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Synthesis and Antimicrobial Studies of New Series of Pyrazoline Bearing *Bis*-Heterocycles *via* 1,3-Dipolar Cycloaddition Reactions

B. JAYASHANKARA and K.M. LOKANATHA RAI*

Department of Studies in Chemistry, University of Mysore,
Manasagangothri, Mysore-570006, India.
jai_shan321@yahoo.co.in

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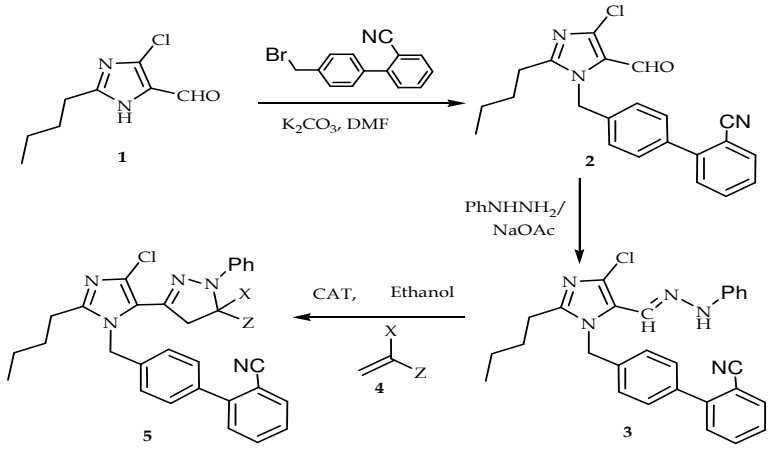
Abstract: Biologically interesting *bis*-heterocycles bearing pyrazoline and imidazole moieties have been synthesized. ^{1}H NMR, ^{13}C NMR, IR and elemental analyses characterized the newly synthesized compounds. All the synthesized compounds were evaluated for their antimicrobial activity and were compared with the standard drugs. All the compounds demonstrated potent to weak antimicrobial activity.

Keywords: Synthesis; *Bis*-Heterocycle; Antimicrobial activity; Chloramine-T

Introduction

The development of simple, facile and efficient synthetic methods for the synthesis of five membered heterocycles from readily available reagents is one of the major challenges in organic synthesis. Among five membered heterocycles**,** pyrazoline and imidazole are represents a class of compounds of great importance in biological chemistry. For instance, pyrazoline derivatives posses the biological activities like, antidepressant[1], anticonvulsant[2] antimicrobial[3], analgesic[4] and antitumour[5] activity and also serves as human acyl-CoA: cholesterol acyltransferase inhibitors.[6] In fact, celecoxib a pyrazole derivative is now widely used in the market as anti-inflammatory drug.[7] Imidazole derivatives are gaining synthetic interest in recent years due to their broad spectrum of biological activities like anti-inflammatory[8], analgesic[9], antibacterial[10], antifungal[11], antituberculosis[12], anticonvolusant[13] and potential anticytokine agents[14]. 2-*n*-Butyl-4-chloro-5-farmyl-imidazole is a key intermediate for the synthesis of Losartan a nonpeptide angiotensin antagonist, which is an orally active antihypertensive drug[15]. Literature studies reveals that *bis*-heterocycles bearing pyrazoline[16,17] were synthesized *via* 1,3-dipolar cycloaddition of aldehyde hydrazone to divinyl ketone / sulfone using chloramine-T (CAT) as dehydrating agent.

1,3-Dipolar cycloaddition reactions are useful tools for constructing biologically potent five membered heterocycles[18]. Apart from the various dipolar reagents known, nitrile imines are used in numerous 1,3-dipolar cycloaddition reactions leading to pyrazoles, pyrazolines, pyrazolidines and other heterocyclic compounds[19]. Huisgen and co-workers[20] first reported the authentic *in situ* generation of nitrile imines by the thermolysis of 2,5-diphenyl tetrazole in the presence of ethyl phenylpropionate and obtained 2,3,5-triphenyl carbethoxypyrazole. Nitrile imines can be generated by photolysis of sydnones[21] and oxidation of aryl aldehyde hydrazones with lead tetraacetate[22], chloramine-T[23] *etc*. In our laboratory Rai *et al* extensively used chloramine-T for the generation of nitrile oxide and nitrile imine from aldoxime and aldehyde hydrazones respectively. With this background, it is considered worthwhile to prepare *bis*-heterocycles using 1,3-dipolar cycloaddition reaction of 2-*n*-butyl-4-chloro-(*N*-substituted)–imidazole substituted nitrile imine with different olefins and screen them for antimicrobial activity. The present communication deals with the synthesis of *bis*-heterocycles via 1,3-dipolar cycloaddition reactions and their antimicrobial activity.



