IJPSR (2014), Vol. 5, Issue 3 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 07 October, 2013; received in revised form, 24 November, 2013; accepted, 03 February, 2014; published 01 March, 2014

A BRIEF REVIEW ON RECENT SYNTHESIS OF 2-AZETIDINONE DERIVATIVES

D.S. Salunkhe and P.B. Piste*

P.G. Department of Chemistry, Y.C. Institute of Science, Satara-415 001, Maharashtra, India

Keywords:

2-Azetidinones, β-lactam, Biological activity

Correspondence to Author:

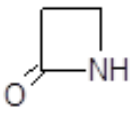
Dr. Mrs. P.B. Piste

Associate Professor in Chemistry, P.G. Department of Chemistry, Y.C. Institute of Science, Satara-415 001, Maharashtra, India

E-mail: ppiste321@gmail.com

ABSTRACT: The chemistry of β-lactams has taken an prestigious place in organic and medicinal chemistry so the review on recent methods in the synthesis of 2-Azetidinone derivatives rendered as a lead molecule for designing potential bioactive agents and it accompanying additional various synthetic information and its orientations would encompass great deal of help to researchers, chemists and pharmacologists to make it the best, most productive, economical and medicinal important compounds which will be expected to show potent pharmacological activities. In future it would be useful to design different new drugs to bring in the market by using rapid, operationally simple, efficient and green procedure. This has led to the discovery of a wide variety of compounds that are of high interest from the point of view antibacterial, anti-inflammatory, antihyperlipidemic, CNS activity, anticancer, antimicrobial, pesticidal, cytotoxic, antidiabetic, antitumor, antifungal, antitubercular activities.

INTRODUCTION: 2-Azetidinones, commonly known as β-lactams, β-lactams ring is a four membered cyclic amide. It is named as such, because the nitrogen atom is attached to the β-carbon relative to the carbonyl.



β-lactam; β-Propiolactam; 2-Azacyclobutanone; 2-Azetidinone; Azetidin-2-one;

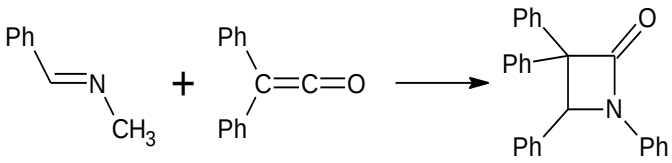
The first synthetic β-lactam was prepared by Hermann Staudinger in 1907 by reaction of the Schiff base of aniline and benzaldehyde with diphenylketene in a [2+2] cycloaddition [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.5(3).666-89

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(3).666-89



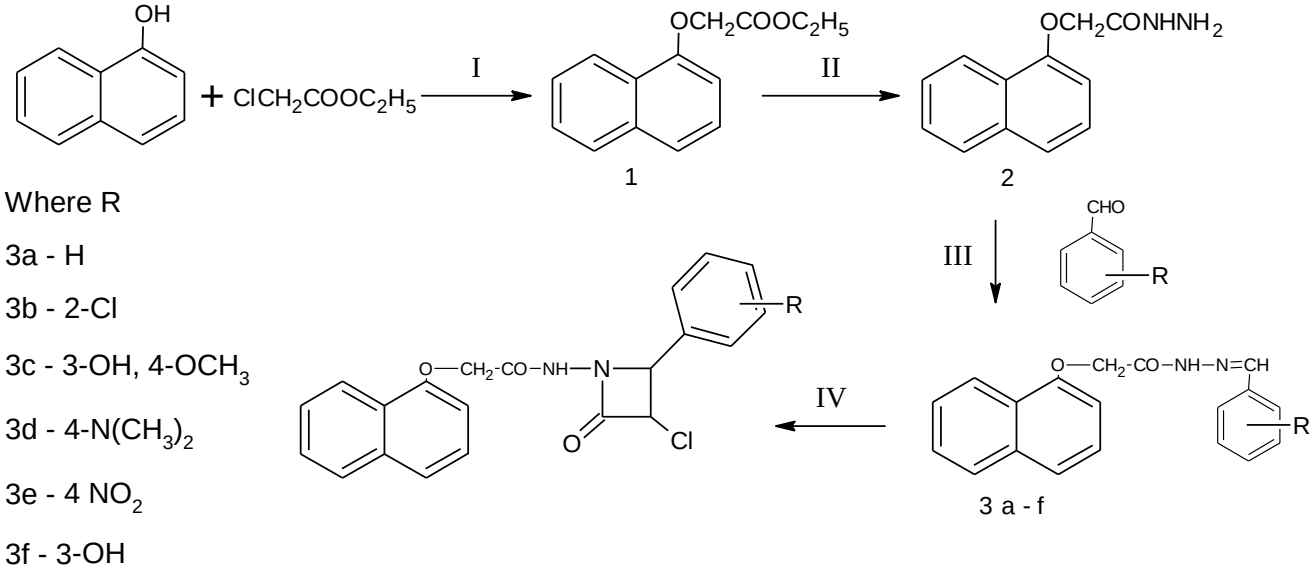
The chemistry of β-lactams has taken an important place in organic chemistry since the discovery of Penicillin by Sir Alexander Fleming in 1928 and shortly thereafter Cephalosporin which were both used as successful antibiotics. Even now the research in this area is stimulated because of development of bacterial resistance to widely used antibiotics of this type. There is a need for functionalized β-lactams or for new active principles in β-lactam series [2]. The 2-azetitinone (β -lactams) ring is a common structural feature of a number of broad spectrum β-lactam antibiotics including penicillins I, cephalosporins II, carbapenems III, nocardicin A IV and monobactams which have been widely used as chemotherapeutic agents to treat bacterial infection and microbial diseases [3, 4].

Azetidinones are very important class of compounds possessing wide range of biological activities such as antibacterial [5], anti-inflammatory [6], antihyperlipidemic [7], CNS activity [8], tryptase inhibitory [9], human leukocyte elastase inhibitory [10], antihyperglycemic [11], vasopressin v1a antagonist [12], and anticancer activity [13], antimicrobial [14], pesticidal [15], antitumor [16], antitubercular [17], cytotoxic [18], enzyme inhibitors [19], elastase inhibitors [20] and cholesterol absorption inhibitors [21].

MATERIALS AND METHODS: We have composed data on recent synthesis of 2-Azetidinone derivatives especially by using International Journals Such as International Journal of Pharm Tech Research, Pure Appl. Chem., Molecules, Eur. J. Med. Chem, Journal of Pharmacy and Pharmaceutical Sciences, Bioorg. Med. Chem. Lett., Tetrahedron, Org. Commun., Asian J. Pharm. Res., World J. Chemistry, Rasayan J. Chem., International Journal of pharmaceutical and Chemical Sciences, International Journal of Drug Design and Discovery, Der Pharmacia Sinica etc. up to 2012. Here, we have selected different methods in synthesis of 2-Azitidinones with different moiety by using different reagents etc.

Brief review on 2-azetidinones derivatives: Kumat *et al* [22] synthesized α-Naphthol into 4-methyl-2*H*-benzo[*h*]chromen-2-one by reacting with ethyl acetoacetate in the presence of bismuth trichloride.

The product was oxidized to 2-oxo-2*H*-benzo[*h*]chromene-4-carbaldehyde and then condensed with aromatic primary amines to give Schiff bases 3a–d. These Schiff bases were then reacted with acid chlorides in the presence of a base in toluene to give 1, 3, 4-substituted 2-azetidinones.



Where R

3a - H

3b - 2-Cl

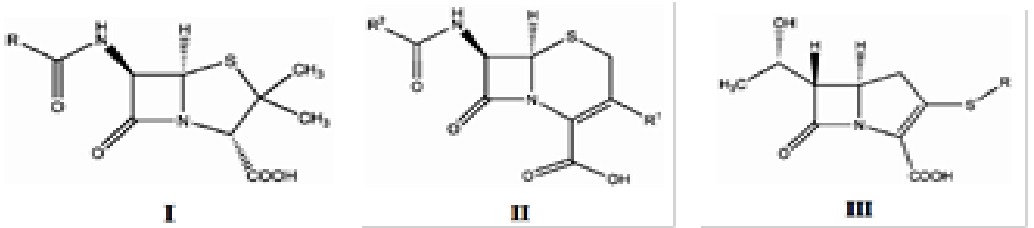
3c - 3-OH, 4-OCH_3

3d - 4-$N(CH_3)_2$

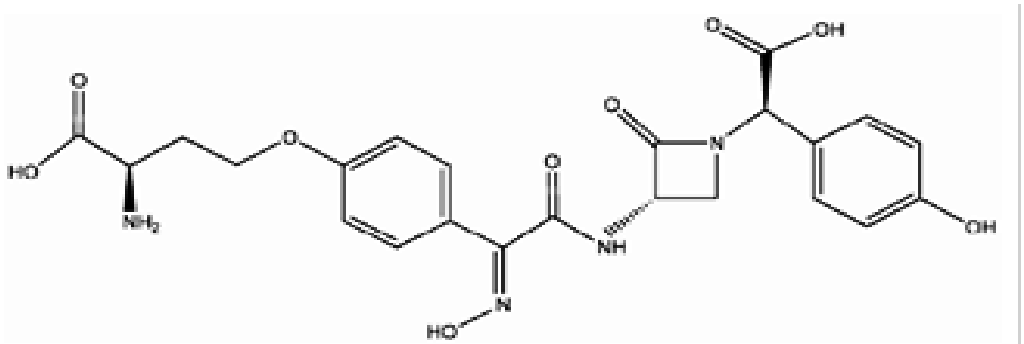
3e - 4 NO_2

3f - 3-OH

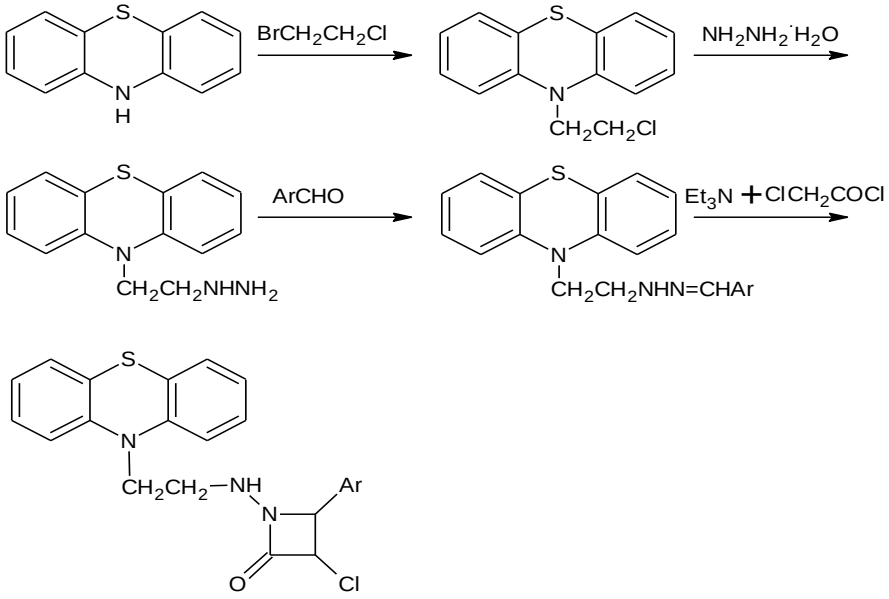
Sharma Ritu *et al* [23] synthesized of N-[2-(10H-phenothiazinyl)ethyl]-4-(phenyl)-3-chloro-2-oxo-1-iminoazetidine. The structures of all the newly synthesized compounds were confirmed by IR, 1H NMR, 13C NMR and FAB-Mass and chemical methods. All synthesized compounds were evaluated for their antibacterial, antifungal and antitubercular activity which displayed acceptable results.



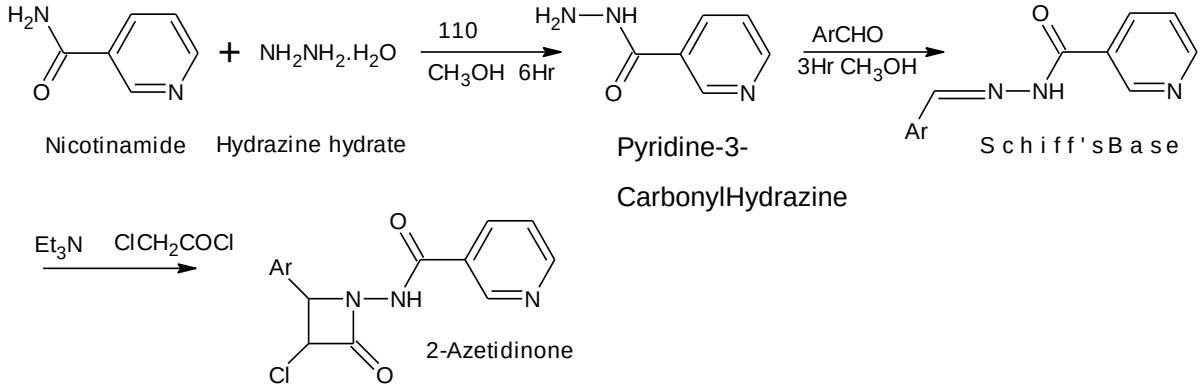
I II III



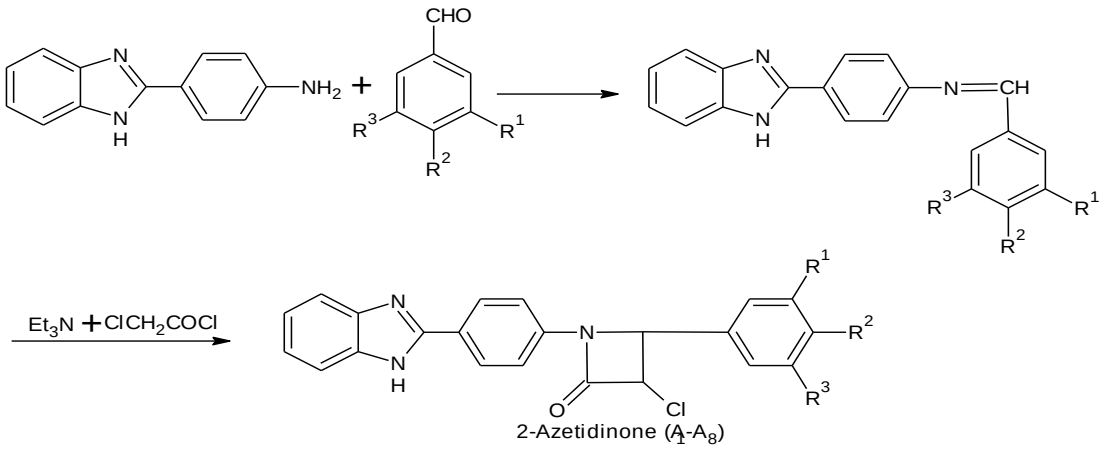
IV



Preethi *et al* [24] synthesized a series of 2-azetidinone derivatives were synthesized by refluxing Schiff bases with different aromatic aldehydes. Schiff bases were synthesized by reaction of nicotinamide with hydrazinehydrate. The chemical structures of the synthesized compounds were confirmed by means of IR, 1H-NMR, mass spectroscopy and elemental analysis.



