

Chapter 5

Green Reactions Under Solvent-Free Conditions



Ghodsii Mohammadi Ziarani, Fatemeh Mohajer, and Razieh Moradi

1 Introduction

The green chemistry movement has promoted the industry to be much cleaner. As it was mentioned, the twelve principles of “green chemistry” were introduced in the 1990s by Paul Anastas and John Warner [1]. These points were implemented by chemists, academia, and even industries based on the synthetic strategy to minimize the production of toxic materials in different reaction conditions [1].

Green chemistry is an increasing agreement to accomplish organic reactions without damaging our environment and the most important way to achieve this goal is by conducting reactions under solvent-free conditions [2–6]. These trends are pretty more widespread due to its many advantages like cost, energy, and time-saving which create cleaner, safer, and more facile reactions. In this scenario, it is worthwhile to design reactions under favorable conditions in water or without any solvent [7].

In this area, there are several reactions to be highlighted through solvent-free approaches, which were accomplished in the presence of different catalysts and functionalized supports such as magnetic types [8, 9] mesoporous [10] graphene oxide [11–15], and other metal oxides [16–19].

Synthesis of various biologically active compounds [20] was reported under solvent-free conditions via different reagents such as pyrimidines [18, 21] which are significant heterocycles present in the core of various biologically active materials [22]. These compounds provided numerous medicinal properties such as antibacterial [23] antidiabetic [24] anticancer [21] antileishmanial [25] antiallergic [26]

G. Mohammadi Ziarani (✉) · F. Mohajer · R. Moradi
Department of Chemistry, Alzahra University, Vanak Square, P.O. Box 1993893973, Tehran, Iran
e-mail: gmohammadi@alzahra.ac.ir

F. Mohajer
e-mail: F.mohajer@alzahra.ac.ir

R. Moradi
e-mail: moradi3452@yahoo.com

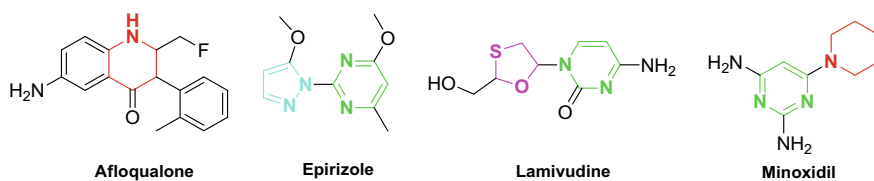


Fig. 1 Some biologically active compounds containing heterocyclic cores

antifungal [27] antipyretic [28] analgesic [29], and antidepressant [30]. Some of the important biologically active compounds such as afloqualone, eprizole, lamivudine, and minoxidil which are applied as anti-inflammatory [31] analgesic [31] anti-HIV [32] and antihypertensive [33] drugs are shown in Fig. 1. Several methods of green synthesis of pyrimidine derivatives under solvent-free conditions are reported.

Another important biologically active heterocyclic core is pyran, which is also synthesized under solvent-free conditions through various methods [34–37]. In this arena, pyrroles [38] quinazolinones [39, 40] benzodiazepines [41], and imidazoles [42, 43] also show biological activities and are synthesized under neat conditions.

A large number of reports dealing with the synthesis of compounds under solvent-free conditions are available. This chapter highlights and summarizes the recent (2016–2020) achievements in the green synthesis of important scaffolds under neat conditions and is classified as shown below [44].

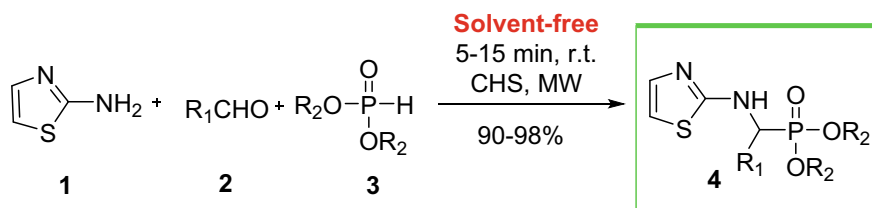
2 Synthesis of Different Scaffolds Under Solvent-Free Conditions

Here, the green chemistry conditions applied in the synthesis of different scaffolds are highlighted.

2.1 The Synthesis of α -Aminophosphonate Derivatives

The α -aminophosphonate derivatives **4**, which are essential from medicinal perspectives [45] are the structural analogues of amino acids wherein a carboxylic moiety is replaced by phosphonic group. Cirandur et al., in 2019, synthesized the anti-oxidant and anti-inflammatory α -aminophosphonate derivatives **4** through a one-pot, three-component coupling reaction from 2-aminothiazole **1** with numerous aldehydes **2** and dialkyl phosphites **3** using caffeine hydrogen sulfate (CHS) as a recyclable catalyst under microwave (MW) irradiation and solvent-free conditions at room temperature in excellent yields as shown in Scheme 1 [46].

Cirandur and co-workers [47] also reported various synthetic α -aminophosphonates **6** from 2-methoxy-5-trifluoromethyl aniline **5**, numerous

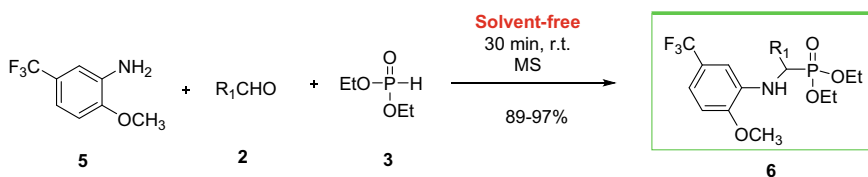


$\text{R}_1 = 4\text{-O}_2\text{NC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 3\text{-OCH}_3\text{-4-HOC}_6\text{H}_3, \text{furfuryl}$
 $\text{R}_2 = \text{CH}_3, \text{C}_2\text{H}_5$

Scheme 1 Synthesis of α -aminophosphonates under neat condition by Cirandur and co-workers

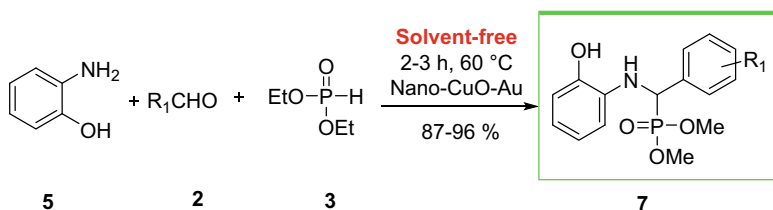
aldehyde derivatives **2**, and diethyl phosphite **3** in the presence of meglumine sulfate (MS) as an eco-friendly catalyst at room temperature under solvent-free conditions in high yields and short reaction time (Scheme 2).