4	a	b	c	d	e	f	g	h
X	H	CH_3	H	H	H	H	H	H
Z	Ph	Ph	CH_2CN	CH_2Cl	CH_2Br	CH_2OH	$COOMe$	$COOEt$

Scheme 1

Experimental

^{1}H NMR spectra were recorded on a Bruker AM 300 MHz spectrometer using $CDCl_3$ as solvent and tetramethylsilane as internal standard. ^{13}C NMR spectra were measured on Jeol 400 (100MHz) instrument. The chemical shifts are expressed in δ and following abbreviations were used: s = singlet, d = doublet, t = triplet and m = multiplet. Infrared (IR) spectra were measured on Shimadzu 8300 spectrometer. Elemental analyses were obtained on a Vaio-EL intrument. Thinlayer chromatography (TLC) was done with pre-coated silica gel G plates using benzene-ethylacetrate as eluent.

Antimicrobial activity

All the synthesized compounds were evaluated for antimicrobial activity by the disc diffusion method[26] and microdilution method[27]. Five bacteria and five fungal species were

used as the antimicrobial test strains namely: *Bacillus substilis, Escherichia coli, Pseudomonas fluorescens, Xanthomonas campestris pvs, Xanthomonas oryzae, Aspergillus niger, Aspergillus flavus, Fusarium oxysporium, Trichoderma species, Fusarium* and *monaliforme. Streptomycin* and *tetracycline* were used as standard drugs against bacteria and *nystatin* was used against fungi. In all the determinations tests were performed in triplicate and the results were taken as a mean of at least three determinations.

Preparation of 4'-(2-Butyl-4-chloro-5-formyl-imidazol-1-ylmethyl)-2-carbonitrile **(2)**

A mixture of 2-butyl-5-chloro-3H-imidazole-4-carbaldehyde (1.0 g, 5.37 mmol) and anhyd. K_2CO_3 (0.90 g, 6.52 mmol) in dimethylformamide (15 mL) were stirred for 15 min at room temperature. 4'-Bromomethyl-biphenyl-2-carbonitrile (1.45 g, 5.33 mmol) was then added and the mixture was stirred at room temperature for 6 h. After completion of the reaction (TLC toluene-ethylacetate; 7:3) the reaction mass was diluted with 25 mL water and the product was extracted with dichloromethane (25 mL). The extract was washed with water (10 mL) and then dried (Na_2SO_4). The solvent was evaporated and the remaining pale yellow oil was crystallized from ethanol to give **2** as a white crystalline solid (1.81 g 89%), mp 108-110 ^oC.

Synthesis of 4,5-dihydro-3-(substituted-imidazole)-1,5-diphenyl-1H-pyrazoline **(5a)**

A mixture of **3** (1.0 g, 2.13 mmol), **4a** (0.23 g, 2.2 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) in ethanol (20 mL) was warmed on a water bath for 2-3 h. TLC monitored the progress of the reaction. After completion of the reaction the solvent was evaporated in vacuum. The residual mass was extracted into ether (25 mL), washed successively with water (2 x 20 mL), 5% NaOH (1 x 10 mL), brine solution (2 x 15 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent afforded crude oily substance, which was purified by column chromatography using benzene-ethylacetate (8:1) as eluent to give the product as thick oil (0.75 g, 62%).

4,5-dihydro-3-(substituted-imidazole)-5-methyl-1,5-diphenyl-1H-pyrazoline **(5b)**

Obtained from **3** (1.0 g, 2.13 mmol), **4b** (0.25 g, 2.12 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.88 g, 70%).

4,5-dihydro-3-(substituted-imidazole)-1-phenyl-1H-pyrazoline-5-carbonitrile **(5c)**

Obtained from **3** (1.0 g, 2.13 mmol), **4c** (0.12 g, 2.20 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.7 g, 63%).

5-(Chloromethyl)-4,5-dihydro-3-(substituted-imidazole)-1-phenyl-1H-pyrazoline **(5d)**

Obtained from **3** (1.0 g, 2.13 mmol), **4d** (0.17 g, 2.23 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.73 g, 63%).

