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Synthesis and Characterization of Some Cyanopyridine Compounds in Therapeutic Interest

K.S.Parikh* & R.P.Patel

Chemistry Department,Sheth Motilal Nyalchand Science College,

Rajmahel Road,PATAN – 384265,INDIA

E-mail : * ksparikh64@yahoo.co.in, rakeshp.patel@alembic.co.in

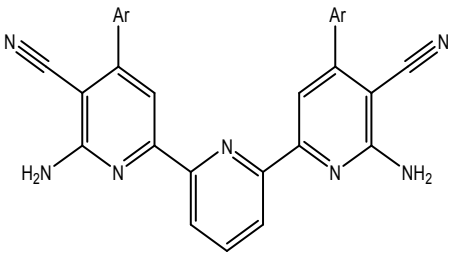
Abstract:4-[6-bromo-2,7,8-trichloroquinoline-3-yl)-6-phenyl-2-methoxy-3-cyanopyridine synthesed by the condensation of malononitrile and sodium methoxide with 3-[6-bromo-2,7,8-trichloro quinoline-3'-yl]-1-arylprop-2-en-1-one.The product is characterized by conventional and instrumental methods.Their structure was found and important biochemical properties were studied.

Key words: Cyanopyridine Compounds.

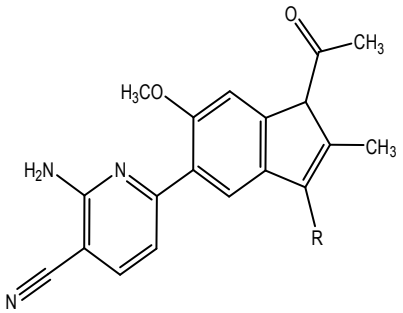
Introduction

Cyanopyridine have attracted considerable attention as they appeared of interest to possess antibacterial, anticholestermic, antifungal, antihypertensive and antidiabetic activities. Thiele Kurt et. al. have studied the analgesic activity of substituted 3-cyanopyridines. N. Latif and co-workers have reported the antibacterial and antifungal activity of 2-amino-3-cyano-4,6- disubstituted pyridines. M. Bernard and co-worker[12] reported the anticonvulsant activity of 3-cyanopyridines. D. G. Bhatt et. al. have prepared 3-cyanopyridines as an immunosuppressive agent. U. Teu and co-worker have shown cyanopyridine as agrochemical fungicides.

Hammana Abou and co-worker have studied anticancer and anti HIV activity of 3-cyanopyridines. Abdallah Navine et. al. have prepared cyanopyridine derivatives which showed analgesic and anti-inflammatory activity. Manna Fedele and co-worker have reported the anti-inflammatory activity of 3-cyanopyridines. H. Yoshida et. al. have studied the antihistamic and antiallergic activity of 3-cyanopyridine derivatives



(IV)



(V)

Abd El-Galil and coworker have prepared 3-cyanopyridines (IV) and studied their pharmacological activity. Gadaginamath and co-worker have synthesized various cyanopyridyl derivatives (V) and documented their variety of biological activities.

