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Microwave assisted synthesis and antifungal activity of some substituted 3(2-furyl) pyrazoline derivatives

Chemistry

KEYWORDS : Pyrazoline,2-furyl acetone,Phenyl hydrazine, antifungal activity,spectral data.ms

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ABSTRACT

Various chalcones were synthesized from 2-furyl acetone with substituted aromatic aldehydes which in treated with phenyl hydrazine resulted in synthesis of final compounds i.e 3(furan-2-yl)-1,5-diphenyl4-5dihydro-1-H-pyrazole;5(4-chorophenyl)-3-(furan-2-yl)-1-phenyl4-5-dihydro-1-H-pyarzole;5(4-nitrophenyl)-3-(furan-2-yl)-1-phenyl4-5-dihydro-1-H-pyarzole etc.have been synthesized employing microwave technique and confirmed by suitable spectroscopic technique such as 1H NMR. The compounds have been evaluated for the antifungal activity.

Introduction:

During the past few decades many infectious diseases have appeared and the old ones which were previously thought to be controlled have reemerged [1]. Antibiotic resistance bacteria and fungi impose a substantial burden on the human population [2]. As antimicrobial drugs lose their potential and effectiveness due to overuse or misuse, new products should be developed to treat and prevent the transmission of the infections. It has become necessary for the development of new broad spectrum antimicrobial agents to keep pace with the continually evolving resistance pathogens. One of the potential approaches to overcome the problem of drug resistance is to design and develop innovative antimicrobial agents with different mode of action so that no cross resistance with available therapeutics can occur [1].

Among the five membered heterocyclics containing two hetero atoms in its ring structure, pyrazole is one of the most important one as large variety of biological activities have been reported for various pyrazole derivatives. Pyrazoline is dihydropyrazole, a five membered heterocyclic compound containing two nitrogen atoms in adjacent positions and possessing only one endocyclic double bond. Among all the pyrazolines, 2-pyrazoline has gained attraction and is frequently studied one [3]. 2-Pyrazolines are very much promising when the biological activities of pyrazolines are taken into consideration. The literature survey reveals that 2-pyrazoline derivatives are reported to possess wide range biological activities like antimicrobial [4,5,6,7], antimycobacterial [8,9] antiamoebic [10,11], anti-inflammatory [12], analgesic [13], anticonvulsant [14], antidepressant [15], anticancer [16], acyl-CoA inhibitory [17], neuroprotective [18], antiviral [19], amine oxidase inhibitory [20] etc.

Considering the above mentioned fact pyrazoline derivatives containing were synthesized and characterized and their antifungal activity against *Rhizopus oryze and Penicillium notatum.* On the other hand,microwave assisted organic reactions have emerged as a new Lead in organic synthesis with important advantages like highly accelerated rate of reaction along with improvement in yield and quality of product[21].

Materials and Methods:

The all reagents used in the present study were of analytical grade. The melting points of the synthesized compounds were determined by open capillary tube method and are uncorrected. The 1H-NMR spectra were recorded at 400 MHz at BRUKER NMR spectrophotometer in DMSO and chemical shifts are expressed in parts per million (δ) relative to tetramethylsilane.

General method:

A solution of 2-furyl acetone(0.05mole) and appropriately substituted benzaldehyde (0.05mole) in ethanol taken in conical flask. Sodium hydroxide was added into reaction mixture.Reaction mixture zapped in microwave oven for 30 sec to 1 min at180 watt and then cooled in refrigerator overnight.The product obtained was filtered and washed with water and recrystallization from ethanol.

Then these synthesized chalcones reacts with phenyl hydrazine in microwave oven at 180 watt gives different substituted pyrazolines.

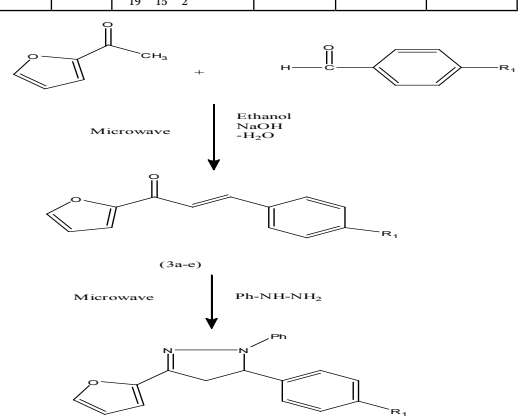
Synthesis of 3-(furan-2-yl)-1,5-diphenyl-4-5-dihydro-1-H-pyrazole(4a-f)

A mixture of substituted chalcone (3a-f)(0.02mole)and phenyl hydrazine(0.02mole) was zapped inside a microwave oven for 1 to 3 min at 180 watt. After cooling ,the solution was poured into crushed ice and the product obtained was filtered and recrystalised using ethanol.

