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A Review: Organic Synthesis of Heterocyclic Compounds and Their Pharmaceutical Therapeutic Applications

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Abstract: Nowadays, the organic synthesis of chemical compounds has become one of the most important fields for chemical specialists in order to prepare various compounds and use them in various fields, including medical, industrial, agricultural, pesticides, water treatment, and other various applications. The complete synthesis of compounds requires a deep understanding of both carbon-carbon bonds formation and functional group conversion processes. Functional group modification represents the majority of chemical processes that occur during the synthesis process.

A comprehensive understanding of both carbon–carbon bond formation and functional group conversion processes is essential for the complete organic synthesis of molecules. The majority of chemical processes used in organic synthesis involve modification of functional groups. The most important benefits of organic synthesis are the preparation of heterocyclic organic compounds and their use as medical therapeutic agents for the treatment of various diseases, as well as the possibility of using others as analgesic agents for diseases. According to what was mentioned, this review will review many of the different chemical methods that have been used in organic synthesis to prepare heterocyclic compounds, with a presentation of their medical and pharmaceutical effectiveness against some different diseases.

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I. INTRODUCTION

The field of chemistry that studied carbon compounds with a connection to biological systems was once known as organic chemistry (organic meaning life). In essence, every chemical reaction that occurs in a biological system is an organic reaction. This is due to the fact that all living things include carbon, including proteins, vitamins, lipids, carbohydrates, haemoglobin, chlorophyll, nucleic acids, and so forth.

The truth is that our reliance on natural resources for food, clothing (cotton, wool, and silk), and energy (petroleum and natural gas) is essentially an organic compound dependency [1]. The goal of organic synthesis is to create carbon-carbon bonds by using recognized or imaginable chemical processes. This results in the connection of two molecular or ionic units, or "synthons". Functional group inversions (FGI), which can increase or decrease the oxidation number of carbon atoms (redox), modify heteroatoms (substitution, addition-elimination), or make molecules bigger (condensation), are the processes that accompany synthesis. This is where most of your time will be spent which is standard procedure in a chemical lab. Probably all you have to do is combine them by condensation processes, swap an OH group for an NH_2 group, or introduce isotopes as molecular identifiers. Companies like Aldrich, Sigma, or Merck will supply your primary carbon material [2].

The entire synthesis of intricate compounds necessitates a comprehensive understanding of processes that form carbon-carbon bonds and those that convert one functional group into another. The majority of chemical processes employed in synthesis entail the alteration of functional groups. Effective synthesis of a molecule is rare without a thorough understanding of all aspects of chemical reactivity, functional group interactions, conformations, and stereochemistry [3]. The technique of organic synthesis necessitates comprehension of chirality and molecular stereochemistry, essential for formulating a synthetic strategy and selecting appropriate reactions and reagents for diverse chemical transformations. Understanding the conformational analysis of each molecule, from the starting material to the end result, is essential, as chemical reactivity and stereochemistry are frequently affected by conformation [4].

The field of chemistry known as "organic synthesis," which involves creating organic compounds by a sequence of carefully planned chemical reactions, has advanced for almost 200 years since Friedrich Wohler's unintentional creation of urea [5]. Two of the most well-known instances of unintentional discoveries made using only the knowledge of elemental compositions—without even the most basic structure and bonding theories—were Wohler's synthesis of urea [6] and Perkin's synthesis of mauveine [7]. Prior to Wohler's accidental synthesis of urea from inorganic materials, chemists thought that organic molecules could only be produced in nature with the vital force of plants and animals, and that they could not be made in a laboratory [8]. After that, chemists began working on synthesizing organic compounds in the laboratory, especially heterocyclic compounds, and introducing them into various industrial, medical, agricultural, and other applications.

Heterocyclic compounds are organic compounds that are cyclical with at least regarded as one heteroatom present. In addition to heterocyclic rings containing other heteroatoms, the most common heteroatoms are nitrogen, oxygen, and sulfur [9]. The word hetero denotes the non-carbon atoms, or heteroatoms, in the ring, while the cyclic portion of heterocyclic means that the chemical has at least one ring structure. Although the general structure of heterocyclic compounds is similar to that of cyclic organic compounds with only carbon atoms in the rings, the physical and chemical characteristics of heterocyclic compounds are frequently very different from those of their all-carbon-ring counterparts [10]. Heterocycles with rings with five or six members and heteroatoms of nitrogen (N), oxygen (O), or sulfur (S) are the most prevalent. Of the simple heterocyclic compounds, pyridine, pyrrole, furan, and thiophene are the most well-known [11].

Heterocyclic compounds are primarily significant in medical chemistry. The most intricate domains in chemistry are often heterocyclic chemistry. It is equally significant for its industrial and physiological importance, its diverse synthetic procedures, and its theoretical implications [12]. Synthetic heterocyclic chemistry has significantly influenced different aspects of human existence and has applications in varied fields such as agriculture, medicine, polymers, and several industries. The majority of synthetic heterocyclic compounds function as pharmaceuticals, serving roles as anticonvulsants, hypnotics, antineoplastics, antiseptics, antihistamines, antivirals, and anti-tumor agents. Each year, a substantial number of heterocyclic medicines is added into pharmacopeias [13,14].

In alignment with the aforementioned points and recognizing the significant relevance of these compounds across diverse domains, a review of the synthetic methodologies employed to produce these compounds will be conducted, alongside an examination of their principal applications in the medical and pharmaceutical sectors, as well as their efficacy as therapeutic agents for various ailments.

II. SYNTHESIS OF SEVEN-MEMBERED HETEROCYCLIC

An intriguing class of organic molecules known as seven-membered heterocyclic compounds has recently attracted attention in the fields of medical chemistry, materials science, and catalysis, among others [15]. Heteroatoms, or atoms other than carbon, added to a seven-membered ring structure, such sulfur, nitrogen, and oxygen, provide compounds new chemical properties compared to compounds with only carbon. Essential building blocks in drug discovery and chemical production, these heterocycles exhibit a wide spectrum of biological activities [16]. This category encompasses several heterocyclic rings having atoms other than carbon (N,O and S), including azepine, thiapine, oxepines, and oxazepine, which will be reviewed in terms of their methods of synthesis and distinct medicinal and biological properties.

➢ *Synthesis of Azepine Derivatives.*

Azepines have important roles in organic chemistry and medicine as seven-membered heterocyclic molecules containing nitrogen. Anticonvulsant, antifungal, antibacterial, anticancer, and anti-inflammatory are only a few of the many biological effects displayed by azepine derivatives [17].

In 2015, M. Yoshimatsu and coworkers reported the synthesis of different substituted azepines (2) by [6+1] cycloaddition reaction of ynenitriles (*N*-Cyanomethyl-*N*-[3-phenyl-2-propyn-1-yl]-*p*-toluenesulfonamide (1)), catalyzed by hafnium triflate, using a Reformatsky reagents (β-hydroxyester Zn/Br $CH_2CO_2R_2$) and using different solvents (dioxane and THF), (equation 1)[18]. The MTT method was used to evaluate the therapeutic effect of several derivatives against HCT-116 human colon tumor cells, revealing significant inhibitory activity on these cells.

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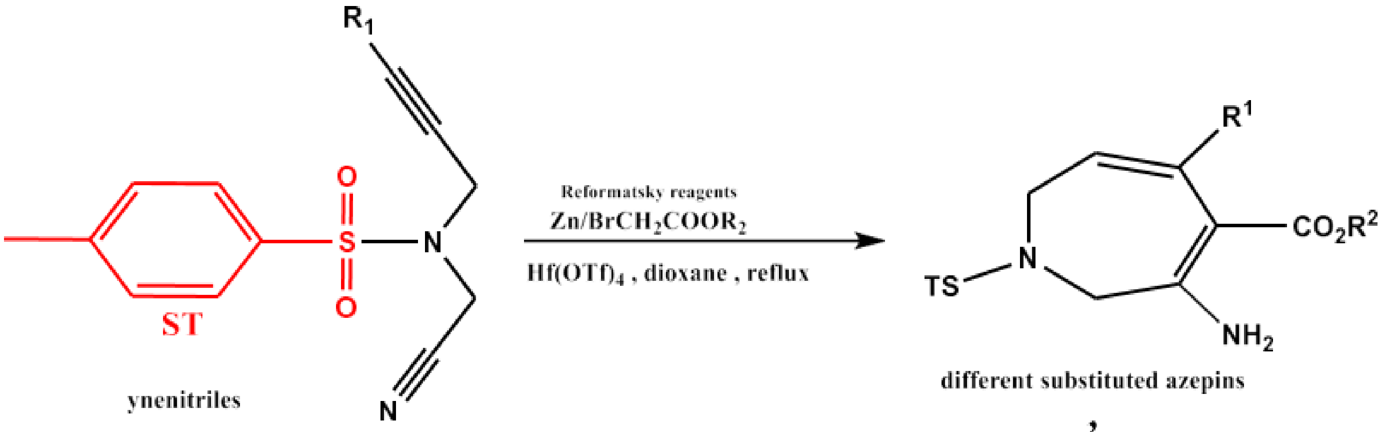


ynenitriles

1

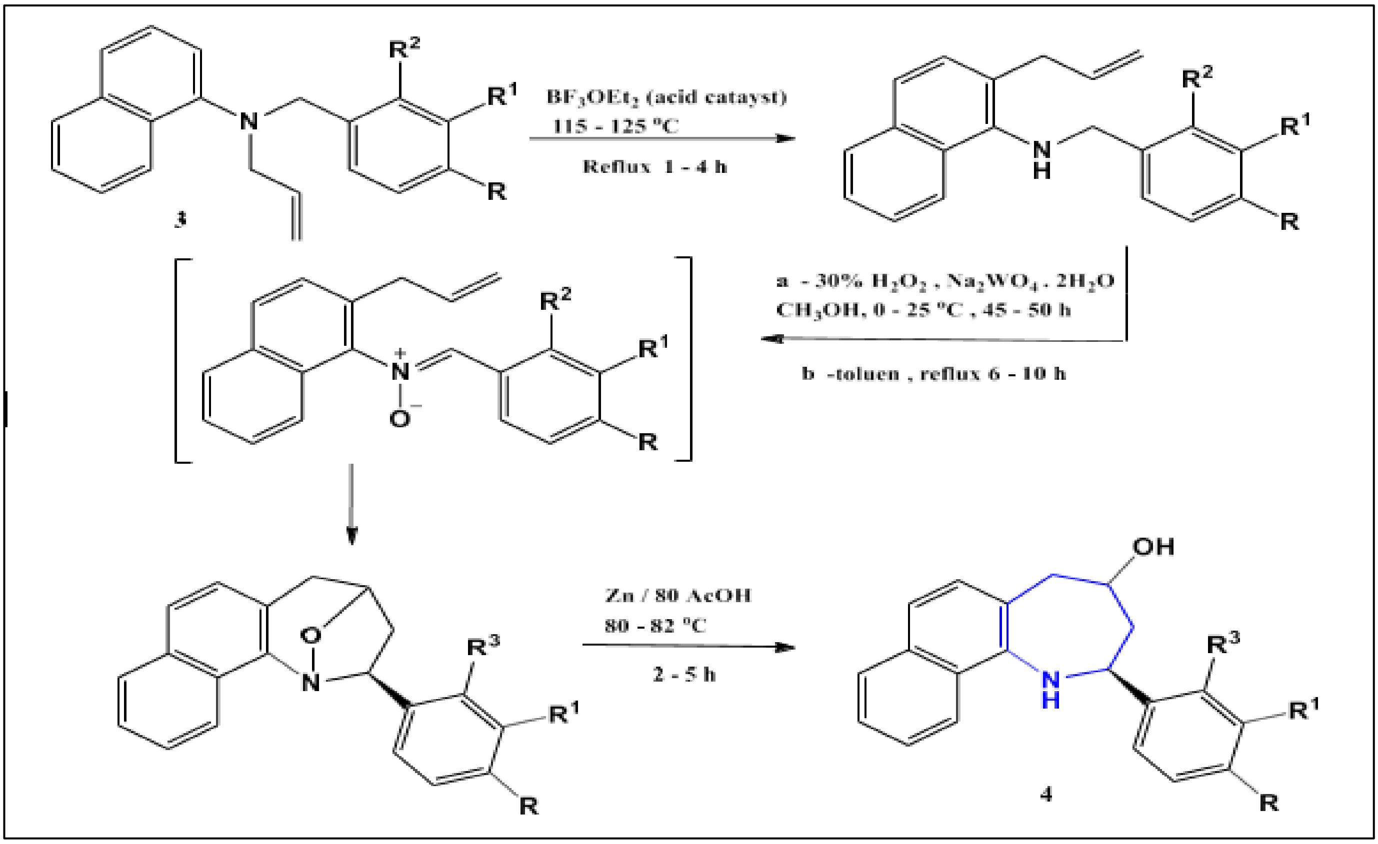
different substituted azepins

2

	R^1	R^2	solvenh	% yield
2a =	Ph ,	Me ,	dioxane, 1h	80
2b =	Ph ,	t.Bu ,	THF , 20 min.	50
2c =	MeC$_6$H$_4$,	Et ,	THF , 33h	78
2d =	MeC$_6$H$_4$,	t.Bu ,	dioxane , 12h	68

Fig 1 Synthesis of Azepine Derivatives.

