



A Review on Recent One Pot Multi-Component Synthesis and Biological Properties of a Class of New Class of Chromenes, Coumarines, Chromeno-Pyrimidines, Pyrido-Pyrimidine and Quinazoline Heterocycles

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The chromenes, coumarines, pyrido-pyrimidine and quinazoline cores possesses a vast number of biological activities such as anticancer, anti-malarial, anti-microbial, anti-fungal, anti-tubercular activities and the conventional classical synthetic methods have harsh conditions having multistep process. Currently, researchers are in search of new methodology to eliminate the use of chemicals, solvents and catalysts, which are hazardous to human health as well as to environment.

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of sp^3 carbon with respect to ring oxygen naming of chromenes are done as *2H*-, *3H*- and *4H*- chromenes and the replacement of sp^3 hybridized carbon by carbonyl group leads to

make *2H*-, *3H*- and *4H*- chromenone or chromone rings [26,27]. A list of various types of chromenes have been shown in (Fig. 2.) containing tricyclic and tetracyclic rings also.

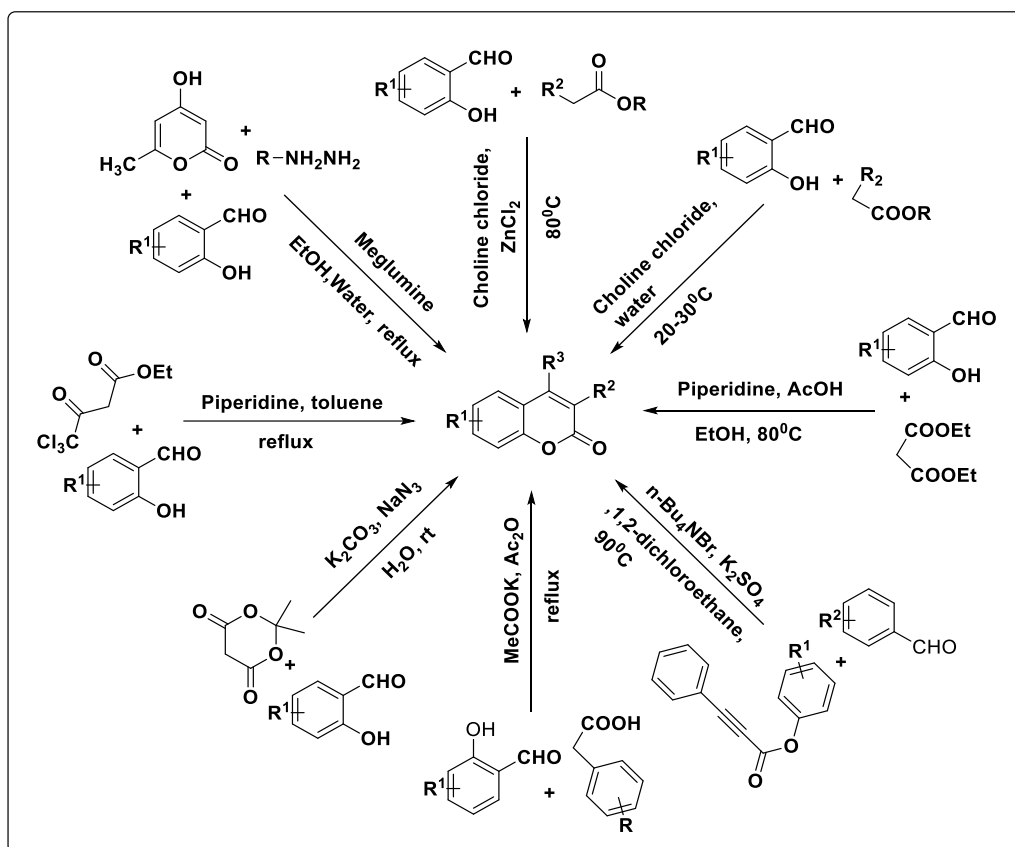


Fig. 1. Diverse synthetic routes for the synthesis of coumarine structures

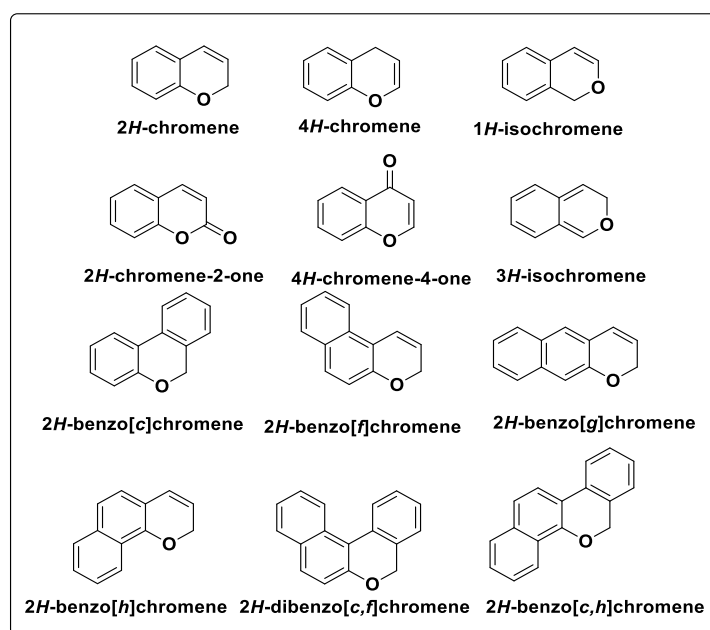


Fig. 2. Different types of chromene scaffolds

Synthetic chromene derivatives possess potent anticancer, antibacterial and antifungal, antirheumatic, anti-inflammatory properties and a vast number of chromene heterocycles are found to have significant biological activity and some of them are used as potent drugs [28]. A large number of potent bioactive chromene heterocycles are reported in literature having anti-HIV, anti-inflammatory, anti-tumour, antihepatic, anticancer, anticoagulant and antagonist activities (Fig. 3.) [29-43]. Therefore, synthetic chemists are always motivated to synthesize such potent analogues for pharmaceutical activities [44-47].

Coumarins possess broad range of biological activities such as- antifungal, anti-bacterial, anti-inflammatory, anti-HIV, anticancer, antituberculosis, anticoagulant, antiviral and significant antioxidant activities (Fig. 4.) [48-59]. Some coumarins are derived as acetylcholinesterase inhibitors and so are useful drug in Alzheimer disease treatment [60].

Dihydro- dichromeno- pyridine- 6,8- dione derivatives also contain coumarin scaffolds which are considered as one of the important fused ring heterocyclic bioactive compounds and thus a variety of scientific research have been made towards the targeted synthesis coumarin analogues to find their significant applications in the field of medicinal chemistry. Coumarins can be derived also from natural resources and scaffold can be used extensively for the preparation of derivatives and their derivatives have no doubt a broad range of biological activities such as anti-fungal, [61] anti-inflammatory, [62] anti-tubercular activities, [63] antiviral, [64] anticancer, [65] etc. A number of fused ring coumarin derivatives have been obtained by following conventional techniques using hazardous chemicals [66] and thus a new sustainable development in synthetic procedure is needed for the synthesis of dihydro-dichromeno-pyridine-6,8-dione derivatives as our targeted product.

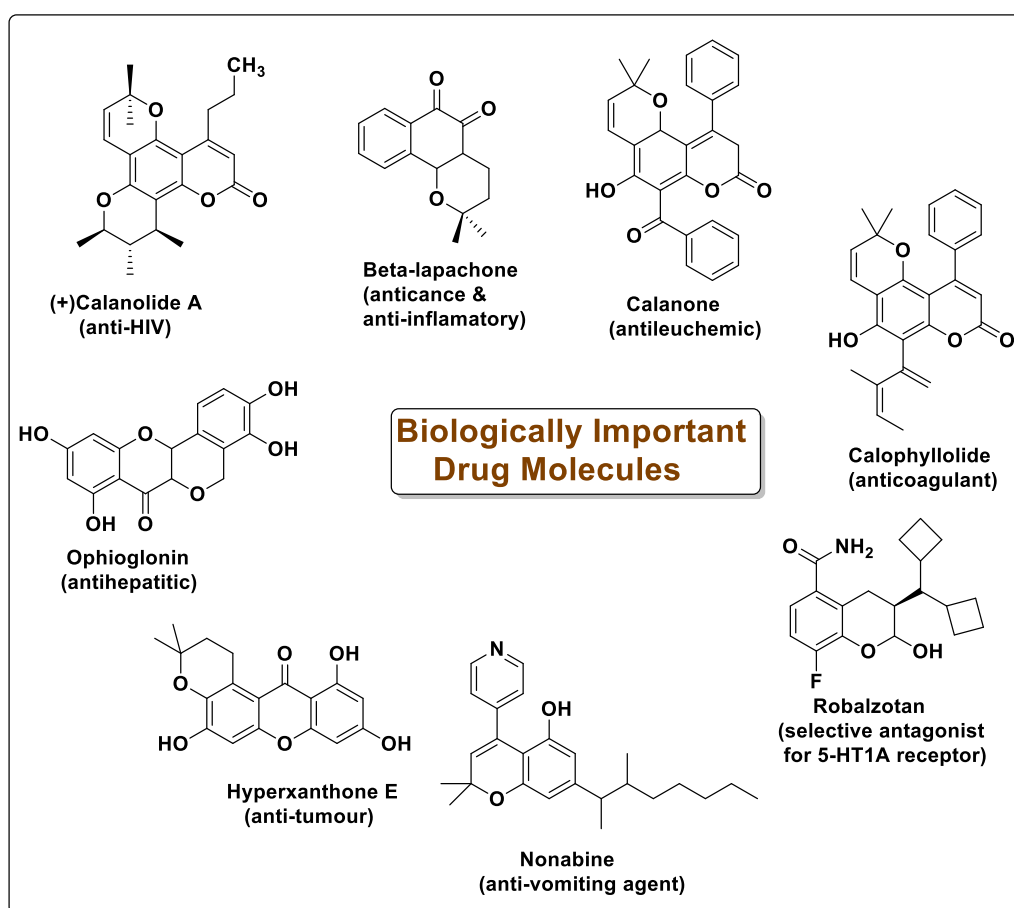


Fig. 3. Some important pharmaceutically active drug molecule containing chromene structural skeletons

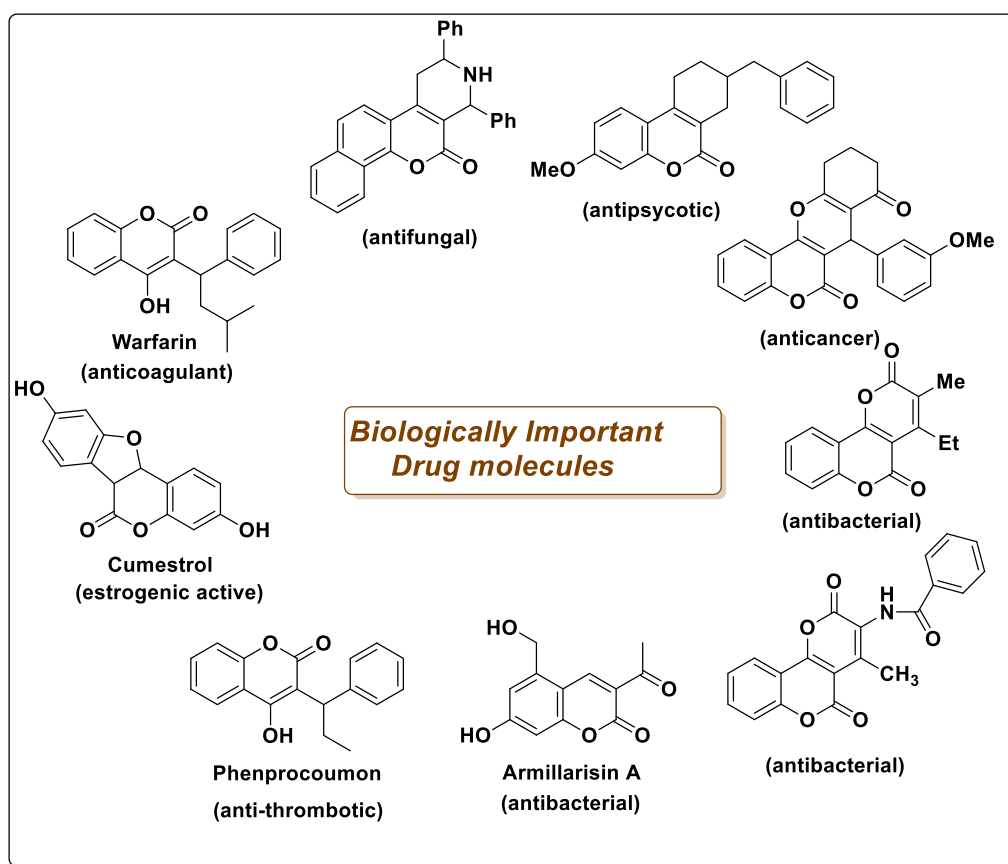


Fig. 4. Some important pharmaceutically active drug molecule containing coumarin structural skeletons

Dihydro-chromeno-pyridines are important class of heterocyclic compounds containing a 1,4-dihydropyridine ring fused with chromene moiety. They are treated as polycyclic 1,4-dihydropyridines and as they also belongs to the class of 1,4-dihydropyridine family they have a broad range of biological importance due to the presence of both dihydropyridine ring and fused chromene ring in it [67,68]. Dihydro-chromeno-pyridines may contain two chromene rings fused with 1,4-dihydropyridine ring or it may contain one chromene ring fused with 1,4-dihydropyridine ring. In spite of having several synthetic procedures of skeletons of 1,4-dihydropyridines there are few reported synthetic procedure for the synthesis of dihydro-chromeno-pyridines skeleton using various catalysts.

