

ISSN 0974-4169 (Print)
0974-4150 (Online)

www.ajronline.org



REVIEW ARTICLE

A Review on Hydrazone, the fascinating field of investigation in medicinal chemistry

Sachin H. Rohane*, Dr. Ashlesha G. Makwana

Department of Chemistry, K.B. Institute of Pharmaceutical Education and Research, Gandhinagar 382023, India

*Corresponding Author E-mail: sachinrohane29@gmail.com

ABSTRACT:

Antibiotic resistance is a global public health threat. There has been considerable interest in the development of novel compounds with antimicrobial, anti-mycobacterial, and antiviral activities etc. keeping Hydrazones as a centre attraction this review has been carried forward. Hydrazone possessing an azometine $-NHN=CH-$ proton constitute an important class of compounds for new drug development. Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities. These observations have been guiding for the development of new hydrazones that possess varied biological activities. Hopefully, this will allow the development of innovative new strategies for the development of novel compounds with different scheme, methods and materials.

KEYWORDS: Antibiotic resistance, Hydrazone, azometine, innovative strategies, broad spectrum.

INTRODUCTION:

Antibiotic resistance is a global public health threat, but nowhere is it as stark as in India. The crude infectious disease mortality rate in India today is 416.75 per 100,000 persons (author calculations based on World Bank data and the Global Burden of Disease, 1990) and is twice the rate prevailing in the United States when antibiotics were introduced (roughly 200 per 100,000 persons). A mix of poor public health systems and hospital infection, high rates of infectious disease, inexpensive antibiotics, and rising incomes is coming together to increase prevalence of resistant pathogens and is increasing the burden of untreatable neonatal sepsis and health-care-associated infections.

New Delhi metallo- β -lactamase (NDM) enzymes, first reported in 2008, are now found worldwide. In India, *Escherichia coli* (n = 1, 815) isolated from the community showed high overall resistance to ampicillin, naladixic acid, and co-trimoxazole (75%, 73%, and 59%, respectively) between 2004 and 2007. Nearly a third of isolates are resistant to injectables like aminoglycosides (represented by gentamicin). From 2008 to 2013, *E. coli* resistance to third-generation cephalosporins increased from 70% to 83%, and fluoroquinolone resistance increased from 78% to 85%. Ten percent of *E. coli* isolates were resistant to carbapenems in 2008, increasing to 13% in 2013. Among *Klebsiella pneumoniae* isolates, third-generation cephalosporin resistance decreased from 90% to 80%, and fluoroquinolone resistance increased from 57% to 73%. Carbapenem resistance among *K. pneumoniae* increased from 2% in 2002 to 52% in 2009 in one tertiary-care hospital in New Delhi. Resistance to fluoroquinolones among invasive *Salmonella Typhi* isolates in India increased from 8% in 2008 to 28% in 2014. However, resistance in 2014 to two older antibiotics—ampicillin,

Received on 28.05.2017 Modified on 26.06.2017
Accepted on 03.07.2017 © AJRC All right reserved
Asian J. Research Chem. 2017; 10(4):417-430.
DOI: 10.5958/0974-4150.2017.00070.0

5%, and cotrimoxazole, 4%—is decreasing, possibly because of a decline in consumption of these two drugs, and is much lower than rates of resistance to fluoroquinolones. Resistance to nalidixic acid in *S. Typhi* is increasing (resistance is about 20%–30%) because of widespread use of other quinolones and not because of nalidixic acid use per se. Among *Enterococcus faecium* isolates, 11% were vancomycin resistant¹.

An antibiotic is a compound or a substance that fights bacterial infections and kills or slow down their growth. The antibiotic market is witnessing high growth due new product innovations and higher investment in R and D activity. Moreover, the other regulatory concerns to control the antibiotic resistance problem are also expected to drive the antibiotics market. The demand for antibiotics is expected to reach USD 44.68 billion by 2016. Since, 2005 this market is seen to grow at an annual rate of 6.6% until 2011.

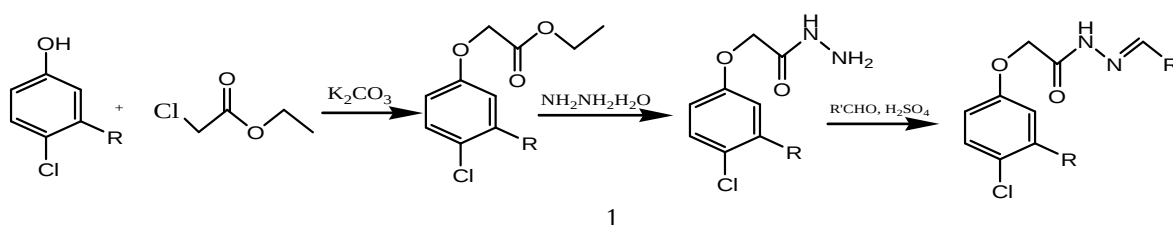
In Hydrazone, the nitrogen is attached to hydrogen; these Hydrazone are stable enough for isolation. However in some cases, especially with simple R group, they rapidly decompose or polymerizes unless there is at least one aryl group on nitrogen or the carbon. When there is an aryl group the compound are quite stable and these compound called as schiff bases and the reaction is best way to prepare them. The reaction is straightforward and proceeds in high yield².

The increased interest in antibacterial over the past few decades has been result of attempts to discover compounds that possess therapeutic effectiveness without considerable side effects during their prolonged therapy³.

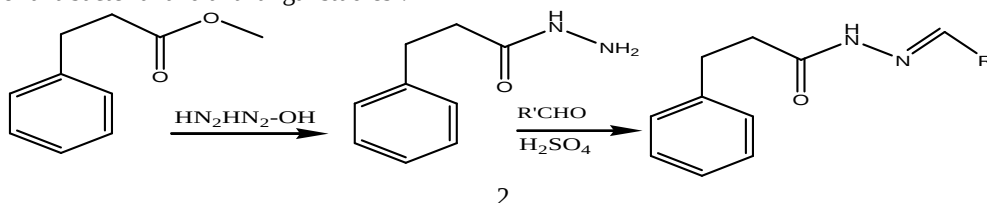
The common and traditional method for preparation of the NAHs involves the treatment of substituted acid hydrazides and carbonyl compounds in the suitable solvents. All the reported approaches include organic classical synthetic methodologies and vary in the selectivity and reaction patterns. A wide variety of methodologies has been developed by the researchers in past decades. Some of the reported methods are described below.

Different methods for hydrazone synthesis:

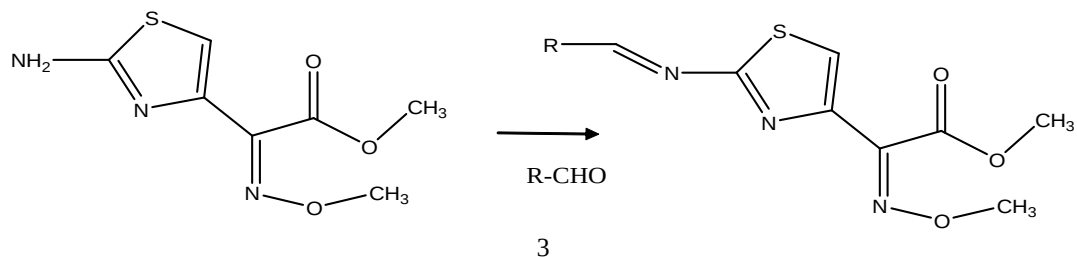
N. Fuloria and *et al* reported synthesis of Imines and Azetidinones derivatives from Haloaryloxy Moiety (**1**). Haloaryloxy moiety on refluxing with chloroethyl acetate in the presence of potassium carbonate and acetone yielded ethyl haloaryloxy acetate, which were reacted with hydrazine hydrate to produce haloaryloxyacetyl hydrazine, which on treatment with aromatic aldehydes yields imines. The novel series of compounds were elucidated on the basis of spectral studies and screened for antibacterial and antifungal studies⁴.