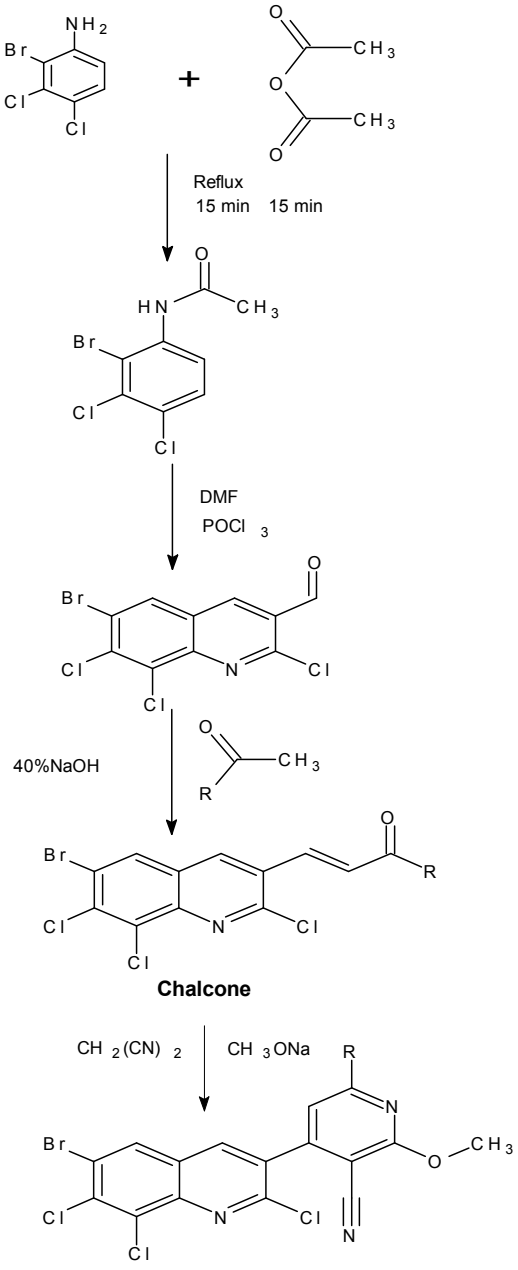
Herein, we reported some Cyanopyridine compounds with excellent antifungal activity and to a some antibacterial activity.

Result and discussion

In the studies reported here, we were able to identify quinoline derivatives that inhibited PrPres accumulation in ScNB cells. The commonly shared structure in these chemicals was a quinoline ring bound at its 2 or 4 position with a side chain containing a nitrogen atom, which was located at a particular distance from a nitrogen atom in the ring. Chemicals with a side chain at the 2 position of a quinoline ring were more effective than those with a side chain at the 4 position. Replacement of a quinoline ring with a pyridine ring or a naphthyridine ring resulted in a weaker inhibiting activity, while modification of biquinoline by a moiety that caused less flexibility in the hinge portion between the quinoline rings completely suppressed the inhibiting activity. These findings suggest that a certain proper alignment of two nitrogens, one in a quinoline ring and the other in a side chain, might be important with regard to inhibiting activity.

The physical and analytical data are presented in table-1. antibacterial and antifungal activity of the compound was determined by agar diffusion method. The result is presented respectively in table-4 and table-5. The antifungal activity of this compound is even similar the standard drug Nystatin. Among all compounds 4gm was found best active agent against C.albicans. The compounds j,d,e,f were found good active against E.coli, S.aureus, and B.subtilis. The compounds e,a were shows good activity against A.Niger.

*** Reaction scheme ***



Where Ar = substituted aromatic Amine.

Experimental

Solvent from Merch,Lancaster & Aldrich were redistilled used in all the experiments. Purity of all starting compounds checked by TLC method (alumina) U/V & iodine vapour as the detecting agent. M.Ps were determined in meltingpoint apparatus. IR Spectra (KBr pellets) were recorded on a Perkin-Elmer 577 Spectrophotometer, NMR Spectra(DMSO) on Brucker spectrophotometer using TMS as internal reference.

SYNTHESIS AND BIOLOGICAL EVALUATION OF 4-[6-BROMO-2,7,8-TRICHLORO QUINOLINE-3-YL)-6- PHENYL-2-METHOXY-3-CYANO PYRIDINE

In the past years, considerable evidence has been accumulated to demonstrate the efficience of cyanopyridines. To further assess the potential of such a class of compounds cyanopyridine derivatives of type (II) have been synthesized by the condensation of malononitrile and sodium methoxide with 3-[6-bromo-2,7,8-trichloro quinoline-3'-yl]-1-arylprop-2-en-1-one.

Spectral Analysis

IR Spectra

IR spectrum of compound IVa showed the appearance of an absorption bands at 2922cm$^{-1.}$ for C-H stretching vibration. Strong C=N stretching bands were observed at1589cm^{-1}.StrongC$^{\equiv}$N were observed at 2221 cm^{-1} Strong Ether C-O-C (sym) observed at 1219 cm^{-1} and C-O-C (asym) observed at 1047 cm^{-1} Strong C-Br stretching bands were observed at 605 cm^{-1}. Strong C-Cl stretching bands were observed at 756cm^{-1}.

