Int. J. Chem. Sci.: 12(4), 2014, 1121-1134
ISSN 0972-768X
www.sadgurupublications.com

ECOFRIENDLY SYNTHESIS OF CHALCONES AND THEIR 2-PYRAZOLINE AND ISOXAZOLINES DERIVATIVES AS POTENTIAL MICROBIAL AGENTS

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ABSTRACT

Microwave assisted synthesis of chalcones under solvent-free conditions resulted in a "green-chemistry" procedure for the preparation of 2-pyrazolines and isoxazoline derivatives in very good yields. Acetone was reacted with appropriately substituted benzaldehydes in the presence of basic alumina to furnish substituted chalcones **(1**, **2** and **3)**. These chalcones undergo facile and clean cyclization with phenyl hydrazine, 2,4-dinitrophenylhydrazine, semicarbazide and thiosemicarbazide to afford substituted 3,5-arylated-2-pyrazoline derivatives **(1a-1d**, **2a-2d** and **3a-3d)**. Reaction of these chalcones with hydroxylamine hydrochloride yielded 3, 5-arylated isoxazoline derivatives (**1e**, **2e** and **3e)**. The structures of synthesized compounds have been confirmed by suitable spectroscopic techniques such as IR and ^{1}H NMR and analytical data. All the compounds were screened for their antibacterial activity against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* and for antifungal activity against *Candida albicans* and *Aspergillus fumigatus.* The compounds exhibited moderate to excellent antibacterial and antifungal activities. The results obtained indicate that unlike classical heating, microwave irradiation results in higher yields in shorter reaction times and cleaner reactions in eco-friendly manner.

Key words: Microwave synthesis, Chalcones, 2-Pyrazoline, Isoxazoline, Phenylhydrazine, 2,4-Dinitrophenylhydrazine, Semicarbazide, Thiosemicarbazide, Hydroxylamine hydrochloride, Antifungal, Antibacterial.

INTRODUCTION

The α, β-unsaturated ketones (chalcones) are considered to be precursors of flavonoids and isoflavonoids and found as naturally-occurring compounds, but it could be considered that their true importance is extended in two branches. The biological activity associated with them, including anti-inflammatory[1-3], antimitotic[4], anti-leishmanial[5],

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anti-invasive[6,7], anti-tuberculosis[8], anti-fungal[9], anti-malarial[10,11], anti-tumor, and anti-oxidant properties[12]; as well as their recognized synthetic utility in the preparation of pharmacologically-interesting heterocyclic systems like pyrazolines and isoxazolines.

Pyrazolines have been largely studied owing to their pharmacological activities, which includes anti-tumor[13], anti-inflammatory[14], anti-parasitary[15], anti-depressive, anticonvulsant[16], antimicrobial[17], antinociceptives[18] and nitric oxide synthase inhibitors, associated with diseases such as alzheimer, Huntington, and inflammatory arthritis[19].

Isoxazolines have also been reported to possess antidiabetic[20], diuretic[21], analgesic[22] antibactrial[23] and hypoglycaemic activity[24].

Microwave radiation has gained the attention of chemists during the last two decades due to its unique advantages, such as shorter reaction times, cleaner reaction products, higher yields and better selectivity. Being a valuable alternative to accomplish more efficient syntheses of a variety of organic compounds with a considerable simplicity of operation and milder reaction conditions, when it is combined with the solvent-free approach, it provides an opportunity to work in open vessels[25-33]. Therefore, we targeted the preparation of the some nitrogen and oxygen containing heterocycles.

Under the framework of, "Green Chemistry", an environmentally benign solvent-free approach has been developed for the synthesis of 1, 5-substituted diphenyl-1, 4-pentadiene-3-one chalcones **(1**, **2** and **3)**, 3, 5-arylated 2-pyrazoline derivatives **(1a-1d**, **2a-2d** and **3a-3d)** and 3, 5-arylated isoxazoline derivatives (**1e**, **2e** and **3e)** by using microwave-assisted dry media reaction conditions and evaluate their antimicrobial activity.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents used were of laboratory grade. The IR spectra (cm^{-1}) were recorded using KBr on Shimadzu FT-IR 8201 PC spectrometer. ^1H NMR spectra ($CDCl_3$/DMSO-d_6) were recorded on Brucker 300 MHz NMR spectrometer using TMS as internal standard (chemical shift in δ ppm.). Mass spectra were recorded on a Jeol-D-300 spectrometer. Elemental analysis was done using Carlo Erba 1106 CHN analyzer and were found within ± 0.5% range of the theoretical values. Follow up of the reactions and the purity of the compounds was ascertained by thin layer chromatography on aluminium plates precoated with silica gel G (Merck) in various solvent systems using iodine vapours as detecting agent. Reactions were carried out in a Ken-Star OM 26 DCF domestic microwave oven at 2450 MHz.

