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Synthesis and antimicrobial studies of 2-(5-substituted)-1, 3, 4-oxadiazole-2-yl)-*H*-imidazo [1, 2, α] pyridine derivatives

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ABSTRACT

A novel series of 2-(5-substituted)-1,3,4-oxadiazole-2-yl)-H-imidazo[1,2,α]pyridine derivatives ***5a-i*** *and* ***6a-d*** *are synthesized and characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass spectral analysis. All the synthesized compounds were tested for there antibacterial and antifungal activity of which compound* ***5b, 5c, 5d, 5e, 5f, 5g, 5h, 5i, 6a, 6c*** *and* ***6d*** *exhibited good antimicrobial activity.*

Keywords: Imidazo [1, 2-*a*] pyridine; 1, 3, 4-oxadiazole; antibacterial; antifungal activity.

INTRODUCTION

It has long been known that imidazo [1, 2-*a*] pyridine derivatives exhibited diverse biological activities [1-3] and are used as antiviral, [4-12] antiulcer, [13-15] antibacterial, [16-17] antifungal, [18-19] antiprotozoal, [20-21] antiherpes, [22] and anti-inflammatory [23] agents. They have also been shown to be selective cyclin dependant Kinase inhibitors, [24] GABA [25] and benzodiazepine receptor agonists, [26-27] and bradykinin B2 receptor antagonists, [28] Cytomegalovirus, [29]. These derivatives also inhibits enzyme like prolyl hydrolase, [30] and some of the derivatives are used to detect β-Amyloid in brain and Alzheimer's disease. [31-32]

Derivatives of 1, 3, 4–oxadiazole have been found to possess a wide spectrum of pharmacological, medical and biological activities [33-34]. Compounds containing 1, 3, 4-oxadiazole nucleus also find unique place in medicinal chemistry and play significant role as they are associated with immense biological activity. The small and simple 1,3,4-oxadiazole nucleus is present in compounds involved in research aimed at evaluating new compounds that posses interesting pharmacological properties like antipanosonal, antibacterial, fungicidal, herbicidal, antitumor, anti-inflammatory, antituberculosis, diuretic, hypoglycemic, anticonvulsant and analgesic. 2, 5-disubstituted-1, 3, 4-oxadiazole derivatives have attracted considerable attention owing to their effective biological activity and extensive use.

In light of the above mentioned findings and in continuation of our work on various heterocyclic compounds as potential antimicrobial agents, we herein report the design, synthesis and antimicrobial evaluation of some novel 2,5-disubstituted 1,3,4-oxadiazole derivatives with imidazo pyridine and substituted phenyl and styryl substitutions.

EXPERIMENTAL SECTION

Melting points of compounds were determined in open capillary tubes in silicon oil bath using a Veego melting point apparatus and are uncorrected. Purity of compounds was monitored by TLC on silica F_{254} coated aluminum plates (Merck) as adsorbent and U.V. light and Iodine chamber as a visualizing agent. IR spectra (KBr in cm^{-1}) were recorded on Shimadzu Model FTIR-435. ^{1}H-NMR spectra were recorded on a Varian mercury TH-300 operating at 300 MHz & 400 MHz using $CDCl_3$ as a solvent and TMS as a internal standard (Chemical shift in ppm) and high

resolution mass spectra were made on a Water Q-T mass spectrometer. The isotopic peak at M+2 was observed in the mass spectrum of all the compounds due to S and Cl or Br.

Synthesis of Ethyl-2-methyl-H-imidazo [1, 2-a] pyridine-3-carboxylate (3):
2-Amino pyridine **1 (**15.0 g, 1.0 mol) was dissolved in absolute ethanol (30 ml). To this potassium carbonate (26.44 g, 1.2 mol) was added and the reaction mixture was stirred for 15 min. To this mixture, ethyl-2-chloro oxobutanoate **2** (31.48 g, 1.2 mol) in ethanol (15 ml) was added drop wise and then refluxed for 8-10 hrs. After completion of reaction as monitored on TLC, the reaction was cooled at room temperature. The solid was filtered and washed with ethanol (15 ml). Ethanol was removed under reduced pressure and 50 gm crushed ice was added and reaction mass was stirred for 15 min. The product was then extracted with dichloromethane (4 x 25 ml), the combined dichloromethane was washed with saturated brine water (50 ml) and dried over sodium sulphate. Dichloromethane was removed under reduced pressure to obtain 24.37 g product.

