



Synthesis and characterization of new quinazoline-4(3H)-one Schiff bases

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ABSTRACT

In this work, 2-chloromethyl-4H-3,1-benzoxazine-4-one (2) has been synthesized via reaction of N-chloroacetyl anthranilic acid (1) and sulfuric acid while treatment of the compound (2) with morpholine gave compound (3). Compound (4) synthesized from compound (3) via reaction with hydrazine hydrate. Moreover the reaction of compound (4) with different aldehydes gave the newly Schiff bases (5- 8). All compounds were confirmed by their melting point, FTIR, and UV-Vis spectra.

INTRODUCTION

Quinazolin-4(3H)-ones and its derivatives are versatile nitrogen heterocyclic compounds^[1] which have long been known as a promising class of biologically active compounds. Pharmacologically, quinazolin-4-ones are among the most important classes of heterocyclic compounds. These compounds possess versatile type of biological activities^[2]. Some of these are well known for their antifungal^[3], antibacterial^[4], anticancer^[5], anti-inflammatory^[6], antitubercular^[7], anti-HIV^[8], and antiulcer^[9]. The most common synthetic method to quinazolin-4-one is based on reaction of anthranilic acid and chloroacetyl chloride.

The chemistry of $>C=N$ is studied extensively because of its high synthesis flexibility, varied coordinating ability and medicinal utility. The compounds containing $>C=N$ include mainly the products of reaction between aldehyde or ketonic components and primary aliphatic or aromatic amines, ammonia, hydrazine, N-phenylhydrazine, hydroxylamine hydrochloride, semicarbazide, thiosemicarbazide and their substituted derivatives. These compounds are generally known as Schiff bases to honor Schiff, who first synthesized such compounds^[10]. These are also known as azomethines. A lot of work has been done on this class of compounds due to its multi applicability^[11-16]. The aim of this work is to synthesize new Schiff bases linked to quinazoline moiety.

Experimental

All chemicals used of reagent grade and used as supplied. Melting points were determined with an electrical thermal melting point apparatus and are uncorrected. The FT-IR spectra in the range (4000 -400) cm^{-1} were recorded by Shimadzu instrument. The UV spectra were performed by Shimadzu instrument.

N-Chloroacetyl anthranilic acid^[17] (1)

This has been synthesized by refluxing a mixture of anthranilic acid (0.01 mol) and (0.01mol) chloroacetyl chloride in 80ml of benzene and two or three drops of pyridine for 6 hrs. Then the reaction mixture was cooled and the product obtained was recrystallized from ethanol: acetone mixture (1:1).

2-Chloromethyl-4H-3,1-Benzoxazine-4-one^[18] (2)

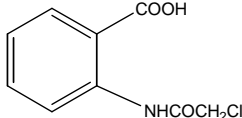
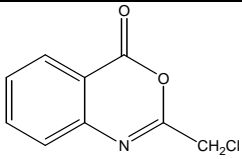
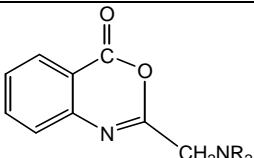
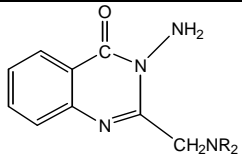
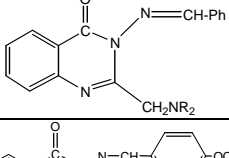
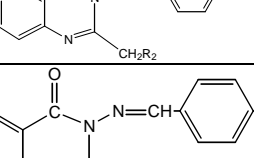
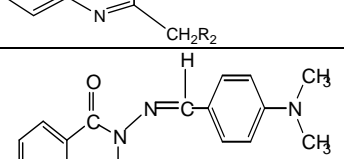
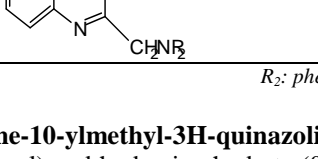
A mixture of (1)(0.02mol), N-chloroacetyl anthranilic acid (1) and sulfuric acid (2mL) in absolute ethanol (25mL) was refluxed for 7 hrs. The excess solvents were distilled off under vacuum condition. Yield (66%).

2-Phenothiazin-10-methyl –benzo [d] [1,3] oxazin -4- one ^[19] (3)

Phenothiazine (0.01 mol) was dissolved in 20 mL of absolute ethanol then was heated in a water bath . The obtained clear solution was added to alcoholic potassium hydroxide solution [(0.01 mol) KOH in 25 mL absolute ethanol] with continuous stirring and cooling, then the obtained precipitate was filtered and dried (phenothiazine potassium salt).

In a suitable round bottomed flask (0.01 mol) of 2-chloromethyl-4H-3,1-benzoxazine-4-one was dissolved in 25 mL of absolute ethanol then (0.01 mol) of phenothiazine potassium salt was added gradually with stirring .The resulted mixture was refluxed for 6 hrs. with continuous stirring then was cooled to room temperature and the formed precipitate was filtered, washed with water and dried

Table (1): Physical properties of the prepared compounds [1-8]

Comp. No.	Compound structure	m. p, °C	Yield %	Color	Rec. Solvent
1.		170-172	70	Light brown	Ethanol:Acetone
2.		182-184	59	dark Brown	Ethanol
3.		154-156	65	Green yellow	Ethanol
4.		oily	68	yellow	Oily
5.		155-157	76	yellow	DMF
6.		154-156	71	Light yellow	CCl ₄
7.		238-240	69	yellow	DMF
8.		178-180	70	Orange	CHCl ₃

R₂: phenothiazine ring.