Compound IVb showed an absorption bands at 2929cm$^{-1.}$ for C-H stretching vibration. Strong C=N stretching bands at1575cm^{-1}.StrongC$^{\equiv}$N at 2229 cm^{-1} Strong Ether C-O-C (sym) observed at1222 cm^{-1} and C-O-C (asym) observed at 1047 cm^{-1} Strong C-Br stretching bands were observed at 687 cm^{-1}. Strong C-Cl stretching bands were observed at 750cm^{-1}.

Table 1: IR spectral data (cm-1) of compounds.

Compound	-C-H Ar	C-O-C(sym)	C$^{\equiv}$N	-C=N	-C-Br	-C-Cl
4a	2922	1219	2221	1589	686	756
4b	2929	1222	2229	1575	687	750
4c	2949	1233	2242	1608	685	768
4d	2958	1226	2230	1582	683	770

NMR Spectra

PMR SPECTRAL STUDY OF 4-[6-BROMO-2,7,8-TRICHLORO QUINOLINE-3-YL)-6- PHENYL-2-METHOXY-3-CYANO PYRIDINE

The 1H NMR spectrum of compound IIIa showed a multiplet at δ 7.46 -7.48 for three protons 'b' & 8.36 for two protons 'c' of benzene ring. A singlet at 4.01 for three proton 'a" as related methoxy group. A multiplet at δ 7.78 & 8.68 accounted for the two protons attached with quinoline ring as proton 'e' and 'f' .A multiplet at δ 7.78 for proton "d" as related to pyridine ring.