Yield, 75 %.; mp 61-65°C; IR (KBr, cm^{-1}) : 1224 (C-N), 1498 (C=C), 1681 (C=O); ^{1}H NMR ($CDCl_3$, 400 Hz)**:** δ 1.39-1.43 (t, 3H, *J*=10.68 Hz, -CH_2CH_3), 2.69 (s, 3H, -CH_3), 4.37-4.43 (m, 2H, -OCH_2CH_3), 6.92-6.96 (t, 1H, d = 7.42, Ar*H*), 7.32-7.37 (t, 1H, *J* = 8.46 Hz, Ar*H*), 7.57-7.59 (d, 1H, *J* = 8.8 Hz, Ar*H*), 9.27-9.28 (d, 1H, *J* = 6.9 Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 Hz): δ 14.47, 16.66, 60.28, 112.60, 113.62, 116.62, 127.58, 127.96, 146.82, 152.70, 161.45.

Synthesis of 2-methylH-imidazo[1,2-a]pyridine-3-carbohydrazide (4).
To a mixture of compound **3** (24.0 g) in methanol (50 ml), hydrazine hydrate (48.0 ml) was added and refluxed for 4 hrs. After completion of the reaction the solid product separated out was filtered and washed with methanol (5 ml) to obtain 12.40 g pure product.Yield, 55 %; mp 187-189ºC; IR (KBr, cm^{-1}): 1244 (C-N), 1494 (C=C), 1626 (C=O), 3288 (NH); ^{1}H NMR ($CDCl_3$, 400 Hz)**:** δ 2.67 (s, 3H, -CH_3), 4.12 (bs, 2H, -NH_2), 6.90-6.93 (t, 1H, *J*= 7.2, Ar*H*), 7.06 (bs, 1H, -N*H*), 7.30-7.34 (t,1H, *J*= 7.2 Hz, Ar*H*), 7.55-7.57 (d, 1H, *J* = 9.0 Hz, ArH), 9.30-9.32 (d, 1H, *J*= 6.8 Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 Hz): δ 15.40, 38.96, 39.16, 39.37, 39.58, 39.79, 40.21, 112.43, 114.42, 115.73, 126.21, 126.93, 145.12, 145.20, 161.77.

General procedure for the synthesis of 5-(3-methyl-H-imidazo [1,2-a]pyridin-2-yl)-1,3,4-oxadiazole-2-thiol (5a-i and 6a-d). To compound **(4) (**1.0 gm, 1.0 mol), phosphors oxychloride (24.0 mL) was added. To this mixture benzoic acid or cinnamic acid (1.1 mol) was then added and refluxed for 8-10 hrs. After completion of the reaction (As checked by TLC) it was poured to ice. Solid product obtained was filtered and purified by column chromatography using hexane: ethyl acetate as eluent.

2-Methyl-3-(5-phenyl-[1,3,4]oxadiozole-2-yl)-imidazo[1,2-a]pyridine (5a)
Yield, 78%; mp 157-159ºC; IR(KBr cm^{-1}): 1096 (C-O), 1261 (C-N), ; ^{1}H NMR($CDCl_3$, 400 Hz): δ 2.82 (s, 3H, -CH_3), 7.27-7.31 (m, 1H, *J= 6.88* Hz, Ar*H*), 7.55-7.59 (m, 1H, *J*= 8.12 Hz, Ar*H*), 7.65-7.68 (m, 3H, *J*= 7.52 Hz, Ar*H*), 7.74-7.76 (m, 1H, *J*= 9.0 Hz, Ar*H*), 8.13-8.28 (m, 2H, Ar*H*), 9.33-9.40 (m, 1H, *J*= 7.64 Hz, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.33, 114.22, 116.43, 123.13, 126.45, 127.29, 127.49, 127.30, 131.77, 146.14, 147.97, 157.76, 161.99; HRMS (EI^+ mode) m/z calcd for $C_{16}H_{12}N_4O$ [M+H] 277.1044 found 277.0800.

