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Novel One Pot Microwave Irradiated Synthesis and Antimicrobial Activities of Some Pyrazolinylbutanediones

B. Bajia, N.S. Rao, M. Nyati and Y.K. Srivastava*
Department of Chemistry, Maharana Pratap Government Postgraduate College
Chittorgarh-312 001, India
E-mail: birbal_bajia@yahoo.com; hariputra_ns@rediffmail.com

New 1-(3,5-diaryl-2-pyrazolinyl)-1,3-butanediones have been synthesized by condensation of 3,5-diaryl-2-pyrazolines with ethyl acetoacetate using microwave irradiation. The synthesized compounds were characterized by their elemental and spectral data and screened for their antibacterial activity.

Key Words: Pyrazolinyl, Ethylacetoacetate, Antibacterial.

INTRODUCTION

In the last few years, there has been a growing interest in the use of microwave irradiation in the chemical reactions. Spectacular results have been obtained giving clear indication on the potentialities and advantage of this technique compared to conventional heating method[1-3]. Virtually all types of thermally driven reactions can be accelerated by microwave. The use of such non-conventional reaction conditions reveal several advantages like a shorter reaction time, increased yield, cleaner reaction, selectivity in the reaction and easy workup. Thus microwave assisted synthesis becomes a part of green chemistry[4,5]. The use of domestic microwave oven in this regard is now a well established procedure in Green Chemistry[5].

Pyrazoline derivatives have been studied extensively because of their ready accessibility, diverse chemical reactivity and variety of industrial applications. Various substituted 2-pyrazolines can be effectively utilized as antimicrobial, anticonvulsant, cardiovascular, antiinflammatory and antidepressant agent[6-10]. In additional pyrazolines have played a crucial role in organic synthesis[11,12].

In view of interesting properties associated with 2-pyrozoline, in the present investigation, the synthesis of some N-substituted 2-pyrozolines using microwave irradiation is reported.

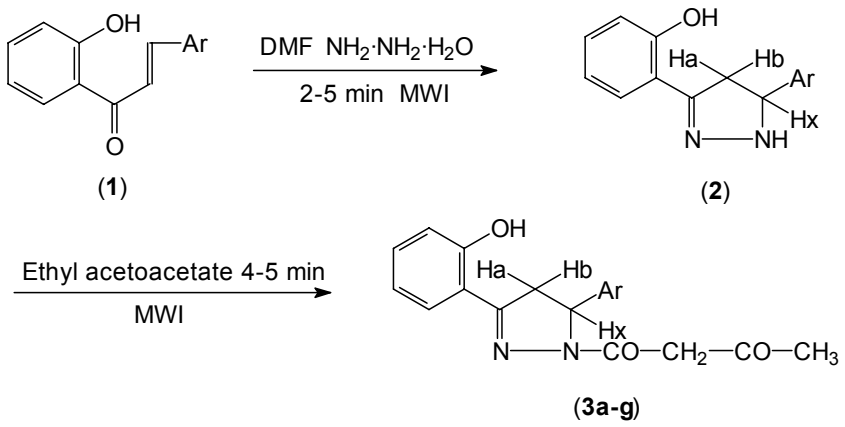
EXPERIMENTAL

All the melting points reported are uncorrected and were taken in open capillaries. The progress of reaction and purity of products was checked by TLC using silica gel-G as adsorbent and benzene-ethyl acetate (9:1) as

eluent. The IR spectra were recorded on Perkins Elmer spectrometer using KBr pellet. The ^{1}H NMR spectra were taken on Bruker-DRx 300 MHz spectrometer using $CDCl_3$ as solvent and TMS as internal standard (chemical shift in δ ppm). Mass spectra were recorded on Jeol-SX-102 mass spectrometer using *m*-nitro benzyl alcohol as matrix. The matrix peaks appear at m/z 107, 136, 154 and 289.

Synthesis of 3,5-diaryl-2-pyrazolines (2a-g): To a slurry of *o*-hydroxychalcone (0.01 mol) in DMF (10 mL), hydrazine hydrate (0.015 mol) was added. The reaction mixture irradiated in microwave oven for 2-3 min. It was then cooled to room temperature. The residue obtained was washed with water and crystallized from ethanol as colourless crystals (**2a-g**).