1,4-dihydropyridines are a class of heterocyclic compound having low molecular weight having both commercial and biological importance. In 1882, the synthesis of a 1,4-dihydropyridines are three component cyclocondensation reaction of acetoacetic ester, aldehyde and ammonia and after that there several methods of synthesis of

1,4-dihydropyridine skeleton are innovated by researchers using various novel catalysts (Fig. 5) [69].

Due to the presence of both chromene moiety and dihydropyridine rings these dihydro-chromeno-pyridine molecules have both biological and pharmaceutical importance. (Fig. 6) Due to the presence of two bioactive chromene and dihydropyridine moieties these types of bioactive compounds largely exhibit diverse activities such as antimicrobial, anticancer, antitumor, antimalarial and antiarrhythmic effects [70-81].

The pyridopyrimidines a of class of heterocyclic organic compounds have 6–6 bicyclic systems containing two or three nitrogen atoms in both six-membered rings. The compounds are also named as diaza- or triaza-naphthalenes which shows the structure of all possible types of pyridopyrimidines such as 4*H*-Pyrido[1,2-*a*]pyrimidin, 1*H*-Pyrido[1,2-*c*]pyrimidin, Pyrido[2,3-*d*]pyrimidin, Pyrido[3,2-*d*]pyrimidin, Pyrido[3,4-*d*]pyrimidin, Pyrido[4,3-*d*]pyrimidin (Fig. 7.).

In spite of the natural abundance of pyridopyrimidines and their derivatives, there are several reported methods of the synthesis of such kind of bicyclic-aza compounds [82]. Among these pyridopyrimidines, 4*H*-Pyrido[1,2-*a*]pyrimidin, 1*H*-Pyrido[1,2-*c*]pyrimidin show

tautomeric effect in solid state and solution phase depend upon the pH condition of the supporting medium and in acidic medium their structure acquires cationic characteristics and in basic medium they show anionic character [83].

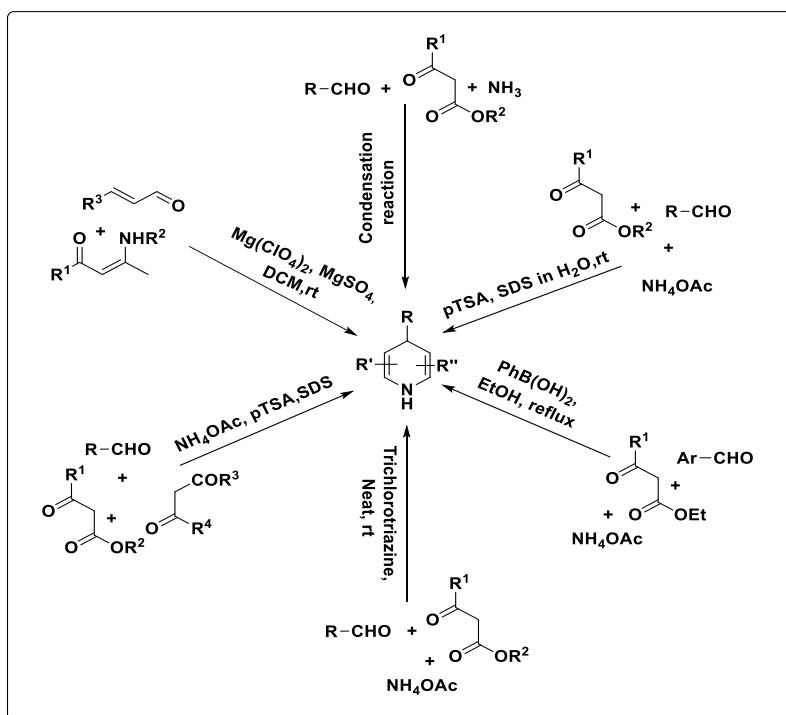


Fig. 5. Diverse synthetic routes for the synthesis of 1,4-dihydropyridine structures

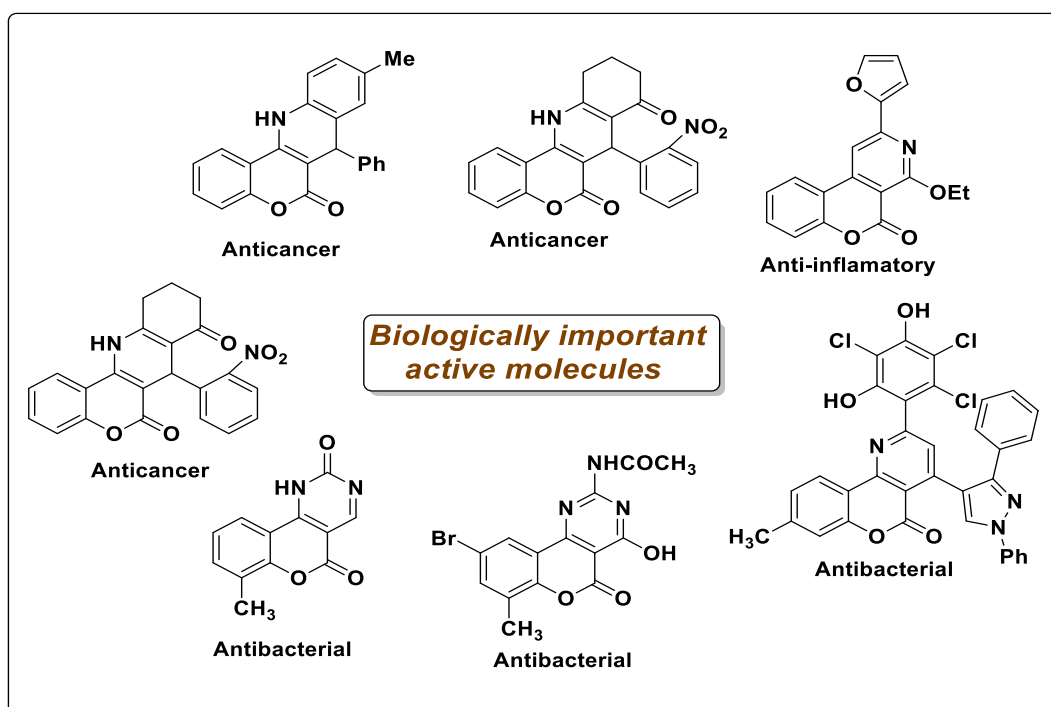


Fig. 6. Some important pharmaceutically active drug molecule

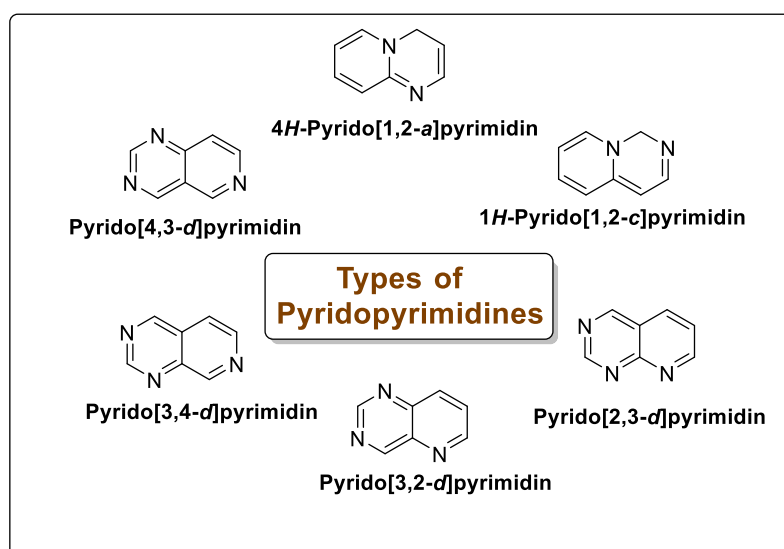


Fig. 7. Various types of pyridopyrimidine skeleton

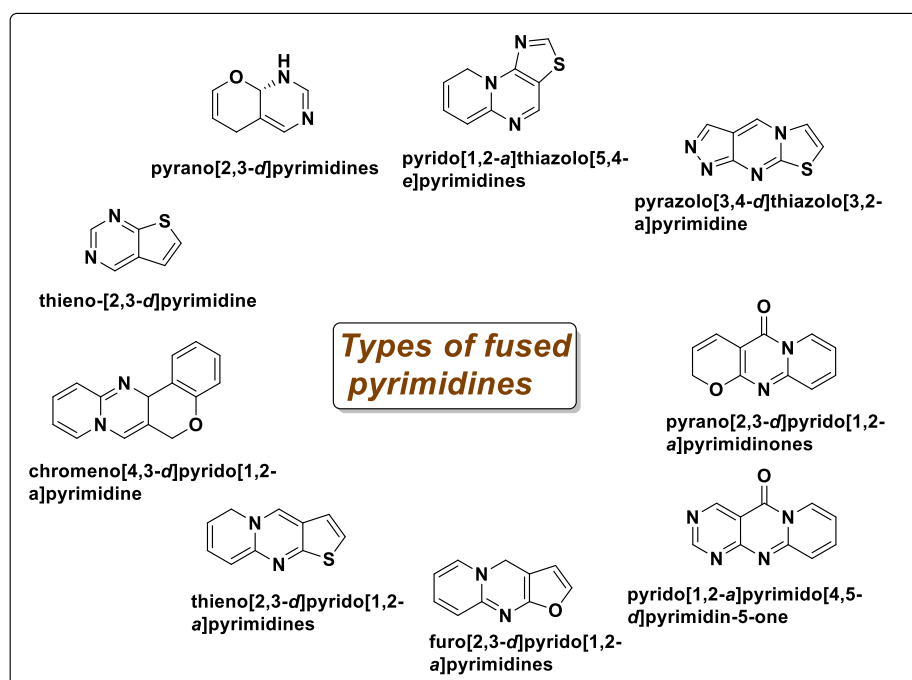


Fig. 8. Various types of fused pyrimidine skeleton

The compounds are generally basic in nature due to the presence of available donatable electron pairs over 'N'-atoms to protons and have broad range of biological importance in medicinal and biochemistry fields. There are also examples of other fused ring pyrimidines such as chromeno[4,3-d]pyrido[1,2-a]pyrimidine, thieno[2,3-d]pyrimidine, pyrano[2,3-d]pyrimidines, pyrazolo[3,4-d]thiazolo[3,2-a]pyrimidine, furo[2,3-d]pyrido[1,2-a]pyrimidines, pyrido[1,2-a]thiazolo[5,4-e]pyrimidines, and pyrido[1,2-

a]pyrimido[4,5-d]pyrimidin-5-one, pyrano[2,3-d]pyrido[1,2-a]pyrimidinones, pyrimidothienopyrido[1,2-a]pyrimidinone, thieno[2,3-d]pyrido[1,2-a]pyrimidines, pyrazolo-pyrido[1,2-a]pyrimidines and isoxazolo-pyrido[1,2-a]pyrimidines (Fig. 8.) have already been reported. Fused pyrimidines can act as interesting scaffolds and key structures in chemistry and medicine as they show diverse biological and medical properties.

Among several types pyridopyrimidines, pyrido[2,3-*d*]pyrimidines are the most abundance isomer in the literature and have wide range of biological activities. Pyrido[2,3-*d*]pyrimidines have anti-inflammatory, antihypertensive, anticancer, antimicrobial, analgesic, antiviral activity and with addition they also act as tyrosine kinase inhibitor, CDK4-inhibitor, and anti-diuretic drugs [84-88]. However, the pyrido[3,2-*d*]pyrimidine, pyrido[3,4-*d*]pyrimidines, pyrido[4,3-*d*]pyrimidines, Pyrido[1,2-*a*]pyrimidines, and pyrido[1,2-*c*]pyrimidines have also biological activities like pyrido[2,3-*d*]pyrimidines such as anti-inflammatory, antimicrobial activities anticancer, antimalarial, anti-psychotropic, antibacterial, antituberculars tyrosine-kinases inhibitor, antiallergic, anti-ulcer, CNS stimulant, urease inhibitor activities activities (Fig. 9.) [89-97].

Another important class of heterocyclic compound is fused ring tetrazole derivatives and tetrazole fused bicyclo aromatic compounds have prominent biological activity in various biological aspect. Tetrahydrotetrazolo[1,5-*a*]quinazolinones falls in the category of fused ring tetrazole derivatives and they are structurally analogous with tetrazolopyrimidines. Tetrazole fused pyrimidines have broad range of biological properties, including antimicrobial, [98] antituberculosis [99] and antidepressant, [100] activities. There are a few examples of methods

reported for the synthesis of tetrazolopyrimidines which involve initial synthesis of base catalysed chalcones followed by cyclocondensation reaction with 5-aminotetrazole. Wang and co-workers had reported also the synthesis of dihydrotetrazolo[1,5-*a*]pyrimidines and tetrahydrotetrazolo[1,5-*a*]quinazolinones catalysed via heavy metal ion Hg^{2+} [101] moreover a variety of catalysts like Iodine, [102] TBBDA, [103] [bmim+][BF₄⁻], [104] acetic acid, [105] di-isopropylammonium trifluoroacetate [106] had been used to mediate the reaction. It remains a challenging task to develop a greener route for the synthesis of a variety of tetrahydrotetrazolo[1,5-*a*]quinazolinones and isolation and purification of final products and therefore, we intended to develop a sustainable and convenient synthetic route for the synthesis of tetrahydrotetrazolo [1,5-*a*]quinazolinones.

Tetrazoles are a class of synthetic organic heterocyclic compound consisting five membered ring containing four nitrogen atoms and one carbon atoms. The first preparation of tetrazole was carried out from HCN and HN₃. There have different types of tetrazole depending upon the position of the double bond and the presence of substitution on Carban atom such as 1*H*,2*H*,3*H*-tetrazole, aminotertazoles, thiotetrazole and several synthetic methods of tetrazole skeletons are reported (Fig. 10., Fig. 11).

