International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 9 Issue 5 ǁ 2021 ǁ PP. 50-54

Synthesis and characterization of N-5{Acridin-9yl)-2-chloro phenyl}alkyl]aryl amides/imides and their studies on their Antimalarial activity

Renu Singh[*1], Akhand Pratap Singh[1], Raghvendra Pratap Singh[2], Saurabh Kumar Singh[3]

[1] *Maharishi University of Information Technology, Lucknow-226020, India*
[2] *Dr. Shakuntala Mishra National Rehabilitation University, Lucknow-226017, India*
3 *Pt. Deen Dayal Upadhyaya Government Girls P.G. College, Lucknow-226017, India*
[*] *Corresponding Author Renu Singh*

Abstract- *An equivalent mixture of Diphenylamine and 4-chloro benzoic acid was heated in the presence of anhydrous $ZnCl_2$ in ethanol. After few hours crude was extracted with benzene, then boiled with charcoal, filtered to get 9-(4-chlorophenyl)-acridine crystal (I). A finally powdered mixture of (I) and an appropriate amido/ imido alkylol (II) was dissolved in concentrated sulphuric acid which furnished N-[5-acridin-9-yl)-2-chlorophenyl}alkyl]-aryl amides/imides(III). Compound (III) were screened for their antimalarial activity involving the standardized method as recommended by National Committee on Clinical Laboratory Standards (NCCLS).*

Index terms- *Acridine derivatives, Animal charcoal, diphenyl derivatives.*

Date of Submission: 16-05-2021 Date of acceptance: 31-05-2021

I. INTRODUCTION

On the basis of literature survey, it is clear that acridine derivatives find great applications as antimalarial agents. Other biological properties of acridine compounds have less extensively investigated and therefore these compounds require more studies in other health areas by way of undertaking the synthesis of more Acridine derivatives with a large number of substituents at different positions in its molecular union and finally subject these compounds for their bio evaluation in animal models. These all valid observations prompted the author to undertake the synthesis of N-[5-acridin-9-yl)-2-chlorophenyl}alkyl]-aryl amides/imides **(III)** Scheme –I for studying for their antimalarial activity.

II. EXPERIMENTAL

Melting points were determined in open capillary tubes in a Toshniwal (Japan) electrical melting point apparatus and therefore values reported are uncorrected. The IR spectra were recorded on an FTIR Perkin Elemer(Model) Spectrophotometer were recorded in CDCl3 on a Bruker instrument at 300MHz and 75MHz respectively. Chemical shifts are expressed in δ scale downfield from TMS, which was used as an internal standard. The Mass spectra (FAB) were recorded on JEOLSX102/DA-600 mass spectrophotometer using Argon as FAB gas. The purity of the compounds was checked by thin layer chromatography (TLC) using silica gel (Acme) and the spots were visualized by Iodine vapours. The intermediate 9-(4-chlorophenyl)-acridine (II) and the target compound N-[5-acridin-9-yl)-2-chlorophenyl}alkyl]-aryl amides/imides (III) were synthesized involving the established protocols.

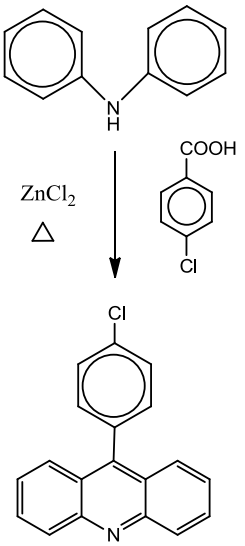
Synthesis of N-[5-acridin-9-yl)-2-chlorophenyl}alkyl]-aryl amides/imides (III)

A powdered mixture of 9-(4-chlorophenyl)-acridine **(II) (0.05 mol)** and an appropriate amido/imido alkylol **(0.05 mol)** was dissolved in concentrated sulphuric acid by stirring and cooling occasionally. The resultant acidic solution of the reactants was vigorously stirred at room temperature for one hour. It was left over-night under refrigeration and pour into ice-cold water slowly with constant stirring. The resultant solid was filtered and washed with cold water. The target compounds synthesized in this way are recorded in **Table-I** along with their characterization data.

