ethanol.

All aromatic acids (a-j) reacted with 3-Mercapto-4-amino-5-[7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4*H*-1,2,4-triazole **5**. The physical data are recorded in Table-1.

Biological Evaluation

The newly synthesized compounds were evaluated for their antibacterial and antifungal activity by Broth Dilution Method. The Broth Dilution Method was performed using Muller-Hinton Broth (Hi-Media) medium. Suspension of each microorganism was prepared and applied to plates with serially diluted compounds (DMSO, solvent control) to be tested and incubated (approx. 20 h) at 37^{o}C. The minimum bactericidal concentration (MBC) was considered to be the lowest concentration that was completely inhibited growth on agar plates. The bacteria strains *Escherichia coli* (MTCC-422), *Pseudomonas aeruginosa* (MTCC-441), *Staphylococcus aureus* (MTCC-96), *Streptococcus pyogenes* (MTCC-443) were used for the study. Ampicillin, Chloramphenicol, Ciprofloxacin, & Norfloxacin were used as the standard drug for evaluating antibacterial activity. The Minimal Bactericidal Concentration was measured in microgram/ml. and recorded in Table-2.

The compounds were evaluated for their anti-fungal activity against fungi using Broth Dilution Method with Saburoud's dextrose agar (Hi-Media). Suspension of each fungus were prepared and applied to agar plates with serially diluted compounds to be tested. The plates were incubated at 26^{o}C for 72 h and MIC's were determined. The fungus strains *Candida albicans* (MTCC-227), *Aspergillus niger* (MTCC-282) and *Aspergillus clavatus* (MTCC-1323) were used for this study. Greseofulvin & Nystatin were used as the standard drug for measuring Minimal Fungicidal Concentration (MFC). The Minimal Fungicidal Concentration is recorded in Table-2.

RESULTS AND DICUSSION

In the present work, ethyl 3-(4-methylphenyl)-3-oxopropanoate **1** was prepared by the coupling reaction of p-methylbenzoyl chloride and 3-ethoxy-3-oxopropanoic acid in presence of 1.6M n-BuLi. Compound **1** was treated with Br_2 in acetic acid, ethyl 2-bromo-3-(p-methylphenyl)-3-oxopropanoate **2** was obtained. The cyclo-condensation of compound **2** with 2-amino-4-methylpyridin in absolute ethanol afforded the ethyl-7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*]pyridine-3-carboxylate **3**. The hydrazinolysis of **3** gave the reaction products 7-methyl-2-(p-methylphenyl)imidazo[1,2-a] pyridine-3-carbohydrazide **4**. The latter compound reacted with CS_2 in the presence of potassium hydroxide, followed by treatment with hydrazine hydrate at reflux temperature to give 4-amino-5-[7-methyl-2-(4-methylphenyl)imidazo[1,2-*a*]pyridin-3-yl]-4*H*-1,2,4-triazole-3-thiol **5**. The condensation of different aromatic acid chlorides (a-j) with 1,2,4-triazole derivative **5** in pyridine leads to the formation of corresponding arylamides **6(a-j)**. While compound **5** was reacted with different aromatic acids (a-j) and smoothly cyclodehydrated by boiling in phosphorous oxychloride affording the corresponding [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazoles **7(a-j)**. All the analytical