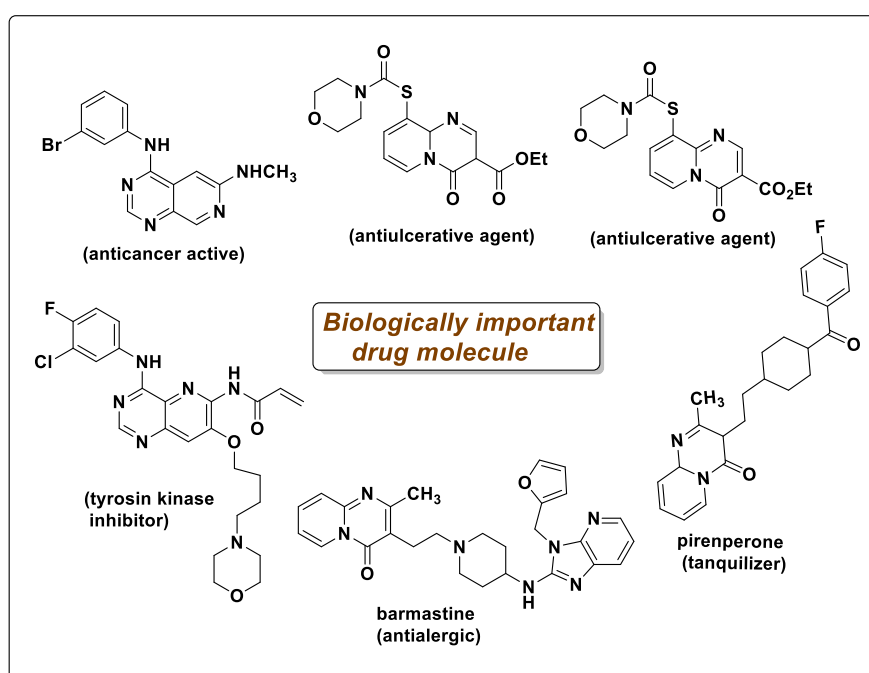


Fig. 9. Some important pharmaceutically active drug molecule

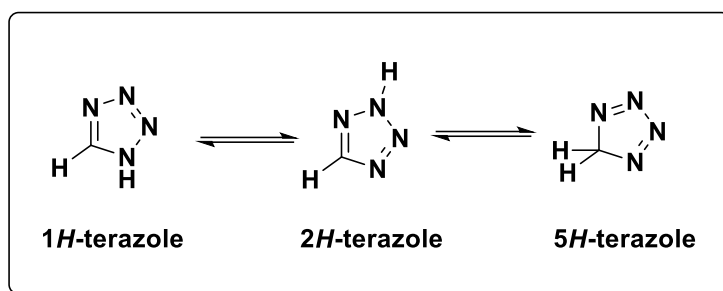


Fig. 10. Structures of 3 types of tautomeric tetrazoles

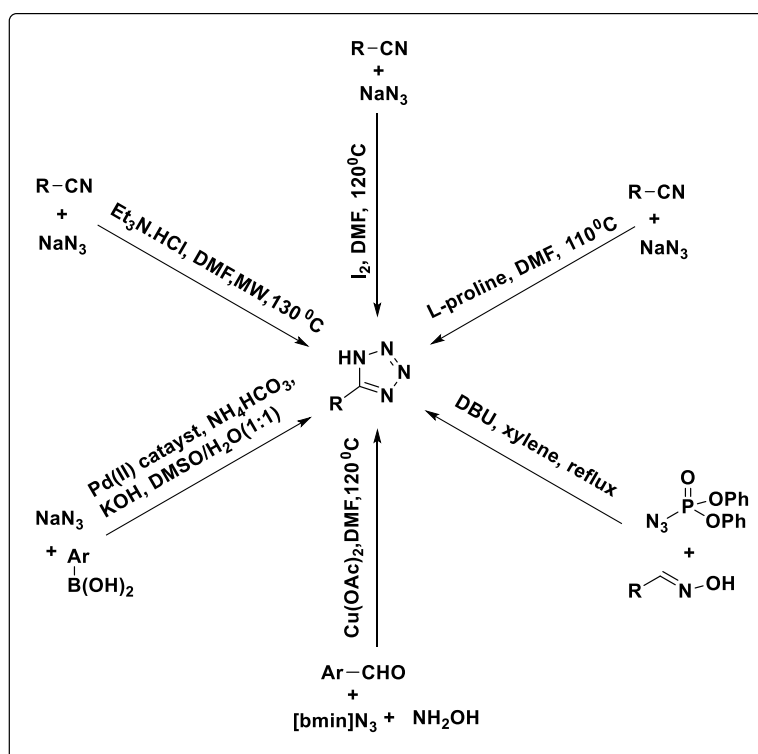


Fig. 11. Diverse synthetic routes for the synthesis of 1,4-dihydropyridine structures

Quinazolinones are generally oxidized derivatives of quinazolines and they are classified into five categories based on the substitution patterns of the ring system (Fig. 12). According to literature 4(3*H*)-quinazolinones are most abundant as natural products and 2(1*H*)-quinazolinones are predominantly a product of benzamides with nitriles [107]. In the most common approach for the synthesis of quinazolinone compounds 2-aminobenzoic acid is used as a precursor. There are other methods reported for the synthesis of various types of quinazolinones below. (Fig. 13).

Tetrazoles have a broad range of biological activities such as antibacterial, antifungal, anticancer, analgesic, anti-inflammatory, anti-

diabetic, antitubercular activities [108-114]. Quinazolinone moiety is a building block for approximately naturally occurring alkaloids and quinazolinone derivatives have attracted significant attention due to their diverse pharmacological activities such as antimalarial, antimicrobial, anti-inflammatory, anticonvulsant, antihypertensive, anti-diabetic, cholinesterase inhibition and anticancer activities and kinase inhibitor properties (Fig. 14) [115-124].

2. METHODS FOR SYNTHESIS OF CHROMENE AND COUMARINE DERIVATIVES

In 2009, Shaabani et al. [125] reported a room-temperature based synthesis of

benzo[*g*]chromene derivatives via one-pot multicomponent reaction of aldehyde, malononitrile with 2-hydroxynaphthalene-1,4-dione or 2,5-dihydroxycyclohexa-2,5-diene-1,4-dione in presence of base catalyst Et₃N in CH₃CN solvent (Scheme 1). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [125].

In 2013, Rajguru et al. [126] had reported a synthetic procedure for the synthesis of 4*H*-chromenes using aromatic aldehyde, malononitrile and C-H activated pyran-2-one to synthesise 2-amino-4*H*-chromene derivatives (Scheme 2). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [126].

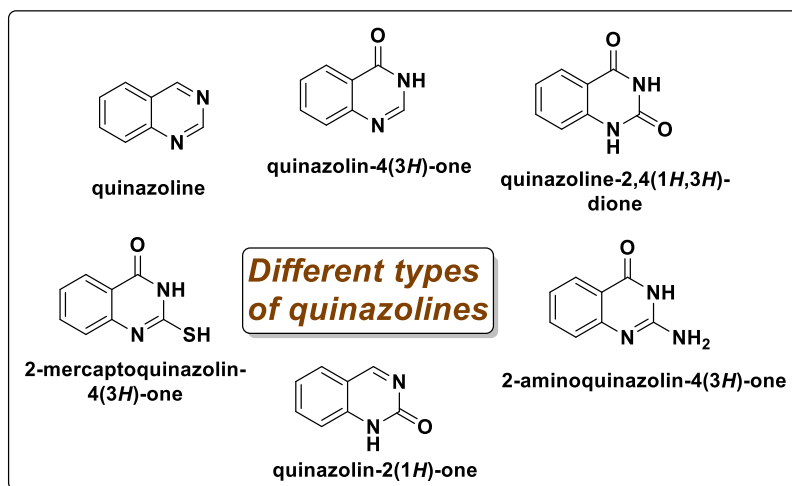


Fig. 12. Different types of quinazoline scaffolds

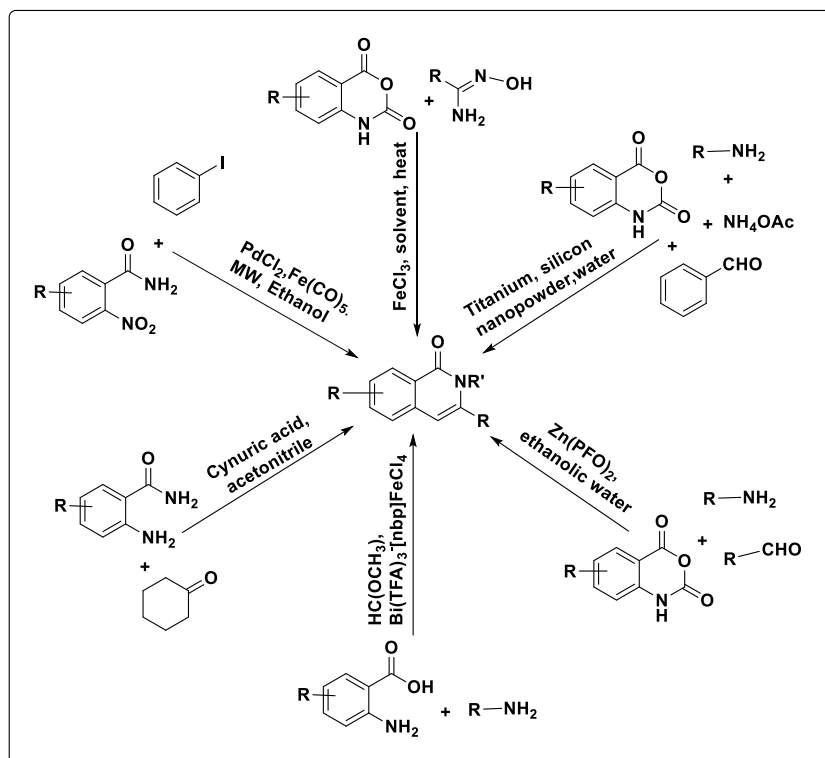


Fig. 13. Different synthetic routes of quinazolinone skeleton

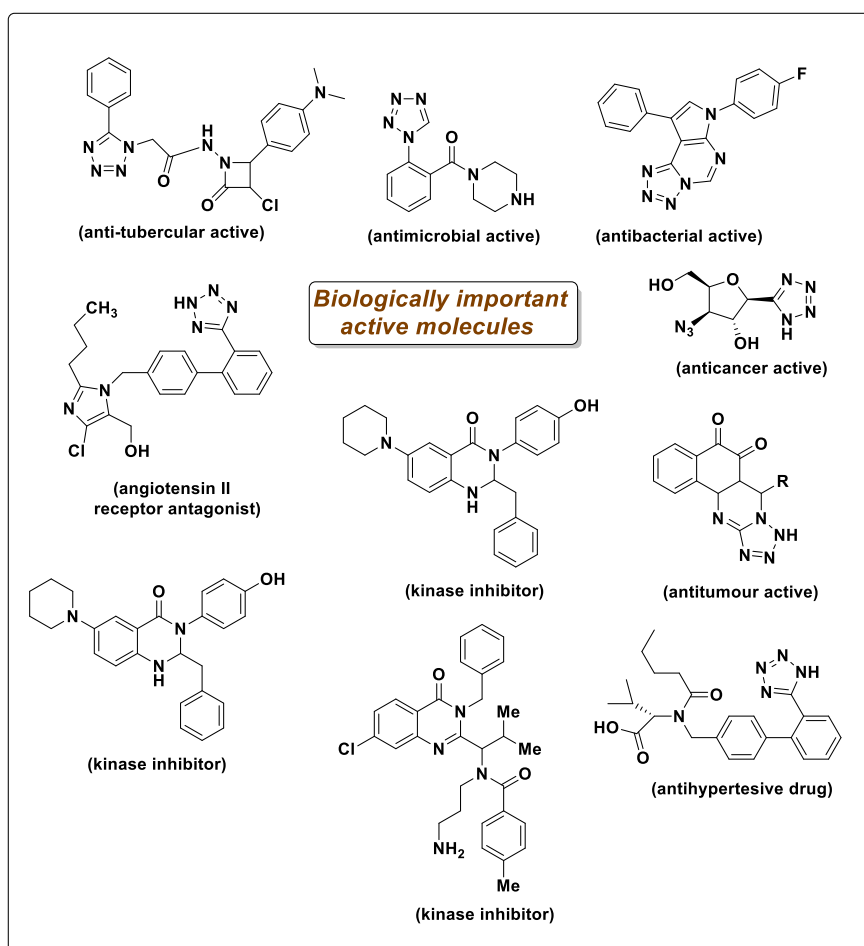
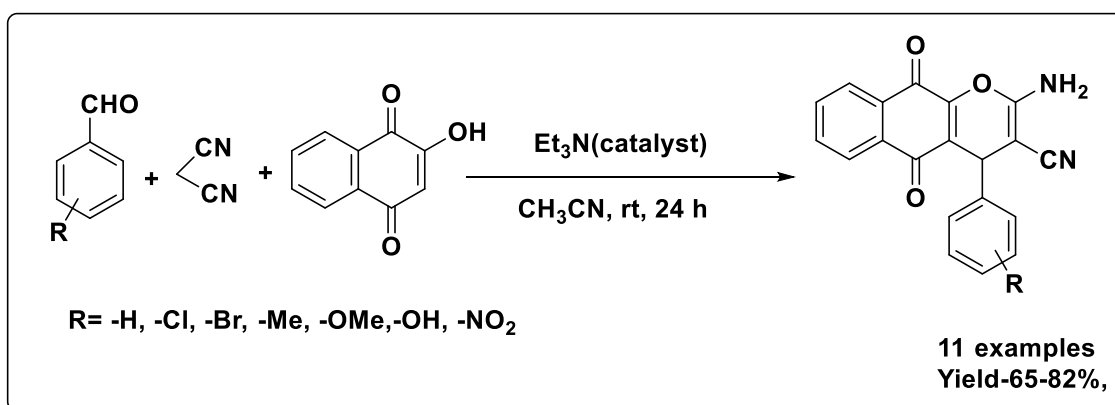


Fig. 14. Some important pharmaceutically active drug molecule



Scheme 1. One pot synthesis of benzo[g]chromene derivatives by Shaabani et al. [125]

In 2010, Khurana et al. [127] reported a synthetic procedure for pyran annulated heterocycles in one pot using DBU catalyst at reflux condition using 4-hydroxycoumarin, 4-hydroxy-6-methylpyrone, 1-naphthol and 2-hydroxynaphthalene-1,4-dione, with good yields

(Scheme 3). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [127].

