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SYNTHESIS OF SCHIFF BASE INCORPORATED NOVEL 2-PYRAZOLINE DERIVATIVES AS PROMISING ANTIBACTERIAL AGENTS

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ABSTRACT

A series of novel 2-Pyrazoline derivatives bearing schiff base unit were synthesized with moderate to good yield. Structures were confirmed with the help of various spectral techniques and compounds were exhibited potential antibacterial activity against selected bacterial strains.

KEY WORDS

Pyrazoline, p-Cl-Benzaldehyde, Grinding technique, Imine, Phenyl hydrazine

INTRODUCTION

Five-membered heterocyclic compounds occupy an important place in the realm of natural and synthetic organic chemistry and are occurred widely in the form of alkaloids, vitamins, pigments, constituents of plants and animal cells. Among these, Pyrazoline based five membered heterocycles plays a crucial role in the development of theory of heterocyclic chemistry and is also extensively used as synthons in organic synthesis [1-8]. The 2-pyrazoline heterocycles are synthesized by using various synthetic methods and are described in the literature [9-11]. However, the most common and popular procedure is reaction between α, β-unsaturated aldehydes or ketones with different hydrazines [12-15]. Schiff base was first reported by Schiff in 1864 which are formed by condensation reaction between carbonyl compounds and amines. These compounds plays important role in the realm of organic chemistry as synthons in the preparation of a number of industrial and biologically active heterocyclic compounds [16-18]. Schiff bases have gained importance in medicinal and pharmaceutical fields due to a broad spectrum of biological activities [19-25]. With keeping important of above compounds and continuations of my previous work [26-30], I attempted to synthesize a series of novel 2-Pyrazoline heterocycles bearing schiff base moiety as potential microbial agents.

EXPERIMENTAL

General procedure to synthesis substituted chalcone (3):

A mixture of 0.01mol of *p*-NH_2-acetophenone **1**, (1 equiv) and p-Cl-benzaldehyde **2** (1 equiv) with 40% aqueous NaOH solution (2 mL) was stirred in ethanol (20 mL) for 3 hrs at room temperature. Progress of the reaction was monitored by TLC and after completion of the reaction mixture was poured in to crush ice and acidified with dilute hydrochloric acid. The solid formed was filtered, dried and recrystalyzed from ethanol.

General procedure to synthesis Schiff base (4):

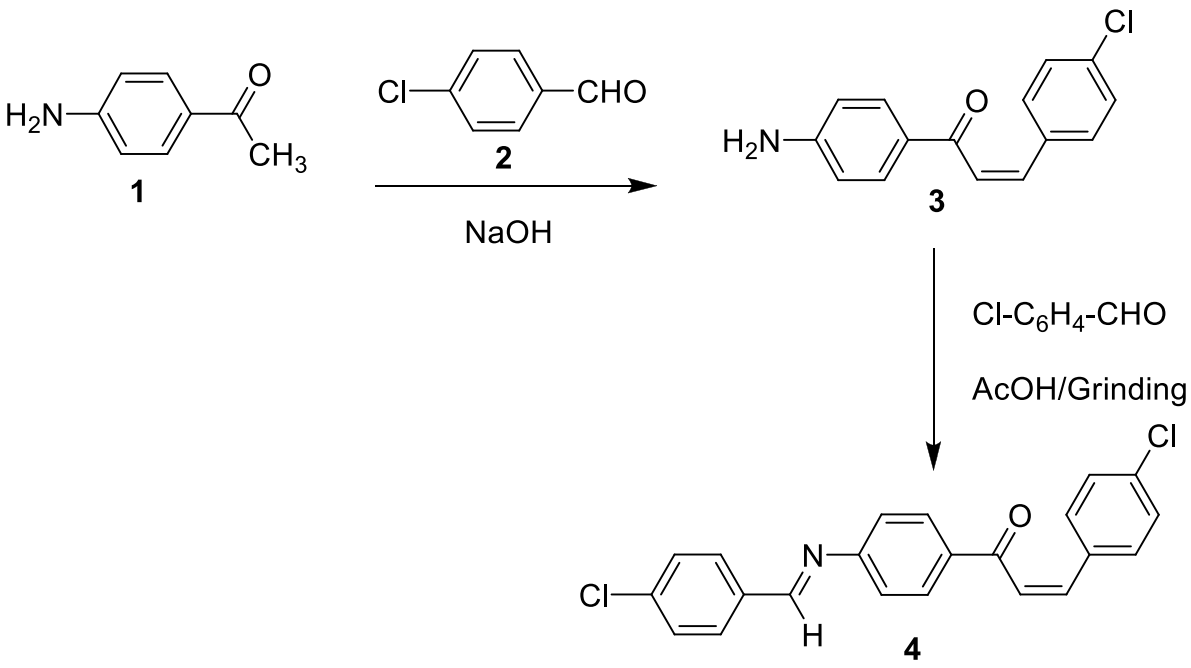
A mixture of substituted chalcone **3** (1 equiv) and p-Cl-benzaldehyde **2** (1 equiv) 2-3 drops of glacial AcOH was added. This mixture was grinded for 5-10mins during that period the solid mixture was started to melt and finally solidified. The progress of the reaction was monitored TLC and the mixture was poured in to ice-cold water after completion of reaction. The solid formed was filtered, washed with water, dried and finally recrystallized from ethanol.

