CHAPTER 1

A brief review on synthesis of heterocyclic compounds via multi-component reaction catalyzed by surface coated metal nanoparticles and graphite oxide
1.1. Introduction:

Sustainable chemistry commonly known as ‘Green chemistry’ is a philosophy of modern day chemical engineering and research which deals with the development of environment friendly procedures\(^1\) for synthesizing biologically significant compounds. In order to guide the practice of green chemistry, Paul Anastas and John C. Warner in the year 1998 proposed twelve principles, which address various ways to diminish environmental pollution and also lay emphasis on research priorities for designing greener technologies.\(^2\) Following these principles, developing newer strategies which relates to the formation and cleavage of chemical bonds symbolize the central topic in modern day organic synthesis.

Scientists around the world are recently focusing on the synthesis of efficient cascades having high structural diversities with least number of steps and without liberating harmful wastes. The best way to achieve this is through one-pot multi-component (MCR) reaction. It is a process in which three or more components react together in a sequential manner to form corresponding product with high atom economy. MCR allow creation of several new bonds in a single step and offer notable advantages like operational simplicity, convergence, simple extraction and purification of desired product etc. One-pot MCR cuts down the reaction time and gives higher yields than the multi-step syntheses, thereby reducing the use of energy and manpower.\(^3\) Because of these above mentioned properties MCRs are applied for the synthesis of diverse drug like molecules with various structural diversities.\(^4\)

Recently field of catalysis has emerged as heart of many chemical protocols because it lowers the activation energy and makes the reaction feasible. Application of clean and reusable catalytic material is one of the principles of green chemistry.\(^5\) So, in this connection search for sustainable, environmentally benign and efficiently reusable catalytic system has become vital. Catalysts can be broadly classified in to two categories viz. homogeneous catalysts and heterogeneous catalysts. Homogeneous catalysts, the catalysts which are in same phase to that of reactants possess many advantages like high turnover number (TON), high entantio-, chemo- and regioselectivity.\(^6\) Although this catalytic system because of the above mentioned superiorities are widely used in various industries but there are certain disadvantages like difficulties in isolation, contamination in final products which makes its
application extremely cumbersome. Heterogeneous catalysts (in different phase to that of reactant) on the other hand can be easily recycled from the reaction mixture and can be re-utilised easily in subsequent reactions but their active sites are not easily accessible. In this sense, heterogenization of homogenous catalyst on solid supports has received utmost importance. Surface modified nano-catalyst which not only provides high catalytic activity (like homogeneous catalyst) but also possesses easy recyclability (like heterogeneous catalyst) is a desirable catalytic system for this purpose.

Nanoparticles have gained lot of attentions recently as catalysts because of its high surface to volume ratio. But, when size of the active site gets reduced to nano range its surface energy increases. Because of this effect, particles get aggregated into small clusters and its catalytic activity decreases. In order to prevent this agglomeration, coating the surface of nanoparticles with appropriate catalytic systems is used. Surface coating technique with active homogeneous counterparts not only increases stability of the nano-catalyst but also increases its catalytic activity because of the presence of various active catalytic site on its surface. Moreover, when size of a particle gets reduced to nano range it becomes very difficult to recycle them by conventional methods like filtration. For overcoming this issue, application of magnetic NPs becomes more viable. Magnetic NPs because of its insoluble and high paramagnetic nature, acts as a perfect solid support for enabling easy and efficient separation of catalyst from the reaction mixture by using an external magnetic field.

Just like nanoparticles, graphite oxide an oxidised form of graphene (allotrope of carbon) gained exceptional interest in the field of catalysis because of its high thermal, mechanical, optical and electronic properties, low cost, bio-compatibility and higher surface area. Moreover, surface of this metal free heterogeneous carbocatalyst consists of various functional groups like epoxy (-O-), carboxyl (-COOH) and hydroxyl (-OH) which accounts for its high oxidising and acidic property. Further, easy recyclability of graphite oxide from the reaction mixture by centrifugation and its re-application in subsequent reactions without much decrease in catalytic activities are the added advantages of this carbocatalyst.

Heterocycles are an important class of compounds which are widely distributed in nature. They also make up more than 50% of the known organic compounds and
are present in variety of drugs, vitamins, agrochemicals and veterinary products.\textsuperscript{17} Heterocyclic compounds like pyrimidines, pyrans, quinazolinones and phthalazine dione/ trione derivatives possess various medicinal and biological activities like anti-cancer, anti-microbial, anti-tumour, anti-malarial, anti-HIV etc.\textsuperscript{18-21} Moreover, some of these heterocycles are of considerable interest because of their ability to function as important intermediates for the synthesis of other vital heterocycles.\textsuperscript{22}

Because of these above cited reasons, research groups throughout the globe recently, is focussing on the application of surface coated metal NPs and other heterogeneous catalysts like graphite oxide for synthesis of biologically relevant heterocyclic compounds by one-pot MCR. Even though application of surface coated magnetic NPs are widely studied but application of metal free carbocatalyst (graphite oxide) in MCR is a very new research avenue. Some of these research protocols which deal with the one-pot multi-component synthesis of heterocyclic compounds catalyzed by surface coated metal NPs and graphite oxide are listed below.

