Research Article

Synthesis of Some Chalcones and Pyrazoline bearing Chloroqunoline Scaffold as Biologically Active Agents

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Abstract

Substituted chalcones 2a-m have been synthesized by the treatment of 2-chloro-6-methyl-3-quinolin-carboxaldehyde[1] with different aromatic ketones. Subsequent reaction with phenyl hydrazine in ethanol furnished desired pyrazolines 3a-m. The compounds [2a-m, 3a-m] have been characterised by means of elemental analyses and spectral data. The products were evaluated for their *in vitro* growth inhibiting activity against several microbes. Some of the compounds showed significant biological activity.

Keywords: Chloroquinolininechalcones, *in vitro* antimicrobial activity, chloroquinolinine pyrazolines, potent pharmacological agents

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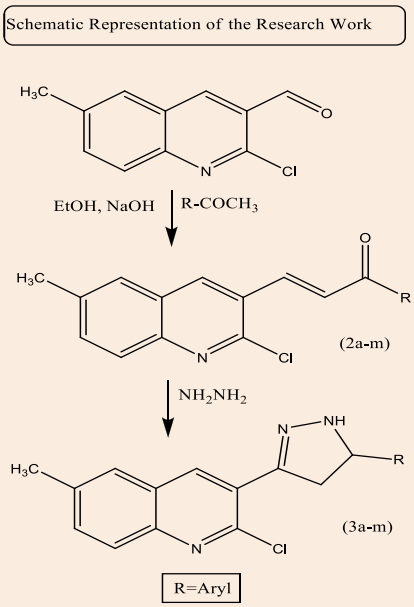

Introduction

Nitrogen containing heterocyclic compounds like quinolones and pyrazolines has received considerable attention in recent years due to their biological activities.

The pharmacological activities associated with quinoline nucleus are as under:
Antimicrobial[1], Anticancer[2], Antimalarial[3], Analgesic[4], Anti-inflammatory[5], Antiviral[6], Anthelmintic[7], Anti-protozoal[8], Cardiovascular activity[9], Hypoglycaemic activity[10], Antialzheimer[11] etc.

Pyrazolines possess biological activities like antiinflammatory[12], analgesic[13], anticonvulsantand Antidepressant[14], insecticidal[15], herbicidal[16], antimicrobial[17], anticarcinogenic[18] and antidiabetic[19], antioxidant[20],antihypertensive[21], antiamoebic[22],cholesterol inhibitory[23].

Some pyrazoline derivatives are applicable as drugs such as azolid / tandearil (antiinflammatory), phenazone/ amidopyrene / methampyrone (analgesic and antipyretic), in doxacarb (insecticidal), anturane (uricosuric) etc. These interesting findings inspired us to synthesis some new pyrazoline derivatives bearing quinoline moiety and made an attempt to evaluate them for the biological potency.

The starting material 2-chloro-6-methyl-3-quinolincarboxaldehyde (1) was condensed with various aromatic ketones to get 3–(2'-chloro-8'-methyl-quinolin-3'-yl)-1-aryl-2-propene-1-ones(2a-m). Compounds 2a-m on treatment with phenyl hydrazine in ethanol afforded 3-(2'-chloro-8-methylquinolin-3-yl)-5-aryl-1-phenylpyrazolines [3a-m].

The structures of the synthesized compounds were assigned on the basis of elemental analyses, IR and PMR spectral data. The antimicrobial profile of the compounds synthesized has been studied against several microbes.

Experimental:

All melting points are uncorrected. Infrared Spectra (KBr) were recorded on a Shimadzu-435 IR Spectrophotometer and ’H NMR spectra on Hitachi NMR-300 using TMS as an internal standard.

Preparation of 3-(2’-chloro-6'-methylquinolin-3'-yl)-1-aryl-2-propene-1-ones (2a-m) :

To a well stirred solution of 2-chloro-8-methyl-3-quinolin-carboxaldehyde[11] (1, 0.01 mol) and aryl ketone (0.01 mol) in ethanol (25 ml) there was added 40% NaOH (3 ml). The reaction mixture was stirred for 24 hr. The contents were poured into ice water, acidified with HCI and resulting solid filtered and crystallized from ethanol. TLC Solvent System: Acetone: Benzene (2:8).

2k: IR (KBr) : 1654 (C=O), 1603 (C=N). 1591 (CH=CH). 763 (C-CI); ^{1}H NMR δ ppm: ($CDCI_3$): 2.4 (s. 3H. -CH_3). 2.5 (s, 3H. -CH_3), 7.18-7.8 (m, 8H, Ar-H), 6.8 (d, 1H, =CH), 7.3 (d, 1H,=CH).
2j: ^{1}H NMR: 2.94 (s, 3H, -ch_3); 3.95 (s, 3H, OCH_3);7.1-8.2 (m, 10H, 8Ar-H + CH=CH).
Similarly, other members of 2 were prepared (Table-1).

