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Synthesis, Characterization and Antimicrobial Activities of Some Pyrazoline Derivatives

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Abstract: ***Some new fused pyrazolines3-methyl-1, 4, 5-triphenyl-1, 3a, 4, 5tetrahydropyrazolo[3-4c]pyrazole, 4(4-Bromophenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole, 4(4-chlorophenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole 4(4-Nitrophenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole, 4(4-methoxyphenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole, 4(4 methyl -2, 6-diphenyl -2, 3, 3a, 6 – tetra hydrophyrozolo [3, 4c] pyrazol-3-yl)phenol, pyrazole are prepared by condensation of 1-phenyl-3-methyl-5-pyrazolone with substituted benzaldehyde under microwave irradiation afford chalcones which under cyclization with phenyl hydrazine to afford fused pyrazolines. Synthesized compound confirmed by suitable spectroscopic technique such as 1HNMR. The compounds were screened for their in antibacterial activity against S. aureus E. coli, S. typhi bacteria.***

Keywords: Microwave irradiation, Pyrazolines, spectral data, antibacterial activity.

1. Introduction

A number of pyrazoline derivatives have been shown to exhibit a broad spectrum of biological & pharmaceutical activities which includes antitumor[1], antibacterial[2-3], antifungal[4-5], antiviral[6] & anticancer[7] activity.

Pyrazolines are well known and important nitrogen-contanining 5-membered hetrocyclic compound and various methods have been worked out for their synthesis[8]. Microwave assisted synthesis ofsome novel 2-pyrazoline derivatives and it's possible antimicrobial activity also reported[9].

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[10]. Thus keeping in view the advantages ofthese techniques and immense biological importance of pyrazolines, it was felt worthwhile to study the reaction under microwave irradiation and to screen the target compounds for antimicrobial activity.

2. Experimental

All melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents used were of laboratory grade. ^{1}H NMR spectra was recorded on Brucker 400MHz, NMR spectrometer using TMS as an internal standard. Reactions were carried out in a domestic microwave oven at 180 watt.

2. 1 General Method

Firstly synthesized 1-phenyl-3-methyl-5-pyrazolone. Then this 1-phenyl-3-metheyl-5-pyrazolone (0. 05mole) and substituted benzaldehyde (0. 05mole) in glacial acetic acid taken in conical flask sodium acetate was added into reaction micture. Reaction mixture zapped in microwave oven for 1 min to 2 min at 180 watt and then cooled in refrigerator overnight. The product obtained was filtered and washed with water and recrystallization from ethanol. Then these substituted benzylidene pyrazolone (3a-f) reacts with phenyl hydrazine in microwae oven for 3 min at 180 watt gives different substituted fused pyrazoline.

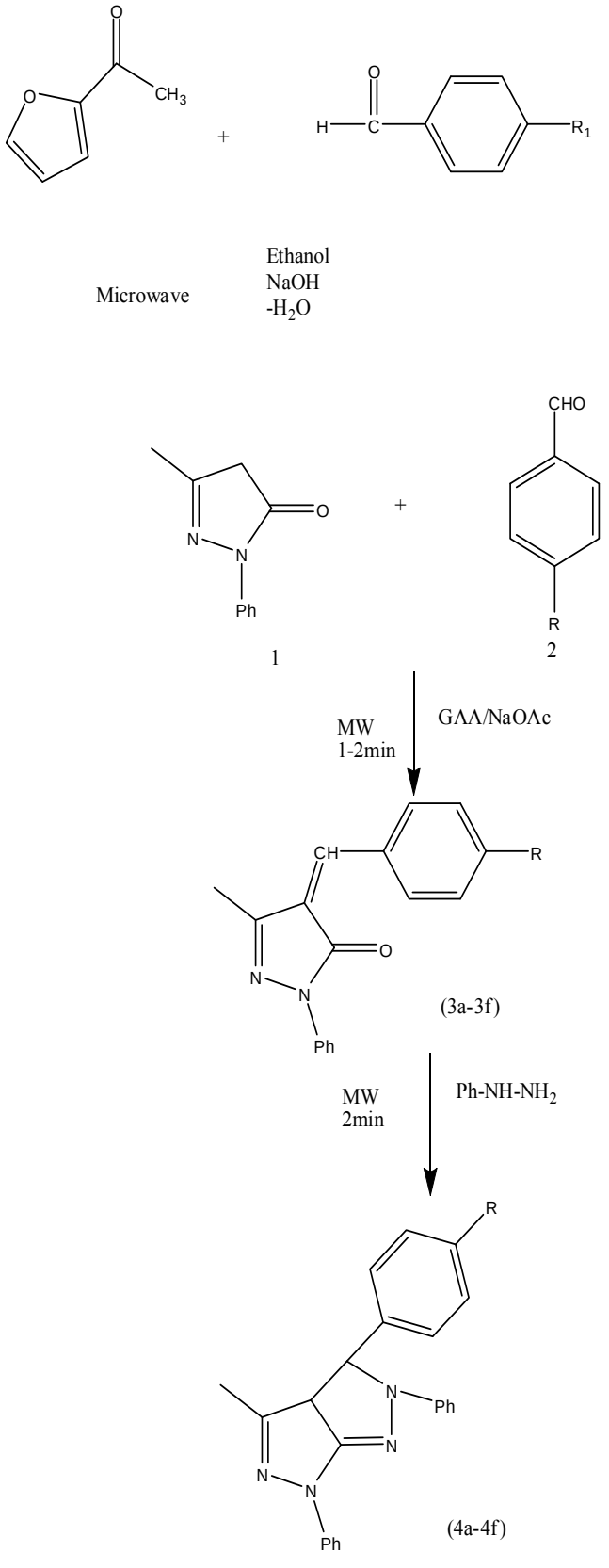
2. 2 Synthesis of 5 substituted phenyl -3-mehtyl -1-phenyl -1, 3a, 4, 5 tetrahydrapyrazolo [3-4c] pyrazole (4a-4f).