2-Methyl-3-(5-p-tolyl-[1,3,4]oxadiozole-2-yl)-imidazo[1,2-a]pyridine (5b):
Yield, 85 %; mp 182-183ºC; IR (KBr cm^{-1}): 1047 (C-O), 1258 (C-N), 1602 (C=O); ^{1}H NMR($CDCl_3$, 400 Hz): δ 2.80 (s, 3H, -CH_3), 2.87 (s, 3H, -CH_3), 7.05-7.10 (t, 1H, *J= 8*.8 Hz, Ar*H*), 7.35-7.47 (m, 4H, Ar*H*), 7.67-7.70 (d, 1H, *J= 11.6* Hz, Ar*H*), 8.01-8.04 (d, 1H, *J*= 10.0 Hz, ArH), 9.52-9.54 (d, 1H, *J*= 9.2 Hz, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.71, 22.31, 113.90, 116.76, 126.32, 127.27, 127.95, 128.52, 131.28, 131.88, 138.43, 146.14, 147.97, 148.46; HRMS (EI^+ mode) m/z calcd for $C_{17}H_{14}N_4O$ [M+H] 291.1086, found 291.0769.

3-[5-(2-Fluro phenyl)-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (5c):
Yield, 80%; mp 194-196ºC; IR (KBr cm^{-1}): 1071 (C-O), 1257 (C-N), 1339, 1449, 1615 (C=O); ^{1}H NMR ($CDCl_3$, 400 Hz): δ 2.80 (s, 3H, -CH_3), 7.40-7.42 (m, 3H, Ar*H*), 7.68-7.70 (m, 2H, Ar*H*), 7.81-7.83 (m, 1H, Ar*H*), 8.13-8.17 (m, 1H, Ar*H*), 9.40-9.42 (m, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 13.92, 106.63, 107.50, 111.39, 115.14, 115.68, 116.93, 117.13, 118.63, 125.16, 127.79, 129.39, 129.89, 134.04, 143.26, 144.10, 145.10, 151.69, 156.66, 157.22, 157.95; HRMS (EI^+ mode) m/z calcd for $C_{16}H_{11}FN_4O$ [M+H] 295.0950, found 295.0617.

3-[5-(2-Iodo phenyl)-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (5d):
Yield,76%; mp 198-199ºC; IR (KBr cm^{-1}): 1019 (C-O),1250 (C-N), 1603 (C=O); ^{1}H NMR($CDCl_3$, 400 Hz): δ 2.90 (s, 3H, -CH_3), 7.09-7.15 (m, 1H, Ar*H*), 7.22-7.26 (m, 1H, Ar*H*), 7.39-7.47 (m, 2H, Ar*H*), 7.51-7.55 (m, 1H, Ar*H*), 7.73-7.76 (m, 1H, Ar*H*), 7.92-7.99 (m, 1H, Ar*H*), 8.01-8.08 (m, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.84, 94.15, 99.99, 107.64, 114.20, 116.72, 127.71, 127.85, 128.07, 128.42, 128.95, 131.02, 131.61, 132.16, 132.52,

141.20, 141.47, 146.78, 148.59, 158.64, 162.56, 169.20; HRMS (EI^+ mode) m/z calcd for $C_{16}H_{11}IN_4O$ [M+H] 402.1892, found 402.9512.

