J. Chemtracks 23 (1&2) 157-162, 2021

Abstracted / Indexed in
A division of the American Chemical Society
Chemical Abstract U.S.A.

ISSN 0973-239X
CODEN:JCOHF7
IMPACT FACTOR : 4.950

Antimicrobial and insecticidal studies of newly synthesized cinnoline based chalcones derivatives

R. N. Singh
Department of Chemistry, Lecturer New Govt. Polytechnic Patna-13
Email : drsinghch@gmail.com

Manuscript received online 25 June 2021, accepted on 30 August 2021

Abstract : 4-methyl-3-propenyl cinnoline used as a precursor to synthesis some new cinnoline based chalcones 3a-1. The reaction of aniline water and sodium nitrite in 1 N HCL at 0ºC gave benzene diazonium chloride solution. Further the benzene diazonium chloride on treatment with acetyl butanone and ethanol gave pheyl hydrazonoacetyl butanone. In this step Griess diazo reaction takes place which on reaction with plyphosphoric acid and after extraction with ethyl acetate has given 4-methyl-3-propenyl cinnoline 2. The spectral of synthesises of synthesized compounds have been confirmed by elemental analysis, IR and NMR spectral studies and evaluated for antibacterial activity against Bacilus subtilis, Escherichia flavus, Fausarium oxysporum, Aspergillus neigther and Trichodama viridae and insecticidal activity against Periplanets Americana.

(Keywords : Cimmoline, antibacterial activity, antifungal activity and insecticidal activity)

Introduction

Heterocyclic nitrogenous compounds and their fused analogs represent in important class of heterocyclic compounds. They exhibit in numerous natural products, displaying a wide spectrum of action on Escherichia coli.[2] Cinno cabominles have been reported as baceteriocides[3] and recent studies have shown that cinnoline and its derrivates exhibit biological activity such as antihypertensive, antiumour, antisecretory, anti-inflamatory, antipyretics and bactericidal.

Experimental

All the melting points were determined in open capillary and are uncorrected. The reactions were mentiored on TLC. The infra red spectra were carried out in KBr pellets on a Shimadzu 8201 PC Spectrophotometer. H^1 NMR spectra on an AVANCE II 400 NMR spectrometer with $CDCl_3$ as a solvent, using TMS as internal reference (Chemical shift in 8 ppm), and elemental analysis of synthesized compounds have been carried out on a Carlo-Elba 1108 model analyser.

Synthesis of phenylhydrazonacetyl butanone:

Benzene diazonium chloride was prepared by dissolving sodium nitrite (7.4g, 0.1 mole) in 26ml of water adding it dropwise to solution analine (10g, 0.1 mole) in N HCl (200 ml) at 0ºC while stirring. The temperature was maintained at 0ºC for another 10 min under stirring. Benzene diazonium chloride solution was added to a well stirred solution of ethanol (39 ml), water (500 ml) and acetyl butanone (10.01g. 0.1 mole) at 0ºC with stirring.

To keep the mixture alkaline to litmus, sodium acetate was added, after 3 hr. stirring at 0ºC, the oxide product was filtered, washed with water and ice dried. Reerystallisation from ethanol afforded yellow needles of purified phenyl hydrazono acetayl butanone with a yield of 16.1g (78%) IR (KB cm^{-1}): 3425 (broad enolic–OH) 2980 (C–H, CH_3), 3080 (Ar–H), 1236.2 (N–N), 1682 (C=O), 824 (disubsitued benzene ring);[3] H NMR ($CDCl_3$) : δ 14.6 (S, enolic OH) 7.3–7.5 (m, Ar-H), 2.3 (s, -CH_3), 2.5 (3,–CH_3), 1.6 (s,–CH), 1.6(s–CH)

Synthesis of 4-methyl-3-propenyl carbodine 2:

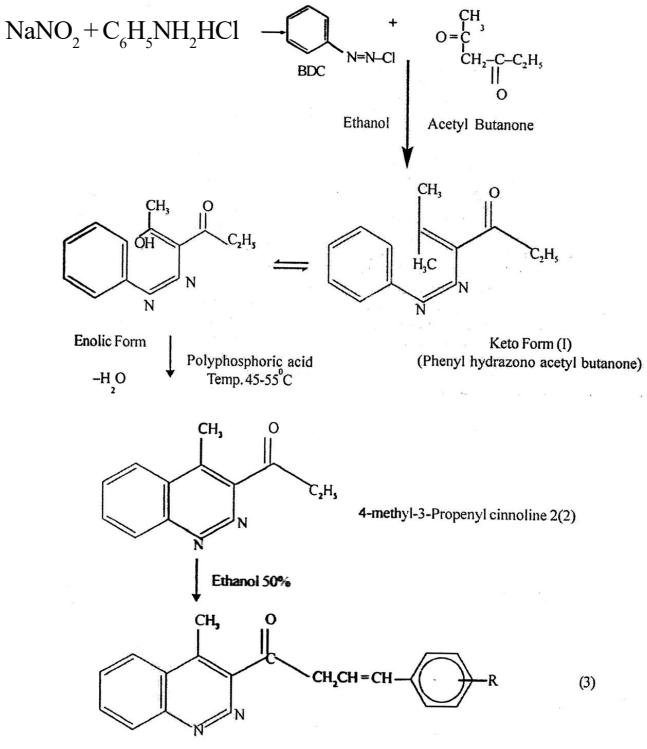
Phynilhydrazono acetyl butanone (10g,

0.05 mole) was added to poly phosphorice acid (15gm, 7.210 ml, 0.03 mole) in small lots over 30 min while maintaining the temperature between 45-55ºC The reaction was maintained for an additional 2 hr. Reaction was monitored by TLC. After the completion of the reaction, Chilled water (200ml) was added carefully to decompose the brownish black residue at 0-5ºC. The product was then extracted with ethyl acetage. Ethyl acetate layer was then treated in with charcoal and concentered to get crude product as a black residue.

After purification by recystallisation from methanol 4-methyl 1-3 propenyl Cinnoline 2 was obtained as pale yellow crystals with a yield of 1.2g (21%); IR (KBr cm^{-1}) (–CN=N) and 1198 cm^{-1} (–N=N-C);^{1}HNMR ($CDCl_3$); δ2.8 (5, $-CH_3$), 9.0(d, Ar-H), 8.2(d, Ar-H), 7.8(t, Ar,H)

Synthesis of 1-(4-methyl cinnoline -3-yl), -3(substituted phenyl) but-2-ene-1-one | cinnoline based chalcone] 3a–1.

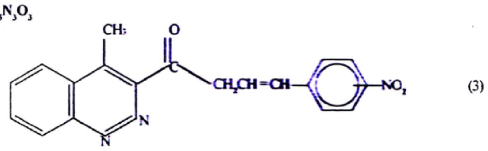
The compound 4-methyle-3-propenyl Cinnoline 2(2.01g, 0.01) and m-nitro benzaldehyde in same ratio (1.50g. 0.01 mole) in ethanol (50ml) was taken at 0-5ºC and added (5-10 ml) 40% NaOH solution till precipited and washed with ice water. Few drops of N 30 for HC was added for complete precipitation and filtered, washed with water and recrystallised from alcohol to afford the compound 3(a). Physical data of synthesized compounds are given Table 3a, IR KBr cm^{-1}) 2988.96 (C–H), 3083 (Ar-H). 1446 (C =C), 1693 (C=O), 882 (cinnoline ring). 1190 (N–N) 822 (cinnoline ring). 1190 (N–NL 822 (disubstituted aromatic ring)^1, H NMR ($CDCl_3$); δ3.408 (s, 3H, CH_3), 4.118 (d 1H; - CH=CH–)4.738 (unsym, m, 4H, $C_6H_4NO_2$)



Analytical data of compound 3a to 31

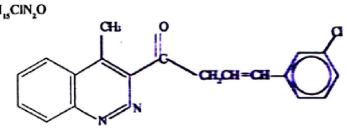
S.No.	Compound	Molecular formula	Mol. Wt.	Yield %	mp °C	Nitrogen
1.	3a	$C_{19}H_{15}N_3O_3$	333.31	87	97°C	12.98
2.	3b	$C_{19}H_{15}ClN_2O$	322.76	82	103°C	9.02
3.	3c	$C_{19}H_{15}ClN_2O$	322.76	79	105°C	9.02
4.	3d	$C_{19}H_{15}ClN_2O$	322.76	78	104°C	9.02
5.	3e	$C_{19}H_{15}BrN_2O$	366.12	98	91°C	8.11
6.	3f	$C_{28}H_{13}N_2O_2$	333.31	95	92°C	11.22
7.	3g	$C_{28}H_{15}N_3O_3$	318.32	91	88°C	9.88
8.	3h	$C_{14}H_{15}N_3O_3$	333.31	90	9°C	11.22
9.	3i	$C_{14}H_{16}N_2O_2$	304.32	89	102°C	13.10
10.	3j	$C_{19}H_{16}N_2O_2$	304.32	88	126°C	13.10
11.	3k	$C_{20}H_{18}N_2O_2$	334.14	87	131°C	10.11
12.	3l	$C_{21}H_{20}N_3O$	333.44	79	134°C	10.11

