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Microwave Assisted One Pot Synthesis and Antimicrobial Activity of 2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1,4,5-triphenyl-1*h*-imidazole Derivatives

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ABSTRACT

Several new promising bioactive derivatives of 1-(2,5-dihydro-2-methyl-5-phenyl-1-(1,4,5-triphenyl-1H-imidazol-2-yl)-1H pyrrol-3-yl) ethanone were synthesized under microwave irradiations. The compounds were obtained in excellent yields via one pot synthesis method. All the titled compounds were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis. Synthesized compounds were evaluated for their preliminary antibacterial and antifungal activity. Antibacterial activity against bacterial strains Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa using ciprofloxacin as standard drug indicated that compounds 4c, 4h, 4k, 4l exhibited moderate to high potency against the parent compound while more potent than the standard drug. Antifungal studies were carried out against fungal strains like Candida albicans and Aspergillus niger using fluconazole as standard drug indicated that all compounds exhibited high potency against the standard compound except 4a, 4b, 4d, 4g, 4j.

Keywords: Microwave synthesis, Imidazole, Pyrrole, Antimicrobial, Antibacterial, Antifungal

INTRODUCTION

Over the past three decades, microwave assisted organic synthesis results in spectacular acceleration of many chemical reactions as a consequence of 3D heating of the reaction mixture and which cannot be reproduced by conventional methods of synthesis [1-3]. These are Multicomponent Reactions (MCRs) which have opened new dimension in synthetic organic chemistry [4-7]. In 1990, Paul Anastas and John Werner defined green chemistry according to them, "Design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances". They also first published their twelve principles of Green Chemistry [8-12]. The fundamentals and significant outcomes of microwave-assisted organic/pharmaceutical synthesis in aqueous medium were reported which have resulted in the development of relatively sustainable and environmentally benign protocols for the synthesis of drugs and fine chemicals [13-15].

One of the important strategies for synthesizing the effective antimicrobial agents in the present research work is to generate effective leads which by further structural modifications, can give potent antimicrobial compounds. The imidazole nucleus is an important structural motif for many natural and synthetic products. Pyrrole nucleus was also observed as one of the important heterocyclic nucleus. Earlier several reports have indicated that, individually both of them possess potent antimicrobial properties.

Motivated by the aforesaid findings, we have prepared imidazole substituted pyrrole derivatives using microwaves emphasizes a strategy that combines two compatible moieties in one molecule followed by *in-vitro* antimicrobial studies of the synthesized compounds. In continuation to our previous work for the synthesis of 2-amino-3,4,5-trisubstituted imidazolines using Radiszewski method using microwaves [16]. All the synthesized compounds have shown excellent to moderate yields. As a result of remarkable proficiency of microwaves, the present research work has been focused towards the microwave assisted synthesis of 1-(2,5-dihydro-2-methyl-5-phenyl-1-(1,4,5-triphenyl-1*H*-imidazol-2-*yl*)-1*H*-pyrrol-3-*yl*) ethanone derivatives (4a-4l) by the method of Hantzsch pyrrole synthesis using 1,3-dicarbonyl compound, α-halo ketones and amines using bismuth nitrate ($Bi(NO_3)_3.5H_2O$), a catalyst acts as eco-friendly for a variety of organic synthesis and is non-volatile, recyclable, non-explosive, easy to handle, and thermally stable and pharmacological evaluation for the search of novel antimicrobials (antibacterial and antifungal) [17,18]. The synthetic route and the sequence of reactions are depicted in Figure 1 and their physical properties are depicted in Table 1. All the synthesized compounds were evaluated for antimicrobial, analgesic and anti-inflammatory activities [19-21].