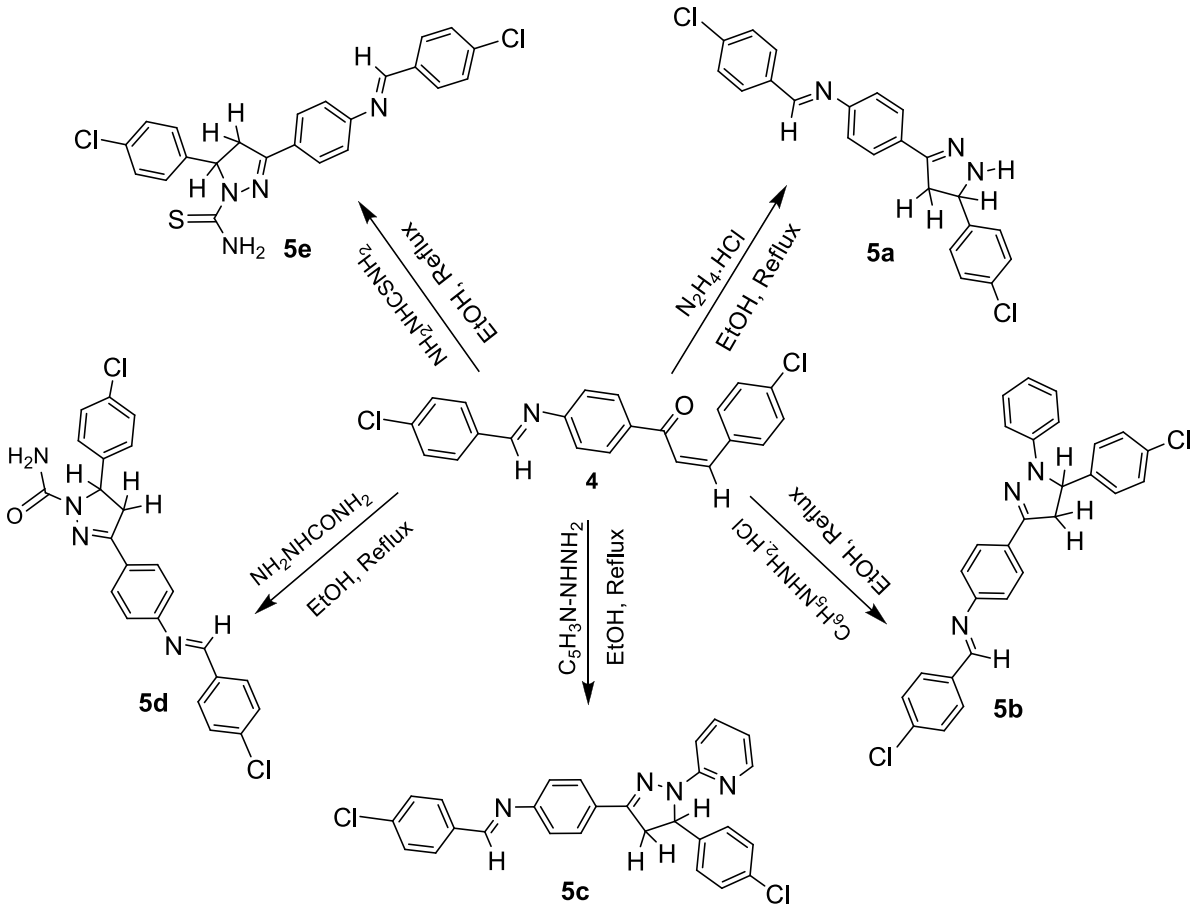
General procedure to synthesis of novel 2-Pyrazoline derivatives (5a-e):

One equivalent of **4** and one equivalent of hydrazine hydrochloride were taken in RB flask with ethanol and fitted with air condenser. The mixture was refluxed for 3hrs and progress of the reaction was monitored by TLC and after completion of the reaction, the ice-cold water was added to reaction mixture. The solid mass was filtered and recrystalyzed from ethanol. The same procedure was followed to prepare remaining derivatives by took different hydrazine derivatives.