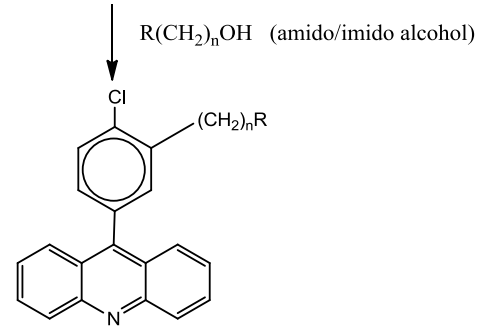
The following synthetic sequences were involved in the synthesis of acridine derivatives-

a) 9-(4-chlorophenyl)-acridine

b) N-[5{(acridin-9-yl)-2-chlorophenyl} alkyl] aryl amides/imides



9-(4-chlorophenyl)-acridine (II)



N-[5-acridin-9-yl)-2-chlorophenyl}alkyl]-aryl amides/imides (III)

Characterization data:-

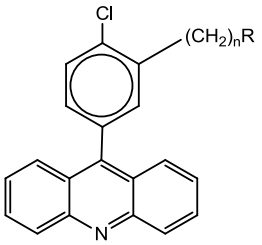


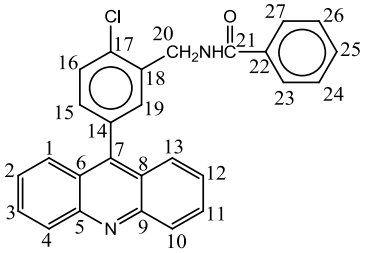
Table-I

Characterization data of N-[5{(acridin-9-yl)-2-chlorophenyl} alkyl] aryl amides/imides (III

Compound no.	R	n	m.p. ^0C	Yield	Colour	Molecular formula	Molecular weight	Analysis	
								Nitrogen, %	
								Calculated	Found
1.	Phthalimido	1	98-100	50	Green	$C_{28}H_{17}O_2N_2Cl$	448.5	6.24	6.45
2.	Phthalimido methyl	2	96-98	53	Green	$C_{29}H_{19}O_2N_2Cl$	462.5	6.05	5.89
3.	Benzamido	1	105-107	56	Green	$C_{27}H_{19}ON_2Cl$	422.5	6.62	6.48
4.	Nicotinamido	1	102-104	52	Green	$C_{296}H_{18}ON_3Cl$	423.5	9.91	9.64

)

Spectral data of N-[5{(acridin-9-yl)-2-chlorophenyl} methyl)]-benzamide



IR (KBr) (v_{max} in cm^{-1})

1636 (C=N), 1685(Sec. amide C=O), 710 (Ar-Cl)

^{1}H NMR (DMSO) (in δ ppm)