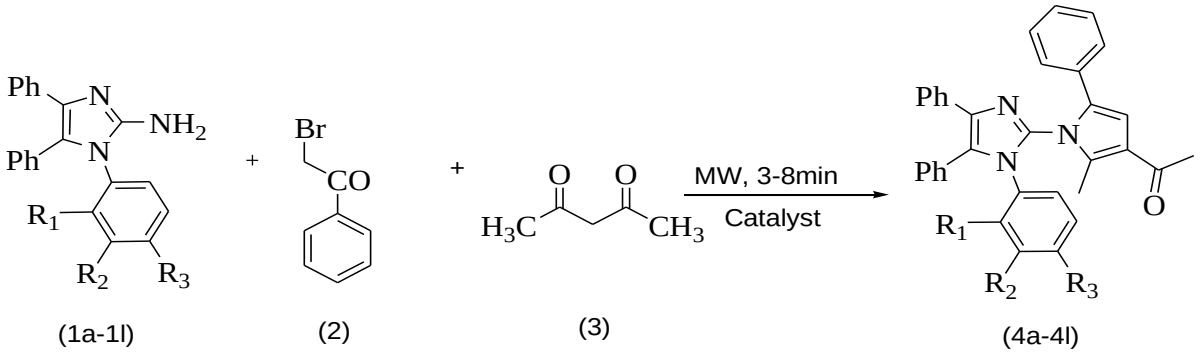
EXPERIMENTAL SECTION

Material and reagents

Chemical reagents for the synthesis of titled compounds were purchased from the Hi-Media, Mumbai, Thomas Baker Chemicals Pvt. Ltd., New Delhi, SD Fine Chemicals Pvt. Ltd., Mumbai, India. All reagents were of commercial grade. All the targeted compounds were synthesized in microwave monomode reactor, IFB. Melting points were determined by an open capillary method which is uncorrected. Infrared spectra's (IR, cm^{-1}) were recorded on Bruker FTIR 550 spectrometer lab India Pvt. Ltd. Hyderabad at CT Institute of Pharmaceutical Sciences, Jalandhar. ^{1}H-NMR, ^{13}C-NMR and mass spectra's were taken as Bruker at Panjab University Chandigarh, using Tetramethylsilane (TMS) as an internal standard and Dimethyl Sulfoxide (DMSO-d_6) as a solvent at radio frequency 400 MHz. Chemical shifts were expressed in δ (ppm) values. All the synthesized compounds exhibited spectral data in consistence with the proposed theoretical structures. Also, Thin Layer Chromatography (TLC) was performed on precoated TLC sheets of silica gel-60 F_{254} visualizing by short and long wavelength UV lamps as well in some cases with the help of oxidizing iodine.

Chemistry

The key intermediate 2-amino-1,4,5-triaryl-1*H*-imidazole (1a-1l) were prepared as per the literature [16]. A mixture of 2-amino-1,4,5-triaryl-1*H*-imidazole (1a-1l), phenacyl bromide (2), 2,4-pentadione (3) and bismuth nitrate ($Bi(NO_3)_3.5H_2O$) 5 mol%, as catalyst was stirred and heated at 300W in microwaves for an optimum time (3-8 min). After completion of the reaction as indicated by TLC, the reaction mixture was dissolved in hot EtOH and catalyst was separated by filtration to obtain the final compounds (4a-4l). The solvent was removed and the product was purified by recrystallization with ethanol. The synthetic reaction for the preparation of triaryl imidazole substituted pyrrolyl derivatives (4a-4l) is given below.



a= R_1=H, R_2= H, R_3=H
b= R_1=H, R_2= H, R_3=OCH_3
c= R_1=H, R_2= H, R_3=NO_2
d= R_1=H, R_2= H, R_3=C_2H_5
e= R_1=Cl, R_2= H, R_3=NO_2
f= R_1=H, R_2= H, R_3=Cl
g= R_1=OCH_3, R_2= H, R_3=H
h= R_1=H, R_2= H, R_3=F
i= R_1=H, R_2= H, R_3=Br
j= R_1=C_2H_5, R_2= H, R_3=H
k= R_1=H, R_2= NO_2, R_3=H
l= R_1=H, R_2= Cl, R_3=H

Figure 1: Synthesis of 2-amino-1,4,5-triaryl-1*H*-imidazole substituted pyrrole derivatives

The present method of synthesis not only affords the products in excellent yields but also avoids the problems associated with catalyst cost, handling, safety and pollution.

