SHORT COMMUNICATION

MICRROWAVE INDUCED SYNTHSIS AND ANTIMICROBIAL ACTIVITIES OF SOME PYRAZOLINYL THIOCARBAMIDES

Y.K.Srivastava
Department of Chemistry, M.P.Govt. P.G. College, Chittorgarh-312001 (Raj.)
E-mail: ys_cor121@yahoo.com

ABSTRACT

Some new 3,5-diaryl-2-pyrazolinyl-1-thiocarbamides have been prepared by condensation of substituted o-hydroxy chalcones with thiosemicarbazide using microwave induced methodology. The synthesized compounds have been screened for their antimicrobial activities in vitro against common bacterial strains.

Key words: *Pyrazoline, Thiocarbamide, Chalcones , Microwave.*

INTRODUCTION

Microwave assisted synthesis in organic chemistry is an important and well established area of research due to a number of advantages over conventional heating methods.[1] The microwave assisted reaction occurs more rapidly safely and with higher chemical yields rendering this method superior to the conventional methods which requires longer reaction period, tedious work up , use of large quantity of solvents and reagents causing environmental pollution. On the other hand microwave induced organic reaction enhancement (MORE) technique provides a non conventional technique for rapid synthesis of organic compounds. In recent years the compounds with hetero atoms are very much used as antimicrobial agents. The literature concerning thio-carbamides is voluminous. These compounds have found their way into almost all branches of chemistry. A number of thio-carbamide derivatives have been reported to possess insecticidal, bactericidal, and herbicidal activities[2-5] The pyrazoline derivatives due to their non toxic properties and a wide range of biological activities [6-9] have been used extensively in medicinal chemistry. It was therefore thought worthwhile to synthesis some new pyrazoline derivatives containing thio-carbamide moiety .Keeping in view of the advantages of microwave heating all the transformations in present investigation have been carried out using MORE technique.

O-Hydroxy chalcones (1) were treated with thiosemicarbazide in presence of anhydrous K_2CO_3 under microwave induced reaction condition to afford 3,5-diaryl-2-pyrazolinyl-1- thio carbamides (3) in 80-85 % yield . Alternatively o- hydroxy chalcones were treated with hydrazine hydrate to get 3,5-diaryl-2-pyrazolines (2) which were then treated with KCNS in presence of catalytic amount of dil. Hcl to afford the desired thiocarbamides.

EXPERIMENTAL

All the melting points reported are uncorrected and were taken in open capillaries. IR spectra were recorded on Perkin Elmer spectrometer using KBr (√ cm-1).[1-]NMR spectra were taken on Brucker DRX-600 spectrometer (δ ppm) and mass spectra were taken on Jeol-sx-100 mass spectrometer using m-nitrobenzyl alcohol as matrix.

(a) Single step microwave assisted process: An intimate mixture of o-hydroxy chalcone (o.o1 mole) ,thiosemicarbazide (o.o15 mole) and anhy. K_2CO_3 were mixed thoroughly in presence of ethanol (5ml) . The solvent was then removed under vaccuo and the residue was subjected to microwave

irradiation for 3-5 minutes. Fter completion of the reaction as indicated by the tlc the reaction mixture was extracted with benzene and separated solid was crystallized from ethanol – benzene(1:1) to afford analytical sample of 3a-g.

(b) Two step microwave assisted process :

(i)Synthesis of 3,5-diaryl -2- pyrazolines:- o-Hydroxy chalcone(0.01mole) and hydrazine hydrate(0.02 mole) were thoroughly mixed to form a paste. It was left at room temperature till it was dried. The solid residue was irradiated under microwave for 1-3 minutes. After completion of the reaction the separated solid was extracted with ethanol , filtered and left at room temperature to get colourless crystals of 2 a-g.

(ii) Synthesis of 3,5-diaryl-2-pyrazolinyl-1-thiocarbamides :- A paste of pyrazolines 2a-g (0.01mole) KCNS (0.02mole) and dil.Hcl (2.0ml) was subjected to microwave irradiation for 3-5 minutes. After completion of the reaction it was cooled at room temperature and treated with ice cold water. The separated solid was filtered and crystallized from ethanol-benzene to give 3 a-g.

