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OXAZOLINES: THEIR SYNTHESIS AND BIOLOGICAL ACTIVITY

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Keywords:

Oxazoline, Antimicrobial, Anti malarial, Antibacterial, Anti-inflammatory, Antioxidant

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ABSTRACT: Heterocyclic chemistry has been known for many years, but in recent years heterocyclics received great attention. In heterocyclic chemistry oxazoline is one of the most important moiety. Oxazoline moiety shows a wide range of application such as in agriculture industry, pharmaceutical, food industry, natural product, medicine, polymers, and various other industries. Oxazoline moiety constitutes the core structure of many biologically active natural compounds. Oxazoline plays a major role in medicinal chemistry. Heterocyclic compounds whose containing oxazoline moiety as core structure reported wide range of biological activities such as antibacterial, antifungal, antimicrobial, antioxidant, antipyretic, anti-HIV, anti-malarial, antitumor, antiviral, anti-inflammatory, CNS stimulant activity, *etc*. Oxazolines synthesized by the reaction of various aromatic substitutes like acids, aldehydes, nitriles, azides, *etc*. The synthetic chemist does great work on the synthesis and application part of oxazolines. In this review we have described various synthetic methodologies and their different biological activities reported by organic synthetic chemist.

INTRODUCTION: Oxazolines have been known for many years, but in recent years the chemical literature has shown considerable activity in this field. A number of review articles [1, 2] were published about the synthesis, reactions, and applications of oxazolines. The literature following publication of those articles indicates a many-fold increase in university and commercial activity involving preparation, reactions, and uses of oxazolines. The oxazoline ring is important constituent of bioactive natural products [3] and pharmaceuticals [4]. The purpose of this review is to assemble the literature dealing with the synthesis and biological activity of oxazolines. Oxazolines are five-membered heterocyclic compounds having one double bond.

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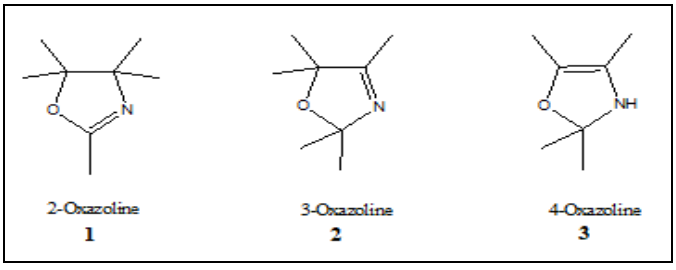
The double bond may be located in one of the three positions in this ring, therefore making the possibility of the existence of three different oxazoline rings. The 2-oxazoline 1 structure is the most common, with 3-oxazolines 2 and 4-oxazolines 3 existing primarily as laboratory research compounds.



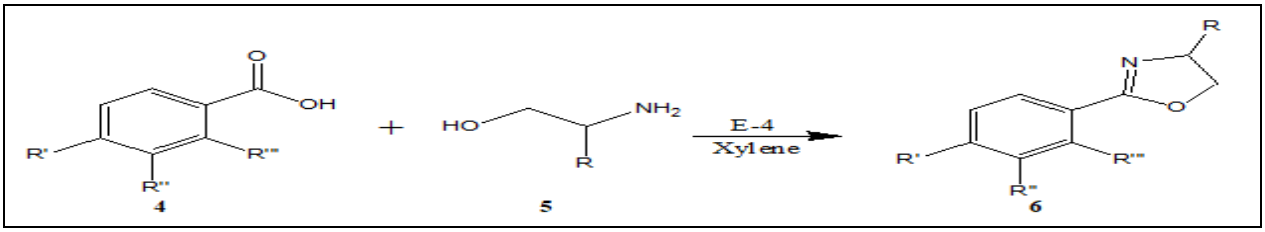
The phenomenal regio- and stereochemical control in synthesis, the 2-oxazoline moiety continues to play a significant role. It has attracted organic chemists from various areas who have discovered its unique properties [5] and its capacity to serve as synthetic precursor [6] or mediator in a multitude of chemical processes [7]. 2-Oxazolines have been used as chiral auxiliaries [8], as ligands for metal

entrapment [9], as protecting groups [10] for carboxylic acids and amino alcohols and of particulars importance as biologically active agent [11]. The oxazoline ring presents an interesting structure on which to build a wide variety of compounds having properties which make them of interest in many fields of application. Hydrogen located on the carbon of an alkyl group in the 2 positions is active and are readily replaced with other groups. The nitrogen of the oxazoline moiety is basic and forms salts with acids and quaternary compounds with alkyl halides. In addition, the 2-oxazoline ring has two sites in the 4 position and two in the 5 position where reactive groups may be located. There are many ways in which oxazoline may be formed. The main interest has been to synthesize 2-oxazoline because of its broad range of application.

SYNTHESIS:

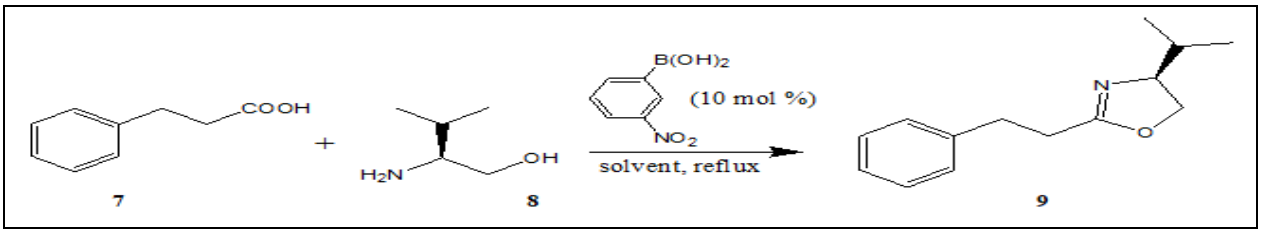
From Acids: Oxazolines are prepared in various ways. The simplest and most inexpensive process involves the reaction of amino alcohol with a carboxylic acid. The amino alcohol must have the NH_2 and OH groups on adjacent carbon atoms, and the acid may be aliphatic or aromatic. When the amino alcohol is completely substituted on the carbon-containing the NH_2 group, the reaction with an acid proceeds smoothly through the amide to the oxazoline with elimination of water.

2- Substituted oxazolines 6 were synthesized from the reaction of 2- amino ethanol 5 with benzoic acid 4 in the presence of Ersorb-4 (E-4) in hot toluene or xylene in good yield [12].



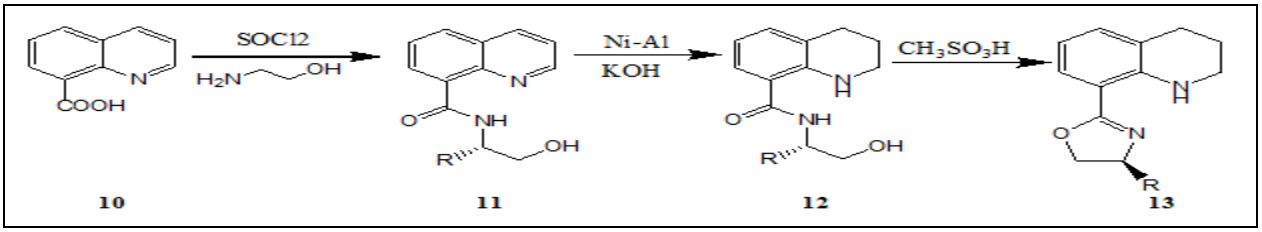
4 5 6

Direct condensation of carboxylic acids 7 with amino alcohols 8 in the presence of 3-nitrophenylboronic acid as a dehydration catalyst was a newly developed methodology for the synthesis of oxazoline 9 in excellent yield [13].



