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Some Synthesis and Antimicrobial Activity of Quinazoline Heterocyclic Compounds: A Review

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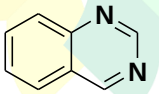
Abstract: Potential bioactive heterocyclic compounds shows antimicrobial activities. Quinazoline having N as heteroatom, bicyclic heterocyclic compounds. These quinazolines heterocyclic compounds having many applications among all these applications they are potential bioactive compounds. Due to applications to human begins synthesized on industrial scale. We have reviewed some synthesis protocols of quinolones and it's derivatives with antibacterial activities.

IndexTerms **- Heterocyclic compounds, synthesis, quinazoline, antimicrobial activity, bioactive compounds**

I. INTRODUCTION

Heterocyclic organic compounds are having importance due to its applications. Heterocyclic organic compounds are cyclic organic compounds having one or more heteroatoms in ring. Element Nitrogen, Sulphur, Oxygen are important heteroatoms present in heterocyclic organic compounds. Heterocyclic organic compounds having one heteroatoms, two heteroatoms or three heteroatoms. This organic compounds are present in monocyclic or bicyclic structures.
These all heterocyclic organic compounds plays important role for living things. Organic compounds are present in plants, Animals, humans majority of organic compounds are heterocyclic organic compounds. Heterocyclic compounds are potentially bioactive. [1]



Stucture:1 Quinazoline

Quinazoline is one of the important bicyclic heterocyclic organic compounds. Quinazoline is made up of two benzene rings and presence of two Nitrogen atoms as heteroatoms. Quinazoline and its derivatives shows important medicinal importance like Anti-viral, Anti-cancer, Anti-tubercular, Anti-microbial, Anti-hypertensive, anti-inflammatory, Analgesic activity others also.