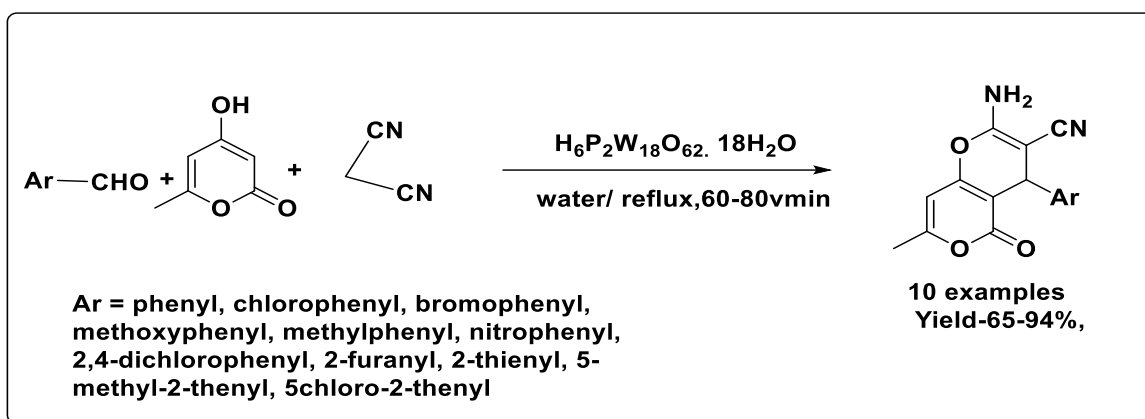
In 2011, Khan et al. [128] reported a three-component condensation reactions between

aromatic aldehydes, ethyl cyanoacetate or malononitrile and diverse C–H activated acidic compounds (Z) in the presence of catalytic amount of DMAP in ethanol under reflux conditions for the synthesis of chromenes (Scheme 4). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [128].

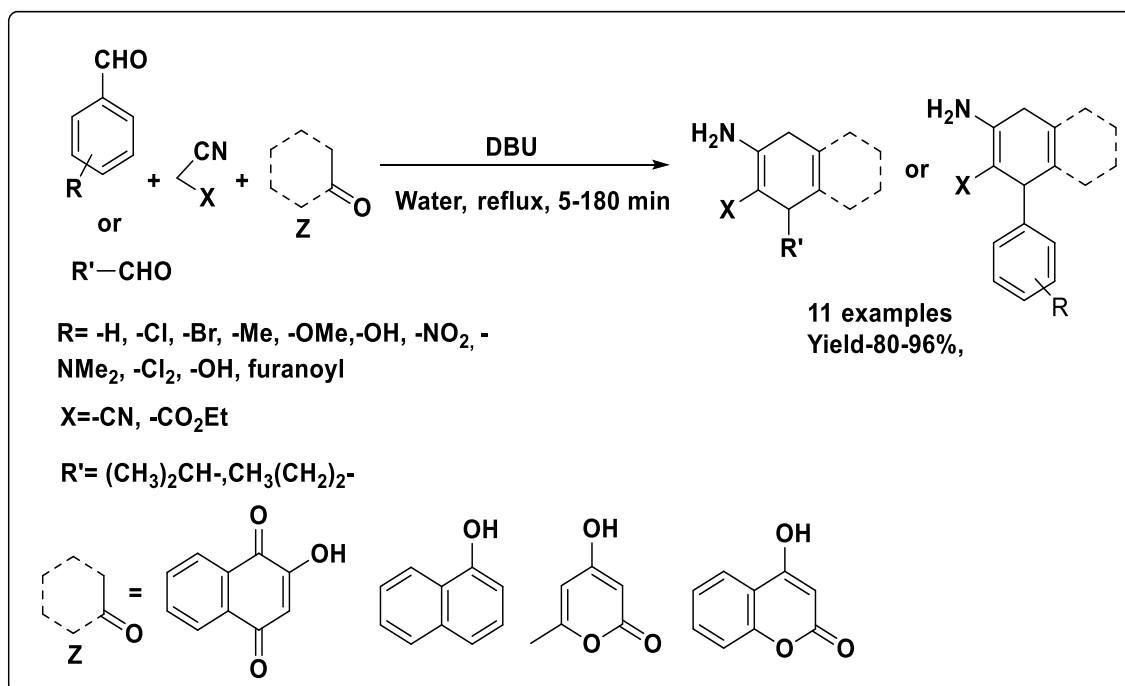
In 2013, Bihani et al. [129] synthesized chromenes and annulated heterocycles using aldehyde, malononitrile and diverse C–H activated acidic compounds (Z) in presence of amberlyst-A21 in ethanolic medium at room temperature (Scheme 5). Then characterization

of the products were done with ^1H and ^{13}C -NMR by the authors in their work [129].

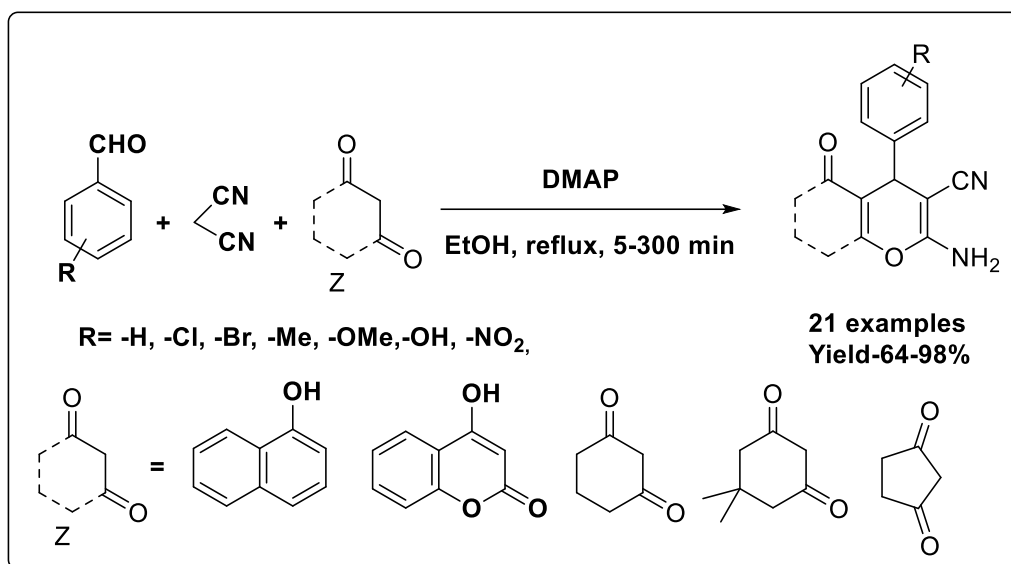
In 2011, Chen et al. [130] reported a three-component reaction between 4-hydroxycoumarin, aldehydes, and cyclic 1,3-dicarbonyl compounds in water at reflux condition to produce a series of 10,11-dihydrochromeno[4,3-*b*]chromene-6,8-(7*H*,9*H*)-dione derivatives in good yields task specific ionic liquid, short reaction time, easy product separation and purification (Scheme 6). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [130].



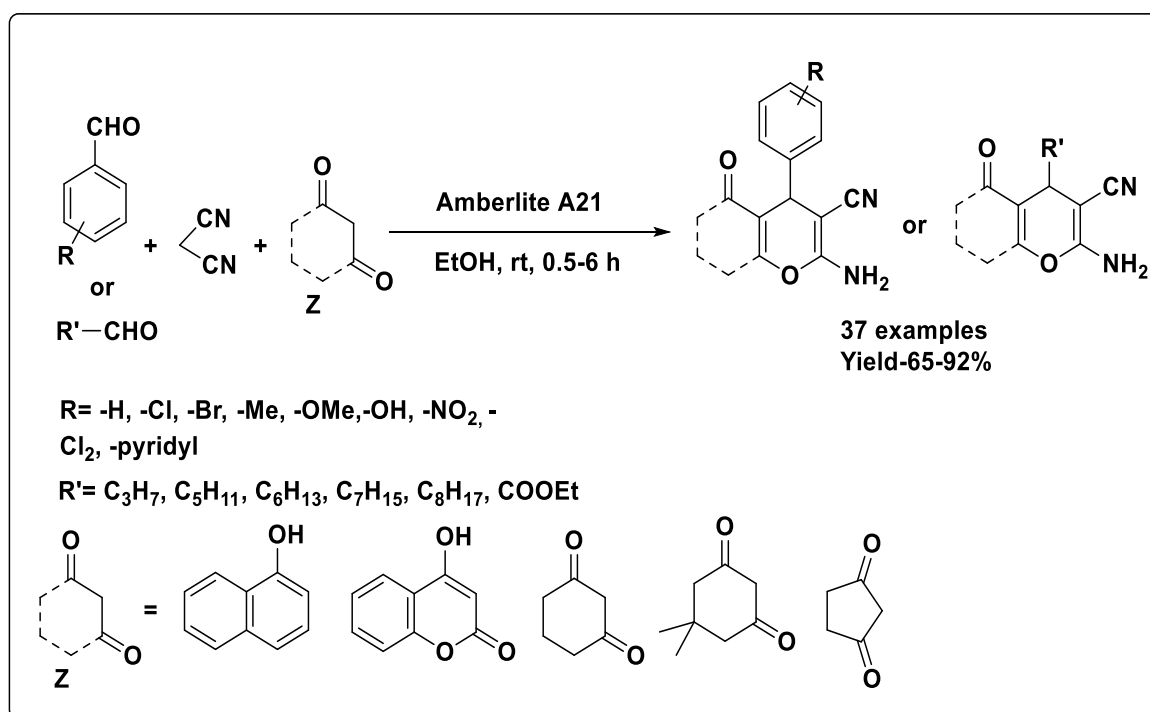
Scheme 2. One pot synthesis of chromene heterocycles derivatives by Rajguru et al. [126]



Scheme 3. One pot synthesis of chromene heterocycles derivatives by Khurana et al. [127]



Scheme 4. One pot synthesis of chromene heterocycles derivatives by Khan et al. [128]



Scheme 5. One pot synthesis of chromene heterocycles derivatives by Bihani et al. [129]

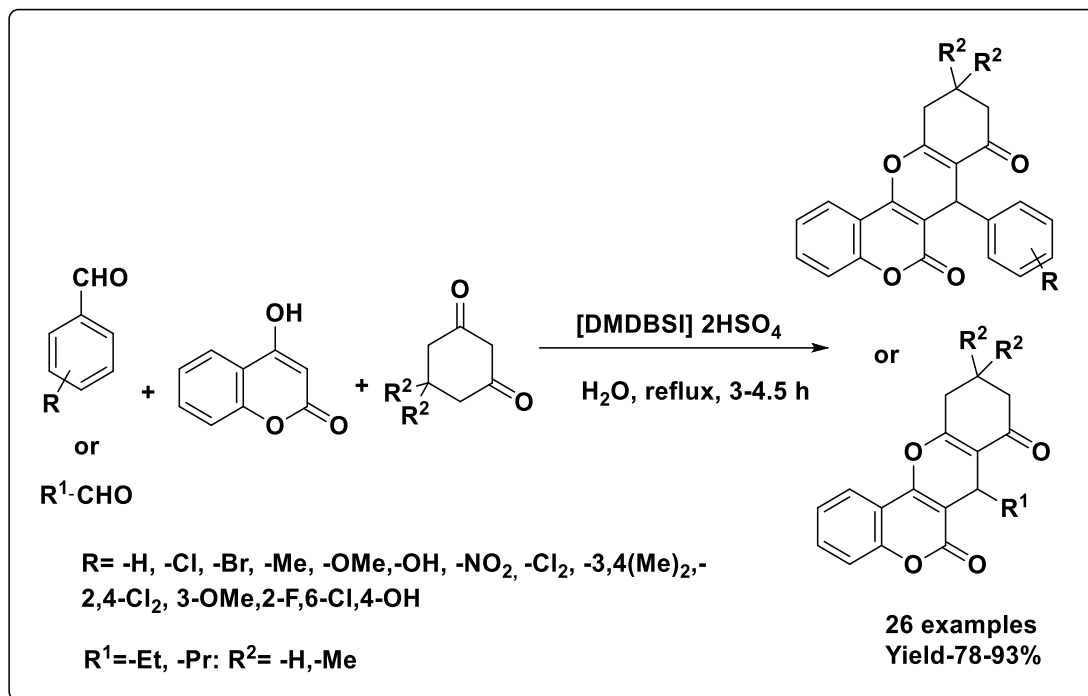
In 2013, Pradhan et al. [131] described the synthesis of a series of chromeno[4,3-*b*]chromene derivatives via three-component reaction of aldehydes, 1,3-diketones, and 4-hydroxycoumarin in aqueous medium under reflux condition by using a Lewis acid-surfactant-combined catalyst [Fe(DS)₃] (Scheme 7). Then characterization of the products were done

with ¹H and ¹³C-NMR by the authors in their work [131].