5-(bromomethyl)-4,5-dihydro-3-(substituted-imidazole)-1-phenyl-1H-pyrazoline **(5e)**

Obtained from **3** (1.0 g, 2.13 mmol), **4e** (0.26 g, 2.14 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.82 g, 66%).

4,5-dihydro-3-(substituted-imidazole)-1-phenyl-1H-pyrazol-yl)methanol **(5f)**

Obtained from **3** (1.0 g, 2.13 mmol), **4f** (0.125 g, 2.15 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.68 g, 61%).

4,5-dihydro-3-(substituted-imidazole)-1-phenyl-1H-pyrazol-5-yl acetate **(5g)**

Obtained from **3** (1.0 g, 2.13 mmol), **4g** (0.185 g, 2.15 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.91 g, 77 %).

4,5-dihydro-3-(substituted-imidazole)-1-phenyl-1H-pyrazol-5-yl propionate **(5h)**

Obtained from **3** (1.0 g, 2.13 mmol), **4h** (0.215 g, 2.15 mmol) and chloramine-T trihydrate (0.6 g, 2.13 mmol) as thick oil (0.92 g, 76%).

Results and Discussion

The general synthetic pathway discussed hereafter is depicted in the Scheme**.** Compound **1** was alkylated using 4'-Bromomethyl-biphenyl-2-carbonitrile and potassium carbonate in DMF. Then farmyl function of **2** was converted into the phenylhydrazone **3.** When oxidative dehydrogenation of **3** by chloramine-T (CAT) afforded nitrile imine, which was *in situ* trapped by the different olefins **4 (a-h)** under refluxing condition in ethanol. Thus produced compound was identified by NMR spectroscopy and elemental analyses as 4,5-dihydro-3-(substituted imidazole)-5-substituted-1-phenyl-1H-pyrazoline **5 (a-h)** in good quality and yield**.** The starting substrate 2-n-butyl-4-chloro-(N-substituted)–imidazole-5-carbaldehyde **1** was prepared according to literature procedure[24]. Imidazole aldehyde phenylhydrazone was prepared by known procedure[25].

Antimicrobial activity

Antimicrobial activity of all the compounds was shown in Table 1 and 2. Among the series of synthesized compounds, **5d** and **5e** shown better inhibition. Remaining compounds shown moderate inhibition. The better inhibition shown by **5d** and **5e** may be due to the presence of chloro and bromo group in the compound.

Table 1. Minimal inhibitory concentration in µg mL^{-1}[**X**] and Inhibitory zone in (diameter) mm [**Y**] of the synthesized compounds against tested bacterial strains by micro dilution method and disk diffusion method respectively

Compound	*Bacillus substilis*		*Escherichia coli*		*Pseudomonas fluorescens*		*Xanthomonas campestris pvs*		*Xanthomonas oryzae*	
	X	Y mm	X	Y mm	X	Y mm	X	Y mm	X	Y mm
5a	21	07	26	13	23	16	25	12	23	12
5b	22	10	21	11	25	14	22	11	24	11
5c	19	13	17	14	20	17	19	14	23	12
5d	17	14	12	13	13	15	10	10	11	10
5e	18	11	14	11	12	16	12	11	14	12
5f	25	07	22	09	28	13	27	10	23	11
5g	22	10	22	10	26	11	23	11	24	12
5h	24	09	22	09	29	15	25	12	23	10
Streptomycin	19	13	13	14	12	17	-	-	-	-
Tetracycline	-		-		-		09	12	13	12

Streptomycin sulfate (25 µg per disc); Tetracycline (25 µg per disc) were used as positive reference standard antibactierial discs, Synthesized compounds (25 µg per disc).

Table 2. Minimal inhibitory concentration in µg mL^{-1}[X] and Inhibitory zone in (diameter) mm [Y] of the synthesized compounds against tested fungal strains by micro dilution method and disk diffusion method respectively

Compound	*Aspergillus niger*		*Aspergillus flavus*		*Fusarium oxysporium*		*Trichoderma species*		*Fusarium monalifome*	
	X	Y mm	X	Y mm	X	Y mm	X	Y mm	X	Y mm
5a	18	08	18	09	14	12	15	14	14	11
5b	18	07	18	07	18	11	17	12	15	09
5c	16	08	16	10	13	13	14	15	11	11
5d	14	09	13	12	10	16	11	17	10	14
5e	15	09	15	11	11	14	13	16	10	12
5f	19	07	19	07	17	11	17	12	15	09
5g	21	07	26	08	23	15	25	12	23	12
5h	22	08	21	10	25	14	22	11	24	11
Nystatin	15	08	15	10	11	14	12	16	09	12

Nystatin (25 µg per disc) was used as positive reference standard antifungal discs, synthesized compounds (25 µg per disc).