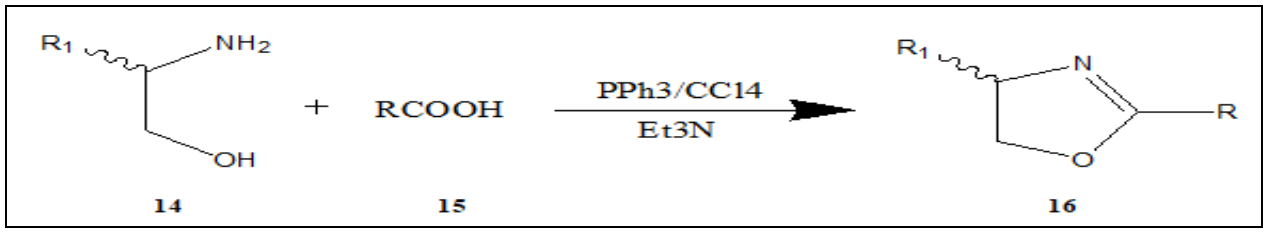
7 8 9

Some new chiral 1, 2, 3, 4-tetrahydroquinolinyl-oxazoline 13 compounds were synthesized from 8-quinolinecarboxylic acid 10 and enantiomerically pure amino alcohols using a convenient procedure [14]. The 1, 2, 3, 4-tetrahydroquinolinyl-oxazoline were synthesized in four steps *via* 11 and 12 intermediate. The reaction is illustrated by the following equation:

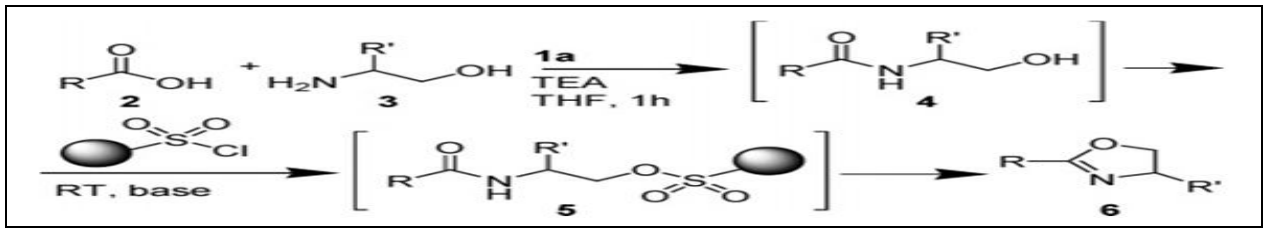


10 11 12 13

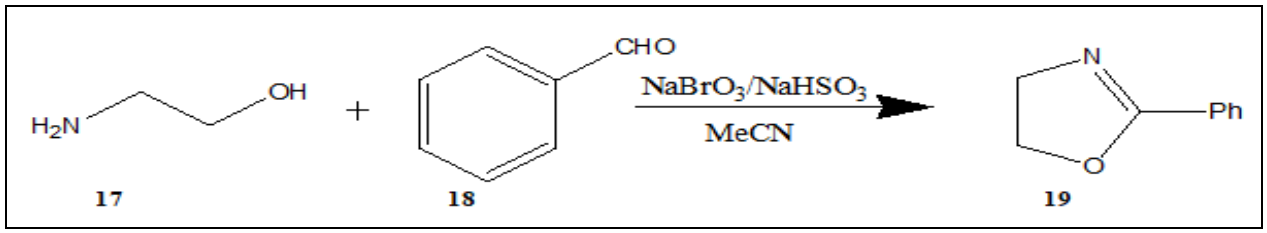
Jiang *et al*., reported a facile one-pot procedure for the synthesis of 1,3-oxazolines 16 bearing fluorinated alkyl groups at the 2-position by the reaction of 14 with 15 [15]. In this reaction amide intermediates were initially formed and then by rapid cyclization its converted into 1, 3-oxazoline product.



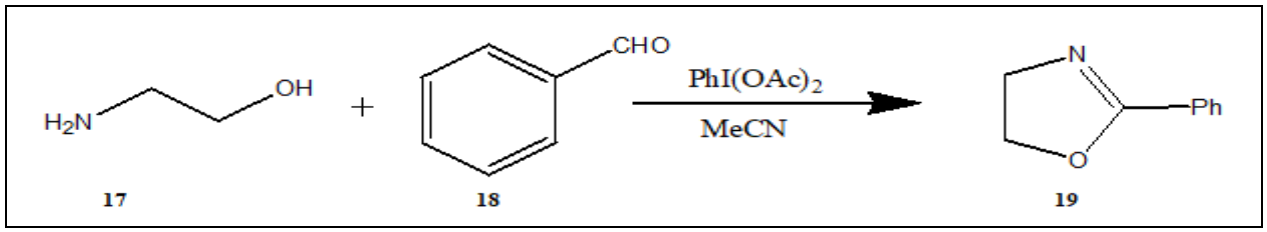
Crosignani *et al*., proposed a protocol for the parallel synthesis of 2-oxazolines using polymer-supported Mukaiyama reagents [16].



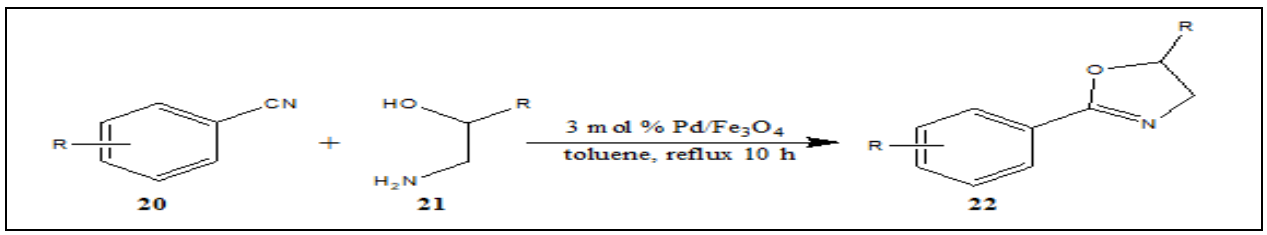
From Aldehydes: 2-Oxazolines 19 also prepared by the reaction of aromatic aldehydes 18 with amino alcohol [17]. This synthetic scheme is performed by many chemists using a different catalyst. Shinde *et al*., [17] were proposed a reaction scheme using $NaBrO_3$ as catalyst.



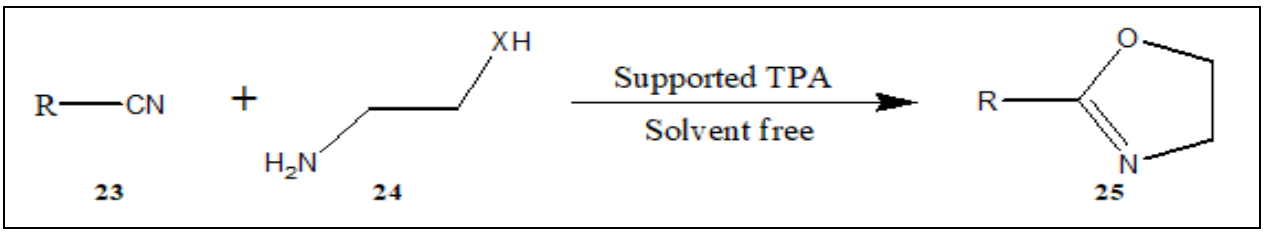
Another reaction mechanism was reported by Karade *et al*. [18] In this mechanism they were treated aldehydes 18 with amino alcohol 17 using $PhI(OAc)_2$ as a catalyst and synthesized oxazolines 19 in good to yield.



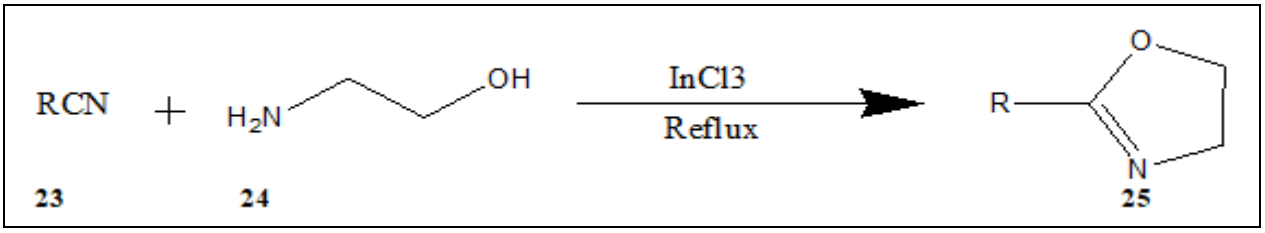
From Nitriles: Oxazoline may also be synthesized from the reaction of aromatic nitriles 20 with amino alcohols 21 [19]. A solution of benzonitrile and amino alcohol in toluene was heated at about 100 °C using Pd/Fe_3O_4 as a catalyst.