details show satisfactory results. The following peaks confirmed the formation of target molecules. The peaks around at 3213 cm^{-1}, 2249 cm^{-1},1690 cm^{-1}, 1590 cm^{-1}, 1036 cm^{-1} and 613 cm^{-1} in FTIR, show the presence of groups N-H, S-H, C=O, C=N, N-N and C-S in arylamides respectively. The peaks at near about 1588 cm^{-1}, 1315 cm^{-1},1016 cm^{-1} and 613 cm^{-1} in FTIR, show the presence of groups C=N, C-N, N-N, and C-S-C in [1,2,4]triazolo[3,4-*b*] [1,3,4]thiadiazoles respectively. In ^{1}H-NMR spectra the peaks at around δppm 2.03-2.19 (s, 1H, -SH) and 7.26-7.42 (m, 5H, Ar-H) confirm the formation of *N*-{3-mercapto-5-[7-methyl-2-(p-methylphenyl)imidazo[1,2-*a*] pyridin-3-yl]-4*H*-1,2,4-triazol-4-yl}arylamide **6**. While in compound **7** absence of the peaks of -SH and $-NH_2$ from triazole intermediate, confirm the formation of triazolothiadiazole ring. All the mass spectra showed the molecular ion peaks for their respective molecular weight apart from fragmentation profile. The spectral results of substituted arylamides **6(a-j)** and [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazoles **7(a-j)** are given in Table-3.

The MBC values of compound 6a(100mg/ml) against E. Coli, compound 6e(100mg/ml) against P. Aeruginosa are similar to the Ampicillin. The compounds 6b(100mg/ml), 6c(200mg/ml) and 6d(250mg/ml), 6e(250mg/ml) show less and similar MBC value against S. Aureus respectively, with reference to Ampicillin. The compounds 6b(25mg/ml) and 6c(50mg/ml) show very less MBC value as compare to Chloramphenicol and Ciprofloxacin against S. Pyogenus, while the MBC value of compound 6i(100mg/ml) and 6j(100mg/ml) are comparable to Ampicillin.

The MBC value of the compounds 7f(25mg/ml) is similar to that of the Ciprofloxacin, while that of compound 7e(50mg/ml) is similar to Chloramphenicol and the compounds 7a, 7d and 7h show similar (100mg/ml) MBC value with reference to the Ampicillin, against E. Coli. The MBC value of 7a(50mg/ml) is similar to Chloramphenicol and the MBC value of the compound 7f(100mg/ml) is similar to the MBC value of Ampicillin, against P. Aeruginosa.

The MFC values of the compounds 6e(250mg/ml) and 4e(200mg/ml) are less, while compounds 6b, 6c, 6f and 6j are similar (100mg/ml) to that of Greseofulvin against C. Albicans. All the compounds show high MFC value against A. Niger and A. Clavatus in comparison to the standard drugs taken.

The MFC values of compounds 7a, 7h and 7j are half (250mg/ml) than the MFC value of Greseofulvin and compounds 7g and 7i show equivalent value (500mg/ml) to that of the standard drug against C. Albicans. The MFC values of all the newly synthesized compounds are quite more against A. Niger and A. Clavatus in comparison to Nystatin and Greseofulvin.