Preparation of 3-(2'-chloro-6'-methylquinolin-3-yl)-5-aryl-1-phenylpyrazolines (3a-m):

A mixture of chalcone (2, 0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (20 ml) was refluxed for 10 hr. The contents were cooled, poured onto crushed ice and separated solid was filtered, dried and crystallized from ethanol. TLC Solvent System: Acetone : Benzene (2:8).

3e : IR (KBr) : 2921 (-CH_3, alkane), 1623 (C=N), 760 (C-CI); ^{1}H NMR ($CDCl_3$ + DMSO-d_6): 2.83 (s, 3H, -CH_3Ar). 3.8 (t. 1H, - CH_{3A}), 4.5 (d. 2H, - CH_{3B}), 6.2 (dd, 1H, CH=CH), 7.1-7.89 (m. 1H. Ar-H).
3m: ^{1}H NMR: 2.8 (s, 3H, -CH_3); 3.42-3.75 (dd, 1H, CH_3); 5.85-6.10 (dd, 1H,-CH=CH-); 7.19-9.14 (m, 12H,Ar).

Similarly, other members of 3 were prepared. The physical constants are given in Table-1.

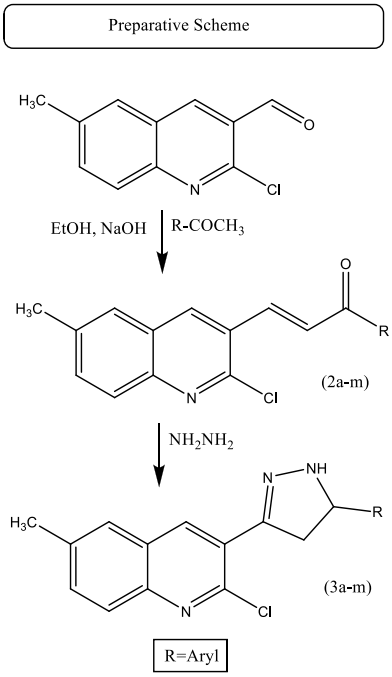

Table 1 Characterization data of the compounds 2a-m and 3a-m

Compd. Code	R	M. Wt.	M.P. (°C)	Yield %	Rf value	N % Calcd.	N % Found
2a	C_6H_5	307.5	180	70	0.45	4.5	4.50
2b	3-$NH_2C_6H_4$	322.5	160	65	0.47	8.68	8.62
2c	4-NH_2-C_6H_4	322.5	178	60	0.36	8.68	8.62
2d	4-Br-C_6H_4	385.5	180	72	0.48	3.63	3.60
2e	4-C*l*-C_6H_4	342.0	180	68	0.67	4.09	4.05
2f	2,4-$(OH)_2$-C_6H_3	339.5	210	72	-	4.12	4.06
2g	C_4H_3O	297.5	150	50	0.57	4.70	4.65
2h	2-OH-C_6H_4	323.5	150	55	0.50	4.32	4.30
2i	4-OH-C_6H_4	323.5	165	58	0.61	4.32	4.30
2j	4-OCH_3-C_6H_4	337.5	160	70	0.50	4.14	4.11
2k	4-CH_3–C_6H_4	321.5	175	65	0.70	4.35	4.31
2*l*	4-NO_2–C_6H_4	352.5	170	74	0.59	7.94	7.91
2m	C_4H_3S	313.5	180	55	-	4.46	4.42
3a	C_6H_5	321.5	120	62	0.50	13.00	13.01
3b	3-NH_2-C_6H_4	336.5	140	64	0.47	16.64	16.60
3c	4-NH_2-C_6H_4	336.5	190	50	0.57	16.64	16.60
3ci	4-Br-C_6H_4	399.5	145	55	0.61	14.01	14.00
3e	4-Cl–C_6H_4	356.0	180	52	0.44	11.79	11.75
3f	2,4-$(OH)_2$-C_6H_3	353.5	185	64	0.64	11.88	11.82
3g	C_4H_3O	311.5	180	53	0.66	13.48	13.41
3h	2-OH-C_6H_4	337.5	160	50	-	12.44	12.41
3i	4-OH-C_6H_4	337.5	140	52	-	12.44	12.41
3j	4-OCH_3-C_6H_4	351.5	120	68	0.55	11.94	11.92
3k	4-CH_3-C_6H_4	353.5	130	65	0.50	12.51	12.48
3l	4-NO_2-C_6H_4	366.5	145	71	0.48	15.27	15.21
3m	C_4H_3S	327.5	185	54	-	12.80	12.80

Antimicrobial activity :

All the compounds reported in Table-2 were tested *in-vitro* for their antimicrobial activity by cup-plate method against various microbes. Under identical conditions, the standard antibiotics showed zones of inhibition penicillin 18-23 mm, ampicillin 15-26 mm, chloramphenicol 15-28 mm against bacterial strains and Griseofulvin showed zones of inhibition of 15-20 mm against *A. niger*.