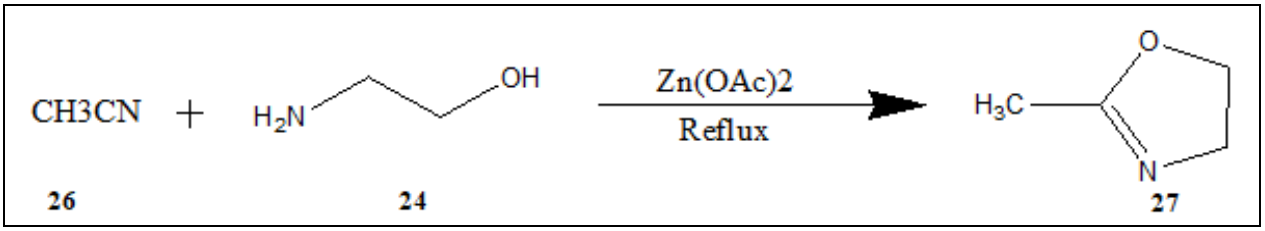
The same product has also been prepared by the reaction of nitriles 23 and amino alcohols 24 by the use of 12-Tungstophosphoric acid (TPA) supported on silica, activated carbon and poly (4 styrylmethyl) pyridinium chloride (PMP) as a reusable catalyst [20].



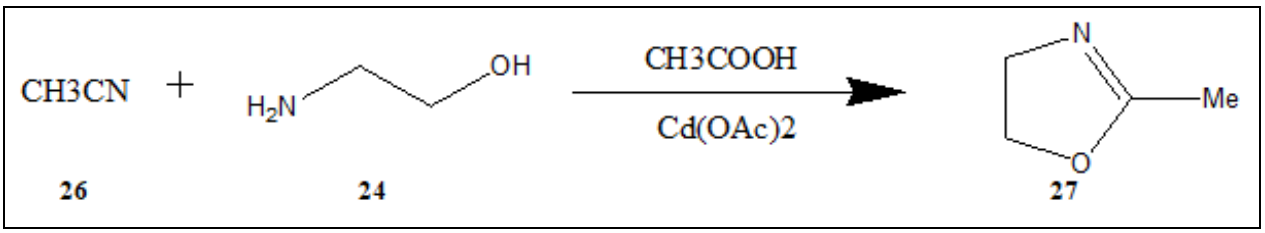
Oxazolines may also be synthesized by the reaction aromatic nitriles 23 with β-amino alcohols 24 using InCl3 as catalyst under reflux conditions [21]. This catalyst can also be successfully applied to the chemoselective conversion of dicyanobenzenes to their corresponding mono- and bis-oxazolines. By using ultrasonic and microwave irradiation improve the yield and reduced the reaction time.



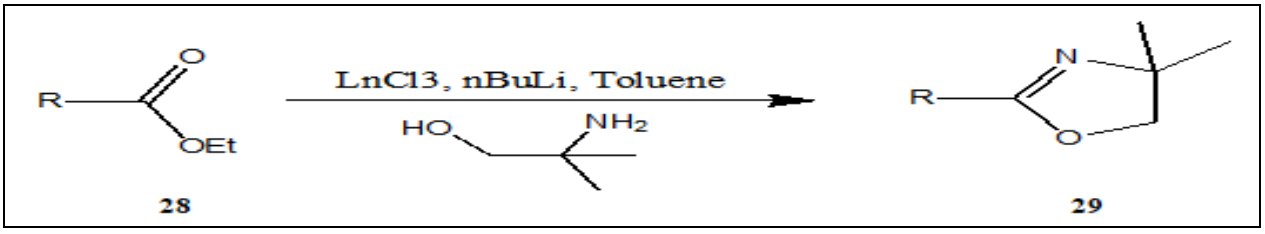
Xiaobo *et al*., [22] were reported a synthetic method for the preparation of 2-oxazolines.



Witte *et al*., proposed a synthetic method for the preparation of 2-oxazolins [23]. In this mechanism, nitriles were treated with amino alcohol in presence of cadmium acetate used as a catalyst forms 2-oxazolines in good yield.

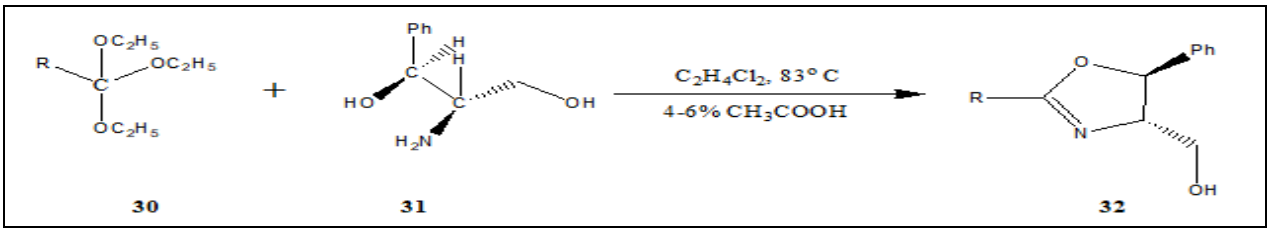


From Ester: There has been a lot of work reported where oxazoline are prepared from esters. Most commonly esters may get converted into oxazoline by the reaction of esters with the amino alcohols. Zhou *et al*., [24] were proposed a new method for the synthesis of 2- oxazolines 29 which had a valuable synthetic application for its simplicity, applicability and efficiency. In this method 2-oxazoline synthesized directly from carboxylic esters 28.

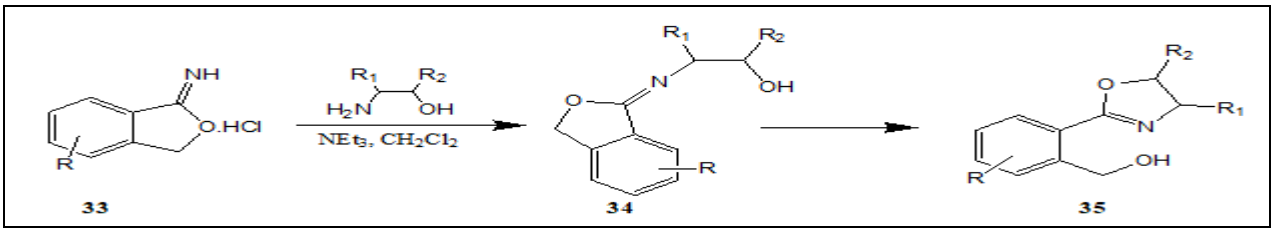


Ezhova et al. were synthesized New chiral N, P-oxazolines. (+) (1S, 2S)-2-Amino-1-phenyl-1, 3-propanediol 31 reacts with ortho-esters 30 to form 4-hydroxymethyl-5-phenyl-1, 3-oxazolines 32.

Subsequent reaction of their toluene sulfonyl derivatives with diphenylphosphinolithium yields the N, P-ligands, (4S, 5S) - 2-R-4-diphenyl-phosphinomethyl-5- phenyl-1, 3-oxazoline [25].

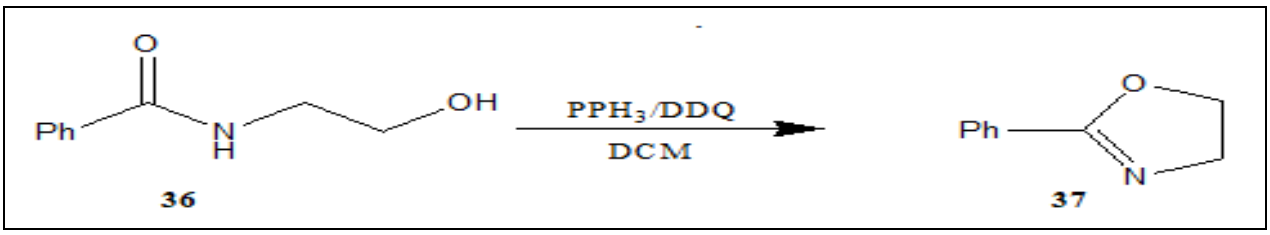


Various chiral bidentate oxazolines 35 were obtained in a one-step synthesis via a cyclic imidate ester rearrangement 33. This reaction was carried out under argon atmosphere in dry solvents under anhydrous conditions [26].

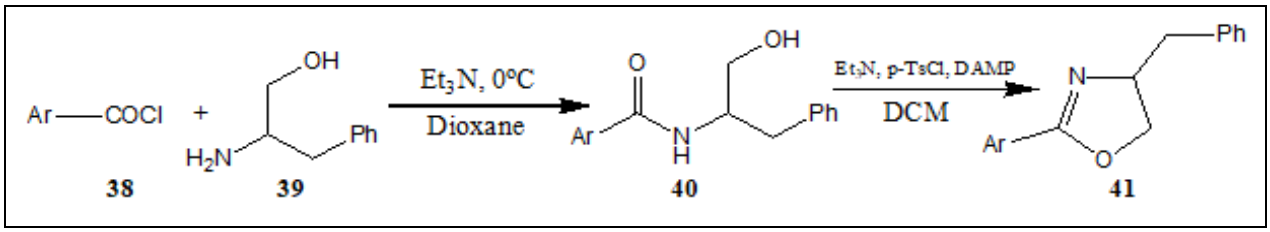


From Amides: A considerable volume of work has been reported where oxazolines are prepared from amides. Some amides cyclize with difficulty, requiring the presence of a dehydrating agent and the use of high temperatures. Others go to the oxazoline with only moderate heat and absence of dehydrating agents.