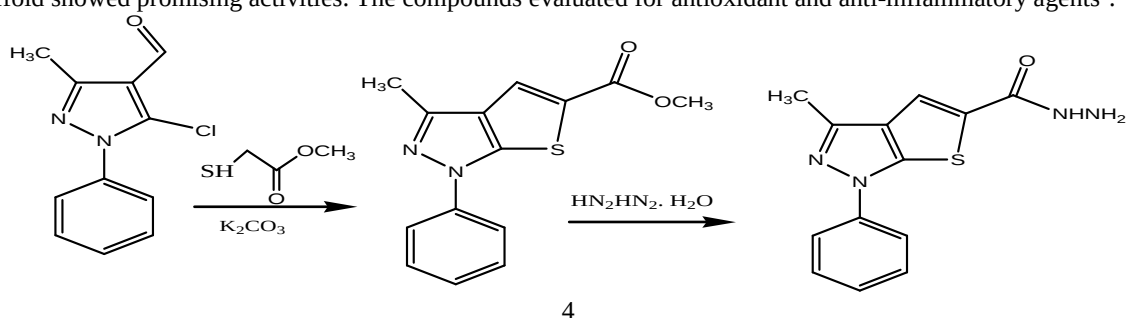
N. Fuloria and *et al* reported synthesis of newer Schiff Bases and Azetidinones from propionic acid derivatives (**2**). Phenyl propionohydrazide, a hydrazinated derivative of methyl phenyl propanoate, when refluxed with aromatic aldehydes yielded Schiff bases. The novel series of compounds were elucidated on the basis of spectral studies and screened for antibacterial and antifungal studies⁵.



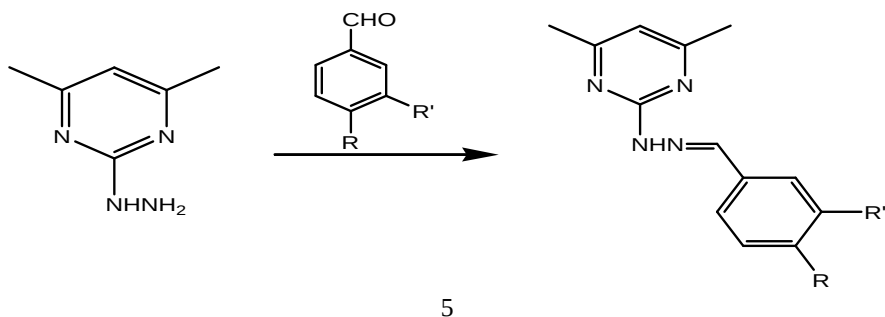
Khyati A. Parikh and *et al* reported synthesis Schiff bases by the condensation reaction between 2-amino-4(2-substituted) thiazole and aromatic aldehydes, which on treatment with Chloroacetyl chloride in the presence of Triethylamine as basic catalyst affords 2-azetidinones (**3**). The synthesized compounds had been tested for their antimicrobial activity against mycobacterium tuberculosis H37R⁶.



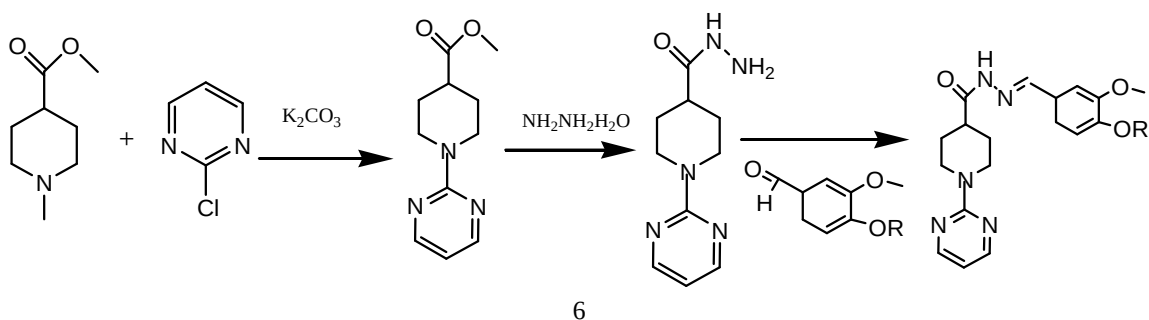
P. S. Mahajan and *et al* reported synthesis three new series of 3-methyl-1-phenyl-1H-thieno[2,3-c]pyrazole-5-carbohydrazide derivatives (**4**). The hydrazones bearing a core pyrazole, chromone and tetrazolo[1,5-a]quinoline scaffold showed promising activities. The compounds evaluated for antioxidant and anti-inflammatory agents⁷.



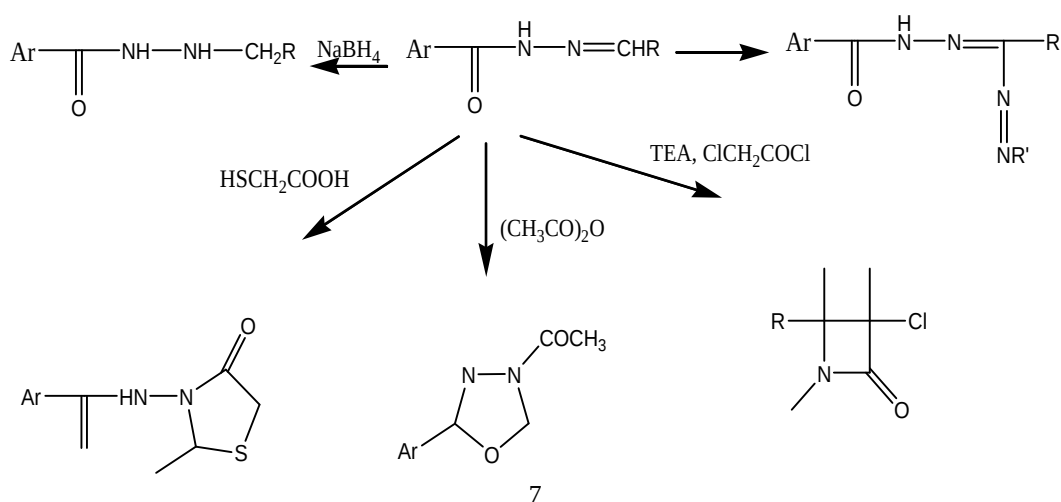
Indu Ravish and Neera Raghav reported the synthesis of Some Pyrimidinyl Hydrazones (**5**). Hydrazones were synthesized by the reaction of 1-(4, 6-dimethylpyrimidin-2-yl)hydrazine, and substituted aldehyde. In the present work they reported the effect of hydrazones on the activities of these two clinically significant enzymes⁸.



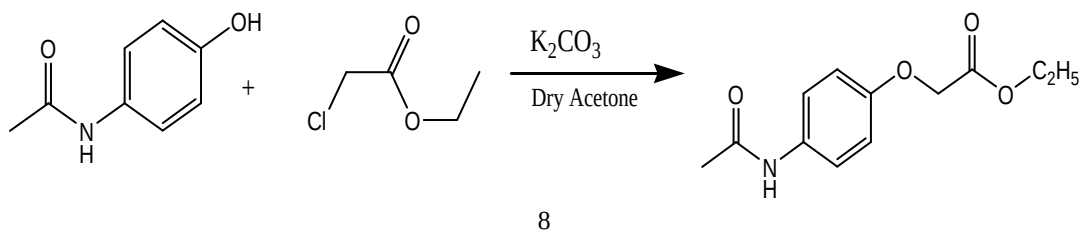
T. Govindasami and *et al* reported synthesis of vanillin related hydrazone derivatives (**6**). New hydrazone derivatives were synthesized from Piperidine-4-carboxylic acid methyl ester. Synthesized hydrazone derivatives were further checked for anti-bacterial activities by paper disc diffusion method against *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacterial strains⁹.



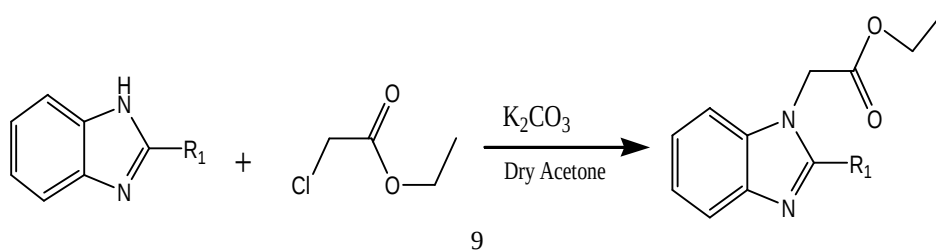
P. Mail kumaran and *et al* reported the synthesis of a number of hydrazone derivatives which were synthesized by using isatin (indole-2, 3-dione) as a starting material, and were purified by crystallization or by column chromatography (**7**). Structures of all the synthesized compounds are supported by correct IR, ¹H NMR, mass spectral and analytical data. Anti-inflammatory activity evaluation was carried out by using carrageenin-induced paw edema assay method¹⁰.