A distinct strategy [19] for synthesizing the azpine ring was employed, commencing with the reaction of *N*-substituted benzyl-a-naphthylamines with a sufficient amount of allyl bromide in the presence of potassium carbonate and dry acetone to yield *N*-allyl-*N*-benzyl-substituted-α-naphthylamines (3), which subsequently were subjected to a series of reactions under varying conditions to form azpine derivatives (4), as shown in (scheme 1) below.



Scheme 1 Different Reagents and Conditions for The Series of Reactions to Synthesize Azpine Derivatives.

Furthermore, from methylene bis chalcones (5), Rajanarendar E. *et al*, [20] were designed azpine derivatives. Methylene bis chalcones (5) was synthesized using the methodology employed [21,22] in the condensation reaction of 5,5'-methylene bis- salicylaldehyde with substituted acetophenones. The reaction of compounds (5) with dimethyl-4-nitroisoxazole (6) was performed in the presence of piperidine in ethanol by condensation by means of Michael addition to yield benzo-triazole (7), that subjected to cyclization reaction with $SnCl_2$- MeOH to form azpine derivatives (8), as shown in scheme (2). Two ER-positive breast cancer cell lines, MCF-7 and MDA-MB-231, were subjected to inhibitory activity tests including these compounds. The chemical structure of these compounds contains substituted benzene rings, which are responsible for the substantial activity that some of these derivatives showed against these cancer cells

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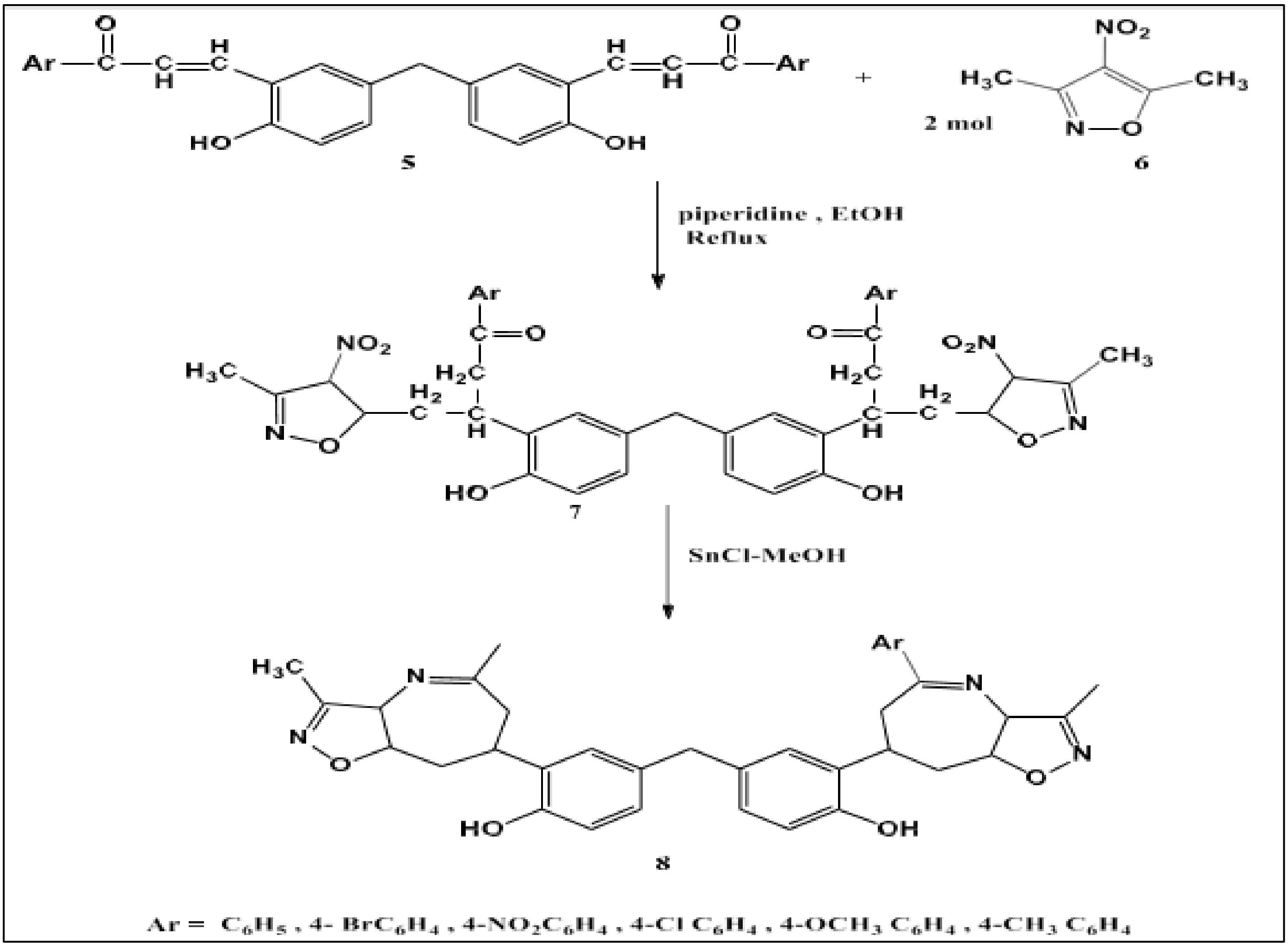


Scheme 2 Synthesis of Alpine Derivatives as Anti-Breast Cancer Agents

➢ *Synthesis of oxazepine derivatives.*

The oxazepine ring is classified as a heterocyclic complex with seven members. This structure contains nitrogen and oxygen atoms, which are not aromatic compounds [23]. The oxazepine structure has an oxygen atom at position (1) and a nitrogen atom at places (2, 3 or 4), (figure 3) [24].

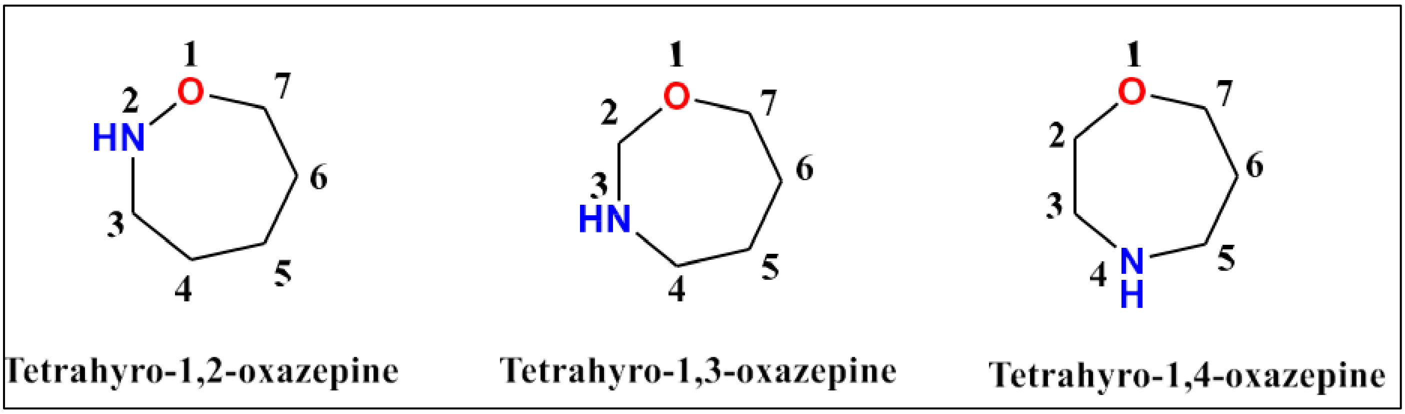
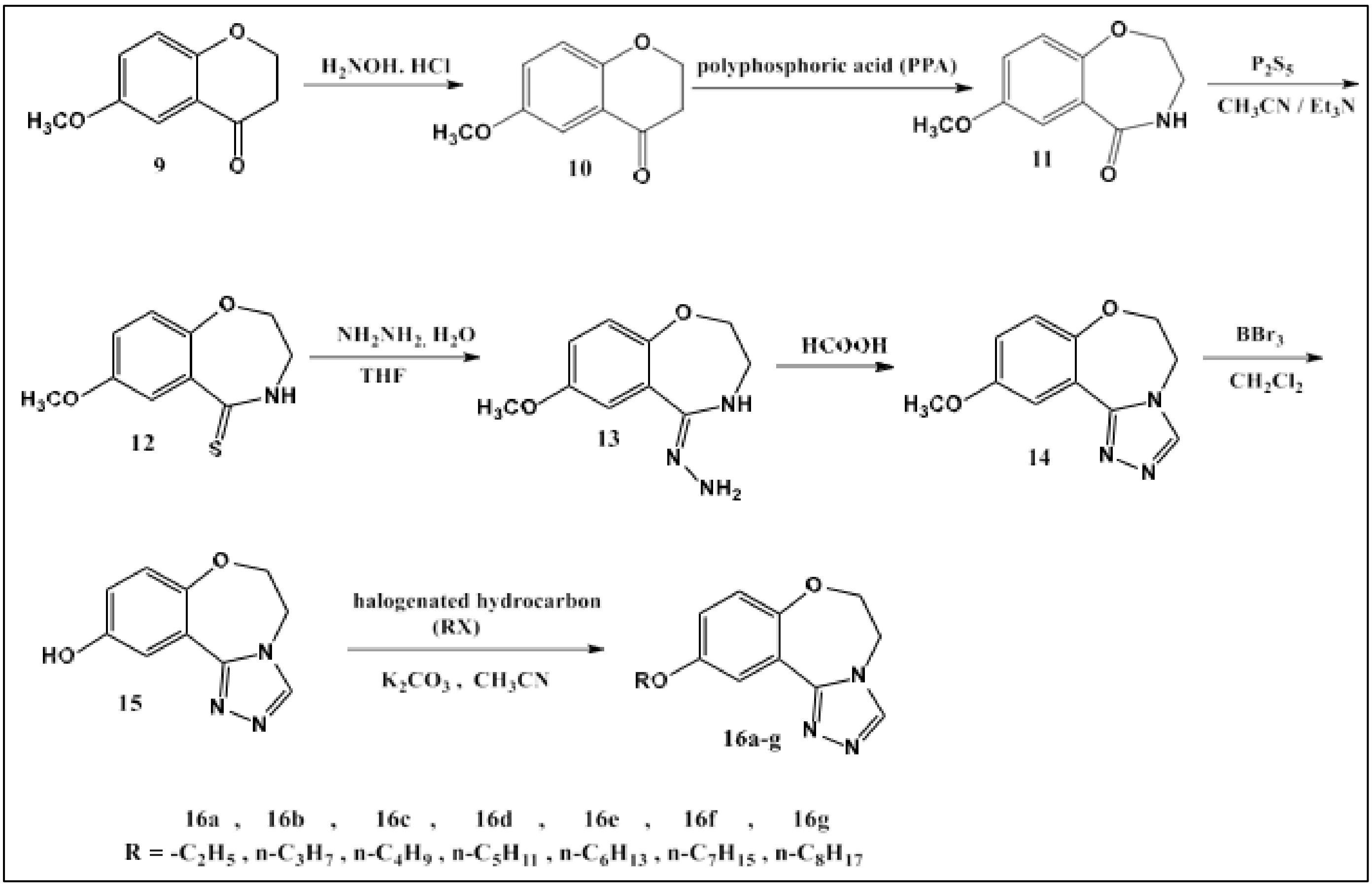