RESULTS AND DISCUSSION

Present work begins with *p*-NH_2-Acetophenone (**1**) which reacted with *p*-Cl-Benzaldehyde aldehyde (**2**) produced corresponding chalcone (**3**). This chalcone further reacted with *p-Cl-benzaldehyde* in the presence of catalytic amount of acetic acid (**3**) afforded schiff base derivative (**4**). The compound **4** reacted with various hydrazine derivatives such as Hydrazine, Phenyl hydrazine, Pyridine hydrazine, Semicarbazide and Thiosemicarbazide afforded desired products **5a-e** with moderate to good yield. Here in, I have applied Aldol condensation, Schiff base formation reaction and Michael type addition reaction to obtain the final products. The physical data such as, melting point, Color, Rf value (Table-1) and spectral data such as, FT-IR, ^{1}H-NMR and ^{13}C-NMR were well supported the formation of the desired products by the agreement of observed signals with expected signals. I was tested antimicrobial activities of selected compounds **5a-d** and obtained results revealed that their potential response against various bacterial pathogens as equal or more than standard. However, tested compounds did not exhibit significant activity against *Pseudomonas aeruginosa* (Table-2).





Scheme: Synthesis of Novel 2-Pyrazoline derivatives **5a-e**

Table-1: Physical data of novel Pyrazoline derivatives 5a-e

Comp.code	Yield (%)	Mp (°C)	Color	Rf value (PE: EA, 2:1)
5a	54	140-142	light yellow	0.50
5b	60	180-182	Yellow	0.40
5c	50	144-146	Dark yellow	0.44
5d	70	156-158	Orange	0.52
5e	75	182-184	Orange	0.50

Table-2: FT-IR Spectral data of novel Pyrazoline derivatives 5a, 5b and 5d

Compounds	Aromatic-CH	Aliphatic-CH	Ar-Cl	C=N	NH
5a	3026.2	2920.18	1119.8	1596.9	3367.4
5b	3065.9	2922.4	1674.9	1528.5	--
5c	3005.0	2933.8	1050.0	1599.0	--
5d	2958.8	2828.3	1090.7	1599.8	3388.4

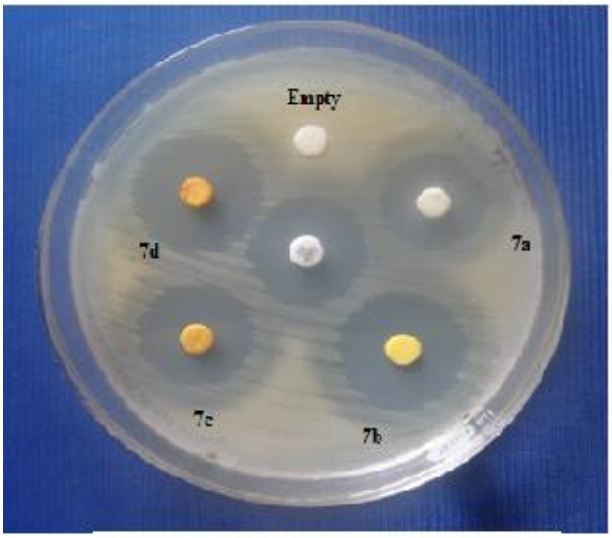
Table-3: ^{1}H-NMR and ^{13}C-NMR Spectral data of novel Pyrazoline derivatives 5a, 5b and 5d

Comp	^{1}H-NMR ($CDCl_3$, δ ppm)	^{13}C-NMR ($CDCl_3$, δ ppm)
5a	3.20-3.28 (dd, 1H, C_4-H), 3.72-3.82 (dd, 1H, C_4-H), 5.42-5.46 (dd, 1H, C_5-H), 6.79-7.86 (m,17Ar-CH), 7.95 (s, 1H, CH=N);	44.17 (C_4), 60.54 (C_5), 112.80, 113.75, 113.97, 114.89, 119.26, 120.32, 120.85, 124.02, 124.76, 126.92, 127.24, 127.41, 128.15, 128.25, 128.84, 129.45, 131.02 (17Ar-CH), 131.48, 133.92, 135.82, 140.79, 144.40, 147.27, (7-Ar-C), 148.0, 151.1 (CH=N).
5b	3.11-3.89 (dd, 1H, C_4-H), 5.20-5.30 (dd, 1H, C_4-H), 5.40-5.50 (dd, 1H, C_5-H), 6.70-8.15 (m, 17Ar-CH), 8.41 (s, 1H, CH=N);	42.86 (C_4), 58.89 (C_5), 113.96, 114.63, 120.26, 124.49, 120.86, 124.49, 124.84, 126.70, 128.07, 128.22, 128.61,129.21, 131.01, 131.26 (17Ar-CH), 131.40, 131.48, 135.60, 136.72, 142.55, 149.38, (7-Ar-C), 156.65 (2CH=N)
5c	3.02-3.09 (dd, 1H, C_4-H), 3.86-3.91 (dd, 1H, C_4-H), 5.28-5.40 (dd, 1H, C_5-H), 6.60-7.93 (m, 16Ar-CH), 8.4 (s, 1H, CH=N)	40.28 (C_4), 54.37(C_5), 112.00, 114.03, 117.12, 119.24, 120.73, 126.07, 126.68, 127.53, 128.19, 128.52, 129.49, 129.64, 130.40(17Ar-CH), 133.37, 133.93, 136.59, 136.80, 141.10 (7-Ar-C), 151.64, 155.51 (CH=N).