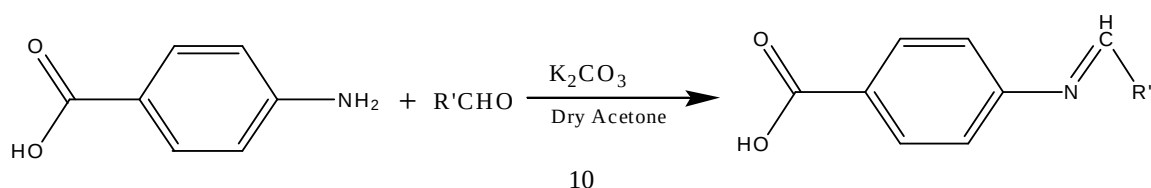
P. Panneerselvam and G. Geete Ganesh synthesized ethyl -4-acetamido phenoxy acetate by using A mixture of p-acetamido phenol and ethyl chloroacetate (**8**). The reaction mixture was refluxed by using dry acetone in presence of anhydrous potassium carbonate (K₂CO₃) for 6 h. The reaction mixture was cooled and then poured in to crushed ice. The solid so product obtained was filtered, dried and recrystallized using ethanol¹¹.



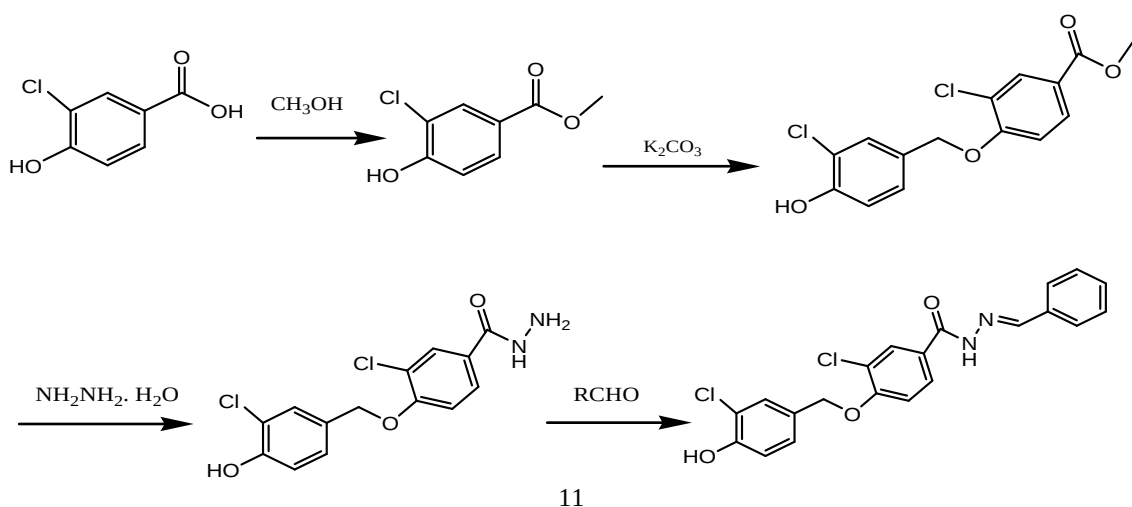
Janardhan Gowda and *et al* reported the synthesis of a new series of 2-substituted-1-[(5-substituted phenyl)- 1,3,4-oxadiazol -2-yl) methyl]- benzimidazole (**9**). The 2-substituted-1H- benzimidazole on reaction with ethyl chloroacetate in presence of potassium carbonate in dry acetone gives ester which on further treatment with hydrazine hydrate gave hydrazide derivatives¹².



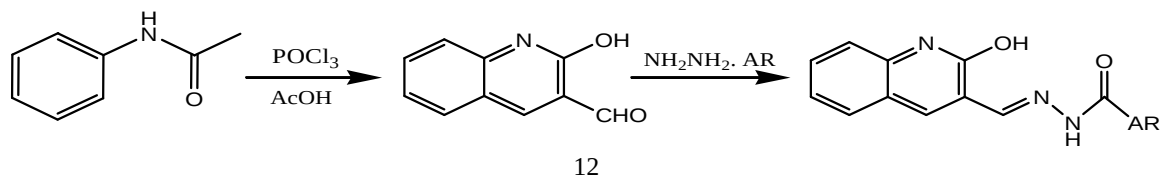
Jigna Parekh and *et al* reported synthesis of some Schiff bases derived from 4-aminobenzoic acid (**10**). They were screened as potential antibacterial agents against a number of medically important bacterial strains¹³.



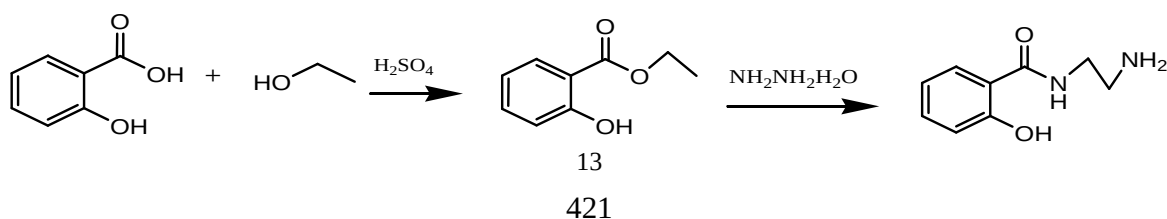
Chandrashekhar K.B. and *et al* reported synthesis of novel hydrazone derivative by using 3-chloro-4-hydroxy benzoic acid (**11**). They screened these compounds for anti bacterial activity. 3-chloro-4-hydroxy benzoic acid was converted to ester by using methanol. Coupling of ester with 3-chlorobenzyl chloride in the presence of potassium carbonate gives intermediate which was treated with hydrazine hydrate in ethanol gives hydrazide derivatives which was finally treated with various benzaldehyde resulted in to Hydrazone derivatives¹⁴.



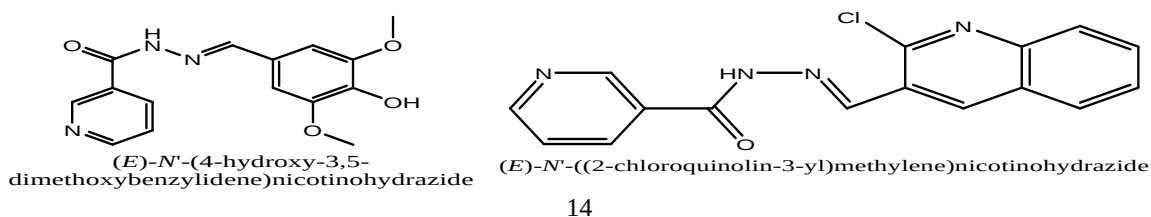
Mustapha C. Mandewale and *et al* reported the synthesis of quinoline hydrazone ligands (**12**). The ligands were synthesized through multi-step reactions. The 2-hydroxy-3-formylquinoline derivatives were prepared from acetanilide derivatives as starting materials using Vilsmeier–Haack reaction. Then the condensation of 2-hydroxy-3-formylquinoline derivatives with hydrazide derivatives yielded quinoline hydrazone ligands. These compounds are screened for anti Tubercular activity¹⁵.



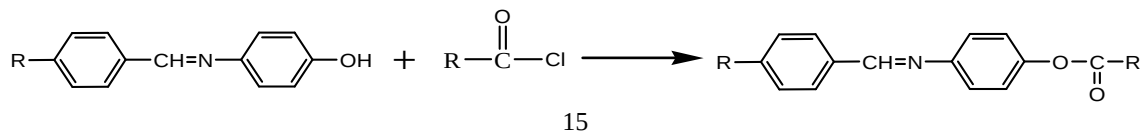
Kui Cheng and *et al* reported synthesis of a series of peptide and Schiff bases (PSB) which were synthesized by reacting salicylic acid, primary diamines with salicylaldehyde or its derivatives (**13**). The inhibitory activities against *Escherichia coli* b-ketoacyl-acyl carrier protein synthase III (ecKAS III) were investigated in vitro and molecular docking simulation also surveyed. Top 10 PSB compounds which posses both good inhibitory activity and well binding affinities were picked out, and their antibacterial activities against Gram negative and Gram-positive bacterial strains were tested, expected to exploit potent antibacterial agent with broad-spectrum antibiotics activity¹⁶.