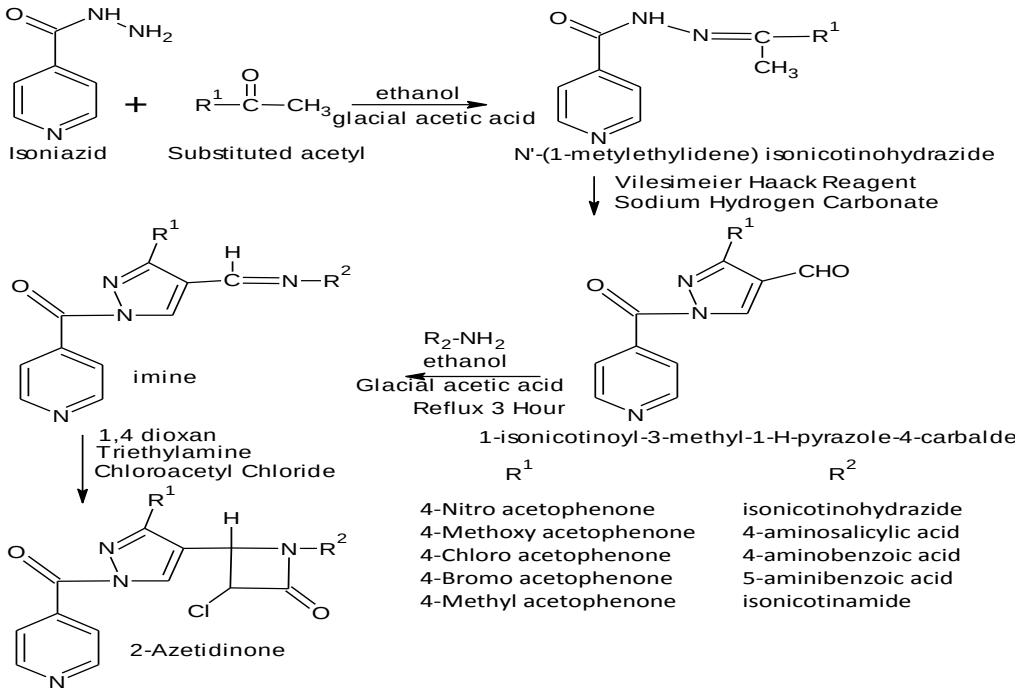
Shanmugapandiyan *et al* [25] prepared series of 2-[4-(azetidin-2-one)-3-Chloro-4-phenyl]-1H-Phenylbenzimidazoles by the reaction of schiff base [2-(4-aminophenyl)-Benzimidazole and substituted Benzaldehyde] with chloroacetyl chloride. The chemical structures of the synthesized compounds were confirmed by IR, 1H-NMR, mass spectral and C, H, N analysis. The synthesized compounds were screened for antibacterial (*Bacillus cereus, Escherichia coli, Micrococcus luteus, Klebssiela pneumoniae, Staphylococcus aureus* and *Salmonella epidermidis*), antifungal (*Aspergillus niger and Candida albicans*), analgesic activity by writhing reflex method and anti-inflammatory activity by carrageenan induced paw edema method.



2-Azetidinone (A_1-A_8)

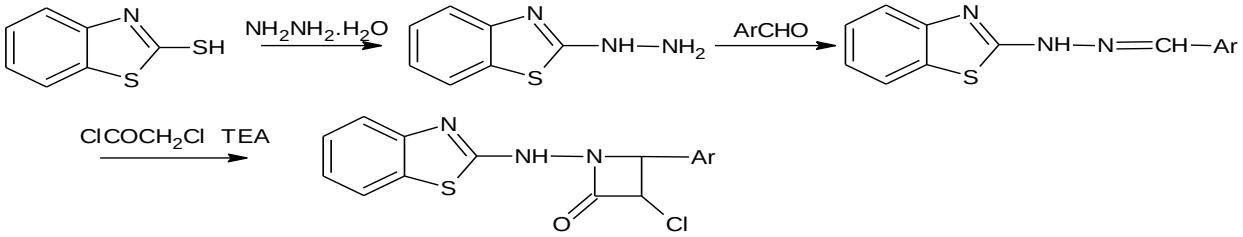
Comp.no.	R_1	R_2	R_3	Comp.no.	R_1	R_2	R_3
A_1	-H	-H	-H	A_5	-H	$-N(CH_3)_2$	-H
A_2	-H	-Cl	-H	A_6	-H	$-OCH_3$	-H
A_3	-H	-OH	-H	A_7	$-OCH_3$	$-CH_3$	-H
A_4	-H	$-CH_3$	-H	A_8	-OCH3	$-OCH_3$	$-OCH_3$

Rathinavel *et al* [26] synthesized novel derivatives of 2-azetidinones by Isoniazid condensed with different derivatives of acetophenone to form hydrazones, using Vilsmerier – Haack reagent to form free aldehyde. The free aldehyde reacts with different free amide ($R\text{-}NH_2$) group to form imines (>C=N) which on react with chloro acetyl chloride and triethylamine to give 2-azetidinone derivatives. The structures of the newly synthesized compounds have been established on the basis of their spectral data and elemental analysis.

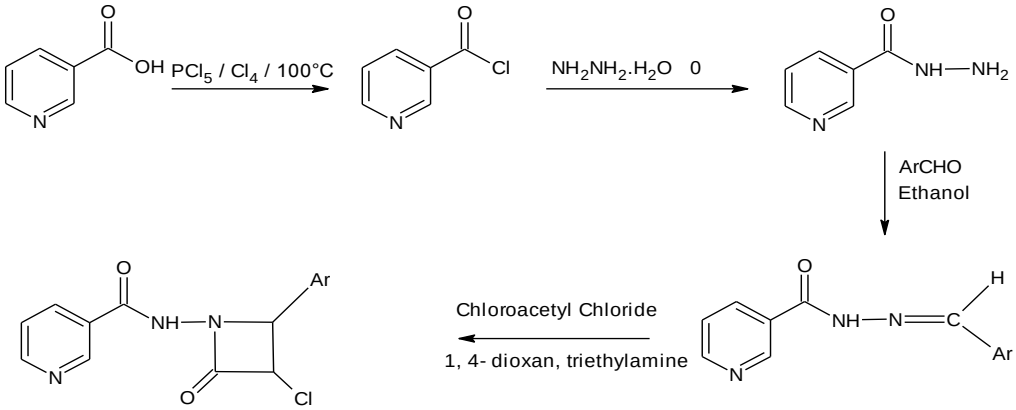


R^1	R^2
4-Nitro acetophenone	isonicotinohydrazide
4-Methoxy acetophenone	4-aminosalicylic acid
4-Chloro acetophenone	4-aminobenzoic acid
4-Bromo acetophenone	5-aminibenzoic acid
4-Methyl acetophenone	isonicotinamide

Dua *et al* [27] reported 2-(4-substituted aryl-3-chloro-2-oxo-azetidine)-2-imino benzothiazoles by the hetrocyclization of 2-substituted arylidene hydrazinobenzothiazoles with chloroacetyl chloride in the presence of triethylamine under microwave irradiation. The reaction rate and yield is enhanced tremendously under MWI as compared to conventional methods.

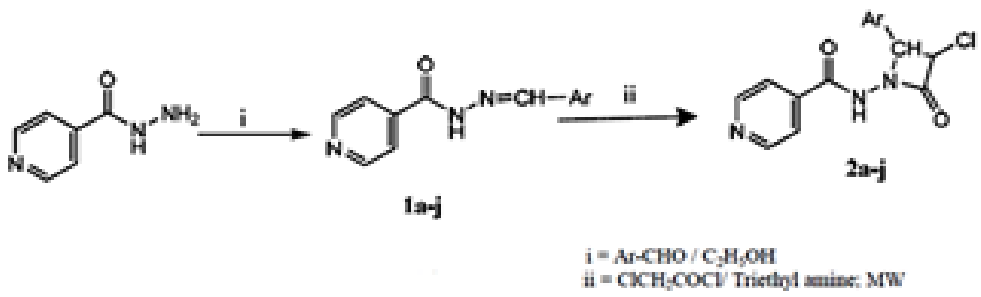


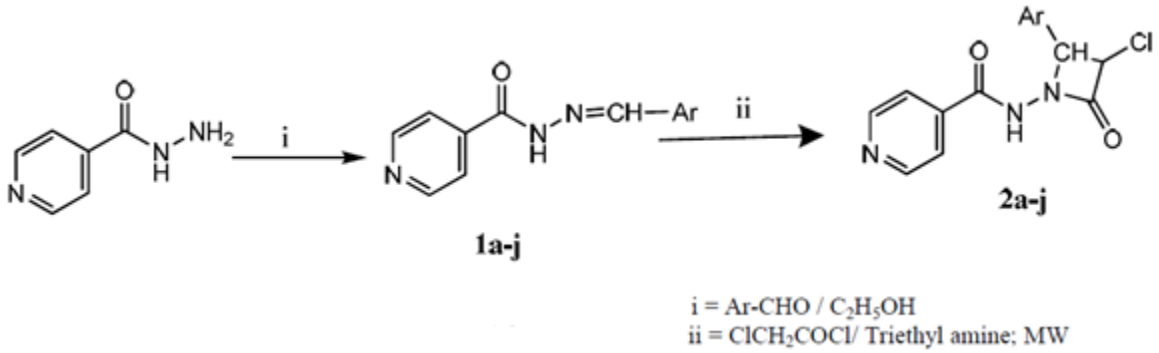
Ramalakshmi *et al* [28] reported novel series of 4 - aryl – 3 - chloro – 1 – nicotinamido – 2 – azetidinones were synthesized and characterized by means of IR, 1H- NMR, Mass spectral analysis. The compounds were screened for anticonvulsant and antimycobacterial activities. Antimycobacterial activity was screened using standard Strain H37RV and two Human Strains (Human strain-I and Human strain-II) isolated from patients suffering from pulmonary tuberculosis.



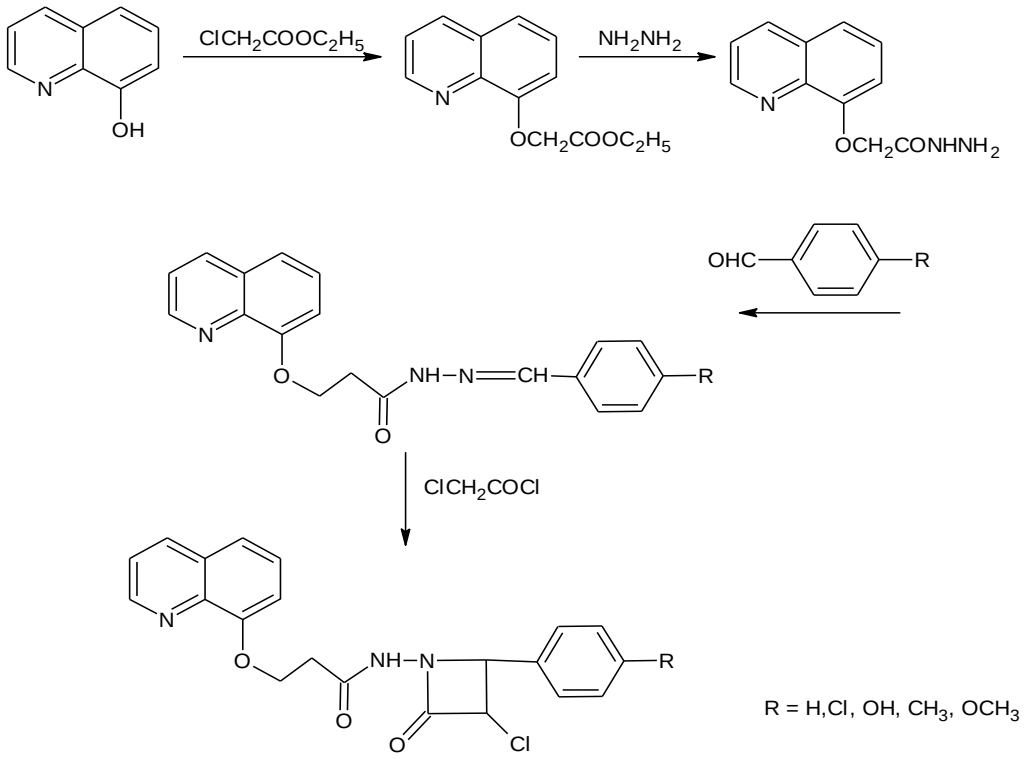
Ar	Ar
2-Hydroxy phenyl	3-Hydroxy phenyl
4-Hydroxy phenyl	3,4-Dihydroxy phenyl
4-Methyl phenyl	4-Methoxy phenyl
3,4,5-Trimethoxy phenyl	4-Hydroxy 3-methoxy phenyl
4-Dimethylaminophenyl	4-Nitro phenyl
3-Nitro phenyl	4-Chloro phenyl
2-Chloro phenyl	Cinnamyl

Shah *et al* [29] reported Pyrazolines are well-known and important nitrogen containing 5-membered heterocyclic compounds and various methods have been worked out for their synthesis. A new series of 3-chloro-1-{4-[5-(Substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-4-(4-hydroxyphenyl) azetidin-2-one are synthesized by reacting 3-chloro-1-{4-[3-(Substituted phenyl)prop-2-enoyl]phenyl}-4-(4-hydroxyphenyl)azetidin-2-one with 99% hydrazine hydrate. All these compounds were characterized by means of their IR, 1H NMR, Spectroscopic data and microanalysis.

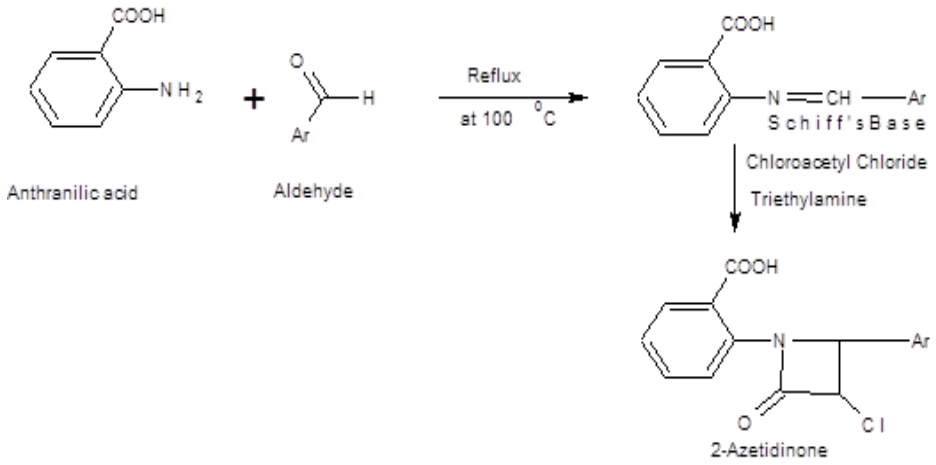




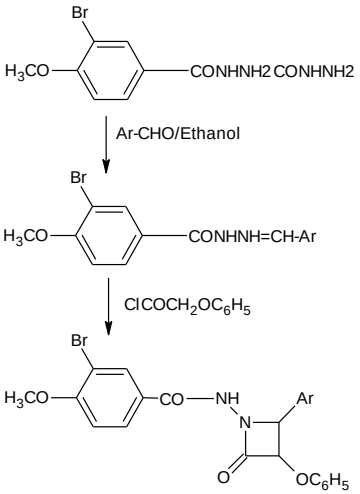
Sangu *et al* [30] synthesized some novel azetidinones from quinolone. Quinoline derivatives are reported to have antimicrobial, anti-inflammatory, analgesic and anticancer activities. The incorporated oxymethylcarbamide at 8th position of the quinoline ring was found to influence the biological activities of the molecules with this some of new quinolinyloxymethylazetidinones were synthesized from 8-hydroxy quinolone through (quinolin-8-yl-oxy) acetyl hydrazide intermediate. All the synthesized compounds were characterized by IR, H1 NMR spectral data and evaluated for their antimicrobial activity.