General procedure for microwave-assisted preparation of 1, 5-substituted diphenyl-1, 4-pentadiene-3-one chalcones (1, 2, 3)

A mixture of acetone (0.01 mol) and appropriately substituted benzaldehyde (0.02 mol) was exposed to microwave irradiation (40% microwave power) for about 3-5 minutes in the presence of basic aluminum oxide. The progress of the reaction and the purity of the compounds were monitored with TLC. The resulting crude solid is extracted with ethanol and filtered to remove basic aluminum oxide. Finally, the products were recrystallized from absolute ethanol to give the pure chalcones **(1**, **2** and **3)** in 76-88% yield.

General procedure for microwave-assisted preparation of 3, 5-arylated 2-pyrazoline derivatives (1a-1d, 2a-2d, 3a-3d)

A slurry of chalcones (0.05 mol) and hydrazines ($RNHNH_2$) (0.05 mol) in ethanol was prepared. The solvent was removed under vacuum and the dry powder was irradiated in a microwave oven (80% microwave power) for about 5-7 minutes in open flask. After completion of the reaction as indicated by TLC, the reaction mixture was cooled at room temperature and extracted with ethanol. The products were recrystallized from absolute ethanol to give good yield (73%-86%) of pure crystals of 2-pyrazolines **(1a-1d**, **2a-2d** and **3a-3d)**.

General procedure for microwave-assisted preparation of 3, 5-arylated isoxazoline derivatives (1e, 2e and 3e)

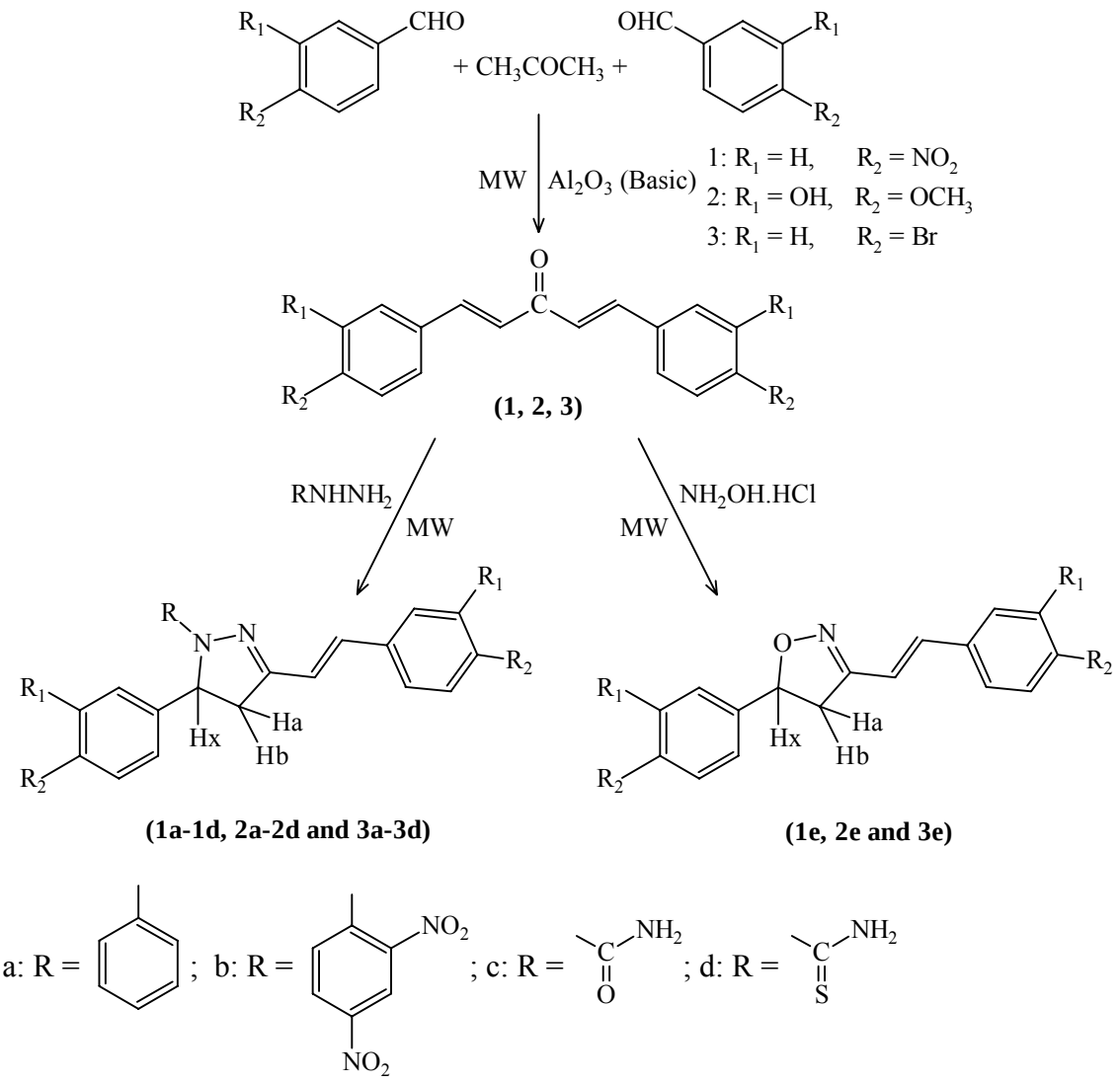
A slurry of synthesized chalcones (0.05 mol) and hydroxylamine hydrochloride (0.05 mol) in ethanol was prepared. The solvent was removed under vacuum and the dry powder was irradiated in a microwave oven (70% microwave power) for about 4-7 minutes in open flask. After completion of the reaction as indicated by TLC, the reaction mixture was cooled at room temperature. The product was eluted and recrystallized from absolute ethanol to give good yield (76%-88%) of pure crystals of isoxazoline derivatives (**1e**, **2e** and **3e**).