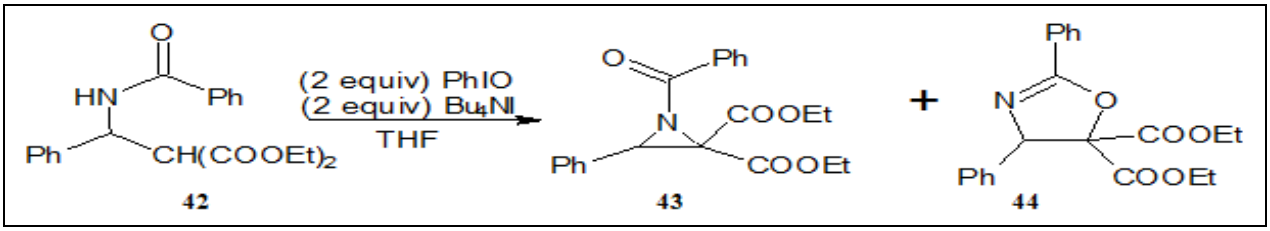
A facile and efficient synthesis of 2-oxazolines 37 from N-(2 hydroxyethyl) amides 36 using triphenylphosphine– 2, 3 - dichloro - 5, 6 - dicyanobenzoquinone (PPh3–DQQ) system was described. The reaction proceeds under neutral and mild conditions and excellent yields were obtained [27].



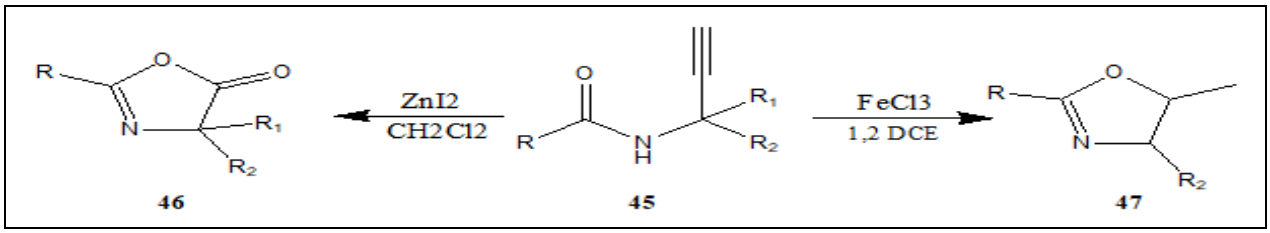
Several new chiral oxazolines 41 were prepared conveniently in good to high yields using a two-step synthesis using microwave irradiations under solvent-free conditions. This method involves the formation of an optically active amide 40, *in-situ* conversion of the amide into tosylate (OTs) and finally rings closing reaction gives substituted oxazolines [28].



R. Fan *et al*., was reported a facile method for the preparation of oxazoline 44 [29]. In this method, they were reported an efficient oxidative cyclization of amidoalkylation 42 adducts of activated methylene compounds with the combination of iodosobenzene and a catalytic amount of tetrabutylammonium iodide under neutral conditions.



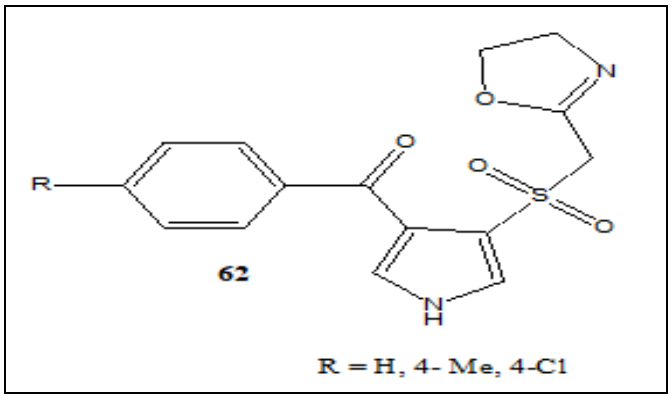
2-Oxazolines can also be prepared from the corresponding hydroxyamides using XtalFluor-E ([Et2NSF2] BF4) as a cyclodehydration agent [30]. M.-F. Pouliot *et al.* were synthesized a wide range of oxazolines under mild conditions in good to excellent. 2- Oxazolines can also be synthesized by the cyclization of acetylenic amide 45. A Lewis acid promoted cyclization of acetylenic amide with various functionalities was well tolerated to give 2-oxazolines 46, 47 and 2-oxazoles in good to excellent yields under mild reaction conditions by ZnI_2 and $FeCl_3$ [31].



A series of 2-oxazoline-1, 10-phenanthrolines (L5–L8) 52 were synthesized by Zhang *et al.*, [32] 2-Methyl-1, 10-phenanthroline 48 and its derivatives were oxidized with selenium dioxide to form their corresponding aldehydes 49. The aldehydes were converted into corresponding oximes 50, which could be further dehydrated in nitriles 51. The methoxyimidates were easily formed in the reaction of nitriles with methanol in the presence of a base. Condensation of the relevant methoxyimidates with aminoethanol gave the corresponding oxazoline-phenanthroline derivatives in acceptable yields.

Application:

Anti-microbial: Oxazolines is one of the most important structural units of among all heterocyclic compounds. Many organic chemists have synthesized various antimicrobial derivatives which contains oxazolines ring system.



V. Padmavathi *et al.*, [36] have prepared Novel sulfone linked bis (heterocycles) 62 having oxazoline moiety in combination with pyrrole from E aroylethenesulfonylacetic acid methyl ester exploiting ester and olefin functionalities. These compounds exhibited greater antimicrobial activity.

These compounds were tested for antimicrobial activity at two different concentrations: 100 and 200 µg/mL, against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Escherichia coli*, *Klebsiella pneumoniae* (Gram-negative bacteria) on nutrient agar plates at 37 ºC for 24 h using chloramphenicol as reference drug. The inhibitory activity of those compounds against the Gram-positive bacteria was higher than that of the Gram-negative bacteria.

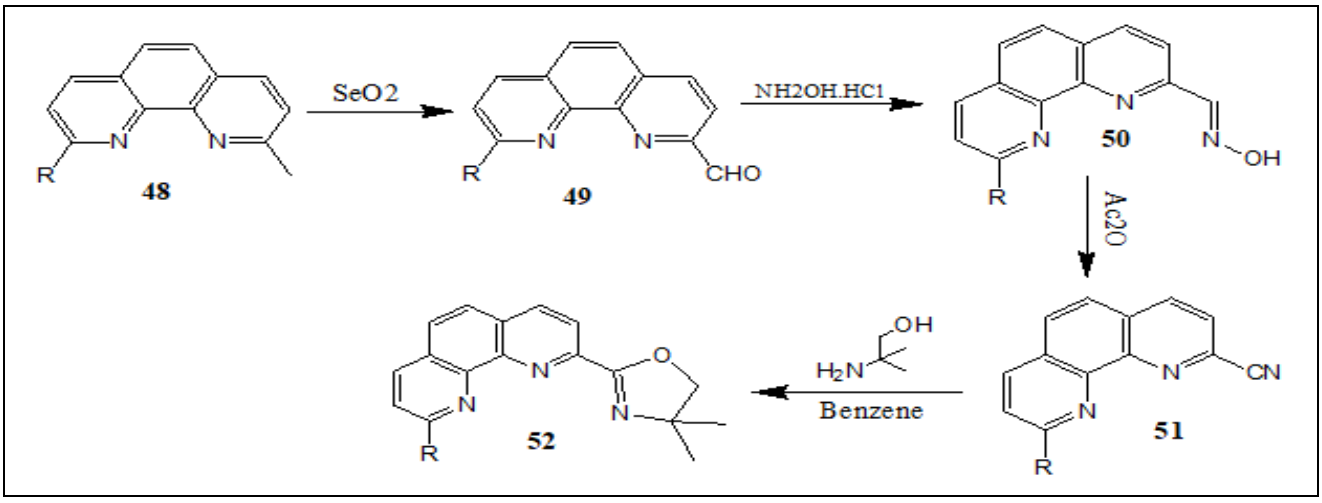
Polyoxazolines of various architectures and chemical functionalities can be prepared in a living and therefore controlled manner *via* cationic ring-opening polymerization. They have found widespread applications [37].