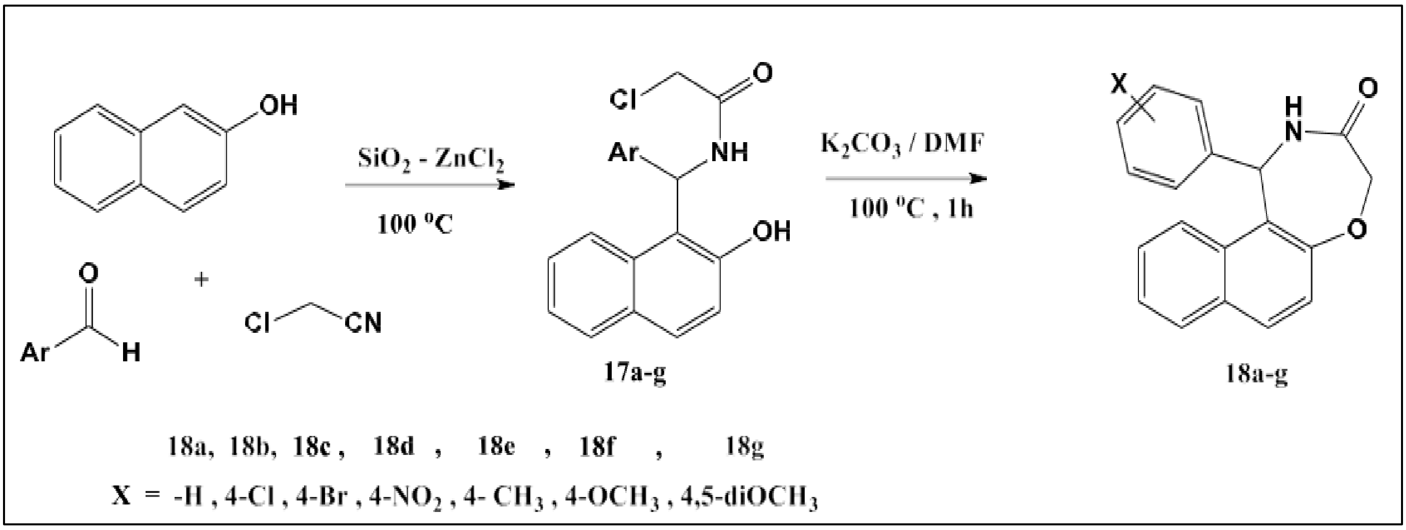
Fig 2 Isomers of Oxazepine (1 . 2 , 1.3, And 1.4-Oxazepine)

As demonstrated in (Scheme 3), Xian-Qing Deng and coworkers have synthesized 10-alkoxy-5,6-dihydro-triazolo[4,3-d] benzo[f] [1,4] oxazepine derivatives (16a-g) starting from 6-methoxy-2,3-dihydrochromen-4-one compound (9) [25]. The maximum electroshock (MES) test was used to screen for anticonvulsant activity in these derivatives, and the rotarod neurotoxicity test (Tox) was used to evaluate their neurotoxicity. Compound10-Heptyloxy-5,6-dihydrotriazolo[4,3d] benzo[f] [1,4]oxazepine (16g) outperformed the commercially available meds carbamazepineand phenytoin in the MES test, with an ED_{50} value of 6.9 mg/kg and a PI value of 9.5, indicating superior anticonvulsant action and increased safety.



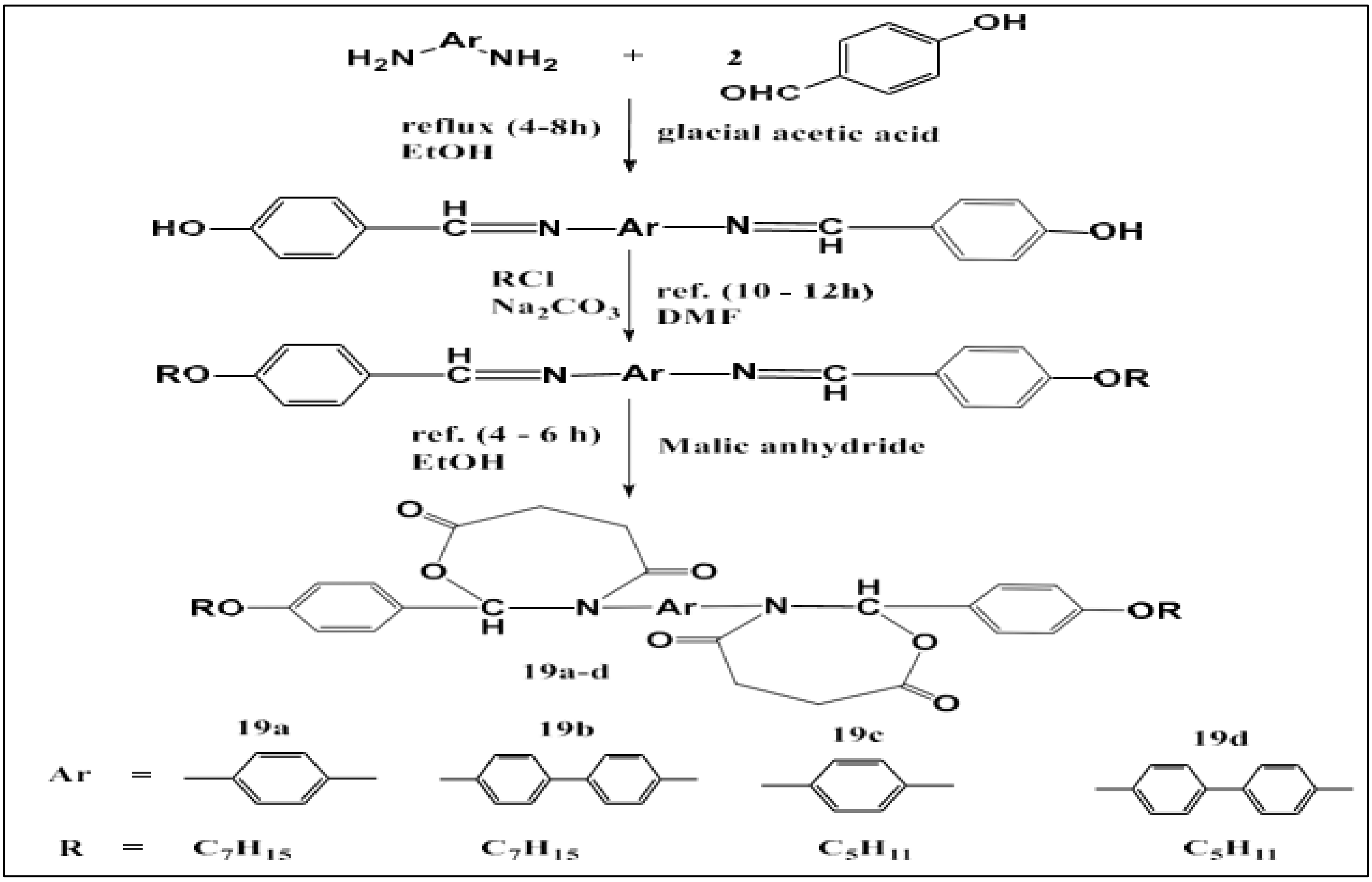
Scheme 3 Some Synthetic 1,4-Oxazepine Derivatives with Anticonvulsant Activity.

On the other hand, a simple and effective method for creating of amidochloroalkylnaphthol derivatives (17a-g) (scheme 4) were developed. It involved a one-pot, three-component condensation of different aldehydes, chloroacetonitrile, and b-naphthol, and it did not involve solvents. The catalyst used was SiO_2-$ZnCl_2$ (silzic), a reusable heterogeneous catalyst. These derivatives after that were refluxed in 5 ml of DMF with stirring at 100°C in the presence of potassium carbonate to obtain 1,2-dihydronaphtho[1,2-f][1,4]oxazepin- 3(4H)-one derivatives (18a-g). Researchers looked at the antioxidant and anticancer effects of oxazepinones formed by cyclizing amidochloroalkylnaphthols [26].



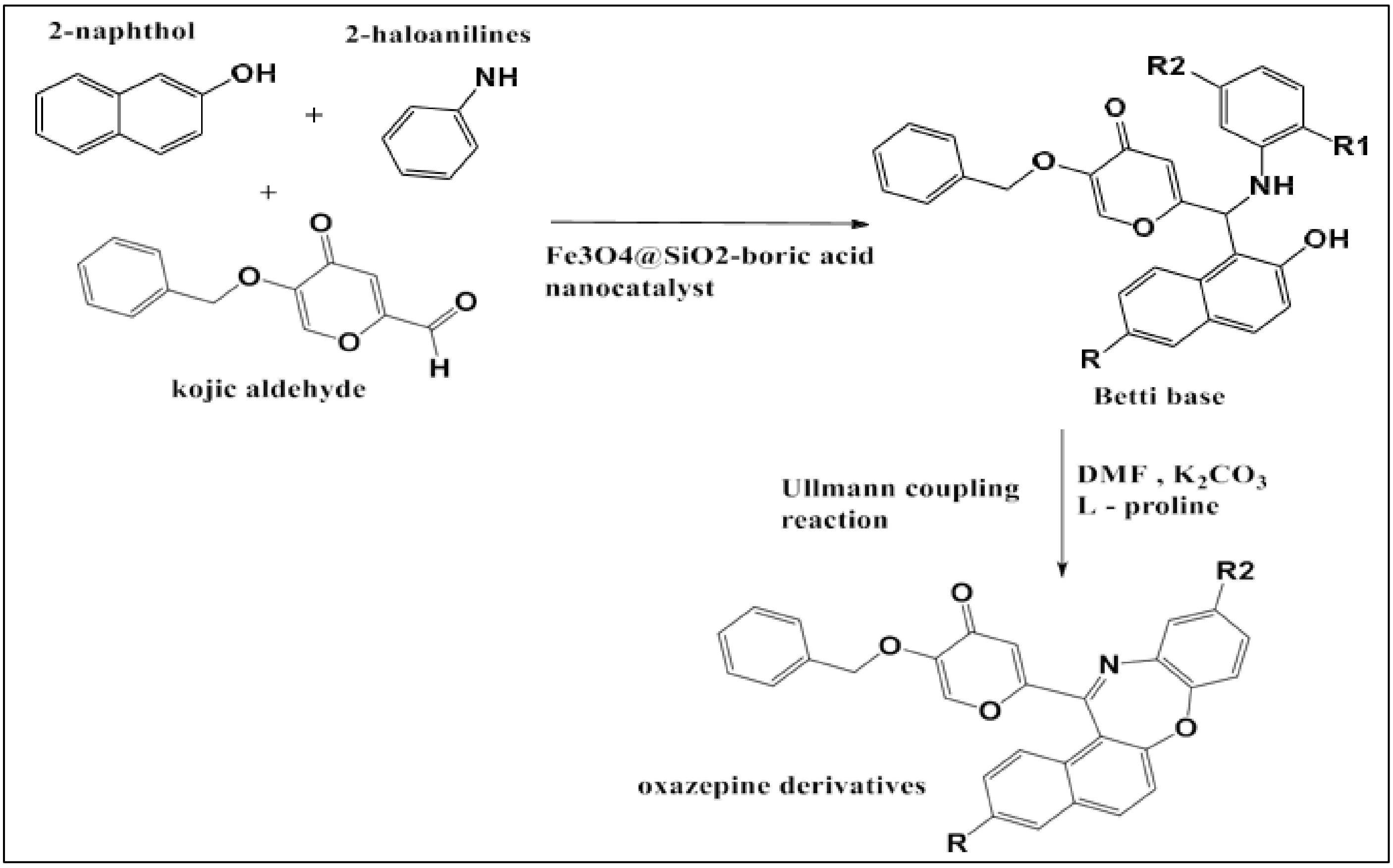
Scheme 4 Synthesis of 1,4-Oxazepine-3-One Derivatives

In another way, through the ring-closer reaction of synthetic Schiff bases, oxazepine derivatives were prepared (scheme 5) by Mohammed Mezher Aftan and coworkers [27]. These derivatives were tested for their biological activity against two bacteria (*E*scherichia coli and *S*taphylococcus), and some of them showed good activity in inhibiting bacterial growth.



Scheme 5 Cyclization Reaction of Schiff Bases to Form 1,3-Oxazepine Derivatives.

New oxazepine derivatives containing kojic acid were synthesised using an innovative tandem Betti/Ullmann/oxidation process [27]. Following a copper-mediated intramolecular Ullmann C-O coupling reaction and aerobic oxidation, this approach incorporates a three-component Betti reaction of 2-naphthol, 2-haloanilines, and kojic aldehyde in the presence of nano Fe_3O_4-SiO_2-boric acid as catalyst. Without using any solvent, the mixture was stirred at 40°C. TLC was used to monitor the reaction. This reaction was cooled after completion nd then ethanol was added to recover the catalyst. Betti base was obtaned from the solid by-product by filtering it. After that, the oxazepine derivative was produced by subjecting the Betti base to a Ullmann reaction using potassium carbonate, L-proline, and DMF as solvents, (scheme 6).



Scheme 6 Synthesis of Oxazepine Derivative from Betti Base.