Scheme 1: Synthesis of studied compounds

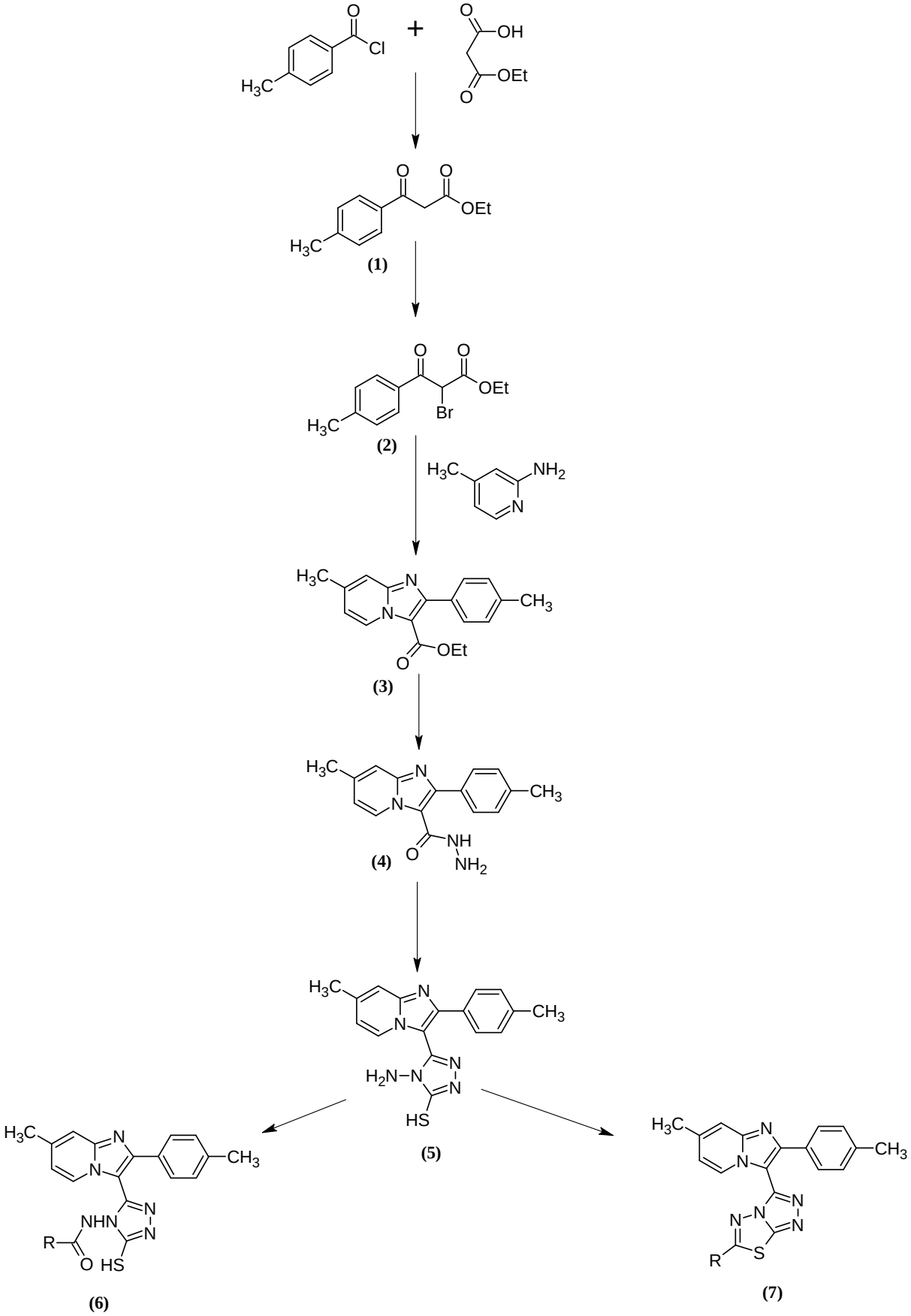


Table-2: Minimal Bactericidal Concentration (MBC) and Minimal Fungicidal Concentration (MFC) values of synthesized compounds

ANTIBACTERIAL ACTIVITY TABLE						ANTIFUNGAL ACTIVITY TABLE		
MINIMAL BACTERICIDAL CONCENTRATION (□g/ml)						MINIMAL FUNGICIDAL CONCENTRATION (□g/ml)		
NO.	CODE NO.	E. COLI MTCC 442	P. AERUGINOSA MTCC 441	S. AUREUS MTCC 96	S.PYOGENUS MTCC 443	C. ALBICANS MTCC 227	A. NIGER MTCC 282	A. CLAVATUS MTCC 1323
1	6a	100	500	500	500	1000	>1000	>1000
2	6b	500	250	100	25	500	1000	1000
3	6c	1000	100	200	50	500	>1000	>1000
4	6d	250	500	250	100	1000	500	500
5	6e	1000	1000	250	500	250	1000	1000
6	6f	500	500	500	250	500	1000	1000
7	6g	250	250	1000	250	1000	500	500
8	6h	1000	1000	500	250	1000	500	500
9	6i	500	250	1000	125	200	500	500
10	6j	250	250	1000	100	500	250	500
11	7a	100	50	500	250	250	500	500
12	7b	500	500	250	500	1000	>1000	>1000
13	7c	250	250	500	500	1000	>1000	>1000
14	7d	100	250	1000	1000	1000	500	500
15	7e	50	125	500	500	1000	>1000	>1000
16	7f	25	100	250	100	1000	500	500
17	7g	500	500	100	1000	500	250	500
18	7h	100	250	500	500	250	500	500
19	7i	500	500	100	250	500	500	500
20	7j	500	500	1000	100	250	1000	1000
21	AMPICILLIN	**100**	**100**	250	**100**	**	**	**
22	CHLORAMPHENICOL	**50**	**50**	**50**	**50**	**	**	**
23	CIPROFLOXACIN	**25**	**25**	**50**	**50**	**	**	**
24	NORFLOXACIN	**10**	**10**	**10**	**10**	**	**	**
25	NYSTATIN	**	**	**	**	**100**	**100**	**100**
26	GRESEOFULVIN	**	**	**	**	500	**100**	**100**

