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SYNTHESIS AND CHARACTERIZATION OF A SERIES OF NOVEL SCHIFFS' BASES OF 1, 3, 4- THIADIAZOLE DERIVATIVES

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ABSTRACT

Literature review showed that 1, 3, 4- Thiadiazole and its derivatives possess wide range of therapeutic effectiveness. In addition, Schiffs' bases also possess broad spectrum anticancer, antibacterial, antifungal and anti-inflammatory activities. Keeping in view of the need for development of novel antimicrobial drugs to combat with the Super bugs developed due to resistance for old drugs, an attempt has been made to develop a series of novel Schiffs' bases of 1,3,4-Thiadiazole derivatives. So they were synthesized and characterized using IR, NMR and mass spectra.

KEYWORDS: Synthesis, Characterization, Schiffs' base, 1, 3, 4-Thiadiazole derivatives.

INTRODUCTION

There are vast numbers of pharmacologically active heterocyclic compounds in regular clinical use. The presence of heterocyclic structures in diverse types of compounds is strongly indicative of the profound effects such structure exerts on physiologic activity, and recognition of this is abundantly reflected in efforts to find useful synthetic drugs.

As 1, 3, 4- thiadiazole and its derivatives, as well as Schiffs' bases, possess wide range of therapeutic effectiveness synergistic action has been expected.

Microwave-assisted synthesis is a branch of green chemistry. Microwave-assisted synthesis has gained much attention in recent years. Microwave irradiation assisted chemical transformations are pollutions free, eco-friendly and offer high yields together with simplicity in processing and handling. The main reasons for this increase include the availability of commercial microwave equipment intended for organic chemistry, development of the

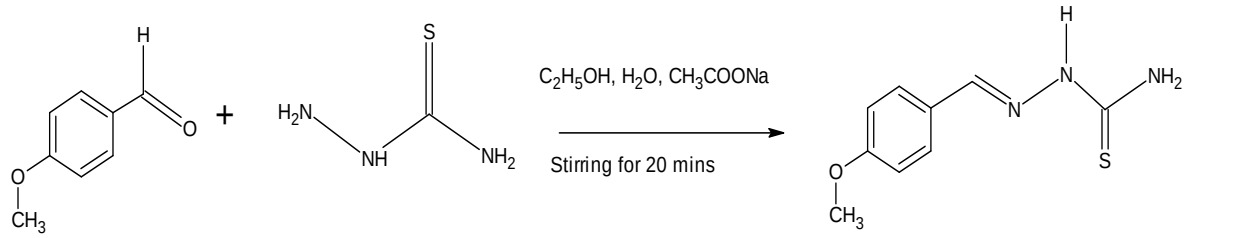
solvent free technique, and shorter reaction time. Therefore an attempt has been made to synthesize 1,3,4-Thiadiazole derivatives by an ecofriendly, less energy consuming microwave method which is more towards green chemistry approach.

MATERIALS AND METHODS

Anisaldehyde (CDH Lab), Sodium acetate (Nice Chem (P) Ltd.), Thiosemicarbazide (Sisco Research Lab), Glaciel acetic acid (S.S Chemicals), Ethanol (Hayman Ltd.), Methanol (Astron Chemicals), Bromine (Merck Ltd), Conc. H_2SO_4 (High Purity Lab Chemicals), p-Nitro benzaldehyde (Sisco Research Lab.), p-Chloro benzaldehyde (CDH Lab), p-Dimethyl amino benzaldehyde (Merck Ltd), o-Methoxy benzaldehyde (Spectrochem), p-Bromo benzaldehyde (CDH Lab), Acetone (SS Chemicals).

