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SYNTHESIS AND CHARACTERIZATION OF 1,3,4-OXADIAZOLE DERIVATIVES

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ABSTRACT
A novel series of 1,3,4-oxadiazoles **(1a-j)** were synthesized by selective cyclization upon reacting Isonicotinic acid hydrazide with cerric ammonium nitrate (CAN) in DMF medium. The structures of the new compounds were elucidated on the basis of IR, ^{1}H- NMR and MASS spectral data.

INTRODUCTION
1,3,4-Oxadiazoles are the five membered heterocyclic compounds with nitrogen and oxygen atom are an imperative part of the pharmaceutical industry and are the parent compound for a vast number of heterocyclics[I].Replacement of two methane (–CH=) groups of furan by two pyridine type nitrogen atoms (–N=) results in the formation of oxadiazole[II]. 1,3,4-oxadiazoles are very commonly reported by the researchers because of their varioussignificant biological and chemical properties.These compounds can be effectively utilized as anti-depressant[III], anti-inflammatory [IV], antitubercular[V], antidiabetic[VI], anticonvulsant[VII], anticancer [VIII], analgesic[IX] and insecticidal agents[X].Certain studies have helped to spot out the antimicrobial activity of oxadiazole. Moreover furamizole a nitrofurantoin derivative with oxadiazole nucleus is a best example of promising antibacterial activity.
The diversified biological activities of 1,3,4-oxadiazoles promoted us to synthesize a new series of 1,3,4-oxadiazole derivatives by using cerric ammonium nitrate as catalyst .1,3,4 oxadiazoles were usually synthesized by reacting hydrazides and acids in presence of $POCl_3$ or with the help of any suitable cyclizing agents like HgO/Iodine, Chloramine-T, iodo benzene diacetateetc[X1].

MATERIALS AND METHODS
Experimental
All the reactions were carried out under the prescribed laboratory conditions. The required solvents were procured from Himedia and Lobachemicals , which were of alalytical grade. IR spectra were recorded by using Alpha bruker IR Spectrometer in KBr discs (cm^{-1}). 1H- NMR

spectra were measured in DMSO-d_6 as the solvent on bruker Avance-II 300 mHz NMR spectrometer using TMS as an internal standard. Mass Spectrum was recorded on Perkin Elmer clarus 680 GCMS spectrometer.

General Procedure for synthesis of 1,3,4-oxadiazole derivatives(1a-j)

Substituted aromatic aldehydes (0.01mol) and INH (1) (0.01mol) is dissolved in DMF (30ml) solution and a pinch of cerric ammonium nitrate (CAN) is added and refluxed for 8-10hrs. The solution is cooled and poured into crushed ice (100ml) with vigorous stirring. The precipitated solid is filtered, washed with cold water and recrystallized from alcohol. The physical data of the compounds **(1a-j)** is reported in the table-1. **(Scheme 01)**

4-(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)phenol: (1a) : IR (KBr,cm^{-1}) ν_{max}: 1002(C-O-C), 1502 (C=C), 1578(C=N), 3064(C-H), ^{1}H-NMR (300 MH_Z, DMSO-d_6) (δ, ppm): 6.81-6.83 (d, Ar-H, 2H), 7.54-7.56 (d, Ar-H, 2H),7.77-7.78(d, Ar-H, 2H), 8.68-8.73 (d, Ar-H, 2H), 10.10(s, 1H, OH). MS(m/z): 239.28(M+).

2-(4-chlorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole: (1b): IR (KBr,cm^{-1}) ν_{max}: 1033 (C-O-C). 1489 (C=C), 1566(C=N), 3032(C-H), ^{1}H-NMR (300 MH_Z, DMSO-d_6) (δ, ppm)**:** 7.46-7.48 (d, Ar-H, 2H),7.72-7.74 (d, Ar-H, 2H), 7.79-7.81 (d, Ar-H, 2H), 8.74-8.75 (d, Ar-H, 2H), MS(m/z): 257.68 (M+).

2-(4-fluorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole: (1d): IR (KBr,cm^{-1}) ν_{max}: 1067(C-O-C). 1551 (C=C), 1614(C=N), 3034(C-H), ^{1}H-NMR (300 MH_Z, DMSO-d_6) (δ, ppm)**:** 6.90-6.92 (d, Ar-H, 2H), 7.62-7.64 (d, Ar-H, 2H), 7.77-.7.79(d, Ar-H, 2H), 8.73-8.74 (d, Ar-H, 2H), MS(m/z):241.22 (M+).