Vidya Desai and Rachana Shinde reported a series of biologically active nicotinic acid hydrazone schiff bases (**14**). Which had been synthesized from nicotinic acid hydrazone and variety of aldehydes using lemon juice as natural catalyst, in moderate to good yields. The schiff bases synthesized, exhibited excellent anti-tubercular activity in comparison to standard drugs used¹⁷.

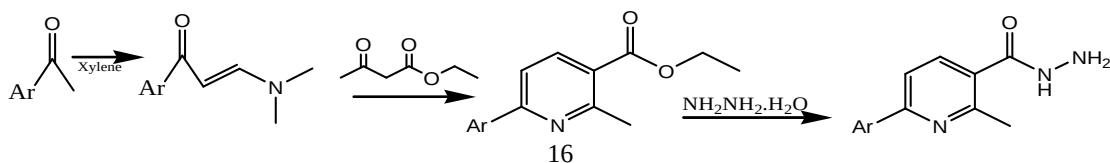


Asma Noureen and *et al* reported the synthesis of some Schiff base esters (**15**) as promising new antitumor, antioxidant and anti-inflammatory agents. The Schiff base esters were synthesized by two synthetic routes using variably substituted hydroxy benzaldehydes with para amino phenol in appreciable yields¹⁸.

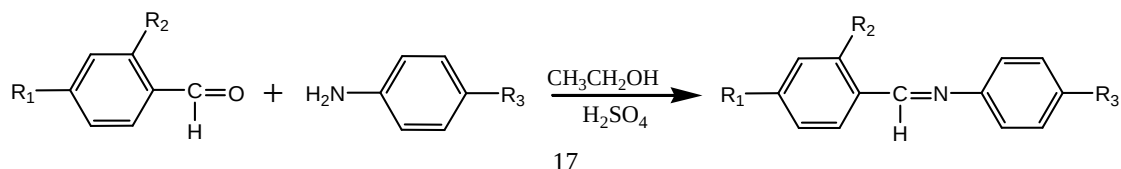


M. Eldehna and *et al* reported the synthesis of Three series of 6-aryl-2-methyl nicotino hydrazides, *N'*-arylidene-6-(4-bromophenyl)-2-methylnicotino hydrazides, and *N'*-(un/substituted 2-oxoindolin-3-ylidene)-6-(4-fluorophenyl)-2-methylnicotino hydrazides (**16**) which were synthesized and evaluated for their potential *in vitro* antimycobacterial activity against *M. tuberculosis*. The synthetic pathways employed to prepare the new targeted derivatives. In a one-pot three-component heterocyclo condensation process, ethyl 2-methyl-6-arylnicotinates was obtained via the reaction of enaminones with ethyl acetoacetate and ammonium acetate in refluxing acetic acid.

Preparation of the nicotinic acid hydrazides in 79%–90% yield was achieved via the hydrazinolysis of ester derivatives with refluxing hydrazine hydrate¹⁹.

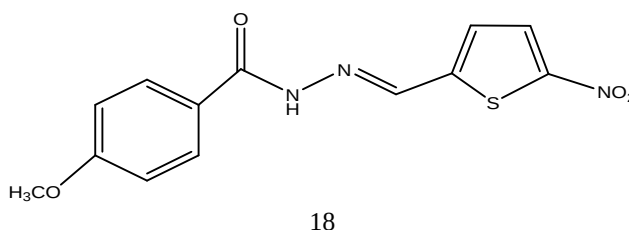


P. B. Raghuwanshi and P. V. Mahalle reported the synthesis of substituted schiff's bases (**17**). The chloro, nitro and methyl substituted benzaldehyde condensed with aniline and nitro aniline in ethanol medium in presence of conc. H₂SO₄ isolate schiff's bases. These compounds were tested for antimicrobial activity against bacteria such as E.coli, S.typhi, S.aureus, P.vulgaris and P.paratyphi are found to have remarkable activity²⁰.

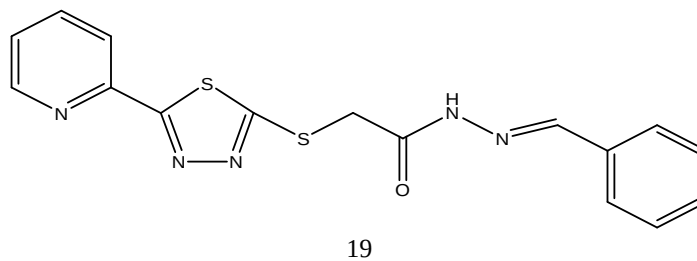


Dr. Kamal Singh Rathore and Gunjan Jadon reported the synthesis of some hydrazone derivatives. A mixture of phenyl acetic acid in acetone, dimethyl Sulphate, anhydrous potassium carbonate was refluxed on a water bath to give methyl 2-phenylacetate. Methyl 2-phenylacetate in alcohol was refluxed with hydrazine hydrate to form 2-phenylacetohydrazide. A mixture of substituted benzaldehyde and 2-phenylacetohydrazide were dissolved in methanol then two drops of conc. HCl were added as catalyst and stirred at room temperature to form *N'*-(2-

chlorobenzylidene)-2-phenylacetohydrazide, N'-(3,4,5-trimethoxybenzylidene)-2-phenyl acetohydrazide, N'-(furan-2-ylmethylene)-2-phenyl acetohydrazide, and N'-(3,4,5-trimethoxybenzylidene) -2-phenylacetohydrazide. Benzoic acid [(5-nitro-thiophene-2-yl) methylene] hydrazide series were synthesized and tested against *M.tuberculosis* H₃₇RV. Rando and co-workers have applied Topliss methodology to a set of nitrogen analogues. 4-methoxybenzoic acid [(5-nitrothiophene-2yl) methylene] hydrazide (**18**) was demonstrated as being the most active compound²¹.



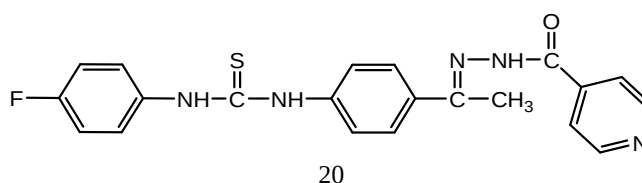
Mamolo M.G. Falagiani, V.; Zampieri *et al* synthesized [5-(Pyridine-2-yl)-1,3,4- thiadiazole-2-yl]thio]acetic acid arylidene-hydrazide (**19**) derivatives and tested for their in vitro antimycobacterial activity²².



Kumar Vasantha and *et al* reported a novel series of *N*-arylidene-2-(2,4-dichloro phenyl)-1-propyl-1*H*-benzo[*d*]imidazole-5-carboxylates having different substitution on the arylidene part were synthesized in good yield. The core nucleus benzimidazole-5-carboxylate was efficiently synthesized by ‘one-pot’ nitro reductive cyclization reaction between ethyl-3-nitro-4-(propylamino) benzoate and 2,4-dichlorobenzaldehyde using sodium dithionite in dimethylsulfoxide. This ‘one-pot’ reaction was preceded very smoothly, in short reaction time with an excellent yield. All the compounds were screened for their in vivo anti-inflammatory and in vitro antimicrobial activity²³.

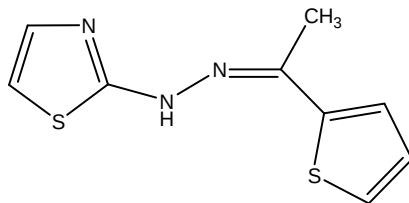
Gregory L. Backes and *et al* reported efficient synthetic procedures for the preparation of acid hydrazines and hydrazides were developed by converting the corresponding carboxylic acid into the methyl ester catalyzed by Amberlyst-15, followed by a reaction with hydrazine monohydrate. Sulfohydrazides were prepared from the corresponding sulfonyl chlorides and hydrazine monohydrate. Both of this group of compounds was condensed with substituted salicylaldehydes using gradient concentration methods that generated a large library of hydrazone, hydrazide and sulfohydrazide analogs. Antifungal activity of the prepared analogs showed that salicylaldehyde hydrazones and hydrazides are potent inhibitors of fungal growth with little to no mammalian cell toxicity, making these analogs promising new targets for future therapeutic development²⁴.