The expanding family of natural products containing oxepine is capturing more and more interest, especially with regard to the structural determination, biological activity, and biogenesis of these compounds. Recently, we announced the first complete synthesis of janoxepin, a natural substance comprising oxepine and pyrimidinone that has anti-plasmodial properties (figure 2). This piqued our interest in the field from a synthetic perspective [28].

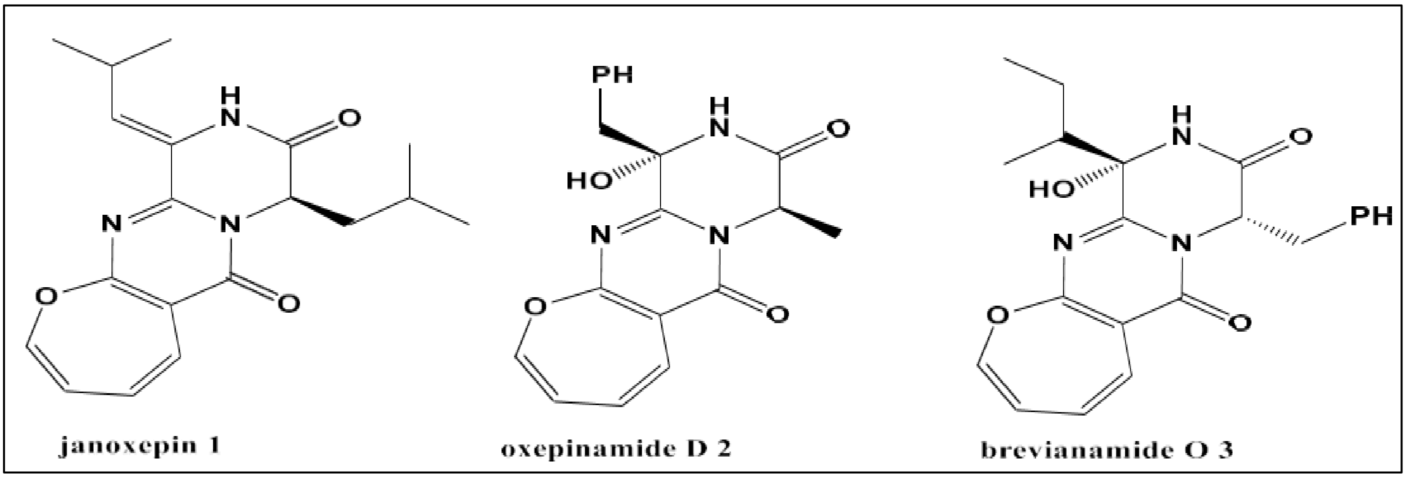
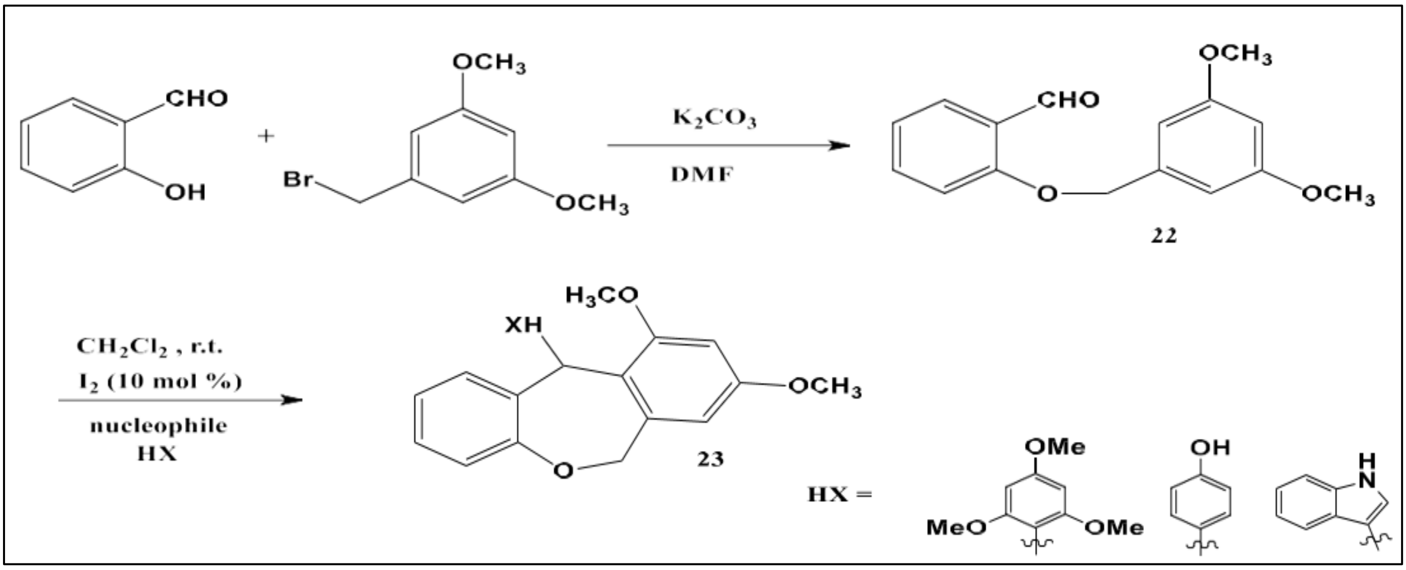


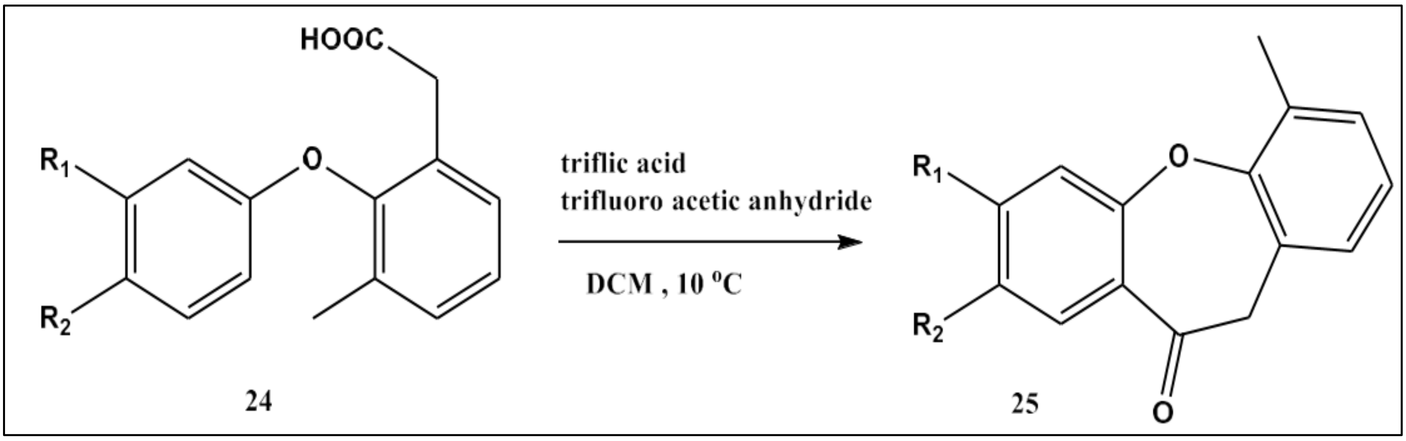
Fig 3 Natural Therapeutic Products Containing the Oxepine Core

O-benzylation of salicylaldehyde using benzyl bromide/K_2CO_3 in DMF readily yielded 2-(benzyloxy)benzaldehyde (22), which undergo a one-pot tandem nucleophilic addition/Friedel-Crafts cyclisation (scheme 7) [29]. In the presence of I_2 (10 mol-%) in dichloromethane at room temperature, the reaction of (22) was performed with different substituted nucleophile (HX) to produce ibenzo[*b*,*e*]oxepines (23).



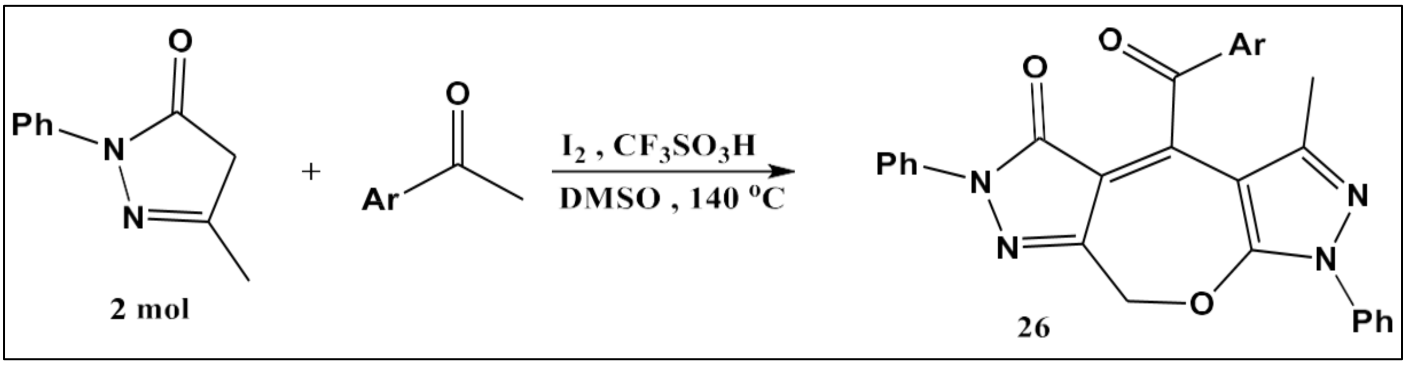
Scheme 7 Friedel Crafts Reaction for Synthesis of Oxepine Ring.

The Friedel Crafts reaction [30] was used on compound (24), which had been synthesised by a series of reactions, to produce dibenzo[b,f]oxepine (25) in the presence of DCM, triflic acid, trifluoro acetic anhydride (scheme 8).



Scheme 8: Friedel Crafts Reaction for Synthesis of Oxepine Ring

The 2,3-Dihydrooxepines (26) were prepared by use of an iodine-catalyzed catalytic formal [3 + 3 + 1] cycloaddition [31]. This method successfully constructed the C_{sp3}–O link by using the reactivity of the methyl and carbonyl groups of 3-methyl-5- pyrazolones (scheme 9). This approach lays forth a simple and effective way to get fused O-heterocycles with different structures by using an iodine-catalyzed cascade reaction that involves iodination, Kernblum oxidation, oxidative coupling, and C−O bond synthesis. This method for building 2,3-dihydrooxepine rings from 3-methyl-5 pyrazolones shows the first simultaneous realisation of the unique reactivity among the methyl, methylene, and carbonyl groups. A large substrate scope also shows a refined synthetic strategy that is diversity-oriented.



Scheme 9 Iodine-Catalyzed Catalytic for Synthesis of 2,3-Dihydrooxepines.

- *Synthesis of six- membered heterocyclic.*

There are several important heterocyclic compounds, but six-membered heterocycles stand out. Pyridines, morpholines, thiazines, dioxanes, isoquinolines, coumarins, quinazolines, chromenes, and many other types of six-membered heterocyclics are available [32]. The nucleotide bases of DNA and RNA, pyrimidines and purines, are symmetrical rings with six members. Additionally, the structures of vitamins B and E also include six-membered heterocycles. Pyridinium, a six-membered heterocycle, is present in the NADP/NADPH redox system and several alkaloids, including nicotine [33]. Quinazolines [34] and isocoumarins [35] have a stellar reputation for their beneficial effects on living things. Displayed here are a few of the most notable six- membered heterocyclic compounds with medicinal potential (figure 3).