Spectral analysis of compounds

Compound 2: ^{1}H NMR $CDCl_3$: δ 0.92 (t, 3H, CH_3), 1.34 (m, 2H, CH_2), 1,66 (m, 2H, CH_2), 2.57 (t, 2H, CH_2), 4.96 (s, 2H, CH_2), 7.12-7.36 (m, 4H, ArH), 7.5-7.65 (m, 4H, ArH), 9.62 (s, 1H, CH), ^{13}C NMR $CDCl_3$: δ 14.2 (C), 23.4 (C), 23.9 (C), 34.8 (C), 42.4 (C), 114.6 (C), 118.5 (C), 127.4 (2C), 128.2 (2C), 129.6 (2C), 132.1 (C), 133.2 (C), 133.4 (C), 136.1 (C), 136.9 (C), 140.9 (C), 142.9 (C), 161.7 (C), 189.1 (C). IR (KBr pellets cm^{-1}) v 3070, .2996, 2241, 1762, 1667, 1576, 1299. Anal. Calcd. For $C_{22}H_{20}ClN_3O$: C, 69.93, H, 5.33, N, 11.12%. Found: C, 69.99, H, 5.38, N11.09%.

Compound 5a: ^{1}H NMR $CDCl_3$: δ 0.94 (t, 3H, CH_3), 1.34 (m, 2H, CH_2), 1,66 (m, 2H, CH_2), 2.57 (t, 2H, CH_2), 3.34 (dd, *J*=6.2, 1H, 4-H), 3.42 (dd, 1H, *J*=6.2, 4-H), 5.17 (dd, 1H, *J*=2.0, 5-H), 5.02 (s, 2H, CH_2), 6.62-7.10 (m, 5H, ArH), 7.18-7.37 (m, 4H, ArH), 7.42-7.65 (m, 4H, ArH), ^{13}C NMR $CDCl_3$: δ 14.1 (C), 23.1 (C), 26.7 (C), 33.2 (C), 39.5 (C), 53.2 (C), 104.7 (C), 113.5 (2C), 115.9 (C), 117.7 (C), 122.2 (C), 126.3 (C), 126.8 (C), 127.2 (2C), 127.8 (2C), 128.4 (C), 128.7 (4C), 129.7 (4C), 132.9 (C), 133.8 (2C), 135.4 (C), 142.7 (C), 143.4 (C), 143.8 (C), 148.6 (C), 156.1 (C). Anal.Calcd. For $C_{36}H_{32}ClN_5$; C, 75.84; H, 5.66; N, 12.28; Found: C, 75.85, H, 5.67, N, 12.28

Compound 5b: ^{1}H NMR $CDCl_3$: δ 0.96 (t, 3H, CH_3), 1.36 (m, 2H, CH_2), 1.62 (s, 3H, CH_3), 1.65 (m, 2H, CH_2), 2.58 (t, 2H, CH_2), 3.32 (s, 2H, 4-CH_2), 5.10 (s, 2H, CH_2), 6.64-7.06 (m, 6H, ArH), 7.13-7.19 (m, 6H, ArH), 7.38-7.68 (m, 6H, ArH). ^{13}C NMR $CDCl_3$: δ 14.2 (C), 23.2 (C), 26.8 (C), 30.1 (C), 33.4 (C), 41.4 (C), 47.3 (C), 56.2 (C), 104.6 (C), 113.5 (2C), 115.9 (C), 117.8 (C), 122.2 (C), 126.2 (C), 126.2 (C), 126.6 (2C), 127.7 (2C), 128.4 (3C), 128.7 (C), 129.9 (4C), 132.9 (C), 133.4 (C), 133.8 (C), 135.4 (C), 142.7 (C), 143.8 (C), 144.4 (C), 148.3 (C), 156.3 (C). Anal.Calcd. For $C_{37}H_{34}ClN_5$; C, 76.08; H, 5.87; N, 11.99; Found: C, 76.10, H, 5.86, N, 11.98%.