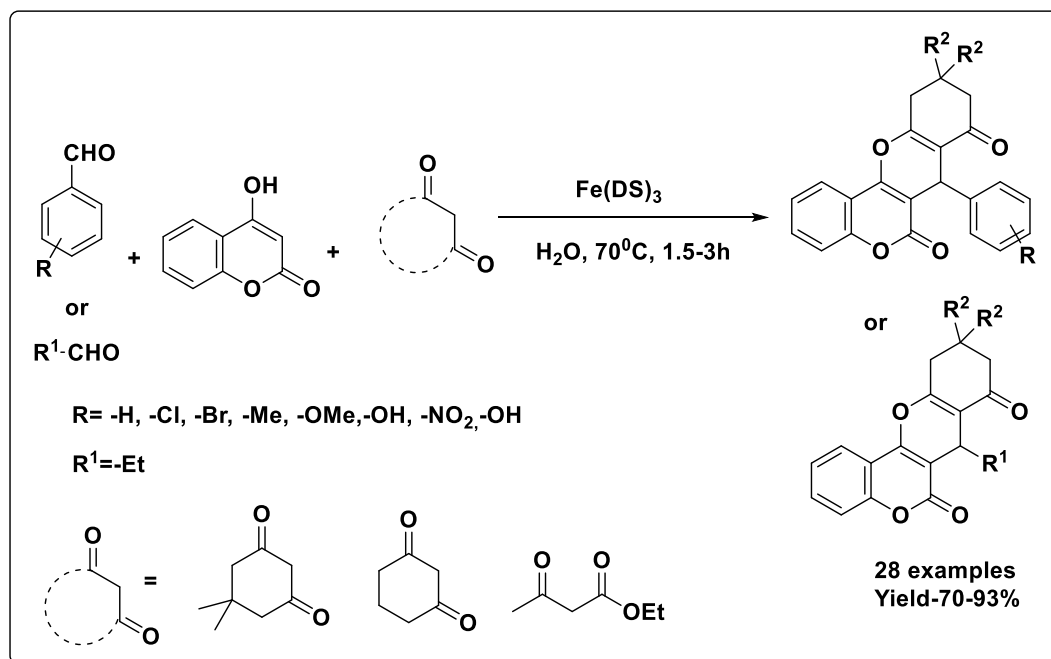
In 2013, Deacamin et al. [132] synthesized chromene derivatives via three component coupling of aldehydes, active methylene compounds, and C-H activated compounds (Z) like dimedone, 4-hydroxycoumarin, 2-

hydroxynaphthalene-1,4-dione, activated phenols in the presence of potassium phthalimide-N-oxyl as organocatalyst in aqueous medium under reflux condition (Scheme 8). Then

characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [132].



Scheme 6. One pot synthesis of chromene heterocycles derivatives by Chen et al. [130]



Scheme 7. One pot synthesis of chromene heterocycles derivatives by Pradhan et al. [131]

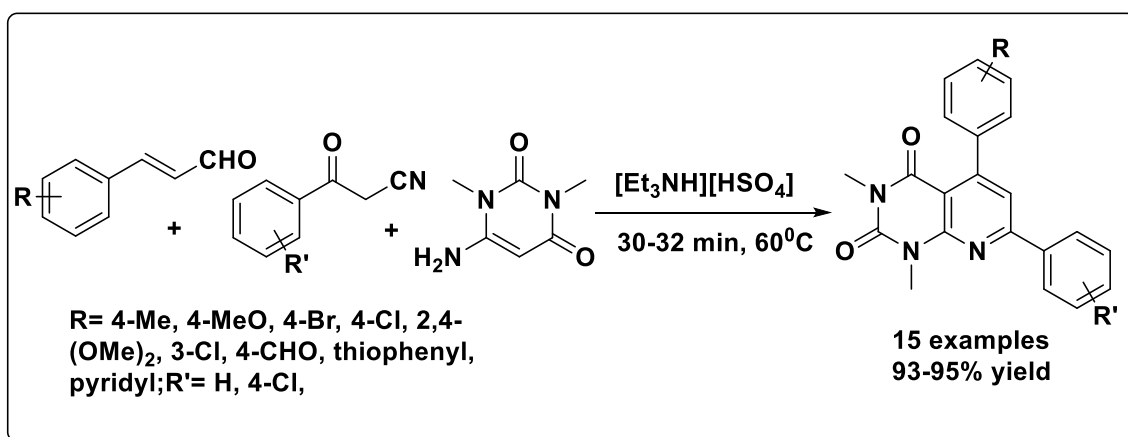
3. METHODS FOR SYNTHESIS OF PYRIDO-PYRIMIDINE DERIVATIVES

In 2021, Jadhav et al. [134] synthesised pyrazolo[3,4-*b*]pyridine derivatives in excellent yields (92–94%) via one-pot multicomponent reaction method using aminouracils and aminopyrazoles, aldehyde, and acyl acetonitrile in presence of $[\text{Et}_3\text{NH}][\text{HSO}_4]$ under solvent-free conditions (Scheme 10). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [134].

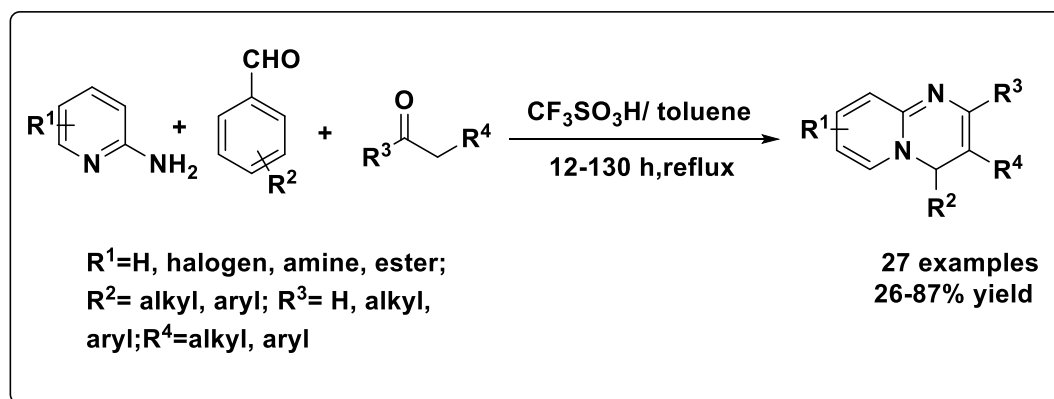
In 2013, Yang et al. [135] reported a one-pot three-component reaction method for the synthesis of 4*H*-pyrido[1,2-*a*]pyrimidines by condensation of 2-aminopyridines, aldehydes, and ketones/ aldehydes in presence of CF_3COOH acid catalyst in toluene solvent (Scheme 11). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [135].

In 2014, Mohssenimehra et al. [136] designed a synthesis for Novel pyrido[2,3-*d*]pyrimidine derivatives were synthesized via one-pot three-component methodology taking 6-amino-2-(methylthio or ethylthio)pyrimidin-4(3*H*)-one, 2,2-dimethyl-1,3-dioxane-4,6-dione and aryl aldehydes using HAp-encapsulated- $\gamma\text{-Fe}_2\text{O}_3$ catalyst at 60°C and under solvent-free conditions (Scheme 12). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [136].

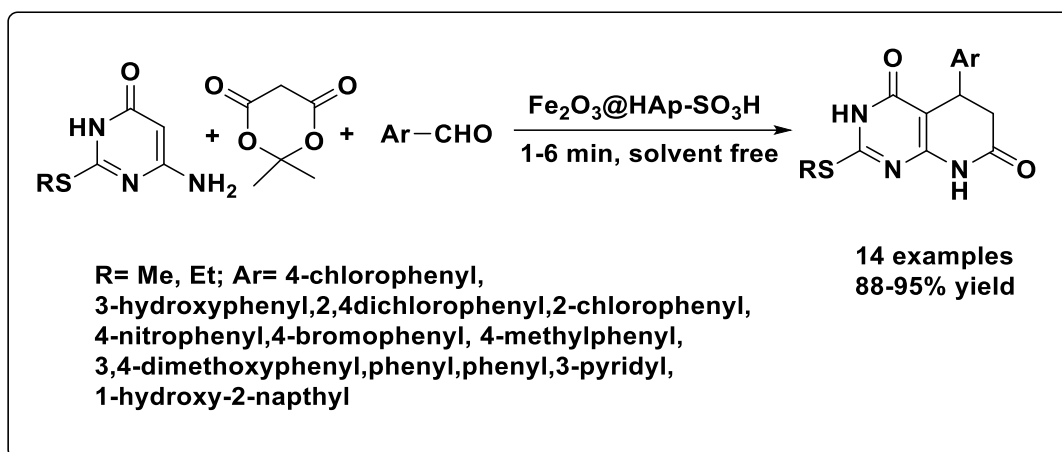
In 2007, Adib et al. [137] had reported a new, one-pot and three-component synthesis of 4*H*-pyrido[1,2-*a*]pyrimidines by using isocyanides, alkynes and *N*-substituted-2-aminopyridines at room temperature condition (Scheme 13). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [137].



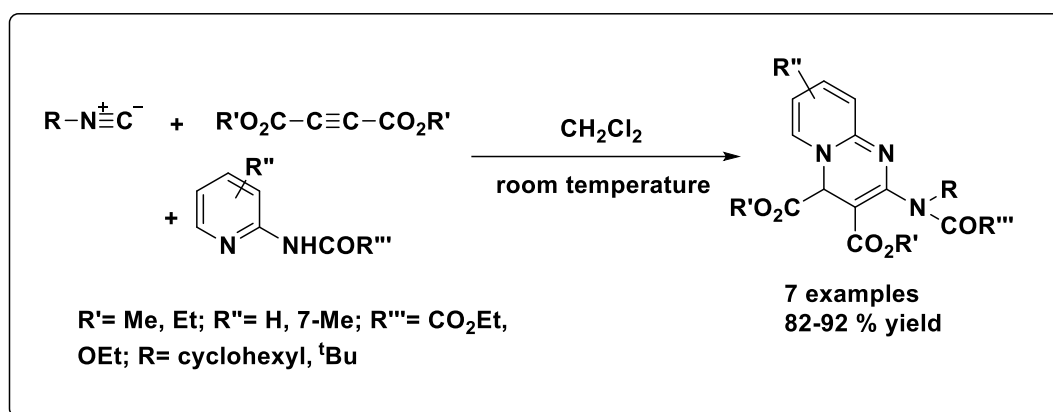
Scheme 10. One pot synthesis of pyrido-pyrimidine derivatives by Jadhav et al. [134]



Scheme 11. One pot synthesis of pyrido-pyrimidine derivatives by Yang et al. [135]



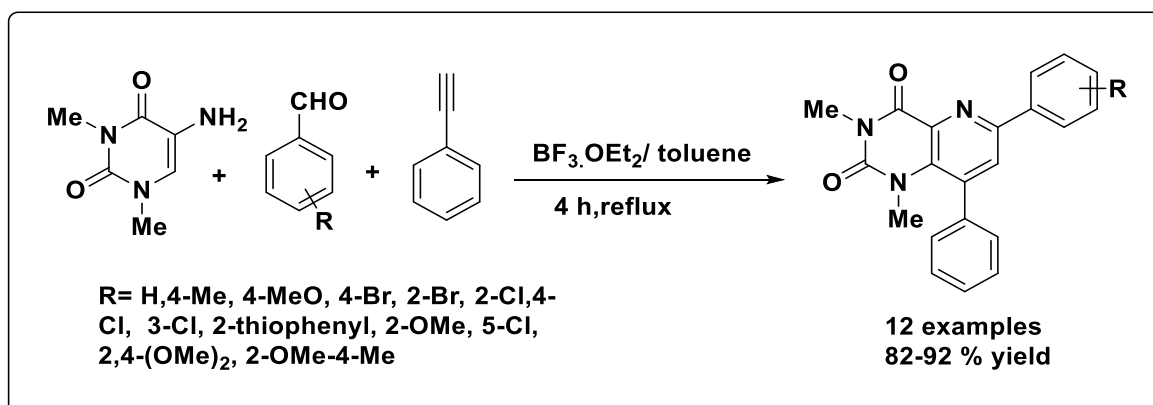
Scheme 12. One pot synthesis of pyrido-pyrimidine derivatives by Mohssenimehra et al. [136]



Scheme 13. One pot synthesis of pyrido-pyrimidine derivatives by Adib et al. [137]

In 2011, Majumdar et al. [138] had reported a mild and efficient synthetic method for the synthesis of pyrido[3,2-*d*]pyrimidine derivatives via three-component reaction between amines, aldehydes, and terminal unactivated alkynes in presence of using $\text{BF}_3 \cdot \text{OEt}_2$ as Lewis acid catalyst in one pot. The features of this

procedure are mild reaction conditions, good to high yields, and shorter reaction time with operational simplicity (Scheme 14). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [138].



Scheme 14. One pot synthesis of pyrido-pyrimidine derivatives by Majumdar et al. [138]

In 2012, Abdolmohammadi et al. [139] synthesised a series of pyrido[2,3-*d*]pyrimidines via one-pot three-component reaction between aminouracil, malononitrile and aromatic aldehydes, using catalytic amount of diammonium hydrogen phosphate (DAHP) in aqueous medium. The reaction proceeds via domino Knoevenagel-Michael-cyclization reactions to give the Pyrido[2,3-*d*]pyrimidine derivatives. (Scheme 15). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [139].

In 2012, Kidwai et al. [140] reported a synthetic procedure for the synthesis of pyrido[2,3-*d*]pyrimidines through environmentally benign process by the reaction of aldehyde, malononitrile, 5-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione and utilizing Fe_3O_4 magnetic nanoparticles at 40°C (Scheme 16). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [140].

