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PEG-OSO_3H CATALYZED SYNTHESIS OF SCHIFF BASES OF ISONIAZIDE AND ITS ANTIBACTERIAL EVALUATION

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Abstract:
Schiff bases are widely used as a precursor of bio-active heterocycles and also applicable as a ligands in Co-ordination chemistry and gaining interest in the area of drug development. Hence, we have developed a highly efficient environmentally benign method to synthesis of biologically active Schiff bases from isoniazide and pyrazole-4-carbaldehyde in water under microwave irradiation.PEG-OSO_3H used as a green catalyst to increase the reaction rate and yield of the corresponding Schiff bases.

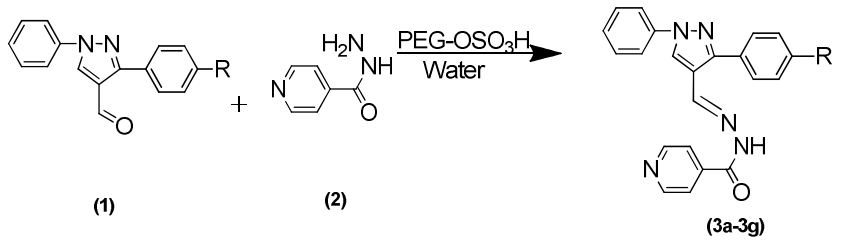
Keywords: Pyrazole-aldehyde; PEG-OSO_3H; Green Chemistry; Microwave, water

Introduction:-
The Cyclic-aldehyde especially with an effective conjugated system, form stable Schiff baseswhereas aliphatic aldehyde are unstable and readily polymerize.[i] A broad range of Schiff bases have extremely diversified and flexible structures [ii]. Schiff bases and amides derived from various heterocyclic compounds displayed broad range of pharmaceutical and biological activities such as antiviral, anticonvulsant, anticancer, antimicrobial, angiotension-II receptor antagonist, anti-inflammatory and antidepressant activity. Schiff base containing heterocycles and their metal complexes have been widely investigated due to their wide range of applications as medicine [iii] catalysts [iv], antioxidant agent [v-vi]. A Schiff base behaves as a co-ordinates and Flexi-dentate ligand of azomethine group [vii]. Moreover, metal complexes of schiff base are important as an analgesic and antibacterial activity [viii]. Schiff bases have been reported in their biological properties, like, antibacterial, anti fungal activities[ix-xii]. Schiff bases and its metal complexes broadly show herbicidal and anticancer applications [xiii-xiv]. Green solvents and catalyst play an important role in modern heterocyclic synthesis to reduced the harm to the environment and economic cost.[xv-xxi]

Herein, A new method has been developed for the preparation of series of Schiff bases of pyrazol-aldehyde and isoniazide using PEG-OSO_3H as a green and efficient catalyst in water.

Synthesis of Schiff bases:-

Scheme 1:-



(1) (2) (3a-3g)

(*E*)-*N*'-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)isonicotinohydrazide

Experimental:

Material and method:-

Melting point are uncorrected taken microcontroller based melting point apparatus CL-726. NMR spectra were recorded by BRUKER 400 MHz spectrophotometer, IR Spectra were recorded on JASCO FT IR 400O INSTRUMENTS. The reactions were monitor by using thin layer chromatography. Reactions were done at Microwave irradiator (MAS-II) (Sineo Technology Co.Ltd.) was irradiation done at 400 watt power.

General procedure for the synthesis of Schiff bases [3a-3g]:-

Schiff bases were prepared by dissolving pyrazole-aldehyde 0.01 mol and isonicotinohydrazide 0.01 mole in $PEGOSO_3H$ and irradiate at 400watt under microwave irradiator at 70^oC-75^oC temperature. This reaction where complete within 3.0 minutes and reaction mixture was allowed to cool and poured on crushed ice. The obtained precipitate was wash with dil. HCl and dried. Products were recrystallized with aqueous ethanol.