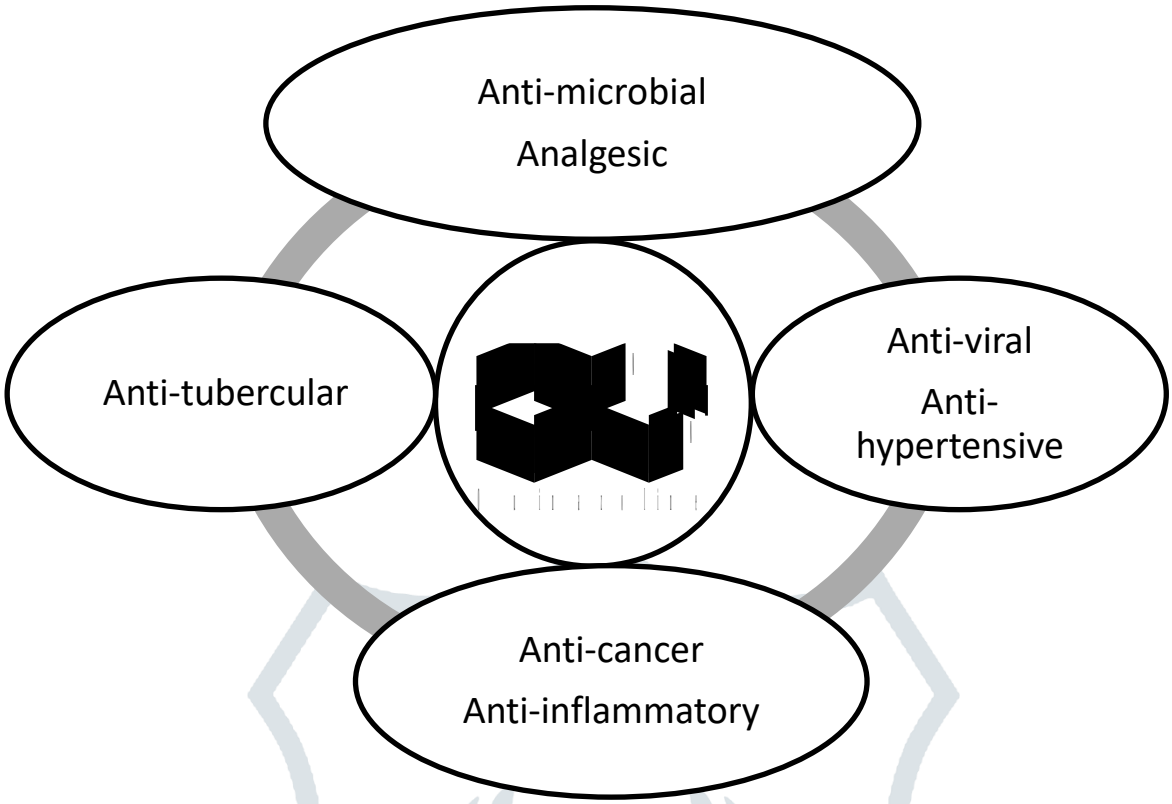


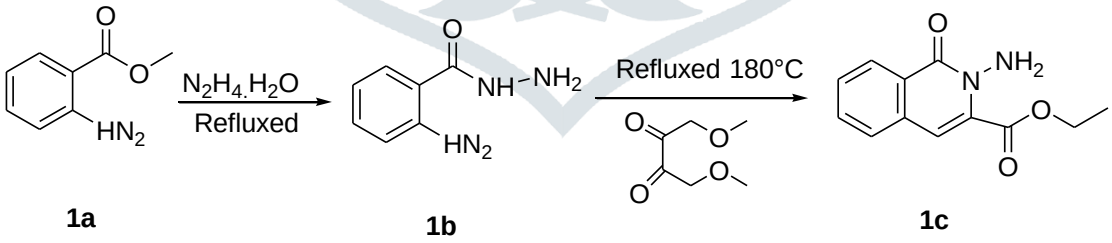
Fig:1 Applications of Quinazolines

Vital importance of quinazolines and its derivatives gives importance's to synthesis of quinazolines and its derivatives. This mini review gives idea and some reported synthesis methods of quinazolines. [2]

A] Synthesis of Quinazolines and its derivatives

A.1 3-amino-2-ethoxycarbonyl quinazolin-4-one

M.K. Kathiravan, Nikhil Vidyasagar, Rahul Khiste, Aparna Chote, Kishor JainMethyl These group synthesized 1 3-amino-2-ethoxycarbonyl quinazolin-4-one with anthranilate as starting material.This is two step synthesis. **(Scheme: 1)** In first step anthranilate (1a) is refluxed with hydrazine hydrate to give Anthranilic acid hydrazide (1b) and in second step this on further reaction with diethyl oxalate to gives 3-amino-2-ethoxycarbonyl quinazolin-4-one (1c)[3**].**

