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Synthesis and Characterization of Some Arylamino Derivatives of Chloroquinoline as Antimicrobial Agents

Bhimani Kanji B., Khunt Ranjan C., Sangani Harhsad G., Dhol Snehal R., Detroja Dilip P., Parikh Arun R.*

Department of Chemistry, Saurashtra University, Rajkot, India

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Abstract

Substituted Schiff's bases (2a-m) have been prepared by the treatment of 2-chloro-6-methxoyquinoline-3-carbaldehyde (1) with different arylamines, which on reaction with $NaBH_4$ furnish our target molecule (3a-m). The structures of the synthesised compounds have been assigned on the basis of elemental analyses, IR, NMR and mass spectral studies. The compounds were evaluated for antimicrobial screening against Gram positive & Gram negative bacteria and fungal strain such as *Aspergillus niger*. Most of the compounds showed significant activity against all the species of bacteria and fungi.

Keywords: Aryl amines, 2-Chloro-6-methoxyquinoline-3-carbaldehyde and antimicrobial activity.

Introduction

Literature survey reveals that arylamines are associated with wide range of pharmacological activities such as anti-infective [1] and other therapeutic activity [2-3]. Moreover quinoline nucleus also possesses bactericidal [4-5], antimalarial [6] and antitumor [7] activity. These valid observations lead us to synthesize same arylamine derivative bearing quinoline nucleus.

The starting compounds 2-chloro-6-methoxyquinolin-3-carbaldehyde **(1)** on treatment with different aromatic amine in ethanol afforded corresponding (2-chloro-6-methoxy quinolin-3-yl methylene)-aryl-amine **(2a-m)**. The reduction of compounds **(2a-m)** with the help of sodium borohydride affords our target compounds arylamino derivative of quinoline **(3a-m)** (scheme-1). The constitutions of all the products have been characterized using elemental analyses, IR, ^{1}H NMR and

mass spectral studies. All the compounds were screened for their antimicrobial activity against different strains of bacteria and fungi.

Materials and Methods

All the melting points are uncorrected. Thin layer chromatography was used for monitoring the reaction. IR spectra recorded on Shimadzu FT IR-8400 on KBr disc. ^{1}H NMR spectra were recorded on 300 MHz spectrophotometer using TMS as an internal standard, FAB mass spectrum was recorded on JEOL SX 102/DA 6000 spectrophotometer. All the compounds gave satisfactory elemental analyses.

Preparation of (2-chloro-6-methoxy quinolin-3-yl methylene)-aryl-amine **(2a-m)**
A mixture of 2-chloro-6-methoxyquinoline-3-carboxaldehyde (2.20 gm, 0.01 M) and *p*-anisidine (1.23 gm, 0.01 M) is refluxed in ethanol (95%) for 6 hrs. with catalytic amount gl. CH_3COOH. The contents were cooled and product was isolated, crystallized from ethanol. Yield 82% (2.67 gm), m.p. 148 ^{o}C, Anal. Calcd for $C_{18}H_{15}O_2N_2Cl$: Found : C, 66.12%; H, 4.59%; N, 8.53%; Required : C, 66.16%; H, 4.63 %; N, 8.57 IR (KBr) cm^{-1} : 1654 (C=N str.); 1571 (C=C str.); 1016 (C-O-C str.) ; 763 (C-Cl str.); ^{1}H NMR ($CDCl_3$) ; δ ppm : 3.85 (s, 3H, Ar-OCH_3), 3.92 (s, 3H, Ar-OCH_3); 6.95-8.95 (m, 9H-Ar-H & vinylic).

Similarly other compounds of (2a-m) have been prepared. The physical data are recorded in Table-1.

Preparation of (6-methoxy-quinolin-3-ylmethyl)-aryl-amine **(3a-m)**
Sodium borohydride (0.15 M, 0.57 gm) was added to a methanolic solution of (2-chloro-6-methoxyquinolin-3-ylmethylene)-(4-fluorophenyl) amine (0.01 M, 3.14 gm) over a period of 30 minutes at temperature 5-10 ^{o}C. The reaction mixture was kept at room temperature for overnight. The excess borohydride was neutralized by adding water and the product was extracted with either. Yield 56% (1.7 gm), m.p. 128 ^{o}C, Anal. Calcd for $C_{17}H_{14}FN_2OCl$; Found: C, 64.44%; H, 4.41%; N, 8.82%. Required : C, 64.46%; H, 4.45%; N, 8.84%. IR (KBr) cm^{-1} : 3062 (C-H str.), 1620 (C=N str.), 788 (C-Cl str.). ^{1}H NMR ($CDCl_3$) : δppm : 3.87 (s, 3H, Ar-OCH_3), 4.5 (s, 2H-CH_2-), 6.53-8.00 (m, 8H, Ar-H).