In another report, Cirandur, and co-workers [48] accomplished the above reaction through Kabachnik–Fields method [49] in the presence of the nano-CuO–Au catalyst to yield α -amino phosphonates **7**, which act as α -glucosidase inhibitor and antioxidant, via three-component reaction of diverse aromatic aldehydes **2**, 2-aminophenol **5**, and dimethyl phosphite **3** in solvent-free conditions at 60 °C (Scheme 3).



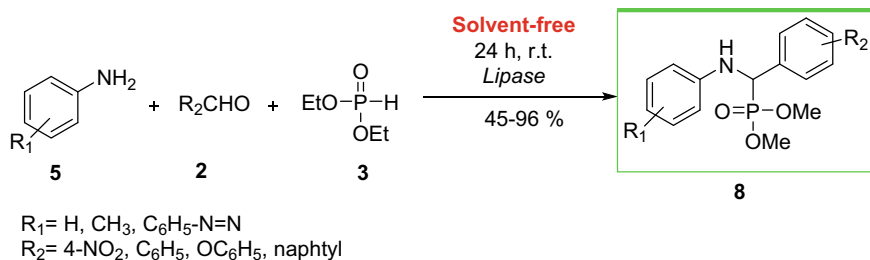
$\text{R}_1 = 4\text{-O}_2\text{NC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 3\text{-OCH}_3\text{-4-HOC}_6\text{H}_3, 4\text{-HOC}_6\text{H}_4$

Scheme 2 Synthesis of α -aminophosphonates under neat conditions by Cirandur and co-workers

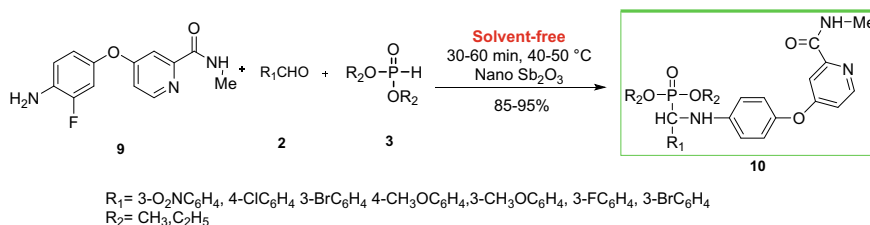


$\text{R}_1 = 4\text{-O}_2\text{NC}_6\text{H}_4, 2\text{-HO-3,4-(H}_3\text{CO)}_2\text{C}_6\text{H}_2, 4\text{-H}_3\text{COC}_6\text{H}_4, 3\text{-OCH}_3\text{-4-HO-4-HC}_3\text{C}_6\text{H}_2, 4\text{-ClC}_6\text{H}_4, 4\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4, 3,4\text{-(CH}_3\text{O)}_2\text{C}_6\text{H}_3, 4\text{-HCOC}_6\text{H}_4, 2\text{-F-5-BrC}_6\text{H}_3, 3\text{-Br-4-OH-5-CH}_3\text{OC}_6\text{H}_2$

Scheme 3 Synthesis of α -aminophosphonates via Kabachnik–Fields reaction under neat conditions by Cirandur and co-workers



Scheme 4 Synthesis of α -aminophosphonates using lipase under neat conditions by Aribi-Zouioueche and co-workers



Scheme 5 Synthesis of α -aminophosphonates under neat conditions using nano-Sb₂O₃ by Cirandur and co-workers

In another report, Aribi-Zouioueche and co-workers reacted different aromatic aldehydes **2**, diverse compounds of aniline **5**, and dimethyl phosphite **3** under solvent-free conditions at room temperature using *Candida Antarctica lipase* as a biocatalyst to produce α -aminophosphonate compounds **8** (Scheme 4) [50]. Also, Esmaeilpour and co-workers [51] disclosed the mentioned process in the presence of Fe₃O₄@SiO₂imid-PMAN without any solvent, at room temperature or by ultrasonic irradiation.

In 2019, Cirandur et al. [52] developed a process for the creation of cytotoxic α -aminophosphonates **10** by a simple and proficient one-pot three-component reaction of 3-(4-amino-3-fluorobenzyl)-*N*-methylbenzamide **9** with diverse aromatic aldehydes **2** and dialkyl phosphite **3** using nano-Sb₂O₃ catalyst under solvent-free conditions in high yields at 40–50 °C as shown in Scheme 5.

2.2 The Synthesis of Pyrimidine Derivatives

In 2019, Esnaashari et al. [53] outlined the preparation of pyrimidines through multi-component reactions using triethylenediamine or imidazole Brønsted acidic, ionic liquid-supported Zr metal-organic structure (TEDA/IMIZ-BAIL@UiO-66). The dihydropyrido[2,3-*d*]pyrimidine compounds **13** were yielded from the reaction

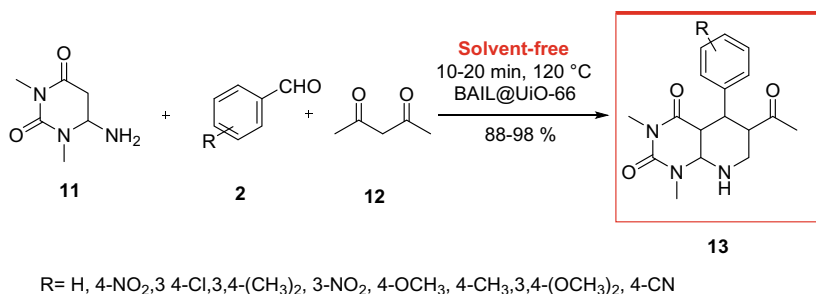
of 6-amino-1,3-dimethyl uracil **11**, several aromatic aldehydes **2**, and acetylacetone **12** in solvent-free conditions (Scheme 6).

The metal–organic structure called MIL-53(Fe) was used as a catalyst to provide the pyrimido[4,5-*d*]pyrimidine compounds **15** in one-step three-component reaction from isothiocyanate **14**, aromatic aldehydes **2**, and 6-aminouracil or *N,N*-dimethyl-6-aminouracil **11** in solvent-free condition at 110 °C in high yield. The other valuable advantage of this study is the recoverable nature of the catalyst supporting green chemistry (Scheme 7) [54].