Panda *et al* [31] reported Schiff bases of anthranilic acid have been synthesized by reaction with different aromatic aldehydes and the azetidinones have been synthesized by cyclocondensation of the Schiff's base with chloroacetyl chloride in the presence of trietylamine. The structures of the newly synthesized compounds have been established on the basis of their spectral data and elemental analysis.

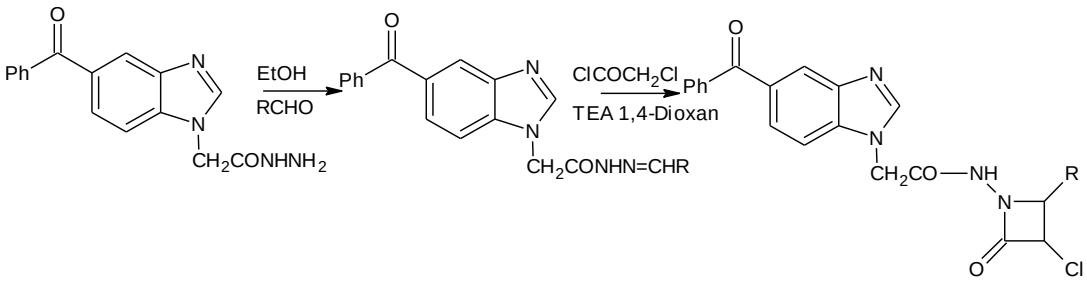


Sahoo *et al* [32] synthesized some novel 2-azetidinone derivatives. 3-bromo-4-methoxybenzoyl hydrazine was prepared from methyl ester of 4-methoxybenzoic acid by bromination and subsequent hydrazinolysis. The acid hydrazide was condensed with different aromatic aldehydes in ethanol as solvent to yield substituted benzal-3-(3'-bromo-4'-methoxybenzoyl) hydrazines. The benzalhydrazines on cyclization with phenoxyacetyl chloride in presence of triethylamine as catalyst afforded 3-phenoxy-4-(substituted phenyl)-1-(3'-bromo-4'-methoxy benzamide)azetidin-2-ones.



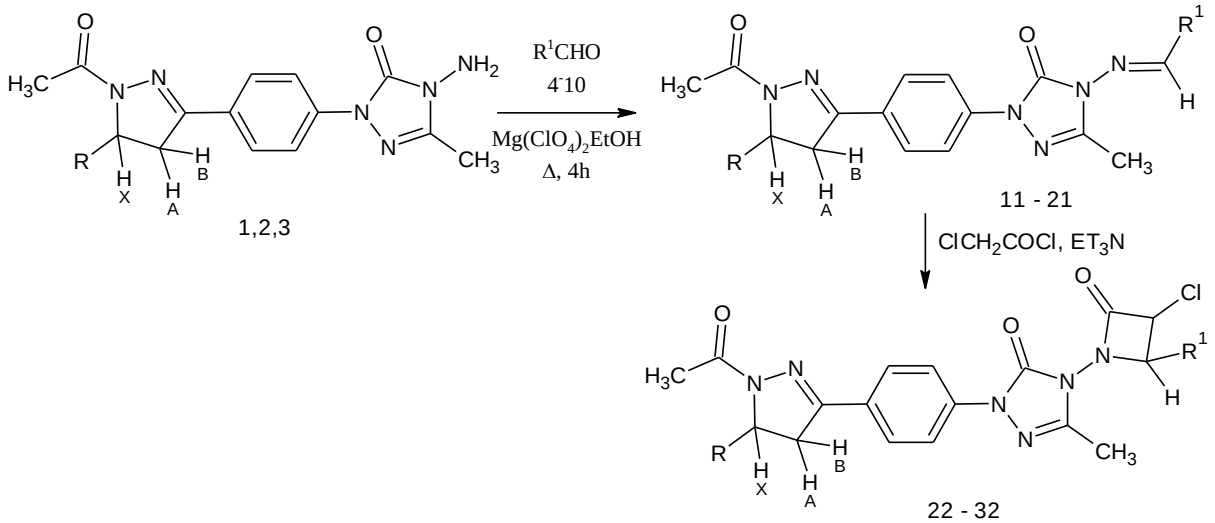
Ar
Phenyl
4-Hydroxyphenyl
4-Hydroxy-3-methoxyphenyl
4-Chlorophenyl
2-Hydroxyphenyl
4-Methoxyphenyl
2-Thienyl
2-Furyl

Kumar *et al* [33], reported that 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl) acetohydrazide undergoes facile condensation with aromatic aldehydes to afford the corresponding 2-(5-benzoyl-1H-benzo[d]imidazol-1-yl)-N'-arylideneacetohydrazide in good yield. Cyclo condensation of compounds with chloro acetyl chloride yields 2-(5-benzoyl-1Hbenzo[d]imidazol-1-yl)-N-(3-chloro-2-aryl-4-oxoazetidin-1-yl)acetamide.

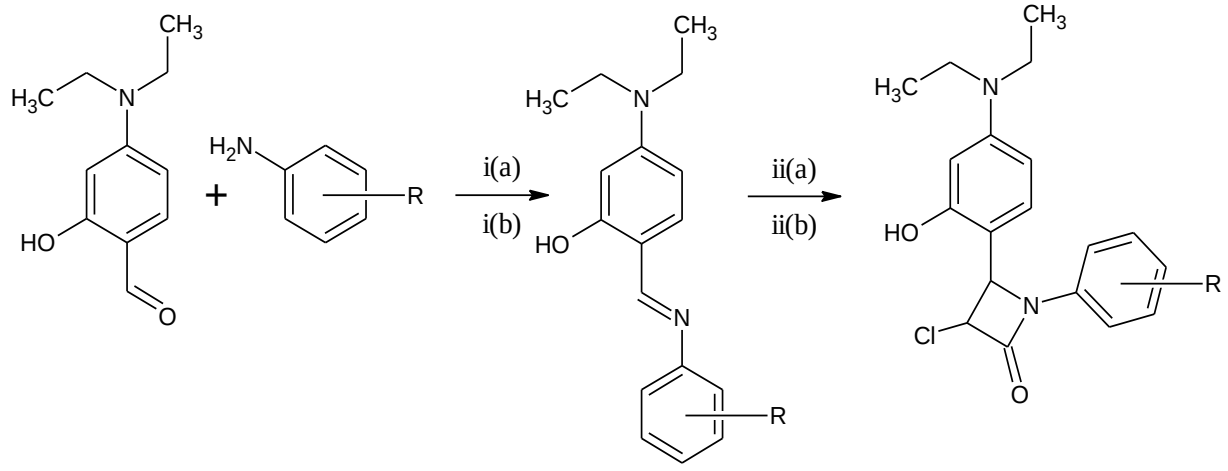


R	$-C_6H_5$	$-OCH_3-C_6H_5$	$-OH-C_6H_5$
	$2-OH-C_6H_5$	$-CH_3-C_6H_5$	$-4CH_2O_2-C_6H_5$
	$4-OH-3-OCH_3-C_6H_5$	$-4-C_2H_5-C_6H_5$	

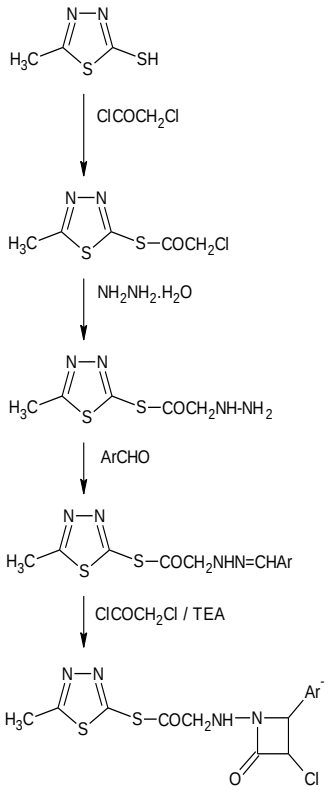
Taj *et al* [34] reported an efficient green approach to the synthesis of Schiff bases (11–21) of 1-amino-2-aryl-3-oxo-1, 2, 4- triazoles (1–3) under Mg(ClO4)2 as catalyst followed by the reaction with chloroacetyl chloride in solvent-free conditions to yield the azetidinones (22–32) with excellent yields. The synthesized compounds were evaluated for the extent of penetration into biological membranes (*clogP*), drug-likeliness and finally drug score was calculated and also screened for antitubercular and antimicrobial activities.



Kumaraswamy *et al* [35] reported the reaction of naphtho[2,1-b]furan-2-carbohydrazide (1) with carbon disulphide and excess of hydrazine hydrate in ethanol produced 4-amino-5-naphtho[2,1-b]furan-2-yl-4H-1,2,4-triazol e-3-thiol (2). The thiol 2 on treatment with aromatic aldehydes yielded 4-{[(4-aryl) methylene]amino}-5-(naphtho[2,1-b]furan-2-yl)-4H-1,2,4-triazole-3-thiols (3a-f). The title compounds, chloro-1-(3-mercapto-5-naphtho[2,1-b]furan-2-yl-1,2,4-triazole-4-yl)-2-(aryl) azetidin-4-ones (4a-f) were obtained by reacting compounds 3a-f with choloro acetyl chloride in presence of triethyl amine.



Dua *et al* [36] reported that systematic investigation of synthesis and biological activity of several new 2-(2'-substitutedbenzylidene-hydrazino-acetyl)-mercapto-5-methyl-1,3,4-thiadiazoles and 2-[2'-{4-substituted-aryl-3-chloro-2-oxo-azetidine}-acetyl-amino-mercapto]-5-methyl-1,3,4-thiadiazoles have been synthesized from 2-(2'-hydrazino-acetyl)-mercapto-5-methyl-1,3,4-thiadiazoles, 2 using 5-methyl-1,3,4-thiadiazole-2-thiol as the starting material.



Where	Ar =
a)	C_6H_5
b)	2-ClC_6H_4
c)	3 – ClC_6H_4
d)	4 – ClC_6H_4
e)	2 – BrC_6H_4
f)	3 – BrC_6H_4
g)	4 – BrC_6H_4
h)	2 – $NO_2C_6H_4$
i)	3 – $NO_2C_6H_4$
j)	4 – $NO_2C_6H_4$
k)	2 – $OCH_3C_6H_4$
l)	3 – $OCH_3C_6H_4$
m)	4 – $OCH_3C_6H_4$
n)	4,4'$(CH_3)_2NC_6H_4$

Bhusari *et al* [37], reported the reaction of 4-methoxybenzaldehyde;

(1) With a substituted hydrazine

(2) In refluxing isopropyl alcohol gave imines

(3) Refluxing glutaric anhydride

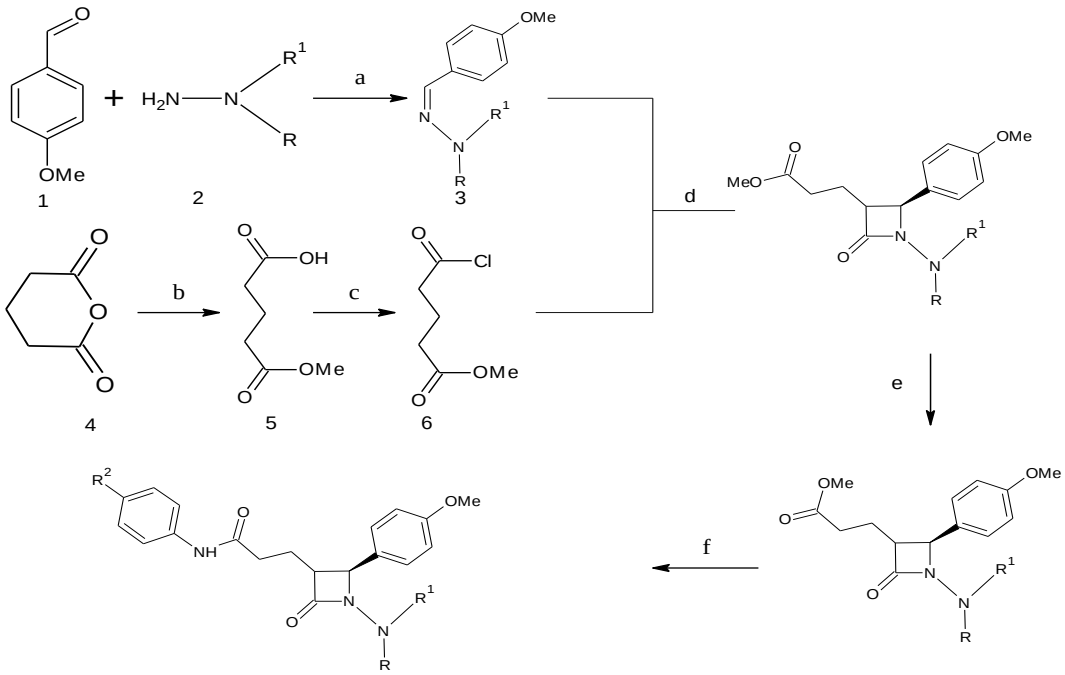
(4) With an equivalent amount of anhydrous MeOH afforded monomethylglutarate;

(5) and treatment of (5) in refluxing $SOCl_2$ yielded methyl 4-(chloroformyl) butyrate

(6) Compound (6) was added to a refluxing solution of imine (3) in anhydrous toluene in the presence of tri(n-butyl)amine. Maintaining the mixture refluxing overnight, gave 2-azetidinone intermediate

(7) Hydrolysis of 7 with LiOH solution affords acid

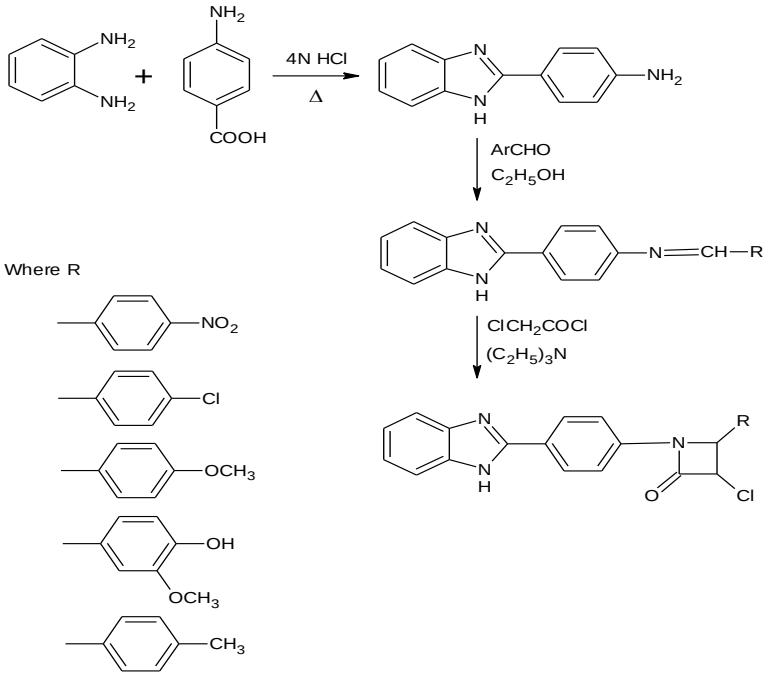
(8) In almost quantitative yield. Finally the reaction of 8 with substituted aromatic amine in the presence of DCC/DMAP in anhydrous CH_2Cl_2 at room temperature gave 2-azetidinone derivatives.