Waschinski *et al.*, [38] were reported the synthesis of a series of PMOXA and PEOXA polymers, terminated with quaternary ammonium groups. The polymers were prepared *via* standard cationic ring-opening polymerization and terminated using a series of N-alkyl-N, N-dimethyl amines as well as pyridine. The materials were investigated regarding

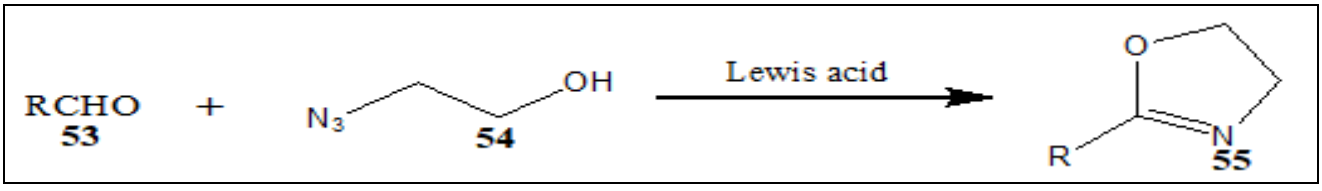
their antimicrobial properties by determining the minimal inhibitory concentration against *Staphylococcus aureus*. The screening showed, that poly (2-methyl-2-oxazoline)-based polymers containing alkyl ammonium functions with alkyl chains of twelve carbon atoms or longer have antimicrobial activity. A pronounced effect of the head group on antibacterial properties was also observed: polymers containing a proton as the head group and a dodecyldimethyl ammonium end group were found to be less bactericidal than the analogous polymer with a methyl head group. Poly (2-methyl-2-oxazoline) containing a BOC-protected NH_2 headgroup, by contrast, showed very high antimicrobial activities, although this effect is not observed in poly (2-ethyl-2-oxazoline)-based polymers.

A further investigation of the influence of the end-groups revealed that head groups consisting of simple alkyl chains of between 4 and 10 carbon atoms in length are most effective in increasing the antimicrobial properties of the ammonium-functionalized polymers [39]. To explain this effect, the authors said that the polymers exist as unimolecular micelles in solution below the critical micellar concentration. Therefore, the end-groups of the polymer would be aggregated and could collaboratively penetrate the cell wall at the same point, which could be more disruptive than the insertion of a single ammonium group.

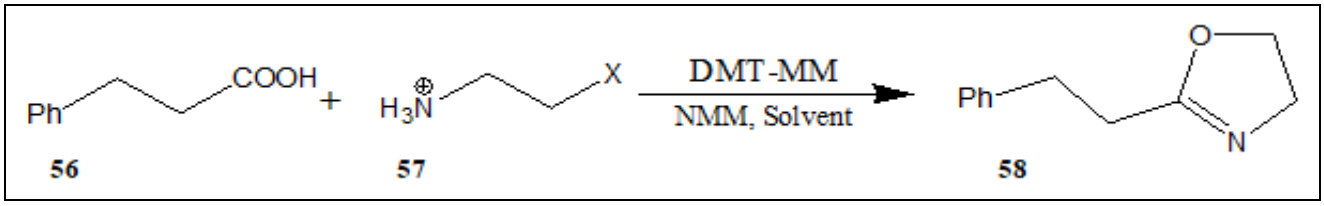
Polyoxazolines with a quaternary ammonium end group were proposed that they are potent biocides. Their antimicrobial activity is controlled by the nature of the distal end group. The nonreactive groups were usually introduced *via* the initiator. A series of poly-methyloxazolines with varying satellite groups including hydroxy, primary amino and double-bond-containing groups were synthesized [40]. The resulting telechelic poly-oxazolines were explored regarding their antimicrobial activity and toxicity. It was found that the functional satellite groups greatly controlled the minimal inhibitory concentrations against the bacteria *Staphylococcus aureus* and *Escherichia coli* in a range of 10 to 2500 ppm.



From Azides: The reactions of 1,2- and 1,3-hydroxyalkyl azides 54 and aldehydes 53 in the presence of Lewis acid result in the one-step construction of oxazolines 55 [33]. This reaction involves initial hemiketal formation and subsequent elimination to form an oxenium ion, which is now set up for intramolecular attack by the azide. The resulting intermediate can then form the product *via* a 1, 2-hydride shift, coupled with N_2 loss, followed by proton loss to give the oxazoline product.

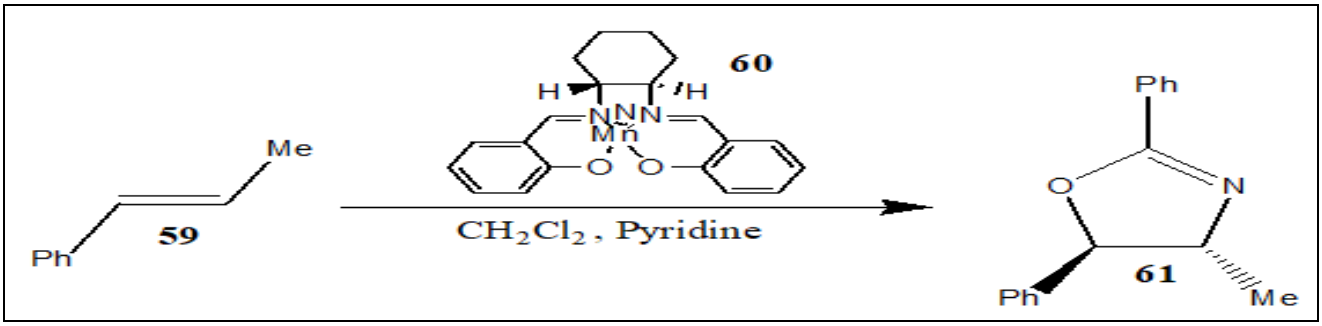


From Ammonium Salt: Reaction of carboxylic acid 56 and 2-haloethylammonium salts 57 gives 2-oxazolines 58 [34]. The reaction involves dehydrocondensation of carboxylic acids and 2-haloethylammonium salts leading to the formation of N-(b - haloethyl) amides, which then converted into 2-oxazolines by the treatment of base. This reaction can proceeds smoothly using 4-(4, 6-dimethoxy-1, 3, 5- triazin- 2- yl)- 4- methyl-morpholinium chloride (DMT-MM).



Chiral Oxazolines: Chiral or optically active oxazolines are highly versatile five-membered heterocycles. They can easily be converted into optically active β-amino alcohols which are useful synthetic intermediates.

Chiral oxazolines 61 are formed by N1 unit transfer to olefins using a chiral nitridomanganese complex 60. When trans-disubstituted styrenes were treated with chiral complex in the presence of an acid chloride, oxazolines were obtained with high enantioselectivities (up to 92%) [35]. In this proposed methodology trans-β-methylstyrene was treated with the chiral nitridomanganese complex in methylene chloride at room temperature in the presence of pyridine, pyridine N-oxide and benzoyl chloride, 4-methyl-2,5-diphenyl-2-oxazoline was obtained with 81% ee. Moreover, the reaction gave exclusively trans-oxazoline with the retention of the stereochemistry of the starting olefin.