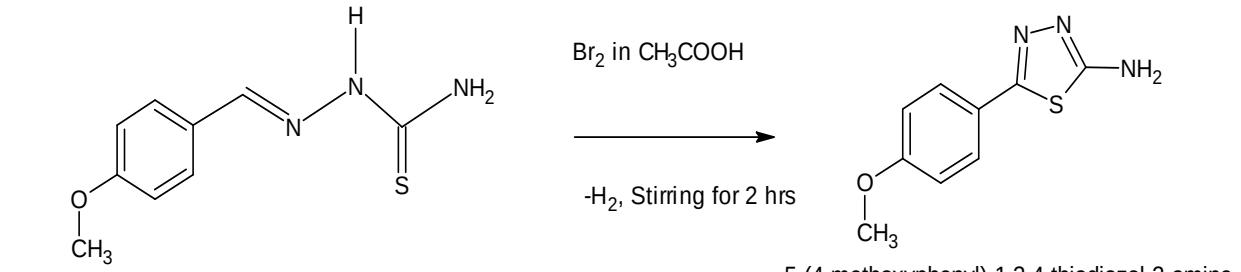
SCHEME

STEP 1



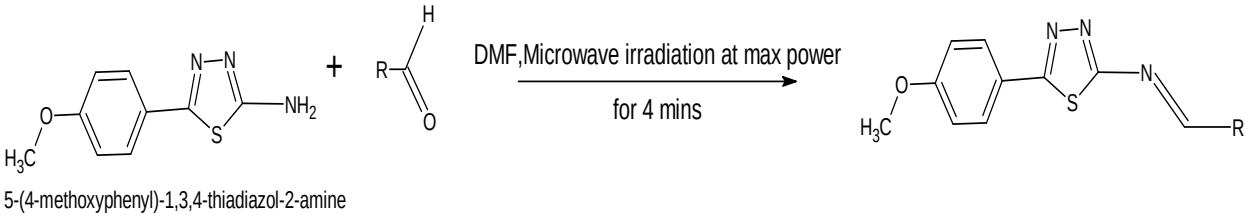
4-methoxybenzaldehyde Thiosemicarbazide (2*E*)-2-(4-methoxybenzylidene)hydrazinecarbothioamide

STEP 2



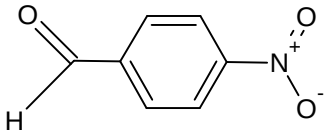
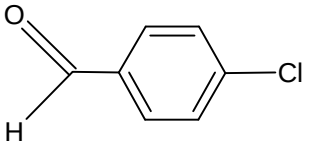
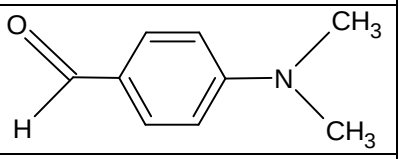
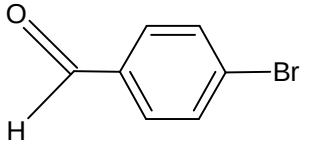
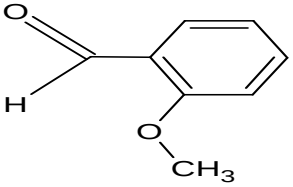
(2*E*)-2-(4-methoxybenzylidene)hydrazinecarbothioamide 5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine

STEP 3



5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine

Different substitutions of R in compounds from DG1 to DG5

COMPOUND	R-CHO
DG1	
DG2	
DG3	
DG4	
DG5	

EXPERIMENTAL

STEP 1: SYNTHESIS OF THIO SEMICARBAZONES

Thiosemicarbazones were synthesized by the addition of an aqueous solution of Thiosemicarbazide (0.01 mol) and Sodium acetate (0.1 mol) to Anisaldehyde (0.02 mol) in 15 ml ethanol by continuous stirring.

After stirring for 20 minutes, the mixture was left undisturbed overnight and the precipitate obtained was collected and purified by recrystallization using ethanol.

STEP 2: SYNTHESIS OF 2- (4-METHOXY BENZYLIDINE) HYDRAZINE-1-CARBOTHIAMIDE

Prepared thiosemicarbazone(0.005 mol) and anhydrous sodium acetate(0.073 mol) were made into slurry by adding 17.5ml acetic acid. To the slurry, bromine (0.016 mol) in acetic acid (5 ml) was added drop wise by stirring.

After addition, stirring was continued for another 2 hours after which the slurry was poured to crushed ice by occasional stirring. The solid obtained was filtered, dried and purified by recrystallisation using absolute ethanol.