Compound 5c: ^{1}H NMR $CDCl_3$: δ 0.94 (t, 3H, CH_3), 1.33 (m, 2H, CH_2), 1,64 (m, 2H, CH_2), 2.55 (t, 2H, CH_2), 3.37 (dd, 1H, *J*=6.0, 4-H), 3.40 (dd, 1H, *J*=6.0, 4-H), 5.19 (dd, 1H, *J*=3.6, 5-H), 5.00 (s, 2H, CH_2), 6.60-7.08 (m, 5H, ArH), 7.16-7.32 (m, 4H, ArH), 7.40-7.65 (m, 4H, ArH), ^{13}C NMR $CDCl_3$: δ 14.2 (C), 23.0 (C), 25.7 (C), 32.6 (C), 33.5 (C), 40.8 (C), 41.1 (C), 104.7 (C), 113.7 (2C), 115.9 (C), 116.6 (C), 117.8 (C), 122.3 (C), 126.3 (C), 127.9 (2C), 128.5 (C), 128.8(C),

129.7 (4C), 132.8 (C) 133.6 (2C), 135.4 (C), 142.7 (C), 144.0 (C), 148.5 (C), 156.7 (C). Anal.Calcd. For $C_{31}H_{27}ClN_6$; C, 71.73; H, 5.24; N, 16.19. Found: C, 71.73; H, 5.23; N, 16.19 %.

Compound 5d: ^{1}H NMR $CDCl_3$: δ 0.98 (t, 3H, CH_3), 1.35 (m, 2H, CH_2), 1,66 (m, 2H, CH_2), 2.57 (t, 2H, CH_2), 3.32 (dd, 1H, *J*=6.4, 4-H), 3.37 (dd, 1H, *J*=6.4, 4-H), 3.46 (dd, 1H, *J*=4.0, CH_2Cl), 3.70 (dd, 1H, *J*=4.0, CH_2Cl), 4.98 (s, 2H, CH_2), 5.10 (m, 1H, 5-H), 6.58-7.08 (m, 5H, ArH), 7.16-7.38 (m, 4H, ArH), 7.42-7.65 (m, 4H, ArH), ^{13}C NMR $CDCl_3$: δ 14.2 (C), 22.8 (C), 26.0 (C), 33.2 (C), 34.6 (C), 40.7 (C), 52.4 (C), 53.4 (C), 104.7 (C), 113.6 (2C), 116.0 (C), 117.5 (C), 122.2 (C), 126.3 (C), 127.8 (2C), 128.4 (C), 128.8 (C), 129.7 (4C), 132.4 (C), 133.5 (2C), 135.4 (C), 142.5 (C), 144.0 (C), 148.4 (C), 156.4 (C). Anal.Calcd. For $C_{31}H_{29}Cl_2N_5$; C, 68.63; H, 5.39; N, 12.91. Found: C, 68.64; H, 5.38; N, 12.93 %.

Compound 5e: ^{1}H NMR $CDCl_3$: δ 0.95 (t, 3H, CH_3), 1.32 (m, 2H, CH_2), 1,63 (m, 2H, CH_2), 2.54 (t, 2H, CH_2), 3.30 (dd, 1H, *J*=6.6, 4-H), 3.35 (dd, 1H, *J*=6.6, 4-H), 3.42 (dd, 1H, *J*=3.2, CH_2Br), 3.68 (dd, 1H, *J*=3.2, CH_2Br), 5.16 (m, 1H, 5-H), 4.98 (s, 2H, CH_2), 6.50-7.08 (m, 5H, ArH), 7.12-7.36 (m, 4H, ArH), 7.42-7.65 (m, 4H, ArH), ^{13}C NMR $CDCl_3$: δ 14.2 (C), 22.6 (C), 26.0 (C), 33.2 (C), 35.9 (C), 36.6 (C), 39.2 (C), 40.5 (C), 54.4 (C), 104.7 (C), 113.6 (2C), 116.0 (C), 117.4 (C), 122.0 (C), 126.2 (C), 127.8 (2C), 128.4 (C), 128.7 (C), 129.7 (4C), 132.5 (C), 133.5 (C), 135.4 (C), 142.6 (C), 143.8 (C), 148.2 (C), 155.4 (C). Anal.Calcd. For $C_{31}H_{29}BrClN_5$; C, 63.43; H, 4.98; N, 11.93. Found: C, 63.45, H, 4.98, N, 11.91 %.