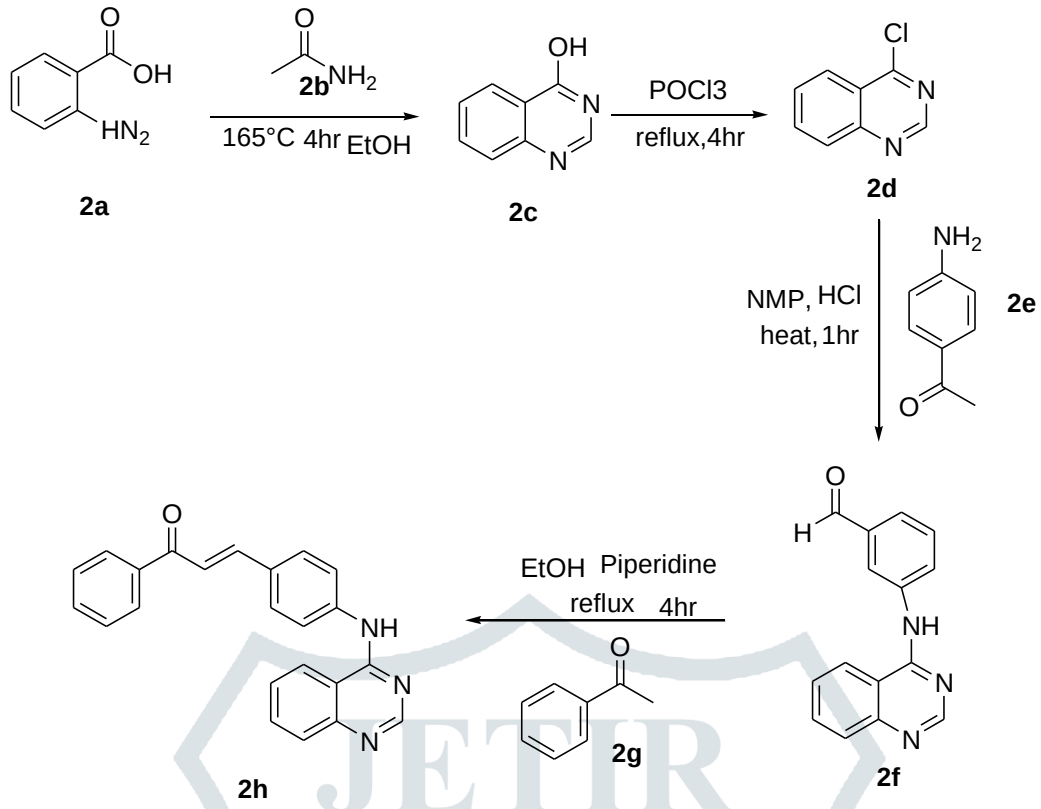


1a **1b** **1c**

Scheme :1 Synthesis of 3-amino-2-ethoxycarbonyl quinazolin-4-one

A.2 Chalcone incorporated quinazoline derivatives

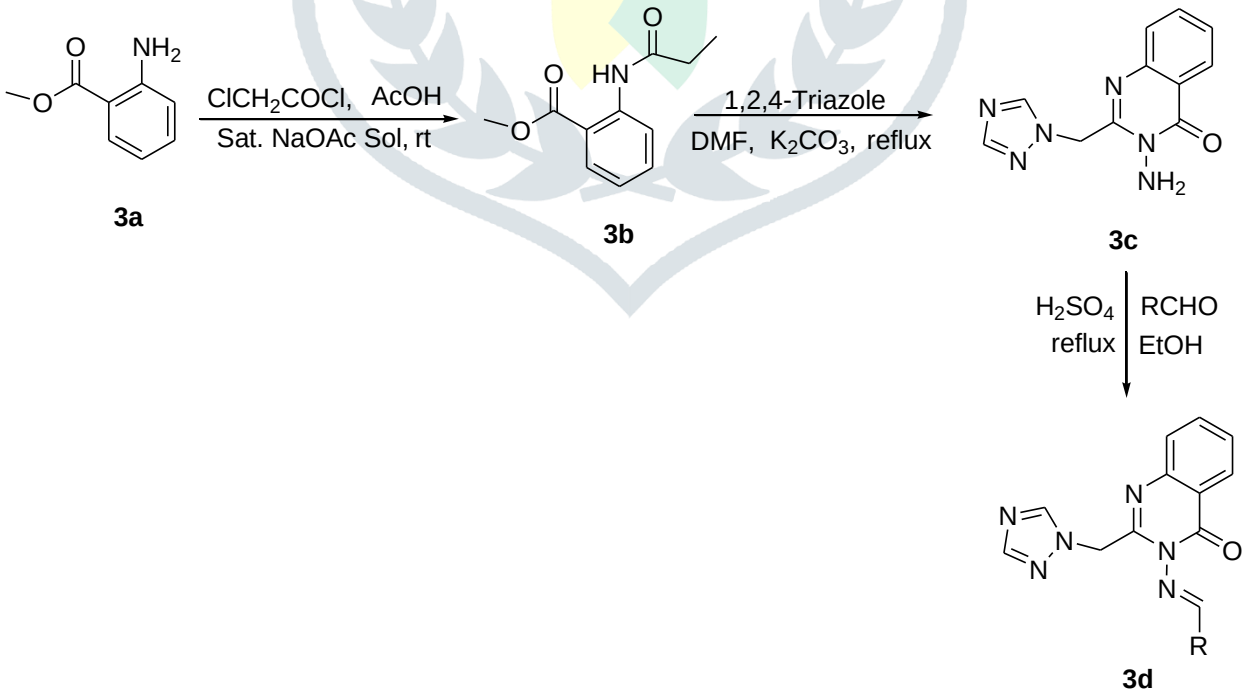
Sapavat Madhavi and its coauthors synthesized quinazoline derivatives incorpated with chalcones. In this synthsis they first react anthranilic acid 2a is refluxed with formamide 2b in presence of absolute ethyl alcohol, at 165°C for 4 hr to give intermediate 2c which is on further refluxed with phosphorus oxycholoride about 4hr to gives 4-choloroquinazoline 2d. This 2d synthesized is reacted with 4-ammino benzaldehyde 2e, in presence of NMP, HCl, refluxed for 4 hr to give 4-(quinazolin-4-ylamino) benzaldehyde 2f. This 2f quinazoline substituted aldehyde is reacted with acetophenone in presence of piperidine, EtOH and reflux for 4h so we get chalcone incorporated quinazoline derivatives 2h**. [4](Scheme: 2)**