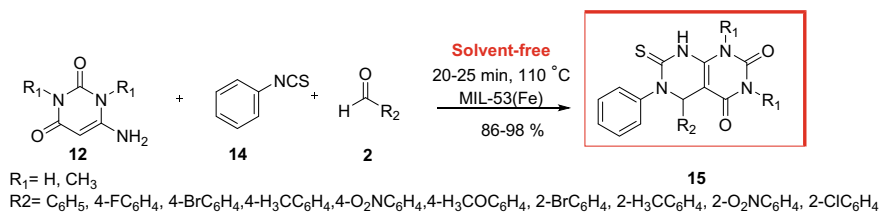
Foroughifar and co-workers [55] reported the synthesis of dihydropyrimidine derivatives **17** as potent antibacterial agents from thiourea or urea **16**, acetylacetone **12**, and different aryl aldehydes **2** under solvent-free conditions in the presence of the $\text{Mn}_{0.5}\text{Fe}_{0.25}\text{Ca}_{0.25}\text{Fe}_2\text{O}_4$ @starch@aspartic acid magnetic nanoparticles ($\text{MnFeCaFe}_2\text{O}_4$ @starch@aspartic acid MNPs) as a catalyst. The merits of this reaction are easy workup, high-yield, and easy separation of catalyst (Scheme 8).

In another study, Bordoloi and co-workers [56] in 2019 demonstrated the synthesis of dihydropyrimidine derivatives **20** from various aldehydes **2**, the benzil **18**, and ammonium acetate **19** under the solvent-free condition at room temperature during 6–8 h in the presence of the water-extractable pomelo (WEP) as citrus fruit (Scheme 9).

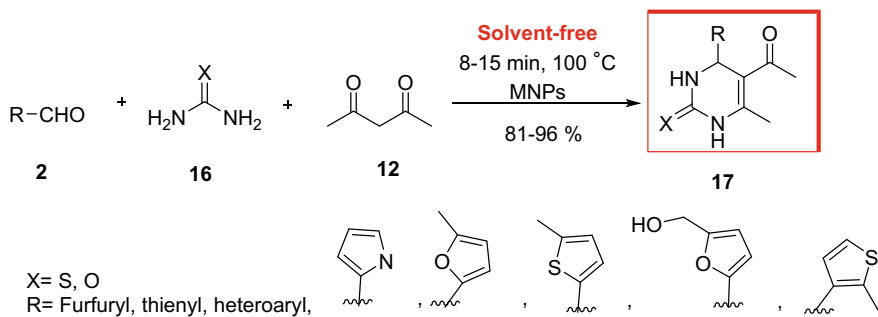
Moradi and co-workers [57], in 2019, demonstrated the synthesis of benzochromenopyrimidines **23** from aldehydes **2**, β -naphthol **21**, and barbituric acids **22** by a green approach without any solvent through aminated multi-walled carbon



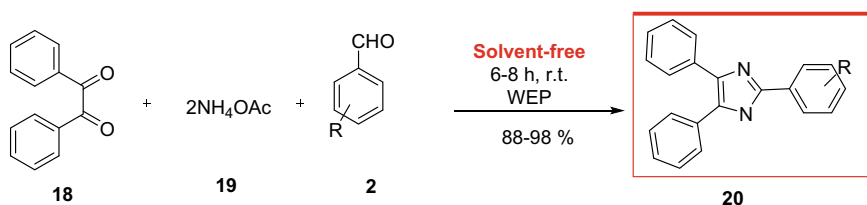
Scheme 6 Synthesis of dihydropyrimidines under neat conditions



Scheme 7 Synthesis of pyrimido[4,5-*d*]pyrimidines under neat condition by Shirirni and co-workers



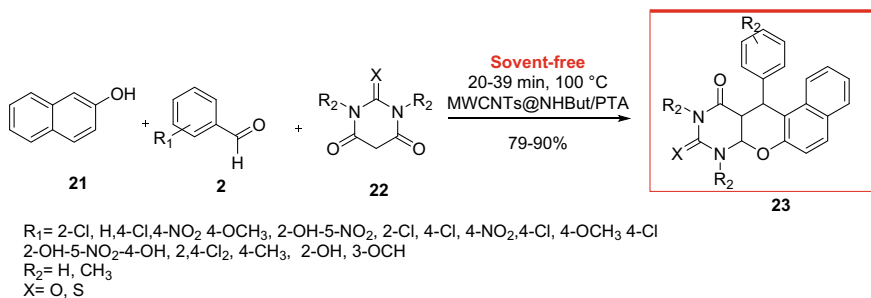
Scheme 8 Synthesis of dihydropyrimidines under neat conditions by Foroughifar and co-workers



Scheme 9 Synthesis of dihydropyrimidines under neat conditions by Bordoloi and co-workers

nanotubes, which were functionalized by phosphotungstic acid and tungsten called (MWCNTs@NHBut/PTA) (Scheme 10).

Saleh and co-workers reported the synthesis of fused pyrimidine compounds **26** from enaminone **24** and various heterocyclic amines **25** under solvent-free conditions in the presence of the nano-like magnesium oxide (MgO) using ball-mill process. The merits of the reaction are easy workup, high-yield, and reusable catalyst. It is



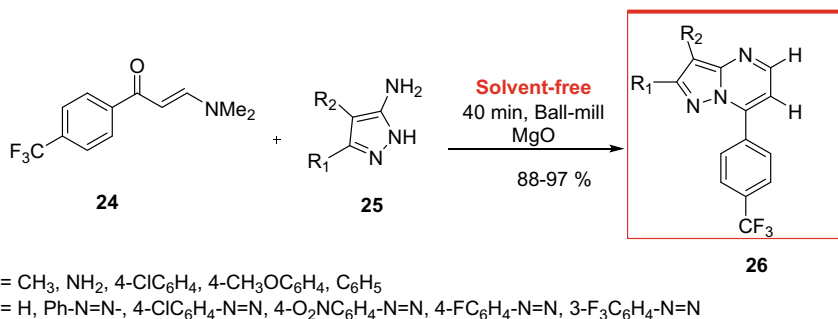
Scheme 10 Synthesis of benzochromenopyrimidines under neat conditions by Moradi and co-workers

important to mention that the aromatic aldehyde with electron-withdrawing groups reacted faster in comparison with electron-releasing groups (Scheme 11) [58].