Compound 5f: ^{1}H NMR $CDCl_3$: δ 0.96 (t, 3H, CH_3), 1.33 (m, 2H, CH_2), 1,63 (m, 2H, CH_2), 2.56 (t, 2H, CH_2), 3.24 (dd, 1H, *J*=6.2, 4-H), 3.30 (dd, 1H, *J*=6.2, 4-H), 3.61-3.86 (m, 2H, CH_2), 5.02 (s, 2H, CH_2), 5.17 (m, 1H, 5-H), 6.52-7.10 (m, 5H, ArH), 7.16-7.37 (m, 4H, ArH), 7.42-7.65 (m, 4H, ArH). ^{13}C NMR $CDCl_3$: δ 14.3 (C), 23.1 (C), 26.0 (C), 33.2 (C), 33.7 (C), 40.9 (C), 53.1 (C), 66.4 (C), 104.5 (C), 113.5 (2C), 115.8 (C), 117.2 (C), 122.2 (C), 126.7 (C), 127.7 (2C), 128.5 (C), 128.9 (C), 129.7 (4C), 132.8 (C), 133.3 (C), 133.8 (C), 135.4 (C), 142.6 (C), 144.0 (C), 148.4 (C), 156.5 (C). Anal.Calcd. For $C_{31}H_{30}ClN_5O$; C, 71.05; H, 5.77; N, 13.36; Found: C, 69.99, H, 6.13, N, 13.03.

Compound 5g: ^{1}H NMR $CDCl_3$: δ 0.94 (t, 3H, CH_3), 1.33 (m, 2H, CH_2), 1,66 (m, 2H, CH_2), 2.02 (s, 3H, CH_3), 2.55 (t, 2H, CH_2), 3.37 (dd, 1H, *J*=6.0, 4-H), 3.42 (dd, 1H, *J*=6.0, 4-H), 5.42 (dd, 1H, *J*=4.0, 5-H), 5.04 (s, 2H, CH_2), 6.57-7.06 (m, 5H, ArH), 7.15 (d, 2H), 7.37 (d, 2H, ArH), 7.42-7.67 (m, 4H, ArH), ^{13}C NMR $CDCl_3$: δ 14.3 (C), 20.8 (C), 23.3 (C), 26.7 (C), 33.5 (C), 37.2 (C), 40.6 (C), 78.4 (C), 104.7 (C), 113.6 (2C), 115.9 (C), 117.3 (C), 122.1 (C), 126.6 (C), 127.8 (2C), 128.4 (C), 128.8 (C), 129.6 (4C), 132.7 (C), 133.5 (C), 133.8 (C), 135.4 (C), 142.7 (C), 144.1 (C), 148.3 (C), 155.9 (C), 170.5 (C). Anal.Calcd. For $C_{32}H_{30}ClN_5O_2$ C, 69.62; H, 5.48; N, 12.69; Found: C, 69.62, H, 5.46, N, 12.70 %.

Compound 5h: ^{1}H NMR $CDCl_3$: δ 0.96 (t, 3H, CH_3), 1.14 (t, 3H, CH_3), 1.34 (m, 2H, CH_2), 1,66 (m, 2H, CH_2), 2.32 (q, 2H, CH_2), 2.57 (t, 2H, CH_2), 3.34 (dd, 1H, *J*=6.4, 4-H), 3.42 (dd, 1H, *J*=6.4, 4-H), 5.38 (dd, 1H, *J*=4.0, 5-H), 5.02 (s, 2H, CH_2), 6.52-7.05 (m, 5H, ArH), 7.14-7.37 (m, 4H, ArH), 7.40-7.66 (m, 4H, ArH), ^{13}C NMR $CDCl_3$: δ 10.1 (C), 14.1 (C), 22.9 (C), 25.7 (C), 27.6 (C), 33.7 (C), 37.5 (C), 40.7 (C), 50.1 (C), 78.9 (C), 104.7 (C), 113.6 (2C), 115.8 (C), 117.7 (C), 122.3 (C), 126.7 (C), 127.8 (2C), 128.4 (C), 128.7 (C), 129.7 (4C), 132.8 (C), 133.5 (C), 135.4 (C), 142.7 (C), 144.0 (C), 148.4 (C), 156.8 (C), 173.2 (C). Anal.Calcd. For $C_{33}H_{32}ClN_5O_2$; C, 70.02; H, 5.70; N, 12.37; Found: C, 70.04, H, 5.70, N, 12.38 %.

Conclusion

In conclusion 4, 5- dihydro -3- (substituted - imidazole) – 5 - substituted-1-phenyl-1H-pyrazoline derivatives were synthesized and their antimicrobial activity have been evaluated. Compounds **5d** and **5e** shows significant inhibition, remaining compounds demonstrated potent to moderate antimicrobial activity. Further research in this area is under progress in our laboratory.

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