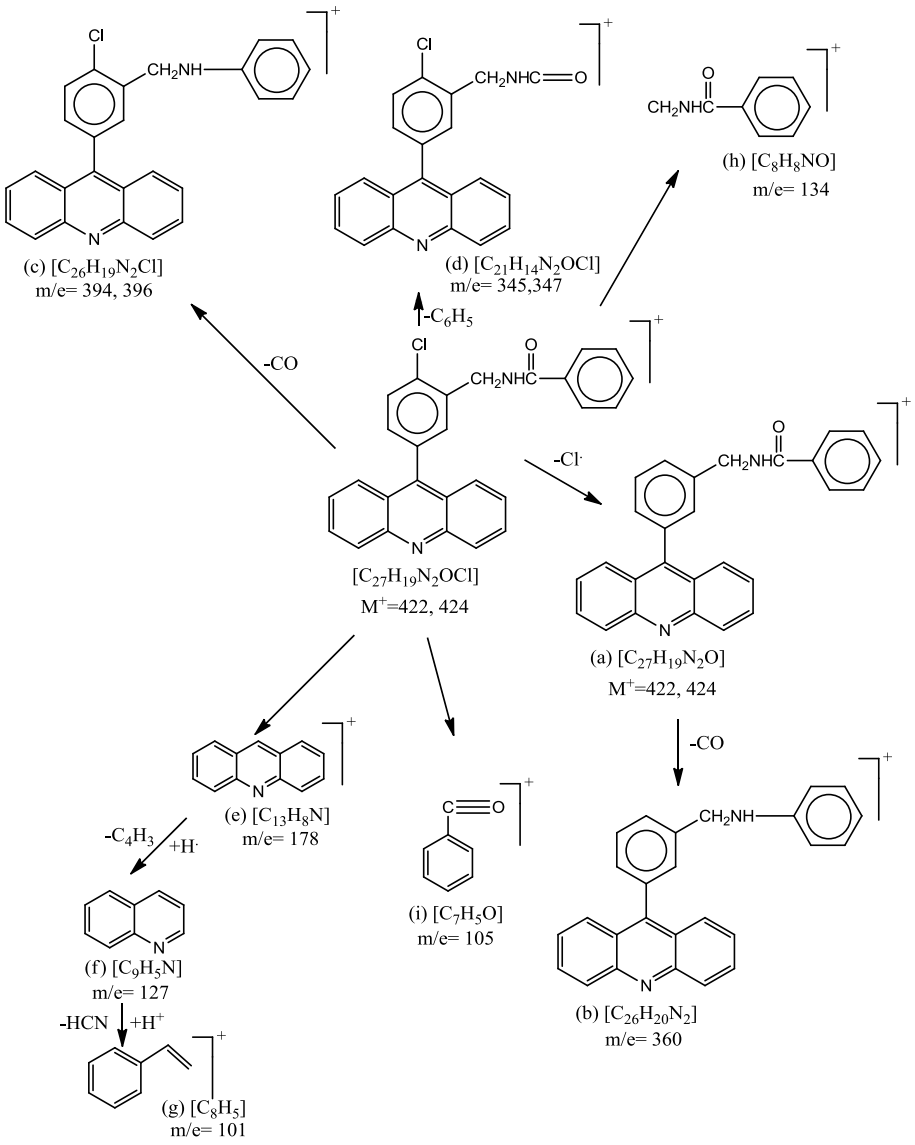
6.85-7.82 (m, 16H, Ar-H), 3.75 (s, 2H, CH_2), 8.85 (brs, 1H, CONH)

^{13}CNMR

69.2 (C-20), 115.5, 116.1, 121.4, 123.7, 125.2, 127.5, 129.2, 131.4, 132.2, 136.4, 141.5 (C-1 to C-6, C-7 to C-13, C-14 to C-19, C-22 to C-27), 175.5 (C-21).

Mass spectra:-

Mass spectral pattern of N-[5{(acridin-9-yl)-2-chlorophenyl} methyl)]-benzamide



Important mass spectral peaks of N-[5{(acridin-9-yl)-2-chlorophenyl} methyl)]-benzamide

Fragment no.	Molecular formula	m/e
M^+	$C_{27}H_{19}N_2OCl$	422, 424
(a)	$C_{27}H_{19}N_2OCl$	397
(b)	$C_{27}H_{19}N_2OCl$	360
(c)	$C_{27}H_{19}N_2OCl$	394, 396
(d)	$C_{27}H_{19}N_2OCl$	345, 347
(e)	$C_{27}H_{19}N_2OCl$	178
(f)	$C_{27}H_{19}N_2OCl$	127
(g)	$C_{27}H_{19}N_2OCl$	101
(h)	$C_{27}H_{19}N_2OCl$	134
*(i)	$C_{27}H_{19}N_2OCl$	105