Table 1: Physical properties of synthesized compounds

Compd.	Molecular formula	Molecular weight	Melting point (^oC)	Yield (%)	Found (Calculated)		
					% C	% H	% N
1	$C_{17}H_{12}N_2O_5$	324	278	76	62.96 (62.99)	3.73 (3.68)	8.64 (8.69)
2	$C_{19}H_{18}O_5$	326	285	88	69.93 (69.90)	5.56 (5.61)	-

Cont…

Compd.	Molecular formula	Molecular weight	Melting point (°C)	Yield (%)	Found (Calculated)		
					% C	% H	% N
3	$C_{17}H_{12}Br_2O$	392	244	76	52.08 (52.05)	3.08 (3.10)	-
1a	$C_{23}H_{18}N_4O_4$	414	281	82	66.66 (66.62)	4.38 (4.40)	13.52 (13.47)
1b	$C_{23}H_{16}N_6O_8$	504	172	78	54.77 (54.73)	3.20 (3.16)	16.66 (16.61)
1c	$C_{18}H_{15}N_5O_5$	381	298	76	56.69 (56.65)	3.96 (3.99)	18.37 (18.41)
1d	$C_{18}H_{15}N_5O_4S$	397	288	74	54.40 (54.35)	3.80 (3.75)	17.62 (17.59)
1e	$C_{17}H_{13}N_3O_5$	339	280	78	60.18 (60.14)	3.86 (3.83)	12.38 (12.33)
2a	$C_{25}H_{24}N_2O_4$	416	293	86	72.10 (72.15)	5.81 (5.76)	6.73 (6.70)
2b	$C_{25}H_{22}N_4O_8$	506	172	73	59.29 (59.24)	4.38 (4.33)	11.06 (11.10)
2c	$C_{18}H_{15}N_5O_5$	383	279	81	62.65 (62.69)	5.52 (5.55)	10.96 (10.91)
2d	$C_{18}H_{15}N_5O_4S$	399	288	79	60.13 (60.10)	5.30 (5.25)	10.52 (10.57)
2e	$C_{19}H_{19}NO_5$	341	272	88	66.85 (66.81)	5.61 (5.56)	4.10 (4.05)
3a	$C_{23}H_{18}Br_2N_2$	482	293	80	57.29 (57.27)	3.76 (3.71)	5.81 (5.85)
3b	$C_{25}H_{22}N_4O_8$	572	172	77	59.29 (59.24)	4.38 (4.33)	11.06 (11.11)
3c	$C_{18}H_{15}Br_2N_3O$	449	294	74	48.13 (48.18)	3.37 (3.32)	9.36 (9.40)
3d	$C_{18}H_{15}Br_2N_3S$	465	286	78	46.47 (46.44)	3.25 (3.30)	9.03 (8.99)
3e	$C_{17}H_{13}Br_2NO$	407	248	76	50.16 (50.11)	3.22 (3.19)	3.44 (3.39)



Scheme

Spectral data of compounds

(1) 1, 5-Bis (4-nitrophenyl) penta-1, 4-diene-3-one

IR (KBr) cm^{-1}: 1619 (C=O α, β-unsat.), 3065 (=C-H str.), 3018 (C-H Ar), 780, 695 (m- disubs.), 953 (CH=CH trans), 1600, 1578, 1501, 1450 (C=C Ar), 1638 (C=C conju.), 1545 (NO_2 asymm.), 1340 (NO_2 symm.), NMR ($CDCl_3$) δ: 7.05 (d, 2H, $H_α$), 7.81 (d, 2H, $H_β$), 6.90-7.25 (m, 8H, Ar-H), Mass m/z : 324 (M^+), 323, 295, 202, 176, 149, 148, 136, 123.

(2) 1, 5-Bis (3-hydroxy-4-methoxyphenyl) penta-1, 4-diene-3-one

IR (KBr) cm^{-1}: 3350 (OH), 1055 (C-O), 1622 (C=O α, β-unsat.), 3026 (=C-H str.), 3010 (C-H Ar), 950 (CH=CH trans), 1605, 1580, 1500, 1452 (C=C Ar), 868, 815 (1, 2, 4-trisub.), 1650 (C=C conjug.), 1250 (C-O-C asymm.), 1042 (C-O-C symm.), 2949, 2836 (CH_3 str.); NMR ($CDCl_3$) δ : 7.03 (d, 2H, H_α), 7.85 (d, 2H, H_β), 6.87-6.88 (m, 2H, Ar-H), 7.10-7.23 (m, 4H, Ar-H), 5.35 (s, 2H, OH), 3.83 (s, 6H, OCH_3), Mass m/z 326 (M^+), 325, 281, 214,137, 203, 192, 123.