It can be concluded from Table-2 that the compounds 2b, 2c, 2d, 2f, 2l, 2m, 3a, 3b, 3k were highly active against *B. megaterium*. The compounds 2c, 2d, 2e, 3a, 3e, 3f showed significant activity against *S. aureus.* In case of *E. coli*, the compounds 2a, 2b, 2d, 2m, 2g, 2i, 3a, 3e, 3fdisplayed maximum activity, while the compounds 2c, 2h. 2k, 2m, 2i, 2j, 2k, 2m exhibited significant activity against *S. typhosa* and *A. niger* respectively.

The compound 3a has been selected for their agrochemical and pharmaceutical screening by Du Pont Agricultural Products, USA.

Table 2 Antimicrobial Activity Screening

Compd. Code	R	*B. megaterium*	*S. aureus*	*E. coli*	*S. typhosa*	Antifungal activity Zone of inhibition in mm 24 hour	48 hour
2a	C_6H_5	16	16	20	12	20	15
2b	3-NH_2-C_6H_4	22	15	22	11	25	20
2c	4-NH_2-C_6H_4	20	17	18	14	25	15
2d	4-Br-C_6H_4	17	18	20	12	30	17
2e	4-Cl-C_6H_4	19	18	14	11	28	20
2f	2,4-$(OH)_2$-C_6H_3	11	16	12	10	27	14
2g	C_4H_3O	10	24	15	13	22	13
2h	2-OH-C_6H_4	14	15	12	10	25	22
2i	4-OH-C_6H_4	14	14	19		27	17
2j	4-OCH_3-C_6H_4	12	12	19	15	20	15
2k	4-CH_3–C_6H_4	17	13	17	12	28	18
2*l*	4-NO_2–C_6H_4	17	12	14	13	25	16
2m	C_4H_3S	15	15	15	14	28	24
3a	C_6H_5	16	19	20	11	20	11
3b	3-NH_2-C_6H_4	15	13	19	10	20	16
3c	4-NH_2-C_6H_4	14	16	16	11	25	18
3d	4-Br-C_6H_4	12	16	20	12	20	10
3e	4-Cl–C_6H_4	12	18	19	11	21	12
3f	2,4-$(OH)_2$-C_6H_3	13	17	21	11	22	20
3g	2-OH-C_6H_4	14	16	23	10	24	18
3h	4-OH-C_6H_4	12	15	19	12	20	20
3i	4-OCH_3-C_6H_4	12	16	18	11	20	10
3j	4-CH_3-C_6H_4	14	14	18	12	18	12
3k	4-NO_2-C_6H_4	16	14	22	11	20	15
3l	C_4H_3O	12	13	18	10	22	16
3m	C_4H_3S	14	12	18	13	25	20

Ensual:

- Out of the 26 compounds synthesized 100 % of them have shown the growth control on microbes used for the investigation.
- 9 Compounds exhibited 107 to 157 % growth control against *B. megaterium* compare to the standard drugs Ampicillin and Penicillin.
- 6 Compounds exhibited 85 to 95 % growth control against *S. aureus* compare to the standard drug Ampicillin.
- 10 Compounds exhibited more than 113 to 160 % growth control against *E. coli* compare to the standard drug Penicillin.
- 10 Compounds exhibited more than 59 to more than 68 % growth control against S. *typhosa*compare to the standard drug Ampicillin.
- 11 Compounds exhibited 105 to 150 % growth control against *A. niger* compare to the standard drug Griseofulvin.

Table 3 Listing of the compounds among (2a – m) and (3a – m); exhibiting the highest activity against the microbes investigated

Antibacterial activity*				**Antifungal activity***
B. megaterium	***S. aureus***	***E. coli***	***S. typhosa***	***A .niger***
2b (22)	2c (17)	2a (17)	2c (14)	2d (30)
2c (20)	2d (18)	2b (22)	2h (13)	2e (28)
2d (17)	2e (18)	2d (20)	2k (15)	2l (27)
2f (19)	3a (19)	2m (24)	2m (14)	2k (28)
2l (17)	3e (18)	3a (20)		2m (28)
2m (17)	3f (17)	3b (19)		3c (25)
3a (16)		3d (20)		3e (21)
3b (15)		3e (19)		3f (22)
3k (16)		3f (21)		3g (24)
		3h (19)		3l (22)
				3m (25)
Ampicillin (14) Penicillin (14) Chloramphenicol (15)	Ampicillin (20) Penicillin (22)	Ampicillin (18) Penicillin (15) Chloramphenicol (18)	Ampicillin (22) Penicillin (23)	Greseofulvin (20)

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