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Research Article

A facile Microwave Induced synthesis of some novel 3-[4'-(4''-nitrophenoxy)-phenyl]-5-(substituted aryl)-2-pyrazoline-1-carboxaldehydes as potential antimicrobial agents

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ABSTRACT

In the present communication, a series of some novel 3-[4'-(4''-nitrophenoxy)-phenyl]-5-(substituted aryl)-2-pyrazoline-1-carboxaldehydes have been synthesized by the treatment of substituted 4'-(4''-nitrophenoxy) chalcones (1a-f) with hydrazine hydrate in hot formic acid under microwave irradiation in 80-85% yield with high purity. The newly synthesized compounds were confirmed by the spectral analysis and elemental data. These compounds were evaluated for their antimicrobial activities.

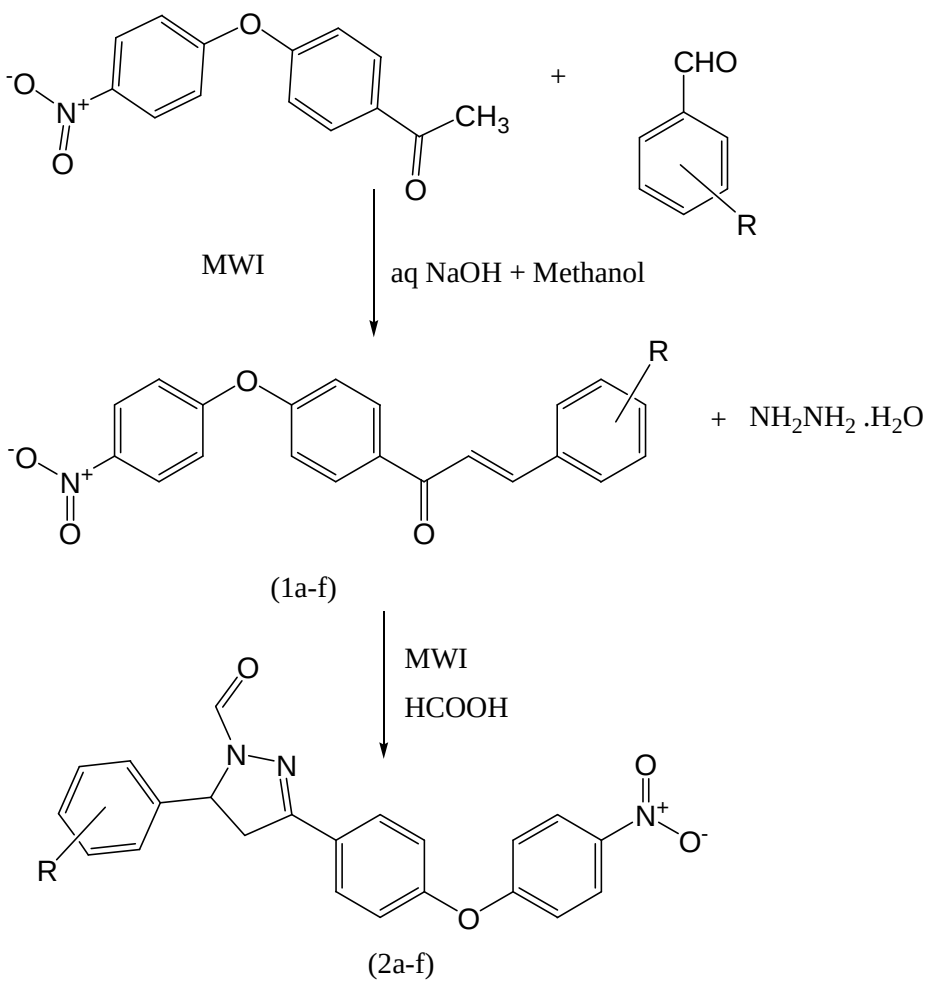
Keywords: Microwave irradiation, 2-pyrazoline, antimicrobial activity.