Table 1: Physicochemical properties of the synthesized compounds (4a-4l)

S. No.	Entry	R_1	R_2	R_3	TLC		Time (min)/Yield (%)	Melting point (°C)
					Eluent	R_f		
1	4a	H	H	H	Ethyl acetate: Methanol (8:2)	8.0	2.2 (97)	123-25
2	4b	H	H	OCH_3	Ethyl acetate: Methanol (8:2)	7.5	0.8 (90)	147-49
3	4c	H	H	NO_2	Ethyl acetate: Methanol (8:2)	7.3	1.5 (34)	112-14
4	4d	H	H	C_2H_5	Ethyl acetate: Methanol (8:2)	6.6	1.2 (85)	125-27
5	4e	Cl	H	NO_2	Ethyl acetate: Methanol (8:2)	7.9	2 (42)	176-78
6	4f	H	H	Cl	Ethyl acetate: Methanol (8:2)	5.9	4.1 (95)	202-04
7	4g	OCH_3	H	H	Ethyl acetate: Methanol (8:2)	8.3	3.5 (82)	84-86
8	4h	H	H	F	Ethyl acetate: Methanol (8:2)	6.7	4 (48)	196-98
9	4i	H	H	Br	Ethyl acetate: Methanol (8:2)	7.8	6 (96)	190-92
10	4j	C_2H_5	H	H	Ethyl acetate: Methanol (8:2)	7.5	3 (94)	188-90
11	4k	H	NO_2	H	Ethyl acetate: Methanol (8:2)	7.7	5 (96)	300 (decomp.)
12	4l	H	Cl	H	Ethyl acetate: Methanol (8:2)	6.5	4 (53)	183-85

Pharmacological activity

Pharmacological Activity of the synthesized compounds was based on standard procedures for antibacterial studies were carried out by micro bath dilution assay method against bacterial strains like *Staphylococcus aureus* (MTCC 96), *Bacillus subtilis* (MTCC 121) (Gram-positive) and *Escherichia coli* (MTCC 614), *Pseudomonas aeruginosa* (MTCC 2453) (Gram-negative) using ciprofloxacin as standard drug. Stock solution (250 µg/ml) of standard and test samples were prepared in 2% DMSO. The Minimum Inhibitory Concentration (MIC) was determined by tube

dilution method. Series of dilutions of tests and standard compounds were prepared in double strength nutrient broth IP and Sabouraud dextrose broth IP. The samples were incubated at 37°C for 48 h. The compounds diffused into the medium produced a concentration gradient. MIC (µg/ml) of the compounds against the test organisms was determined. The lowest concentration, MIC, which inhibited the growth of microorganisms was found to be 100 µg/ml for standard and test samples and was further taken for the measurement of zone of inhibition (in mm) for the studies of antimicrobial activity. It has observed that the majority of the compounds possessed significant antibacterial activity. Antifungal studies were carried out against fungal strains like *Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 282) using fluconazole as standard drug. All the compounds were dissolved in dimethyl formamide (DMF)/DMSO. Proper drug controls were used.

RESULTS AND DISCUSSION

Several methods have been used for the synthesis of tetra-substituted imidazoles and their derivatives. There is no doubt that some of the methods were good in terms of reactivity, however they suffer from longer reaction time and low percent yield. Due to the above reaction problems development of an efficient and versatile method for the synthesis of target compounds with the help of microwaves as well an acidic catalyst, bismuth nitrate ($Bi(NO_3)_3.5H_2O$). Therefore, in technical terms the present synthesis method can be termed as total green synthesis, which is already an area of active research and it offers an attractive feature such as reduced reaction times, higher percentage yields and ecofriendly reaction, which is proved to have wide scope in organic synthesis when compared with conventional method of synthesis. We further claim that there is a room for further improvement of reaction conditions which could be an area of future research in this direction. Also synthesized compounds were better synthetic moieties of medicinal interest.