Scheme: 2 Synthesis of Chalcone incorporated Quinazoline derivatives

A.3 3-amino-2-(1H-1,2,4-triazol-1-ylmethyl)quinazolin-4(3H)-one

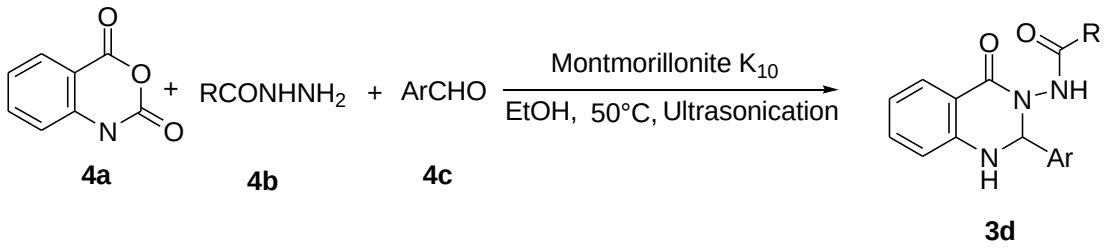
Methyl anthranilate 3a is on reaction with chloroacetyl chloride with acetic acid and sat. sodium bicarbonate solution at room temperature to gives methyl 2-(2-chloroacetamido)benzoate 3b. This 3b compound is further reaction with 1,2,4-Triazole, in presence of DMF, K2CO3, and reflux to get 3-amino-2-(1H-1,2,4-triazol-1-ylmethyl)quinazolin-4(3H)-one 3c. 3c on reaction with aldehyde in presence of Ethyl alcohol, sulphuric acid and refluxing we get quinazolin-4(3H)-one Schiff base conjugates 3d.[5].



Scheme:3 Synthesis of 3-amino^{-2}-(1H^{-1},2,4-triazol^{-1}-ylmethyl)quinazolin^{-4}(3H)-one

A.4 2-aryl substituted N-(4-oxo-1,2-dihydroquinazolin-3(4H)-yl)aryl.

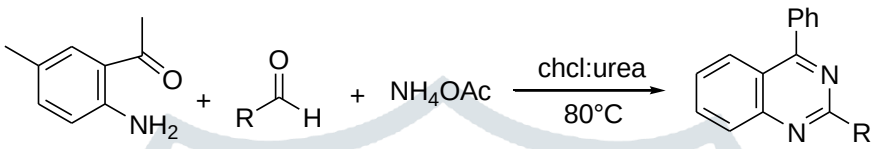
Isatoic anhydride 3a is on reaction with acid hydrazides 3b and Aldehyde 3c in presence of Montmorillonite k10, EtOH, at 50°C and with ultrasound irradiation we get 2-aryl substituted N-(4-oxo-1,2-dihydroquinazolin-3(4H)-yl)aryl.[6].



Scheme:4 Synthesis of 2-aryl substituted N-(4-oxo-1,2-dihydroquinazolin-3(4H)-yl)aryl.

A.5 Quinazolin derivatives

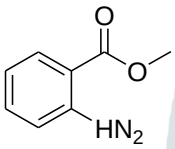
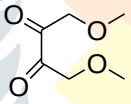
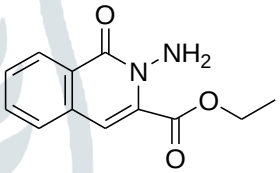
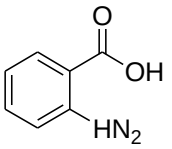
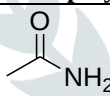
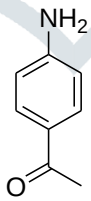
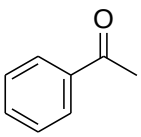
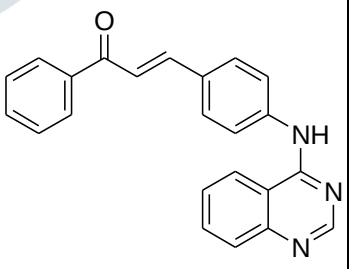
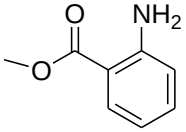
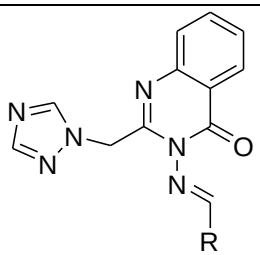
2-amino-5-cholorobenzophenone 5a , aromatic aldehyde5b and ammonium acetate5c all this three component on reaction in presence of ch:cl as deep eutectic solvent gives quinazoline 5d[7].