3-[5-(3-Chloro phenyl)-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (5e):
Yield, 70%; mp 174-176ºC; IR (KBr cm^{-1}): 1080 (C-O), 1256 (C-N), 1606 (C=O); ^1H NMR($CDCl_3$, 300 Hz): δ 3.03 (s, 3H, -C*H*$_3$), 7.41-7.54 (m, 1H, Ar*H*), 7.58-7.60 (m, 2H, Ar*H*), 7.79-7.80 (m, 1H, Ar*H*), 8.04-8.05 (m, 1H, Ar*H*), 8.12-8.17 (m, 2H, Ar*H*), 9.73-9.74 (m,1H, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.59, 100.09, 114.47, 116.70, 122.04, 127.95, 128.18, 129.64, 138.16, 158.34, 162.18; HRMS (EI^+ mode) m/z calcd for $C_{16}H_{11}ClN_4O$ [M-H] 311.0591, found 311.0376.

3-[5-(4-Chloro phenyl)-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (5f):
Yield, 89%; mp 178-179ºC; IR (KBr cm^{-1}): 1088 (C-O), 1262 (C-N), 1595 (C=O); ^1H NMR($CDCl_3$, 400 Hz): δ 2.82 (s, 3H, -C*H*$_3$), 7.04-7.07 (m, 1H, Ar*H*), 7.38-7.42 (m, 1H, Ar*H*), 7.45-7.47 (m, 2H, Ar*H*), 7.66-7.69 (m, 1H, Ar*H*), 7.98-8.02 (m, 2H, Ar*H*), 9.43-9.44 (m, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.58, 100.06, 114.43, 116.73, 122.08, 127.99, 128.16, *129.69, 138.19, 158.30, 162.13; HRMS* (EI^+ mode) m/z calcd for $C_{16}H_{11}ClN_4O$ [M+H] 311.0591, found 311.0376.

3-[5-(4-Fluro phenyl)-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (5g):
Yield, 87%; mp 163-167ºC; IR (KBr cm^{-1}): 1065 (C-O), 1260 (C-N), 1604 (C=O); ^1H NMR ($CDCl_3$, 400 Hz): δ 2.93 (s, 3H, -C*H*$_3$), 7.18-7.26 (m, 4H, Ar*H*), 7.52-7.53 (m, 1H, Ar*H*), 7.80-7.84 (m, 1H, Ar*H*), 8.14-8.15 (m, 1H, ArH), 9.55-9.57 (m, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.92, 114.65, 116.42, 116.71, 119.70, 128.11, 128.43, 129.14, 129.25, 157.81, 162.08, 163.12, 166.57, 183.76; HRMS (EI^+ mode) m/z calcd for $C_{16}H_{11}FN_4O$ [M+H] 295.0950, found 295.0617.

2-Methyl-3-[5-(4-nitro-phenyl)-[1,3,4]oxadiozole-2-yl]-imidazo[1,2-a]pyridine (5h):
Yield, 82%; mp 188-191ºC; IR (KBr cm^{-1}): 1065 (C-O), 1263 (C-N), 1592 (C=O); ^1H NMR ($CDCl_3$, 400 Hz): δ 2.88 (s, 3H, -C*H*$_3$), 7.12-7.14 (m, 1H, Ar*H*), 7.45-7.50 (m, 3H, Ar*H*), 7.62-7.63 (m, 1H, Ar*H*), 7.75-7.78 (m, 1H, Ar*H*), 8.06-8.13 (m, 1H, Ar*H*), 9.51-9.54 (m, 1H, Ar*H*); HRMS (EI^+ mode) m/z calcd for $C_{16}H_{11}N_5O$ [M+H] 322.0895, found 322.0797.