RESULTS AND DISCUSSION

O-Hydroxy chalcones were transformed into corresponding 3,5-diaryl-2-pyrazolinyl-1-thiocarbamides under microwave irradiation either by a single step or a two step process (scheme-1). For the sake of comparision the reaction weas also carried out using conventional heating condition. In the conventional method the reaction time was 6-7 hrs. for both single and two step process with low yields,(60-65%) whereas in microwave assisted method the reaction was completed within 3-5 minutes with enhanced yield (80-85%) . Further more the reaction was carried out under solvent free condition to minimize the environmental pollution.

The identity of the newly synthesized compounds was confirmed on the basis of their analytical and spectral data. The IR spectra of these compounds gave prominent peaks at 3350-3300 cm-1(NH_2) , 1650-1640 cm-1 (CO) , and 1375-1310cm-1 (C=S and C=C combined) .The 1NMR spectra gave singlet at δ 7.88-8.61 (2H,NH_2), a multiplet at δ 6.95-8.2 (aromatic protons), double doublet at δ2.5-2.7 (1H,C_4-Ha), 3.2-3.4 (1H C_4-Hb), and 5.05-5.7 (1H,C_5-Hx) confirming the presence of typical ABX pattern of the pyrazoline system. The mass spectra (FAB) of these compounds gave molecular ion peaks corresponding to their molecular masses.

Antimicrobial activity :

All the synthesized compounds were screened for their antibacterial activity invitro against E.coli , S.aureus ,S.albus ,K.pneumonae ,and P.vulgaris at a concentration of 200µg /ml using paper disc method[10]. The standerd drugs used were coffrioxane and Amoxyclove.at concentration of 30µg/disc. All the compounds were found to possess moderate to good activity .

Table-1: Physical data of 3,5-diaryl-2-pyrazolinyl-1- thiocarbamides 3a-g

Compd.	Ar.	Mol. Formula (Mol.wt.)	M.P. ^{0}C	Reaction time (min)		%Yield	
				a	b	a	b
3a	C_6H_5	$C_{16}H_{15}N_3OS$(297)	236	4.0	5.0	82	81
3b	4-omeC_6H_4	$C_{17}H_{17}N_3O_2S$(327)	241	3.0	5.0	83	82
3c	3,4-diomeC_6H_3	$C_{18}H_{19}N_3O_3S$(357)	230	3.0	5.0	84	83
3d	3,4,5-triomeC_6H_2	$C_{19}H_{21}N_3O_4S$(387)	234	4.0	5.0	85	85
3e	4-Cl-C6H4	$C_{16}H_{14}N_3OS$(331.5)	198	3.0	6.0	85	83
3f	4-Nme_2-C_6H_4	$C_{18}H_{20}N_4OS$ (340)	224	5.0	6.0	83	81
3g	4-OH-C_6H_4	$C_{16}H_{15}N_3O_2S$(313)	268	5.0	5.0	82	81

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REFERENCES

1. S.V.Kasi and T.K.Raja., *Indian J.Heterocyclic Chem.*.,**16**, 195,(2006)
2. J.R.Krazer and B.Sidney., Ger.Offen.,1900018, *Chem. Abstr.*, **72**, 32043. (1970)
3. Ciba Ltd., Fr. Pat., 1,511325, *Chem. Abstr*.,**71**, 91052, (1969)
4. L.Stadnyk., R.S. Campbell and B.T.Johnson., *Bull. Environ. Contaim. Toxicol.*,**6,** 108, (1971)
5. H.D.Sally., *J.Pharmacol.* **90**,260, (1947)
6. J.C.Maruzella and P.A.Henery., *J.Am.Pharm.Assoc.*, **47,**298, (1958)
7. J.G.Vincent., and H.W. Vincent., *Proc.Expt. Biol. Med.* **55,** 162, (1955)
8. T.C.Sharma., M.M.Bokadia and N.J.Reddy., *Indian J.Chem*.**19B**,228 (1980)
9. G.D.Thorn., *Phytopathology.*, **51**,77 (1961)

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