Spectral data

Spectral data of the synthesized final compounds is described as follows

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1,4,5-triphenyl-1*H*-imidazole (4a): IR (KBr, cm^{-1}): 2920.40 (sp^3 C-H, CH_3), 3020.23 (sp^2, Ar-C-H), 1688.83 (C=N, imidazole), 1568.52 (Ar-C=C), 1195.25 (C-N, imidazole), 1683.83 (C=O, $COCH_3$); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 7.11-7.93 (m, Ar-5H, phenyl), 6.91-7.08 (m, Ar-15H, phenyl), 6.2 (s, 1H, imidazole), 2.3 (s, 3H, C-CH_3), 1.2 (s, 3H, $COCH_3$); ^{13}CNMR (δ, ppm, 400 MHz, DMSO-d_6): 151.30, 144.20, (phenyl carbon), 20.10 (C-CH_3), 48.20 ($COCH_3$), 160.22, 156.40 (C-imidazole), 131.33, 129.12, 126.12, 124.78 (C-pyrrole); MS (*m/z*, M^+): 493.6, $C_{34}H_{27}N_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(4-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole (4b): IR (KBr, cm^{-1}): 2918.26 (sp^2, Ar-C-H), 2850.61 (sp^3CH, CH_3), 1620.63 (C=N, imidazole), 1379.81 (Ar-C=C), 1180.14 (C-N, imidazole), 1092.90 (C-O, OCH_3), 1468.04 (C=O, $COCH_3$); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 8.70 (dd, 4H, *p*-substituted phenyl), 8.91 (m, Ar-15H, phenyl), 5.90 (s, 1H, imidazole), 2.20 (s, 3H, C-CH_3), 1.20-1.40 (s, 3H, $COCH_3$); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 144.20 (C-phenyl), 20.10 (C-CH_3), 115.45 (OCH_3), 39.20 ($COCH_3$), 138.40 (C-imidazole), 122.78 (C-pyrrole); MS (*m/z*, M^+): 541.2, $C_{35}H_{30}N_3O_2$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*l*-1-(1-(4-nitrophenyl)-4,5-diphenyl-1*H*-imidazole (4c): IR (KBr, cm^{-1}): 2870 (sp^3 C-H, CH_3), 2960 (sp^2, Ar-C-H), 1669.59 (C=N, imidazole), 1467.79 (Ar-C=C), 1166.22 (C-N, imidazole), 1030.69 (C-O, OCH_3); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 7.70-7.75 (dd, 4H, *p*-substituted phenyl), 6.91-7.08 (m, Ar-15H, phenyl), 6.20- 6.40 (s, 1H, imidazole), 2.30-2.50 (s, 3H, C-CH_3), 1.30-1.50 (s, 3H, $COCH_3$); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 154.30, 127.10 (C-phenyl), 31.30, 28.10 (CH_2CH_3), 42.20 ($COCH_3$), 163.22, 158.40 (C-imidazole), 133.33, (C-pyrrole); MS (*m/z*, M^+): 538.6, $C_{36}H_{31}N_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(4-ethylphenyl)-4,5-diphenyl-1*H*-imidazole (4d): IR (KBr, cm^{-1}): 2677.75 (sp^3 C-H, CH_3), 2928.92 (sp^2, Ar-C-H), 1627.50 (C=N, imidazole), 1472.52 (Ar-C=C), 1298.28 (C-N, imidazole), 1173.52 (C-O, OCH_3); ^{1}H-NMR (δ, ppm, 400MHz, DMSO-d_6): 7.75 (dd, 4H, *p*-substituted phenyl), 7.28 (m, Ar-15H, phenyl), 7.00 (s, 1H, imidazole), 2.20 (s, 3H, C-CH_3), 3.20 (s, 3H, $COCH_3$), 1.15 (q, 2H, CH_2CH_3), 1.2(t, 3H, CH_2CH_3); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 113.10 (C-phenyl), 40.30 (CH_2CH_3), 39.20 ($COCH_3$), 142.40 (C-imidazole), 133.33 (C-pyrrole); MS (*m/z*, M^+): 521.1, $C_{36}H_{31}N_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(2-chloro-4-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole (4e): IR (KBr, cm^{-1}): 2950 (sp^3 C-H, CH_3), 3140 (sp^2, Ar-C-H), 1620 (C=N, imidazole), 1517 (Ar-C=C), 1205 (C-N, imidazole), 1725 (C=O), 750 (C-Cl), 820 (*p* disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 7.70-7.75 (dd, 4H, *p*-substituted phenyl), 6.50-7.80 (m, Ar-15H), 8.61 & 8.82 (d, Ar-4H), 1.9 (s, 1H), 2.10 (s, 3H, $COCH_3$), 1.33 (d, 3H, C-CH_3); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 135.50 (C-phenyl), 39.30 (CH_2CH_3), 40.20 ($COCH_3$), 175.22, 140.40 (C-imidazole), 118.12, 127.78 (C pyrrole); MS (*m/z*, M^+): 573.0, $C_{34}H_{25}ClN_4O_3$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole (4f): IR (KBr, cm^{-1}): 2900.54 (sp^3 C-H, CH_3), 3040.36 (sp^2, Ar-C-H), 1648.32 (C=N, imidazole), 1517.76 (Ar-C=C), 1205.26 (C-N, imidazole), 1725.57 (C=O), 750.24 (C-Cl), 820.65 (*p*-disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 7.70-7.75 (dd, 4H *p*-substituted phenyl), 6.50-7.80 (m, Ar-15H), 8.61 & 8.82 (d, Ar-4H), 1.9 (s, 1H), 2.10 (s, 3H, $COCH_3$), 1.3 (d, 3H, C-CH_3); ^{13}CNMR (δ, ppm, 400 MHz, DMSO-d_6): 155.30 (C-phenyl), 39.30 (CH_2CH_3), 40.20 ($COCH_3$), 163.22, 158.40 (C-imidazole), 128.12, 127.78 (C pyrrole); MS (*m/z*, M^+): 527.2, $C_{34}H_{26}ClN_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(2-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole (4g):
IR (KBr, cm^{-1}): 3060.34 (sp^2, Ar-C-H), 2961.31 (sp^3 C-H, CH_3), 1629.22 (C=N, imidazole), 1572.34 (phenyl, Ar-C=C), 1234.56 (C-N, imidazole), 1727.54 (C=O), 1034.36 (C-O), 760.58 (*o*-disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 6.50-7.80 (m, Ar-10H), 8.62 (d, Ar-2H), 7.80 (dd, Ar-2H), 7.5 (m, Ar-5H), 3.90 (s, 3H, $COCH_3$), 1.75 (d, 3H, C-CH), 1.80 (q, 1H, CH_3-C), 3.90 (s, 3H, C-OCH_3); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 135.30, 110.10 (C-phenyl), 39.30 (CH_2CH_3), 40.20 ($COCH_3$), 175.22, 140.40 (C-imidazole), 118.12, 127.78 (C pyrrole); MS (*m/z*, M^+): 523.6, $C_{35}H_{29}N_3O_2$.