2-Methyl-3-[5-(2,4-Dichloro-phenyl)-[1,3,4]oxadiozole-2-yl]-imidazo[1,2-a]pyridine (5i):
Yield, 85%; mp 183-186ºC; IR (KBr cm^{-1}): 1084 (C-O), 1263 (C-N), 1600 (C=O); ^1H NMR($CDCl_3$, 400 Hz): δ 2.88 (s, 3H, -C*H*$_3$), 7.41-7.49 (m, 3H, Ar*H*), 7.59-7.62 (m, 1H, Ar*H*), 7.77-7.80 (m, 1H, Ar*H*), 8.05-8.11 (m, 1H, Ar*H*), 9.50-9.53 (m, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 15.46, 100.05, 114.48, 116.79, 121.46, 127.83, 127.91, 128.06, 131.03, 131.40, 131.42, 131.96, 132.08, 132.90, 133.74, 134.05, 138.35, 138.53, 146.80, 148.60, 158.75, 160.74; HRMS (EI^+ mode) m/z calcd for $C_{16}H_{10}Cl_2N_4O$ [M-H] 345.1828, found 345.0135.

3-{5-[2-(4-Fluorophenyl)-vinyl]-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (6a):
Yield, 75%; mp 194-197ºC; IR (KBr cm^{-1}): 1244 (C-O), 1626 (C=C), 3217(=C-H); ^1H NMR($CDCl_3$, 400 Hz): δ 2.77 (s, 3H, -C*H*$_3$), 7.20-7.24 (m, 2H, -Ar*H*), 7.35-7.39 (m, 1H, -Ar*H*), 7.43-7.47 (m, 1H, -Ar*H*), 7.65-7.70 (m, 1H, -Ar*H*), 7.81-7.88 (m, 4H, -Ar*H*), 9.38-9.39 (m,1H, -Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 13.42, 108.18, 114.31, 115.85, 116.06, 116.66, 125.18, 125.77, 127.78, 128.35, 130.22, 130.31, 138.18, 152.90, 156.37, 162.64; HRMS (EI^+ mode) m/z calcd for $C_{18}H_{13}FN_4O$ [M+H] 321.1106, found 321.0735.

3-{5-[2-(4-tert butyl-phenyl)-vinyl]-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (6b):
Yield, 89%; mp 181-184ºC; IR (KBr cm^{-1}): 1244 (C-O), 1626 (C=C), 3217 (C-H); ^1H NMR($CDCl_3$, 400 Hz): δ 1.17-1.33 (s, 9H, -C(C*H*$_3$)$_3$), 2.82 (s, 3H, -C*H*$_3$), 7.36-7.38 (m, 1H, -Ar*H*), 7.41-7.44 (m, 1H, -Ar*H*), 7.46-7.48 (m, 2H, -Ar*H*), 7.73-7.75 (m, 1H, -Ar*H*), 7.78-7.80 (m, 3H, -Ar*H*), 7.86-7.88 (m, 1H, ArH), 9.41-9.42 (d, 1H, *J*= 6.8 Hz, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): 14.09, 30.89, 34.58,108.64, 115.01, 115.90, 125.16, 125.73, 127.73, 128.03, 129.09, 130.24, 131.94, 138.92, 152.90, 156.37, 162.64; HRMS (EI^+ mode) m/z calcd for $C_{22}H_{22}N_4O$ [M+H] 359.1872, found 359.1660.

3-{5-[2-(2-Fluro-phenyl)-vinyl]-[1,3,4]oxadiazole-2-yl]-2-methyl-imidazo[1,2-a]pyridine (6c):
Yield, 79%; mp 186-188ºC; IR (KBr cm^{-1}): 1244 (C-O), 1626 (C=C), 3217(=C-H); ^1H NMR($CDCl_3$, 400 Hz): δ 2.90 (s, 3H, -C*H*$_3$), 7.36-7.42 (m, 2H, Ar*H*), 7.54-7.61 (m, 3H, -Ar*H*), 7.80-7.84 (d, 1H, *J*= 16.56 Hz, Ar*H*), 7.90-7.94 (d, 1H, *J*= 15.44 Hz, ArH), 8.00-8.02 (m, 1H, Ar*H*), 8.06-8.10 (m, 1H, Ar*H*), 9.51-9.53 (d, 1H, *J*= 6.68 Hz, Ar*H*); ^{13}C NMR ($CDCl_3$, 100 Hz): δ 13.42, 108.16, 112.05, 114.43, 116.06, 116.61, 125.15, 125.74, 127.76, 128.29, 128.86, 130.31, 138.18, 152.90, 156.37, 162.64; HRMS (EI^+ mode) m/z calcd for $C_{18}H_{13}FN_4O$ [M+H] 321.1106, found 321.0735.