Similarly other members of (3a-m) have been synthesized. The physical data are recorded in Table-1.

Antimicrobial Activity
Compound **2a-m** & **3a-m** were screened for their antibacterial and antifungal activity using cup-plate agar diffusion method [8] at a concentration of 40 µg/ml, using Gram positive bacterial strains such as *Bacillus megaterium, Staphylococcus aurous* and Gram negative bacterium strain such as *Proteus vulgaris* and *Escherichia coli*. The antifungal testing was carried out against *Aspergillus niger*. Known antibiotics like Ampicillin, amoxicillin, Norfloxacin, penicillin and greseofulvin were used for comparison purpose. By visualizing the antimicrobial data, it could be observed that most of the compounds exhibited significant activity (Table-2).

Table-I: Physical constant of the compounds 2a-m and 3a-m

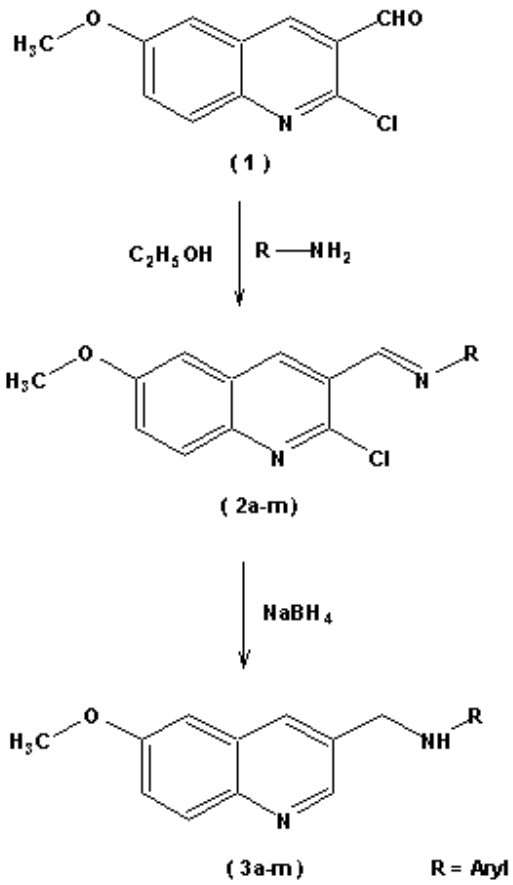
Sr. No.	R	Molecular Formula	M.P. ^{o}C	Yield %	Rf* Value	% of Nitrogen Calcd.	Found
2a	C_6H_5-	$C_{17}H_{13}ON_2Cl$	96	0.43	68	9.44	9.41
2b	2-Cl-C_6H_4-	$C_{17}H_{12}ON_2Cl_2$	125	0.58	65	8.46	8.43
2c	3-Cl-C_6H_4-	$C_{17}H_{12}ON_2Cl_2$	152	0.55	63	8.46	8.42
2d	4-Cl-C_6H_4-	$C_{17}H_{12}ON_2Cl_2$	155	0.56	63	8.46	8.45
2e	4-CH_3-C_6H_4-	$C_{18}H_{15}ON_2Cl$	120	0.53	69	9.01	9.04
2f	3-CH_3-C_6H_4-	$C_{18}H_{15}ON_2Cl$	131	0.50	68	9.01	9.06
2g	4-CH_3-C_6H_4-	$C_{18}H_{15}ON_2Cl$	174	0.61	65	9.01	9.00
2h	2-NO_2-C_6H_4-	$C_{17}H_{12}O_3N_3Cl$	164	0.57	64	12.30	12.34
2i	3-NO_2-C_6H_4-	$C_{17}H_{12}O_3N_3Cl$	188	0.50	83	12.30	12.28
2j	4-NO_2-C_6H_4-	$C_{17}H_{12}O_3N_3Cl$	236	0.53	81	12.30	12.27
2k	3-Cl,4-F-CH_3-	$C_{17}H_{11}ON_2Cl_2F$	130	0.48	73	8.02	8.00
2l	4-OCH_3-C6H4-	$C_{18}H_{15}O_2N_2Cl$	148	0.47	82	8.57	8.53
2m	4-F-C_6H_4	$C_{17}H_{12}ON_2FCl$	182	0.51	68	8.90	8.87
3a	C_6H_5-	$C_{17}H_{15}ON_2Cl$	108	0.43	53	9.38	9.34
3b	2-Cl-C_6H_4-	$C_{17}H_{14}ON_2Cl_2$	87	0.45	61	8.41	8.45
3c	3-Cl-C_6H_4-	$C_{17}H_{14}ON_2Cl_2$	102	0.58	58	8.41	8.46
3d	4-Cl-C_6H_4-	$C_{17}H_{14}ON_2Cl_2$	155	0.61	57	8.41	8.37
3e	2-CH_3-C_6H_4-	$C_{18}H_{17}ON_2Cl$	80	0.57	54	8.96	8.91
3f	3-CH_3-C_6H_4-	$C_{18}H_{17}ON_2Cl$	104	0.55	55	8.96	8.91
3g	4-CH_3-C_6H_4-	$C_{18}H_{17}ON_2Cl$	115	0.51	59	8.96	8.93
3h	2-NO_2-C_6H_4-	$C_{17}H_{14}O_3N_3Cl$	176	0.52	51	12.22	12.26
3i	3-NO_2-C_6H_4-	$C_{17}H_{14}O_3N_3Cl$	123	0.49	63	12.22	12.18
3j	4-NO_2-C_6H_4-	$C_{17}H_{14}O_3N_3Cl$	175	0.47	56	12.22	12.19
3k	3-Cl,4-F-C_6H_3-	$C_{17}H_{13}ON_2Cl_2F$	143	0.52	52	7.47	7.93
3l	4-OCH_3-C_6H_4-	$C_{18}H_{17}O_2N_2Cl$	198	0.53	61	8.52	8.53
3m	4-F-C_6H_4-	$C_{17}H_{14}ON_2ClF$	128	0.48	56	8.84	8.82

