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Synthesis of phenyl pyrazolines and their derivative as antimicrobial and antifungal agents

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ABSTRACT

A series of 2-Chloro-3-(1-phenyl-3-aryl-4,5-dihydro-1H-pyrazole-5-yl)-7-(trifluoromethyl) quinoline was synthesized by the action of -[2-Chloro-7-(trifluoromethyl) quinoline-3-yl]-1-phenylpre-2-en-1-one on phenyl hydrogen. The structures of the synthesized compounds have been established on the basis of their elemental analysis and spectral (IR, ^{1}H NMR) studies. Further they have been screened for their antibacterial and antifungal activity.

Keywords: Quinoline-3-carbaldehyde, Phenyl pyrazolines, Antifungal. Antibacterial.

INTRODUCTION

Pyrazoline and its derivatives are better therapeutic agents like Analgesic, bacterial, cardiovascular, Diuretic, fungicidal, herbicidal, hypoglycemic, insecticidal, tranquilizer, ant allergic, anticonvulsant, anti-diabetic, anti-implantation, anti-inflammatory, antitumor, antineoplastic, antimicrobial.[1-20] some new phenylcarbonyl pyrazolines (V) as an insecticides and at 40% concentration shows 100% mortality of spodopetra litura larvae after seven drops.[21]

MATERIALS AND METHODS

All the chemicals used were of pure grade (Finar and Sigma Aldrich). The melting points of all compounds were determined by open capillary method and were uncorrected.

Synthesis of 2-Chloro quinoline-3-carbaldehyde:
To an ice-cooled solution of N,N-dimethylformamide (10.95 g,11.6 ml,0.15 mol)was added drop wise with stirring phosphoryl chloride (53.7 g, 32.3 ml, 0.35 mol). m-trifloromethyl acetanilide (10.15g, 0.05M) was then added and the reaction raised to 75°c and stirred for 20 hrs. The reaction mix poured into ice-water (300 ml)and stirred for 0.5h at <10°C.the solid precipitated solid was collected by filtration and wash with water and recrystalized from ethyl acetate to afford the product (9.77 g,68 %), m.p 170-175°C ($C_{11}H_5ClF_3NO$) ; Requires : C, 50.89 ; H, 1.94; N,5.40%; found; C, 50.59; H, 1.90; N,5.47%).

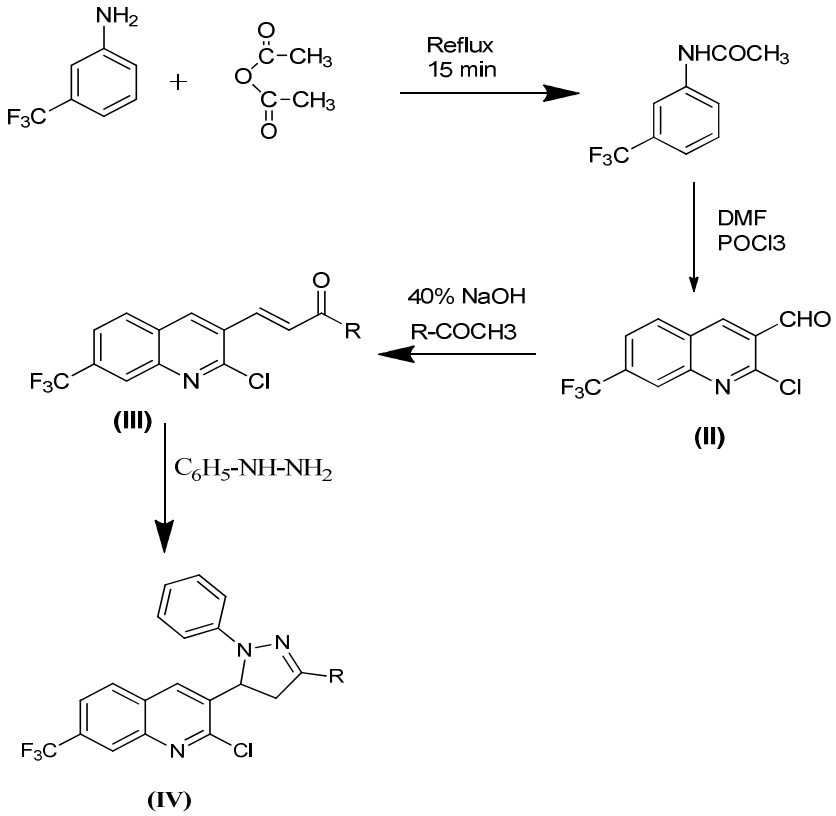
Synthesis of 3-[2-Chloro-7-(trifluoromethyl) quinoline-3-yl]-1-phenylpre-2-en-1-one:
To a well stirred solution of 2-Chloro quinoline-3-carbaldehyde (2.59 g, 0.01 M) and acetophenone (1.5 g, 0.01 M) in ethanol (25 ml), 40% NaOH added till the solution become basic. The reaction mixture was stirred for 24 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol. Yield, 3.72 g (94%), m.p.160-164°C.

($C_{19}H_{11}ClF_3NO$; Requires: C, 63.08; H, 3.06; N, 3.87%; found: C,63.92; H, 3.15; N, 3.80%). TLC solvent system Acetone: Benzene (1:9).

Synthesis of 2-chloro-3-(-1,3-diphenyl-4,5-dihydro-1H-pyrazole-5-yl)-7-(trifluoromethyl) quinoline

A mixture of 3-[2-Chloro-7-(trifluoromethyl) quinoline-3-yl]-1- Phenylpre-2-en-1-one (3.6 g, 0.01 M), phenyl hydrazine (1.08 g, 0.01 M) in 25 ml methanol was reflux for 12 hrs. in presence of basic catalyst piperidine. The reaction product was poured into ice, crude product was isolated, crystallized from dioxan. Yield, 3.6 g (81%), m.p. 244°C. (C25H17ClF3N3; Requires: C, 66.45; H, 3.79; N, 9.30%; found : C, 66.50; H, 3.75; N, 9.36%). TLC solvent system Acetone : Benzene (2:8).