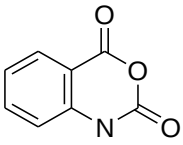
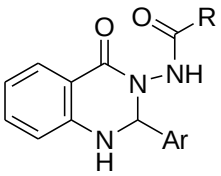
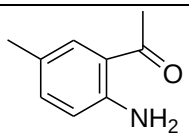
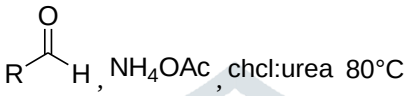
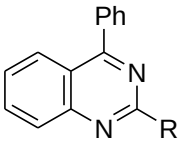


Scheme: 5 Synthesis of quinazoline derivatives

All this synthesis of quinazolines and its derivatives are summarized in **Table:1**

Table 1: Quinazoline and its derivatives synthesis methods with starting materials, reagents, conditions, and product with stuctures

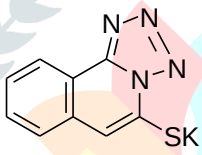
Sr. No	Starting Material	Reactant/Reagent/Conditions	Quinazoline	Ref.
1	 **Methyl anthranilate**	1. $N_2H_4.H_2O$, Refluxed  2. Refluxed 180°C **Two Step Synthesis**	 **3-amino-2-ethoxycarbonyl quinazolin-4-one**	[3]
2	 **Anthranilic acid**	1.  165°C 4hr EtOH POCl3 2. reflux,4hr NMP, HCl heat, 1hr  3. EtOH Piperidine reflux 4hr  4	 **4-(quinazolin-4-ylamino) benzaldehyde**	[4]
3	 **Methyl anthranilate**	1. $ClCH_2COCl$, AcOH Sat. NaOAc Sol, rt 2. 1,2,4-Triazole, DMF, K_2CO_3, reflux 3. RCHO, EtOH, H_2SO_4, reflux		[5]

		Three Steps Synthesis	**3-amino-2-(1H-1,2,4-triazol-1-ylmethyl)quinazolin-4(3H)-one**	
4	 **Isatoic anhydride**	$RCONHNH_2$, ArCHO, Montmorillonite K_{10} EtOH, 50°C, Ultrasonication	 **2-aryl substituted N-(4-oxo-1,2-dihydroquinazolin-3(4H)-yl)aryl.**	[6]
5	 **2-amino-5-cholorobenzophenone**		 **quinazoline**	[7]

B] Antimicrobial Activities

Quinazoline and derivatives shows antimicrobial activities against microbial species, some derivatives and its antimicrobial activities are explained in this short review.

B1. N-aryl(benzyl, heteryl)-2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetamides

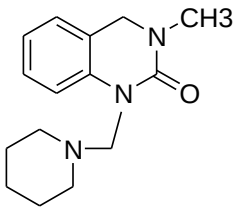


N-aryl(benzyl, heteryl)-2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetamides

Author and co-author first synthesized N-aryl(benzyl, heteryl)-2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetamides. As quinazoline derivatives. Then this derivatives are checked for antimicrobial activities for various gram positive and gram negative bacteria. They used agar diffusion method for preliminary antimicrobial testing. All about this antimicrobial testing is summarized in Fig.2 [8].

Sr. No.	Microgranism	Quinazoline	Zone of Inhibition(mm)	Reference Compound	Zone of Inhibition(mm)	Ref.
1	*Escherichia coli*	N-aryl(benzyl, heteryl)-2-(tetrazolo[1,5-c]quinazoline-5-ylthio)acetamides	6	Ampicillin	26	[8]
2	*Staphylococcus aureus*		6		22	
3	*Enterobacter aerogenes*		6		16	
4	*Enterococcus faecalis*		6		17	
5	*Pseudomonas aeruginosa*		6		-	
6	*Klebsiella pneumoniae*		8		-	
7	*Candida albicans*		6		-	

B2 3-Methyl-1-(piperidin-1-ylmethyl)-3, 4-dihydroquinazolin-2(1H)-one



3-Methyl-1-(piperidin-1-ylmethyl)-3, 4-dihydroquinazolin-2(1H)-one

Samra Farooq and its co-author First synthesized quinazoline derivatives, then they are checked with antimicrobial activities with some gram positive and gram negative microorganisms. There zone of inhibition is compared with Cefixime. *P. aeruginosa* this microorganism shows good antimicrobial activity against this quinazoline compound. This is given in Table: 2 [9].

Sr. No.	Microgranism	Quinazoline	Zone of Inhibition(mm)	Reference Compound	Zone of Inhibition(mm)	Ref.
1	*S.aureus*	Methyl-1-(piperidin-1-ylmethyl)-3, 4-dihydroquinazolin-2(1H)-one	52	Cefixime	75	[9]
2	*E.coli*		38		70	
3	*K. pneumoniae*		51		76	
4	*P.aeruginosa*		74		70	

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