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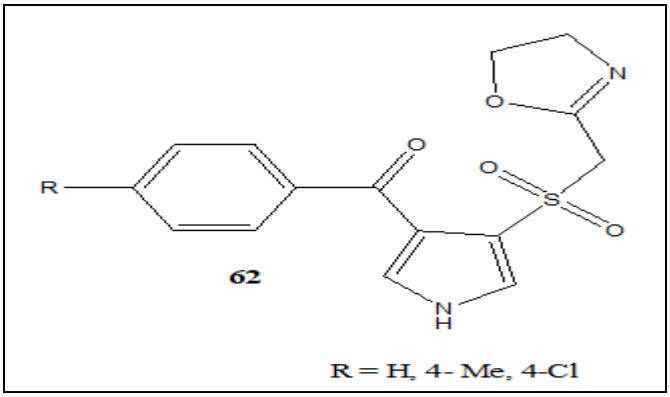

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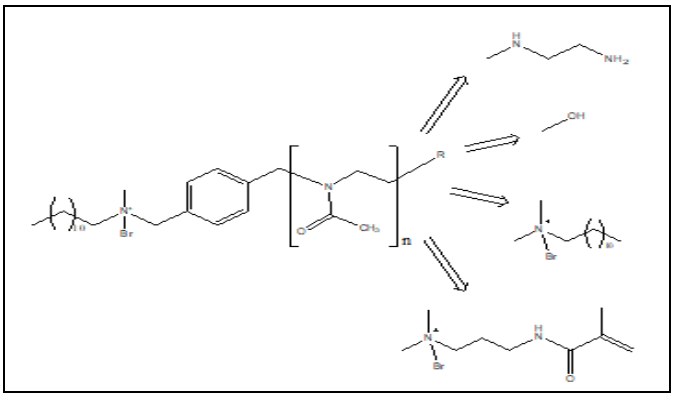
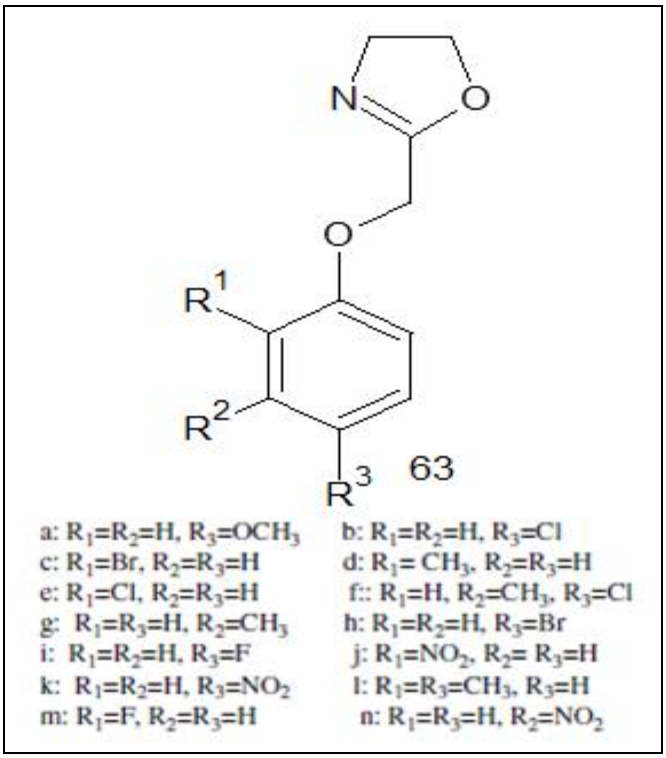
A further investigation of the influence of the end-groups revealed that head groups consisting of simple alkyl chains of between 4 and 10 carbon atoms in length are most effective in increasing the antimicrobial properties of the ammonium-functionalized polymers [39]. To explain this effect, the authors said that the polymers exist as unimolecular micelles in solution below the critical micellar concentration. Therefore, the end-groups of the polymer would be aggregated and could collaboratively penetrate the cell wall at the same point, which could be more disruptive than the insertion of a single ammonium group.

Polyoxazolines with a quaternary ammonium end group were proposed that they are potent biocides. Their antimicrobial activity is controlled by the nature of the distal end group. The nonreactive groups were usually introduced via the initiator. A series of poly-methyloxazolines with varying satellite groups including hydroxy, primary amino and double-bond-containing groups were synthesized [40]. The resulting telechelic poly-oxazolines were explored regarding their antimicrobial activity and toxicity. It was found that the functional satellite groups greatly controlled the minimal inhibitory concentrations against the bacteria *Staphylococcus aureus* and *Escherichia coli* in a range of 10 to 2500 ppm.

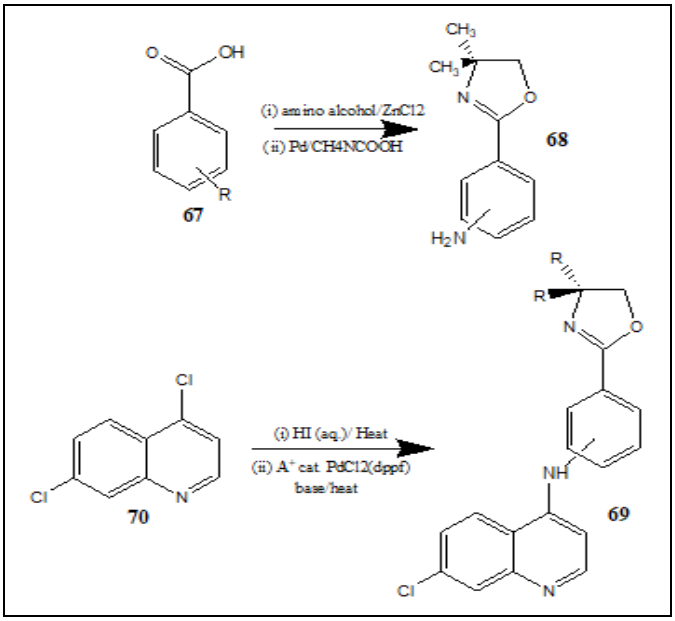


Anti-inflammatory: Oxazolines analogs are very useful in pain control and particularly in the management of oncological pain is the main and important target for the researcher. Oxazoline show good efficiency as chemotherapeutic agent especially as analgesic and anti-inflammatory agent.



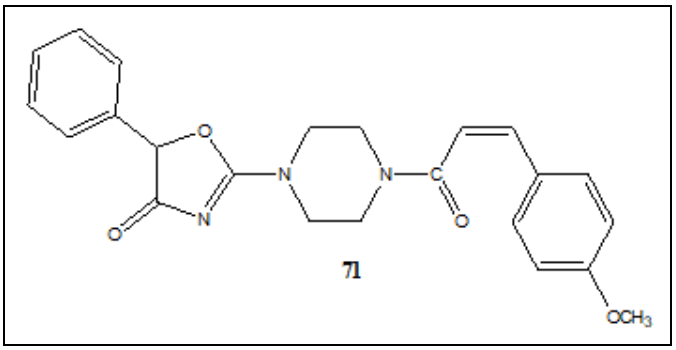
Khanum *et al.*, [41] has been synthesized a series of potential biologically active 2-aryloxy methyl oxazolines 63 from substituted hydroxybenzenes. These synthesized compounds were screened for their anti-inflammatory ulcerogenic, cyclo-oxygenase activities. The potency of the compounds was compared with that of the standard drugs, aspirin and phenylbutazone which indicates that these compounds were offered significant anti-inflammatory activity with low ulcerogenic activity than the standard drugs.

Anti-malarial: Malaria is a very infectious disease, and malaria infection results in over 300 million clinical cases and 1.5–2.7 million deaths worldwide per year. Most of these cases are caused by *Plasmodium falciparum*, the most virulent human malaria species. 2-oxazolines have long been recognized for their potent biological activity and cost-effective. Oxazoline derivative 69 as a potential anti-malarial agent has been investigated by E. E. Gordey *et al.* [42]



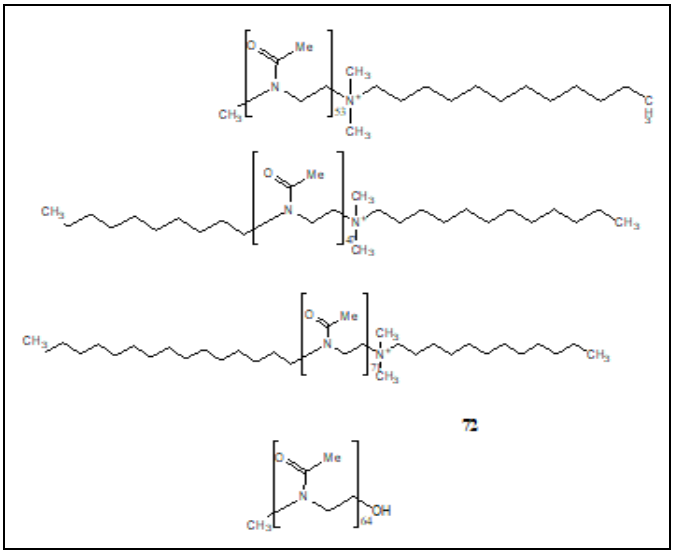
In this the synthesis and *in-vitro* antimalarial testing of a series of quinoline–oxazolehybrids had been carried out. These compounds were initially screened on cultures of P. falciparum clone 3D7A and they exhibited antimalarial activity in the 1 µM range.

Herrin *et al.*, [43] have been prepared the derivatives of 1-(4-methoxycinnamoy1)-4-(5-pheny1-4-oxo-2-oxazolin-2-yl) piperazine 71 and evaluate their activity against *Plasmodium berghei*. They all compound were exhibited blood schizonticidal activity against *Plasmodium berghei* in mice.