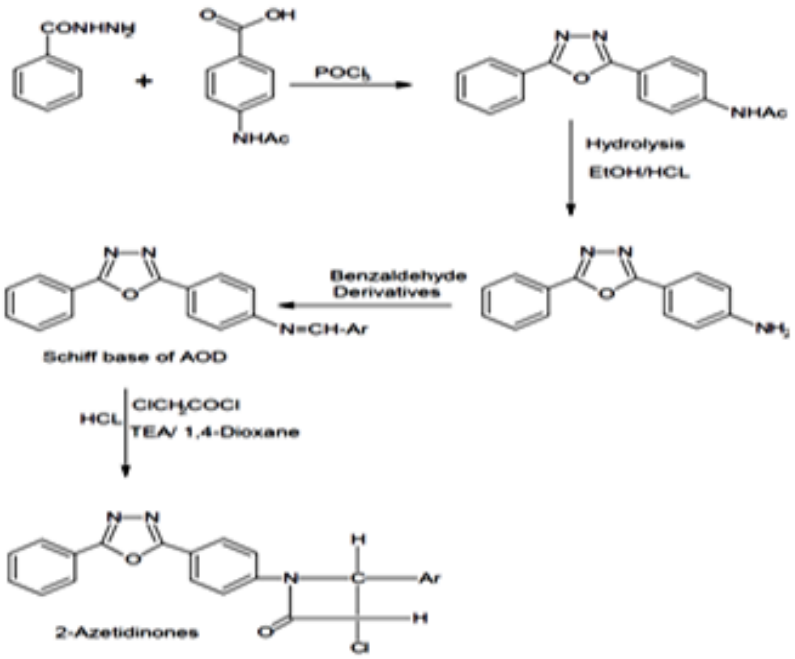
Reagent and condition: (a)iPrOH, reflux; (b)CH_3OH, reflux (c)$SOCl_2$, reflux (d)n-Bu3N, Toluene, reflux (e) LiOH, THF/H_2O (f) substituted aromatic amine, DCC/DMAP, CH_2Cl_2

Selvam *et al* [38] reported that thiazolidinone derivatives synthesized by equimolar quantities of o-phenylenediamine, p-amino benzoic acid in 4N HCl was refluxed for 30 min. to give 4-(1H-benzo[d] imidazol-2-yl) benzenamine. A mixture of equimolar quantities of aromatic aldehyde and 4-(1H-benzo[d]imidazol-2-yl) benzenamine was refluxed for 20 min in 20 mL of ethanol to give

schiff base N-(4-substituted benzylidine)-4-(1H-benzo[d]imidazol-2-yl) benzenamine. A mixture of schiff base, triethylamine, 1,4– Dioxan and chloro acetyl chloride was stirred yield 1-(4-(1Hbenzo[d]imidazol-2-yl) phenyl)-3-chloro-4-(4-substituted phenyl) azetidin-2-one.

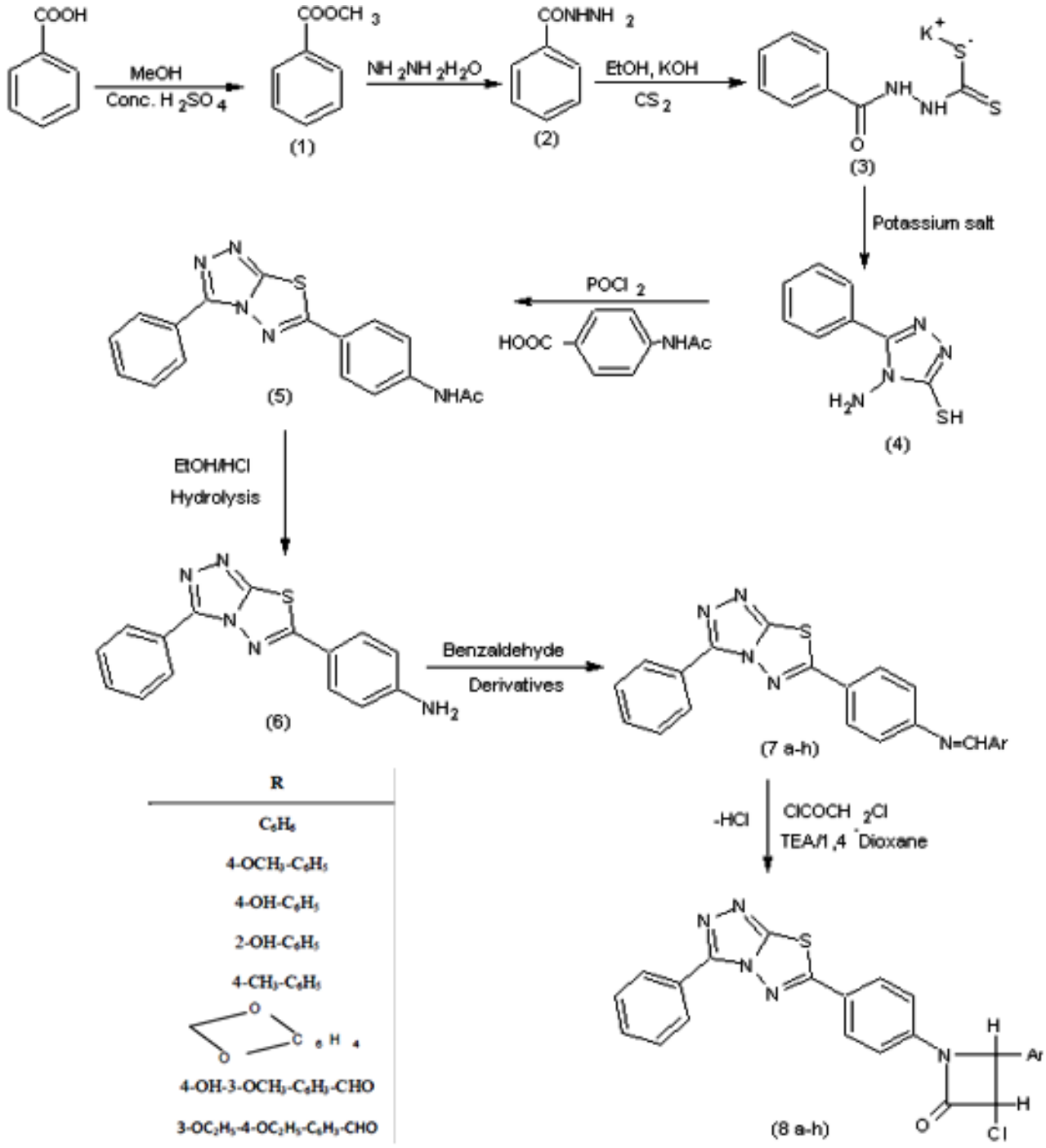


Parmar *et al* [39] reported synthesis of 2 – azetidinones. The N-acetyl aryl amino-1,3,4-oxadiazole were prepared by Benzohydrazide in phosphorus oxychloride, N-acetyl-4-amino benzoic acid and ethanol. The aryl amino-1,3,4-oxadiazole (AOD) were prepared by hydrolysis of N-acetyl aryl amino-1,3,4-oxadiazole. N-acetyl aryl amino-1,3,4-oxadiazole and ethanol-HCl mixture The Schiff bases of AOD were prepared by Benzaldehyde derivatives, 3-chloro-1-[4(5-phenyl-1,3,4-oxadiazole-2-yl)phenyl]-4-phenyl azetidin-2-ones were synthesized with Schiff bases on treatment with Chloroacetylcloride in the presence of triethylamine



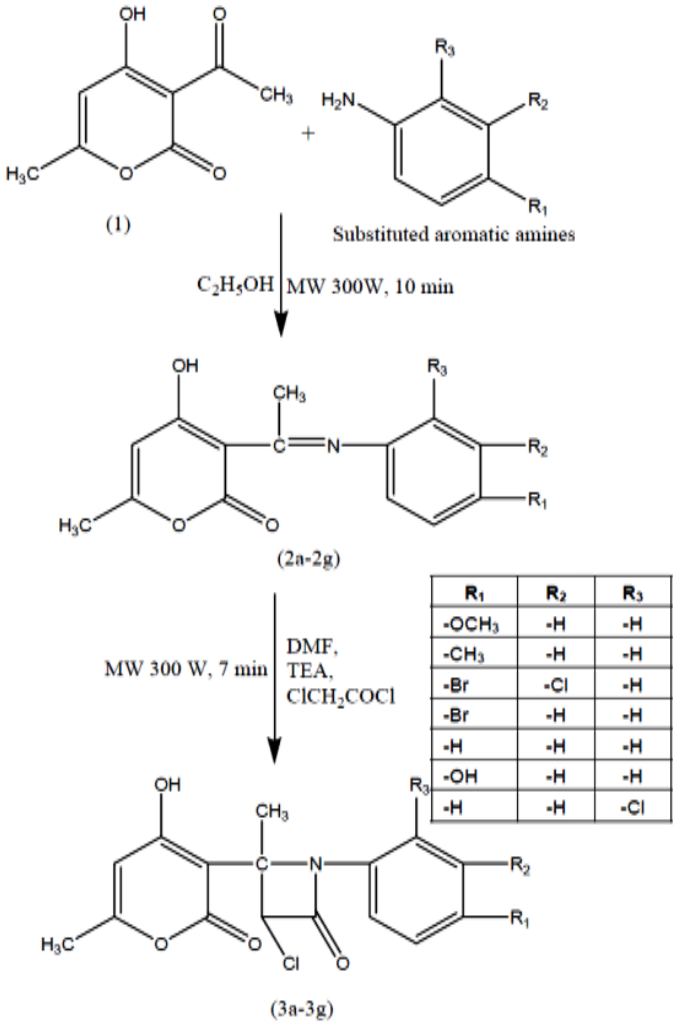
Parmar *et al* [40] reported series of novel 2-Azetidinones (8a-h) have been synthesized by cyclocondensation of various Schiff bases based of ATT with chloroacetyl chloride in presences of triethylamine. Various Schiff bases were synthesized by condensation of ATT with various

aryl aldehydes (7a-h). The synthesized compounds 8a-h was screened for their antibacterial activity.



Pulate *et al* [41] reported the reaction of dehydroacetic acid with primary aromatic amines to yield Schiff bases (2a-2g) by using microwave system. Schiff bases irradiated with dimethyl formamide in presence of triethyl amine and chloroacetyl chloride to afford azetidinones (3a-3g) in excellent yields.

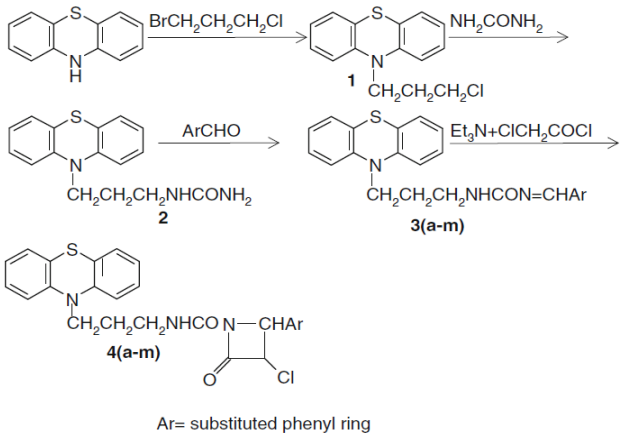
The products, characterized on the basis of spectral data, have shown moderate to good antimicrobial activity against some bacteria and fungi



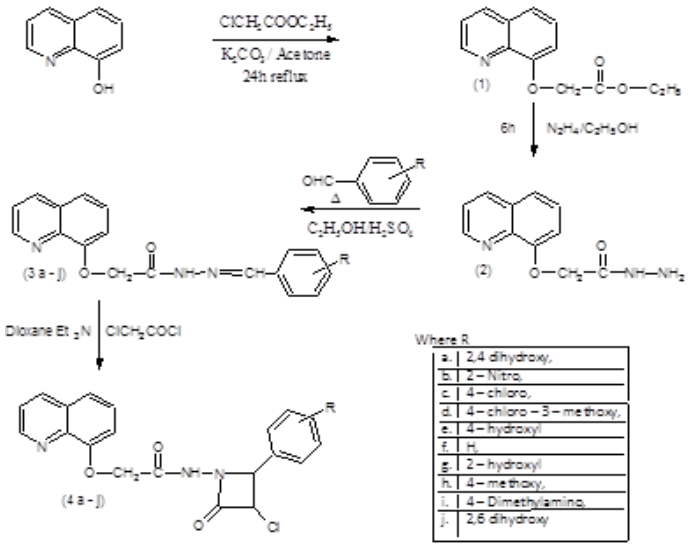
R_1	R_2	R_3
-OCH_3	-H	-H
-CH_3	-H	-H
-Br	-Cl	-H
-Br	-H	-H
-H	-H	-H
-OH	-H	-H
-H	-H	-Cl

Sharma *et al* [42] reported a new series of N-[3-(10H-phenothiazin-1-yl)propyl]-4-(substituted phenyl)-3-chloro-2-oxo-1-azetidinecarboxamide 4(a–m) have been synthesized from phenothiazine in four steps. Phenothiazine on reaction with $Cl(CH_2)_3Br$ at room temperature gave 1-(3-chlorophenyl)-10H-phenothiazine, 1. The compound 1 yielded the condensation product with urea at room temperature, N-[3-(10H-phenothiazin-1-yl)propyl]urea 2.

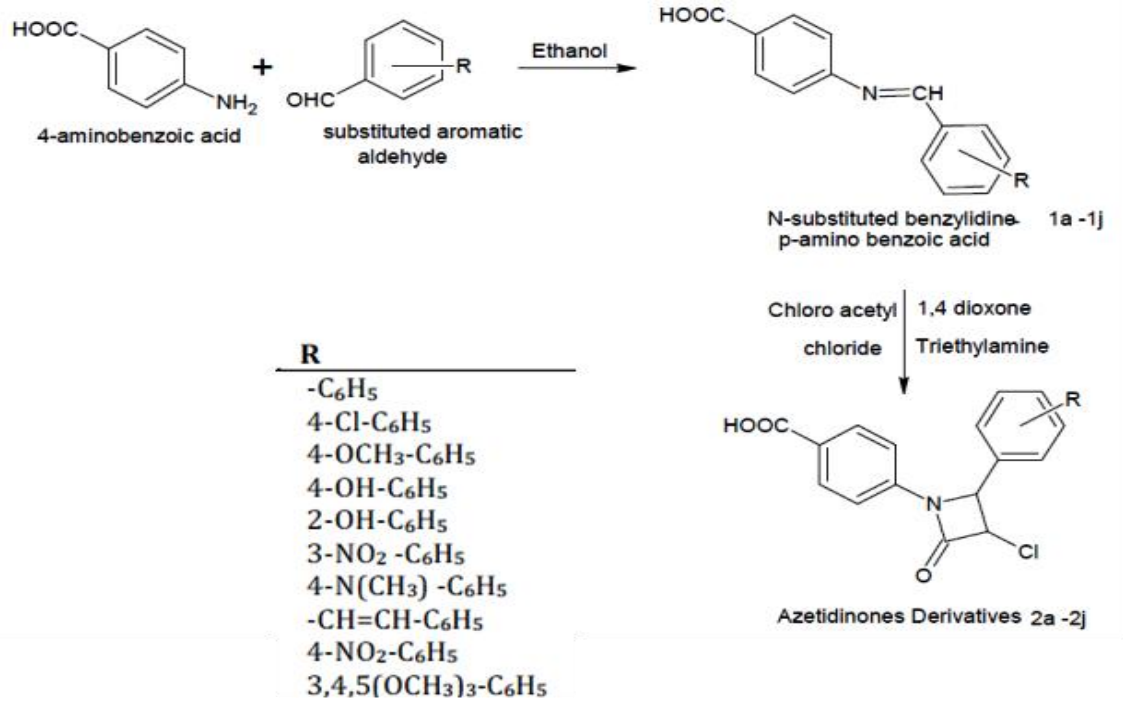
The compound 2 on further reaction with several substituted aromatic aldehydes produced N-[3-(10Hphenothiazin-1-yl)propyl]-N_-[(substituted phenyl)methylidene]-urea 3(a–m). The compounds 3(a–m) on treatment with $ClCH_2COCl$ in the presence of Et_3N furnished final products 2-azetidinone 4(a–m).