Table-3: Spectral data of synthesized compounds

Sr. No.	No	Spectral data
1	6a	IR (KBr, cm^{-1}) : 3213, 3062, 2831, 2249, 1690, 1604, 1590, 1481, 1170, 1117, 1036, 825, 613. ^{1}H-NMR (DMSO-d_6, δppm) : 2.07 (s, 1H, -SH), 2.28 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Py-CH_3), 7.19–7.87 (m, 12H, Ar-H). Mass (m/z) : 441.5 (M+1)
2	6b	IR (KBr, cm^{-1}) : 3218, 3043, 2791, 2261, 1678, 1598, 1582, 1473, 1191, 1121, 1042, 836, 621. ^{1}H-NMR (DMSO-d_6, δppm) : 2.10 (s, 1H, -SH), 2.29 (s, 3H, Ar-CH_3), 2.42 (s, 3H, Py-CH_3), 4.10 (s, 3H, Ar-OCH_3), 6.99–8.10 (m, 11H, Ar-H). Mass (m/z) : 471.7 (M+1)
3	6c	IR (KBr, cm^{-1}) : 3308, 3112, 2821, 2271, 1680, 1605, 1576, 1483, 1176, 1131, 1022, 849, 616. ^{1}H-NMR ($CDCl_3$, δppm) : 2.05 (s, 1H, -SH), 2.21 (s, 3H, Ar-CH_3), 2.34 (s, 3H, Py-CH_3), 4.20 (s, 6H, Ar-OCH_3), 7.00–7.91 (m, 10H, Ar-H). Mass (m/z) : 501.5 (M+1)
4	6d	IR (KBr, cm^{-1}) : 3215, 3085, 2843, 2283, 1691, 1612, 1575, 1521, 1479, 1348, 1178, 1123, 1036, 847, 619. ^{1}H-NMR ($CDCl_3$, δppm) : 2.07 (s, 1H, -SH), 2.23 (s, 3H, Ar-CH_3), 2.32 (s, 3H, Py-CH_3), 6.13 (s, 1H, -NH), 7.06–8.31 (m, 10H, Ar-H) . Mass (m/z) : 531.5 (M+1)
5	6e	IR (KBr, cm^{-1}) : 3216, 3046, 2793, 2258, 1670, 1596, 1591, 1470, 1189, 1118, 1038, 831, 618. ^{1}H-NMR (DMSO-d_6, δppm) : 2.08 (s, 1H, -SH), 2.26 (s, 3H, Ar-CH_3), 2.31 (s, 3H, Py-CH_3), 6.80–8.03 (m, 11H, Ar-H). Mass (m/z) : 442.5 (M+1)
6	6f	IR (KBr, cm^{-1}) : 3211, 3041, 2831, 2278, 1698, 1573, 1561, 1451, 1193, 1136, 1041, 836, 614. ^{1}H-NMR (DMSO-d_6, δppm) : 2.06 (s, 1H, -SH), 2.26 (s, 3H, Ar-CH_3), 2.32 (s, 3H, Py-CH_3), 6.79–8.01 (m, 11H, Ar-H). Mass (m/z) : 442.5 (M+1)
7	6g	IR (KBr, cm^{-1}) : 3306, 3056, 2783, 2257, 1679, 1576, 1562, 1463, 1186, 1170, 1046, 841, 629. ^{1}H-NMR (DMSO-d_6, δppm) : 2.06 (s, 1H, -SH), 2.27 (s, 3H, Ar-CH_3), 2.30 (s, 3H, Py-CH_3), 6.80–8.01 (m, 11H, Ar-H). Mass (m/z) : 442.5 (M+1)
8	6h	IR (KBr, cm^{-1}) : 3215, 3064, 2833, 2244, 1694, 1608, 1586, 1486, 1378, 1178, 1121, 1026, 827, 612. ^{1}H-NMR ($CDCl_3$, δppm) : 2.03 (s, 1H, -SH), 2.23 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Py-CH_3), 6.45–7.83 (m, 9H, Ar-H). Mass (m/z) : 495.5 (M+1)
9	6i	IR (KBr, cm^{-1}) : 3302, 3118, 2831, 2274, 1678, 1618, 1570, 1471, 1368, 1128, 1025, 851, 721, 619. ^{1}H-NMR ($CDCl_3$, δppm) : 2.05 (s, 1H, -SH), 2.18 (s, 3H, Ar-CH_3), 2.21 (s, 3H, Py-CH_3), 6.05 (s, 1H, -NH), 7.00–8.13 (m, 9H, Ar-H). Mass (m/z) : 511.9 (M+1)
10	6j	IR (KBr, cm^{-1}) : 3298, 3108, 2834, 2275, 1683, 1611, 1581, 1478, 1351, 1158, 1121, 1019, 846, 729, 621. ^{1}H-NMR ($CDCl_3$, δppm) : 2.05 (s, 1H, -SH), 2.21 (s, 3H, Ar-CH_3), 2.39 (s, 3H, Py-CH_3), 5.98 (s, 1H, -NH), 6.10–7.91 (m, 8H, Ar-H). Mass (m/z) : 429.9 (M+1)
11	7a	IR (KBr, cm^{-1}) : 3030, 2960, 2866, 1612, 1581, 1496, 1460, 1357, 1180, 1066, 1020, 715. ^{1}H-NMR (DMSO-d_6, δppm) : 2.31 (s, 3H, Ar-CH_3), 2.92 (s, 3H, Py-CH_3), 7.02–7.94 (m, 12H, Ar-H). Mass (m/z) :