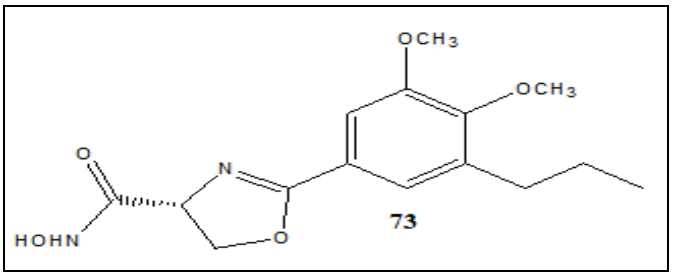
Anti-bacterial Bacterial infections are one of the major health problems for human mankind. Particularly, the increasing resistance against antibiotics demands the development of conceptually new agents active against bacteria. Oxazolines and its derivatives act as a good antibacterial agent.

Waschinski *et al.*, [44] investigated selected PMOX-DDA polymers with different satellite groups regarding their aggregation behavior in solution and their interactions with liposome as a model for the bacterial phospholipid membrane. The antibacterial activities of these polymer oxazolines were determined with the bacterial strains S. aureus, *S. epidermidis, E. coli,* and *P. aeruginosa*. In this experiment N, N Trimethyl-dodecylammonium chloride was used as a reference.



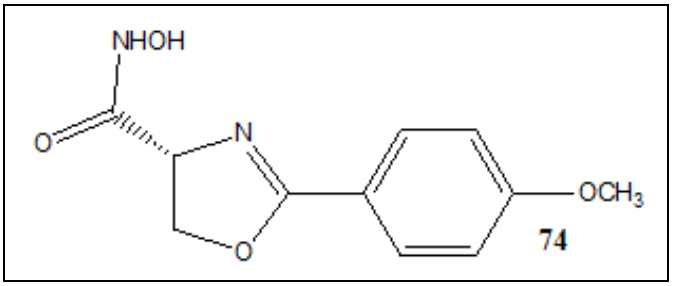
Strains of three bacteria *i.e. Enterococcus faecalis*, Mycobacterium tuberculosis, and Pseudomonas aeruginosa have recently shown resistance to every

clinically available antibiotic. Therefore Pirrung et al [45] have been synthesized UDP-3-O-[R-3-hydroxymyristoyl]-GlcNAc deacetylase (LpxC) a zinc amidase 73 that inhibit Gram-negative bacteria. The inhibitors of this enzyme are oxazolines.



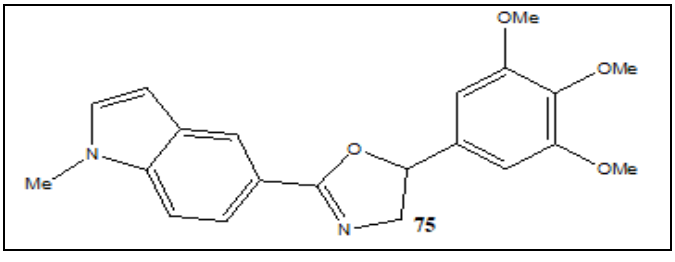
73

Some of the enzyme inhibitors exhibit antibacterial activity through their inhibition of LpxC which is a zinc amidase that catalyzes the second step of lipid biosynthesis in Gram-negative bacteria. Pirrung *et al.*, [46] developed a method for the synthesis of oxazolines 74 and evaluated these compounds against wild-type and LpxC inhibitor-sensitive strains of *Escherichia coli*, as well as wildtype Pseudomonas aeruginosa with the range of (~2 µg/mL.



74

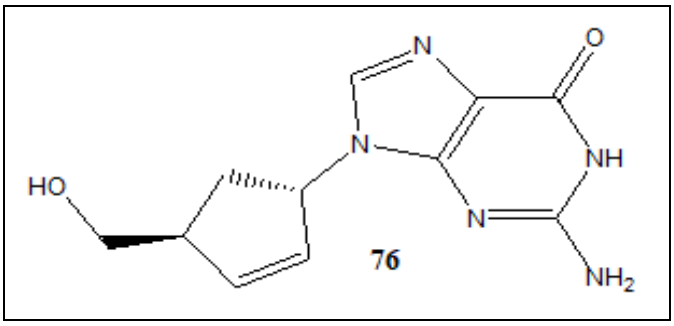
Anti-tumor: There are many derivatives of oxazolines were reported which shows activity against cancer [47]. Q. Li *et al.*, [47 b] have been synthesized a series of indole containing oxazolines 75. The compounds exert their anticancer activity through inhibition of tubulin polymerization by binding at the colchicines site. This compound was identified as an orally antimitotic agent active against various cancer cell lines.



75

These optically active 5-aryl oxazolines were synthesized by coupling of the amino alcohol with either the acids or the nitriles. These oxazoline derivatives were evaluated for their antiproliferative activity against the human lung carcinoma cell line NCI-H460 and the MDR positive human colon adenocarcinoma cell line HCT-15 and their anticancer activity of was evaluated in the syngeneic M5076 murine ovarian sarcoma flank tumor model.

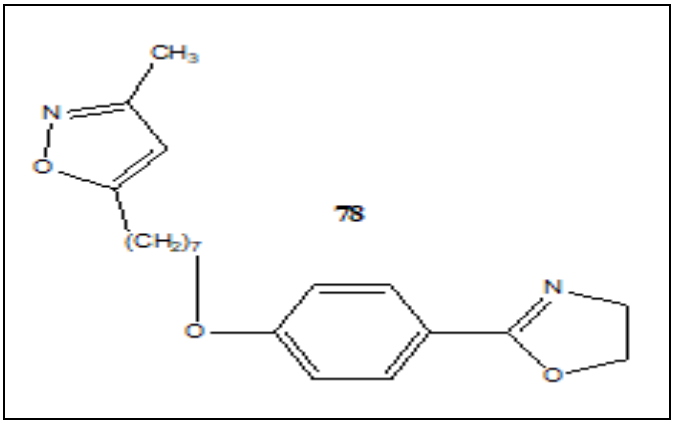
Anti-viral: Berranger *et al.*, [48] has been synthesized a potent antiviral agent carbovir by using chiral oxazoline-N-oxide 76.



76

Peculiarly (-)-Carbovir was reported as a potential agent in treating AIDS [49]. And because of this it has been the subject of strong interest and turned out a new kind of (+)-Carbovir whose exhibited antiviral activity.

A series of substituted phenyl analogs of 5- [[4-(4, 5-dihydro-2 oxazolyl) phenoxy]alkyl]-3-methylisoxazoles 78 have been synthesized and screened *in-vitro* against several human rhinovirus (HRV) serotype [50].

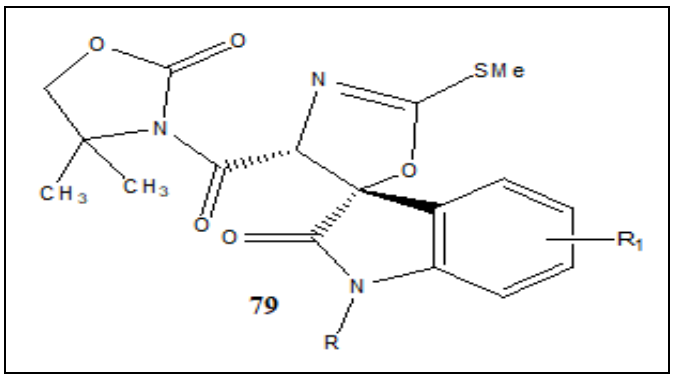


78

This compound is a broad-spectrum antipicornavirus agent that inhibits replication of 36 out of 45 rhinovirus serotypes at levels ranging

from 0.3 to 3.0 µM. And it also prevents paralysis when administered intraperitoneally to mice infected subcutaneously with Echo-9 virus.

Anti-pyretic: Jiang *et al.*, [51] reported a unique optically active spiro[oxazoline-3,3′- oxindole]s 79, a new antipyretic agent.