3-{5-[2-(3-Nitro-phenyl)-vinyl]-[1, 3, 4] oxadiazole-2-yl]-2-methyl-imidazo [1, 2-a] pyridine (6d):

Yield, 81%; mp 190-194ºC; IR (KBr cm^{-1}): 1244 (C-O), 1626 (C=C), 3217 (C-H); ^{1}H NMR ($CDCl_3$, 400 Hz): δ 2.87 (s, 3H, -C*H*$_3$), 7.48-7.51 (m, 1H, Ar*H*), 7.80 (m, 2H, Ar*H*), 7.91-7.95 (m, 1H, Ar*H*), 8.17-8.24 (m, 2H, Ar*H*), 8.24-8.26 (m, 2H, Ar*H*), 8.35-8.37 (m, 1H, Ar*H*), 8.66-8.71 (m, 1H, Ar*H*), 9.45-9.46 (d, 1H, *J*= 6.88 Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 Hz): 13.44, 108.14, 114.34, 115.82, 116.09, 116.63, 125.15, 125.74, 127.74, 128.38, 130.26, 130.29, 138.16, 152.94, 156.39, 162.60. HRMS (EI^+ mode) m/z calcd for $C_{18}H_{13}N_4O$ [M+H] 348.1051, found 348.0791.

Antimicrobial Activity

The antibacterial activity of all the newly synthesized compounds was done by the Muller-Hinton agar-well diffusion assay technique. The stock solutions of all test compounds (100 µg/mL) were prepared by dissolving 100 µg of the test compound in DMSO (1 mL). Chloramphenicol and DMSO were used as positive and negative controls, respectively. Twenty milliliter of molten and cooled MHA and 320 µL of each test bacterial culture were mixed (separate flasks were used for each bacterial culture) and poured in sterilized and labeled petri plates. The wells of 6 mm were punched in the solidified petri plates, aseptically. Fifty micro litters from stock solutions of all compounds as well as controls was added to each well of labeled petri plates and incubated at 35^{o}C for 24 h. The diameter of the zone of growth inhibition around each well was measured after incubation using vernier caliper.

The minimum inhibitory concentration (MIC) of compounds against Gram-positive and Gram-negative test bacteria was determined in the range 100 to 40 µg/mL. All the test cultures were streaked on SCDA and incubated overnight at 37^{o}C. Stock solution of each compound was prepared in DMSO and was appropriately diluted to get a final concentration of 100, 90, 80, 70, 60, 50 and 40 µg/mL. Standard antibiotic chloramphenicol was also diluted to get a final concentration in the same manner.

For the antifungal activity, Potato dextrose agar (Hi media) medium was used. This sterilized hot medium (15 mL) was pipette out into flat petri plates. When it solidified 15 mL of warm seeded agar was applied over it. The seeded agar was made by cooling the medium to 40 ^{o}C and then adding spore suspension to seeded medium. Nystatin and DMSO were used as positive and negative controls, respectively. Concentration 100 µg/mL of the synthesized compounds were prepared by dissolving the required quantity of compounds in DMSO, sterilized Whatman filter paper number 541 discs were prepared by cutting 6 mm diameter were spread individually with needle and planted upon the chilled seeded medium. The culture plates were then incubated for 24–72 h at 37^{o}C and inhibition zone around each disc was measured from the centre of the discs. The diameter of growth inhibition zone was calculated by vernier caliper. For minimum inhibitory concentrations (MIC) of synthesized compounds were determined in the range of concentrations from 100 to 40 µg/mL.