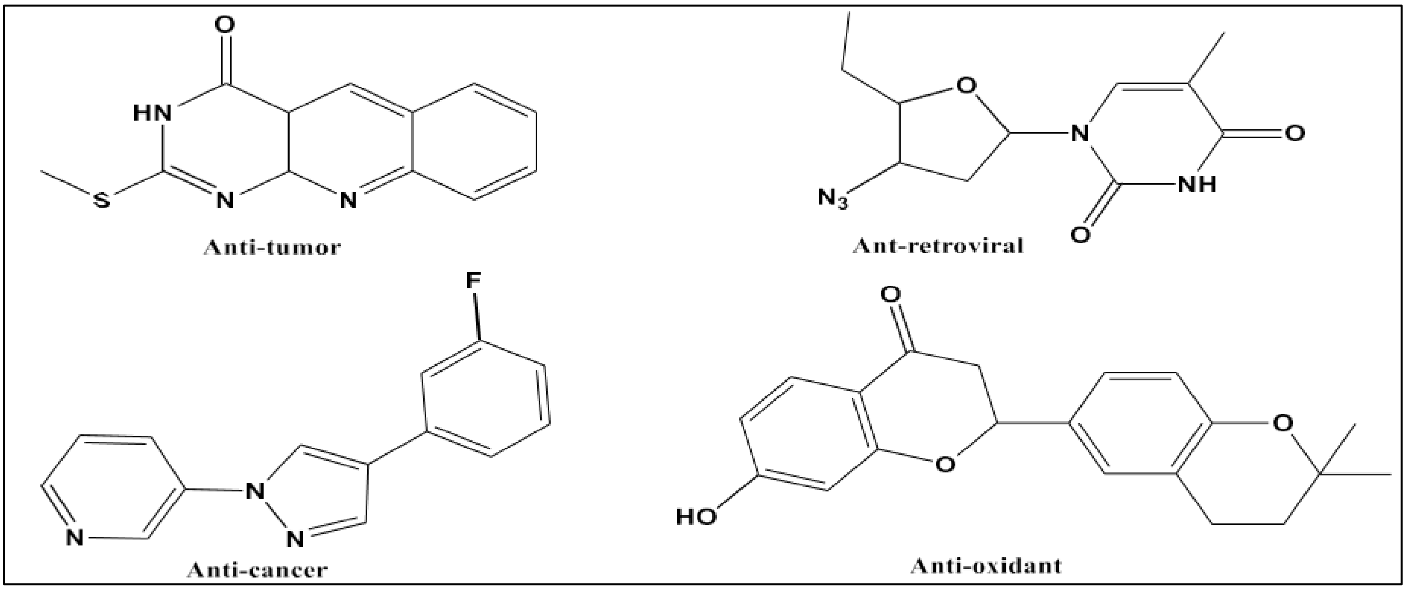
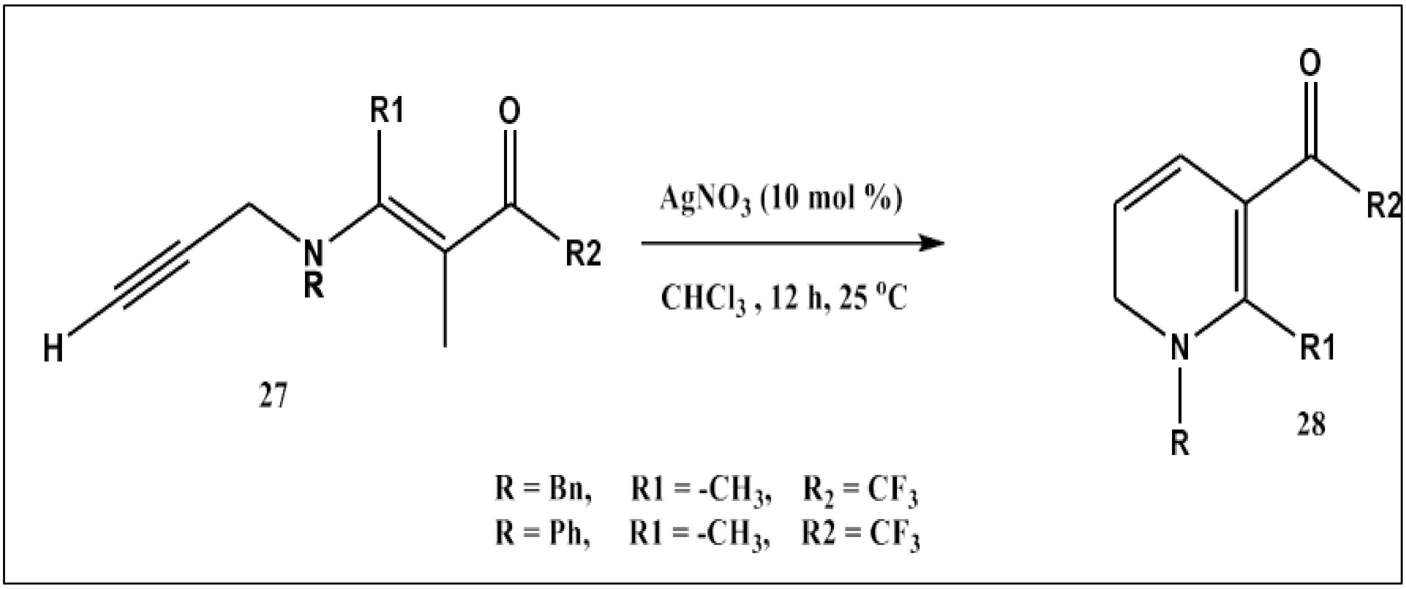


Fig 4 Some Compounds Have a Six-Membered Heterocyclic Ring Structure That Have Medicinal Significance.

- *Synthesis of pyridines.*

A new approach to the 1,2-dihydropyridine synthesis (28) using silver nitrate as a catalyst has been proposed by Martins *et al* [36]. The results of the intramolecular cyclization of several N-propargylic β-enaminones (27) were obtained in satisfactory to excellent yields in a chloroform solvent (scheme 10).



Scheme 10 Various Enaminones Undergo Intramolecular Cyclization to Produce 1,2-Dihydropyridines

Vasam et al.[37] developed a procedure for the synthesis of various fused pyridines (33) using a multi-component silver-catalyzed system. In a one-pot reaction conducted at room temperature for 10 minutes, a mixture of aldehydes (29), ketone (30), ammonium acetate (31), and dicyanomethane (32) were subjected to a 2-mol% Ag(I)- N-heterocyclic carbene in ethanol medium. The result was pyridines with good to outstanding yields (scheme 11).

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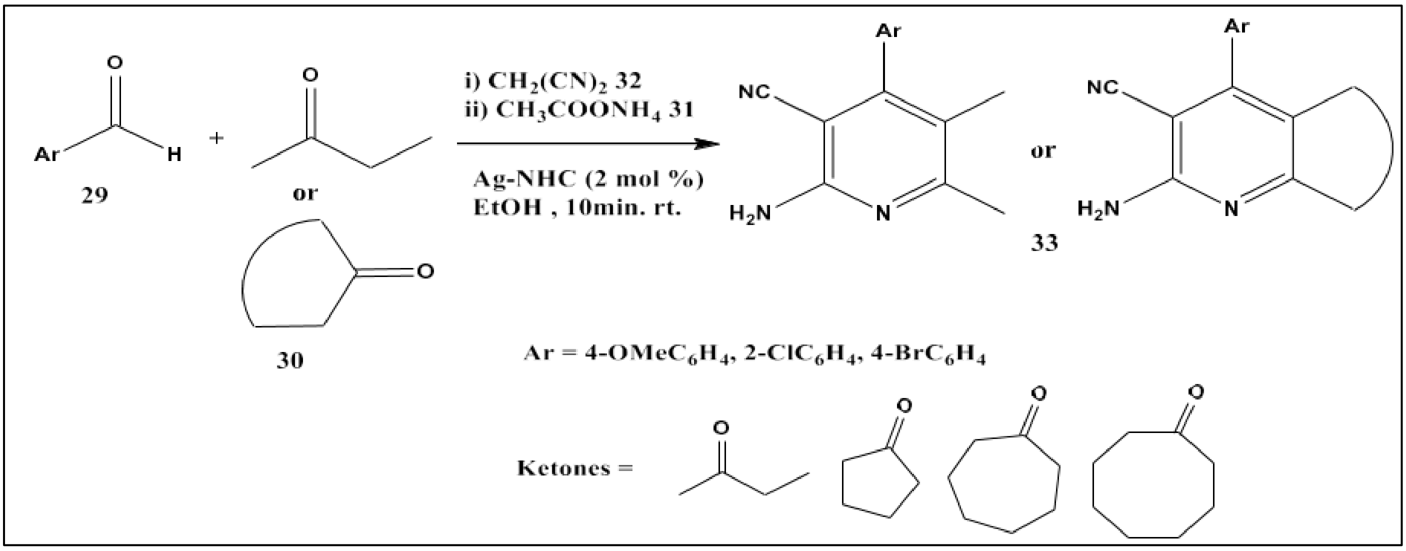
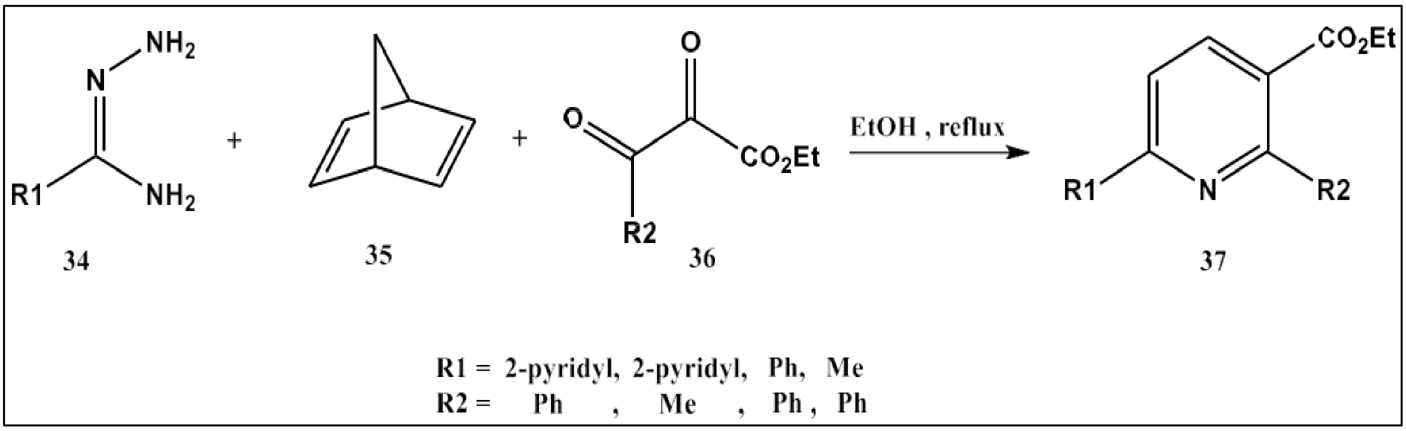


Scheme 11 Fused Pyridines Synthesized by Multi-Component Silver-Catalyzed System.

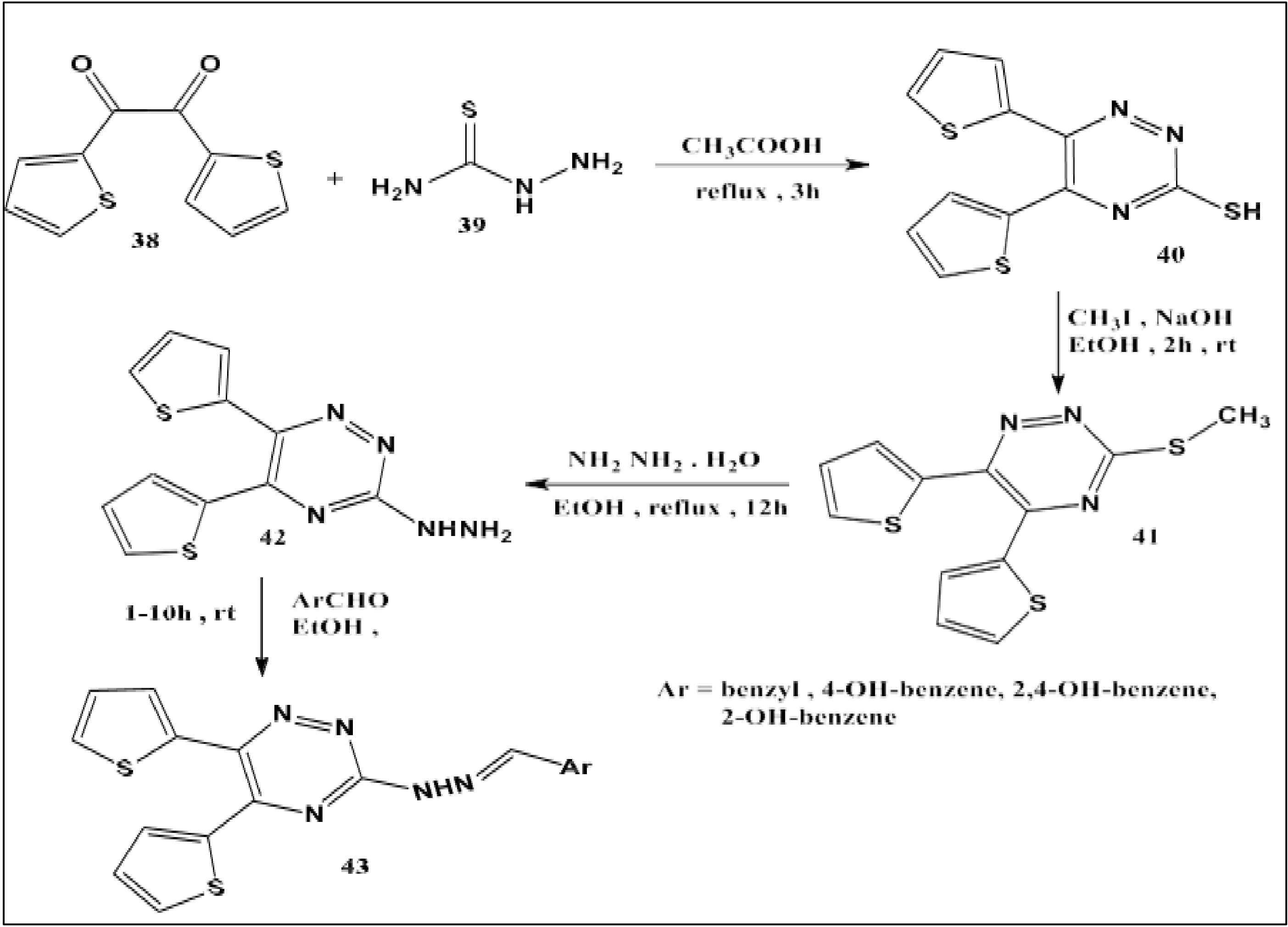
In the presence of an electron-deficient group R1 (2-pyridyl), the inverse electron- demand aza Diels-Alder reaction between amidrazones (34), 2,5 norbornadiene (35) and hydrated α,β-diketo-esters (36) in refluxing ethanol yielded pyridines (37). Therefore, amidrazones (2-pyridyl) may be easily converted into pyridines in a "one-pot" synthesis (scheme 12). This method for pyridine synthesis was put into action by Marta Altuna-Urquijo and co-workers [38].



