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Synthesis, Characterization and antimicrobial activity of 6/7-Substituted Quinolines-4-thiazolidinones

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ABSTRACT

A series of total fifteen novel Quinoline Schiff bases [4a-e,5a-e,6a-e] were prepared from 6/7 substituted quinoline carbaldehyde . All quinoline schiff bases were refluxed with thioacetic acid in presence of anhydrous zinc chloride and solvent N,N-dimethyl formamide to afforded novel series of 4-thiazolidinone (7a-e,8a-e,9a-e) . All synthesized 4-thiazolidinone were screened for their antimicrobial activity.

Keywords: 4-Thiazolidinones, Schiff bases, Quinoline ,antimicrobial activity.

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INTRODUCTION

Quinoline and its derivatives exhibit antimalarial, antitubercular, antibacterial, antihistaminic, antitumor activities. On the other hand 4-thiazolidinone derivatives are known to possess antimicrobial, antifungal, antiviral, antituberculosis properties. These properties stimulate us to synthesize new potential compounds in which biologically active quinoline Schiff bases reacted with thioacetic acid to form Quinoline 4-thiazolidinones. It is surmised that these compounds would exhibit interesting pharmacological activities. In present investigation we report here in synthesis of 6/7 - substituted Quinoline 4-thiazolidinones [1-21].

MATERIAL AND METHODS

Experimental

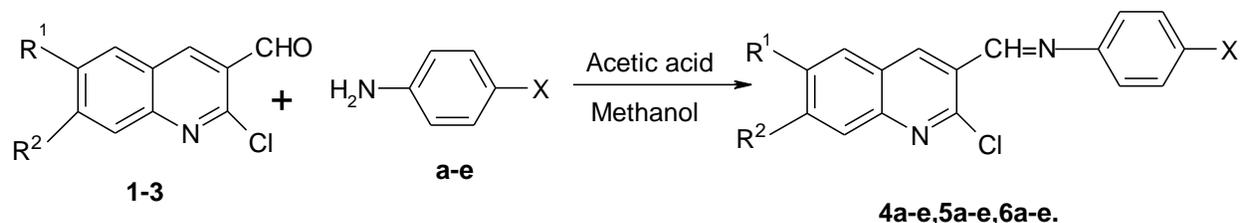
Melting points were determined in capillary tube and are uncorrected. IR spectra were recorded in potassium bromide pellets on a Bomem MB 104 FT infrared spectrometer. ¹H NMR spectra were obtained on a FT Gemini 60 (60MHz) spectrophotometer with TMS as an internal standard. Mass spectra were recorded on FTVG-7070H. Mass spectrometer using the EI technique at 70 eV. Micro analysis was performed on Heraeus CHN-O rapid analyser. Purity of compounds was checked by TLC.

6/7-Substituted Quinoline Schiff bases (4a-e,5a-e,6a-e)

A mixture of 2-chloro-6-methoxy-3-quinoline carboxyaldehyde (1), 2-chloro-7-methoxy-3-quinoline carboxyaldehyde (2), 2-chloro-6-methyl-3-quinoline carboxyaldehyde (3) (0.005mol) and 4-nitroaniline /4-chloro aniline/ 4-toluidine/ 4-anisidine /4-amino phenol (0.005mol) in 10 ml methanol was refluxed independently on water bath for 3-4 hrs. The reaction mixture was allowed to cool and separated solid was filtered, washed with water dried and recrystallised from ethanol to give products 4a-e,5a-e,6a-e. (**Table-1**).

6/7-Substituted Quinoline-4-Thiazolidinones 7a-e, 8a-e, 9a-e.

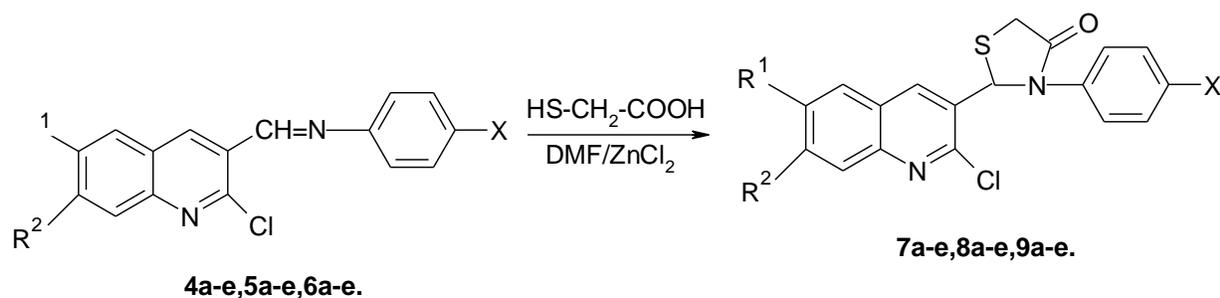
0.01 Mol of 4a-e, 5a-e and 6a-e was refluxed with thioacetic acid (0.01mol) in 10 ml of N,N-dimethyl formamide in presence of anhydrous zinc chloride were refluxed for 4-6 hrs. After complete heating reaction mixture was cooled, which was then poured in ice water, the solid obtained, filtered, dried and recrystallized from ethanol (**Table-2**).