		423.5 (M+1)
12	7b	IR (KBr, cm^{-1}) : 3042, 2956, 2862, 1610, 1582, 1498, 1461, 1351, 1189, 1059, 1018, 833, 721. ^{1}H-NMR (DMSO-d_6, δppm) : 2.28 (s, 3H, Ar-CH_3), 2.43 (s, 3H, Py-CH_3), 4.13 (s, 3H, Ar-OCH_3), 6.95–8.10 (m, 11H, Ar-H). Mass (m/z) : 453.7 (M+1)
13	7c	IR (KBr, cm^{-1}) : 3043, 2961, 2853, 1608, 1572, 1484, 1461, 1373, 1187, 1182, 1012, 830, 718. ^{1}H-NMR ($CDCl_3$, δppm) : 2.21 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Py-CH_3), 4.18 (s, 6H, Ar-OCH_3), 7.03–7.89 (m, 10H, Ar-H). Mass (m/z) : 483.5 (M+1)
14	7d	IR (KBr, cm^{-1}) : 3048, 2950, 2856, 1614, 1565, 1521, 1485, 1459, 1371, 1250, 1178, 1106, 836. ^{1}H-NMR ($CDCl_3$, δppm) : 2.18 (s, 3H, Ar-CH_3), 2.31 (s, 3H, Py-CH_3), 7.02–8.36 (m, 10H, Ar-H). Mass (m/z) : 513.5 (M+1)
15	7e	IR (KBr, cm^{-1}) : 3041, 2951, 2863, 1619, 1562, 1493, 1460, 1364, 1248, 1180, 1116, 841. ^{1}H-NMR (DMSO-d_6, δppm) : 2.25 (s, 3H, Ar-CH_3), 2.31 (s, 3H, Py-CH_3), 6.78–8.00 (m, 11H, Ar-H). Mass (m/z) : 424.5 (M+1)
16	7f	IR (KBr, cm^{-1}) : 3040, 2978, 2843, 1620, 1532, 1484, 1461, 1341, 1239, 1187, 1110, 846. ^{1}H-NMR (DMSO-d_6, δppm) : 2.27 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Py-CH_3), 7.00–8.11 (m, 11H, Ar-H). Mass (m/z) : 424.5 (M+1)
17	7g	IR (KBr, cm^{-1}) : 3043, 2953, 2861, 1618, 1568, 1476, 1451, 1364, 1251, 1173, 1102, 828. ^{1}H-NMR (DMSO-d_6, δppm) : 2.22 (s, 3H, Ar-CH_3), 2.35 (s, 3H, Py-CH_3), 6.78–7.86 (m, 11H, Ar-H). Mass (m/z) : 424.5 (M+1)
18	7h	IR (KBr, cm^{-1}) : 3050, 2947, 2853, 1614, 1553, 1485, 1445, 1352, 1230, 1181, 1109, 824. ^{1}H-NMR ($CDCl_3$, δppm) : 2.18 (s, 3H, Ar-CH_3), 2.23 (s, 3H, Py-CH_3), 7.18–8.13 (m, 9H, Ar-H). Mass (m/z) : 477.5 (M+1)
19	7i	IR (KBr, cm^{-1}) : 3044, 2970, 2862, 1617, 1581, 1493, 1470, 1364, 1250, 1191, 1101, 849, 736. ^{1}H-NMR ($CDCl_3$, δppm) : 2.19 (s, 3H, Ar-CH_3), 2.39 (s, 3H, Py-CH_3), 6.35–7.81 (m, 9H, Ar-H). Mass (m/z) : 493.9 (M+1)
20	7j	IR (KBr, cm^{-1}) : 3062, 2971, 2870, 1607, 1561, 1473, 1454, 1362, 1246, 1165, 1109, 833, 729. ^{1}H-NMR ($CDCl_3$, δppm) : 2.26 (s, 3H, Ar-CH_3), 2.33 (s, 3H, Py-CH_3), 6.13–7.84 (m, 8H, Ar-H). Mass (m/z) : 511.9 (M+1)

CONCLUSION

It can be concluded from the MBC values that the simple phenyl substituted arylamide show equivalent activity with that of Ampicillin against E. Coli, while 3-methoxyphenyl and 2,3-dimethoxyphenyl substituted compounds show remarkable activity against S. Aureus and P. Aeruginosa respectively as compare to Ampicillin. Further these compounds show excellent and equivalent activity respectively, against S. Pyogenus with reference to Chloramphenicol and Ciprofloxacin. The low MFC values indicate that the 4-chloro, 2,5-difluorophenyl and 2-

pyridine substituted arylamide show good activity against C. Albicans as compared to Greseofulvin.

Phenyl and pyridine substituted thiadiazole show equivalent activity against P. Aeruginosa and E. Coli respectively with that of Chloramphenicol. 2,4,5-trifluoro, 2-chloro,4,5-difluoro and 3-chloro,2,4,5-trifluoro substituted compounds show equivalent activity against E. Coli, S. Aureus and S. Pyogenus in comparison to Ampicillin. The low MFC values indicate that the simple, 2,4,5-trifluoro and 3-chloro,2,4,5-trifluoro substituted thiadiazoles shows good activity against C. Albicans as compared to Greseofulvin.

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