Recently in 2021 Khalaj et al. synthesized a variety of chromeno[4,3-*d*]pyrido[1,2-*a*]pyrimidine derivatives via the three-component condensation reaction between 4-hydroxycoumarin, aldehydes, and 2-aminopyridines in presence of $\text{NiFe}_2\text{O}_4@\text{SiO}_2$ grafted di(3-propylsulfonic acid) nanoparticles (Scheme 17). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [141].

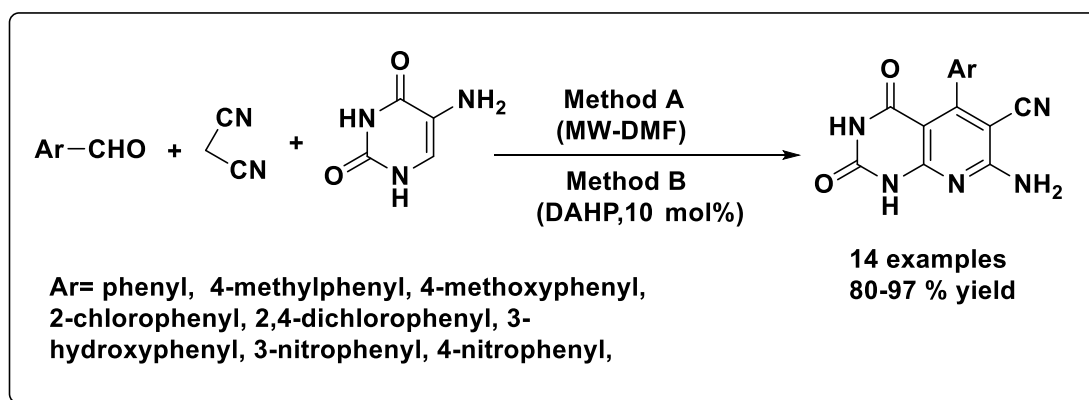
In 2018, Brahmachari et al. applied an ultrasound-assisted methods for one-pot synthesis of a new series of pharmaceutically relevant and diversely functionalized 7-

aryl/heteroarylchromeno[4,3-*d*]pyrido[1,2-*a*]pyrimidin-6(7*H*)-ones. A one pot three-component tandem reaction between 4-hydroxycoumarin, substituted aromatic aldehydes, and 2-aminopyridines were subjected for doing reaction in the presence of sulfamic acid as a catalyst (Scheme 18). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [142].

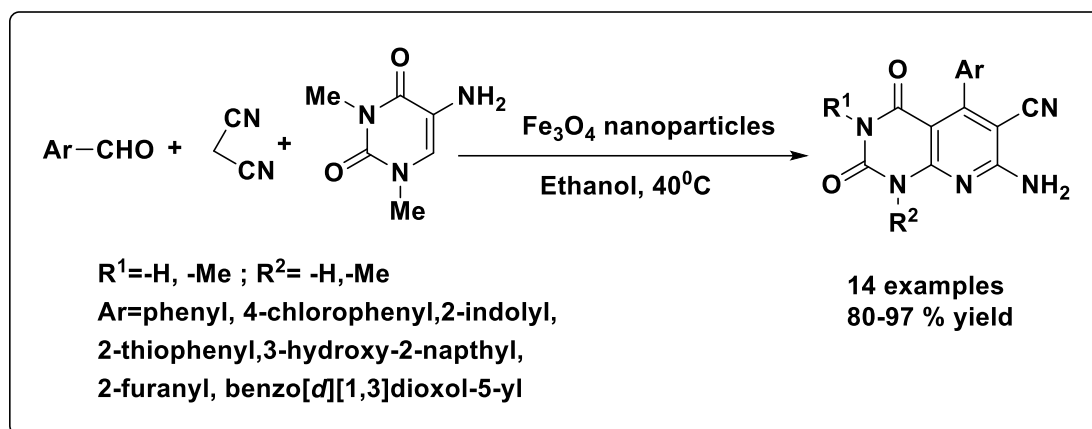
4. METHODS FOR SYNTHESIS OF DIHYDRO-DICHROMENO-PYRIDINE-DIONE DERIVATIVES

In 2017, Zeynizadeh et al. [143] reported the synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives via one-pot condensation reaction of 1,3-diketones (ethyl acetoacetate or 4-hydroxycoumarin), aromatic aldehydes and aqueous ammonia in H_2O (70°C) as a green solvent by using silica-layered nickel ferrite, ($\text{NiFe}_2\text{O}_4@\text{SiO}_2@\text{SO}_3\text{H}$) with excellent yield (Scheme 19). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work. [143].

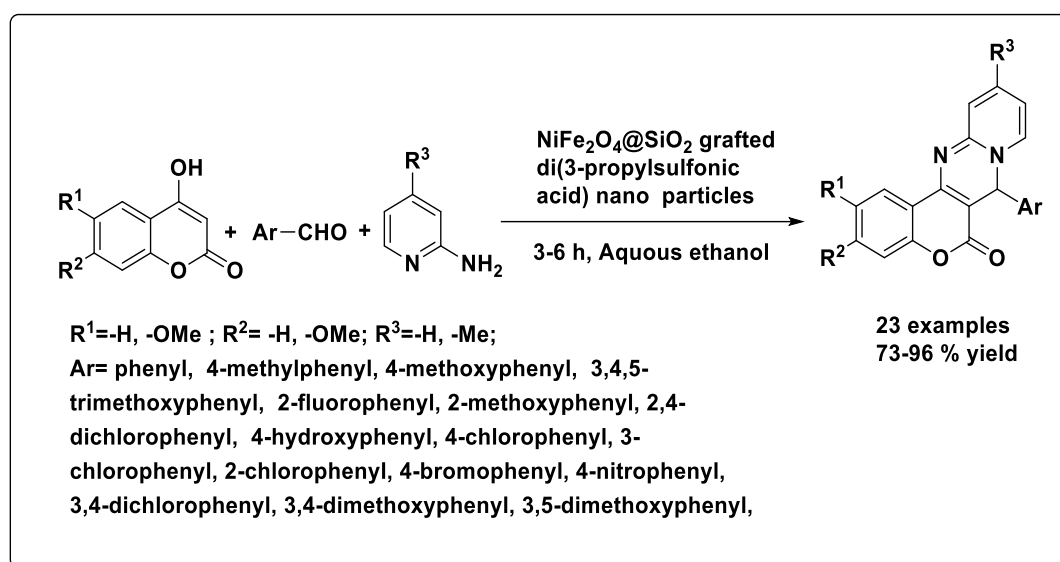
In 2019, Gilanizadeh et al. [144] had reported an efficient ecofriendly approach has been developed for one-pot multicomponent synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives by Tandem condensation of aromatic aldehydes, 4-hydroxycoumarin, and ammonium acetate by using heterogeneous $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{Ni-Zn-Fe}$ hydrotalcite catalyst under solvent-free conditions (Scheme 20). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [144].



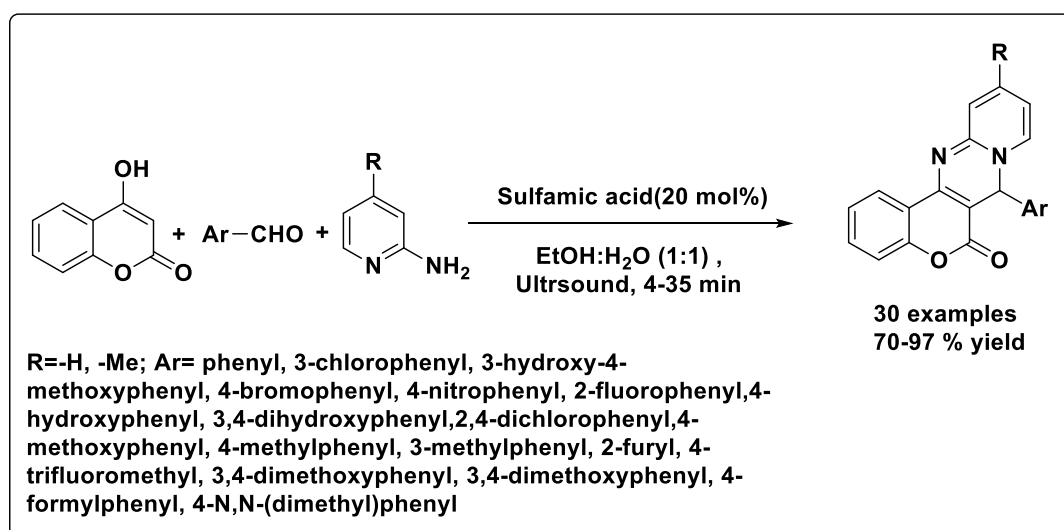
Scheme 15. One pot synthesis of pyrido-pyrimidine derivatives by Abdolmohammadi et al. [139]



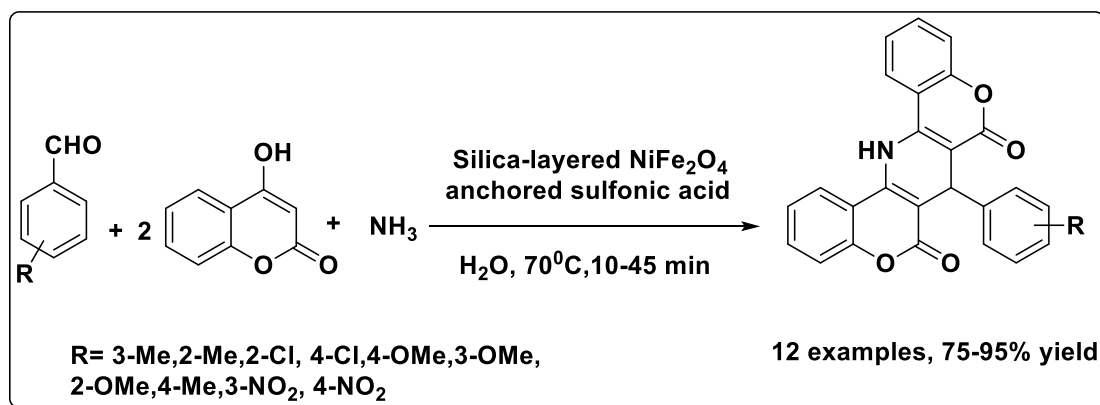
Scheme 16. One pot synthesis of pyrido-pyrimidine derivatives by Kidwai et al. [140]



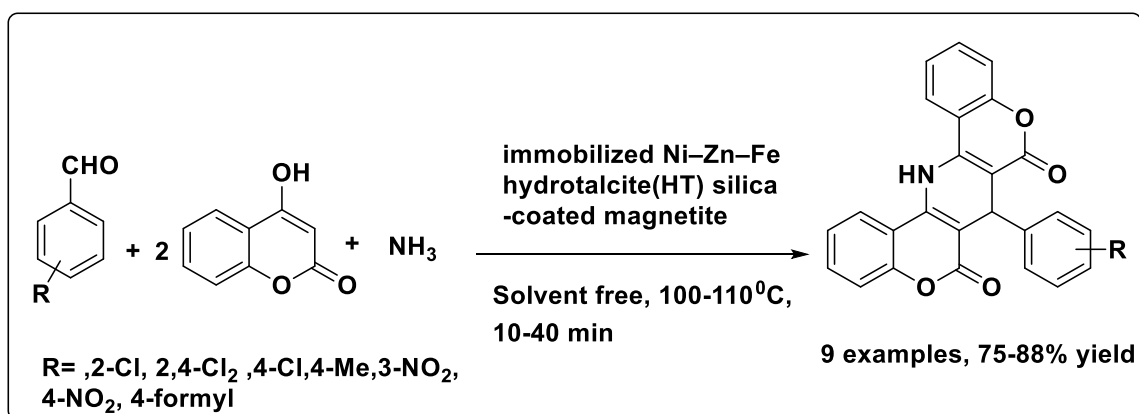
Scheme 17. One pot synthesis of pyrido-pyrimidine derivatives by Khalaj. *et al.*



Scheme 18. One pot synthesis of pyrido-pyrimidine derivatives by Bramhachari et al. [133]



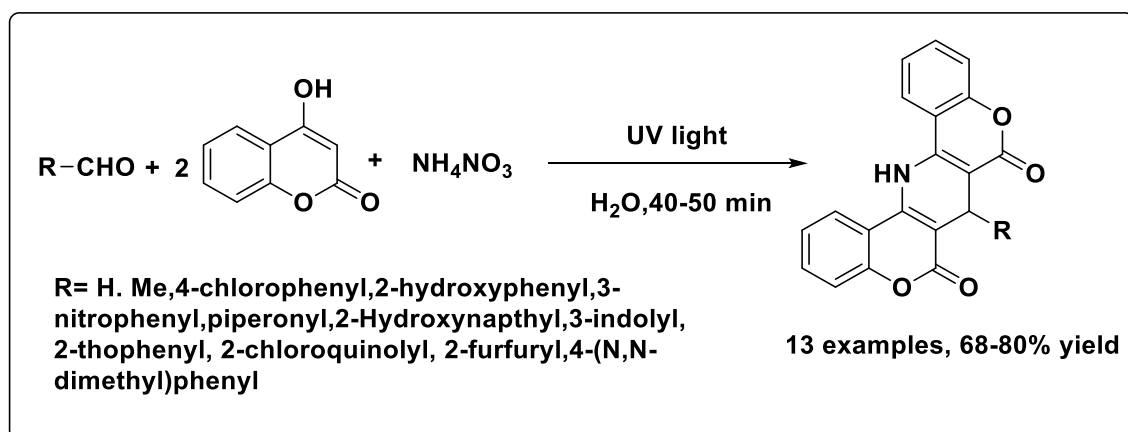
Scheme 19. One pot synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives
Zeynizadeh et al. [143]



Scheme 20. One pot synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives
Gilanizadeh et al. [144]

In 2004, Kidwai et al. [140] reported an ecofriendly approach for one-pot multicomponent synthesis of fused dihydro-dichromeno-pyridine-6,8-dione derivatives by condensation of aromatic aldehydes, 4-hydroxycoumarin, and

ammonium acetate using UV light in presence of water solvent with considerable good product yield (Scheme 21). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [145].