INTRODUCTION

Pyrazolines are well known nitrogen containing five membered heterocyclic compounds. Pyrazolines and their derivatives have been found to possess a broad spectrum of biological activities such as antibacterial[1], antifungal[2], antidepressant[3], antiinflammatory[4], antitubercular agents[5], immunosupp - ressive[6], anticonvulsant[7] and bactericidal[8-9]properties. Certain pyrazolines due to their non toxic properties have been used as local anesthetics also[10]. Pyrazolines are used extensively as useful synthon in organic synthesis[11-14]. Among various pyrazoline derivatives, 2-pyrazolines seem to be most frequently studied pyrazoline. A variety of methods have been reported for the preparation of this class of compounds. The pyrazoline function is quite stable and has inspired chemists to utilize this stable fragment in bioactive moieties to synthesize new compounds. High speed microwave assisted chemistry is being utilized in recent years successfully in various field of synthetic organic chemistry[15]. Literature reviews prove the synthetic utility of MORE chemistry in routine organic synthesis[16-18]. It can be termed as e-chemistry because it is easy, effective, economical easy, eco- friendly and in believed to be a step towards

green chemistry. Pollution free synthesis, shorter reaction time easy work-up and minimum use of solvent are the major advantages of this technique[19-21]. Under the framework of "green chemistry" we were, therefore, interested in developing a microwave assisted protocol for the synthesis of the title compound.

Here in we report a microwave induced synthesis of some novel 3-[4'-(4''-nitrophenoxy)-phenyl]-5-(substituted aryl)-2-pyrazoline-1-carboxaldehyde. Substituted 4'-(4"-nitrophenoxy) chalcones (1a-f) on the reaction with hydrazine hydrate in hot formic acid under MWI resulted in the formation of the title compounds (2a-f). The yields of the products formed under microwave irradiation were high. The purity of compounds was monitored by TLC and the structure of the synthesized compounds was confirmed by elemental analysis and spectral data (IR, ^{1}H-NMR, Mass) which are summarized in Table-I and Table-II respectively.



R= (a) H, (b) 4-N $(CH_3)_2$ (c) 4-C l

(d) 3,4(OCH_3) (e) 4-OCH_3 (f) 3,4,5$(OCH)_3$

Reaction Scheme

Table-I: Physical data of synthesized compound 3-[4'-(4''-nitrophenoxy)-phenyl]-5--(substituted aryl)-2-pyrazoline-1-carboxaldehydes (2a-f).

Com.	R	Molecular formula (Mol. Wt.)	M.P. (^{0}C)	Yield %	Reaction Time (MWI)		R_f value	%N	
					Power (watt.)	Time (min.)		Cal.	Found
2a	H	$C_{22}H_{17}N_3O_4$ (387)	172	85	600	4	0.69	10.85	10.72
2b	4-N$(CH_3)_2$	$C_{24}H_{22}N_4O_4$ (430)	155	81	600	2	0.71	13.02	12.98
2c	4-Cl	$C_{22}H_{16}N_3O_4Cl$ (421.5)	166	85	600	2	0.70	9.96	9.75
2d	3,4-$(OCH_3)_2$	$C_{24}H_{21}N_3O_6$ (447)	106	84	600	3	0.76	9.39	9.04
2e	4-OCH_3	$C_{23}H_{19}N_3O_5$ (417)	161	83	600	4	0.72	10.07	9.96
2f	3,4,5-$(OCH_3)_3$	$C_{25}H_{23}N_3O_7$ (477)	169	80	600	2	0.73	8.80	8.56

EXPERIMENTAL

Melting points were determined by open capillaries and are uncorrected. The chemicals and solvents are used of laboratory grade and were purified. The purity of compounds was checked by TLC on silica gel-G using benzene-ethyl acetate (9:1 v/v) as the eluent. The IR spectra were recorded on Shimadzu FT-IR spectrometer using KBr (cm^{-1}). ^{1}H-NMR spectra were measured on Brucker-DR_x-600 spectrometer using TMS as internal standard and $CDCl_3$ or DMSO-d_6 as solvent. Mass spectra were obtained on an Agilent 6520-QTOF LCMS having a ESI source in positive mode. Matrix peaks appeared at m/z 387, 430, 421.5, 447, 417 and 477 corresponding to their molecular masses. All the transformations were carried out in a domestic microwave oven Samsung 30N with power out-put 600 watts.

General procedure for the synthesis of substituted 4'-(4"-nitrophenoxy) chalcones (1a-f): A solution of 4-(4'-nitrophenoxy) acetophenone (0.01 mole) and variously substituted aryl aldehyde (0.01 mole) in methanol (15 mL) were taken in beaker, then added aq. Sodium hydroxide (40%, 15 mL) and the reaction mixture was irradiated under microwave irradiation for 3-4 minutes at 300 watts. The progress of the reaction was checked by TLC on silica gel-G using benzene-ethyl acetate (9:1 v/v) as the eluent. After completion of the reaction, the reaction mixture was cooled at room temperature then poured into ice cold water, neutralized with dil.HCl. The solid obtained was filtered, washed with water,dried followed by recrystallization from alcohol and benzene to give product (1a-f).