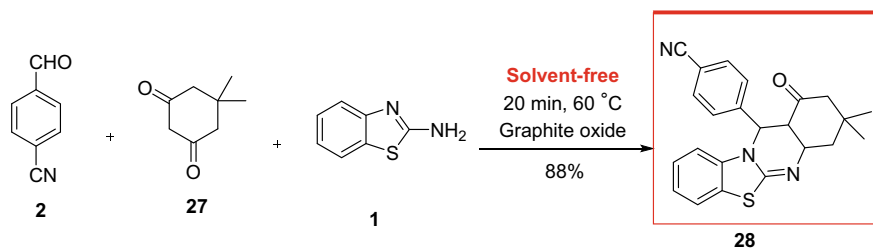
A series of biologically active pyrimidine derivatives were successfully synthesized by Pal et al. [22] using graphite oxide as a green metal-free carbon catalyst (Scheme 12). In this method, cyanobenzaldehyde **2**, dimedone **27**, and 2-aminobenzothiazole **1** were reacted in the presence of graphite oxide under solvent-free reaction conditions (SFRC) at 60 °C for 20 min to provide the product **28** in 88% yield.

The synthesis of the pyrimidine derivatives **30** and **31** was developed through one-step multi-component reactions from 6-amino-1,3-dimethyl uracil **11**, 3,4-methylenedioxyphenol **29** or naphthalen-2-ol **21** and the suitable aryl aldehyde **2** in solvent-free conditions in the presence of SMA/Py/ZnO, which was prepared by the reaction of poly(styrene-co-maleic anhydride) with 3-aminopyridine and zinc oxide (Scheme 13) [59].

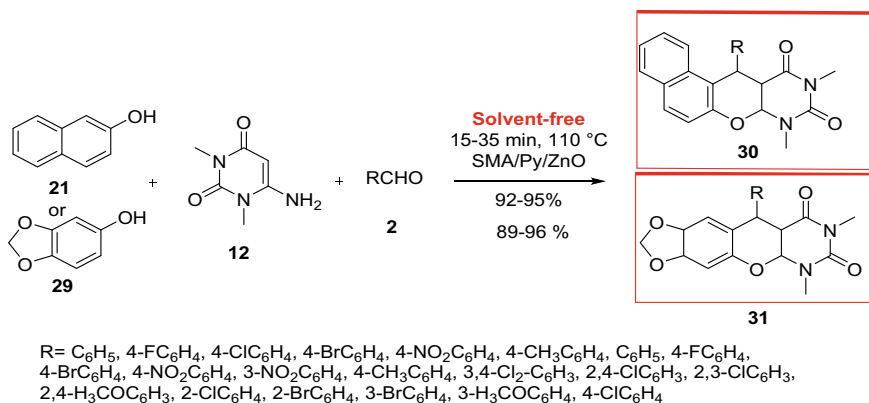
Pyrimidine scaffold was fused with triazole and pyrazole via a three-component reaction between 3-methyl-1-phenyl-2-pyrazolin-5-one **33**, various aromatic aldehydes **2**, and 3-amino-1,2,4-triazole **32** or pyrazole to yield the 4-aryl-substituted dihydropyrimidine derivatives **34** under solvent-free condition using tungstate sulfuric acid (TSA) as the green catalyst (Scheme 14) [60].



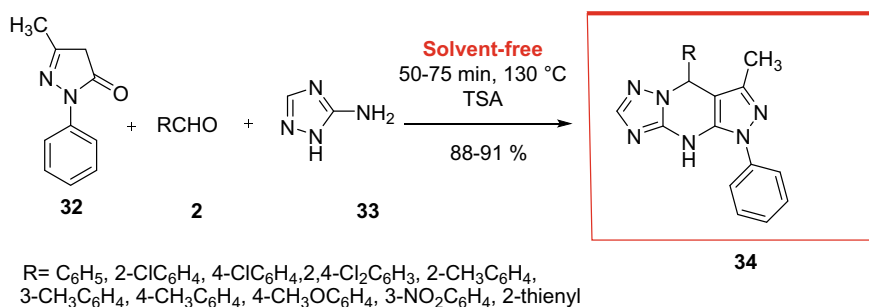
Scheme 11 Synthesis of fused pyrimidines under neat conditions by Saleh and co-workers



Scheme 12 Synthesis of fused pyrimidines under neat conditions by Pal and co-workers



Scheme 13 Synthesis of chromeno[2,3-*d*]pyrimidin-2(1H)-ones under neat conditions by Heravi and co-workers

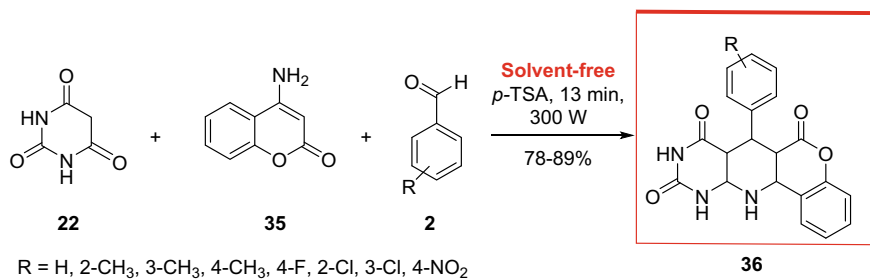


Scheme 14 Synthesis of fused dihydropyrimidines under neat conditions by Farahi and co-workers

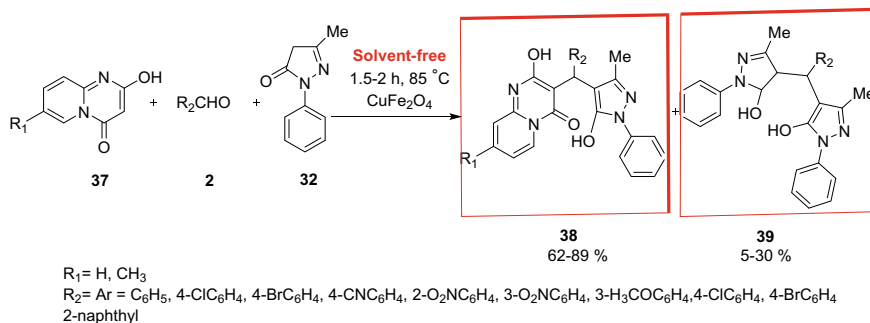
This attempt reported the synthesis of the pyrimidine-triones **36** from various benzaldehydes **2**, barbituric acid **22**, and 4-amino-2*H*-chromene-2-one **35** using *p*-toluenesulfonic acid as catalyst under microwave irradiation and solvent-free conditions in high yields (Scheme 15) [61].