(3) 1, 5-Bis (4-bromophenyl) penta-1, 4-diene-3-one

IR (KBr) cm^{-1}: 1625 (C=O α, β-unsat.), 3049 (=CH str.), 3015 (C-H, Ar), 1649 (C=C conjug.), 958 (CH=CH trans), 1606, 1584, 1509, 1456 (C=C Ar), 832 (p-disub.); NMR ($CDCl_3$) δ: 7.03 (d, 2H, H_α), 7.80 (d, 2H, H_β), 6.70-7.21(m, 8H, Ar-H); Mass m/z: 392 (M^+), 394, 396, 391, 393, 395, 397, 366, 368, 370, 360, 362, 364, 314, 316, 234, 236, 208, 210, 180, 182, 183, 168, 170, 155, 157, 156, 154.

(1a) 5-(4-Nitrophenyl)-1-phenyl-3-(4-nitrostyryl)-2-pyrazoline

IR (KBr) cm^{-1}: 1582 (C=N), 3070 (C-H, Ar), 3035 (=C-H), 2946, 2839 (CH_2), 963 (CH=CH trans), 1605, 1510, 1481, 1455 (C=C Ar), 842 (p-disub.), 1530 (NO_2 asymm.), 1335 (NO_2 symm.); NMR ($CDCl_3$) δ: 3.15 (dd, 1H, C_4-H_A), 3.41 (dd, 1H, C_4-H_B), 5.26 (dd, 1H, C_5-H_x), 7.80 (d, 1H, H_α), 7.10 (d, 1H, H_β), 6.74-6.85 (m, 3H, Ar-H), 7.25-7.29 (m, 2H, Ar-H), 7.50-7.58 (m, 2H, Ar-H), 8.01-8.04 (m, 2H, Ar-H), 8.19-8.23 (m, 4H, Ar-H); Mass m/z: 414 (M^+), 338, 337, 174, 148, 90, 78.

(1b) 1-(2, 4-Dinitrophenyl)-5-(4-nitrophenyl)-3-(4-nitrostyryl)-2-pyrazoline

IR (KBr) cm^{-1}: 1589 (C=N), 3019 (C-H, Ar), 3051 (=C-H), 2956, 2853 (CH_2 str.), 962 (CH=CH trans), 1608, 1579, 1500, 1458 (C=C Ar), 818, 893 (1,2, 4- trisub.), 1545 (NO_2 asymm.), 1363 (NO_2 symm.), 1623 (C=C conju.), 829 (p-disub.); NMR ($CDCl_3$) δ: 3.18 (dd, 1H, C_4-H_A), 3.45 (dd, 1H, C_4-H_B), 5.19 (dd, 1H, C_5-H_x), 7.67 (d, 1H, H_α), 6.98 (d, 1H, H_β) 7.79-8.81 (m, 11H, Ar-H); Mass m/z: 504 (M^+), 458, 433, 382, 369, 330, 270, 176.

(1c) 5-(4-Nitrophenyl)-3-(4-nitrostyryl)-2-pyrazoline-1 carboxamide

IR (KBr) cm^{-1}: 1582 (C=N), 3351 (NH-asymm.), 3115 (NH-symm.), 3013 (C-H, Ar), 3050 (=C-H), 2956, 2841 (CH_2 str.), 967 (CH=CH trans), 1600, 1509, 1450, 1581 (C=C Ar), 810 (p- disub.), 1552 (NO_2 asymm.), 1384 (NO_2 symm.); NMR ($CDCl_3$) δ: 3.21 (dd, 1H,

C_4-H_A), 3.44 (dd, 1H, C_4-H_B), 5.32 (dd, 1H, C_5-Hx), 7.69 (d, 1H, H_α), 6.98 (d, 1H, H_β), 7.48-7.79 (m, 8H, Ar-H), 8.96 (s, 2H, NH_2); Mass m/z: 381 (M^+), 379, 365, 339, 336, 174.

(1d) 5-(4-Nitrophenyl)-3-(4-nitrostyryl)-2-pyrazoline-1-carbothioamide

IR (KBr) cm^{-1}: 1571 (C=N), 1468, 1099 (C=S), 3021 (C-H, Ar), 3346 (N-H asymm.), 3128 (N-H symm.), 3065 (=C-H), 2955 2862 (CH_2 str.), 960 (CH=CH trans), 1600, 1508, 1449, 1583 (C=C Ar), 819 (p-disub.), 1565 (NO_2 asymm.), 1390 (NO_2 symm.); NMR ($CDCl_3$) δ: 3.28 (dd, 1H, C_4-H_A), 3.42 (dd, 1H, C_4-H_B), 5.28 (dd, 1H, C_5-Hx), 7.70 (d, 1H, H_α), 7.01 (d, 1H, H_β), 7.38-7.63 (m, 8H, Ar-H), 8.57 (s, 2H, NH_2); Mass m/z: 397 (M^+), 381, 352, 339, 276, 208.