J. Safari \textit{et. al.}\textsuperscript{23} reported rapid synthesis of amidomalkyl naphthols (4) by condensation of aldehydes (1), $\beta$-naphthol (2), and amides (3). For this one-pot MCR the research group applied sulfuric acid functionalized magnetic nano-Fe$_3$O$_4$ as a reusable catalyst. After characterization of solid acid catalyst by FT-IR, XRD, SEM, TGA and VSM, authors carried out systematic standardization for various reaction parameters in order set up perfect experimental condition. 0.02 g of sulfuric acid functionalized magnetic nano-Fe$_3$O$_4$ (MNPs-SO$_3$H) was found to be good enough to catalyze the reaction under SFRC at 100 $^\circ$C (the optimized condition) (Scheme 1). Reaction went smoothly with both aliphatic and aromatic aldehydes and effect of electron withdrawing and electron donating group was insignificant on the yield of the desired product. Catalyst was recycled by using external magnetic field and reused in six consecutive runs without much decrease in catalytic activity.

\begin{center}
\textbf{Scheme 1}
\end{center}
F. Alonso and his team\textsuperscript{24} reported a multi-component click synthesis of 1,2,3-triazoles (8, 9) using epoxides (5), azides (6) and acetylenes (7) in water at 70 °C, catalyzed by copper nanoparticles on activated carbon (Scheme 2). Procedure for the preparation of catalyst as reported by the research group is an easy one and catalyst showed excellent catalytic activity at low copper loading (0.5 mol %). The stereo and regiochemistry of the said reaction was established on the basis of X-ray crystallographic technique. For unmistakable determination of regiochemistry of the process an NMR experiment was carried out. A mechanistic study was carried out which revealed participation of copper (I) acetylides and triazolides as reaction intermediates.

\begin{equation}
\text{R}_1\text{O} + \text{NaN}_3 + \text{R}_2\text{Cu NPs/C (0.5 mol %) H}_2\text{O, 70 °C}}
\end{equation}

Scheme 2

A magnetically separable nano-Fe\textsubscript{3}O\textsubscript{4}@mesoporous SBA-15 catalyst with high surface area was synthesized by J. Mondal and co-workers\textsuperscript{25} by chemical conjugation of nano-Fe\textsubscript{3}O\textsubscript{4} with functionalized SBA-15. Nano-Fe\textsubscript{3}O\textsubscript{4}@mesoporous SBA-15 containing amino group and carboxyl group at its surface was synthesized via thiol-ene click reaction of vinyl functionalized SBA-15 and cysteine hydrochloride. After carrying out a detailed characterization of catalyst, the group applied it in Biginelli reaction involving aldehyde (1), ethylacetoacetate (10) and urea (11) under milder condition for the synthesis of 3,4-dihydropyrimidin-2(1H)-one derivatives (12) (Scheme 3). Easy magnetic separation of catalyst and its reusability in 7 consecutive runs without much decrease in catalytic activities are the plus points of this reported protocol.
Scheme 3

L-Cysteine functionalized magnetic NPs (LCMNP), a novel magnetically separable nano-organocatalyst was reported by A. K. Nezhad et al.26 After carrying out a detailed characterization of catalyst, the group applied it in one-pot MCR of various salicaldehydes (1), nucleophiles (13) and malononitrile (14) for the synthesis of 2-amino-4H-Chromene-3-carbonitriles (15) in water (Scheme 4). In order to render LCMNP best for the above said reaction, the authors compared its catalytic activity with various corresponding amino acids and NPs. Catalyst after the reaction was over can be easily separated from the reaction mixture by using an external magnet and can be reused in seven corresponding runs without much decrease in catalytic activity.

\[
\text{Nu} + \text{RCHO} + \text{O} + \text{H}_2\text{N} + \text{NH}_2 \rightarrow \text{Nu} + \text{O} + \text{H}_2\text{N} + \text{NH}_2
\]

\[
\text{Nu} = \text{Indoles, N,N-dimethylaniline, malononitrile and TMSCN}
\]

Scheme 4

Poly(4-vinyl pyridine) supported copper (I) iodide NPs (P4VPy-CuI) were synthesised by Albadi and co-workers.27 The research group have successfully applied it as a catalyst for the one-pot regioselective synthesis of 1,4-disubstituted-1,2,3-triazoles (17) using benzyl halides (16), NaN₃ (6) and terminal alkynes (7) in water. The catalyst can be recovered by simple filtration and recycled up to eight consecutive runs without any loss of its efficiency (Scheme 5).

\[
\text{Br} + \text{R} + \text{NaN}_3 \rightarrow \text{P4VPy-CuI} \rightarrow \text{Water, reflux} \rightarrow \text{17}
\]