Sriram *et al.*, synthesized a new series of antimycobacterial agents containing INH hydrazide-hydrazone.1-(4-Fluorophenyl)-3-(4-{1-[pyridine-4- carbonyl]hydrazono} ethyl} phenyl) thiourea (**20**) was found to be most potent compound²⁵.



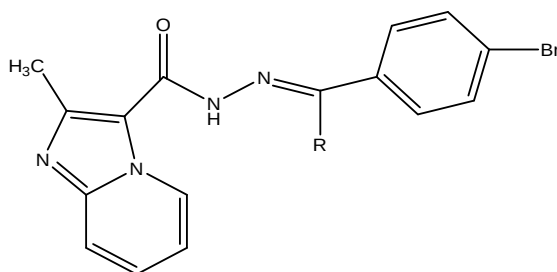
2-acetylthiophene-2-thiazolyl-hydrazone (**21**) inhibits 5-lipoxygenase activity in polymorpho-nuclear leucocytes (PMNS), 12-lipoxygenase and cyclooxygenase in platelets. Inhibition of the two pathways of arachidonic acid

cascade could lead to additional beneficial antiinflammatory activity. In fact, inhibitors of both cyclooxygenase and lipoxygenase.



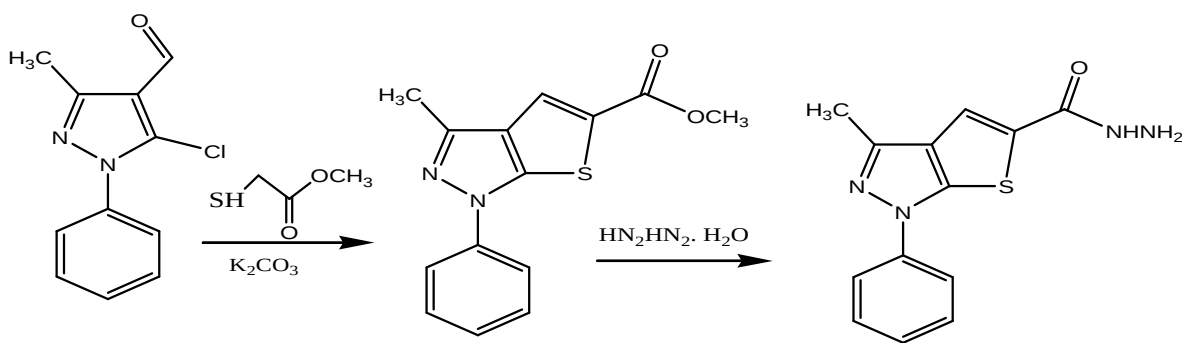
21

N-heterocyclic functionalized acyl aryl hydrazone (**22**) compounds were synthesized and evaluated for their analgesic and anti-inflammatory activity. These compounds were structurally planned applying classical ring bioisosterism strategies on 4-acyl-(N-phenyl pyrazolyl)-aryl hydrazone. The para-substituent at the pharmacophore acyl aryl hydrazone moiety gives good and persistent anti-inflammatory activity



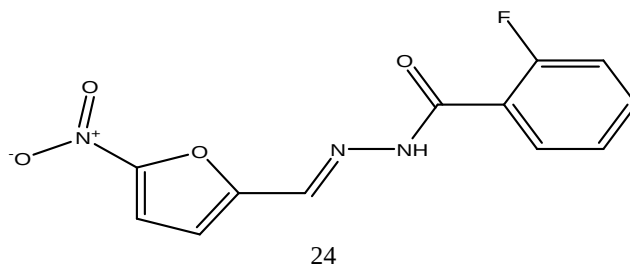
22

Pravin S. Mahajan and *et al* reported three new series of 3-methyl-1-phenyl-1H-thieno[2,3-c]pyrazole-5-carbohydrazone (**23**) derivatives had been synthesized and evaluated for their in vitro antioxidant and anti-inflammatory activities. The hydrazones bearing a core pyrazole, chromone and tetrazolo[1,5-a]quinoline scaffold showed promising activities. Furthermore, molecular docking studies also revealed a significant correlation between the binding score and biological activity for these compounds to describe the molecular basis for the structure activity relationship (SAR) results. As these compounds are good cyclooxygenase inhibitors, isoenzyme inhibitory potency studies are warranted²⁶.

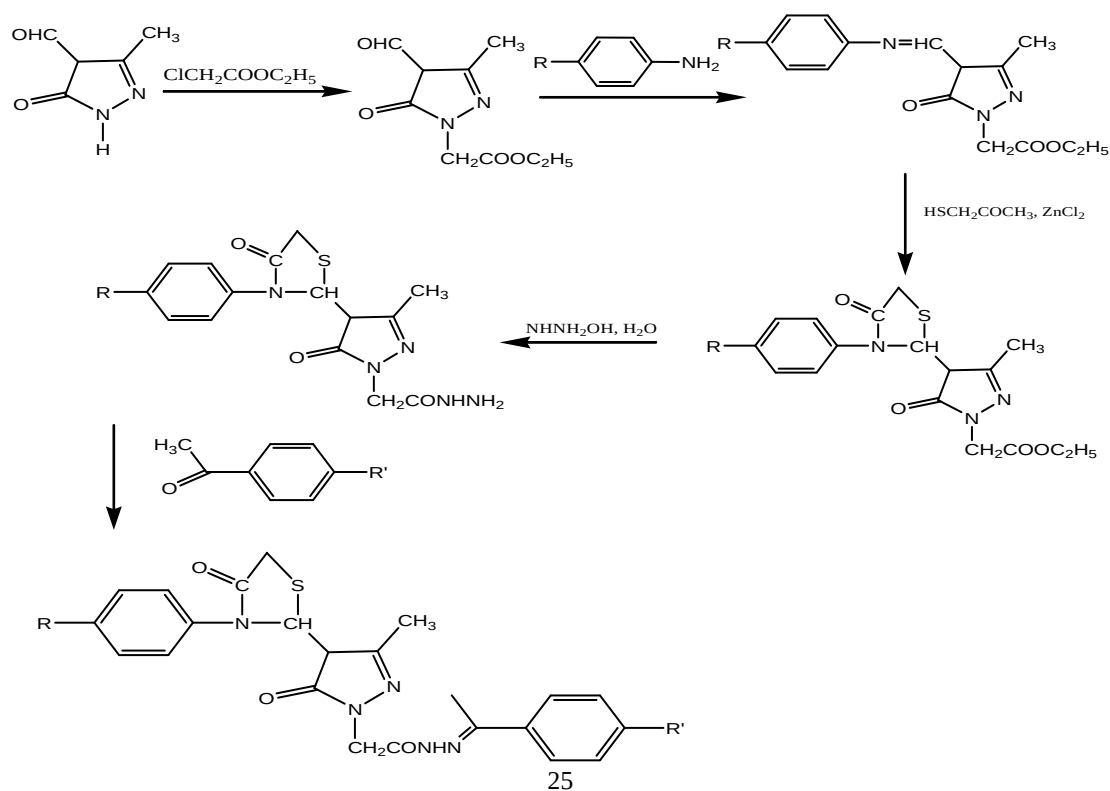


23

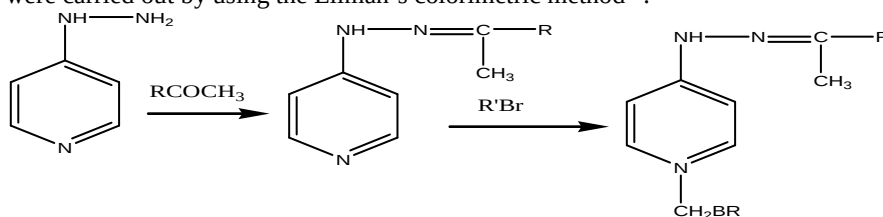
Rollas et al. synthesized a series of hydrazide hydrazones and 1,3,4-oxadiazolines (**24**) of 4-fluorobenzoic acid hydrazide as potential antimicrobial agents and tested these compounds for their antibacterial and antifungal activities against *S. aureus*, *E. coli*, *P. aeruginosa* and *C. albicans*. From these compounds, 4-fluorobenzoic acid [(5-nitro-2-furyl)methylene] hydrazide showed equal activity as ceftriaxone against *S. aureus*. In addition, the MIC values of compounds and for the same strain were in the range of those reported for ceftriaxone²⁷.