(1e) 5-(4-Nitrophenyl)-3-(4-nitrostyryl)-isoxazoline

IR (KBR) cm^{-1}: 1579 (C=N), 860 (N-O), 3040 (=C-H), 3015 (C-H Ar), 1609, 1581, 1503, 1452 (C=C Ar), 1626 (C=C Conju.), 968 (CH=CH trans), 2948, 2853 (CH_2 str.), 846 (p-disub.), 1575 (NO_2 asymm.), 1375 (NO_2 symm.); NMR ($CDCl_3$) δ : 2.77 (dd, 1H, C_4-H_A), 3.02 (dd, 1H, C_4-H_B), 5.64 (dd, 1H, C_5-H_x), 6.74 (d, 1H, H_α), 6.54 (d, 1H, H_β), 6.80-8.30 (m, 8H, Ar-H); Mass m/z : 339 (M^+), 337, 218, 192, 191, 189, 175, 165, 150, 148.

(2a) 5-(3-Hydroxy-4-methoxyphenyl)-1-phenyl--3-(3-hydroxy-4-methoxystyryl)-2-pyrazoline

IR (KBr) cm^{-1}: 1586 (C=N), 3079 (C-H, Ar), 3029 (=C-H), 3353 (O-H), 1058 (C-O), 2959, 2842 (CH_2 str.), 952 (CH=CH trans), 1608, 1581, 1502, 1451 (C=C Ar), 814, 899 (1, 2, 5-trisub.), 1248 (C-O-C asymm.), 1043(C-O-C symm.); NMR $CDCl_3$) δ: 3.18 (dd, 1H, C_4-H_A), 3.46 (dd, 1H, C_4-H_B), 5.26 (dd, 1H, C_5-H_x), 7.38 (d, 1H, H_α), 6.60 (d, 1H, H_β) 6.71-7.24 (m, 11H, Ar-H), 5.34 (s, 2H, OH), 3.84 (s, 6H, OCH_3); Mass m/z: 416 (M^+), 415, 414, 338, 241, 176.

(2b) 1-(2,4-Dinitrophenyl)-5-(3-hydroxy-4-methoxyphenyl)-3-(3-hydroxy-4-methoxy styryl)-2-pyrazoline

IR (KBr) cm^{-1}: 1589 (C=N), 3024 (C-H, Ar), 3312 (O-H), 3056 (=C-H), 2922, 2860 (CH_2 str.), 951 (CH=CH trans), 1600, 1501, 1449, 1589 (C=C Ar), 868, 815 (1,2, 4-trisub.), 1526 (NO_2 asymm.), 1319 (NO_2 symm.), 1622 (C=C conju.); NMR ($CDCl_3$) δ: 3.19 (dd, 1H, C_4-H_A), 3.44 (dd, 1H, C_4-H_B), 5.24 (dd, 1H, C_5-H_x), 7.67 (d, 1H, H_α), 6.98 (d, 1H, H_β), 7.79-8.98 (m, 9H, Ar-H), 5.39 (S, 2H, OH), 3.82 (s, 6H, OCH_3); Mass m/z: 506 (M^+), 504, 489, 475, 458, 433, 383, 370, 331, 319, 175, 136.

(2c) 5-(3-Hydroxy-4-methoxyphenyl)-3-(3-hydroxy-4-methoxystyryl)-2-pyrazolines-1- carboxamide

IR (KBr) cm^{-1}: 1587 (C=N), 1112 (C-O), 1637 (C=O), 3361 (N-H asymm.), 3112 (N-H symm.), 3017 (C-H Ar), 3072 (=C-H str.), 2951, 2862 (CH_2 str.), 970 (CH=CH trans), 1602, 1504, 1582, 1457 (C=C Ar), 898, 813 (1, 2, 4 trisub.), 3310 (O-H), 1256 (C-O-C asymm.), 1048 (C-O-C symm.); NMR ($CDCl_3$) δ: 3.16 (dd, 1H, C_4-H_A), 3.40 (dd, 1H, C_4-H_B), 5.19 (dd, 1H, C_5-H_x), 7.56 (d, 1H, H_α), 6.87 (d, 1H, H_β), 6.71-7.75 (m, 6H, Ar-H), 8.88 (s, 2H, NH_2), 5.38 (s, 2H, OH), 3.79 (s, 6H, OCH_3); Mass m/z : 383 (M^+), 381, 341, 337, 321.