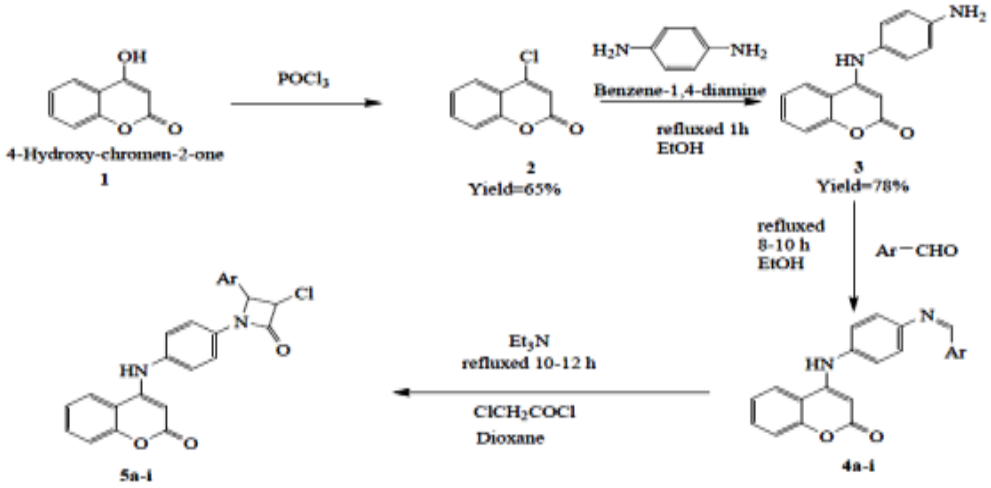
Maity *et al* [43], reported the reaction of 8 – hydroxyl quinolone with ethyl chloro acetate to give 8 – hydroxyl quinoline ethyl acetate, which on hydrazonolysis gave 8 – hydroxyl quinoline acetyl hydrazide. This compound was converted to corresponding Schiff's bases of 8 – hydroxyl quinoline acetyl hydrazide by the reaction with different aromatic or heterocyclic aldehydes. Finally, the cyclization of Schiff's bases with chloroacetyl chloride in the presence of triethylamine and dioxane resulted in the formation of corresponding 2 – azetidinonederivaties.



Pawar *et al* [44] reported that Para-amino benzoic acid on addition with different aromatic aldehyde gives schiff's bases. The Schiff base so formed on treatment with chloroacetylchloride and triethyl amine as a base catalyst in 1-4 dioxan gives various substituted 4-[3-chloro-4-substituted phenyl-2-oxo-azetidin-1-yl] benzoicacid containing different functional groups(2a-2j). The lead compounds were characterized by melting point, TLC, IR, and 1HNMR studies.



Patel *et al* [45] reported a series of novel azetidinones 5a-i have been synthesized by cyclocondensation of various Schiff bases of coumarin with chloro acetyl chloride in presence of triethyl amine. The reaction of 4-hydroxy coumarin with $POCl_3$ yielded 4-chloro coumarin 2 and 4-chloro-3, 4', 3', 4''-tercoumarin 2a. Compound 2 was reacted with p-phenylenediamine to yield 4-[(4-aminophenyl)amino]-2H-chromen-2-one. Various Schiff bases of coumarin were synthesized by condensation of 4-[(4-aminophenyl)amino]-2H-chromen-2-one with different aldehydes

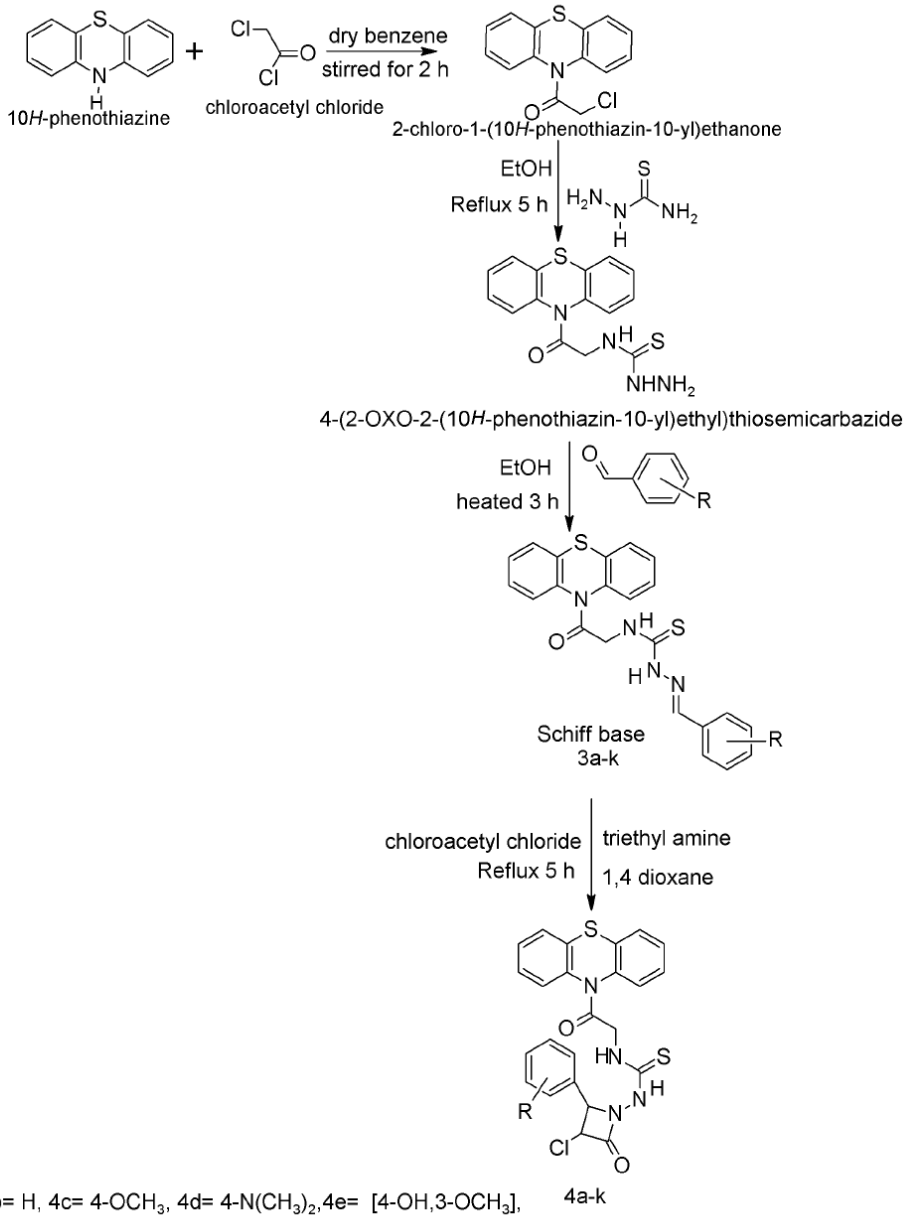


	Ar		
a	Phenyl	e	4-chloro phenyl
b	4-Nitro phenyl	f	4-methyl phenyl
c	3-Nitro phenyl	g	Phenyl-2-carboxaldehyde
d	3,4-dimethoxy phenyl	h	Naphthyl
		i	2-chloro quinonyl

Chavan *et al* [46] have been synthesized several 2-azetidinones 2a-e and 4-thiazolidinones 3a-e from halo-substituted Schiff bases using conventional as well as microwave technique. The newly synthesized compounds were established on the basis of spectroscopic technique. Further, all compounds screened for antimicrobial activity against *Bacillus subtilis*, *Escherichia coli*, *Aspergillus niger* and *Aspergillus flavus*. Most of the titled compounds show potent activity.

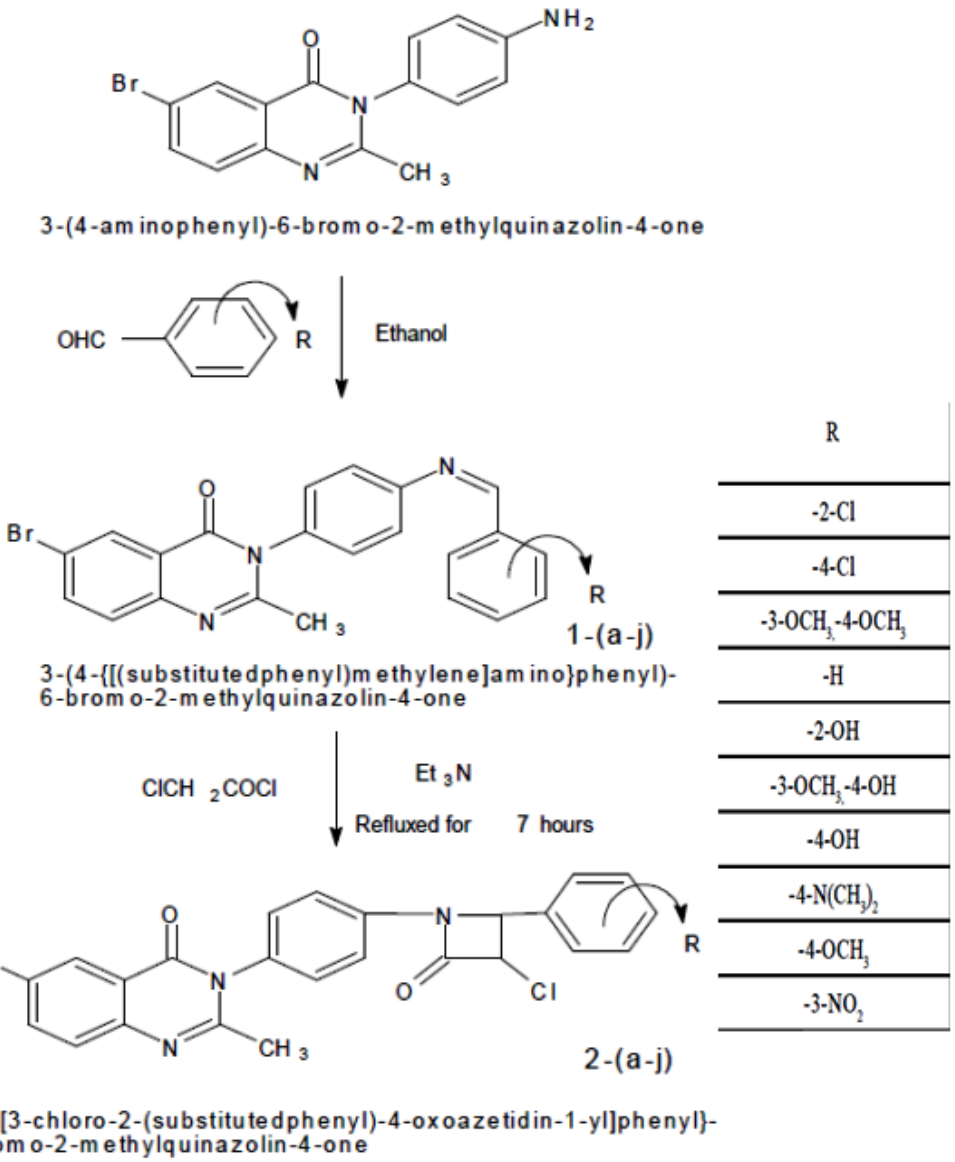
Rajasekaran *et al* [47] reported reaction of chloroacetyl chloride and phenothiazine in dry benzene to give 2-chloro-1-(10H-phenothiazin-10-yl) ethanone. A mixture of 2-chloro-1-(10H-phenothiazin-10-yl)ethanone and thiosemicarbazide in absolute ethanol yields 4-(2-oxo-2-(10H-phenothiazin-10yl)ethyl)thiosemicarbazide.

Mixture of 4-(2-oxo-2-(10H-phenothiazin-10-yl) ethyl) thiosemicarbazide and substituted benzaldehyde in ethanol give Schiff's base and Chloroacetyl chloride was added drop wise to the mixture of triethylamine and solution of substituted Schiff bases Azetidinones.

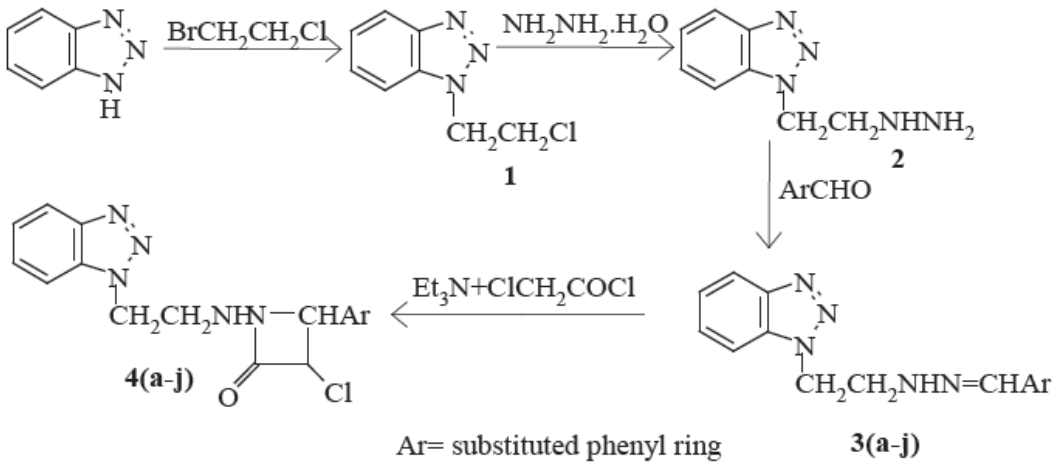


4a= H, 4b= H, 4c= 4-OCH_3, 4d= 4-$N(CH_3)_2$,4e= [4-OH,3-OCH_3], 4f= 4-NO_2, 4g= 2-Cl, 4h= 4-Cl, 4i= 4-OH, 4j= 3-Cl, 4k= 3-F