2-(3'-Acetyl-2'-Methyl-5'-Phenyl)-Pyrrol-1-*yl*-1-(1-(4-Fluorophenyl)-4,5-Diphenyl-1*H*-Imidazole (4h): IR (KBr, cm^{-1}): 3232.26 (sp^2 Ar-C-H), 1688.20 (C=N), 1630.10 (Ar-C=C), 1213.17 (C-N), 1702.25 (C=O), 1460.50 (N=O), 1286.01 (N-O), 820 (*p*-disubstituted), 773.74 (C-Cl) 832.29 (*p*- disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 6.50 (m, Ar-15H), 7.80 (d, Ar-2H), 7.50 (d, Ar-2H), 1.9 (s, 1H), 2.10 (s, 3H, $COCH_3$), 1.50 (d, 3H, C-CH), 1.8 (q, 1H, CH_3-C), 1.7 (t, 0H, CO-C-(CH), 1.2 (d, 0H, C-CH); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 135.30, (C-phenyl), 39.30 (CH_2CH_3), 40.20 ($COCH_3$), 175.22, 140.40 (C-imidazole), 118.12, 127.78 (C pyrrole); MS (*m/z*, M^+): 511.1, $C_{34}H_{26}FN_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(4-bromophenyl)-4,5-diphenyl-1*H*-imidazole (4i): IR (KBr, cm^{-1}): 3095.34 (sp^2, Ar-C-H), 2850.54 (sp^3 C-H, CH_3), 1648.77 (C=N, imidazole), 1525.33 (phenyl, Ar-C=C), 1205.32 (C-N, imidazole), 1725.40 (C=O), 800.32 (C-Br), 820.12 (*p*-disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 6.50-7.80 (m, Ar-10H), 8.65 & 8.80 (d, Ar-4H), 7.5 (m, Ar-5H), 1.9 (s, 1H),