Result and Discussion

We are continuously working on green solvents and here we find that with this $PEGOSO_3H$ solvent there is no catalyst required for schiff bases as it act as an acid catalyst also. Hence we have design the green protocol for the synthesis of schiff bases where no external catalyst required only dissolving solvent act as catalyst and take part in reaction. The solvent also recovered and reused. The pyrazole aldehyde and isoniazide is taken in PGSO3 solvents and irradiated at 400wat. The schiff base formation was observed within 3 minutes. The reaction were monitored with Thin layer chromatography and when the formation schiff base observed then reaction mask was poured on crushed ice. Solid product observed which filtered and recrystalised. To generalise the scope of this reaction differently substituted pyrazolyl carbaldehyde is taken with isoniazide and same treatment is given. The results were obtained with excellent yield **(Refer scheme 1 table 1).**

Table 1 Evaluation of compounds [4a-4g]

compounds	R=	Yield%	M.P (^oC)
3a	**-CH_3**	**91**	**194-195**
3b	**-Br**	**93**	**183-184**
3c	**-OCH_3**	**93**	**202-203**
3d	**-H**	**90**	**142-146**
3f	**-OH**	**92**	**262-263**
3e	**-NO_2**	**94**	**170-171**
3g	**-F**	**93**	**148-149**

The IR spectra of the compound 3ashows prominent peaks at 3417 cm^{-1} for N-H, 1691 cm^{-1} for C=O attached to N-H and Schiff base formation conforms i.e. C=N with 1588 stretching. ^{1}H NMR of compound 3ashows characteristic δ12.01 0f one proton connected nitrogen exchangeable with D2O (N-H), δ 7.40- δ 8.80 H of benzene ring, pyridine ring and δ 9.13 of pyrazole hydrogen. The most important that shows the δ8.61 1H because of schiff proton i.e. H-C=N. All the above spectral data clearly shows the formation of title compound **3a**.

Antibacterial activities:

The antibacterial activities of all the compounds were studied against gram-positive bacteria (*Staphylococcus aureus and Bacillus subtilis*) and gram-negative bacteria (*E.coli, and klebsiella promioe*) at a concentration of 50µg/ML byagar cup plate method. A methanol system was used as control in this method. Similar conditions using doxycyclineas a control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds found more toxic to moderate active for microbes, shown in **Table 2.**

Table 2: Antibacterial Activity of Compound:

Compounds	Gram +Ve		Gram –Ve	
	Bacillus subtilis	***Staphylococcus aureus***	***E. coli***	***Klebsiella promioe***
Given Sample	49	54	58	51
Standard Doxycycline	66	67	70	76

Characterization ofsynthesis of products:

^{1}H NMR (400 MHz):

(1,3-diphenyl-1H-pyrazol-4-yl) methylene isonicotinohydrazide (3a):-
δ 7.40 to 8.80 (10H, aromatic H and 4H, pyridine-H), δ 8.61 (s, 1H, Schiff base -CH=N-), δ 9.13 (s, 1H, Pyrazole Proton) and δ 12.01 (s, 1H, NH, exchangeable with D2O).

(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene isonicotinohydrazide (3e) :-
δ 7.38 to 9.05 (9H, aromatic H and 4H, pyridine-H), δ 8.69 (s, 1H, Schiff base -CH=N-), δ 9.01 (s, 1H, Pyrazole Proton) and δ 11.98 (s, 1H, NH, exchangeable with D2O).

IR analysis (cm^{-1}):
(1,3-diphenyl-1H-pyrazol-4-yl) methylene isonicotinohydrazide (3a):-
3417 (for N-H stretching), 1691 (for C=O stretching) and 1588 (for C=N stretching).

(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene isonicotinohydrazide (3e):-
3422 (for N-H stretching), 1688 (for C=O stretching) and 1575 (for C=N stretching).