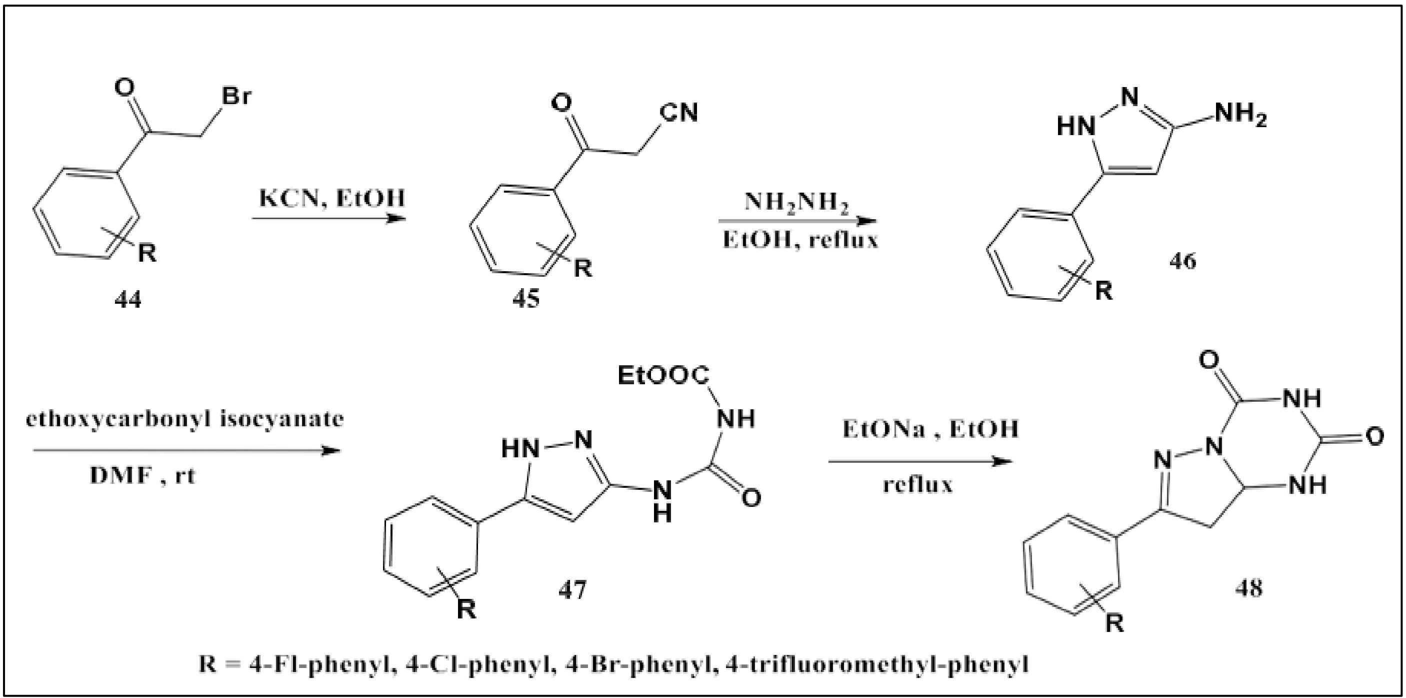
Scheme 12 Synthesis of Pyridines Ring by Inverse Electron-Demand Aza Diels- Alder Reaction.

- *Synthesis of triazine derivatives.*

A reaction using thenil (38) and thiosemicarbazide (39) in refluxing ethanol has been developed for synthesis of 1,2,4-triazine derivatives (40) (scheme 13) [39]. The following steps involve the reaction of these derivatives with methyl iodide to yield compound (41), which in turn reacts with hydrazin hydrate to produce compound (42), and finally with a number of aromatic aldehydes that have different substituents to form compound (43). Some of these 1,2,4-triazine derivatives with various aryl hydrazone moieties showed potential as antioxidants without causing major harm to brain cells, and they inhibit the BACE1 enzyme and interfere with Aβ aggregation through metal chelatory action. To the contrary, a number of triazole derivatives (scheme 14) were produced by a sequence of reactions that began with the conversion of 2-bromo-1-phenyl-ethanone (44) to 3-Oxo-3-phenylpropionitrile (45) by treating it with potassium cyanide. After reacting with hydrazine, this chemical forms 5-Phenyl-1H-pyrazol-3-ylamine (46). Then, it is treated with ethoxycarbonyl isocyanate to create N-ethoxycarbonyl-N'-(pyrazol-3-yl) ureas (47). The synthesis of 1,3-dihydropyrazolo[1,5-a][1,3,5]triazin- 2,4-diones (48) occurs when these ureas go through an intramolecular ring annulation reactionthat is catalyzed by sodium ethoxide [40].

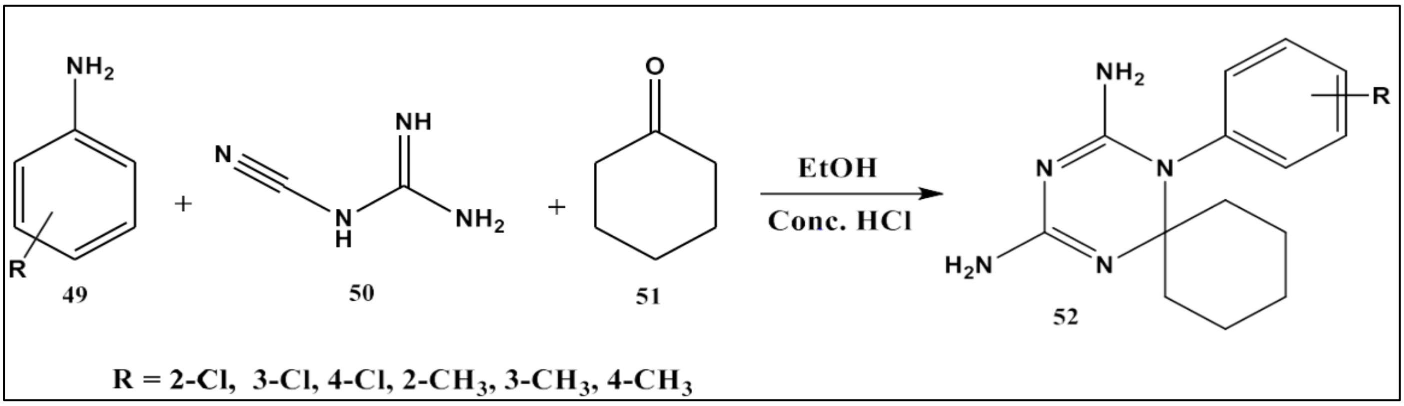


Scheme 13 Synthesis of 1,2,4-Triazine Derivatives



Scheme 14: Synthesis of 1,3,5-Triazine Derivatives.

(Scheme 15) describes the well-known '3-component' approach [41] that was used to synthesize 5-aryl-1,3,5-triazaspiro [5.5] undeca-1,3-diene-2,4-diamine(52). These compounds were obtained by refluxing three components aniline (49), cyanoguanidine (50), and cyclohexanone (51) in the presence of a catalytic quantity of strong hydrochloric acid in alcohol.



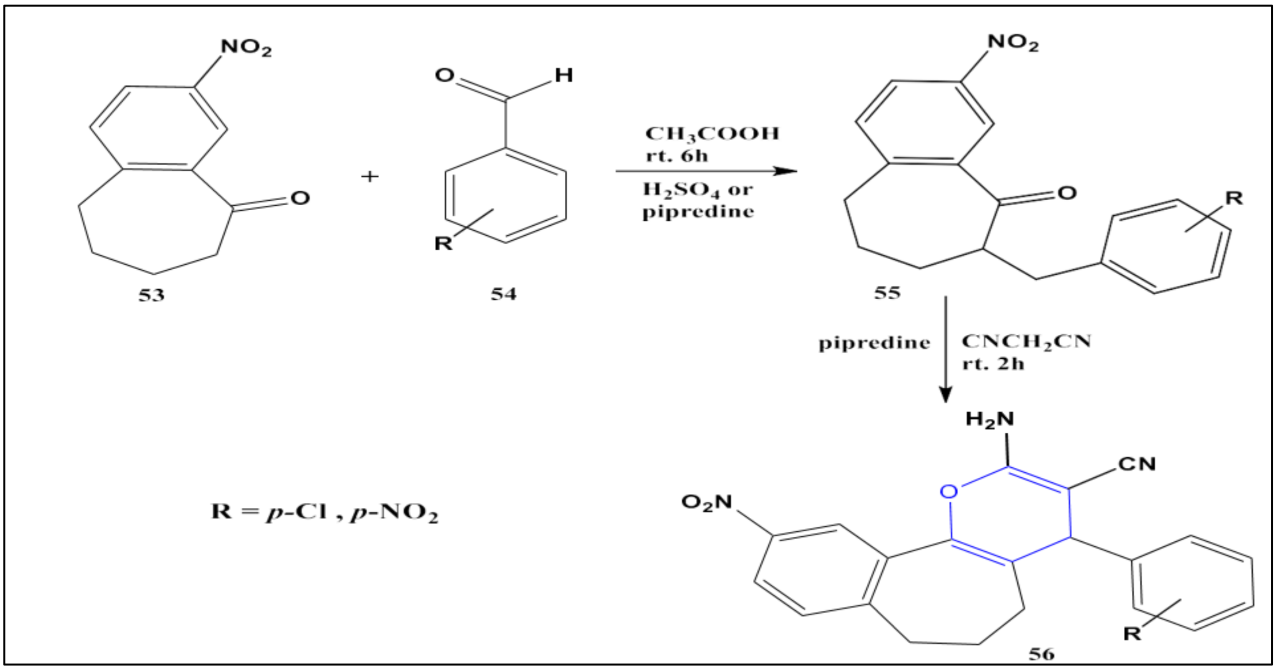
Scheme 15 Synthesis of 1,3,5-Triazine Derivatives by Three Component' Approach