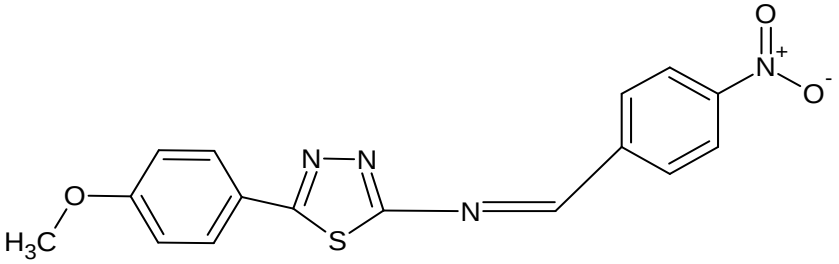
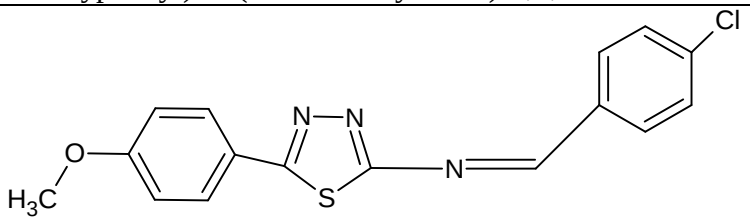
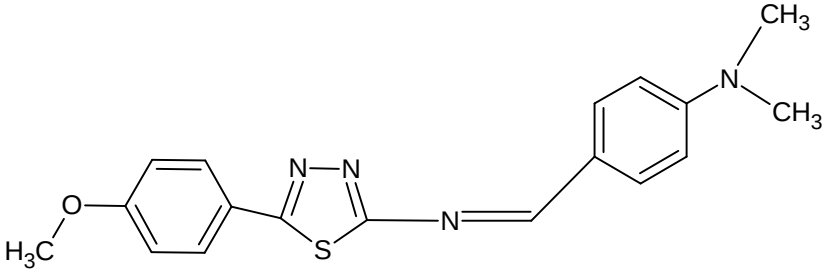
STEP3: SYNTHESIS OF SCHIFFS' BASES WITH VARIOUS ALDEHYDES

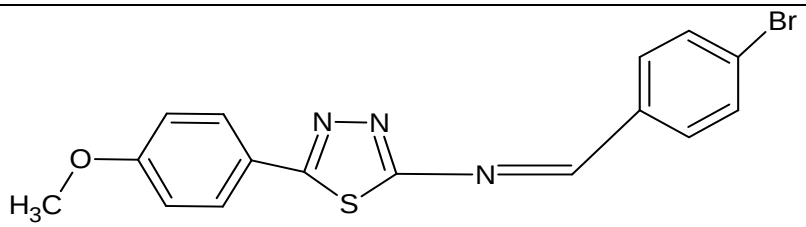
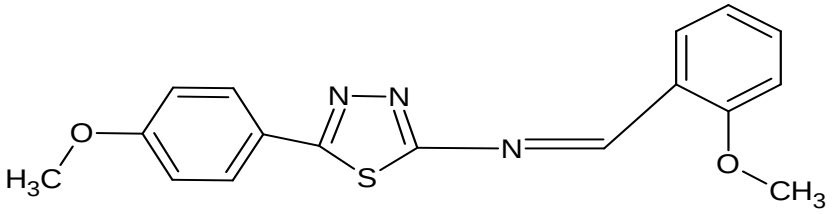
Prepared 2-(4-methoxy benzylidine) hydrazine-1-carbothiamide was suspended in DMF and any aromatic aldehyde (0.015 mol) were added with 2-3 drops of con. H_2SO_4. The reaction mixture was then heated in a microwave oven at maximum power for 4 mins. The resultant contents were poured into crushed ice. The crude product was filtered, purified, dried and recrystallized using methanol. Purity of the compounds were checked by TLC and the spots were located using iodine chamber and UV light.

RESULTS AND DISCUSSION

Melting points were determined using open capillary tube method and the values are presented uncorrected. IR spectra were recorded on FTIR(Shimadzu, IR-Affinity-1) spectrometer using KBr pellets technique. ^{1}HNMR were recorded using Bruker, Avance Ⅲ HD NMR spectrometer using $CDCl_3$ as solvent and TMS as internal standard. The chemical shift was expressed in δppm. Mass spectra were recorded on Jeol GCmate mass spectrometer.