Physical data of synthesized compound are presented as-

Table No.1

compound	R1	Reaction time(min)	Mol. formula	Yield	Mol.wt.	m.pt °c
4a	-H	1.51	$C_{19}H_{16}N_2O$	60%	288	175°c
4b	-Cl	2.35	$C_{19}H_{15}N_2OCl$	61.24%	322.5	190 °c
4c	$-CH_3$	1.56	$C_{20}H_{18}N_2O$	50%	302	180 °c
4d	-NO2	1.35	$C_{19}H_{15}N3O_3$	53%	333	210°c
4e	-Br	2.56	$C_{19}H_{15}N_2OBr$	65%	366	185 °c



Scheme 1:-Synthesis of title compound (4a-e)

3-(furan-2-yl)-1,5-diphenyl-4-5-dihydro-1-H-pyrazole

^{1}H NMR 7.75(CH,S,of 2-furan),5.19(CH,t ,of methine),3.90(C

H2,d,methylene),6.83(CH,S,of 1-benzene ,1-N-C),7.40(CH,S,of 1-benzene 1-C

5(4-Chlorophenyl)-3-(furan-2-yl)-1,5-diphenyl-4-5-dihydro-1-H-pyrazole

^{1}H NMR 7.75(CH,S,of 2-furan),5.19(CH,t ,of methine),3.90(CH2, d,methylene),7.44(CH,of-C-Cl),6.83(CH,S,1-benzene,1-N-C)

5(4-Nitrophenyl)-3-(furan-2-yl)-1,5-diphenyl-4-5-dihydro-1-H-pyrazole

^{1}H NMR 7.75(CH,S,of 2-furan),5.19(CH,t ,of methine),3.90(CH2,d,methylene), 6.83(CH,S,1-benzene,1-N-C),8.21(CH,of 1-benzene ,1-N(=o)=o)

5(4-Bromophenyl)-3-(furan-2-yl)-1,5-diphenyl-4-5-dihydro-1-H-pyrazole

^{1}H NMR 7.75(CH,S,of 2-furan),5.19(CH,t ,of methine),3.90(CH 2,d,methylene),7.92(CH,of –C-Br), 6.83(CH,S,1-benzene,1-N-C)

3-(furan-2-yl)-1-Phenyl-5$_p$-tolyl-4,5-dihydro-1-H-pyrazole

^{1}H NMR 7.75(CH,S,of 2-furan),5.19(CH,t ,of methine),3.90(C H2,d,methylene)7.12(CH,of –C-O), 6.83(CH,of 1-benzene,1-N-C).2.35(for –CH_3)

Antimicrobial activities

Antifungal activity

The following fungal strains Rhizopus oryze and Penicillium notatum were used for the present study. Sabouraud dextrose agar (SDA) medium was used for the growth of fungi and testing was done in Sabouraud dextrose broth (SDB) medium.

The antifungal activities of synthesized pyrazolines are represented in table no.2. Synthesized compound effective towards fungal strain.

Table No.2

Compounds	Antifungal Activity (Zone of Inhibition in mm)	
	Rhizopus oryze	Penicillium notatum
4a	12	10
4b	20	15
4c	20	10
4d	Resistant	20
4e	15	Resistant

Result & Discussion:

Chalcone (3a-e)were prepared by following the standard protocol[22] and were reacted with phenyl hydrazine to yield 3(furan-2-yl)1,5diphenyl 4-5-dihydro-1-H-pyrazole & its derivatives.the synthetic procedure for preparation of title compounds is given in scheme 1.The assigned structure & molecular formula of the newly synthesized compound (4a-e)were confirmed and supported by ^{1}H NMR as well as elemental analysis which was in full agreement with proposed structures.the compounds were screend in vitro antifungal potential by filter paper disc method against fungi.The results of antifungal activities expressed in terms of inhibition zone are reported in Table no.2.Even though the synthesized compound shows appreciable antifungal activity.

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