RESULTS AND DISCUSSION

The synthesis of the target molecules was achieved as per the synthetic scheme given in Figure 1. Accordingly, 2-amino pyridine was treated with chloro-oxobutanoate to obtain compound **3** which was converted to its corresponding carbazide derivative **4** using hydrazine hydrate. Compound **4** was further reacted with either substituted benzoic acids or cinnamic acids in presence of $POCl_3$ to afford target compounds **5a-i** and **6a-d** in almost quantitative yields. All the synthesized compounds were analyzed by spectroscopic analysis.

Structure of compound **3** was established by ^{1}H NMR which showed presence of ethyl group 1.40 (-CH_3) and 4.40 (-CH_2-). Formation of compound **4** was confirmed by ^{1}H NMR and IR which showed the absence of ethyl ester peaks 1.40 and 4.40 δ and presence of carbazide peaks peak 4.14 (-NH_2) & 7.01 (-NH-) δ. All the target compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectrometric techniques. The representative ^{1}H NMR spectrum of compound **5a** shows disappearance of carbazide proton at δ 4.14 (-NH_2) and 7.01 (-NH-), while disappearance of carbazide amide at 1626 cm^{-1} in IR confirmed the structure. Further the structure was confirmed beyond doubt by HRMS which shows the M+1 peak at 277.0800. calcd for $C_{16}H_{12}N_4O$ [M+H] 277.1044.

Similarly, the structures of all the other derivatives were confirmed by analytical data, the results are presented in the experimental part.