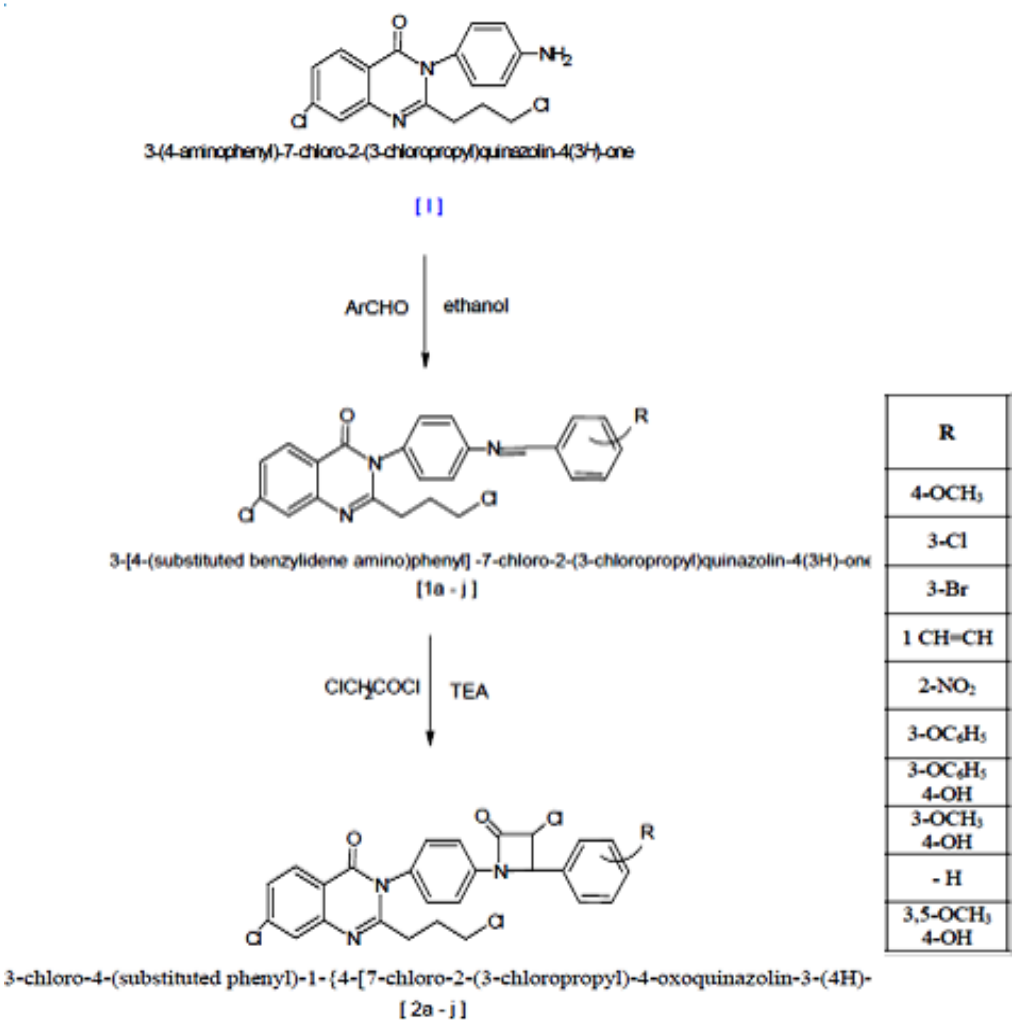
Gor *et al* [48] reported the reaction of 3-(4-aminophenyl)-6-bromo-2-methylquinazolin-4-one in absolute ethanol, substituted aldehydes and a few drops of glacial acetic acid to get compound 3-(4-{[(substitutedphenyl)methylene]amino}phenyl)-6-bromo-2-methyl quina- zolin-4-one(1a-j). The mixture of compound 1 in benzene was taken. Chloro acetyl chloride was added at room temperature with constant stirring and triethylamine to produced 3-{4-[3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl]phenyl}-6-bromo-2-methylquinazolin-4-one.[2-(a-j)]



Sharma *et al* [49] reported the reaction of 1,2,3-Benzotriazole and 1-bromo-2-chloroethane in methanol yield compound 1-(2-chloroethyl)-1H-1,2,3-benzotriazole (1).The compound 1 and hydrazine hydrate were stirred on a magnetic stirrer to yield compound N-[2-(1H-1,2,3-benzotriazol-1-yl)ethyl]-hydrazine (2). The compound 2 and different substituted benzaldehyde in methanol in the presence of 2-4 drops glacial acetic acid to furnish compound N-[2-(1H-1,2,3-benzotriazol-1-yl)ethyl]-N'-[(substituted phenyl)methylidene]-hydrazine (3). The compound 3, Et3N and chloroacetyl chloride in methanol were first stirred followed by reflux on a steam bath to furnish compound N-[2-(1H-1,2,3-benzotriazol-1-yl)ethyl]-4-(substituted phenyl)-3-chloro-2-oxo-1-iminoazetidine (4).

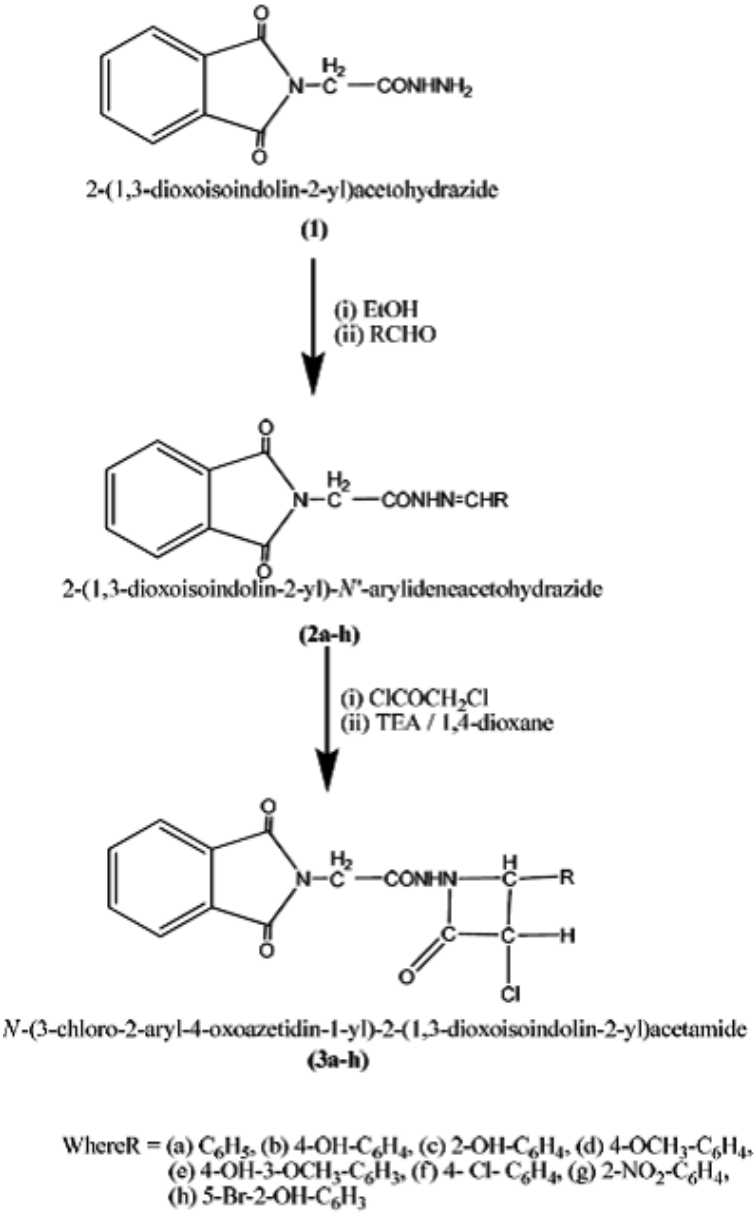


Lokhandwala *et al* [50] reported the reaction of 7-chloro-2-(3-chloropropyl)-4H-3,1-benzoxazin-4-one (1) was allowed to react with different aromatic aldehydes in presence of ethanol and acid catalyst to get the corresponding Schiff bases. various substituted 3-chloro-4-(substitutedphenyl)-1-{4-[7-chloro-2-(3-chloropropyl)-4-oxoquinazolin-3(4H)-yl}azetidin-2-ones (2a-j) containing different functional groups have been synthesized by treating 7-chloro-2-(3-chloropropyl)-3-{4-[(substitutedbenzylidene)amino]phenyl} quinazolin-4-(3H)-ones (1a-j) with chloroacetylchloride in presence of triethyl amine at reflux temperature.



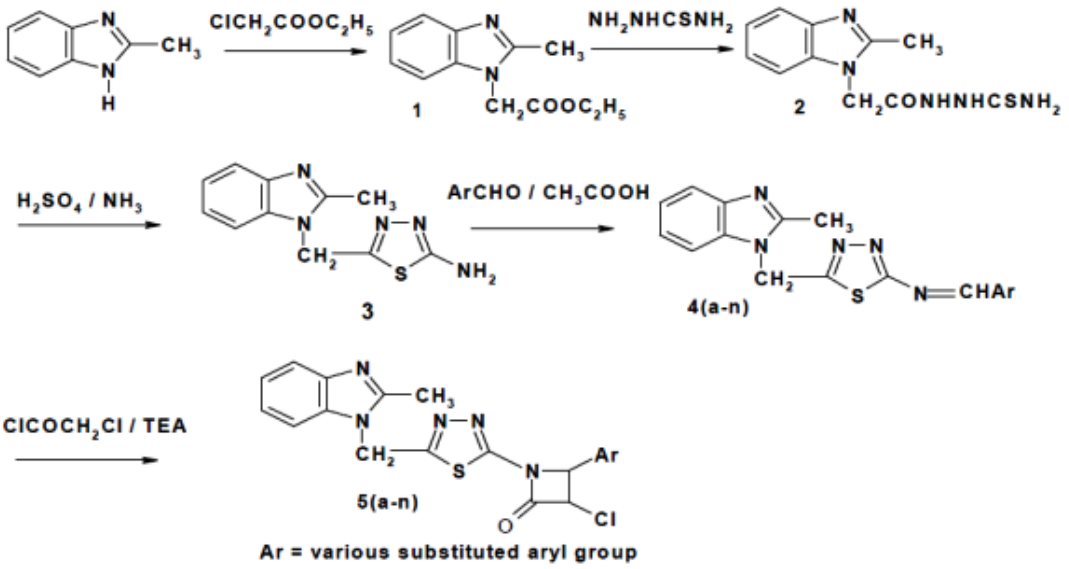
R
4-OCH_3
3-Cl
3-Br
1 CH=CH
2-NO_2
3-OC_6H_5
3-OC_6H_5 4-OH
3-OCH_3 4-OH
- H
3,5-OCH_3 4-OH

Dhameliya *et al* [51] reported the reaction of 2-(1, 3-dioxoisoindolin-2-yl) acetohydrazide (1) with aromatic aldehydes to afford the corresponding 2-(1,3-dioxoisoindolin-2-yl)-N'-arylideneacetohydrazide (2a-h) in good yields. Cyclocondensation of compounds (2a-h) with chloro acetyl chloride yields N-(3-chloro-2-aryl-4-oxoazetidin-1-yl)-2-(1,3-dioxoisoindolin-2-yl)acetamide (3a-h).



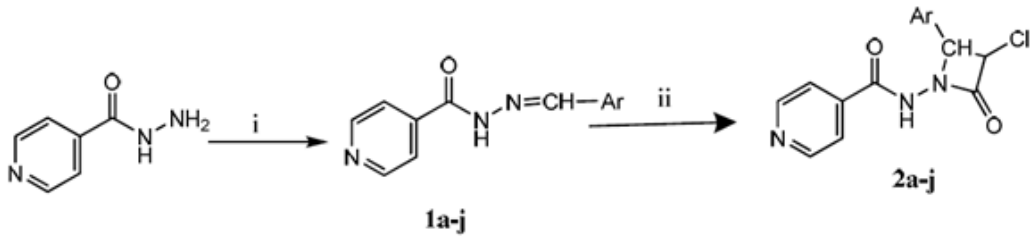
WhereR = (a) C_6H_5, (b) 4-OH-C_6H_4, (c) 2-OH-C_6H_4, (d) 4-OCH_3-C_6H_4, (e) 4-OH-3-OCH_3-C_6H_3, (f) 4- Cl- C_6H_4, (g) 2-NO_2-C_6H_4, (h) 5-Br-2-OH-C_6H_3

Sonwane *et al* [52] reported Conventional Method and Microwave Method for the synthesis of N1–[2'-(4-substituted phenyl-3-chloro-azetidin-2-one-5'-methylene)-1',3',4'-thiadiazole]-2-methylbenzimidazole, the reaction of 2-methylbenzimidazole and ethylchloroacetate with K_2CO_3 in methanol give N1-Ethylacetate-2-methylbenzimidazole (1). The compound 1 and thiosemicarbazide in methanol give N1-Acetylthiosemicarbazide-2-methylbenzimidazole (2). The solution of compound 2 and concentrated H_2SO_4 in methanol give N1–(2'-amino-5'-methylene)-1',3',4'-thiadiazole-2-methylbenz-imidazole (3). The mixture of compound 3 and different substituted benzaldehyde in ethanol with 4-5 drops of glacial acetic acid give N1–[(2-substituted-benzylidene-imino-5'-methylene)-1',3',4'-thiadiazole]-2methylbenzimidazoles, (4). The compound 4 and triethylamine in methanol with chloroacetyl chloride gives N1–[2'-(4-substitutedphenyl-3-chloro-azetidin-2-one-5'-methylene)-1',3',4'-thiadiazole]-2-methyl ben-zimidazole(5).



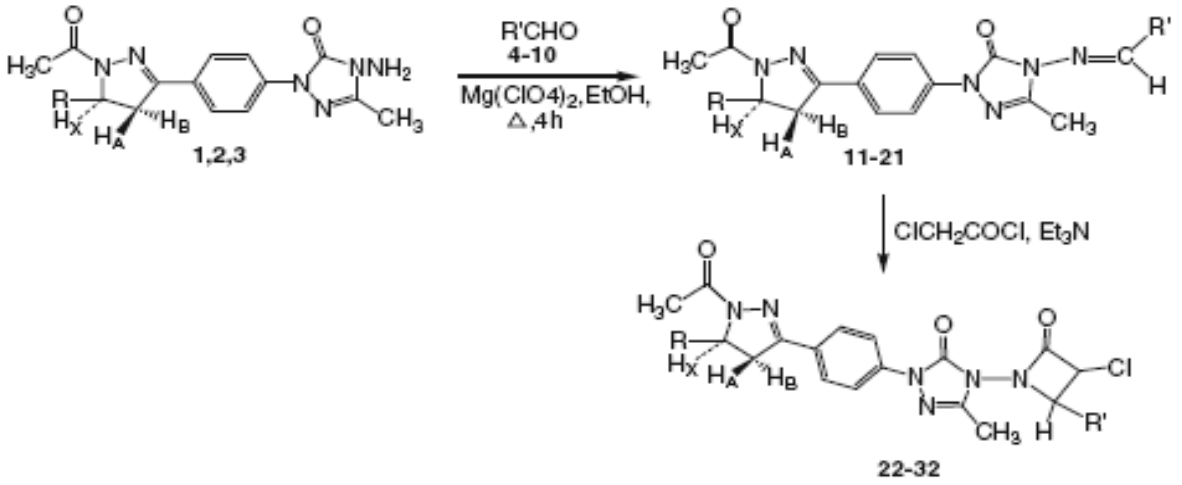
a	C_6H_5	b	2-ClC_6H_4	c	3-ClC_6H_4
d	4-ClC_6H_4	e	2-BrC_6H_4	f	3-BrC_6H_4
g	4-BrC_6H_4	h	2-$OCH_3C_6H_4$	i	3-$OCH_3C_6H_4$
j	4-$OCH_3C_6H_4$	k	2-$NO_2C_6H_4$	l	3-$NO_2C_6H_4$
m	4-$NO_2C_6H_4$	n	4, 4'-$(CH_3)_2NC_6H_4$		

Nikalje *et al* [53] reported the reaction of the synthesis of N'-(substituted- aryl/heterylidene) isonicotinohydrazide1 (a-j) were prepared by reaction between equimolar quantities of isoniazid and substituted aldehydes in ethanol. A mixture of Schiff base 1 and chloroacetyl chloride in dimethylformamide was taken inErlenmeyer flask. Triethyl amine was added to the reaction mixture, as a catalyst. The mixture was irradiated in microwave oven to give N-(3-chloro-2-oxo-4-substitutedazetidin-1- yl) isonicotinamide(2a-j)