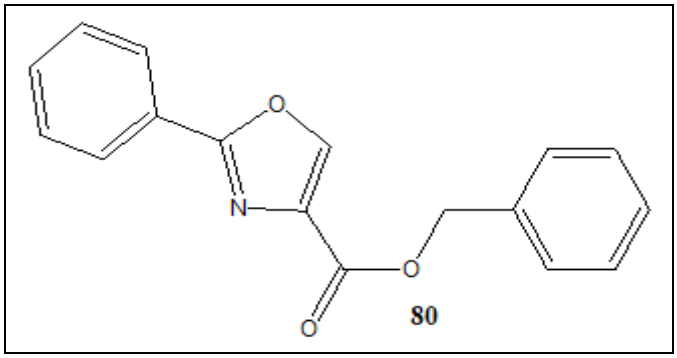


79

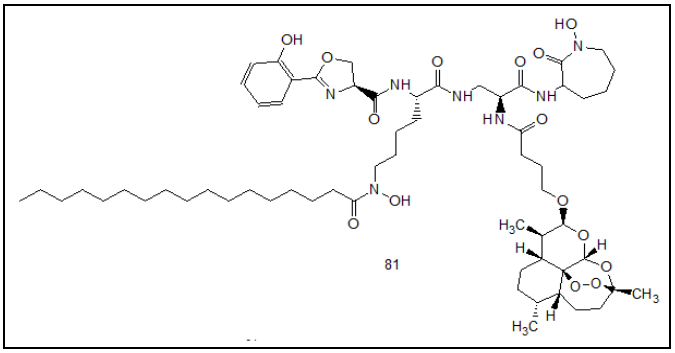
These compounds were synthesized through the organocatalyzed asymmetric synthesis of spiro-cyclic thiocarbamates via an aldol reaction and the biological activity of spirooxazolines is evaluated on fever by intracerebroventricular (icv) injection of lipopolysaccharide (LPS, a component of the outer membrane of Gram-negative bacteria) using a model of acute neuroinflammation in mice.

Anti-tuberculosis: Tuberculosis (TB) is a very infectious disease resulting in a death every 20 s. Thus, new drugs are urgently needed for the treatment of tuberculosis. The increase in cases of TB/HIV co-infection and the spread of multiple-drug resistant TB and extensively drug-resistant TB are making matters worse.

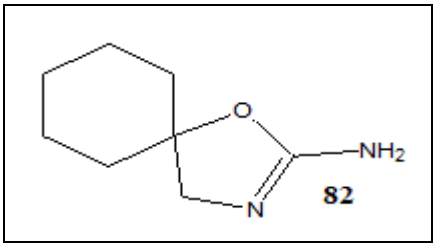
Moraski *et al.*, [52] reports the structure-activity relationship (SAR) starting from the oxazoline/ oxazole benzyl ester and leading to the identification of imidazo [1, 2-a] pyridines 80 as a new class of potent and metabolically robust antitubercular agents.


80

Miller *et al.*, [53] have been synthesized an artemisinin conjugate 81 with mycobactin T analog, and they found that it not only retains antimalarial activity similar to that of artemisinin itself but is exquisitely microbe-selective and has shown remarkably potent activity against *Mycobacterium tuberculosis*. The mycobactin-arteminisin conjugate is active against not only H37Rv *Mycobacterium tuberculosis* [minimum inhibitory concentration (MIC) = 0.39 µg/mL] but also both MDR Mycobacterium tuberculosis (MIC = 0.16-1.25 µg/mL) and XDR Mycobacterium tuberculosis (MIC = 0.078-0.625 µg/mL).

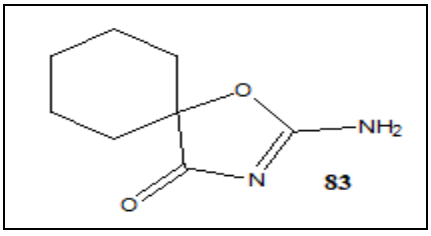

81

CNS Stimulant Activity: Harnden *et al.*, [54] proposed the synthesis of some 5-spiro-substituted 2-amino-2-oxazoline 82 and their effects on the central nervous system.



82

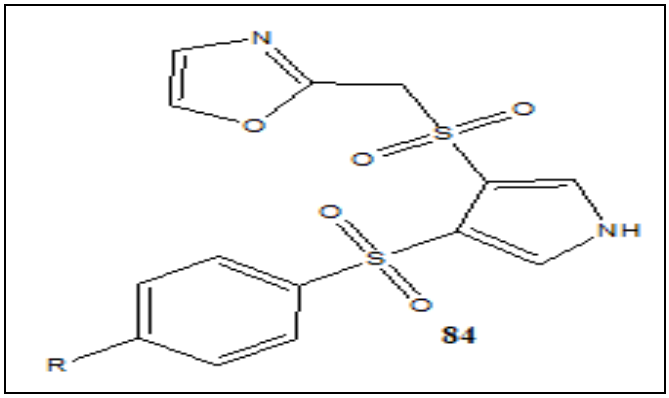
These compounds were synthesized from cyclic ketones involving reduction of the ketone cyanohydrins and reaction of the resultant 2-hydroxyethylamines with CNBr. The effect of CNS activity was evaluated by the observation of albino Swiss-Webster mice for gross changes in behavior. Harnden et al [55] synthesized another CNS stimulant oxazoline moiety 83.



83

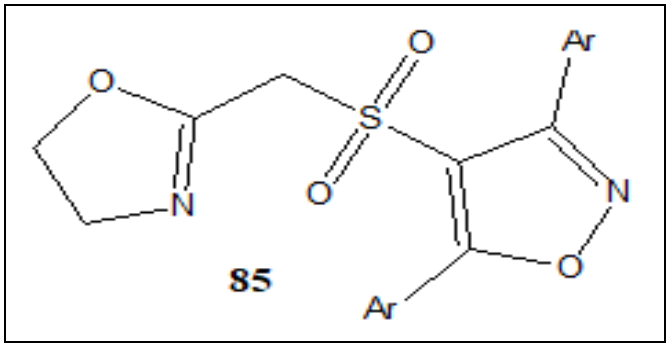
They synthesized a series of 5-spiro-substitued-2-amino-2oxazoline-4-ones and their effects on CNS were screened by the observation of albino Swiss-Webster mice for gross changes in behavior.

Anti-oxidant: A new class of sulfone linked pyrrolyl oxazolines 84 and thiazolines were synthesized from E-arylsulfonylethene-sulfonylacetic acid methyl ester and studied their antimicrobial and antioxidant activities [56]. The compounds were tested their antioxidant activity by nitric oxide, DPPH methods and reducing power method. These compounds exhibited high antioxidant property in all the three methods at 100 µM concentration.



84

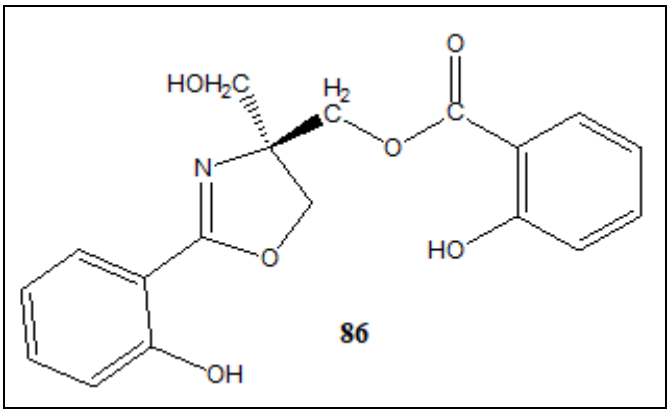
It was observed by Padmaja *et al*., [57] that the compounds having isoxazole in combination with oxazoline 85 exhibited greater antioxidant activity.



85

These compounds were prepared from the synthetically vulnerable intermediate E-styryl sulfonylacetic acid methyl ester and evaluate their antioxidant property by 1, 1-diphenyl-picrylhydrazyl (DPPH), nitric oxide and hydrogen peroxide methods. They showed good radical scavenging activity in all three methods. The presence of electron-donating substituents on the aromatic ring enhances the antioxidant activity of these compounds.

Djurendić *et al*., [58] has been synthesized a series of some new 2-oxazoline derivatives 86 and tested their antioxidant property. These compounds were prepared by methyl salicylate and 2-amino-2-(hydroxymethyl) propane-1, 3-diol. The antioxidant activity of these compounds was screened by DPPH method.



86

CONCLUSION: 2-oxazoline nucleus has formed a large number of potentially biologically active molecules on modifications. The synthesis, structures and biological activities of oxazoline derivatives have long been focused on research interest of organic chemists in the field of medicine, due to the potential biological activities exhibited by them. Looking into the medicinal importance of oxazoline moiety, it will be worthwhile to synthesize certain newer derivatives of oxazolines and evaluate them for their biological activities.

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CONFLICT OF INTEREST: Nil

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