2.10 (s, 3H, $COCH_3$), 1.3 (d, 3H, C-CH), 1.8 (q, 1H, CH_3-C); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 135.30 (C-phenyl), 39.30 (CH_2CH_3), 40.20 ($COCH_3$), 175.22, 140.40 (C-imidazole), 118.12, 127.78 (C pyrrole); MS (*m/z*, M^+): 572.5, $C_{34}H_{26}BrN_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(2-ethylphenyl)-4,5-diphenyl-1*H*-imidazole (4j): IR (KBr, cm^{-1}): 3100.34 (sp^2, Ar-C-H), 2900.54 (sp^3 C-H, CH_3) 1650.30 (C=N, imidazole), 1525.36 (Ar-C=C), 1205.49 (C-N, imidazole), 1725.39 (C=O), 760.40 (*o*-disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 6.50-7.80 (m, Ar-10H), 8.62 (d, Ar-2H), 7.80 (dd, Ar-2H), 7.5 (m, Ar-5H), 1.9 (s, 1H), 2.10 (s, 3H, $COCH_3$), 1.3 (d, 3H, C-CH), 1.8 (q, 1H, CH_3-C), 1.6 (q, 2H, C-CH_3), 1.2(t, 3H, C-CH_2); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 161.30, 156.20, 128.10 (C-phenyl), 20.10 (C-CH_3), 30.30, 28.10 (CH_2CH_3), 70.50 (OCH_3), 35.20 ($COCH_3$), 160.22, 156.40 (C-imidazole), 132.33, 129.12, 124.78 (C-pyrrole); MS (*m/z*, M^+): 521.1, $C_{36}H_{31}N_3O$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(3-nitrophenyl)-4,5-diphenyl-1*H*-imidazole (4k): IR (KBr, cm^{-1}): 3050.30 (sp^2, Ar-C-H), 2870.20 (sp^3 C-H, CH_3) 1650.30 (C=N, imidazole), 1505.29 (Ar-C=C), 1210.10 (C-N, imidazole), 1725.30 (C=O), 900.30, 850.20 & 760.37 (*m*-disubstituted); ^{1}H-NMR (δ, ppm, 400MHz, DMSO-d_6): 6.50-7.80 (m, Ar-10H), 8.62 (d, Ar-2H), 7.80 (dd, Ar-2H), 7.5 (m, Ar-5H), 1.9 (s, 1H), 2.10 (s, 3H, $COCH_3$), 1.8 (q, 1H, CH_3-C), 1.6 (q, 2H, C-CH_3), 1.2(t, 3H, C-CH_2); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 161.30, 132.50, 128.10 (C-phenyl), 20.10 (C-CH_3), 30.30, 28.10 (CH_2CH_3), 70.50 (OCH_3), 35.20 ($COCH_3$), 160.22, 156.40 (C-imidazole), 132.33, 129.12, 124.78 (C-pyrrole); MS (*m/z*, M^+): 539.6, $C_{34}H_{27}N_4O_3$.