The heterogeneous copper ferrite (CuFe₂O₄) was used as a nanocatalyst to synthesize benzylpyrazolyl pyrido[1,2-*a*]pyrimidine derivatives **38** and pyrazole **39** through a three-component reactions from various aryl aldehydes **2**, 2-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidine-4-ones **37**, and 3-methyl-1-phenyl-1*H*-pyrazol-5-one **32** in solvent-free conditions, and here, the catalyst could be easily removed magnetically from the mixture of reaction (Scheme 16) [62].

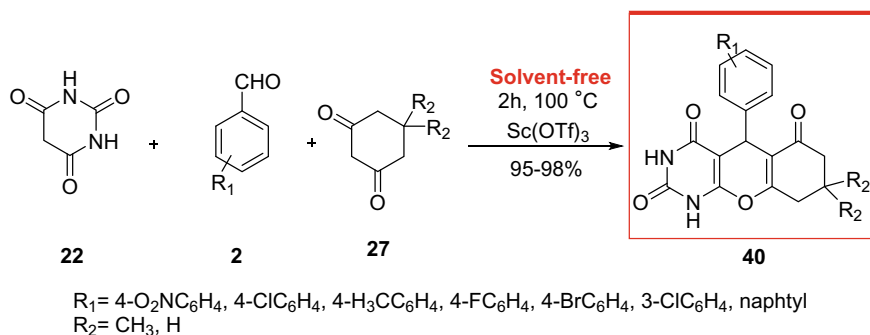
Through one-pot multi-component reactions, chromeno[2,3-*d*]pyrimidinetrione derivatives **40** were yielded from numerous aromatic aldehydes **2**, dimedone **27**, or cyclohexane-1,3-dione and barbituric acid **22** in the presence of Sc(OTf)₃ as catalyst under solvent-free condition at 100° C for 2 h (Scheme 17) [63].



Scheme 15 Synthesis of pyrimidines under neat conditions by Foroumadi and co-workers

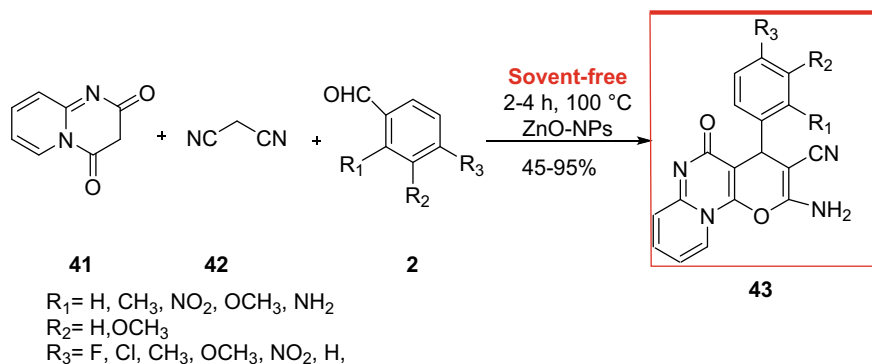


Scheme 16 Synthesis of pyrimidines under neat conditions by Esmaeili and co-workers



Scheme 17 Synthesis of chromeno[2,3-*d*]pyrimidinetriones under neat conditions by Kumari and co-workers

Pyrimidine-3-carbonitriles **43** were produced through multi-component condensation reaction of various aromatic aldehydes **2**, 3*H*-pyrido[1,2-*a*]pyrimidine-2,4-dione **41**, and malononitrile **42** using ZnO nanoparticles as suitable catalyst under solvent-free conditions (Scheme 18) [64].

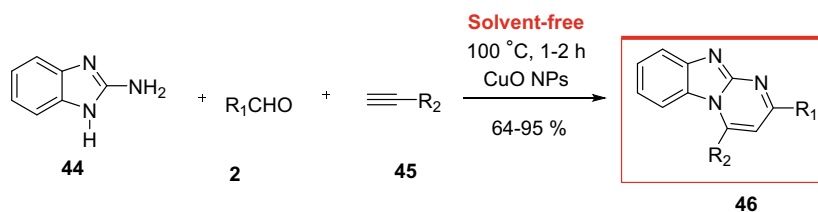


Scheme 18 Synthesis of pyranopyridopyrimidines under neat conditions by Mahmoud and co-workers

In 2018, Rawat and co-workers [18] synthesized the biologically active fused imidazo[1,2-*a*]pyrimidines **46** through coupling reaction involving 2-aminobenzimidazole **44**, aldehyde **2**, and terminal alkyne **45** in the presence of copper oxide nanoparticles as catalyst under solvent-free condition (Scheme 19).

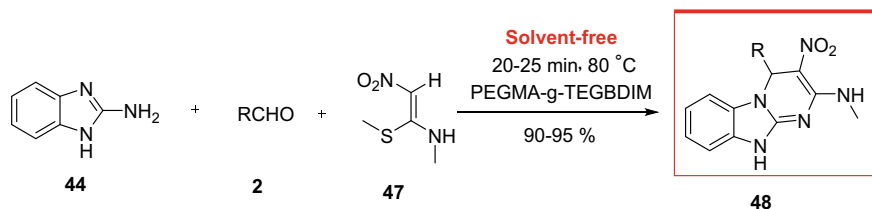
In a similar study, Kim and co-workers [65] outlined a process to synthesize pyrimidine amine scaffolds **48** from 1*H*-benzo[*d*]imidazol-2-amine **44** and (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine **47** with various aldehydes **2** under solvent-free condition at 80 °C using catalytic amounts of PEGMA-*g*-TEGBDIM (Scheme 20).

A series of pyrazolopyranopyrimidines **51** were obtained from four-component reaction of different aromatic aldehydes **2**, substituted barbituric acids **22**, hydrazine monohydrate **49**, and ethyl acetoacetate **50** in three methods (Method A: using SB-DABCO⁺Cl⁻; Method B: using SB-DBU⁺Cl⁻; and Method C: using NSB-DBU⁺Cl⁻) under solvent-free conditions (Scheme 21) [66].