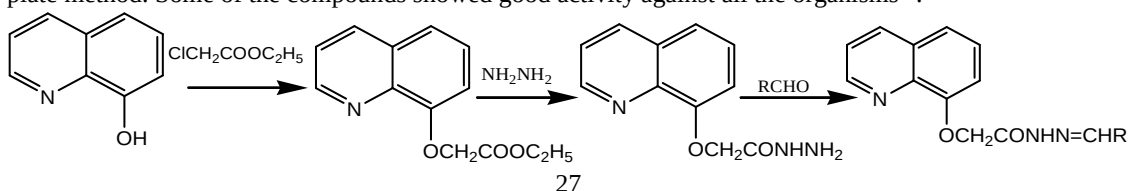
A series of novel Pyrazolone Schiff bases (25) bearing thiazolidinone and oxadiazoles systems were prepared by K. Kishore Kumar from ethyl-2-(4-formyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate and substituted amines. All pyrazolone Schiff bases were refluxed with mercapto acetic acid in presence of anhydrous zinc chloride and solvent N,N-dimethyl formamide to afforded novel series of Ethyl-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl) acetate. The prepared compounds have been screened on some strains of bacteria and fungi²⁸.



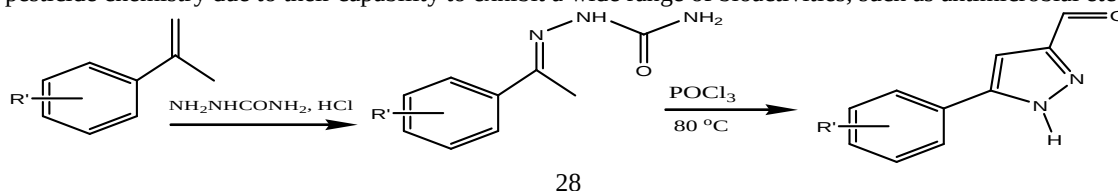
Sulunay Parlar and et al reported a series of pyridinium salts (26) were synthesized bearing alkylphenyl groups at 1 position and hydrazone structure at 4 position of the pyridinium ring and evaluated for the inhibition of both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) enzymes. The cholinesterase (ChE) inhibitory activity studies were carried out by using the Ellman's colorimetric method²⁹.



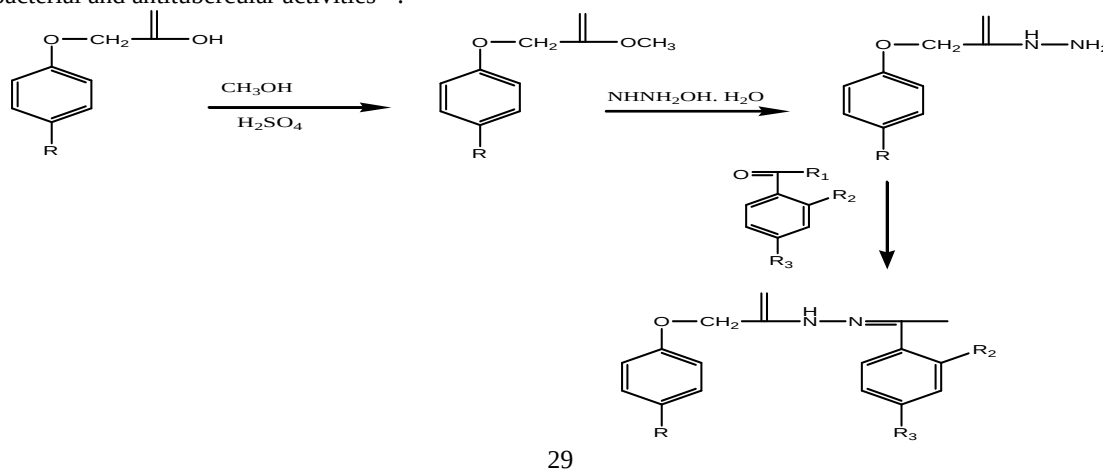
B.C.Revanasiddappa and *et al* reported synthesis of hydrazones derived from 8-hydroxy quinoline moiety. 8-Hydroxyquinoline reacts with ethyl chloroacetate in the presence of anhydrous K_2CO_3 to yield ethyl (quinolin-8-yloxy) acetate. The ethyl ester reacts with hydrazine hydrate and forms 2- (quinolin-8-yloxy) acetohydrazide, which on condensation with various aldehydes gives N'-benzilidine-2-(quinolin-8-yloxy)}acetohydrazides (**27**). The hydrazide upon reaction with various substituted acetophenones yields N'-(1-phenylethylidene)-2-(quinolin-8-yloxy)} acetohydrazides. All the compounds have been screened for their antibacterial and antifungal activity by the cup-plate method. Some of the compounds showed good activity against all the organisms³⁰.



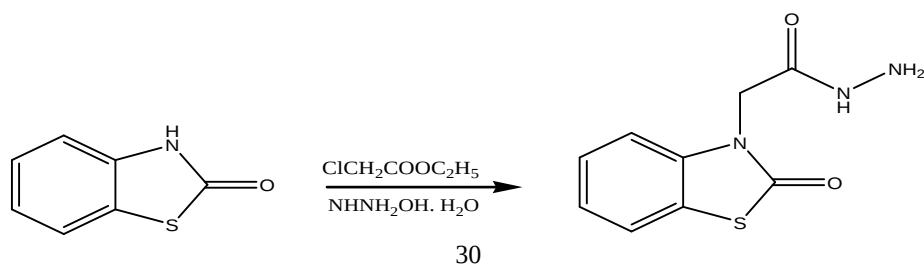
Shridhar Malladi and *et al* reported synthesis, characterization and antibacterial activity of some new pyrazole based Schiff bases (**28**). Pyrazoles represent a key motif in heterocyclic chemistry and occupy a prime place in medicinal and pesticide chemistry due to their capability to exhibit a wide range of bioactivities, such as antimicrobial etc³¹.



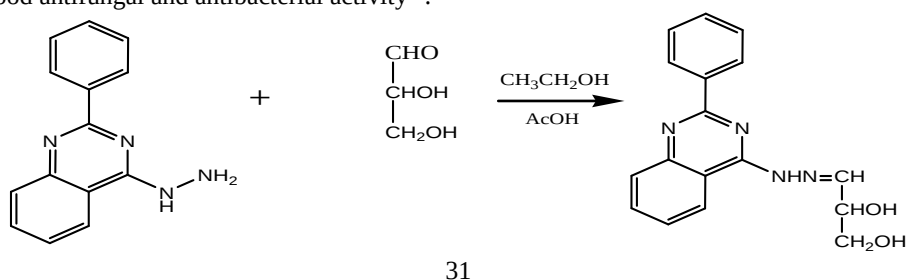
A.S. Raja and *et al* reported the synthesis of some diphenyl hydrazone and semicarbazones (**29**). In this reaction they condensed phenoxy or 4-bromophenoxy acetic acid hydrazide and substituted aryl semicarbazides with appropriate carbonyl compounds yield corresponding hydrazones and semicarbazones. They investigated all this compounds for antibacterial and antitubercular activities³².



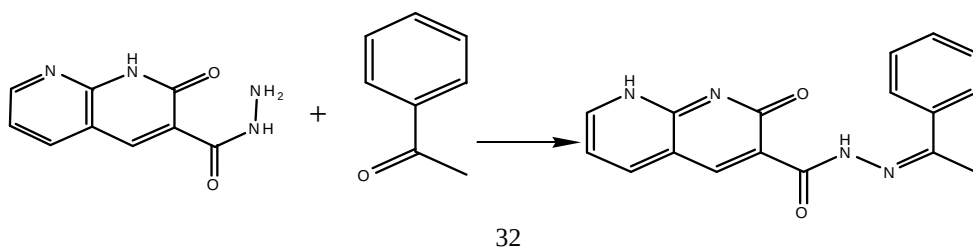
Hydrazones are an important class of compounds found in many synthetic products. Due to their importance in synthetic chemistry, Ahmet Ozdemir and *et al* reported the synthesis of a new series of ten compounds based on the coupling of 2-oxo-3(2*H*)-benzothiazoleacetic acid, hydrazide and 2-thioxo-3(2*H*)-benzothiazoleacetic acid, hydrazide with different aldehydes (**30**). The nucleophilic substitution of 2(3*H*)-benzothiazolone shows an important difference when compared with that of 2-mercaptobenzothiazole. The enolizable character of the amide moiety allows several useful substitutions at the level of the *N* position of the 2(3*H*)-benzothiazolone under base-catalyzed conditions. On the other hand, the nucleophilic reactivity of 2-mercaptobenzothiazole associated with the presence of nitrogen and sulfur atoms holding a pair of electrons on either side of the $>C=S$ group increases the electron donating capacity of "S" to form a bond with a halogenated carbon atom³³.