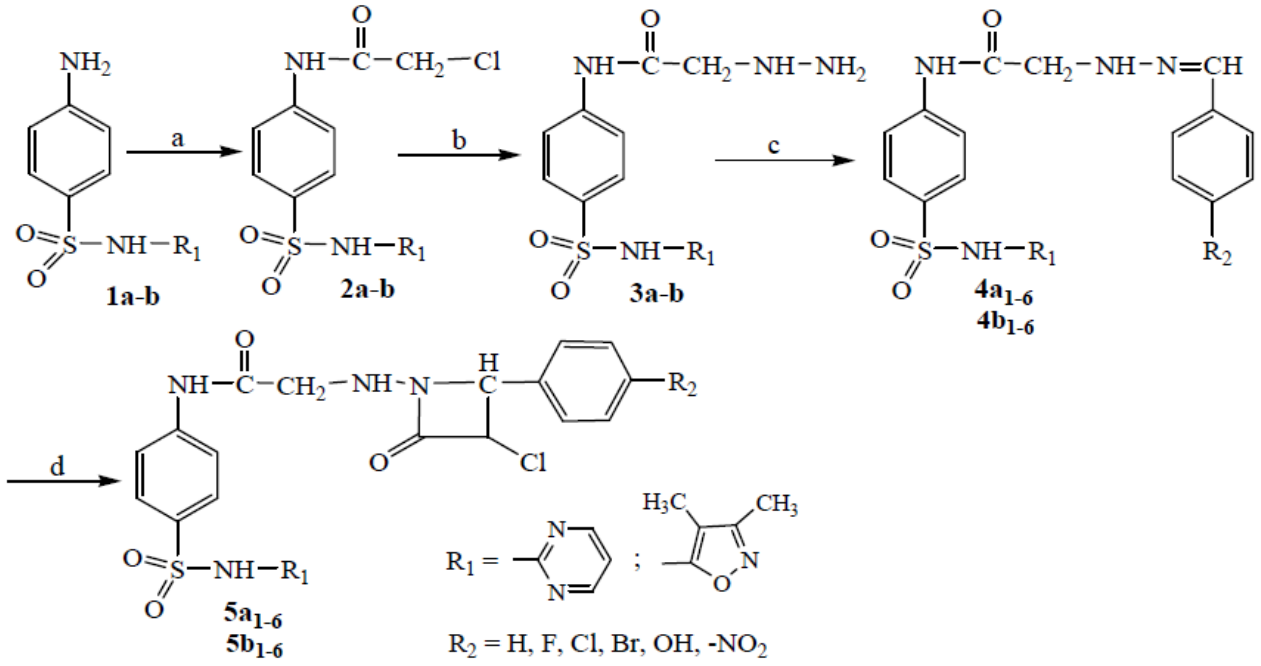


i = Ar-CHO / C_2H_5OH
ii = $ClCH_2COCl$/ Triethyl amine; MW

Taj *et al* [54] reported an efficient green approach to the synthesis of Schiff bases (11–21) of 1-amino-2-aryl-3-oxo-1,2,4- triazoles (1–3) under Mg(ClO4)2 as catalyst followed by the reaction with chloroacetyl chloride in solvent-free conditions to yield the azetidinones (22–32) with excellent yields. The synthesized compounds were evaluated for the extent of penetration into biological membranes (*clogP*), drug-likeliness and finally drug score was calculated and also screened for antitubercular and antimicrobial activities.



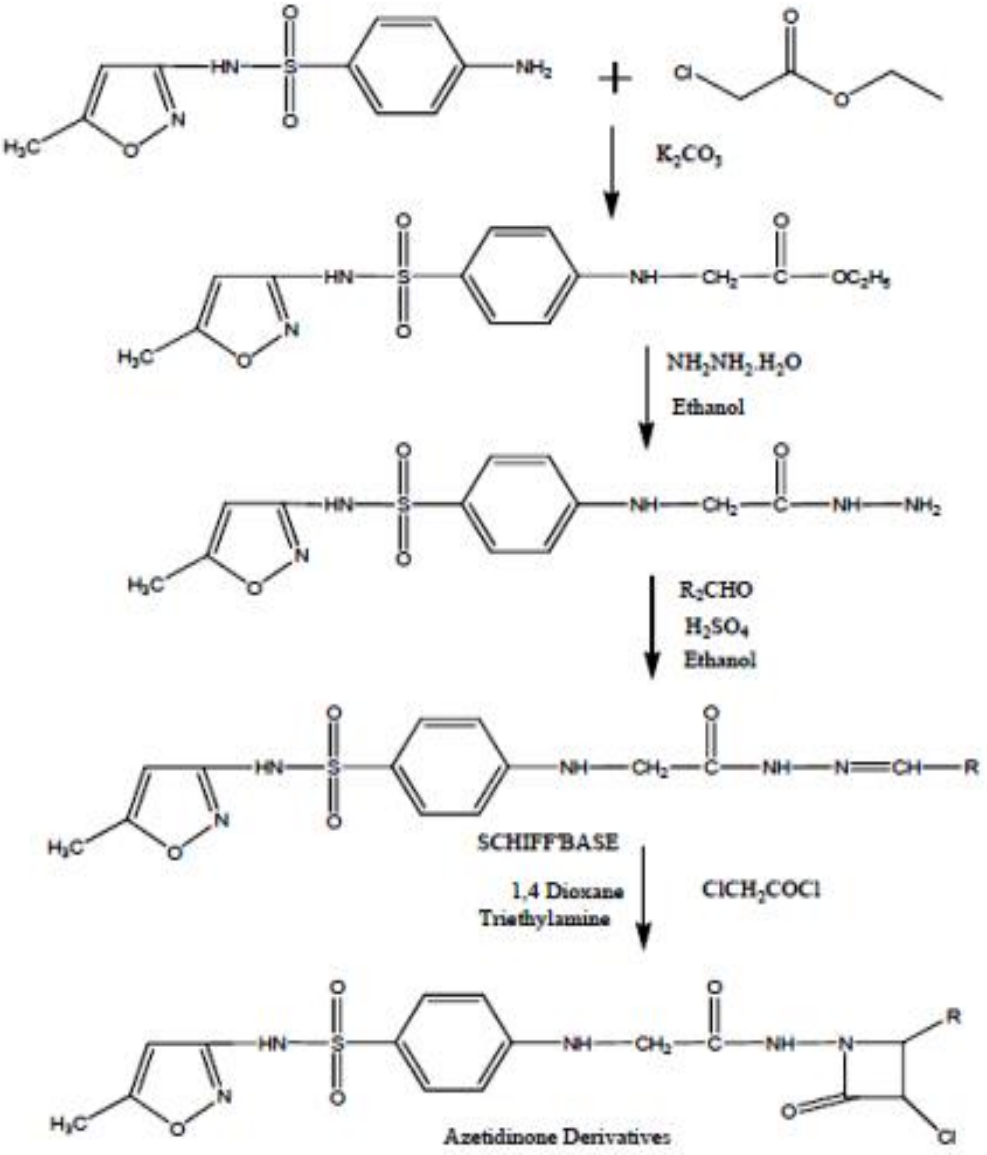
Dragostin *et al* [55] reported the synthesis of Azetidinone derivatives 5a1.–6, 5b1.–6. First, sulfadiazine (4-amino-*N*-pyrimidin-2-yl-benzensulfonamide, 1a) and sulfisoxazole [4-amino-*N*-(3,4-dimethyl-1,2-oxazol-5-yl)benzensulfonamide, 1b] were reacted with chloroacetyl chloride whereby the corresponding chloracetyl derivatives 2a.–b were obtained. Compounds 2a.–b on amination with hydrazine hydrate afforded hydrazinoacetyl sulfonamide derivatives 3a.–b. The condensation reaction of compounds 3a.–b with various aromatic aldehydes yielded *N*-(arylidene)hydrazinoacetyl sulfonamide derivatives 4a1.–6, 4b1.–6. Finally, the compounds 4a1.–6, 4b1.–6 upon reaction with chloracetyl chloride in the presence of triethylamine afforded *N*-(4-aryl-3-chloro-2-oxoazetidin-1-yl)aminoacetyl sulfonamides 5a1.–6, 5b1.–6.



Reagents and Conditions: (**a**) chloracetyl chloride, dry acetone, anhydrous K_2CO_3, heating 12 h; (**b**) hydrazine hydrate 99%, ethanol, heating 10 h; (**c**) aromatic aldehydes, acetic acid, ethanol 50%, heating 8 h; (**d**) chloracetyl chloride, anhydrous 1,4-dioxane, triethylamine, room temperature, stirrer 3 h.

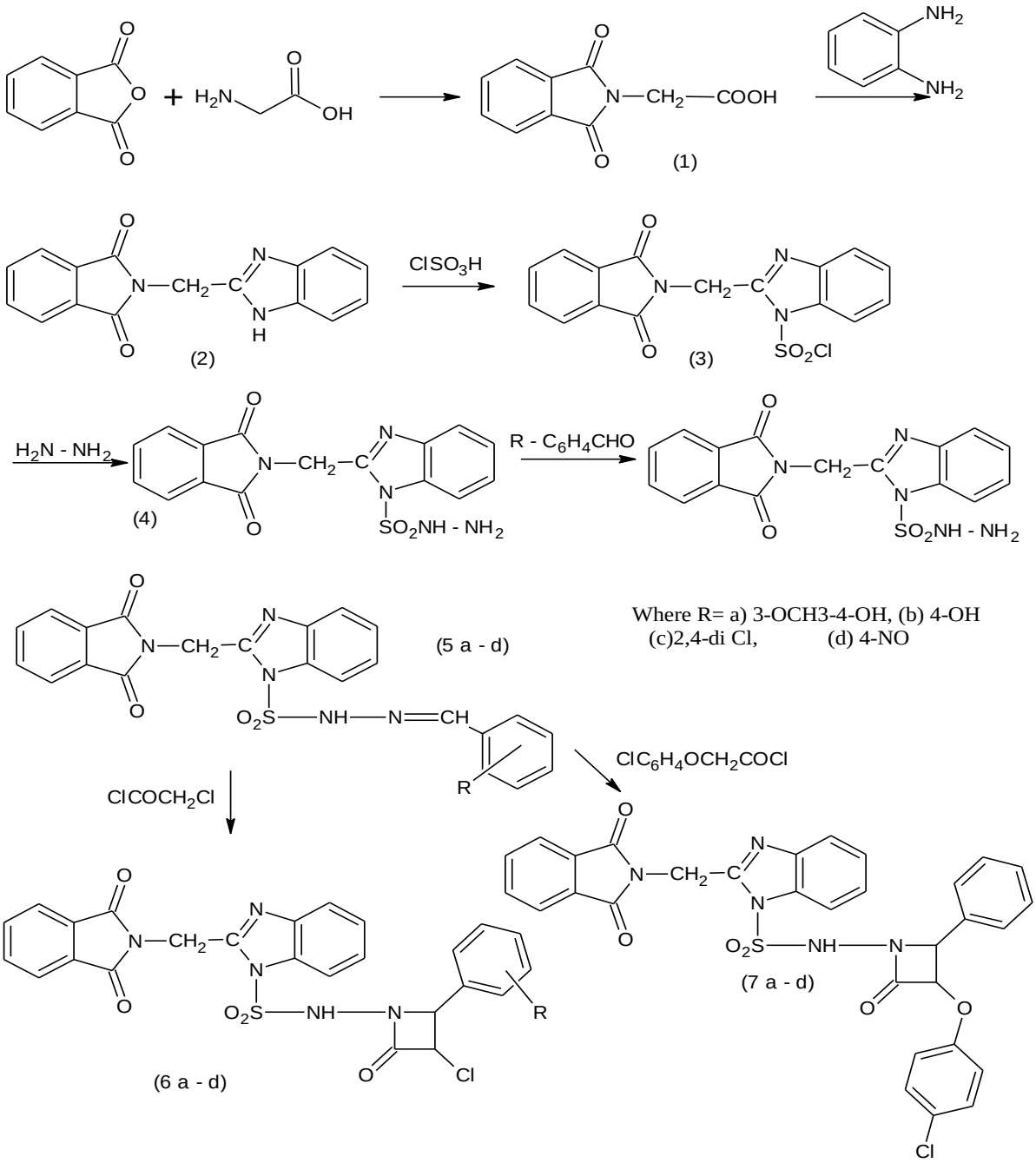
Bhat K *et al* [56] reported reaction of Sulphamethox-azole, ethylchloroacetate and anhydrous potassium carbonate in dry ethanol refluxed to give Sulphamethoxazoleethylacetate. A mixture of Sulphamethoxazoleethylacetate, Hydrazine hydrate in ethanol give Sulphamethox-azole acetyl

hydrazide mixture of Sulphamethoxazole acetyl hydrazide dissolved in minimum quantity of ethanol and different aromatic or heterocyclic aldehydes was refluxed together by employing sulphuric acid to give Schiff's bases of Sulphamethoxazole acetyl hydrazide. Chloroacetylchoride was added dropwise to Schiff's base and triethylamine in dioxane at 5-10°C to give azetidinone.

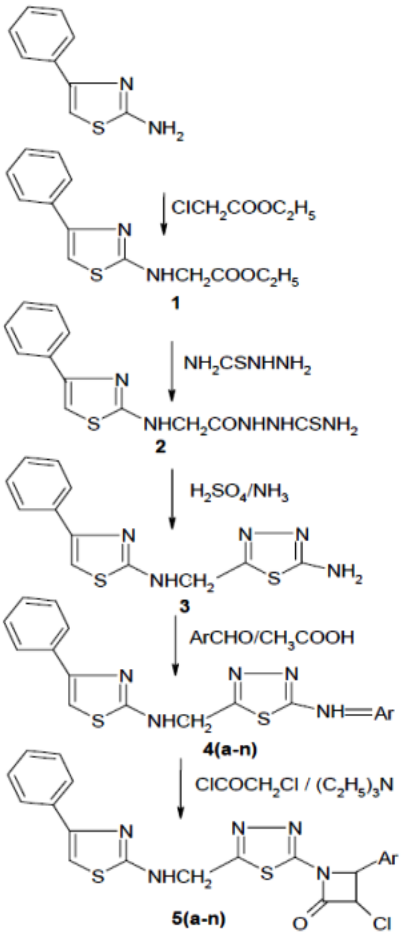


Seth *et al* [57] reported two series of chloro/p-chlorophenoxy substituted azetidinones were synthesized incorporating benzimidazole moiety. Phthalimide and glycine were reacted to give N-phthalyl acetic acid (1) which was further cyclized to give N-methyl phthalylbenzimidazole (2) on treatment with o-phenylenediamine.

Further treatment with chlorosulphonic acid and then with hydrazine hydrate, followed by reaction with different aromatic aldehydes gave the Schiff bases (5a-d). These schiff bases formed when treated with chloro/ p-chlorophenoxy acetyl chloride underwent cyclization to give the azetidinones (7a-d).



Sonwane *et al* [58] reported synthesis of a new 2-[(4-substituted-phenyl-3-chloroazetidin-2-one)-5-(2'-methylamino 4-phenyl-1', 3'-thiazolyl-]-1, 3, 4-thiadiazoles, 5(a-n)from 2-substituted-benzylideneamino-5-[2'-methylamino-4'-phenyl-1',3'-thiazolyl]-1,3, 4-thiadiazole, 4(a-n) using 2-amino-4phenyl-1, 3-thiazole as a starting material.



	Ar
a	C6H5
b	2-ClC6H4
c	3-ClC6H4
d	4-ClC6H4
e	2-BrC6H4
f	3-BrC6H4
g	4-BrC6H4
h	2-OCH3C6H4
i	3-OCH3C6H4
j	4-OCH3C6H4
k	2-NO2C6H4

CONCLUSION: The informational data, available in literature so far, rendered 2 – azetidinones has become one of the most important heterocycles in current chemistry research**,** due to its important pharmaceutical applications, especially in biological science, and medicinal chemistry**.** All the 2 – azetidinones derivatives exhibited varied activity against different bacteria. These studies may serve as a basis for the chemical modifications directed towards the development of a new class of 2 – azetidinones derivatives. We hope that, our brief review on 2 – azetidinones will assist all those interested in this promising class of heterocyclic compounds to reach decisions in the choice of targets and tasks for further investigations.