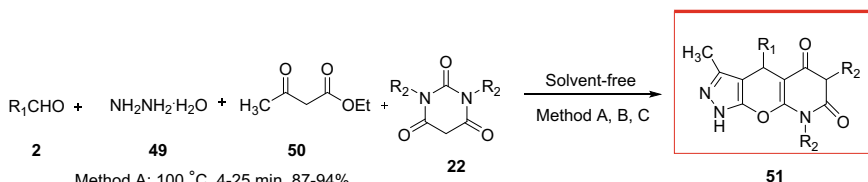
$R_1 = \text{C}_6\text{H}_5, 4\text{-ClC}_6\text{H}_4, 4\text{-O}_2\text{NC}_6\text{H}_4, 4\text{F-C}_6\text{H}_4, 4\text{-H}_3\text{CC}_6\text{H}_4, \text{thienyl, 3-pyridyl, methylenedioxyphenyl}$
 $R_2 = \text{C}_6\text{H}_5, \text{CH}_3\text{OC}_6\text{H}_4, 4\text{F-C}_6\text{H}_4, 4\text{-H}_3\text{CC}_6\text{H}_4$

Scheme 19 Synthesis of imidazo[1,2-*a*] pyrimidines under neat conditions by Rawat and co-workers



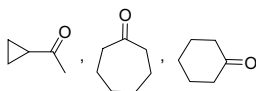
R = 4-BrC₆H₄, 4-ClC₆H₄, 4-FC₆H₄, 4H₃CC₆H₄, 4-CH₃OC₆H₅, 4-HOC₆H₄, 3-BrC₆H₄, 3-ClC₆H₄, 3-FC₆H₄, 3-CH₃C₆H₄, 2-BrC₆H₄, 2-ClC₆H₄, 2-FC₆H₄, 2-H₃CC₆H₄, 2-HOC₆H₄, pyridyl, thionyl, pyridyl, 2,3,4-(CH₃O)₃C₆H₂

Scheme 20 Synthesis of pyrimidine amines under neat conditions by Kim and co-workers



Method A: 100 °C, 4-25 min, 87-94%
Method B: 100 °C, 3-32 min, 87-95%
Method C: 100 °C, 3-30 min, 83-95%

R₁ = 4-H₃CC₆H₄, 3-O₂NC₆H₄, 4-O₂NC₆H₄, 4-ClC₆H₄, 2-CH₃OC₆H₄, 4-ClC₆H₄, 2-CH₃OC₆H₄, 3-ClC₆H₄, 2-ClC₆H₄, 3(CH₃O)₃C₆H₂, 3-O₂NC₆H₄, 4-CH₃OC₆H₄, 3-CH₃OC₆H₄, 2-HOC₆H₄,



R₂ = CH₃, H

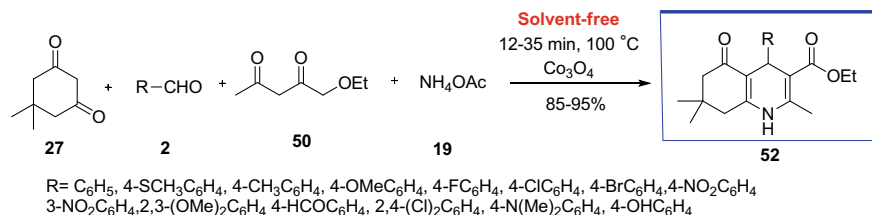
Scheme 21 Synthesis of pyrazolopyranopyrimidines under neat conditions by Shaterian and co-workers

2.3 The Synthesis of the Pyran Derivatives

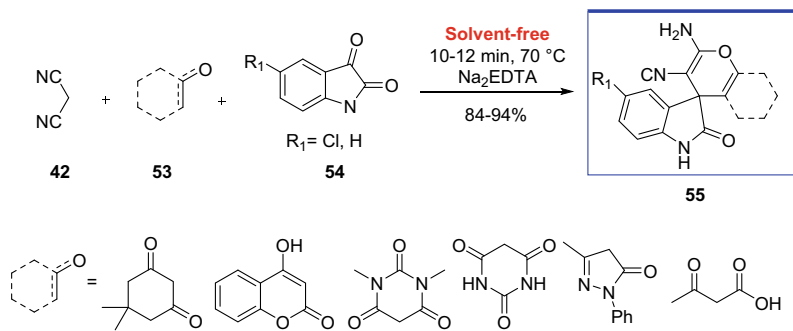
Ghasemzadeh and co-workers [36] synthesized tetrahydrobenzopyran derivatives **52** from different aromatic aldehydes **2**, dimedone **27**, ammonium acetate **19**, and ethyl acetoacetate **50** through a four-component coupling reaction in the presence of Co₃O₄ as nanocatalyst under solvent-free condition at 100 °C (Scheme 22).

Maghsoodlou and co-workers [37] reported the synthesis of the spiro-2-amino-4H-pyran derivatives **55** through a one-step three-component condensation reaction from malononitrile **45**, CH-acids **53**, and isatin **54** using Na₂EDTA as catalyst under solvent-free conditions at 70 °C (Scheme 23).

Siddiqui and co-workers [67] performed the synthesis of pyranopyrazole moieties **58** in the presence of the functionalized mesoporous silica and NdCl₃ called Nd-SM at 70 °C under solvent-free condition by Knoevenagel condensation [68] between various aromatic aldehydes **2** and ethyl cyanoacetate **56** [69]. The resulting



Scheme 22 Synthesis of pyrans under neat conditions by Ghasemzadeh and co-workers



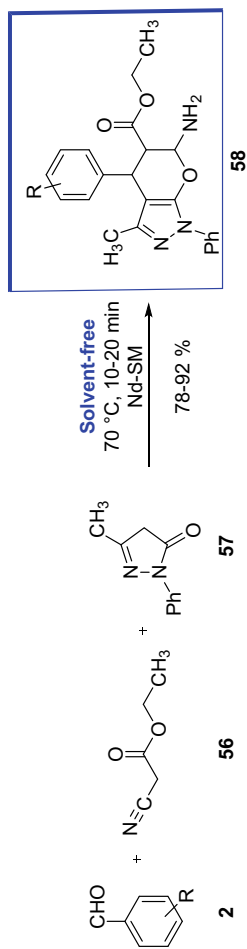
Scheme 23 Synthesis of spiro-2-amino-4H-pyrans under neat conditions by Maghsoodlou and co-workers

product reacts with substituted pyrazoline **57** through cyclization reaction to provide pyranopyrazole scaffolds (Scheme 24).