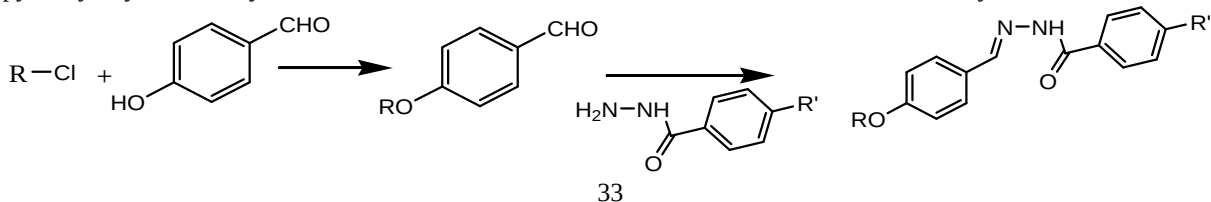
Gamal A. and *et al* reported the synthesis of hydrazone from novel sugar. In this reaction condensation of equimolar amounts of 4-hydrazino-2-phenylquinazoline and a number of monosacchaide glucose, D-galactose etc took place which gives corresponding hydrazones (**31**). These compounds were screened for antimicrobial activity and some of them shows good antifungal and antibacterial activity³⁴.



K. Mogilaiah and *et al* synthesized hydrazone by condensing 1,8-naphthyridin-2-one-3-carboxylic acid hydrazide with different acetophenone gives respective acetophenone 1,8-naphthyridin-2-one-3-carbonylhydrazone (**32**). All the compounds were screened for their antibacterial activity against specific microorganism³⁵.

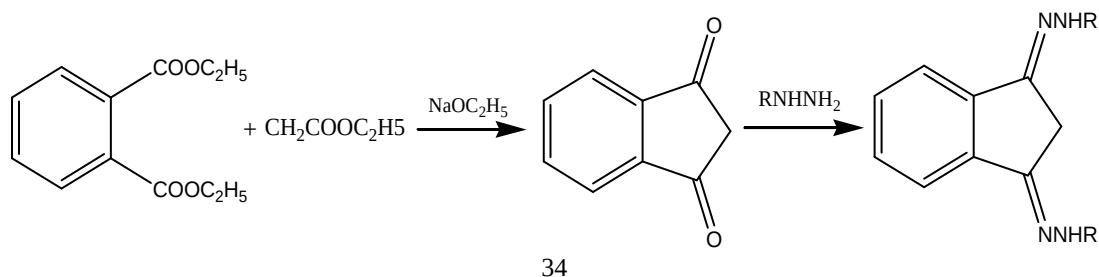


1,3,4-oxadiazole are a class of 5-membered heterocyclic compound that with wide range of pharma and biological activity. M. Shailaja and *et al* reported the synthesis of derivatives of 1,3,4-oxadiazole (**33**) by using substituted pyridinyloxy benzaldehyde. These oxadiazole derivatives were tasted for antimicrobial activity³⁶.

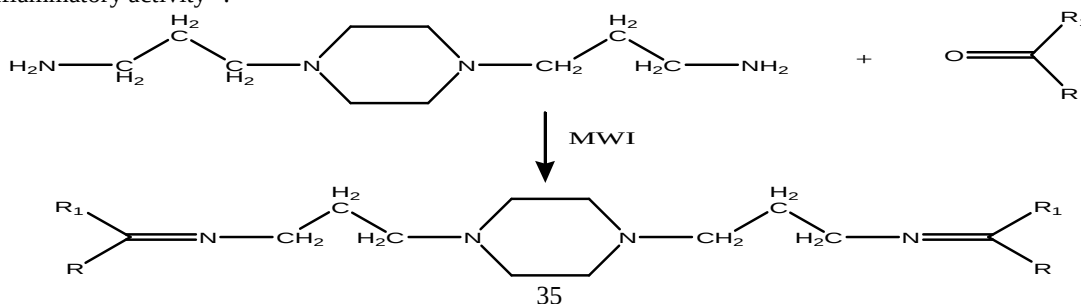


N. Linganna and *et al* reported synthesis of bishydrazone by thermolysis of aldehyde hydrazone under reduced pressure. In this typical reaction a solution of semicarbazone and tetrahydrofuran heated in a sealed tube for 12 to 14 hrs and bishydrazone obtain³⁷.

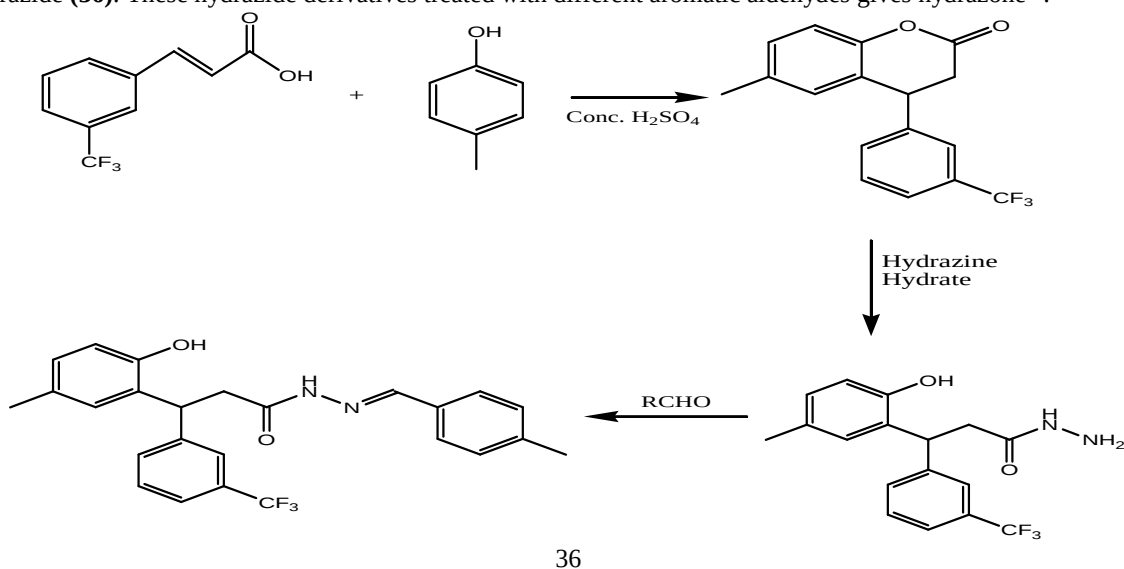
S. Jubie and *et al* reported the synthesis of some hydrazones and carbazones of indane-1, 3-Dione. Diethyl phthalate when treated with ethyl acetate in sodium ethoxide gives sodium salt of ester derivative which on neutralization by sulphuric acid gives indane-1,3-dione (**34**). This intermediate reacts with ethanol under reflux result in hydrazone and carbazone. All these compounds evaluated for antimicrobial activity³⁸.



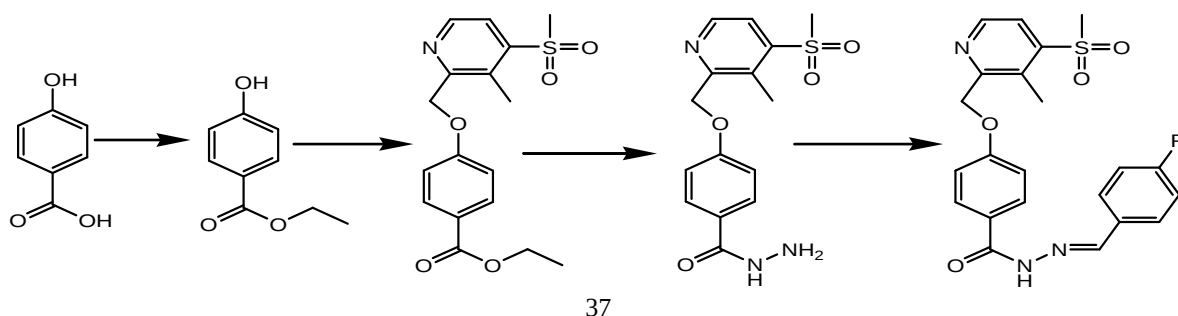
S.M. Sondhi and *et al* reported a number of bis schiff's bases (**35**) which had been synthesized by condensation of 2,4,10 tetraoxaspiro undecane dipropanamine with furfural, indole-3-aldehyde, 2-acetylpyridine, 4-acetylpyridine and by condensation of 1,4-bis(3-aminopropyl) piperazine with indole-3-aldehyde, 2-acetylpyridine, in high yields using microwave irradiation. Bis hydrazone derivatives were obtained by condensation of 2,6-diacetylpyridine with various arylsulfonylhydrazide using microwave irradiation. These compounds were tested for anagesic and antiinflammatory activity³⁹.