(2d) 5-(3-Hydroxy-4-methoxyphenyl)-3-(3-hydroxy-4-methoxystyryl)-2-pyrazoline-1-carbothioamide

IR (KBr) cm^{-1}: 1558 (C=N), 1121, 1505 (C=S), 3342 (N-H symm.), 3162 (N-H symm.), 3008 (C-H, Ar), 3038 (=C-H str.), 2951, 2865 (CH_2 str.), 976 (CH=CH trans), 1607, 1509, 1583, 1448 (C=C Ar), 905, 820 (1, 2, 4-trisub.), 3320 (O-H), 1245 (C-O-C asymm.), 1040 (C-O-C symm.); NMR ($CDCl_3$) δ: 3.17 (dd, 1H, C_4-H_A), 3.42 (dd, 1H, C_4-H_B), 5.18 (dd, 1H, C_5-H_x), 7.32 (d, 1H, H_α), 6.67 (d, 1H, H_β), 7.34-7.59 (m, 6H, Ar-H), 8.56 (s, 2H, NH_2), 5.32 (s, 2H, OH), 3.89 (s, 6H, OCH_3); Mass m/z: 398 (M^+), 353, 341, 337, 217.

(2e) 5-(3-Hydroxy-4-methoxyphenyl)-3-(3-hydroxy-4-methoxystyryl) isoxazoline

IR (KBR) cm^{-1}: 1572 (C=N), 3358 (OH), 1057 (C-O), 3013 (C-H, Ar), 3045 (=C-H str.), 964 (CH=CH trans), 861 (N-O), 1598, 1576, 1504, 1454 (C=C Ar), 1625 (C=C conjug.), 2957, 2892 (CH_3 str.), 1244 (C-O-C asymm.), 1041 (C-O-C symm.); NMR ($CDCl_3$) δ: 2.79 (dd, 1H, C_4-H_A), 3.07 (dd, 1H, C_4-H_B), 5.63 (dd, 1H, C_5-H_x), 6.76 (d, 1H, H_α), 6.51 (d, 1H, H_β), 6.80-8.32 (m, 6H, Ar-H), 5.35 (S, 2H, OH), 3.88 (s, 6H, OCH_3); Mass m/z: 341 (M^+), 339, 324, 312, 310, 293, 192, 189, 176, 166, 149.

(3a) 5-(4-Bromophenyl)-1-phenyl-3-(4-bromostyryl)-2-pyrazoline

IR (KBr) cm^{-1}: 1588 (C=N), 3075 (=C-H), 3018 (C-H Ar), 1603, 1583, 1454 (C=C Ar), 968 (CH=CH trans), 2920, 2869 (CH_2 str.), 831 (p-disub.); NMR ($CDCl_3$) δ: 3.20 (dd, 1H, C_4-H_A), 3.44 (dd, 1H, C_4-H_B), 5.31 (dd, 1H,C_5-H_x), 7.19 (d, 1H, H_α), 6.58 (d, 1H, H_β), 6.83-7.57 (m, 13H, Ar-H); Mass m/z: 482 (M^+), 484, 486, 483, 485, 477, 479, 481, 401, 403, 405, 274, 276, 273, 275, 277, 257, 259, 221, 223, 209, 211, 206, 208, 180, 182, 78, 90, 207, 130, 103, 77.

(3b) 1-(2, 4-Dinitrophenyl)-5-(4-bromophenyl)-3-(4-bromostyryl)-2-pyrazoline

IR (KBr) cm^{-1}: 1591 (C=N), 3046 (=C-H), 3002 (C-H Ar), 1602, 1583, 1453 (C=C Ar), 969 (CH=CH trans), 2949, 2857 (CH_2 str.), 829 (p-disub.), 1218 (C-N str.), 805, 883 (1, 2, 4-tri sub.); NMR ($CDCl_3$) δ: 3.17 (dd, 1H, C_4-H_A), 3.40 (dd, 1H, C_4-H_B), 5.17 (dd, 1H, C_5-H_x), 7.24 (d, 1H, H_α), 6.92 (d, 1H, H_β), 7.44-8.85 (m, 11H, Ar-H); Mass m/z: 572 (M^+), 493, 495, 481, 483, 468, 470, 416, 418, 403, 405, 364, 366, 350, 352, 208, 210, 169, 171, 156, 158.

(3c) 5-(4-Bromophenyl)-3-(4-bromostyryl)-2-pyrazoline-1-carboxamide

IR (KBr) cm^{-1}: 1586 (C=N), 1651 (C=O), 3349 (N-H asymm.), 3105 (N-H symm.), 3036 (=C-H), 3013 (-CH Ar), 1608, 1508, 1449 (C=C Ar), 970 (CH=CH trans), 2920, 2858 (CH_2 str.), 818 (p- disub.); NMR ($CDCl_3$) δ: 3.20 (dd, 1H, C_4-H_A), 3.46 (dd, 1H,C_4-H_B), 5.30 (dd, 1H, C_5-H_x), 7.28 (d, 1H, H_α), 6.63 (d, 1H, H_β), 6.90-8.15 (m, 8H, Ar-H), 6.79 (s, 2H, NH_2); Mass m/z: 449 (M^+), 451, 453, 431, 433, 405, 407, 409, 371, 373, 294, 296.