General procedure for the synthesis of 3-[4'-(4''-nitrophenoxy)-phenyl]-5-(substituted aryl)-2-pyrazoline-1-carboxaldehydes (2a-f):- A mixture of substituted 4'-(4''-nitrophenoxy) chalcone (0.01 mole) was dissolved in hot formic acid (10mL). Hydrazine hydrate (0.03 mole) was added to it and the mixture was irradiated under microwave oven at 600 watt. for 2-4 minutes. The progress of reaction was monitored by TLC on silica gel-G using benzene-ethyl acetate (9:1 v/v) as eluent. After completion of the reaction, the content were cooled and poured into crushed ice. The solid mass separated was filtered, washed with cold water and recrystallized from methanol to give pure products 2(a-f) in (80-85%) yield.

Table-II: Spectral data of synthesized compound 3-[4'-(4''-nitrophenoxy)-phenyl]-5-(substituted aryl)-2-pyrazoline-1-carboxaldehydes (2a-f).

S.No.1	Name of Compound	**3-[4'-(4''-nitrophenoxy)-phenyl]-5-phenyl-2-pyrazoline-1-carboxaldehyde (2a).**
(2a).	IR (KBr, υ cm^{-1})	2941 (C-H stret.), 1647 (-CHO), 1508-1427 (C=C, C=N)
	^{1}H NMR ($CDCl_3$, ppm):	3.21-3.25 (dd, 1H, H_a), 3.80-3.86 (dd, 1H, H_b),5.56-5.59 (dd, 1H, H_x),7.02-8.20 (m, 13H, Ar-H), 8.97 (s, 1H, -CHO)
	Mass (FAB, m/z)	$M^{+\cdot}$ 387
S.No.2	Name of Compound	**3-[4'-(4''-nitrophenoxy)-phenyl]-5-(4-N,N-dimethylamino phenyl)-2-pyrazoline-1-carboxaldehyde (2b).**
2b	IR (KBr, υ cm^{-1})	2933 (C-H stret.), 1651(-CHO), 1516-1431 (C=C, C=N)
	^{1}H NMR ($CDCl_3$, ppm):	2.17 (s, 6H, -N(CH_3)$_2$), 2.92-3.25 (dd, 1H, H_a), 3.69-3.80 (dd, 1H, H_b) 5.48-5.51 (dd, 1H, H_x), 6.68-8.25 (m, 12H, Ar-H), 8.93 (s, 1H, -CHO)
	Mass (FAB, m/z)	$M^{+\cdot}$ 430
S.No.3	Name of Compound	**3-[4'-(4''-nitrophenoxy)-phenyl]-5-(4-chloro phenyl))-2-pyrazoline-1-carboxaldehyde (2c).**
2c	IR (KBr, υ cm^{-1})	2945 (C-H stret.), 1656 (-CHO), 1506-1429 (C=C, C=N)
	^{1}H NMR ($CDCl_3$, ppm):	3.17-3.21 (dd, 1H, Ha), 3.69-3.86 (dd, 1H, Hb), 5.52-5.55 (dd, 1H, Hx) 7.06-8.25 (m, 12H, Ar-H) ,8.94 (s, 1H, -CHO)
	Mass (FAB, m/z)	$M^{+\cdot}$ 421.5
S.No.4	Name of Compound	**3-[4'-(4''-nitrophenoxy)-phenyl]-5-(3,4-dimethoxy phenyl)-2-pyrazoline-1-carboxaldehyde (2d).**
2d	IR (KBr, υ cm^{-1})	2920 (C-H stret.), 1670 (-CHO),1512-1425 (C=C, C=N)
	^{1}H NMR ($CDCl_3$, ppm):	3.20-3.24 (dd, 1H, Ha), 3.77-3.83 (dd, 1H, Hb), 3.95 (s, 6H, OCH_3) 5.51-5.53 (dd, 1H, Hx) , 6.74-8.25 (m, 11H, Ar-H) 8.97 (s, 1H, -CHO)
	Mass (FAB, m/z)	M+. 447
S.No.5	Name of Compound	**3-[4'-(4''-nitrophenoxy)-phenyl]-5-(4-methoxy phenyl)-2-pyrazoline-1-carboxaldehyde (2e).**
2e	IR (KBr, υ cm^{-1})	2926 (C-H stret.), 1657 (-CHO), 1516-1429 (C=C, C=N)
	^{1}H NMR ($CDCl_3$, ppm):	3.19-3.24 (dd, 1H, H_a) , 3.71-3.79 (dd, 1H, H_b),3.83 (s, 3H, OCH_3), 5.51-5.54 (dd, 1H, H_x) , 6.87-8.25 (m, 12H, Ar-H),8.94 (s, 1H, -CHO)
	Mass (FAB, m/z)	$M^{+\cdot}$ 417
S.No.6	Name of Compound	**3-[4'-(4''-nitrophenoxy)-phenyl]-5-(3,4,5-trimethoxy phenyl)-2-pyrazoline-1-carboxaldehyde (2f).**