ACKNOWLEDGEMENT: We are very thankful to the Department of Chemistry, Yashavantrao Chavan Institute of Science, Satara, for providing necessary facility.

* Image quality: As received from the Author.

REFERENCES:

1. Tidwell, Thomas T: Hugo (Ugo) Schiff, Schiff Bases, and a Century of β-Lactam Synthesis. Angewandte Chemie International Edition. 2008; 47 (6): 1016.
2. Brabandt WV, Dejaegher Y, and Kimpe ND: New reactions of functionalized β-lactams. Pure Appl. Chem. 2005; 77(12) 2061–2071.
3. Mehta PD and Pathak AK: Two Dimensional QSAR Study of Some Novel 2-Azetidinone Series for Their Antibacterial Activity against Bacillus subtilis. International Journal of PharmTech Research .2012;4 (2): 676-688.
4. Bandyopadhyay D, Cruz J, Yadav RN and Banik BK: An Expeditious Iodine-Catalyzed Synthesis of 3-Pyrrole-substituted 2-Azetidinones. Molecules. 2012; 17:11570 – 11584.
5. Chavan AA and Pai NR: Synthesis and Biological Activity of N-Substituted-3-chloro-2-azetidinones. Molecules. 2007; 12(11): 2467 – 2477.
6. Kumar A and Rajput CS: Synthesis and anti-inflammatory activity of newer quinazolin-4-one derivatives. Eur. J. Med. Chem. 2009; 44: 83–90.
7. Leach CA, Deirdre MB: Lipoprotein-associated PLA2 inhibition — a novel, non-lipid lowering strategy for atherosclerosis therapy. II Farmaco .2001; 56: 45 – 50.
8. Goel RK, Singh A, Naidu PS, Mahajan MP and Kulkarni SK: PASS-assisted search and evaluation of some as CNS active agents. Journal of Pharmacy and Pharmaceutical Sciences. 2005; 8: 182 – 189.
9. Bisacchi GS, Slusarchyk WA: Synthesis of potent and highly selective non guanidineazetidinone inhibitors of human tryptase. Bioorg. Med. Chem. Lett. 2004; 14: 2227 – 2231.
10. Stephane G, Moreno G, Georges D, and Jacqueline M: Synthesis and evaluation of N1/C4-substituted β-lactams as PPE and HLE inhibitors. Bioorganic & Medicinal Chem. 2004; 12: 129 – 138.
11. Goel RK, Mahajan MP and Kulkarni SK: Evaluation of anti–hyperglycemic activity of some novel monocyclic betalactams. J Pharm PharmaceutSci 2004; 7(1):80 – 83.
12. Guillon CD, Koppel GA, Brownstein MJ: Azetidinones as vasopressin V1a antagonist. Bioorg. Med. Chem. 2007; 15: 2054 – 2080.
13. Banik BK, Banik I, Becker FF: Stereocontrolled synthesis of anticancer β-lactams via the Staudinger reaction. Bioorg. Med. Chem. 2005; 13: 3611 – 3622.
14. Patel KH and Mehta AG: Synthesis and antifungal activity of azetidinones and thiazolidinones derivative of 2-amino-6- (2-naphthalenyl) thiazolo [3, 2-d] thiadiazole, EJ. Chem. 2006, 3(13), 267- 273
15. Madhu G, Jayaveera KN, Ravindranath LK, Santosh Kumar B, Nagarjuna Reddy P: Synthesis, Characterization and biological evaluation of novel quinoline linked 1,3,4-oxadiazoles possessing azetidin-2-one, thiazolidin-4-one and tetrazole moieties. International Journal of Chem Tech Research. 2013; 5(5): 2381 – 2389
16. Veinberg G, Shestakova I, Vorona M, Kanepe I and Lukevics E: Synthesis of antitumor 6-alkylidenepenicillanate sulfones and related 3-alkylidene-2-azetidinones. Bioorg. Med. Chem. Lett. 2004; 14(1): 147 – 150.
17. Narute AS, Khedekar PB and Bhusari KP: QSAR studies on 4-thiazolidinoes and 2-azetidinones bearing benzothiophene nucleus as potential anti-tubercular agents. Indian Journal of Chemistry. 2008; 47B:586 – 591.
18. Veinberg G, Bokaldere R, Dikovskaya K, Vorona M, Kanepe I, Shestakova I, Yashchenko E and Lukevics E:

Synthesis of Cytotoxic 1,3,4-trisubstituted 2-azetidinones. Chemistry of Heterocyclic Compounds .2003; 39(5): 587-593.

19. Beauve C, Bouchet M, Touillaux R, Fastrez J and Marchand-Brynaert J: Synthesis, Reactivity and Biochemical Evaluation of 1,3-Substituted Azetidin-2-ones as Enzyme Inhibitors. ChemInform. 2000; 31(4)
20. Gerard S, Dive G, Clamot B, Touillaux R and Marchand-Brynaert J:Synthesis, hydrolysis, biochemical and theoretical evaluation of 1,4-bis(alkoxycarbonyl)azetidin-2-ones as potential elastase inhibitors. Tetrahedron. 2002; 58: 2423 – 2433.
21. Wang Y, Zhang H, Huang W, Kong J, Zhou J and Zhang B: 2-Azetidinone derivatives: Design, synthesis and evaluation of cholesterol absorption inhibitors. European Journal of Medicinal Chemistry. 2009; 44(4) 1638 – 1643.
22. Kumar S, Kumar P and Sati N: Synthesis and biological evaluation of Schiff bases and azetidinones of 1-naphthol. J Pharm Bioallied Sci. 2012; 4(3): 246–249.
23. Sharma R, Samadhiya P, Srivastava SD and Srivastava SK: Synthesis and biological activity of 2-oxo-azetidine derivatives of phenothiazine. Org. Commun. 2011; 4(2) 42-51.
24. Jaya Preethi P, BinduSree K,Pavan Kumar K,Rajavelu R andSivakumar T: Synthesis, Characterization and Its Biological Evaluation of Some Novel4-Thiazolidinone and 2-Azetidinone Derivatives. Asian J. Pharm. Res. 2012;2(2): 63-70.
25. Shanmugapandiyan P, Denshing KS, Ilavarasan R, Anbalagan N, Nirmal R: Synthesis and Biological Activity of 2-(Thiazolidin-4-One) Phenyl]-1h-Phenylbenzimidazoles and 2-[4-(Azetidin-2-One)-3-Chloro-4- Phenyl] -1h-Phenyl Benzimidazoles. IJPSDR. 2010; 2(2): 115-119.
26. Rathinavel G, Senthilkumar KL, Sathish SD: Synthesis and antibacterial studies on some novel derivatives of azetidin-2-ones. Int. J. Pharm & Ind. Res. 2011; 1(3): 187-194.
27. Rajiv D, Sonwane SK, Srivastava SK and Srivastava SD: Greener and Expeditious synthesis of 2-azetidinone derivatives from 2-mercaptobenzothiazole and their pharmacological screening of the synthesized compounds using microwave irradiation. World J. Chemistry. 2010; 5(1):52-56.
28. Ramalakshmi N, Vijayakumar R, Ilango K, Arunkumara S and Puratchikody A: Synthesis and biological evaluation of 4-aryl -3-chloro –1– nicotinamido–2–azetidinonesas potential anticonvulsant and antimycobacterial agents. Int. J. Chem. Sci. 2008; 6(3): 1213-1222.
29. Shah SH and Patel PS: Synthesis and Antimicrobial Activity of Azetidin-2-one containing Pyrazoline Derivatives. Research Journal of Chemical Sciences. 2012; 2(7): 62-68.
30. Srinivas S, Aparna V, Rajkamal B, Saikiran G: Synthesis and antimicrobial evaluation of some novel quinolone incorporated azetidinones, Thiazolidinones. JPSI. 2012; 1: 41 – 43
31. Pande HY, Wadher SJ, Jani DK: Synthesis and biological svaluation of novel Schiff bases and their derivatives as antimicrobial agents. Journal of Pharmaceutical and Scientific Innovation.2012; 44 – 46.
32. Sahoo U, Seth AK, Sen A, Dhanya B, Patel J and Chawla R:Synthesis and characterization of certain novel azetidinone derivatives as antibacterial and antifungal agents. RJPBCS 2010; 1(2): 102 – 107.
33. Kumar D, Bux FB, and Singh A: Synthesis and biological activity of azetidinone. Rasayan J. Chem. 2010; 3(3):497-502.
34. Taj T,Kambale RR, Gireesh T and Badami BV: An expeditious green synthesis of Schiff bases and azetidinones derivatised with 1,2,4-triazoles. J. Chem. Sci. 2011;123(5): 657–666.
35. Kumaraswamy MN, Vaidya VP, Chandrasekhar C, Mathias DAP, Shivakumar H and Mahadevan KM: Synthesis and Pharmacological Investigations of Azetidinones Involving 3-Mercapto-4-amino-5-naphtho[2,1-b]furan-1,2,4-triazole. International journal of pharmaceutical and chemical sciences. 2013; 2 (1) 159 – 168.
36. Dua R. andSrivastava SK: Synthesis, characterization and antimicrobial activity of 2-(2'-substituted - benzylidene - hydrazino -acetyl) – mercapto -5-methyl - 1, 3, 4-thiadiazoles and 2 -[2'- {4 - substituted -aryl - 3 - chloro - 2 - oxo –azetidine } –acetyl-aminomercapto]- 5-methyl - 1, 3, 4 –thiadiazoles. International Journal of Pharma and Bio Sciences .2010; 1(2) 1 – 7.
37. Bhusari KP, Charbe NB, Mehere AP, Warokar AS , Kakde JW and Mishra AP: Synthesis, cholesterol absorption inhibition and anti-bacterial activity of some novel 2-azetidinone derivatives. IJRPC. 2011; 1(4) 1066 – 1074.
38. Panneer ST., Radhika PP, Janagaraj S, Kumar AS: Synthesis of novel 2-substituted benzimidazole derivatives as potential anti-microbial agents. Research in Biotechnology 2011; 2(3):50-57.
39. Parmar K, Modi V, Prajapati S, and Patel R: A Facile And Expeditious Approach For The Synthesis of 2-Azetidinone Derivatives With Microbial Activity. Asian Journal of Biochemical and Pharmaceutical Research. 2011; 2 (1): 612 – 620.
40. Parmar K, Patel R, Prajapati S, Joshi S and Patel R: Synthesis and antimicrobial activity of novel 3-Chloro- [1-(3,6-Diphenyl) [1,2,4] Triazolo [3,4b][1,3,4] Thiadiazole)] -4-(3,4-Diethoxy Phenyl-Azetidin-2-One and their derivatives. Journal of Applied Pharmaceutical Science. 2012; 2 (1) 114-118.
41. Pulate CP, Gurubasavrajswamy PM, Antre RV and Divakar G: Microwave-Assisted Synthesis and Antimicrobial Activity of Novel Azetidinones from Dehydroacetic Acid. International Journal of Drug Design and Discovery 2011; 2(2): 483-487.
42. Sharma R, Samadhiya P, SrivastavaSD and Srivastava SK: Synthesis and pharmaceutical importance of 2-azetidinone derivatives of phenothiazine. J. Chem. Sci. 2012; 124(3) 633–637.
43. Maity S., Khan SA and Ahmad S: Synthesis and characterization of some novel β lactam condensed bioactive 2 – azetidinone derivatives as prospective antimicrobial agent. International research journal of pharmacy. 2012; 3(4): 296 – 299.
44. Pawar PY, Kalure SU, Kulkarni RB: Synthesis and Pharmacological Screening of Some New Azetidinone Derivatives. International Journal of Pharmacy and Pharmaceutical Sciences. 2012; 4: 464 – 467.
45. Patel D, Patel N, Kumari P and Patel N: Synthesis and Characterization of Some New Azetidin-2-ones Containing Coumarin moiety and their Antimicrobial Study. International Journal of Chemistry. 2011; 3(2): 117 – 123.
46. Chavan S, Zangade S, Vibhute A, Vibhute Y: Synthesis and antimicrobial activity of some novel 2-azetidinones and 4-thiazolidinones derivatives. European Journal of Chemistry 2013; 4 (2): 98-101.
47. Rajasekaran A, Sheejadevi K: Synthesis and Biological Evaluation of 1-(3-chloro-2-oxo-4- Phenylazetidin-1-yl)-3-(2-oxo-2-(10H-Phenothiazine-10-yl)ethyl) Thiourea

Derivatives. International Journal of Advances in Pharmaceutical Research. 2013;4(7): 1909 – 1920
48. Gor DG, Patel PA, Patel PS: Synthesis, Characterization and Anti-microbial Activity of 3-{4-[3-chloro-2-(substitutedphenyl)-4-oxoazetidin-1yl] phenyl}-6-bromo-2-methylquinazoline-4-one. International Journal for Pharmaceutical Research Scholars. 2012;1(3): 12 – 15.
49. Sharma R, Samadhiya P, Srivastava SD, and Srivastava SK: Synthesis and Biological Significance of Some 2-Azetidinone Derivatives. Journal of Sciences, Islamic Republic of Iran. 2012; 23(2): 139-146.
50. Lokhandwala S and Patel D: In vitro microbial studies of some newly synthesized azetidinones derivatives. Archives of Applied Science Research 2013; 5 (3): 27-30.
51. Dhameliya DR and Patel MC: Synthesis and Biological Activity of Novel Azetidinones. Pelagia Research Library Der Chemica Sinica. 2011; 2(4):190-196.
52. Sonwane SK, Dua R, Srivastava SK and Srivastava SD: Synthesis of some novel 2-azetidinone derivatives of 2-methylbenzimidazoleby conventional and microwave assisted and evaluation of their antimicrobial efficacy. Scholars Research Library Der Pharmacia Lettre. 2010; 2(2): 159-167.
53. Nikalje APG,Pathan M, Narute AS, Ghodke MS andRajani D: Synthesis and QSAR Study of Novel N-(3-chloro-2-oxo-4-substituted azetidin-1-yl) isonicotinamide derivatives as Anti mycobacterial Agents. Pelagia Research Library Der Pharmacia Sinica. 2012; 3(2):229-238.
54. Taj T, Kambale RR, Gireesh T and Badami BV: An expeditious green synthesis of Schiff bases and azetidinones derivatised with 1,2,4-triazoles. J. Chem. Sci. 2011; 123(5): 657–666.
55. Dragostin OM, Lupascu F,Vasile C, Mares M,Nastasa V,MoraruRF,Pieptu D, and Profire L: Synthesis and Biological Evaluation of New 2-Azetidinones with Sulfonamide Structures. Molecules. 2013; 18: 4140-4157.
56. BhatIK, Mishra SK, James JP, Shastry CS: Antimicrobial studies of synthesized azetidinone derivatives from sulfamethoxazole moiety. Journal of Chemical and Pharmaceutical Research. 2011; 3(3):114-118
57. Seth M and Sah P: Synthesis and antimicrobial activity of 2- azetidinones derived from benzimidazole. Journal of Chemical and Pharmaceutical Research .2012; 4(1):146-153.
58. Sonwane SK, Srivastava SD, and Srivastava SK: Synthesis and Antimicrobial Activity of Some 2-[(4-Substituted-Phenyl-3-Chloro-Azetidin-2-One)-5-(2'-Methylamino-4-Phenyl-1',3'-Thiazolyl-]-1,3,4-Thiadiazoles. Journal of Sciences, Islamic Republic of Iran .2009; 20(3): 227-232.

How to cite this article:
Salunkhe DS and Piste PB: A brief review on recent synthesis of 2-azetidinone derivatives. *Int J Pharm Sci Res* 2014; 5(3): 666-89.doi: 10.13040/IJPSR.0975-8232.5(3).666-89