2-(3'-acetyl-2'-methyl-5'-phenyl)-pyrrol-1-*yl*-1-(1-(3-chlorophenyl)-4,5-diphenyl-1*H*-imidazole (4l): IR (KBr, cm^{-1}): 2950.30 (sp^2, Ar-C-H), 2760.20 (sp^3 C-H, CH_3) 1630.30 (C=N, imidazole), 1542.29 (Ar-C=C), 1214.10 (C-N, imidazole), 1745.30 (C=O), 850.20 & 760.37 (*m*-disubstituted); ^{1}H-NMR (δ, ppm, 400 MHz, DMSO-d_6): 6.50-7.80 (m, Ar-10H), 8.42 (d, Ar-2H), 7.80 (dd, Ar-2H), 7.5 (m, Ar-5H), 1.9 (s, 1H), 2.10 (s, 3H, $COCH_3$), 1.8 (q, 1H, CH_3-C), 1.6 (q, 2H, C-CH_3), 1.2(t, 3H, C-CH_2); ^{13}C-NMR (δ, ppm, 400 MHz, DMSO-d_6): 161.30, 156.20, 132.50, 128.10 (C-phenyl), 20.10 (C-CH_3), 30.30, 28.10 (CH_2CH_3), 70.50 (OCH_3), 35.20 ($COCH_3$), 160.22, 156.40 (C-imidazole), 132.33, 124.78 (C-pyrrole); MS (*m/z*, M^+): 528.0, $C_{34}H_{26}ClN_3O$.

Pharmacological activity

SAR studies revealed that compound having electron withdrawing groups like NO_2, Cl are responsible for increase in the antimicrobial activity (antibacterial and antifungal both) when compared with standard reference drugs that was found to be most significant for the compounds 4c, 4h, 4k, 4l which possess nitro group which draw electron density away from the π-system while other compounds like 4d, 4i, 4j showed moderate antimicrobial activity due to unsubstituted phenyl groups or electron donating groups which exhibited lipophilicity seemed to provide moderate activity. The observations are given hereunder in Table 2.

Table 2: Antibacterial and antifungal activities of the compounds synthesized

Entry	Zone of inhibition (mm) at 100 µg/ml				Fungi	Fungi
	Gram-positive organisms		Gram-negative organisms			
	Staphylococcus aureus **(MTCC 96)**	***Bacillus subtilis*** **(MTCC 121)**	***Escherichia coli*** **(MTCC 614)**	***Pseudomonas aureginosa*** **(MTCC 2453)**	***Candida albicans*** **(MTCC 227)**	***Aspergillus niger*** **(MTCC 282)**
4a	4	3	2	4	ND	2
4b	6	3	3	3	12	5
4c	24	19	12	17	12	24
4d	ND	3	12	5	3	ND
4e	23	18	12	19	12	21
4f	3	21	4	12	6	12
4g	6	3	2	3	6	3
4h	25	18	ND	19	12	20
4i	6	12	6	12	11	12
4j	ND	7	6	12	4	3
4k	22	12	20	12	ND	20
4l	24	18	12	20	12	22
Control	-	-	-	-	-	-
Ciprofloxacin	25	20	21	20	-	-
Fluconazole	-	-	-	-	23	21

*=Average zone of inhibition in mm; ND= Not defined

All other remaining compounds revealed low biological activity when compared with standard drug. In general, most of the tested compounds revealed better activity against the Gram-positive bacteria rather than the Gram-negative bacteria. N-1 Substituted imidazole derivatives exhibited high antimicrobial activity. In general it was observed that most of the compounds with substituted phenyl rings showed better antimicrobial activity *p*-substituted phenyl causes an increase in activity.

CONCLUSION

This work demonstrates the microwave assisted synthesis of a library of novel imidazoles substituted pyrrole derivatives and *in vitro* evaluation of antimicrobial (Antibacterial and antifungal) activity. Further, results indicated that by microwave technique there was a reduction from hours to few minutes. Structure activity relationship also proved that electron withdrawing groups were responsible for increasing biological potency of the synthesized compounds when compared with standard drug. Therefore, these molecular hybrids make them certain promising molecules for further lead optimization in the development of novel antimicrobial drugs for further studies and development of biologically active molecules. These chemical entities may serve as lead for further modification to render them clinically useful drug agents having least side effects as compared to drugs presently available in the market.

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