2.4 The Synthesis of the Pyrrole Derivatives

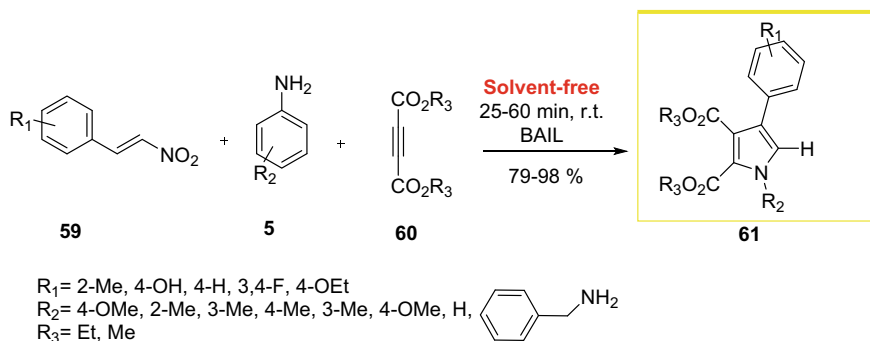
Pyrroles are one of the most significant moieties found in many natural compounds and biologically activate compounds [70]. Atar and co-workers disclosed the synthesis of tetrasubstituted pyrroles **61** which by the reaction of various types of amines **5**, substituted dialkyl acetylenedicarboxylates **60**, and β -nitrostyrene **59** in presence of the imidazolium Brønsted acidic ionic liquid as a metal-free catalyst under solvent-free condition. In this attempt, functionalized tetrasubstituted pyrroles were produced in acceptable yields (Scheme 25) [71].

After finding optimized conditions, nitromethane **62**, various aryl aldehydes **2**, 1,3-dicarbonyl derivatives **51**, and amine **5** were treated at room temperature through a one-step four-component reaction to afford polysubstituted pyrrole scaffolds **63** using functionalized Fe_3O_4 as the magnetic nanoparticle (Scheme 26) [72]. In the same study, the biologically active substituted pyrrole derivatives were formed from various ethyl acetoacetate, nitromethane, different benzaldehydes, and a variety of

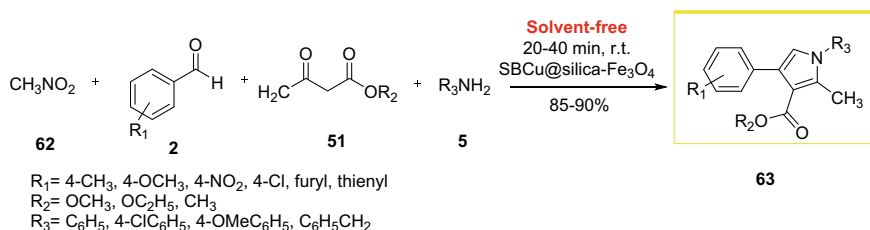


R = 4-Br, 3-Br, 3-OCH₃, thieryl, 3-NO₂, H, 4-OCH₃

Scheme 24 Synthesis of pyranopyrazoles under solvent-free conditions by Siddiqui and co-workers



Scheme 25 Synthesis of pyrroles under neat conditions by Atar and co-workers



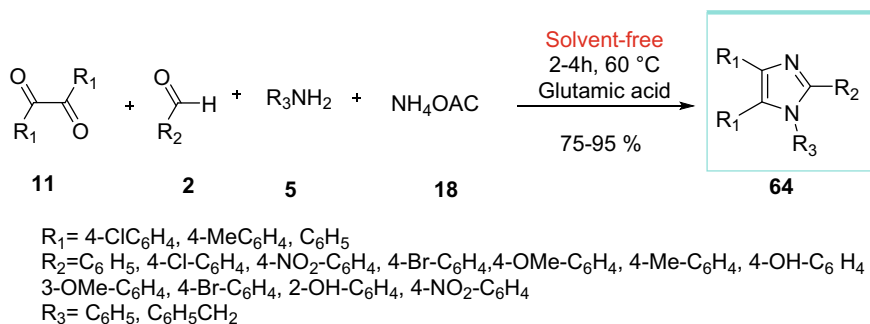
Scheme 26 Synthesis of pyrroles under neat conditions by Salehzadeh and co-workers

anilines in the presence of Cu@imine/ Fe_3O_4 MNPs at 100°C under solvent-free conditions in 15-25 min in 89–97% yield [38].

2.5 The Synthesis of the Imidazole Derivatives

Imidazole is a beneficial heterocyclic moiety found in many synthetic or natural compounds that attracted much attention through diverse and multi-purpose biological activity [73]. These properties marked them as valuable scaffolds for further study. Thus, Khandan-Barani and co-workers [74] designed the synthesis of 1,2,4,5-tetrasubstituted imidazoles **64** through multi-component reaction between various aryl aldehydes **2**, 1,2-dicarbonyl derivatives **11**, different amines **2**, and ammonium acetate **18** using glutamic acid as catalyst under solvent-free condition at 60°C during 2–4 h in acceptable yields (Scheme 27).

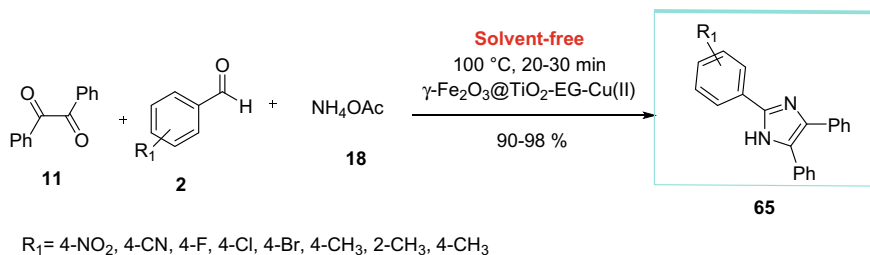
In a study, the functionalized catalyst called $\gamma\text{-Fe}_2\text{O}_3@\text{TiO}_2$ ($g\text{-Fe}_2\text{O}_3@\text{TiO}_2\text{-EG-Cu(II)}$) yielded the tetrasubstituted imidazole scaffolds **65** from different types of aldehydes **2**, benzil **11**, and ammonium acetate **18** and substituted amines **5** under solvent-free conditions at 100°C [75]. The mentioned catalyst was made