Biological Activity:-

1. Antibacterial activity-

Acridine derivatives **(Table-I)** bearing Phthalimidomethyl and Benzamido substituents **(compounds 2 and 3)** respectively were examined for their antibacterial activity against four bacterial strains *in vitro* involving the macro broth dilution technique as recommended by National committee for Clinical Laboratory Standard (NCCLS)[1,2]. Both these compounds shows no observable degree of antibacterial activity against the four bacterial strains viz; Eischerichia coli(Ec) (ATCC-9367), Pseudomonas aeruginosa(Pa) (ATCCBAA-427), Staphylococcus Aureus (Ea) (ATCC-25923) and Klebsiella Pneumonia (Kp) (ATCC-27736) . Gentamycin was taken as standard drug having MIC 0.18, 0.18, 25, 6.25 µg/mL against Kp, Ec, Pa and Sa respectively. None of the compounds under investigation showed appreciable antibacterial activity. The complete loss of antibacterial activity of these two acridine derivatives **(compounds 2 and 3)** is mainly attributed to their inability for ionization and in sufficient areas of flatness to permit Vander Waal's bonding at the receptor site, since this view of the importance of the flat area has been strengthened by incorporation of styryl group on the 4-aminoquinolino and 4-aminopyridine derivatives. The antibacterial data of these compounds have been incorporated in **table II.**

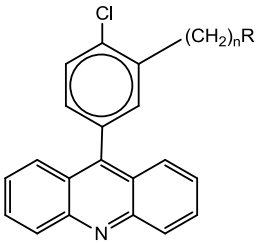


Table-II

Antibacterial activity data of N-[5{(acridin-9-yl)-2-chlorophenyl} alkyl] aryl amides/imides

Compound No.	R	n	Minimum inhibitory concentration (MIC) in µg/mL			
			Ec	Pa	Sa	Kp
2.	Benzamido	1	>50	>50	>50	>50
3.	Phthalimidomethyl	2	>50	>50	>50	>50

2. Antifungal activity-

The two same acridine derivatives **(Table-I)** bearing Phthalimidomethyl and Benzamido substituents **(compounds 2 and 3)** respectively were also examined against six fungi viz. Candida albicans (ca), Cryptococcus neoformans (cn), Sporothrix schenckii (Ss), Trichophyton mentagrophytes (Tm), Aspergillus fumigatus (Af), and Candida parapsilosis (Cp) involving the macro broth dilution method *in vitro* as recommended by National committee for Clinical Laboratory Standard (NCCLS)[1,3,4]. Fluconazole was taken as standard drug having MIC 0.5, 1.0, 2.0, 1.0, 2.0 and 1.0 µg/mL against Ca, Cn, Ss, Tm, Af and Cp respectively.

None of the above compounds showed appreciable extent of antifungal activity. The antifungal data of these compounds have been incorporated in **table III.**

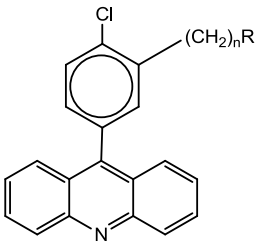


Table-III

Antifungal activity data of N-[5{(acridin-9-yl)-2-chlorophenyl} alkyl] aryl amides/imides

Coumpound No.	R	n	Minimum inhibitory concentration (MIC) in μg/mL					
			Ca	Cn	Ss	Tm	Af	Cp
2.	Benzamido	1	>50	>50	>50	>50	>50	>50
3.	Phthalimidomethyl	2	>50	>50	>50	>50	>50	>50

REFERENCES:

[1]. National Committee for Clinical Laboratory Standards (NCCLS), Mewthods for dilution in antimicrobial susceptibility tests:Approved Standards M2-A5 Villanova, P.A., NCCLS, 1993.
[2]. Dhar, M.L., Dhar, M.N., Dhawan, B.N. Mehrotra and Roy, C., Ind. J. Exp. Biol., 6,232, (1968).
[3]. Wahab, S., Tandon, R.N., Jacob, Z., Sagar, P. and Srivastava, O.P., J. Ind. Bot. Soc., 60, 278 (1981).
[4]. Mishra, B.K. in "Designing and synthesis of some heterocyclic compounds containing amido/amino alkyl groups for their bioevaluation", A Ph. D. Thesis, Chemistry Department, Lucknow University, Lucknow, p. 143 (2003).