(3d) 5-(4-Bromophenyl)-3-(4-bromostyryl)-2-pyrazoline-1-carbothioamide

IR (KBr) cm^{-1}: 1563 (C=N), 1157 (C=S), 3348(N-H asymm.), 3152 (N-H symm.), 3033 (=C-H), 3019 (C-H Ar), 1583, 1605, 1448 (C=C Ar), 947 (CH=CH trans), 2926, 2863 (CH_2 str.), 829 (p-disub.), 1262 (C-N); NMR ($CDCl_3$) δ: 3.19 (dd, 1H, C_4-H_A), 3.42 (dd, 1H, C_4-H_B), 5.94 (dd, 1H, C_5-H_x), 7.21 (d, 1H, H_α), 6.65 (d, 1H, H_β), 6.91-7.59 (m, 6H, Ar-H), 8.54 (s, 2H, NH_2); Mass m/z: 465 (M^+), 467, 469, 450, 452, 405, 407, 409, 386, 388, 309, 311, 207, 211.

(3e) 5-(4-Bromophenyl)-3-(4-bromostyryl)-isoxazoline

IR (KBr) cm^{-1}: 1579 (C=N), 870 (N-O), 3090 (=C-H), 3015 (C-H Ar), 1504, 1608, 1586, 1457 (C=C Ar), 1629 (C=C conjug.), 972 (CH=CH trans), 2918, 2863 (CH_2 str.), 824 (p-disub.); NMR ($CDCl_3$) δ: 2.78 (dd, 1H, C_4-H_A), 3.02 (dd, 1H, C_4-H_B), 5.61 (dd, 1H, C_5-H_x), 7.64 (d, 1H, H_α), 6.49 (d, 1H, H_β), 6.82-8.35 (m, 8H, Ar-H); Mass m/z: 407 (M^+), 409, 411, 413, 252, 254, 182, 184, 225, 227, 209, 211, 410, 412, 414, 383, 385, 387, 331, 333, 184, 186, 223, 225, 156, 158, 255, 257, 199, 201.

Biological activity

The antimicrobial activity was determined using disc diffusion method[28] by measuring the inhibition zone in mm. All the newly synthesized compounds, i.e. **(1**, **2** and **3)** and **(1a-e, 2a-e** and **3a-e)** were screened *in vitro* for their antibacterial activity against one Gram-positive strain (*Staphylococcus aureus*) and two Gram-negative strains (*Escherichia*

coli and *Pseudomonas aeruginosa*) at a potency of 200 µg. Antifungal activity was also tested against *Candida albicans* and *Aspergillus fumigatus* at 200 µg potency. Ciprofloxacin and Amoxyclav were used as standard drug for antibacterial screening and Amphotericin B and Voriconazole were used as standard for antifungal screening. All the synthesized compounds exhibited moderate to excellent antibacterial activities and significant antifungal activities. Each experiment was done in triplicate and the average reading was taken. The *in vitro* microbial activity of the synthesized compounds is represented in Table 2 and Table 3.

Table 2: Antibacterial activity of synthesized compounds

Compound	Antibacterial activity					
	E. coli	***S. aureaus***	***P. aeruginosa***	***E. coli***	***S. aureaus***	***P. aeruginosa***
1	19 (0.86)	20 (0.86)	13 (0.50)	19 (0.95)	20 (0.68)	13 (0.65)
2	23 (1.04)	24 (1.04)	21 (0.80)	23 (1.15)	24 (0.82)	21 (1.05)
3	20 (0.90)	18 (0.78)	17 (0.65)	20 (1.00)	18 (0.62)	17 (0.85)
1a	18 (0.81)	22 (0.95)	18 (0.69)	18 (0.90)	22 (0.75)	18 (0.90)
1b	14 (0.63)	18 (0.78)	10 (0.38)	14 (0.70)	18 (0.62)	10 (0.50)
1c	19 (0.86)	22 (0.95)	21 (0.80)	19 (0.95)	22 (0.75)	21 (1.05)
1d	19 (0.86)	23 (1.00)	19 (0.73)	19 (0.95)	23 (0.79)	19 (0.95)
1e	25 (1.13)	23 (1.00)	24 (0.92)	25 (1.25)	23 (0.79)	24 (1.20)
2a	17 (0.77)	19 (0.82)	21 (0.80)	17 (0.85)	19 (0.65)	21 (1.05)
2b	15 (0.68)	16 (0.69)	17 (0.65)	15 (0.75)	16 (0.55)	17 (0.85)
2c	18 (0.81)	23 (1.00)	13 (0.50)	18 (0.90)	23 (0.79)	13 (0.65)
2d	18 (0.81)	24 (1.04)	15 (0.57)	18 (0.90)	24 (0.82)	15 (0.75)
2e	25 (1.13)	21 (0.91)	19 (0.73)	25 (1.25)	21 (0.72)	19 (0.90)
3a	16 (0.72)	18 (0.78)	17 (0.65)	16 (0.80)	18 (0.62)	17 (0.85)
3b	11 (0.50)	16 (0.69)	10 (0.38)	11 (0.55)	16 (0.55)	10 (0.50)
3c	23 (1.04)	25 (1.08)	19 (0.73)	23 (1.15)	25 (0.86)	19 (0.95)
3d	21 (0.95)	23 (1.00)	17 (0.65)	21 (1.05)	23 (0.79)	17 (0.85)
3e	18 (0.81)	15 (0.65)	09 (0.34)	18 (0.90)	15 (0.51)	09 (0.45)
Ciprofloxacin	**22**	**23**	**26**	-	-	-
Amoxyclav	-	-	-	**20**	**29**	**20**