A mixture of substituted benzylidene pyrazolone (0. 025) (3a-f) reacts with phenyl hydrazine (0. 025) in microwave oven for 1 to 3 min at 180 watt. After cooling the solution was poured in to crushed ice and the product obtained was filtered & recrystallized using ethanol.

2. 3 Physical data of synthesized compounds.

Table 1

Compd. No.	R	Reaction time in (Min)	Mol.formula	Yield	Mol. Wt.
4a	-H	38 Sec.	$C_{23}H_{20}N_4$	60	352
4b	-CL	2 Min.	$C_{23}H_{19}N_4Cl$	58	386.5
4c	-Br	37 Sec.	$C_{23}H_{19}N_4Br$	58	430.9
4d	-NO2	37 Sec.	$C_{23}H_{19}N_5O2$	57	397
4e	-OCH3	1.6 Min.	$C_{24}H_{22}N_4O$	67	370
4f	-OH	1.3 Min.	$C_{23}H_{20}N_4O$	62	368



synthesis of compounds (4a-4f)

1) **3 – Methyl 1, 4, 5 triphenyl, 1, 3a, 4, 5 tetrahydropyrazolo [3-4c] pyrazole (4a)**
^{1}HNMR (400MH$_Z$ DMSO, δPPM)
7. 8 (m, Ar-H), 7. 44 (m, Ar-H), 7. 2(m, Ar-H), 1. 96(3H, -CH$_3$), 3. 5(CH, methine) 2. 32 (CH, methine)
2) **4(4-chlorophenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole (4b)**
^{1}HNMR (400MH$_Z$ DMSO, δPPM)
7. 8 (m, Ar-H), 7. 45 (m, Ar-H)7. 35 (m, Ar-H)7. 35 (m, Ar-H), 7. 47(S, c-cl)2. 33 (3H, methyl), 5(S, C- N)
3) **4(4-Bromophenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole (4c)**
^{1}HNMR (400MH$_Z$ DMSO, δPPM)
7. 82(m, Ar-H), 8. 0(m, Ar-H), 7. 5(m, Ar-H), 7. 36(S, C-Br), 5. 32(S, C-N), 3. 41(CH, methine), 6. 73(1-benzene, 1-N)
4) **4(4-Nitrophenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole (4d)**
^{1}HNMR (400MH$_Z$ DMSO, δPPM)
8. 1(m, Ar-H), 7. 8(m, Ar-H), 7. 25(m, Ar-H), 7. 54(S, NO_2), 2. 37(CH, methine)
5) **4(4-methoxyphenyl) – 3 methyl -1, 5-diphenyl -1, 3a, 4, 5 – tetra hydrophyrozolo [3, 4c] pyrazole (4e)**
^{1}HNMR (400MH$_Z$ DMSO, δPPM)
8. 02(m, Ar-H), 7. 81(m, Ar-H), 7. 83(m, Ar-H), 6. 97(S, C-O), 1. 97(S<methyl), 3. 80(CH, methine), 4. 95(n-Ar)
6) **4(4 methyl -2, 6-diphenyl -2, 3, 3a, 6 – tetra hydrophyrozolo [3, 4c] pyrazol-3-yl)phenol (4f)**
^{1}HNMR (400MH$_Z$ DMSO, δPPM)
7. 84 (m, Ar-H), 7. 49(m, Ar-H), 7. 16(m, Ar-H)6. 84(1-benzene, -N-C)6. 71(1-benzene, C-O)8. 17(Aromatic-OH), 2. 3(CH, methine), 3. 47(CH, methine), 1. 94(3H, methyl).

3. Antimicrobial Activities

3. 1 Antibacterial Activity

Staphylococcus aureus was taken as gram positive strain, and Escherichia coli and Salmonella typhi species were taken as gram negative strains; they have been used for the present study. The antimicrobial activity was determined using disc diffusion method[11] by measuring the inhibition zone in mm. All the synthesized compounds exhibited significant antibacterial activity.

Table 2

Compounds	Antimicrobial Activity (Zone of Inhibition in mm)		
	S.aureus	E.coli	S.typhi
4a	18	18	12
4b	15	14	22
4c	12	12	Resistant
4d	12	10	Resistant
4e	12	12	15
4f	22	20	20

4. Results and Discussions

Chalcones (3a-f) wre prepared by followings the standard protocol (II) and were reacted phenyl hydrazine to yield 4-substituted phenyl-3-methyl, 5-diphenyl–1, 3a, 4, 5–tetrahydropyrazolo [3-4c] pyrazole (4a-4f). The synthetic procedure for preparation of compounds is given in scheme I. The assigned structure of newly synthesized compounds (4a-4f) were confirmed and supported by ^{1}HNMR which was in full agreement with proposed structures. The

compounds were screened in vitro antibacterial potential by disc diffusion method against pathogenic bacteria. The results of antibacterial activities expressed in terms of inhibition zone are reported in Table no. 2. Even though the synthesized compound shows appreciable antibacterial activity.

5. Conclusion

Few novel pyrazoline derivatives (4a-4f) have been synthesized and evaluated for antimicrobial activity. The results of antimicrobial studies of newly synthesized compounds related that they possess significant antibacterial activities.

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