3-Amino-2-Phenothiazin-10-ylmethyl-3H-quinazolin-4-one^[20](4)

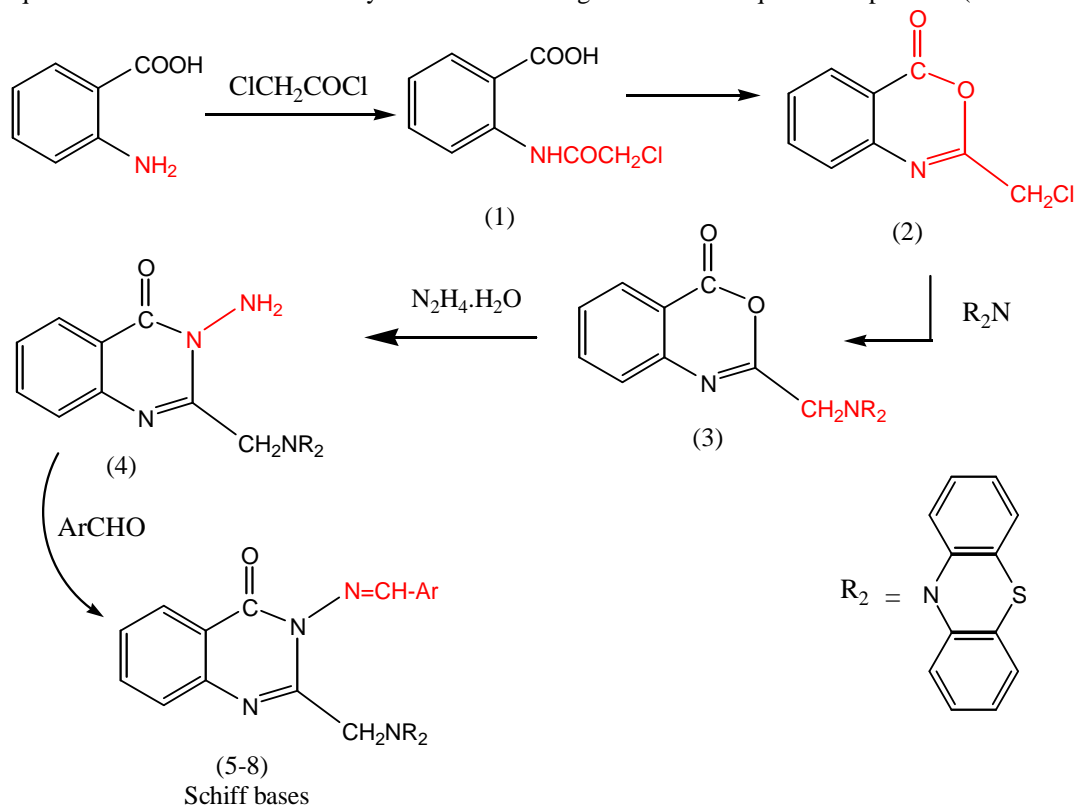
A mixture of (3) (0.01 mol) and hydrazine hydrate (0.01 mol) in absolute ethanol (30mL) was refluxed for 12 hrs. excess solvent was distilled off and the product recrystallized from appropriate solvent.

Synthesis of the new Schiff bases ^[21] (5-8)

A mixture of compound (4) (0.01mol) and appropriate aryl aldehyde (0.01mol) was refluxed in absolute ethanol (20mL) for 6-8 hrs. The reaction mixture was cooled and the product obtained recrystallized from appropriate solvent.

RESULTS AND DISCUSSION

The new quinazolinone derivatives were synthesized following the reaction sequences depicted in (Scheme -1-).



Ar CHO: PhCHO, 4-NO₂-PhCHO, 4-methoxy-PhCHO, 4-N,N-dimethyl-PhCHO

Scheme -1-

The starting material for the synthesis of the target compounds was synthesized by the reaction of anthranilic acid with chloroacetyl Chloride. FT-IR spectrum of compound(1) showed the appearance of new absorption characteristic bands at 1693cm⁻¹ and 1651cm⁻¹ which belonged for functional groups νC=O and ν C=N respectively. UV spectra showed mainly electronic transitions corresponding to(n →π*) and (π →π*).

Table (2): U.V and IR spectral data for the prepared compounds (1-8) .

Comp. No.	U.V. λ _{max} (nm)	FT-IR, cm ⁻¹
1	256, 313	3468, 3425, 1693, 1639, 1585,752
2	304	1693, 1639,1585, 752
3	311	1693, 1643, 1585
4	326	3336, 3320, 1666, 1612, 1577
5	304	1693, 1620, 1581
6	323	1624, 1600, 1573
7	326	1685, 1631, 1597
8	390	1681, 1600, 1550

FT-IR spectrum of compound (2) was showed the appearance of new bands at 3205cm⁻¹ for ν NH. Condensation of (4) with aryl aldehyde in absolute ethanol afforded the newly synthesized Schiff bases(5-8) as shown in Scheme (1)

The formation of the newly Schiff bases was indicated by the presence in their IR spectra of azomethine (CH=N) stretching band at (1606-1643) cm^{-1} combined with the disappearance of the NH_2 stretching band.

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