Table 3: Antifungal activity of synthesized compounds

Compound	Antifungal activity			
	C. albicans	***A. fumigatus***	***C. albicans***	***A. fumigatus***
1	26 (1.85)	24 (0.96)	26 (0.81)	24 (0.92)
2	21 (1.50)	20 (0.80)	21 (0.65)	20 (0.76)
3	18 (1.28)	19 (0.76)	18 (0.56)	19 (0.73)
1a	22 (1.57)	20 (0.80)	22 (0.68)	20 (0.76)
1b	20 (1.42)	18 (0.72)	20 (0.62)	18 (0.69)
1c	23 (1.64)	26 (1.04)	23 (0.71)	26 (1.00)
1d	27 (1.92)	24 (0.96)	27 (0.84)	24 (0.92)
1e	18 (1.28)	30 (1.20)	18 (0.56)	30 (1.15)
2a	30 (2.14)	32 (1.28)	30 (0.93)	32 (1.23)
2b	28 (2.00)	29 (1.16)	28 (0.85)	29 (1.11)
2c	30 (2.14)	29 (1.16)	30 (0.93)	29 (1.11)
2d	31 (2.21)	33 (1.32)	31 (0.96)	33 (1.26)
2e	22 (1.57)	27 (1.08)	22 (0.68)	27 (1.03)
3a	27 (1.92)	19 (0.76)	27 (0.84)	19 (0.73)
3b	19 (1.35)	20 (0.80)	19 (0.59)	20 (0.76)
3c	28 (2.00)	25 (1.00)	28 (0.87)	25 (0.96)
3d	15 (1.07)	33 (1.32)	15 (0.46)	33 (1.26)
3e	19 (1.35)	22 (0.88)	19 (0.59)	22 (0.84)
Amphotericin B	**14**	**25**	-	-
Voriconazole	-	-	**32**	**26**

RESULTS AND DISCUSSION

In this paper, microwave assisted synthesis of chalcones **(1**, **2** and **3)** has been reported by the reaction of acetone and substituted benzaldehydes in the presence of basic alumina. These chalcones were treated with hydrazines **(a-d)** and hydroxylamine hydrochloride (**e)** under microwave irradiation to yield 2-pyrazolines **(1a-d**, **2a-d** and **3a-d),** and isoxazolines (**1e**, **2e** and **3e)**, respectively in 3-7 minutes. The synthetic procedure for preparation of title compounds is given in reaction scheme. The assigned structure and

molecular formula of the newly synthesized compounds **(1**, **2**, **3**, **1a-e**, **2a-e** and **3a-e)** were confirmed and supported by ^{1}H NMR, Mass and IR data as well as elemental analysis, which was in full agreement with proposed structures. All the compounds were screened *in vitro* for their antibacterial and antifungal potential by disc diffusion assay against selected pathogenic bacteria and human pathogenic fungi. The results of antibacterial and antifungal activities expressed in terms of zone of inhibition are reported in Table 2 and Table 3. The results of antimicrobial studies of synthesized compounds revealed that they possess antibacterial activities to certain extent, but significant antifungal activities. Compound **(2**, **3**, **1e**, **2e** and **3c)**, **(2**, **3**, **1d**, **1e**, **2c**, **2d**, **3c**, and **3d)** and **(2**, **1c**, **1e** and **2a)** have shown excellent activity against *E. coli, S. aureaus* and *P. aeruginosa*, respectively. All the synthesized compounds have shown significant to excellent activity against both, *C. albicans* and *A. fumigatus.*

CONCLUSION

In summary, this work demonstrates a rapid, efficient and environment friendly method for the synthesis of these compounds (chalcones, 2-pyrazolines and isoxazoline derivatives) under microwave irradiation. The results obtained confirm that the microwave assisted synthesis is a dry media reaction condition that leads to considerable saving in reaction time and energetically profitable over the conventional method. The results of antimicrobial studies of synthesized compounds revealed that they possess moderate to potent antibacterial activities and significant antifungal activities against the tested gram positive and gram negative microorganisms. The data reported in this paper may be helpful as a guide for the medicinal chemists, who are working in this area.

ACKNOWLEDGEMENT

The authors are thankful to Principal and Head, Department of Chemistry, S. G. G. Government College, Banswara (Raj.) for providing laboratory facilities. The authors are grateful to Director, CDRI, Lucknow for elemental and spectral analysis. Thanks are also due to Dr. Renu Bansal, Microbiologist, Haryana for providing screening facilities (including pathogens, media and instruments) for biological analysis of the compounds.

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Accepted : 29.09.2014