Structure and IUPAC name of the synthesized compounds

COMPOUND CODE	STRUCTURE AND IUPAC NAMES
DG1	 5-(4-methoxyphenyl)-*N*-(4-nitrobenzylidene)-1,3,4-thiadiazol-2-amine
DG2	 *N*-(4-chlorobenzylidene)-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine
DG3	 *N*-[4-(dimethylamino)benzylidene]-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine

DG4	 *N*-(4-bromobenzylidene)-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine
DG5	 *N*-(2-methoxybenzylidene)-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine

5-(4-methoxyphenyl)-*N*-(4-nitrobenzylidene)-1,3,4-thiadiazol-2-amine(DG1)

Yellow solid, yield:81.5%, m.pt.: 136^0-138^0C, R_f:0.51,IR: ϑ_{max} cm^{-1}: 3109(Ar.CH Str), 1529(Ar.NO_2Str), 1604(C=N Str), 677(C-S-C Str),1691(-CH=N-Str),1082(C-O-C Str) ^{1}HNMR($CDCl_3$-d_6/TMS):1.25(s,1H,C=CH),7.27-8.42(m,8H,Ar-H),3.9(m,6H,OCH_3) MS:m/z(M+)340^+

***N*-(4-chlorobenzylidene)-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine(DG2)**

Pale yellow solid, yield:75.8%, m.pt.: 144^0-146^0C, R_f:0.8,IR: ϑ_{max} cm^{-1}: 2927(Ar.CH Str), 761(C-Cl Str), 1598(C=N Str), 761(C-S-C Str),1685(-CH=N-Str),1091(C-O-C Str) ^{1}HNMR($CDCl_3$-d_6/TMS): 1.25(s,1H,C=CH),7.35-8.05(m,8H,Ar-H),3.84(m,6H,OCH_3) MS:m/z(M^+)330^+

***N*-[4-(dimethylamino)benzylidene]-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine(DG3)**

Reddish brown solid, yield:88.2%, m.pt.: 194^0-196^0C, R_f:0.36,IR: ϑ_{max} cm^{-1}: 2918(Ar.CH Str), 1440(N(CH_3)$_2$ Str), 1597(C=N Str), 727(C-S-C Str),1657(-CH=N-Str),1064(C-O-C Str)^{1}HNMR($CDCl_3$-d_6/TMS) 1.3(s,1H,C=CH),7.3-8.3(m,8H,Ar-H),3.09(m,6H,Ar-N(CH_3)$_2$) 3.83(m,6H,OCH_3):MS:m/z(M^+)338^+

***N*-(4-bromobenzylidene)-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine(DG4)**

Yellow solid, yield:64.8%, m.pt.: 157^0-159^0C, R_f:0.6,IR: ϑ_{max} cm^{-1}: 3167(Ar.CH Str), 509(C-Br Str), 1460(C=N Str), 710(C-S-C Str),1660(-CH=N-Str),1068(C-O-C Str) ^{1}HNMR($CDCl_3$-d_6/TMS): 1.25(s,1H,C=CH),7.3-8.3(m,8H,Ar-H),3.84(m,6H,OCH_3) MS:m/z(M^+)374^+

***N*-(2-methoxybenzylidene)-5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-amine(DG5)**

Pale brownish yellow solid, yield:46%, m.pt.: 173^0-175^0C, R_f:0.7,IR: ϑ_{max} cm^{-1}: 2837 (Ar.CH Str), 1598(C=N Str), 754(C-S-C Str),1658(-CH=N-Str),1089(C-O-C Str)^{1}HNMR($CDCl_3$-d_6/TMS): 1.3(s,1H,C=CH),7.3-8.3(m,8H,Ar-H),3.8(m,6H,OCH_3) MS:m/z(M^+)325^+

IR Spectra of all the synthesized compounds showed the absence of aldehyde stretching and the presence of Ar.CH Str, C=N Str, C-S-C Str,-CH=N-Str, C-O-C Str and the stretching specific to the prepared compounds.

NMR Spectra also showed the absence of aldehyde group and the presence of aromatic protons, alkyl protons and methoxy protons.

Mass Spectra confirms the molecular weight of assigned compounds.

CONCLUSION

In general, Schiff-thiadiazole derivatives are prepared by appropriate rearrangements, ring opening and substitution reaction. The assigned structure of the compounds are confirmed by IR, NMR and mass spectra. These derivatives have vast range of biological activities which benefits us. The area of the synthesis of these heterocyclic rings continues to grow, providing more and better methods for synthesis of this interesting heterocycle, permitting the discovery of more active, more specific and safer new drug candidates.

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