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Refrences:-

i. Türkkan, B., Sarıboğa, B. and Sarıboğa, N., 2011. Synthesis, characterization and antimicrobial activity of 3, 5-di-tert-butylsalicylaldehyde-S-methylthiosemicarbazones and their Ni (II) complexes. *Transition Metal Chemistry*, *36*(6), p.679.
ii. K. C. Gupta and A. K. Sutar, "Catalytic Activities of Schiff Base Transition Metal Complexes," *Coordinatio try Reviews*, Vol. 252, No. 12-14, 2008, pp. 1420-1450. http://dx.doi.org/10.1016/j.ccr.2007.09.005.
iii. Hazra, K.; Nargund, L.V.G.; Rashmi, P.; Narendra Sharath Chandra, J.N.; Nandha, B.; *Der Chemica Sinic.,* **2011**, 2, 149.
iv. Prajwal, L.L.; Boja, P.; Manjunatha, K.; Vinaya, C.; Nalilu, S.K.; Chandrashekar, K.R.; *Med. Chem. Res.,* 2013, 22, 1689-1699. doi:10.1007/s00044-012-0154-3.
v. D.Worku, M.Negussie, V.J.T.Raju, R.Negussie, Bull. Chem. Soc.Ethiop. 17, 30(2002).
vi. M.Fujita, Doguro, M.Miyazawa, H.Oka, K.Yamaguchi And K.Ogura,Nature,378,469(1995).
vii. P.Paul,Proc. Indian Acad. Sci(Chem. Sci.),114,269(2002).
viii. L.A.Paquette, W.A.Benjamin, Principles of Modern Heterocyclic Chemistry 318(1968). [8]. M.Yoshizawa, J.Am.Chem.Soc,127, 2798(2005).
ix. D.R. Williams, Chem. Rev., 72, 203 (1972).
x. A. Campos, J.R. Anacona and M.M. Campos-Vallette, Mian group Metal chem., 22, 283 (1999).
xi. N. Sari, S. Arslan, E. Logoglu and I. Sakiyan, G.U.J. Sci, 16, 283 (2003).
xii. M. Verma, S.N. Pandeya, K N. Singh, J P. Stabler and Acta Pharm., 54, 49 (2004).
xiii. P.G. Cozzi, Chem. Soc. Rev., 410 (2004).
xiv. S. Chandra, J. Sangeetika, J. Indian Chem. Soc, 81, 203 (2004).
xv. M. H., Shaikh; D. S., Wagare; M., Farooqui; A., Durrani; "Facile and green one-pot synthesis of 2-aminothiazole in glycerol-water" Heterocyclic Lett. 2017, 7, 4, 1061-1064.
xvi. D. S., Wagare; S., Mujahed; F., Mazahar; D., Ayesha; "PEG-1500 in water: A green, recyclable catalyst for the one-pot synthesis of imidazo[1,2-a]pyrimidines under microwave irradiation", Chem. & Biol. Inter. 2016, 6, 6, 405-409.
xvii. D. S., Wagare; M., Farooqui; T. D., Keche; D., Ayesha; "Efficient and green microwave-assisted one-pot synthesis of azaindolizines in PEG-400 and water", Syn. Comm. 2016, 46, 21, 1741–1746.

xviii. D. S., Wagare; D., Lingampalle; M., Farooqui; D., Ayesha; "An enviornmentally benign one-pot synthesis of 3-aryl-furo[3,2-c]coumarins in PEG-400 and water", Der. Phar. Chemica, 2016, 8, 1, 408-411.

xix. D. S., Wagare; D. N., Prashant; S., Mujahed; F., Mazahar; D., Ayesha; "Highly efficient microwave-assisted one-pot synthesis of 4-aryl-2-aminothiazoles in aqueous medium", Env. Chem. Lett. (2016),6, 6, 405-409. **DOI: 10.1007/s10311-017-0619-1**.

xx. M., Shaikh; D., Wagare; M., Farooqui; A., Durrani; "Rapid and environmentally benign protocol for the synthesis of pyrazolyl-4-thiazolidinone" Asian Journal of Pharmacy and Pharmacology 2019; 5(3):576-581.

xxi. M., Shaikh; D., Wagare; M., Farooqui; A., Durrani; "Trimethylsilyl Chloride Catalyzed Highly Efficient Synthesis of Schiff Bases of Thiazole in Glycerol under Microwave Irradiation" Asian J. Org. Med. Chem., 2019 ,4(2), 109-112, **DOI:10.14233/ajomc.2019.AJOMC-P170.**

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