Int. J. Chem. Sci.: 13(4), 2015, 1844-1848
ISSN 0972-768X
www.sadgurupublications.com

SYNTHESIS AND BIOLOGICAL ACTIVITY OF 4-(4-BROMOPHENYL)-2-[4-(ARYLHYDRAZONO-3-METHYL-5-(5-BROMOPYRIDIN-2-YL) IMINO-4,5-DIHYDRO PYRAZOL-1-YL]-1,3-THIAZOLE DERIVATIVES

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ABSTRACT

4-(4-Bromophenyl)-2-[4-(arylhydrazono-3-methyl-5-(5-bromopyridin-2-yl)imino-4, 5-dihydro pyrazol-1-yl]-1,3-thiazole derivatives have been synthesized using conventional method and microwave irradiation. The structure of the synthesized compounds have been confirmed by IR and NMR spectroscopy. These compounds were evaluated for their biological efficacy.

Key words: Thiazole, Pyrazole, Biological, Synthesis.

INTRODUCTION

Compounds containing thiazole ring systems are known to possess pharmacological properties like antimicrobial[1], analgesic[2], antiinflammatory[2], anticancer[3], and antitubercular[4] activities. Pyrazole exhibits pharmacological properties such as anticancer[5], analgesic[2], antiinflammatory[6] and antimicrobial[7] activities. Pyridine derivatives are found to exhibit fungicidal[8], insecticidal[9] activities.

In view of this heterocycles having thiazole, pyrazole and pyridine moiety have been synthesized. Synthesis of 1-thiocarboxamido-3-methyl-4-(arylhydrazono)-2-pyrazolin-5-ones **(3)** has been reported[10]. Further derivatives of compound **(4)** are reported by one pot synthesis[11]. Compound **(3)** was treated with *p*-bromophenacyl bromide to obtain 4-(4-bromo phenyl)-2-[(4-arylhydrazono)-3-methyl-5-oxo-2-pyrazolin-1-yl] thiazole derivatives **(4)**,

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which on treatment with 5-bromo-2-aminopyridine gave 4-(4-bromophenyl)-2-[4-(arylhydrazono-3-methyl-5-(5-bromopyridin-2-yl) imino-4,5-dihydro pyrazol-1-yl]-1,3-thiazole derivatives **(5)**. The synthesis of **(5)** has been carried out using conventional method as well as by microwave irradiation.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr on Shimadzu Corporation, IR Affinity-I and PMR on a Agilant Technology 400/54 premium shielded using TMS as internal standard (chemical shift in δ ppm).

The reactions were monitored on TLC.

4-(4-Bromophenyl)-2- [4-(4-nitrophenylhydrazono-3 -methyl-5 -oxo-4, 5-dihydro pyrazol- 1-yl)-1,3-thiazole derivatives (4g)

A mixture of 1-thiocarboxamido-3-methyl-4-(4-nitrophenylhydrazono)-2-pyrazolin-5-one **(3g)** (0.01 mol) in DMF (10 mL) and *p*-bromophenacyl bromide (0.01 mol) in ethanol was stirred at room temperature for 2 hrs. The separated solid was filtered, dried and recrystalized from DMF. IR (KBr): 1676 cm^{-1} (> C=O), 1568 cm^{-1} (C=N), 1340 cm^{-1} (NO_2).

4-(4-Bromophenyl)-2-[4-(4-nitrophenylhydrazono-3-methyl-5-(5-bromopyridin-2-yl) imino-4,5-dihydro pyrazol-1-yl]-1,3-thiazole derivatives (5g)

Conventional method

Compound **(4g)** (0.005 mol) and 5-bromo-2-aminopyridine (0.005 mol) were refluxed in 20 mL of DMF for 4 hrs. After completion of reaction, the reaction mixture was cooled and poured in to crushed ice with stirring. The solid obtained was filtered, washed with water and then recrystallized from toluene.

Microwave assisted synthesis

Compound **(4)** (0.005 mol) and 5-bromo-2-aminopyridine (0.005 mol) were refluxed in 20 mL of DMF for 7 min. After completion of reaction, the reaction mixture was cooled and poured into crushed ice with stirring. The solid obtained was filtered, washed with water and then recrystallized from toluene.

Other compounds were obtained by the same method.

Compound **(5g)**: IR (KBr): 1520 cm^{-1} (C=N), 1332 cm^{-1} (NO_2) NMR ($CDCl_3$): 2.62 (s, 3H, -CH_3), 8.45 (s, 1H, -NH), 7.97 (s, 1H, thiazole 5-H), 7.2-7.65 (m, Ar-H, 11H)

RESULTS AND DISCUSSION

Synthesis of 4-(4-bromophenyl)-2-[4-(arylhydrazono-3-methyl-5-(5-bromopyridin-2-yl) imino-4,5-dihydro pyrazol-1-yl]-1,3-thiazolederivatives has been carried out using conventional method as well as by microwave irradiation. The reaction rate is enhanced tremendously under microwave irradiation as compared to the conventional method with improved yields. The IR spectrum of compound **(4)** shows peak at 1676 cm^{-1} indicating the presence of carbonyl group whereas the IR spectrum of compound **(5)** does not show peak in this region indicating the absence of carbonyl group.