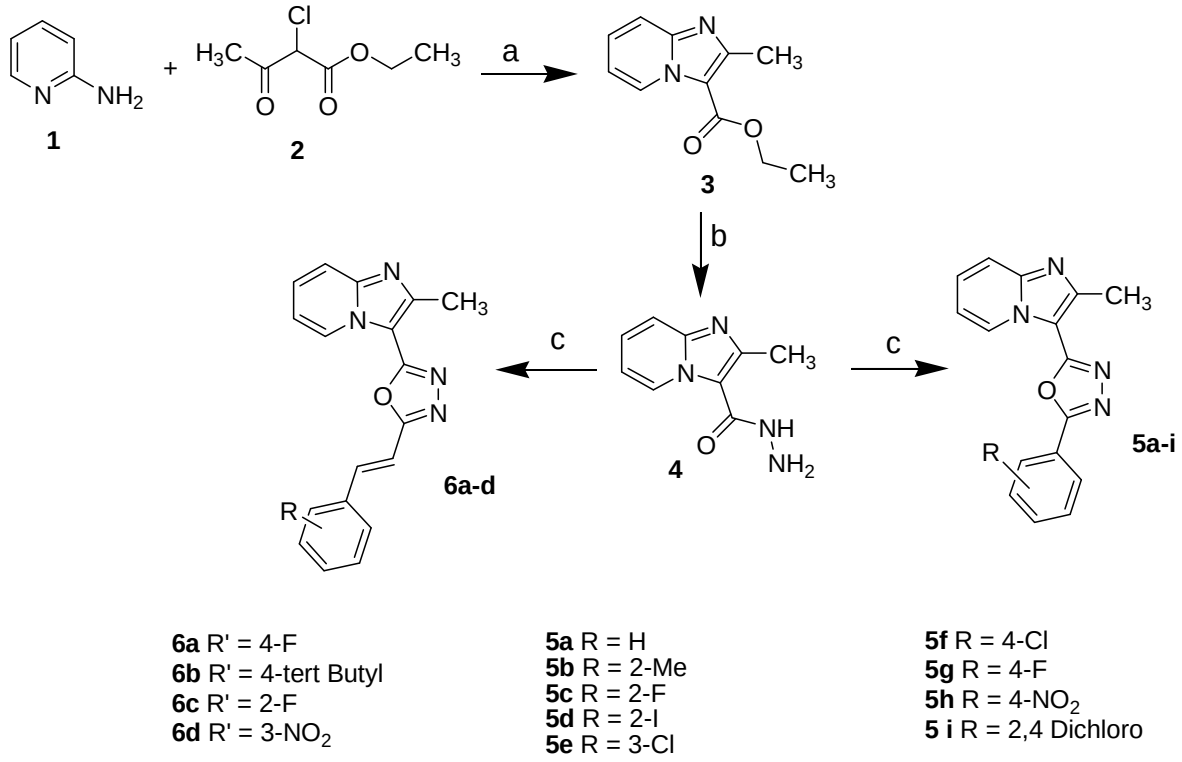

Figure 1. Synthesis of compounds 6a-k. Reagents and conditions: (a) ethanol, K_2CO_3, reflux, 10 h; (b) ethanol, $N_2H_4.H_2O$,reflux, 5 h; (c) Ar-COOH,$POCl_3$, reflux, 6 h

Table 1:Antibacterial activty of the compounds (5a-i and 6a-d) as MIC (µg/ml)

Compound	*S.aureus*	*E.coli*	*B.subtilis*	*P.aeruginosa*	*S.pyogens*	*K.terrigena*	*K.pneumonae*
4	70	90	90	80	--	--	--
5a	90	80	80	90	--	60	70
5b	70	80	70	60	60	--	60
5c	70	70	60	80	80	70	80
5d	60	60	70	60	80	80	70
5e	70	70	50	70	80	50	70
5f	70	90	70	90	70	60	60
5g	90	80	100	70	60	80	70
5h	80	70	80	70	70	80	60
5i	60	80	90	70	70	70	80
6a	90	--	90	70	--	90	60
6b	70	90	80	70	--	--	--
6c	70	70	70	90	90	50	60
6d	60	70	70	70	70	80	60
Chloramphenicol	50	50	40	40	50	40	50

Table 2: Antifungal activty of the compounds (5a-i and 6a-d) as MIC (µg/ml)

Compound	*T. Viride*	*A flavus*	*A brasillansis*	*C. albicans*
NCIM	1051	944	545	3471
4	--	--	--	90
5a	80	90	80	90
5b	--	--	--	100
5c	80	70	80	100
5d	70	60	70	90
5e	80	100	90	70
5f	90	70	90	90
5g	60	--	--	100
5h	--	--	--	50
5i	90	80	80	90
6a	--	90	90	--
6b	--	--	--	80
6c	70	80	80	60
6d	90	80	70	80
Nystatin	60	50	40	40

The newly synthesized compounds **5a-i** and **6a-d** were tested for their antibacterial activity against *S.aureus, E.coli, B.subtilis, P.aeruginosa, S.pyogens, K.terrigena and K.pneumonae.* All the synthesized compounds were dissolved in DMSO and antibacterial activity studied by disc diffusion method. Compound **5b, 5c, 5d, 5e, 5f, 5g, 5h, 5i, 6a, 6c** and **6d** shows good antibacterial activity against several species. The results are summarized in Table 1. Compound **6a-k** were also tested for antifungal activity against *T.viride, A.flavus, A.brasillansis* and *C.albicans.* Among the all synthesized compounds **5d, 5g, 5h** and **6c** shows good antifungal activity. The results are summarized in Table 2. It is evident from the table that there is very little effect of the various substituents [electron donating CH_3, electron withdrawing (NO_2) or halogens (F, Cl, Br)] on the antimicrobial activity. Compound **5a** with no substitution also show significant activity which suggests that activity is due to oxadiazole ring clubbed with imidazo pyridine.

CONCLUSION

We have synthesized a new series of 2-(5-substituted)-1, 3, 4-oxadiazole-2-yl)-*H*-imidazo [1, 2, α] pyridine derivatives **5a-i** and **6a-d.** Most of the newly synthesized compounds exhibited promising *in vitro* antibacterial and antifungal activity. Among the investigated compounds **5b, 5c, 5d, 5e, 5f, 5g, 5h, 5i, 6a, 6c** and **6d** were more potent towards bacterial strains and **5d, 5g, 5h** and **6c** were effective against fungal strains. Remaining compounds also showed moderate to weak antimicrobial activities.

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