- *Synthesis of pyran derivatives.*

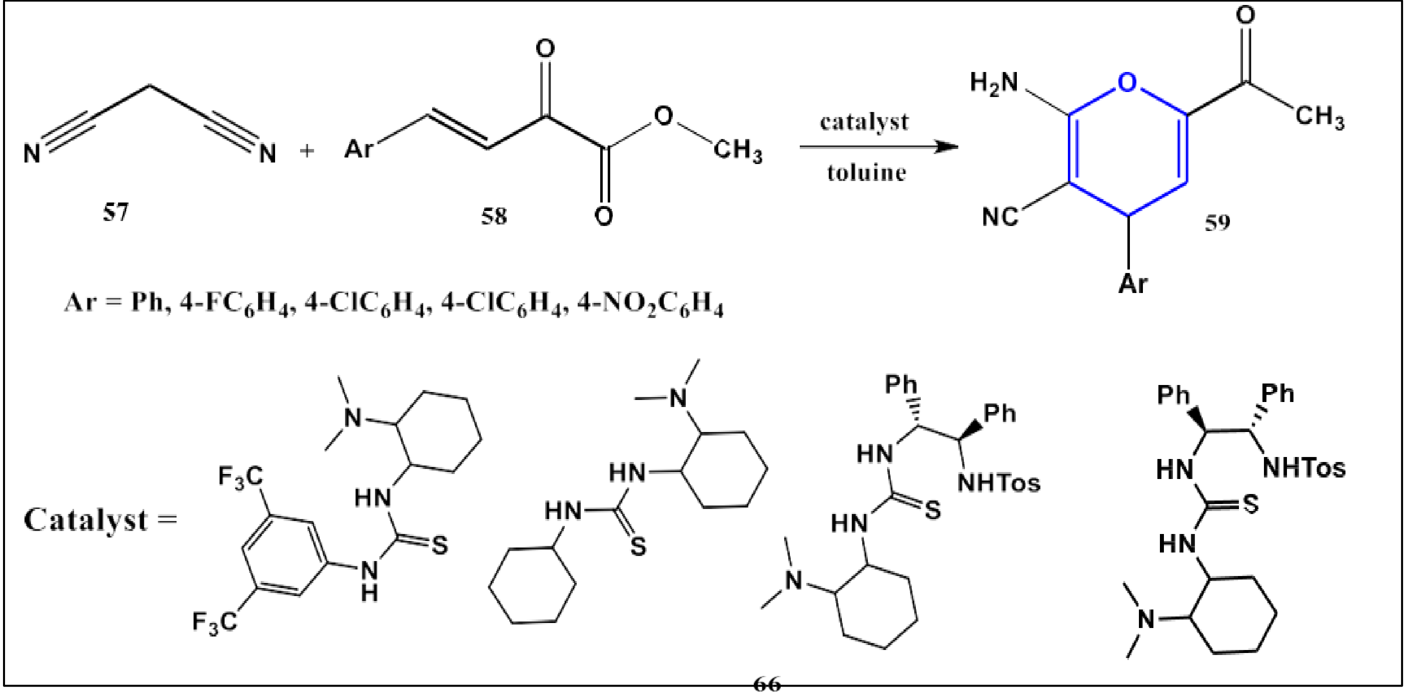
There is a key function for six-membered heterocyclic compounds containing oxygen, such as 4H-pyrans, in bioorganic chemistry and they remain an intriguing class of naturally occurring and synthetically produced physiologically active substances [42]. Indeed, pyrans and fused pyrans are intriguing chemicals in the biological realm due to their antibacterial [43], antifungal [44], anticancer [45], anticoagulant, diuretic, spasmolitic, and antianaphylactic properties [46,47].

Abdel-Galil E. Amr and coworkers [48] have developed an approach for producing pyran derivatives by reaction of 3-Nitro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5- one (53) with substituted aromatic aldehydes (54) in the presence of sulfuric acid or piperidine as a catalyst . This gave rise the formation of arylmethylene derivatives (55), which was further converted to pyran derivatives (56) by condensation with malononitrile in the same catalyst solution (scheme 16). To find those with potential anticancer effects, researchers tested a number of the synthetic derivatives. Leukemia, lung, colon, central nervous system, melanoma, ovarian, renal, prostate, and breast cancer cell lines were utilized to examine each chemical at five distinct doses.

Alternatively, a variety of novel chiral multifunctionalized 4H-pyran derivatives (59 were easily obtainable by employing chiral bifunctional thiourea-tertiary amine catalysts in a one-pot asymmetric Michael addition-cyclization synthesis including malononitrile (57) and β,γ-unsaturated α-keto esters (58). The enhanced reaction conditions allowed for the production of the target products with yields ranging from 50 to 68% and efficiencies ranging from 72 to 88% (scheme 17) [49].

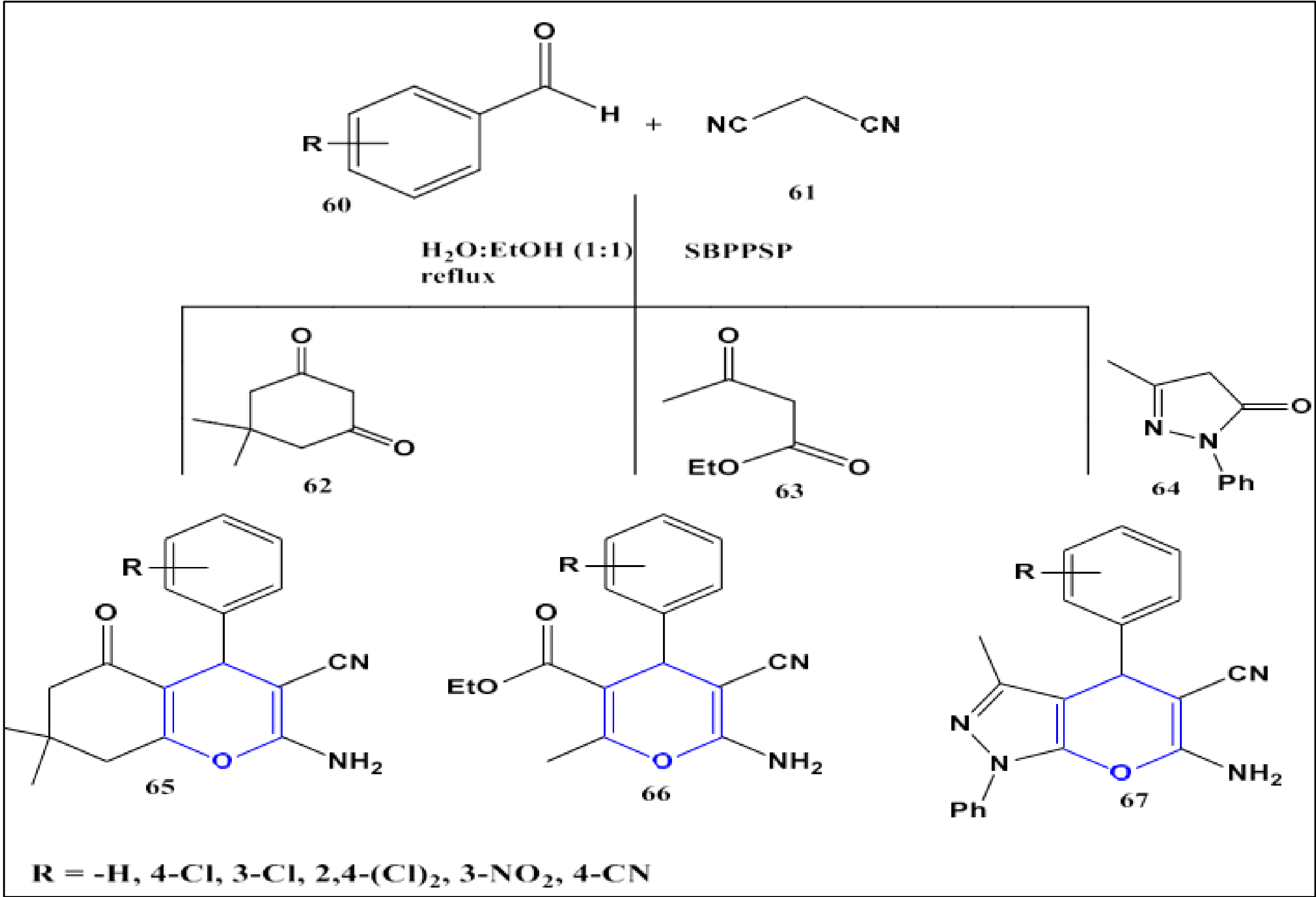


Scheme 16 Synthesis of Pyran Derivatives.



Scheme 17 One-Pot Asymmetric Michael Addition-Cyclization for Synthesis of Pyrane Derivatives.

Different substituents aromatic aldehydes (60) were reacted with malononitriles (61) and different carbonyl compounds (62-64) in aqueous ethanol in the presence of silica- Bonded-*N*-propylpiperazine sodium-*n*- propionate (SBPPSP) as a solid-phase catalyst to prepare 4*H*- benzo[b]pyran derivatives (65-67) (scheme 18). This strategy was implemented by Niknam K. and coworkers [50].



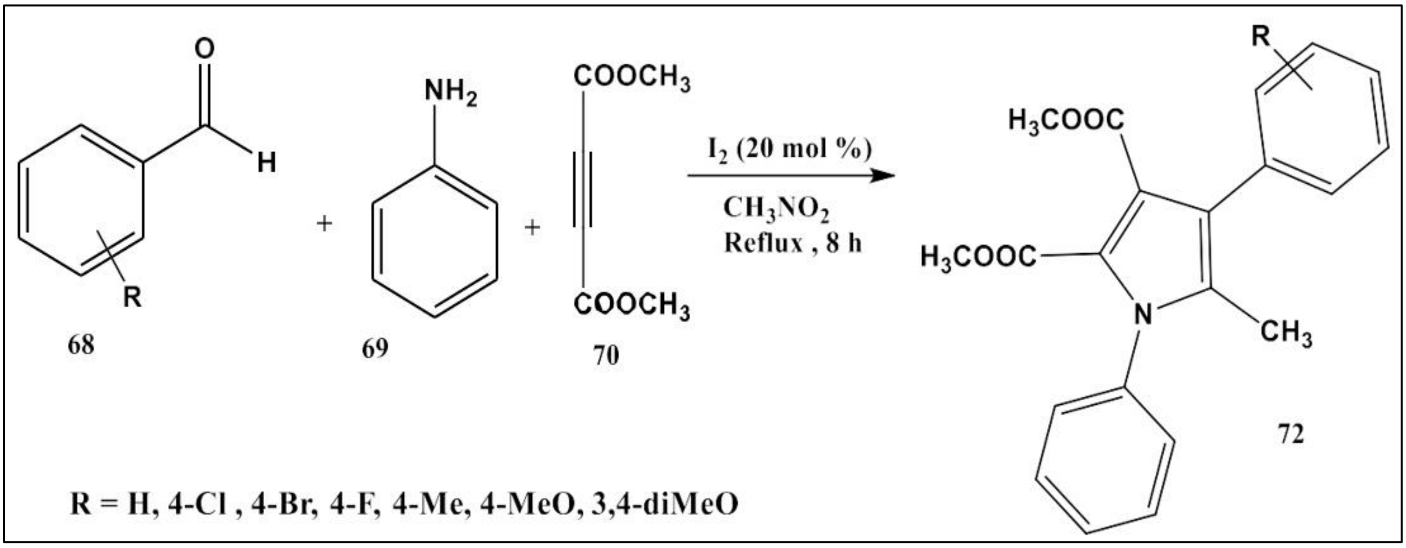
Scheme 18 Use of SBPPSP as A Catalyst for The Synthesis of 4*H*- Benzo[B]Pyran Derivatives.

III. SYNTHESIS OF FIVE- MEMBERED HETEROCYCLIC

Five-membered aromatic heterocycles containing a single heteroatom, namely pyrrole, furan, and thiophene, are regarded as derivatives of the cyclopentadienyl anion, achieved by substituting the CH group with NH, O, and S, respectively. So, these five- membered heterocycles should behave like conjugated dienes and acyclic amines, ethers, and sulfides, respectively. They also have aromaticity-related properties, like (i) electrophilic substitution reactions, (ii) resonance stabilization, and (iii) an aromatic sextet involving the lone pair on the heteroatom, in addition to their tendency to undergo addition reactions [51].