2f	IR (KBr, υ cm^{-1})	2945 (C-H stret.), 1666 (-CHO),1506-1423 (C=C, C=N)
	^{1}H NMR ($CDCl_3$, ppm):	3.18-3.23 (dd, 1H, H_a) ,3.78-3.84 (dd, 1H, H_b),3.95 (s, 9H, OCH_3) 5.49-5.52 (dd, 1H, H_x), 6.44-8.25 (m, 12H, Ar-H), 9.00 (s, 1H, -CHO)
	Mass (FAB, m/z)	$M^{+\cdot}$ 477

RESULTS AND DISCUSSION

As a result of our studies related to the development of synthetic protocols using microwave irradiation, we report here a novel and easy access to substituted 2-pyrazolines using a one-pot procedure and demonstrate its superiority over previously reported classical heating methods. Newly synthesized some substituted 3-[4'-(4''-nitrophenoxy)-phenyl]-5- (substituted aryl)-2-pyrazoline-1-carboxaldehydes were prepared by microwave irradiation. All the synthesized compounds were characterized on the basis of their spectral analysis (FT-IR, ^{1}H-NMR, Mass).

The IR spectra of 2-pyrazoline exhibited absorption bands at 3066-2941 cm^{-1} for (-CH stret.), 1670cm^{-1} for (-CHO), 1508-1427 cm^{-1} for (C=C, C=N), and aromatic nitro group shows the bands in regions 1595-1560 cm^{-1} (asymm.) and 1354 cm^{-1} (symm). IR absorption bands in the region at 850-746 cm^{-1} are due to para substituted phenyl ring. The PMR spectrum of synthesized compounds, the three hydrogen atoms attached to C-4 and C-5 carbon atoms of the heterocyclic ring gave an ABX spin system proved the 2-pyrazoline structure. The high field double doublet at δ3.21-3.25 (due to H_a at C-4), double doublet at δ3.80-3.86 (due to H_b at C-4), and double doublet at δ5.56-5.59 (due to H_x at C-5) are characterized for compound (2a). And δ7.02-8.20 due to multiplets of 13H from aromatic ring, a singlet at δ8.97 also observed due to –CHO group. The mass spectra of 2-pyrazoline were showed molecular ion peaks corresponding to their molecular formula.

ANTIMICROBIAL ACTIVITY

All the synthesized compounds (2a-f) were screened for their antimicrobial activities which are summarized in **Table III.**

Table III: Biological screening results of compounds (2a-f), Zone of inhibition in (mm)

Compd.	Antibacterial activity			Antifungal activity		
	E.coli	*Pseudomonas*	*K.pneumoniae*	*B.subtilis*	*C. albicans*	*A. Fumigatus*
2a	19	18	17	20	20	18
2b	21	22	15	18	16	17
2c	20	19	21	17	18	22
2d	22	23	19	19	17	19
2e	17	19	16	18	19	15
2f	18	21	18	14	21	17
Ciprofloxacin	40	40	40	40	-	-
Fluncazole	-	-	-	-	40	40

(Note: - Zone of inhibition in (mm) will substract from borer size.)

CONCLUSION

The use of microwave irradiation technique leads to considerable saving in the reaction time and is energetically profitable. The reaction under MWI is clean, efficient, eco-friendly,economic easy, easy work-up and integral part of green chemistry. The yields of newly synthesized compounds were found to be in range 80-85%. The structure of the synthesized compounds were confirmed and characterized with the help of spectral data (IR, PMR, Mass) and some of compounds show potential antimicrobial activities.

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