Scheme 21. One pot synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives
Kidwai et al. [140]

In 2020, Saffarian et al. [146] has reported a synthetic method of dihydro-dichromeno-pyridine-6,8-dione derivatives by using $\text{Fe}_3\text{O}_4@\text{SiO}_2@(\text{CH}_2)_3\text{-urea-quinoline}$ sulfonic acid chloride, as nanomagnetic catalyst bearing under solvent free condition at 80°C temperature with reasonable yield (Scheme 22). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [146].

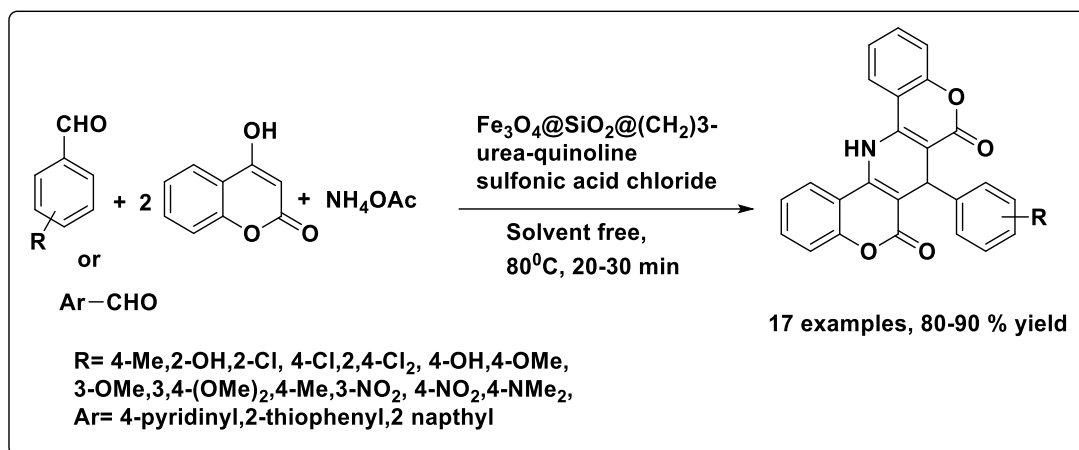
In 2016, Shaabani et al. [125] reported a synthetic protocol for the synthesis of dihydro-dichromeno-pyridine-6,8-dione scaffolds with reasonable yield by using guanidinium-based sulfonic acid as a Brønsted acid as well as organocatalyst in water medium under reflux condition (Scheme 23). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [147].

In 2004, Brahmabhatt et al. [148] reported a synthetic protocol for the synthesis of dihydro-

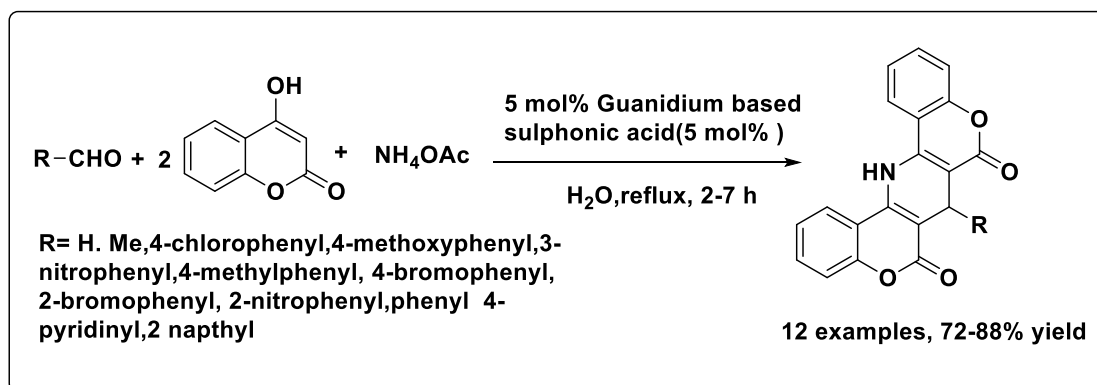
dichromeno-pyridine-6,8-diones with reasonable yield by using acetic acid as a Brønsted acid as well as organocatalyst as well as solvent at 130°C temperature (Scheme 24). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [148].

5. METHODS OF SYNTHESIS OF TETRAHYDROTETRAZOLO[5,1-B]QUINAZOLINONE DERIVATIVES

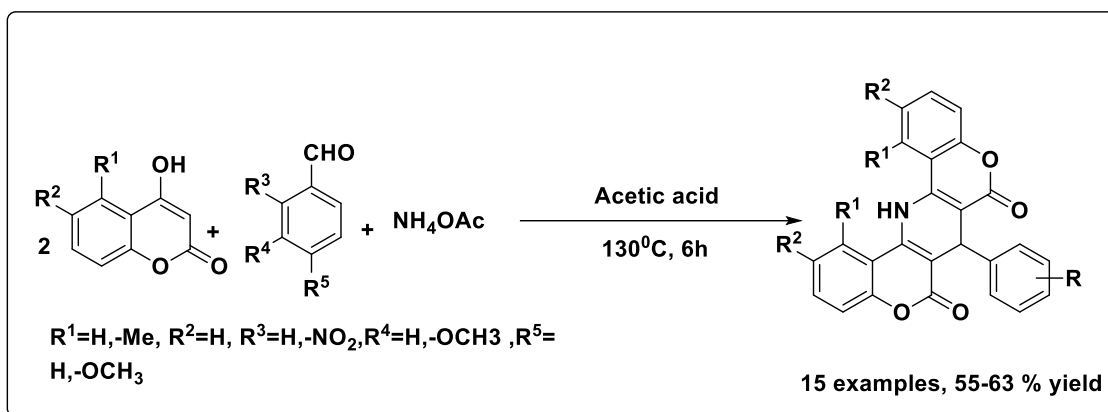
In 2019, Basha et al. [149] reported a facile one-pot synthesis of tetrazolo[1,5-a]pyrimidine derivatives via a one pot three-component reaction between aldehydes, 5-aminotetrazole and 1,3-diketones in PEG-400 under microwave irradiation at 110°C (Scheme 25). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [149].



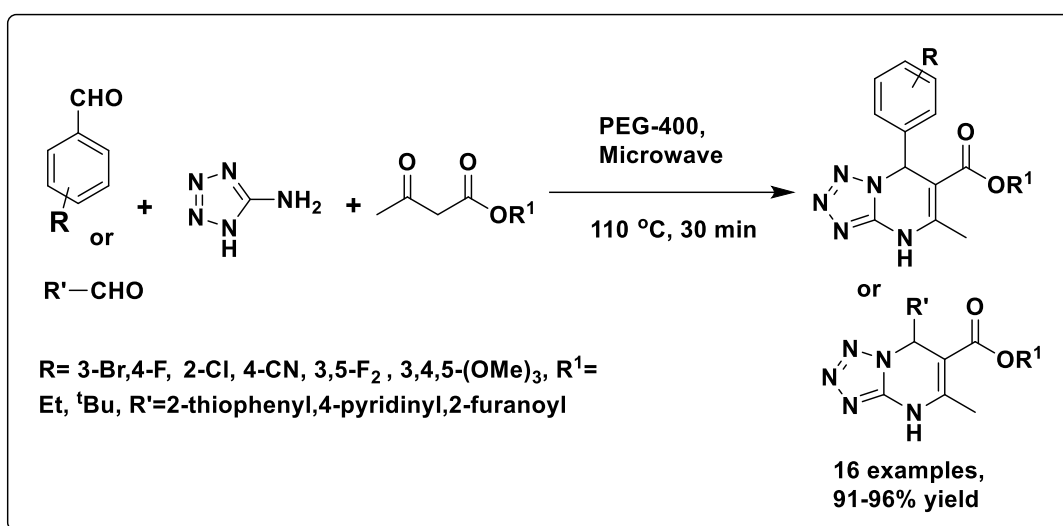
Scheme 22. One pot synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives Saffarian et al. [146]



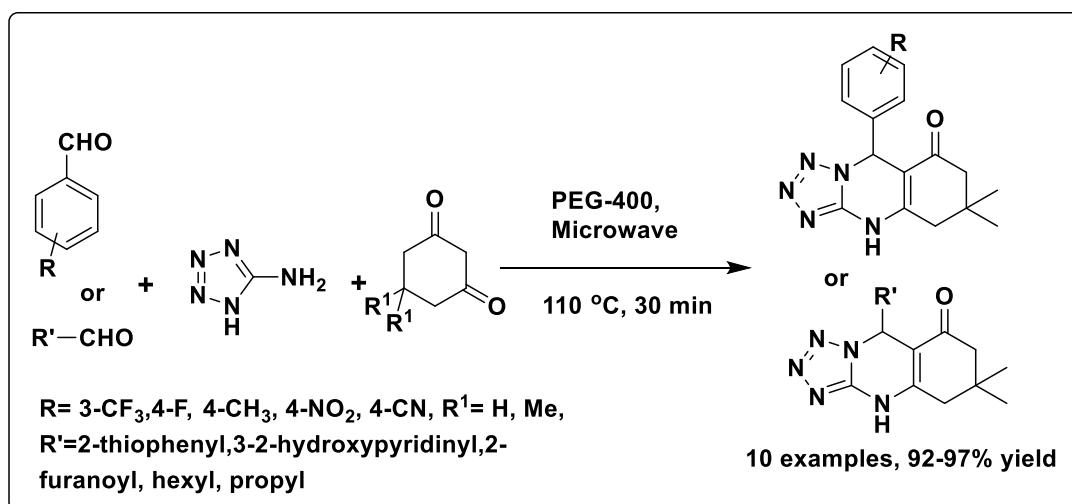
Scheme 23. One pot synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives Shaabani et al. [125]



Scheme 24. One pot synthesis of dihydro-dichromeno-pyridine-6,8-diones derivatives
Brahmbhatt et al. [148]



Scheme 25. One-pot synthesis of tetrazolo[1,5-a]pyrimidine derivatives by Basha et al. [149]



Scheme 26. One-pot synthesis of tetrahydrotetrazolo [5,1-b]quinazolinones derivatives by
Basha et al. [150]

In 2019, Basha et al. [150] also reported a facile synthesis of tetrahydro-tetrazolo [5,1-*b*]quinazolinones via one pot method by the reactions of aldehydes, 5-aminotetrazole and dimedone in presence of PEG-400 solvent under microwave irradiation at 110°C temperature (Scheme 26). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [150].

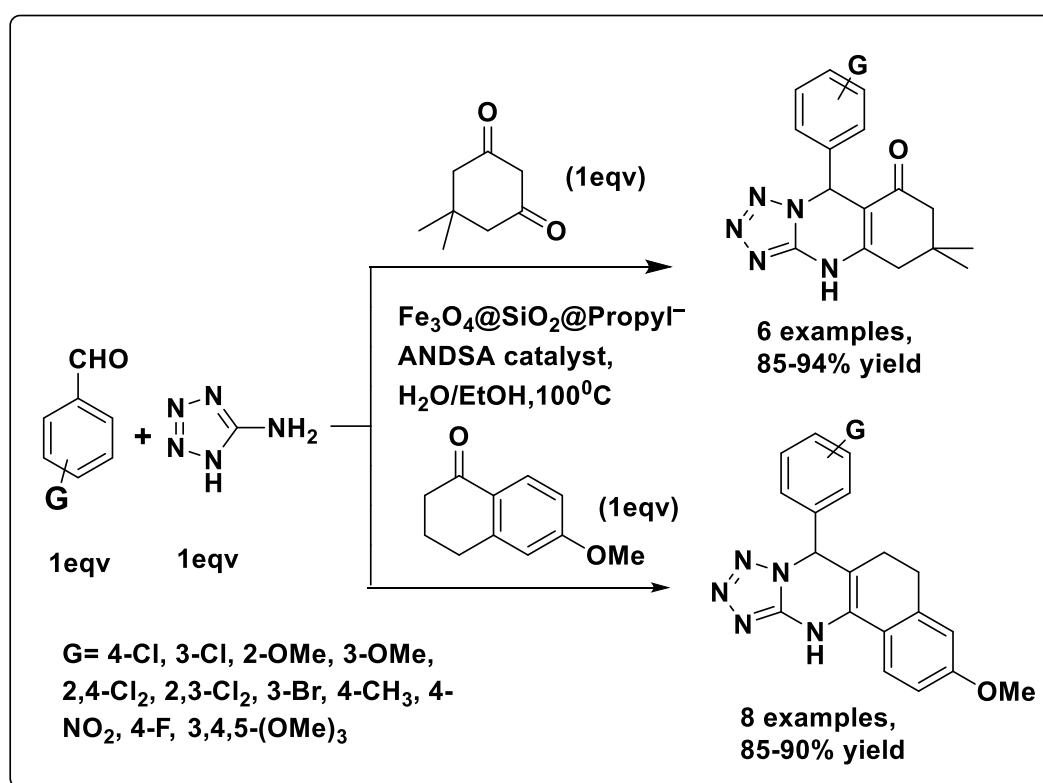
In 2019, Ghorbani-Vaghei et al. [151] has reported a facile synthesis of tetrahydro-tetrazolo[1,5-*b*]quinazolines and tetrahydrobenzo[*h*]-tetrazolo[5,1-*b*]quinazolines from the reaction of aldehydes, 5-aminotetrazole, and dimedone as cyclic 1,3 diketone in presence of Fe₃O₄@SiO₂@Propyl-ANDSA catalyst at 100°C in H₂O/EtOH as the solvent (Scheme 27). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [151].