3(a) $C_{19}H_{15}N_3O_3$

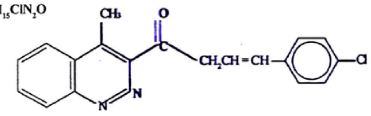


(3)

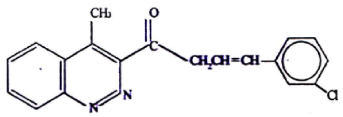
3(b) $C_{19}H_{15}ClN_2O$



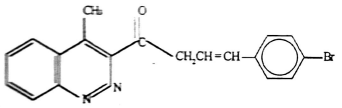
3(c) $C_{19}H_{15}ClN_2O$



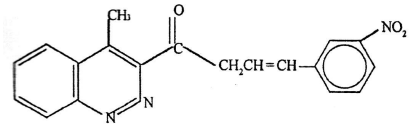
3(d) $C_{19}H_{15}ClN_2O$



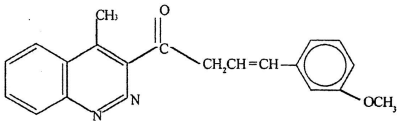
3(e) $C_{19}H_{15}BrN_{2O}$



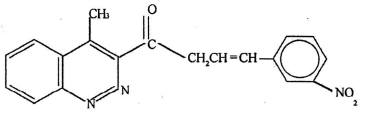
3(f) $C_3H_{25}N_3O_3$



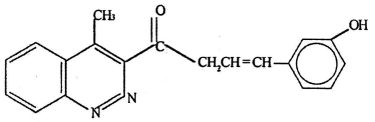
3(h) $C_{22}H_{18}N_2N_2$



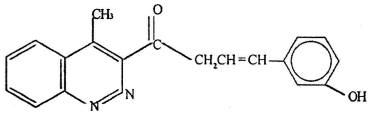
3(g) $C_{19}H_{15}N_3O_3$



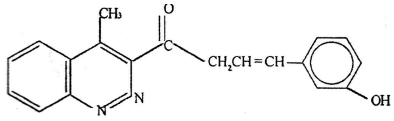
3(h) $C_5H_5N_2O_3$



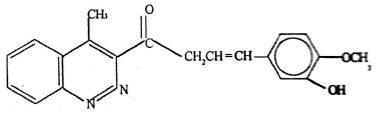
3(i) $C_5H_5N_2O_3$



3(j) $C_{19}H_{16}N_2O_2$



3(k) $C_{20}H_{18}N_2O_2$



3(l) $C_{21}H_{20}N_3O$

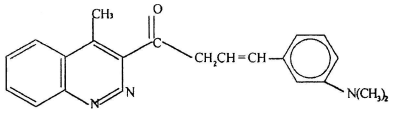


Table - II Antibacterial activity of the compounds 3a-1

Compound	*B.sublilis* (conc. ppm)		*E.coli* (conc. ppm)		*K.pneumonia* (conc. ppm)		*S.aureus* (conc. ppm)	
	100	500	100	500	100	500	100	500
3a	+	++	++	++	+	++	++	+++
3b	++	+	+	++	+	++	-	-
3c	++	++	+	++	++	+++	+	++
3d	++	++++	++	++	++	++	+++	++
3e	++	++	++	++	+	++	+	++
3f	++	++	+	++	++	++	++	+++
3g	+	++	++	++	+	++	++	++
3h	+	++	++	++	+	++	++	++
3i	+	++	++	++	++	++	++	+++
3j	++	++	+	+++	+	++	+	+
3k	+	++	+	++	++	++	+	+
3l	+	++	+	++	++	++	+	+
Std	+++	++++	++++	++++	++++	++++	++++	++++

Std. Streptomycin; inhibition diameter in mm : (-) 4; (+) 5-11; (++) 11-15; (+++) 15-19, (++++) 19-24

Table - II
Antibacterial activity of the compounds 3a-1

Compound	*B.sublilis* (conc. ppm)		*E.coli* (conc. ppm)		*K.pneumonia* (conc. ppm)		*S.aureus* (conc. ppm)	
	100	500	100	500	100	500	100	500
3a	+	++	++	++	+	++	++	+++
3b	++	+	+	++	+	++	-	-
3c	++	++	+	++	++	+++	+	++
3d	++	++++	++	++	++	++	+++	++
3e	++	++	++	++	+	++	+	++
3f	++	++	+	++	++	++	++	+++
3g	+	++	++	++	+	++	++	++
3h	+	++	++	++	+	++	++	++
3i	+	++	++	++	++	++	++	+++
3j	++	++	+	+++	+	++	+	+
3k	+	++	+	++	++	++	+	+
3l	+	++	+	++	++	++	+	+
Std	+++	++++	++++	++++	++++	++++	++++	++++