Reaction Scheme



RESULTS AND DISCUSSION

All the synthesized final compounds were first purified by successive recrystallization using appropriate solvents. The purity of the synthesized compounds was checked by performing thin layer chromatography and determining melting points. Then the synthesized compounds were subjected to spectral analysis such as IR and NMR to confirm the structures. All the analytical details show satisfactory results. Our titled compounds are known to possess antimicrobial activity; the compounds were screened for their antibacterial and antifungal activity by cup-plate method. Two gram positive bacteria such as *B.mega*, and *S.aureus* two gram negative bacteria such as *E.coli* and *P.valgaris* and a fungal species such as *A.Niger* is tested for the activities. The concentration of 40 μg/ml of our titled compounds has been used. Ampicillin, Amoxicilline, Norfloxacin and Penicilline have been used as standards for anti-bacterial activity and greseofulvin have been used as standards for anti-fungal activity. All the compounds have shown mild to moderate activities.

^{1}H NMR Spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy is one of the latest physical methods of investigating organic compounds. The scale of the spectrum is usually marked in parts per million (ppm) of the applied field or infrequency units (Hz). ^{1}H-NMR spectra were recorded on Bruker WM 400FT MHz NMR instrument using $CDCl_3$

or DMSO-d_6 as solvent and TMS as internal reference. The data of compounds of pyrazoline is summarized in Table -2.

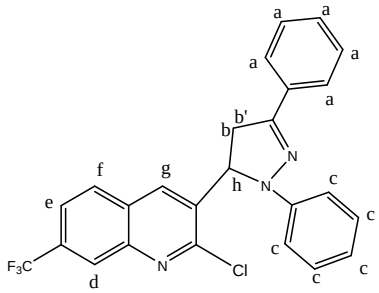
Infrared spectra

The systematic interpretation of the infra-red spectrum is based upon the empirical data obtained by assigning infrared absorption values to the structural units a characteristic of different structural units. Infra-red spectra were recorded in KBr on a Shimadzu FTIR spectrophotometer. The data of the structure is summarized in Table-3.

Table-1: Characterization Table of Physical constants of 2-chloro-3-(1-phenyl-3-aryl-4,5-dihydro-1H-pyrazole-5-yl)-7-(trifluoromethyl) quinoline

Sr No	Molecular Formula	R	Molecular Weight	M.P °C	Yield %
1a	$C_{25}H_{17}ClF_3N_3O$	4-OH-C_6H_4-	467.87	218	75
1b	$C_{25}H_{16}ClF_3N_4O_2$	4-NO_2- C_6H_4-	496.87	293	82
1c	$C_{22}H_{14}ClF_3N_4S$	2-C_4H_3S -	458.89	272	76
1d	$C_{25}H_{16}Cl_2F_3N_3$	2-Cl- C_6H_4-	486.32	280	70
1e	$C_{26}H_{19}ClF_3N_3O$	4-OCH_3-	481.90	250	88
1f	$C_{25}H_{16}BrClF_3N_3$	4-Br-C_6H_4-	530.77	273	86
1g	$C_{25}H_{16}ClF_4N_3$	4-F- C_6H_4-	469.86	258	73
1h	$C_{25}H_{16}Cl_2F_3N_3$	4-Cl- C_6H_4-	486.32	268	85
1i	$C_{26}H_{19}ClF_3N_3$	4-CH_3- C_6H_4-	465.90	215	71
1j	$C_{25}H_{17}ClF_3N_3$	C_6H_5-	451.87	244	81

Table-2



Proton value				
signal	Signal Position (δ ppm)	Relative No of Protons	multiplicity	Inference
1	3.81-3.82	1H	d	b
2	4.21-4.22	1H	d	b’
3	5.41-5.43	1H	m	h
4	7.08-7.27	5H	m	a
5	7.41-7.43	2H	d	e,g
6	7.80-7.82	1H	d	d
7	7.85-7.98	5H	m	c
8	8.21-8.24	1H	d	f

Table-3

Type	Vibration mode	Frequency in cm-1
Amine	C=N stretching	1596
Alkenes	C-H stretching	2925
Halide	C-F stretching	1319
	C-Cl stretching	756

Table:4- Biological Activity

Compounds	*B.mega*	*S.aureus*	*E.coli*	*P.valgaris*	*A.niger*
1a	20	19	20	10	13
1b	15	15	17	14	22
1c	11	12	14	12	14
1d	10	20	14	9	10
1e	23	18	13	17	21
1f	13	14	11	18	16
1g	9	13	16	11	14
1h	10	19	10	13	10
1i	12	15	15	18	18
1j	14	12	19	13	20
Ampicillin	23	22	21	25	-
Amoxicillin	22	23	21	24	-
Norfloxacin	24	17	23	19	-
Penicillin	25	24	19	20	-
Greseofulvin	-	-	-	-	25

CONCLUSION

The work has approached towards the synthetic and biological approach of these wonder molecules. Anti-bacterial property of the synthesized compounds has exhibited very good inhibition; all compounds have exhibited mild activity towards gram positive bacteria *B. mega, S. aureous*, when all compounds shows mild activity against gram negative bacteria *E. coli* and *P. aeruginosa* as compare to four standard. But the systematic substitution at various position and other derived compounds have shown remarkable antifungal properties. The compounds 1e have exhibited outstanding activity towards *B.mega* and no any other compound has shown good antifungal activity.

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