In 2012, Raju et al. has reported a facile synthesis of tetrazolo[1,5-*a*]pyrimidine derivatives from the reaction of aldehydes, 5-aminotetrazole, and ethylacetoacetate as acyclic 1,3 diketone in

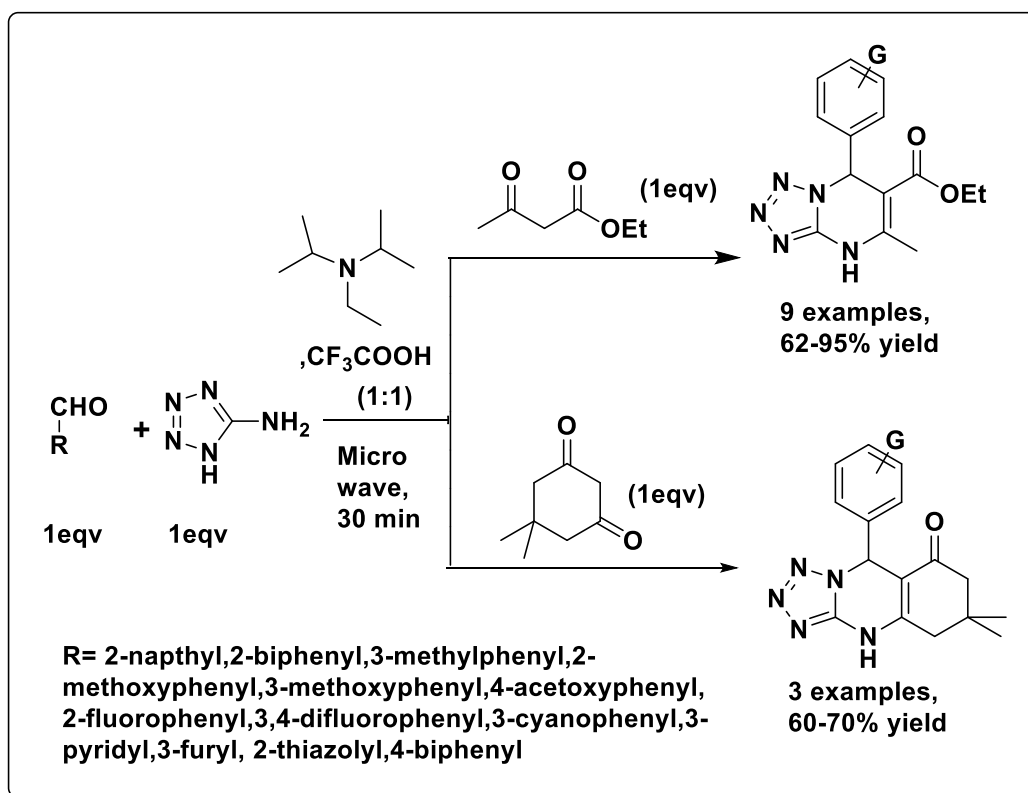
presence of a 1:1 mixture of N,N,N-triisopropylamine and CF₃COOH under microwave condition having reasonable yield (Scheme 28). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [152].

In 2010, Zeng et al. [153] reported a novel reaction for the synthesis of dihydro-tetrazolo[1,5-*a*]pyrimidines by the reaction of 5-aminotetrazole with aryl aldehydes and acetophenone catalyzed by iodine in presence of isopropyl alcohol under refluxing condition in one pot method (Scheme 29). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [153].

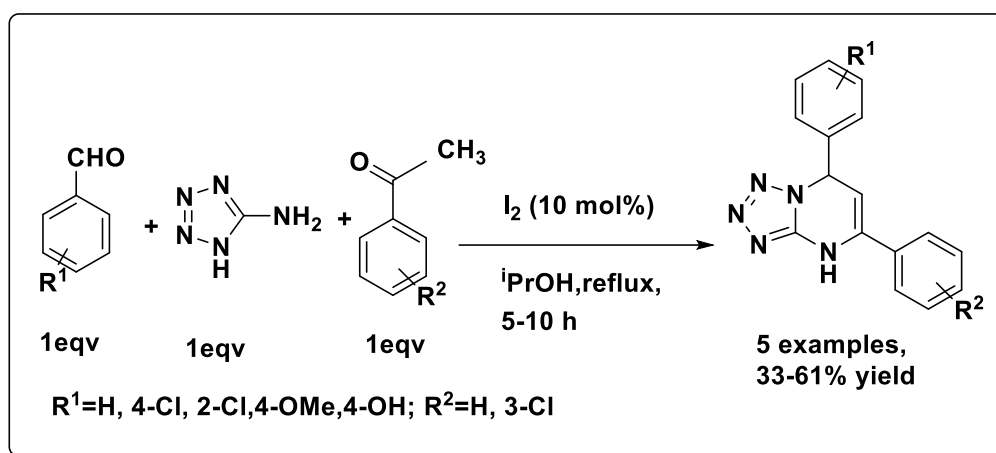
In 2010, Zeng et al. [154] also reported methods for the synthesis of dihydro-tetrazolo[1,5-*a*]pyrimidine and tetrahydro-tetrazolo[5,1-*b*]quinazolinone derivatives in one pot method in presence of iodine in isopropyl alcohol under reflux condition (Scheme 30). Then characterization of the products were done with ¹H and ¹³C-NMR by the authors in their work [154].



Scheme 27. A facile synthesis of tetrahydro-tetrazolo[1,5-*b*]quinazolines and tetrahydrobenzo[*h*]tetrazolo[5,1-*b*]quinazolines by Ghorbani-Vaghei et al. [151]



Scheme 28. A facile synthesis of tetrazolo[1,5-a]pyrimidine derivatives by Raju et al. [152]

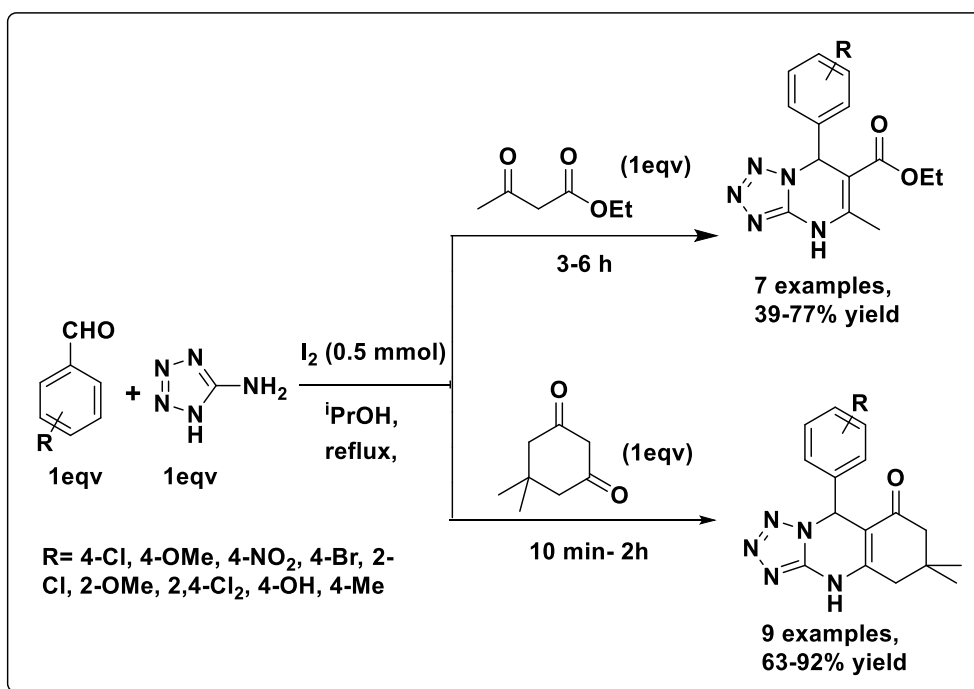


Scheme 29. A facile synthesis of dihydrotetrazolo[1,5-a]pyrimidines by Zeng et al. [153]

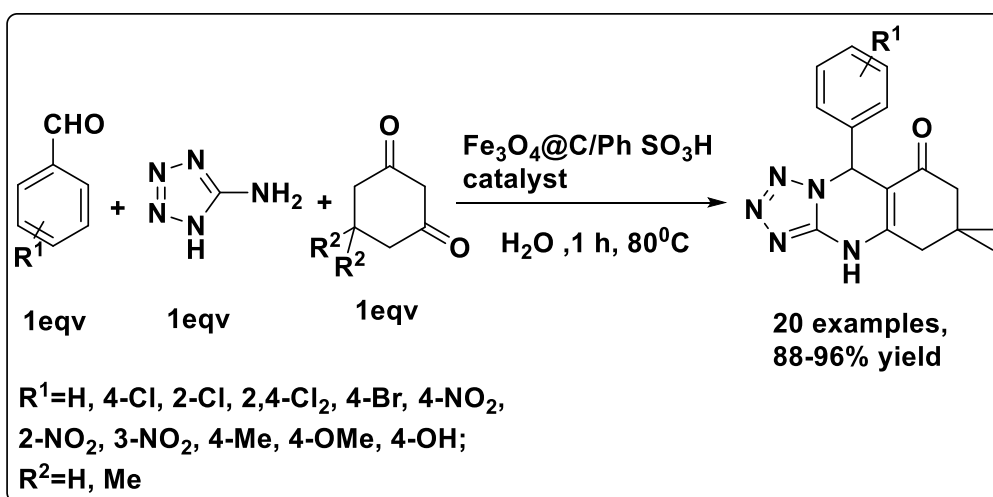
In 2021, Hassankhani et al. [155] reported a synthetic method for the synthesis of tetrahydrotetrazolo[5,1-b]quinazolinone derivatives by using synthesized Fe_3O_4 @meso-C immobilized with activated 4-aminobenzenesulfonic acid as catalyst in presence of water at 80°C with good yields (Scheme 31). Then characterization of the products were done with ^1H and ^{13}C -NMR by the authors in their work [155].

In 2017, Kour et al. reported facile synthetic methods for the synthesis of dihydrotetrazolo[1,5-a]pyrimidines and tetrahydrotetrazolo[1,5-a]quinazolinones via one pot multi-component method by the reaction of 5-aminotetrazole, aldehyde and active methylene compounds (e.g. acetophenone, alkylacetoacetates, dimedone) in presence of AlCl_3 catalyst under reflux condition in acetonitrile solvent with

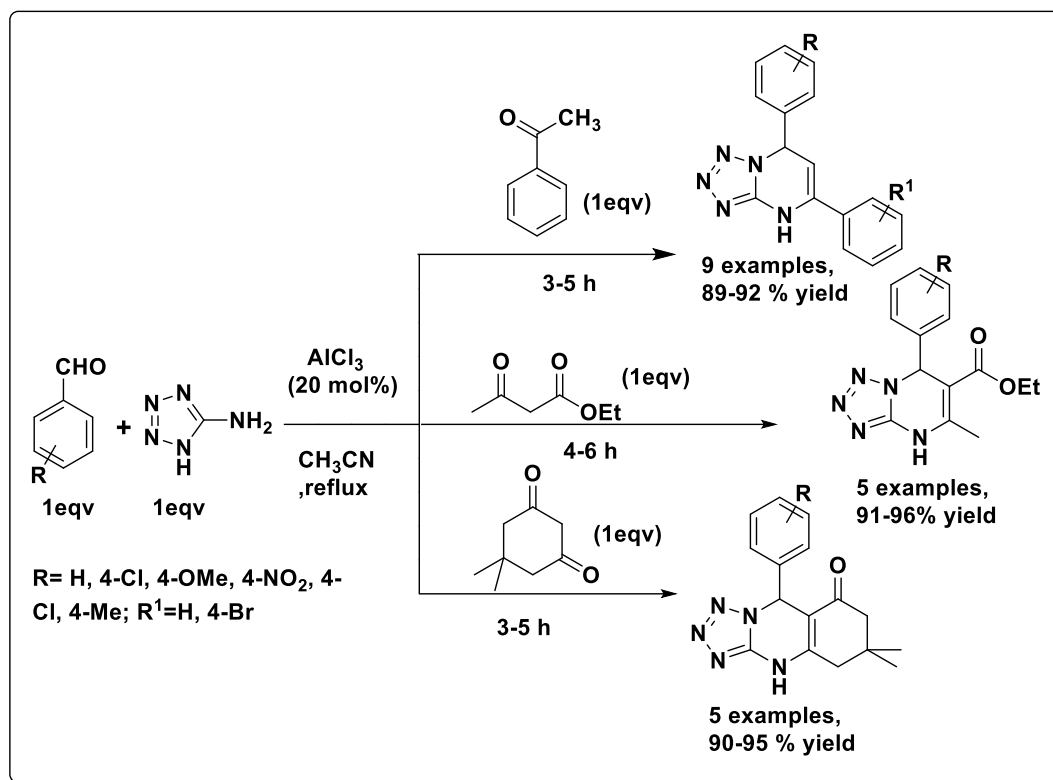
reasonable yields (Scheme 32). Then with ^1H and ^{13}C -NMR by the authors in their work characterization of the products were done [156].



Scheme 30. Synthesis of dihydrotetrazolo[1,5-a]pyrimidine and tetrahydrotetrazolo[5,1-b]quinazolinone derivatives by Zeng et al. [154]



Scheme 31. Synthesis of tetrahydrotetrazolo[5,1-b]quinazolinone derivatives by Hassankhani et al. [155]



Scheme 32. One pot synthesis of dihydrotetrazolo[1,5-a]pyrimidines and tetrahydrotetrazolo[1,5-a]quinazolinones by Kour et al. [156]

6. CONCLUSION

This review is an overview of new dimensions of one pot multi-component synthetic approaches in designing chromenes, coumarines, pyridopyrimidine and quinazoline scaffolds. This paper will play an important role in providing scientific ideas to synthesis a variety of heterocyclic moieties in a new synthetic way following the one-pot multi-component method.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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