	R1	R2
1	-OCH ₃	H
2	H	-OCH ₃
3	-CH ₃	H

Scheme-1

	X
a	-NO ₂
b	-Cl
c	-CH ₃
d	-OCH ₃
e	-OH



Scheme-2

	R ¹	R ²	X
4a	-OCH ₃	H	-NO ₂
4b	-OCH ₃	H	-Cl
4c	-OCH ₃	H	-CH ₃
4d	-OCH ₃	H	-OCH ₃
4e	-OCH ₃	H	-OH
5a	H	-OCH ₃	-NO ₂
5b	H	-OCH ₃	-Cl
5c	H	-OCH ₃	-CH ₃

	R ¹	R ²	X
5d	H	-OCH ₃	-OCH ₃
5e	H	-OCH ₃	-OH
6a	-CH ₃	H	-NO ₂
6b	-CH ₃	H	-Cl
6c	-CH ₃	H	-CH ₃
6d	-CH ₃	H	-OCH ₃
6e	-CH ₃	H	-OH

Table-1: Physical and spectral data of Compounds 4a-e,5a-e,6a-e.

Sr.No	Compounds	M.P. (°c)	Yield (%)
1	4a	160	65
2	4b	209	70
3	4c	184	72
4	4d	156	70
5	4e	201	69
6	5a	184	72
7	5b	178	55
8	5c	210	69
9	5d	189	70
10	5e	169	40
11	6a	172	45
12	6b	170	60
13	6c	182	48
14	6d	189	49

All compounds gave satisfactory CHN analysis

Table-2: Physical and spectral data of Compounds 7a-e,8a-e,9a-e.

Sr.No	Compounds	M.P. ($^{\circ}$ C)	Yield (%)
1	7a	80	72
2	7b	170	55
3	7c	210	69
4	7d	180	70
5	7e	165	39
6	8a	163	65
7	8b	209	70
8	8c	187	72
9	8d	159	70
10	8e	205	69
11	9a	270	65
12	9b	268	72
13	9c	256	68
14	9d	260	89
15	9e	250	40

All compounds gave correct CHN analysis. IR spectra showed the absence of absorption bond in the region.1500- 1525 cm^{-1} due to $-\text{CH}=\text{N}-$ stretch.

RESULTS AND DISCUSSION

The starting compound 2-chloro-6-methoxy quinoline carboxyaldehyde (1), 2-chloro-7-methoxy quinoline carboxyaldehyde (2), 2-chloro-6-methyl quinoline carboxyaldehyde (3), were condensed independently with 4-nitro aniline (a) / 4-chloro aniline(b) / 4-toluidine(c) / 4-anisidine(d) / 4-amino phenol (e) to afford respective schiff bases 4a-e,5a-e and 6a-e (**Scheme-1**).

The structure of 1-3, 4a-e,5a-e, 6a-e were supported by their spectral data. IR spectra in KBr showed the absence of absorption band in the region $2830-2700\text{ cm}^{-1}$ due to C-H and $1730-1690\text{ cm}^{-1}$ due to C=O of -CHO groups respectively and the presence of absorption band in the region $1500-1525\text{ cm}^{-1}$ due to -CH=N- stretch. Mass spectra of these products exhibit molecular ion peaks at M^{+2} (1/3 intensity of M^{+}) and M^{+} which corresponds to their molecular weight. ^1H NMR (DMSO-d_6) spectra of these compounds revealed signals in the region δ 7.2-8.2 (m, due to Ar-H), δ 8.3-8.4 ppm (s,1H due to C-CH in quinoline).

These 6/7 -substituted quinoline schiff bases 4a-e,5a-e,6a-e were heating with thioacetic acid in the presence of anhydrous zinc chloride which act as a catalyst and solvent N,N-dimethyl formamide(DMF) under go cyclisation to afford 2-chloro-6/7- substituted quinoline-4-thiazolidinones 7a-e,8a-e,9a-e. (**scheme -2**). All the newly synthesized compounds gave satisfactory C,H and N analysis and spectral data.

The IR in KBr showed absence of absorption in the region $1500-1525\text{ cm}^{-1}$ due to -CH=N- and presence of absorption band in the range $1730-1740\text{ cm}^{-1}$ due to >C=O of thiazolidinone. ^1H NMR (DMSO-d_6) signals appeared at δ 3.7-4.12 ppm due to methylene group and at δ 5.86-6.3 ppm assigned for -CH= (methylinic proton) of 4-thiazolidinone. In ^1H -NMR spectra methylene proton of the 4-thiazol- dinone ring displayed two signals appearing as doublet at δ 3.61-3.98 and δ 3.7-4.12 ppm due to non equivalent germinal methylene protons.

Antimicrobial activity

All the compounds were tested for their antimicrobial activity using disc diffusion technique against *S.aureus*, *B.substilis*, *S. Typhi*, *E.Coli*. the standard antibiotics showed zones of inhibition penicillin 20-24 mm, ampicillin 18-25 mm and Norflaxacin 18-26mm against bacterial strains. Compounds 4a-b,5a-b,6a-b,7a-b,8a-b,9a-b were highly active against *B.substilis*. The compounds 4d,5d,6d,7d,8d,9d. Showed significant activity against *E.Coli*. 4c,4e,5c,5e, 6c,6e, 7c, 7e, 8c, 8e,9c,9e. display maximum activity against *S.aureus*. and *S. Typhi*. respectively.

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