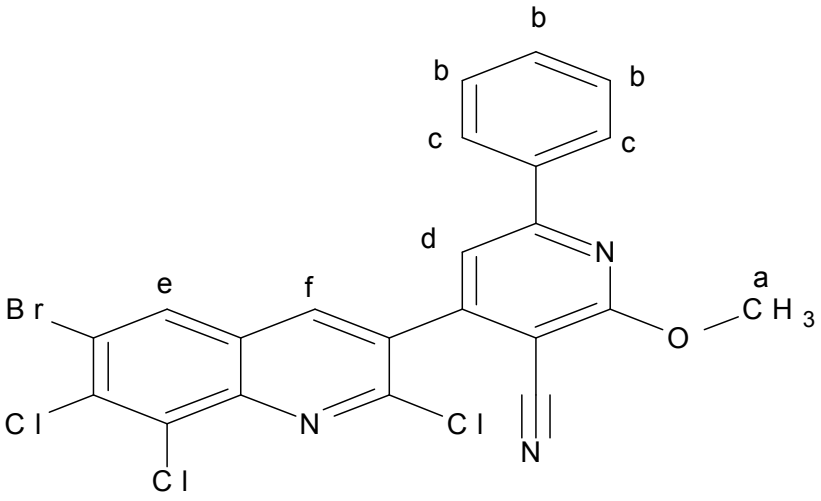


Table-2

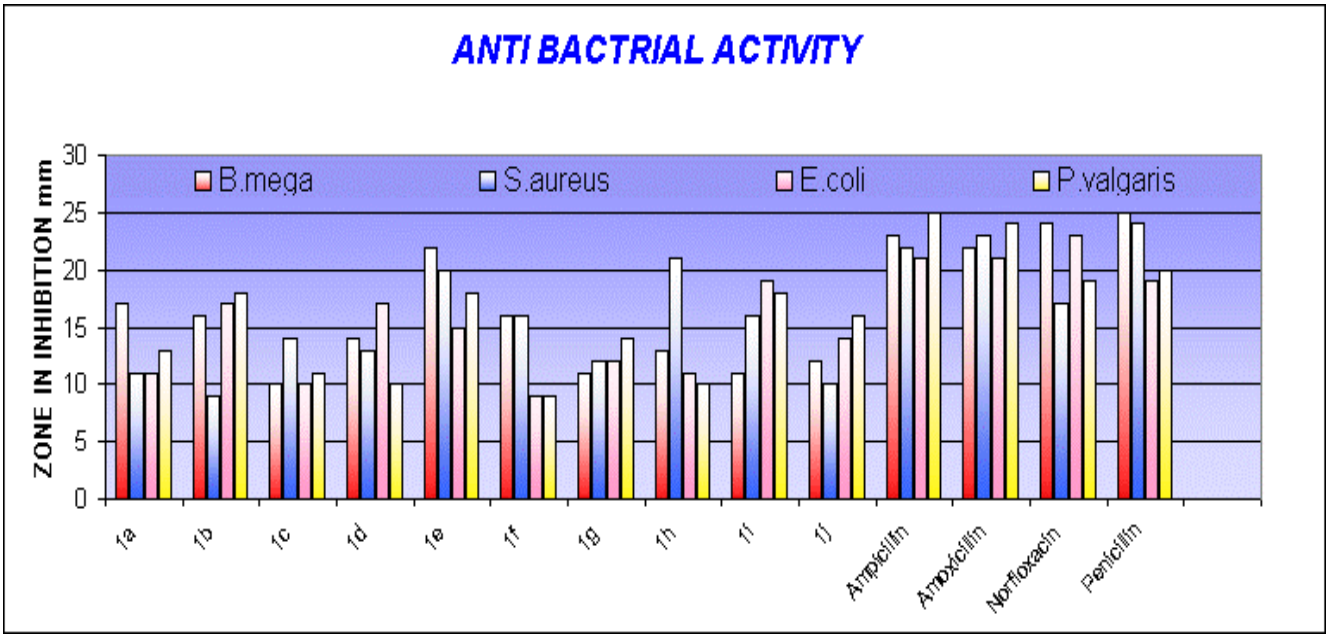
Signal No	Signal Position (δ ppm)	Relative No Of Protons	Multiplicity	Inference
1	4.01	3H	Singlet	-OCH3 a
2	7.46-7.48	3H	Multiplet	-Ph b
3	8.30	2H	Multiplet	-Ph c
4	7.78	1H	Multiplet	CH d
5	7.86	1H	Multiplet	CH e
6	8.63	1H	Multiplet	CH f

Table-3

Sr No	Molecular Formula	R	M.W.	M.P °C	Yield %	%Br Cal. (found)	%C Cal. (found)	%N Cal. (found)
1a	**$C_{22}H_{11}BrCl_3N_3O_2$**	4-OH-C_6H_4-	535.6	179°C	69	14.92 (14.88)	19.86 (19.81)	7.85 (7.82)
1b	**$C_{22}H_{10}BrCl_3N_4O_3$**	4-NO_2- C_6H_4-	564.6	186°C	74	14.15 (14.11)	18.84 (18.81)	9.92 (9.86)
1c	**$C_{19}H_8BrCl_3N_4OS$**	2-C_4H_3S -	526.6	188°C	71	15.17 (15.14)	20.20 (20.16)	10.64 (10.59)
1d	**$C_{22}H_{10}BrCl_4N_3O$**	2-Cl- C_6H_4-	554	172°C	76	14.42 (14.46)	25.60 (25.57)	7.58 (7.54)
1e	**$C_{23}H_{13}BrCl_3N_3O_2$**	4-OCH_3-	549.6	189°C	69	14.54 (14.49)	19.35 (19.31)	7.65 (7.62)
1f	**$C_{22}H_{10}Br_2Cl_3N_3O$**	4-Br-C_6H_4-	598.5	177°C	76	26.70 (26.68)	17.77 (17.73)	7.02 (7.06)
1g	**$C_{22}H_{10}BrCl_3FN_3O$**	4-F- C_6H_4-	537.6	166°C	69	14.80 (14.77)	19.78 (19.81)	7.82 (7.78)
1h	**$C_{22}H_{10}BrCl_4N_3O$**	4-Cl- C_6H_4-	554	183°C	78	14.42 (14.38)	25.60 (25.58)	7.58 (7.56)
1i	**$C_{23}H_{15}BrCl_3N_3O$**	4-CH_3- C_6H_4-	533.6	168°C	71	14.97 (14.98)	19.93 (19.91)	7.87 (7.85)
1j	**$C_{22}H_{11}BrCl_3N_3O$**	C_6H_5-	519.6	196°C	78	15.38 (15.42)	20.47 (20.43)	8.09 (8.04)