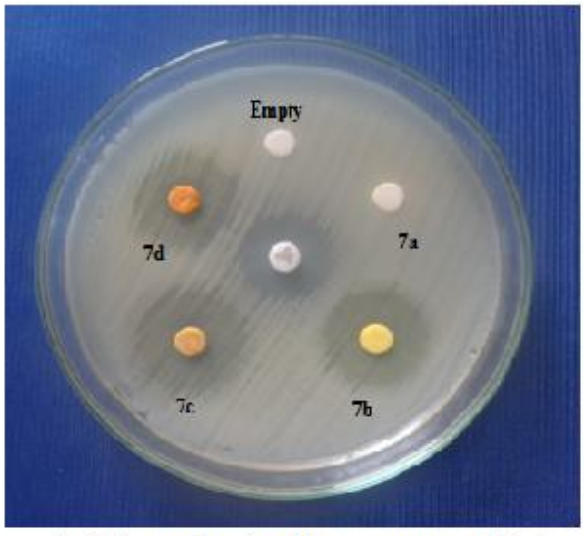
Table-4: Antibacterial activity of novel Pyrazoline derivatives 5a-d against various bacterial pathogens where Gentamicin (30mg) used as standard

S. No.	Bacteria	Zone of inhibition mm in diameter					
		Standard	Empty	7a	7b	7c	7d
1	*Staphylococcus aureus*	17	-	-	18	20	21
2	*Bacillus subtitles*	20	-	19	23	22	25
3	*Pseudomonas aeruginosa*	17	-	-	-	-	-
4	*Escherichia coli*	24	-	24	29	25	24

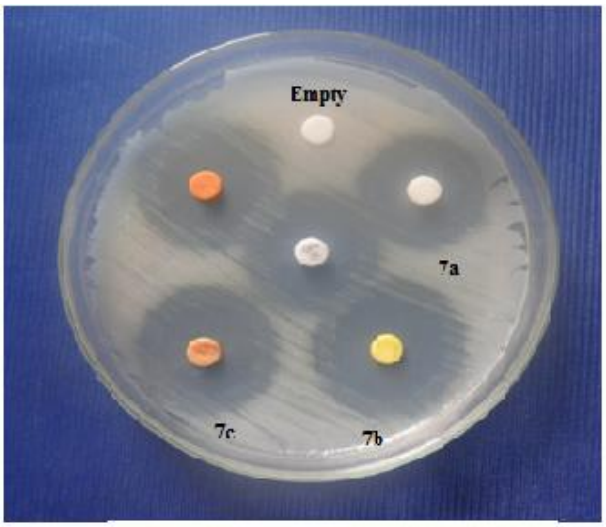
Figure-1: Images of antibacterial studies of 5a-d against different bacteria



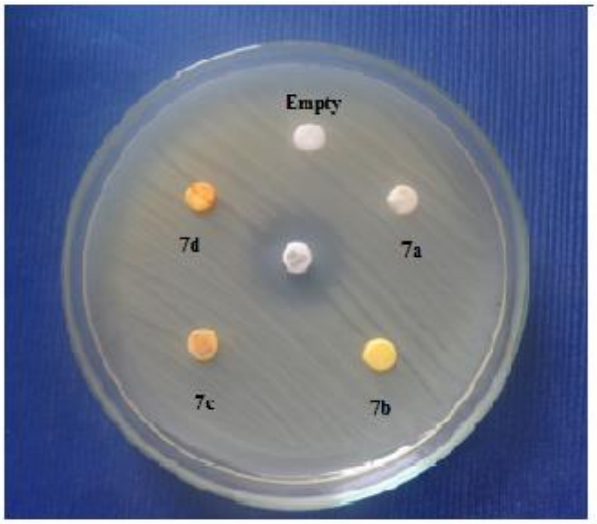
Activity against *Bacillus subtitles* (G+)



Activity against *Staphylococcus aureus* (G+)



Activity against *Escherichia coli* (G-)



Activity against *Pseudomonas aeruginosa* (G-)

CONCLUSION

I have reported synthesis of some novel 2-pyrazoline derivatives consisting schiff base moiety with moderate to good yield. All the synthesized compounds were characterized by using analytical and spectral data. Disc diffusion method showed that potential activity of selected compounds except *Pseudomonas aeruginosa.*

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