2-(4-nitrophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole: (1e): IR (KBr,cm^{-1}) ν_{max}: 1066(C-O-C). 1550 (C=C), 1598(C=N), 2965(C-H), ^{1}H-NMR (300 MH_Z, DMSO-d_6) (δ, ppm)**:** 7.24 (d, Ar-H, 2H), 7.51 (d, Ar-H, 2H),8.41 (d, Ar-H, 2H), 8.72(d, Ar-H, 2H), MS(m/z): (M+).

2-phenyl-5-(pyridin-4-yl)-1,3,4-oxadiazole: (1f): IR (KBr,cm^{-1}) ν_{max}: 1064(C-O-C). 1487 (C=C), 1551(C=N), 2993(C-H), ^{1}H-NMR (300 MH_Z, DMSO-d_6) (δ, ppm)**:** 7.66-7.68 (d, Ar-H, 2H),7.77-7.78 (d, Ar-H, 2H), 8.74-8.49 (d, Ar-H, 2H),8.73 (d, Ar-H, 2H), MS(m/z):268.23(M+).

2-(3,4-dimethoxyphenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole: (1g): IR (KBr,cm^{-1}) ν_{max}: 1069(C-O-C). 1595 (C=C), 1595(C=N), 3043(C-H), ^{1}H-NMR (300 MH_Z, DMSO-d_6) (δ, ppm)**:** 3.33 (s, 2XOCH_3, 6H), 7.43-7.44 (d, Ar-H, 2H), 7.71-7.73 (d, Ar-H, 2H), 7.78-7.80 (d, Ar-H, 2H),8.74-8.76 (d, Ar-H, 2H), MS(m/z): 283.28 (M+).

Table 1: Physical data of 1,3,4-Oxadiazoles (1a-j)

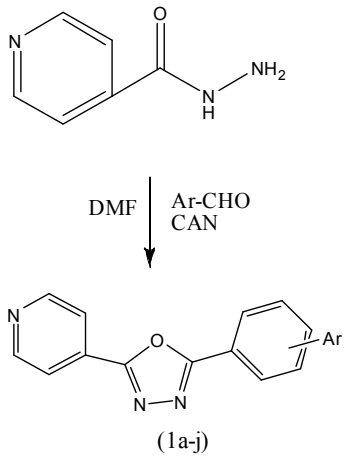
Comp	Ar-CHO	Molecular Formula	Molecular Weight	MP (^{o}C)	Yield (%)
1a	4-OH	$C_{13}H_9N_3O_2$	239.23	201-03	87.96
1b	4-Cl	$C_{13}H_8N_3OCl$	257.68	191-93	80.00
1c	4-OCH_3	$C_{14}H_{11}N_3O_2$	253.26	176-78	75.43
1d	4-F	$C_{13}H_8N_3OF$	241.22	151-53	72.23
1e	4-NO_2	$C_{13}H_8N_4O_3$	268.23	143-45	66.87
1f	C_6H_5	$C_{13}H_{10}N_3O$	223.23	108-10	78.57
1g	3,4-$(OCH_3)_2$	$C_{15}H_{13}N_3O_3$	283.28	121-23	63.88
1h	4-Br	$C_{13}H_8N_3BrO$	302.13	135-37	65.00

1i	3-OH-4-OCH_3	$C_{14}H_{11}N_3O_3$	269.26	141-43	78.95
1j	3,4,5-$(OCH_3)_3$	$C_{15}H_{13}N_3O_4$	299.28	111-13	86.00

RESULTS AND DISCUSSION

All the new compounds **(1a-j)** were obtained by the reaction between INH and aromatic aldehydes in the DMF medium. The synthetic route for the preparation of the title compounds is depicted in **Scheme -1**.All the synthesized compounds were characterized by their physical and spectral data .The ^{1}H -NMR spectrum of compounds confirmed the conversion of the INH into the 1,3,4-oxadiazole ring . The new compounds were further characterized by mass spectra and the compounds showed the presence of prominent molecular ion peak and they are consistent with assigned molecular formula.

Scheme-01



(1a-j)

CONCLUSION

A very simple and effective method was demonstrated for the synthesis of 1,3,4-oxadiazoles by using cerric ammonium nitrate as catalyst. The main advantage of this catalyst is easy to handle, nontoxic and yielded in good products.

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