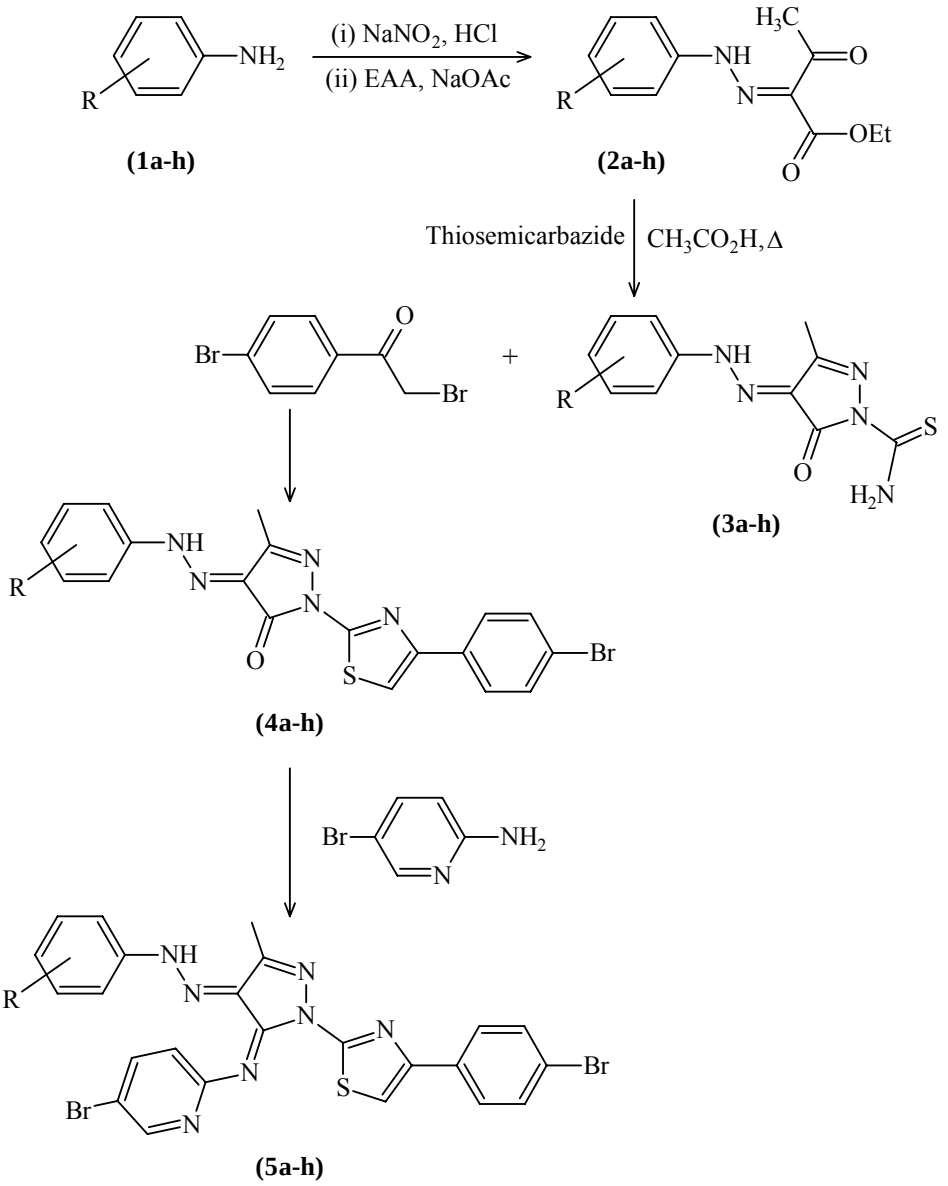
Biological activities

All the newly synthesized compounds i.e. **(5a)** to **(5h)** were screened for their antibacterial activity against *E. coli*, *S. aureus*, *P. aeroginosa* and *S. typhi* using ciprofloxacin as a standard. The zone of inhibition was measured in mm. DMF was used as diluent control.

Table 1: Characterization data of (5a-h)

Deriv.	R	M.P. (Comp. No. 4)	M.P. (Comp. No. 5)	Conventional method (Comp. No. 5)		Microwave irradiation (Comp. No. 5)	
				(Time in hrs.)	% Yield	(Time in min.)	% Yield
a	H	216	187	3	54	6	62
b	2-OCH_3	226	200	3	58	6	69
c	4-OCH_3	162	128	3	48	6	62
d	4-Br	262	246	3	71	6	82
e	4-Cl	258	240	3	50	6	62
f	4-CH_3	200	178	2	55	5	67
g	4-NO_2	278	264	4	58	7	75
h	3-NO_2	254	230	4	56	7	69

Compound **(5f)** was found to be moderately active against all four micro organisms whereas Compound **(5b)**, **(5c)**, **(5d)**, **(5f)**, and **(5g)** were found mildly active against *S. aureus*. Rest all were found inactive.



Scheme 1

R = (a) H, (b) 2-OCH_3, (c) 4-OCH_3, (d) 4-Br, (e) 4-Cl, (f) 4-CH_3, (g) 4-NO_2, (h) 3-NO_2.

ACKNOWLEDGEMENT

One of the authors (PRR) is thankful to University of Mumbai for awarding Minor Research Grant.

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Accepted : 11.11.2015