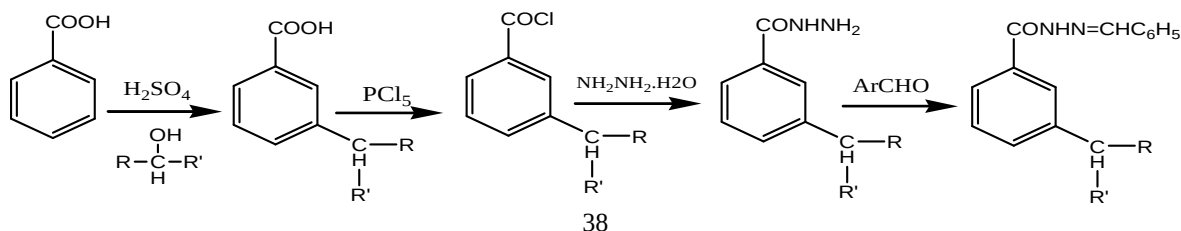
Srinivasrao and *et al* reported the synthesis of some new potent antibacterial hydrazide-hydrazone derivatives. The synthesis involved preparation of substituted chrome-2-one from starting material 3-(3-trifluoromethyl) phenyl)-acrylic acid with p-cresol which in treatment with hydrazine hydrate in methanol gives substituted propane hydrazide (**36**). These hydrazide derivatives treated with different aromatic aldehydes gives hydrazone⁴⁰.



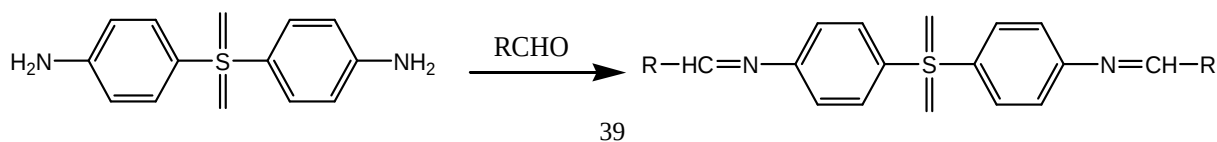
Swamy Saidugari and *et al* reported the synthesis of some new benzohydrazide derivatives (**37**) from commercially available 4-hydroxybenzoic acid and 2-chloromethyl-4-methanesulphonyl-3-methyl pyridine as a starting material. These compounds were tested for antibacterial activity⁴¹.



Pandey V.K. and *et al* reported synthesis of substituted azetidinone (**38**) by using phenyl-3-hydroxyethyl quinazolinone with benzoic acid in the presence of conc. sulphuric acid, and with further treatment with hydrazine hydrate affords hydrazides with condensation with an aromatic aldehydes in acetic acid gives hydrazone. The compounds were tested for antiviral and antibacterial activity⁴².



A series of Schiff base and 2-azetidinones (**39**) of 4,4'-diaminodiphenylsulphone have been synthesized by S.J. Wadher and *et al*. 4,4'-diaminodiphenylsulphone was condensed with various aromatic or heterocyclic aldehyde in ethanol in the presence of concentrated sulphuric acid as a catalyst to yield the Schiff base. These Schiff's bases on treatment with chloroacetylchloride in the presence of triethylamine gave substituted 2-azetidinone. All these compounds were evaluated for their *in vitro* activity against several microbes. Compound exhibited potent antibacterial activity with the reference standard ciprofloxacin and fluconazol⁴³.



CONCLUSION:

This review totally focused on development of hydrazone by using different scheme of synthesis and raw materials. This information become the benchmark for researchers who have synthesized variety of hydrazone derivatives and screened them for their various biological activities viz. anticonvulsant, antidepressant, analgesic, anti-inflammatory, antiplatelet, antimalarial, antimicrobial, antimycobacterial, anticancer, vasodilator, antiviral, antischistosomiasis, anti-HIV, anthelmintic, antidiabetic, and trypanocidal activities. These observations based on the present review have been becoming a helpful tool to guide researchers for the development of new hydrazones that possess varied biological activities.

REFERENCE:

1. Ramanan L and Ranjit RC, PLOS Med, 13(2016) 1.
2. Jerry March, Advanced Organic Chemistry, (John Wiley and Sons Publication, New York) 1992, p. 896.
3. Metzger JV, The Chemistry of heterocyclic compound, (John Wiley and Sons Publication, New York) 1979, p. 9.
4. Neeraj KF and et al, Asian J Chem, 20 (2006) 1.
5. Neeraj KF and et al, Asian J Chem, 20 (2008) 1.
6. Parikh KA and et al, Ind J Chem, 39B (2000) 716.
7. Mahajan PS and et al, Res Chem Intermed, 13 (2004) 197.
8. Ravish I and Raghav N, Biochem Anal Biochem, 5 (2016) 1.
9. Govindasami T and et al, International J Org Chem, 1 (2011) 71.
10. Mail kumaran P and et al, Asian J Pharma Ana and Med Chem, 1 (2013) 104.
11. Panneerselvam P and Geete Ganesh G, E-Journal of Chemistry, 8S1 (2011) S149.
12. Janardhan Gowda and et al, Indian J of chem, 49B (2010) 1130.
13. Parekh J and et al, J. Serb. Chem Soc, 70 (2005) 1155.
14. Chandrashekhara K B and Narisetty R, Indian J of chem. 54B (2015) 902.
15. Mustapha C and et al, J of Saudi Chemical Soc, 73 (2016) 1.

16. Kui C and et al, Bioorganic and Medi Chem, 17 (2009) 7861.
17. Desai V and Shinde R, Int J Pharm, 5 (2015) 930.
18. Noureen A and et al, Pak. J. Pharm. Sci, 26 (2013)113.
19. Eldehna M and et al, Molecules, 20 (2015) 8800.
20. Raghuwanshi PB and Mahalle PV, Der Pharma Chemica, 6 (2014) 262.
21. Dr. Rathore K and Jadon G, J of Drug Delivery and Therapeutics, 4 (2014)131.
22. Padmini K and et al, Int J of Pharma Research and Review 2 (2013)43.
23. Kumar V and et al, Bioorg and Med Chem Letters, 25 (2015)1420.
24. Gregory L and et al, Bioorg and Med Chem Letters, 22 (2014) 4629.
25. Sriram, D and et al, Bioorg Med Chem 14 (2006) 876.
26. Mahajan PS and et al, Res Chem Intermed, 10 (2015) 1.
27. Rollas S and et al, Farmaco, 57 (2002)171.
28. Kishore Kumar K and et al, Der Pharma Chemica, 4 (2012)1603.
29. Parlar S and et al, Chem. Pharm. Bull, 64 (2016)1281.
30. Revanasiddappa BC and et al, Int J of ChemTech Res, 1 (2009) 1100.
31. Malladi S and et al, Arabian J of Chem,6 (2013) 335.
32. Raja AS and et al, Indian J of Chem, 49 B (2010) 1384.
33. Ahmet O and et al, J of Serb Chem Soc,77 (2012) 141.
34. Gamal and et al, Indian J of Chem, 39B (2000) 368.
35. Mogilaiah K and et al, Indian J of Chem, 40B (2001) 1270.
36. Shalaja M and et al, Indian J of Chem, 49B (2010) 1088.
37. Linganna N and et al, Indian J of Chem, 38B (1999) 1126.
38. Jubie S and et al, Indian J of Chem, 49B (2010) 1261.
39. Sondhi and et al, Indian J of Chem, 48B (2009) 1128.
40. Yatcheria and et al, Indian J of Chem, 54B (2015) 1162.
41. Saidugari S and et al, Indian J of Chem, 56B (2017) 177.
42. Pandey VK and et al, Indian J of Chem, 44B (2005) 158.
43. Wadher SJ and et al, Int J of PharmTech Res, 1 (2009) 22.