All the compounds gave satisfactory elemental analysis.
*TLC Solvent System: Acetone : Benzene (2 : 8) for compounds 2a-m.
*TLC Solvent System: Acetone : Benzene (1 : 9) for compounds 3a-m.

Table-2 Antimicrobial screening results of compounds 2a-m and 3a-m

Sr. No.	R	Antimicrobial activity Zone of inhibition (mm)				Antifungal activity Zone of inhibition (mm)
		B. mega	***S. aureus***	***P. vulgaris***	***E. coli***	***A. niger***
2a	C_6H_5-	18	15	12	16	15
2b	2-Cl-C_6H_4-	12	12	15	15	14
2c	3Cl-C_6H_4-	15	18	16	12	17
2d	4-Cl-C_6H_4-	**22**	20	20	14	19
2e	2-CH_3-C_6H_4-	17	17	17	18	20
2f	3-CH_3-C_6H_4-	**22**	18	18	20	18
2g	4-CH_3-C_6H_4-	16	19	19	13	15
2h	2-NO_2-C_6H_4-	20	**22**	15	15	13
2i	3-NO_2-C_6H_4-	14	15	17	21	14
2j	4-NO_2-C_6H_4-	13	21	12	14	16
2k	3-Cl,4-F-C_6H_5-	18	16	14	21	18
2l	4-OCH_3-C_6H_4-	20	17	16	16	14
2m	4-F-C_6H_4-	18	14	15	12	22
3a	C_6H_5-	15	**21**	15	15	21
3b	2-Cl-C_6H_4-	16	15	12	16	15
3c	3Cl-C_6H_4-	17	17	16	17	14
3d	4-Cl-C_6H_4-	12	12	15	12	13
3e	2-CH_3-C_6H_4-	14	14	19	14	12
3f	3-CH_3-C_6H_4-	18	18	15	19	14
3g	4-CH_3-C_6H_4-	19	17	14	21	18
3h	2-NO_2-C_6H_4-	15	16	17	14	15
3i	3-NO_2-C_6H_4-	17	19	18	16	17
3j	4-NO_2-C_6H_4-	19	**21**	17	19	16
3k	3-Cl,4-F-C_6H_5-	20	20	16	12	22
3l	4-OCH_3-C_6H_4-	17	13	15	14	17
3m	4-F-C_6H_5-	15	12	18	17	14
	Ampicillin	23	22	15	21	-
	Amoxycillin	22	23	18	21	-
	Norfloxacin	24	17	17	23	-
	Penicillin	25	24	20	19	-
	Greseofulvin	-	-	-	-	25

SCHEME – I



Results and Discussion

Compounds-1 possess aldehyde group which shows the IR absorption at 1685 cm^{-1} but when it condensed with aryl amine due to this peak will be disappeared and new peak found at 1654 cm^{-1} c .which is related to –C=N– str. The compounds 2a-m on reduction with the help of sodium borohydride, C=N group converts in to $–CH_2$-NH- due to this the peak related to -CH_2 appears at 4.5 δppm in NMR spectrum. So spectral analysis fully supported to synthesis of compounds 2a-m and 3a-m. By the comparison of antimicrobial data with standard drug, it is concluded that when phenyl ring system posses $–CH_3$, -Cl or NO_2 are shows remarkable activity against *B. megaierium* in case of compound **2d** and **4f**, but nitro group present at position 2- and 4- then it is active against *S. aureus* such as **2h** and **3j**. Compound **2c**, it possess Cl group at position 4- shows remarkable activity against *P. vulgaris*. Remaining compounds are moderately active against all experimental strains of bacteria and fungi.

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