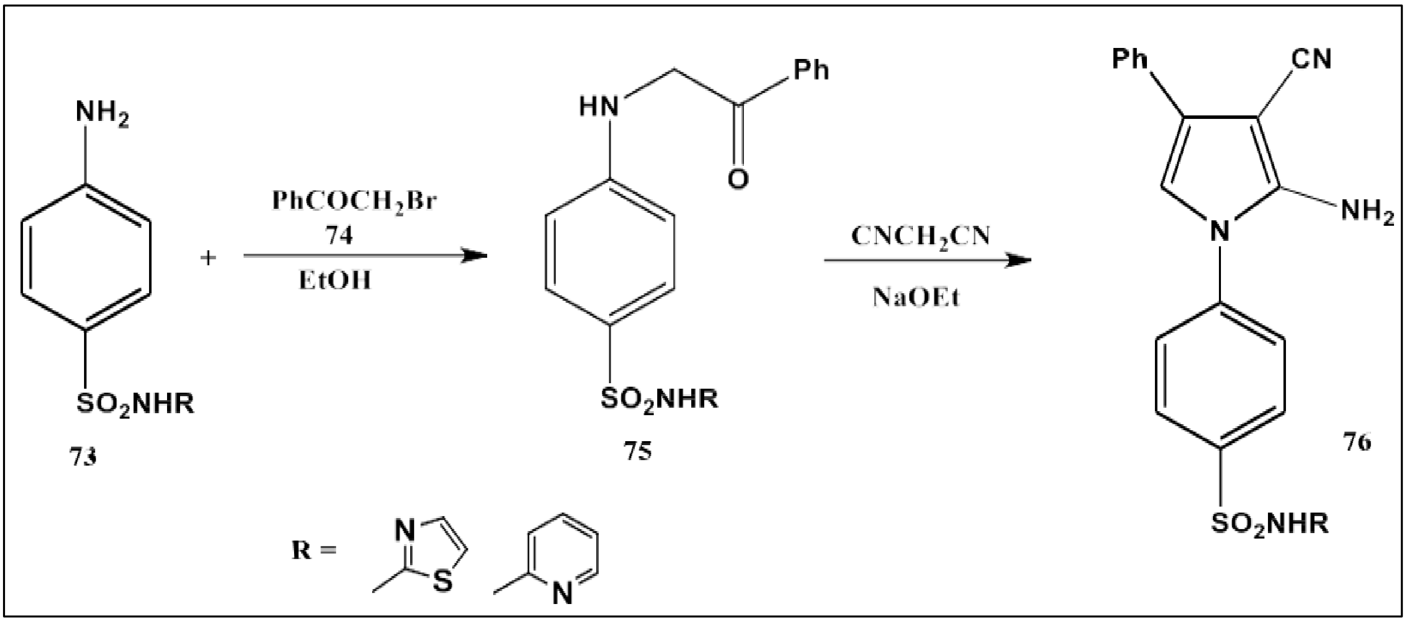
- *Synthesis of Pyrrole Derivatives.*

Sanchicol and co-workers [52] proposed a procedure for synthesizing pyrrole derivatives (72) via a four-component coupling reaction involving aldehydes (68), aniline (69), diamethyl acetylenedicarboxylates (70), and nitromethane (71), utilizing iodine as a catalyst (scheme 19).



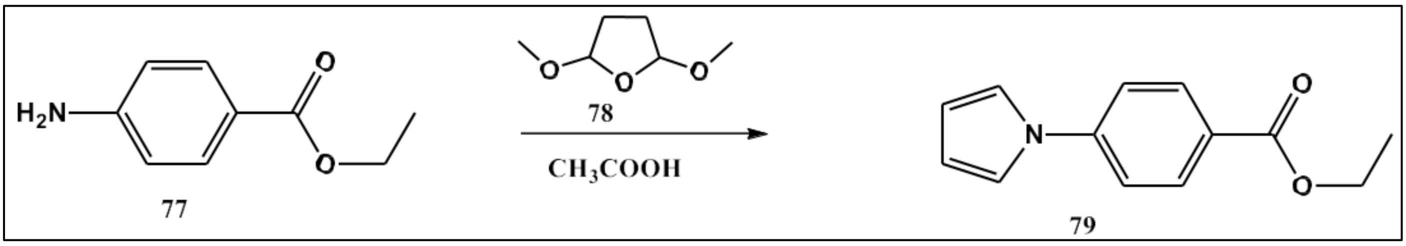
Scheme 19 Four-Component Coupling Process for The Synthesis of Pyrrole Derivatives.

On the other hand, pyrrole derivatives were synthesized in two steps described in a scheme as shown in (Scheme 20). The first step involved the reaction of different substituted aniline (73) with phenacyl bromide (74) to form 4-(2-oxo-2-phenyl-ethylamino)-benzenesulfonamide derivatives (75), which undergoes a reaction in the second step with malononitrile in the presence of sodium ethoxide to form pyrrole derivatives (76) [53]. These compounds' activity against breast and liver cancer cell lines has been evaluated in vitro. When compared to compounds 74 (IC50 = 6.78 and 6.75 lM), the pyrrole derivatives 75 shown higher activity (IC50 = 5.36 and 5.3 lM), and they were discovered to be almost as active as doxorubicin (IC50 = 5.23 lM).



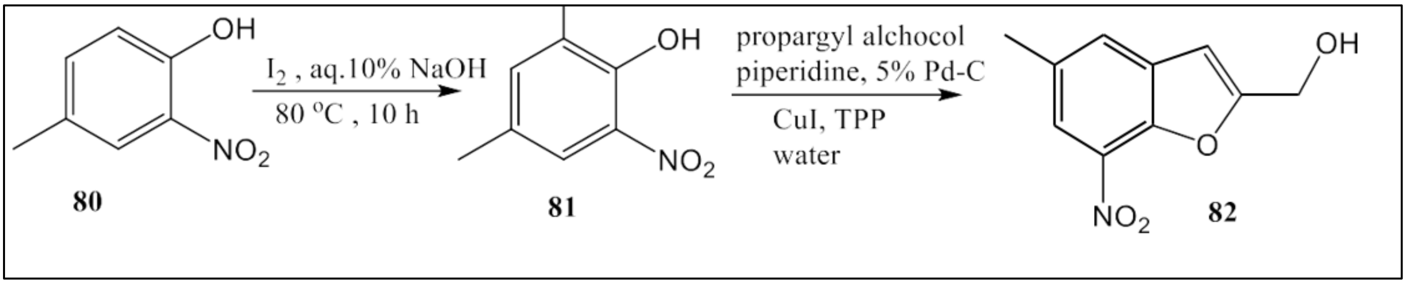
Scheme 20 Synthesis of Pyrrole Derivatives.

In order to create pyrrole derivative (79), Ethyl 4-aminobenzoate (77) was subjected to the Paal–Knorr reaction by reacting with 2,5-dimethoxytetrahydrofuran (78) in the presence of dried acetic acid [54].



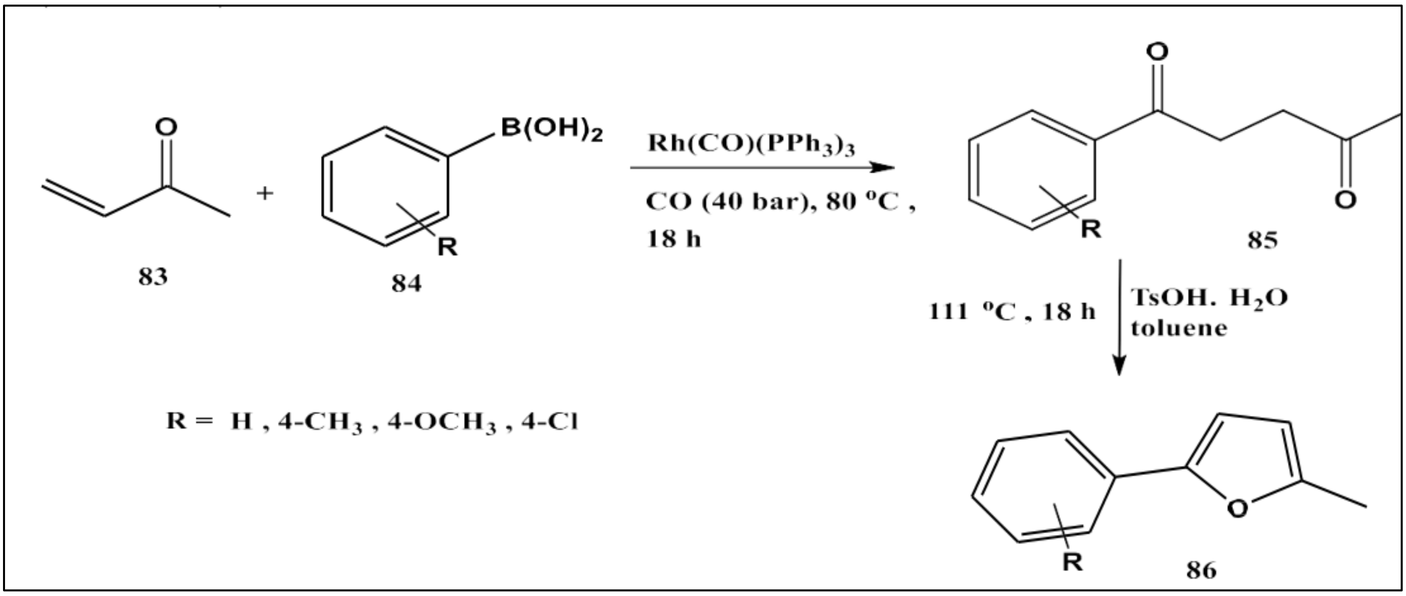
Scheme 21 Synthesis of Furan Derivatives.

Venkateshwarlu T. et. al. [55] have synthesized a furan derivative by reacting 4-methyl- 2-nitrophenol (80) with iodine in the presence of an aqueous solution of sodium hydroxide to form 2-iodo-4-methyl-6-nitrophenol (81). Then, the ring closure of this compound was performed with triphenylphosphine in the presence of CuI forming furan derivatives (82) (scheme 22).



Scheme 22: Copper Iodide-Catalyzed Ring-Closure to Form Furan Derivatives.

By another method [56], radium salts were used to catalyze the reaction between chalcones (*α,β*-enones) (83) and arylboronic acid (84) under pressure of carbon monoxide to form 1,4-diketones (85), which then undergoes ring-closure and the furan derivatives (86) is formed in the presence of *p*-toluenesulfonic acid monohydrate (scheme 23).



Scheme 23 Synthesis of Furan Derivatives Catalyzed by Radium Salts.

- *Biological activity of heterocyclic compounds*

Heterocyclic compounds are active in a wide variety of diseases, making them an important class of organic chemicals with applications across many scientific disciplines. There is a heterocyclic ring in the main skeleton of many biological compounds, including DNA and RNA, chlorophyll, hemoglobin, vitamins, and countless more. For example, triazine derivatives have antibacterial, herbicide, and urinary antiseptic and anti-inflammatory properties, among many other uses for heterocyclic chemicals that have found utility in the treatment of common ailments. Antimicrobial, antifungal, antiviral, anthelmintic, and other biological actions have been documented for benzo imidazole derivatives [57].

An emerging discipline of chemistry, medicinal chemistry seeks to understand common ailments and develop effective treatments by bridging the gap between the chemical and medical communities. From the time that scientists all around the globe began to concentrate on microorganisms and the fermentation products they produce,as well as on plants and animals, this area of contemporary chemistry has been expanding at a dizzying rate. Traditional medicinal chemistry draws from areas of physics, biology, and organic chemistry, among other classical chemistry subfields [58].

Heterocycles are useful in many fields, such as agriculture, medicine [59], and animal husbandry. A wide variety of goods, including sanitizers, copolymers, antioxidants, dyestuffs, and corrosion inhibitors, include heterocyclic groups. Heterocycles are being utilized in the production of many chemical compounds. Antibiotics (such as cephalosporin) and a number of naturally occurring substances, including morphine, vinblastine, and reserpine, among others [60].

Vitamins and antibiotics are just two examples of the many cellular biochemicals composed of heterocyclic [61]. The most significant class of chemical compounds is known to consist of heterocyclic compounds that contain nitrogen atoms. Many planned and proven methods for the systematic synthesis of heterocyclic compounds containing nitrogen have been developed in earlier years [62].

Scientists have demonstrated a great deal of interest in various heterocycles, including sulfur-containing heterocyclic compounds, in addition to conducting extensive research on heterocycles, particularly those containing nitrogen heteroatoms [63].

Numerous medicinal and therapeutically effective chemicals include sulfur-containing heterocyclic compounds. These chemicals possess a wide range of beneficial qualities, including those that pertain to diabetes, cancer, bacteria, viruses, inflammation, hypertension, malaria, Alzheimer's disease, and fungal infections. There is a wide variety of natural items and medications that contain sulfur-containing heterocyclic compounds. These compounds are frequently used in chemical research. Vegetables, meat, peanuts, coffee, and chocolate are just few of the items that use a range of heterocyclic compounds containing sulfur to impart flavor [64]. To treat peripheral artery disease and other conditions, the FDA has authorized sulfur heterocycles such as raloxifene and others [65]. One such famous antiviral medication is ritonavir. Infections caused by fungus can also be treated with thiabendazole. In addition, the Food and Drug Administration has authorized a number of medications containing sulfur heterocycles for the treatment of numerous medical conditions [66].

IV. CONCLUSIONS

Heterocyclic compounds constitute a significant category of organic molecules utilized in medicinal chemistry, serving as pharmaceuticals for the treatment of many ailments. Heterocyclic compounds have a variety of medical applications, evidenced by numerous notable achievements. Due to their intriguing biological roles, heterocyclic compounds are sought-after synthetic targets and vital constituents in click chemistry and the pharmaceutical domain. The pharmaceutical industry has demonstrated significant interest in the potential applications of heterocycles as anticancer, antifungal, antibacterial, anti-inflammatory, anti-Alzheimer's, antiviral, and antidiabetic agents, among other therapies. In the realm of active medication research, it is worth noting that an increasing number of heterocycles are being contemplated as potential therapeutic possibilities.

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