Std. Streptomycin; inhibition diameter in mm : (-) 4; (+) 5-11; (++) 11-15; (+++) 15-19, (++++) 19-24

Table - IV
Insecticidal activity of compound 3a-1 against periplaneta Americana (K1) value in mintues

Compound	Time 1%	(minutes) 2%
3a	9	8
3b	6	4
3c	7	3
3d	5	4
3e	11	10
3f	14	9
3g	9	8
3h	11	8
3i	11	9
3j	12	9
3k	13	11
3l	12	10
Std.	7	5

Results and Discussion

The reaction of aniline water and sodium nitrite in 1N HCl at 0^0C gave benzene diazonium chloride solution. Further the benzene diazonium chloride on treatment with acetyl butanone and ethanol gave phenyl hydrazonoacetyl butanone. In this step Griess diazo reaction takes plac -[5] which on reaction with polyphosphoric acid and after extraction with ethyl acetae have given[4] methyl-3-propenyl cinnoline 2 was carried out by intramolecular. The use of phosphoric acid is only for cyclisation.

4-methyl-3-propenyl cinnocline 2 reached with various substituted aldehydes to give cinnoline based chakcone 3a-1 of corresponding aldehyde in quantative yield. The compounds 3a-1 were screened for their antimicrobial and insectual activities (Table 1-III).

The compounds have been screened for their antifungal activity against *Aspergillus flavus*. *Fusarium oxysporum*, *Aspergillus niger* and *Trichderma virdae* by filter paper disc plate method at two different concentrations (100 ppm and 500 ppm) and antibuterial activity against *Bascillus subtills*. *Escherichia coli, Stapyloccus auraeaus* and *Klebsiella pneumniae* at two different concetrations (50 ppm and 100 ppm) by filter paper disc plate method standard antifungal drug griseflavin and antibacterial drug streptomycin

have also been screened under the similar conditions for comparison.

The cockroach (*Periplanta americana*) has been selected for insecticidal activity study and 1% and 2% solutions of prepared compounds (0.1 mole) were injected in the abdominal region of cockroach with the help of micro-syringe. The time of death was noted as KD (Knock Down) value standard drug cypermethrin was also used under similar conditions for comparison.

At the time of death the antennae became motionless the appendages shrunk and folded towards the ventral side and cockroach laid dorsally.

On going through the result of biological activity of synthesized compounds 3a-1 shows that 3d, 3f and 3h are highly active against both selected bacteria and fungi and rest of compounds have shown good to moderate activity. All chloro derivatives of 3 series 3b, 3c, and 3d have shown better insecticidal activity in compounds have been shown good to moderate activity.

The compounds which were synthesized in laboratory shown significant application in antimicrobial, anticancer and insecticidal properties. This may fruitful to render sercies to humanity.

Acknowledgements

The authors feel a lot of gratitude to TERI, New Delhi for providing NMR and analytical data of compound. The authors are also thankful to our rev. Chairman Mr. Dev Murti Sir for providing smooth research facilities.

References

1. H.G. Sangani, K.B. Bhimani and R.C. Khunt, *J. Serb. Chem. Soc*. **71(6)**, 587 (2009)
2. J.C.E. Simpson, Condensed Pridazines and Pyrazine rings (Cinnolines, Phthalzines and Quinoxalins), (Interscience Publishers, New York), (1953).
3. H.Eisako, JP 7010349, *Cem. Abstr.* **73**, 45529 (1970)
4. P.Griess. *Annulenes,* **106**, 123 (1858)
5. V. K. Ahulwalia and agarwal Rena, Comprehensive Practical Organic Chemistry, 54(2000)
6. A. Pandey and V. K. Saxena , *Indian J.Chem.* **16B,** 390 (1987)
7. H.V. Patel, P.S. Fernades and K.A. Vyas *Indian J. Chem.* **29B,** 135 (1990)
8. H.S. Cen and Z.M. Li, *Chinese J.Chem.* **11**, 596 (2000)
9. B.Narayan, K.K. Vijaya Raj Ashalana B. Indian J. Chem. 45B, 1704 (2006)
10. R.G. Menon and E. Purushotoman, *Indian J. chem.* **35B**, 1115 (1996)