Chart No-6.1

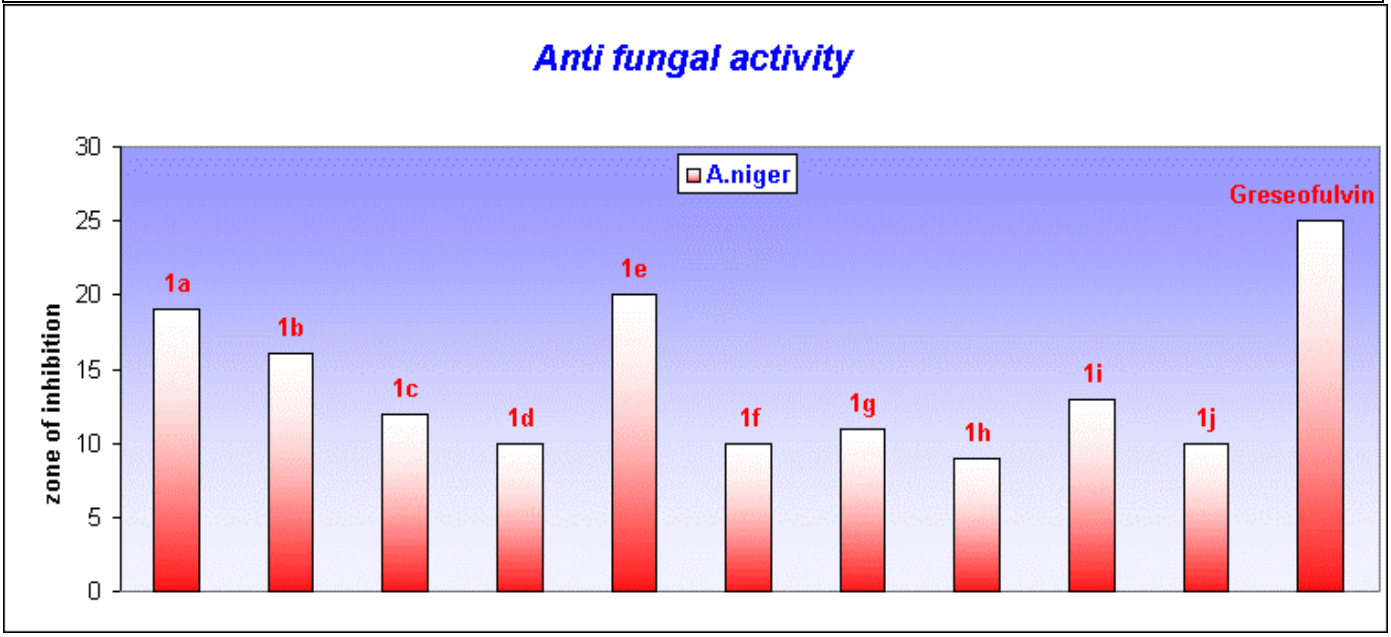
COMPARATIVE STUDY OF ANTIMICROBIAL ACTIVITY OF 6-BROMO-2,7,8-TRICHLORO QUINOLINE-3-YL)-6- PHENYL-2-METHOXY-3-CYANO PYRIDINE.



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

Chart No-6.2

COMPARATIVE STUDY OF ANTIFUNGAL ACTIVITY OF 6-BROMO-2,7,8-TRICHLORO QUINOLINE-3-YL)-6- PHENYL-2-METHOXY-3-CYANO PYRIDINE.



	1a	1b	1c	1d	1e	1f	1g	1h	1i	1j	Greseofulvin
A.niger	19	16	12	10	20	10	11	9	13	10	25

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