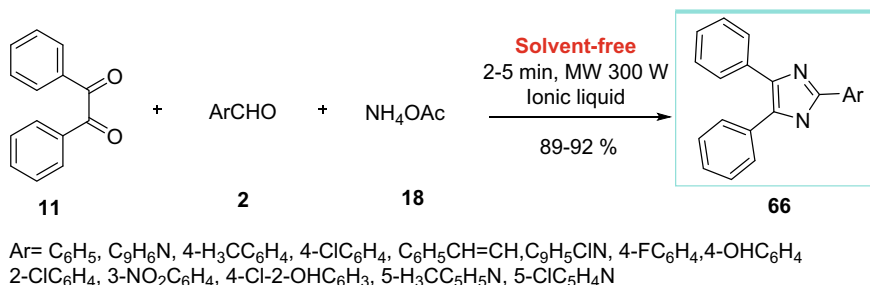
Scheme 27 Synthesis of imidazoles under neat conditions by Khandan-Barani and co-workers

up of $\gamma\text{-Fe}_2\text{O}_3$ core and TiO_2 as a shell which was functionalized with guanidinated epibromohydrin and Cu (II) (Scheme 28).

In 2018, Sakram's group [42] developed a process by the condensation reaction of the benzil **11**, different aldehydes **2**, and ammonium acetate **18** under solvent-free condition to yield 2,4,5-trisubstituted imidazoles **66**. The best result was obtained at 300 W within 2–4 min in the presence of the poly(4-vinylpyridinium) bromide APVPB as an ionic liquid catalyst (Scheme 29).



Scheme 28 Synthesis of imidazoles under neat conditions by Nejatianfar and co-workers



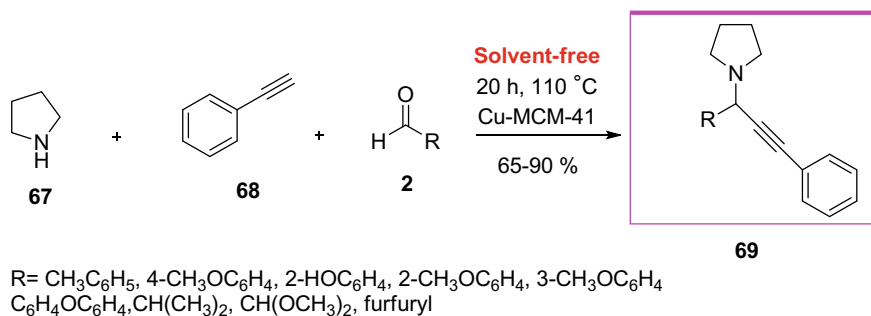
Scheme 29 Synthesis of imidazoles by MW irradiation under neat conditions by Sakram and co-workers

2.6 The Synthesis of the Propargylamine Derivatives

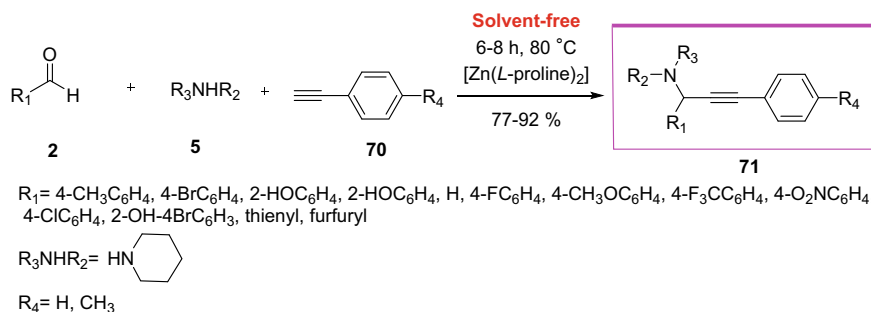
Negrón-Silva and co-workers [76] demonstrated the synthesis of diastereoselective propargylamine **69** using Cu functionalized mesoporous catalyst called Cu-MCM-41 [77]. The pyrrolidine **67**, phenylacetylene **68**, and different aldehydes **2** reacted through C–H activation to obtain various propargylamines using Cu-MCM-41 (Scheme 30).

Layek and co-workers [78] disclosed the synthesis of propargylamines **71** through one-pot multi-component reaction of different types of aldehydes **2** with various alkynes **70** and amines **5** using $[Zn(L\text{-proline})_2]$ as the catalyst (Scheme 31).

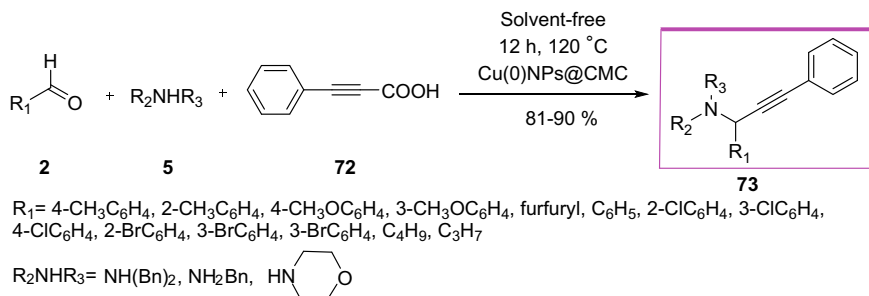
Zhang and co-workers [79] reported the synthesis of various propargylamines **73** using Cu(0)NPs@CMC as copper nanoparticle catalyst assembled on carboxymethylcellulose in solvent-free condition at 120 °C. To simplify the reaction process, several amines **5** were reacted with phenylpropionic acid **72** and various aldehydes **2** in presence of the catalyst under neat conditions (Scheme 32).



Scheme 30 Synthesis of propargylamines under neat conditions by Negrón-Silva and co-workers



Scheme 31 Synthesis of imidazoles by under neat conditions by Layek and co-workers



Scheme 32 Synthesis of propargylamines under neat conditions by Zhang and co-workers

3 Conclusion

The synthesis of different compounds through green reactions under solvent-free conditions is highly demanding in chemistry due to the great concern on our environment. There has been a great interest in developing environmentally benign reactions using green solvents and protocols, which lead to a series of reports using solvent-free green chemistry. A significant merit of this reaction is that many of these methods are simple and well organized. It is seen that α -amino phosphonates, pyrimidines, pyrans, pyrroles, imidazoles, and propargylamines are easily accessible by green chemistry process. The many successful models reported are applied in medicinal chemistry, drug discovery, organic synthesis, and material science. There is a future study to synthesis vast amounts of reactions in green chemistry under solvent-free conditions which reduce the cost of designing reactions.

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