Synthesis of 1-(3,5-diaryl-2-pyrazolinyl)-1,3 butane-diones (3a-g): An intimate mixture of 3,5-diaryl-2-pyrazoline (0.01 mol) and ethyl acetoacetate (0.02 mol) was subjected to microwave irradiation for 4-5 min with occasional disruption of 30 s. After completion of reaction as indicated by TLC the residue obtained was washed thoroughly with water, dried and crystallized from ethanol as colourless crystals (Table-1).



Scheme-I

Antibacterial activity: Cup plate method[13,14] was employed to evaluate the preliminary antibacterial activity of (**3a-g**) against gram positive *S. aureus* and *S. albus* and gram negative *E. coli, K. pneumoneae* and *P. vulgaris* organism. Preparation of nutrient broath, subculture base layer medium, agar medium and peptones walls was done as per standard procedure.

Amicacin used as standard drug. The zone of inhibition produced by each compounds was measured in mm. (Table-2)

TABLE-1
PHYSICAL DATA OF SYNTHESIZED COMPOUNDS (**3a-g**)

Compd.	Ar	m.f.	m.p. (ºC)	Yield (%)	Reaction time (min)
3a	Phenyl	$C_{19}H_{18}N_2O_3$	186	80	3.5
3b	4-Methoxyphenyl	$C_{20}H_{20}N_2O_4$	176	70	4.0
3c	3,4-Dimethoxyphenyl	$C_{21}H_{22}N_2O_5$	130	75	4.5
3d	3,4,5-Trimethoxyphenyl	$C_{22}H_{24}N_2O_6$	160	85	4.0
3e	4-Chlorophenyl	$C_{19}H_{17}N_2O_3Cl$	188	80	3.5
3f	4-Dimethylaminophenyl	$C_{21}H_{23}N_2O_3$	200	60	4.0
3g	4-Hydroxyphenyl	$C_{19}H_{18}N_2O_4$	172	72	4.5

TABLE-2
ANTIBACTERIAL ACTIVITY OF SYNTHESIZED COMPOUNDS (**3a-g**)

Compd.	Zone of inhibition in mm				
	S. aureus	*S. albus*	*E. coli*	*K. pneumoniae*	*P. vulgaris*
3a	–	08	09	10	–
3b	–	09	08	14	–
3c	–	09	10	11	–
3d	–	11	13	09	–
3e	–	11	10	12	–
3f	–	12	09	09	–
3g	–	08	10	12	–
Amicacin	22	24	14	20	–

RESULTS AND DISCUSSION

The reactions of 2-pyrazolines with ethyl acetoacetate by conventional heating have been reported to afford pyrazoline enamine ester[15]. However during present study under microwave induced reaction condition the product obtained was identified as 1-(3,5-diaryl-2-pyrazolinyl)-1,3-butanediones. The structure of the compound was confirmed on the basis of elemental analysis and spectral data. The IR spectra of compounds showed absorption band at 3430 cm^{-1} (broad peak -OH), 2965 cm^{-1} (C-H str. of aromatic ring), 2837 cm^{-1} (C-H str. of -CH_2- group), 1700-1680 cm^{-1} (C=O str.), 1230-1220 cm^{-1} (C=N str.) and 1130-1120 cm^{-1} (N-N str.). The ^1H NMR spectra showed signal as double doublet at δ 2.24-2.30 (C-H_a), 2.54-2.60 (C-H_b), 4.86-4.90 (C-H_x) confirming the presence of ABX pattern of pyrazoline ring. Aromatic protons gave multiplate at δ 6.51-7.10 and OH

proton gave a singlet at δ 10.09. The methylene proton gave singlet at 1.70 and methyl proton showed a singlet at 1.50. The mass spectra of synthesized compounds gave molecular ion peak corresponding to their molecular mass besides other peaks.

The antibacterial screening results show that all compounds are active against *S. albus, K. pneumoniae* and *E. coli* and none of the compound was found active against *S. aureus* and *P. vulgaris*.

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