Scheme 5

N. Koukabi and group28 after synthesizing γ-Fe₂O₃-SO₃H carried out its successful characterization by FT-IR, TGA, XRD, XPS etc. After synthesis and characterization, the desired synthesized catalyst was applied for synthesis of 1,4-dihydropyridines (1,4-DHP) (20). Authors employed 0.025g of γ-Fe₂O₃-SO₃H in one-pot MCR of
aldehydes (1), ethylacetoacete (10) or methylacetoacete (18) and ammonium acetate (19) and stirred it under SFRC at 90°C (Scheme 6). Other added advantages of this methodology are less tedious work-up procedure, high yield of desired product, easy catalyst separation and its reusability in successive reactions.

\[
\text{R}_1\text{CHO} + \text{R}_2\text{O} + \text{NH}_4\text{OAc} \xrightarrow{\gamma-\text{Fe}_2\text{O}_3\cdot\text{SO}_3\text{H}(0.025g)} \text{90}^\circ\text{C, SFRC}} \quad \text{R}_3\text{O} + \text{NH}_4\text{OAc} \xrightarrow{\gamma-\text{Fe}_2\text{O}_3\cdot\text{SO}_3\text{H}(0.025g)} \text{90}^\circ\text{C, SFRC}} \quad \text{R}_3\text{O} \quad \text{R}_3\text{O} \quad \text{R}_3\text{O} \quad \text{R}_3\text{O}
\]

**Scheme 6**

B. Hemmati and his group\(^2^9\) worked on the synthesis of a nano-biocatalyst, in which they coated surface of nano-Fe\(_3\)O\(_4\) with Irish moss (IM). IM is derived from algae. The catalyst was characterized by FT-IR, TEM, SEM, EDX, VSM and XRD analyses. Afterwards its first catalytic report was carried out in MCR of aldehyde (1), 2-aminobenzimidazole (21) and C-H acidic compounds (14/22) for the synthesis of imidazopyrimidine derivatives (23/24) using ethanol as solvent under reflux condition. Amount of Fe\(_3\)O\(_4\)@IM applied in the reaction is 20mg (Scheme 7). After conclusion of reaction, solid residue was recrystallized from ethanol to afford pure product. Magnetically recycled catalyst was reused in six cycles.

\[
\text{N}\text{H}_2 + \text{R}_1\text{CHO} \xrightarrow{\text{Fe}_3\text{O}_4\cdot\text{IM}(20 \text{ mg}) \text{ EtOH, reflux}}} \text{23}
\]

**Scheme 7**
An efficient, heterogeneous nano-catalyst was synthesized by grafting nano-Fe$_3$O$_4$ and TiO$_2$ NPs to 2, 4-toluene diisocyanate. The novel nano-catalyst was characterized by FT-IR, field emission scanning electron microscopy (FE-SEM), XRD, TGA and VSM analyses. Catalyst, nano-Fe$_3$O$_4$@TDI@TiO$_2$ (0.028 g) was enough for catalyzing synthesis of hexahydroquinoline (25) and tetrahydrobenzo[b]pyran derivatives (26) at 70 °C under SFRC. 1,3-cyclic di-ketone (22), aldehydes (1), malononitrile (14) and ammonium acetate (19) was taken in a one-pot in the molar ratio of 1:1:1:2.5 for the synthesis of hexahydroquinolines (25) and for synthesizing tetrahydrobenzo[b]pyran derivatives (26) only 1,3-cyclic di-ketone (22), aldehydes (1), malononitrile (14) were taken (Scheme 8). Catalysts were separated by external magnet and recycled in consecutive reactions. Pure products were recrystallized by using ethanol.

![Scheme 8](image_url)

Silica encapsulated γ-Fe$_2$O$_3$ coated with L-Leucine (MNPs-L-Leucine) was synthesized by Z. Arabpoor and group. After synthesis and characterization by various analytical techniques like powder XRD, SEM, EDX, VSM, TGA and FT-IR, authors applied that for the one-pot synthesis of thiazoloquinolines (30) via four-component reaction of aldehydes (1), dimedone (29), cysteamine (28) and α-enolicdithioesters (27) under SFRC (Scheme 9). The novel superparamagnetic NP was easily separated from the reaction mixture by external magnetic field.
Superparamagnetic nanoparticles of modified sulfuric acid ($\gamma$-Fe$_2$O$_3$@SiO$_2$-OSO$_3$H) was used as a green reusable catalyst in Ugi like Groebke-Blackburn-Bienaymé reaction (Scheme 10) by using aldehydes (1), isocyanide (31) and a primary amine source (32) for the synthesis of biologically important aminoimidazopyridine derivatives (33). S. Rostamnia and his research group in this work recycled the catalyst easily by external magnetic field and reused that in five reaction cycles without much decrease in catalytic activity. Products were synthesized under solvent-free reaction condition.

B. L. Li and co-workers had reported nano-CoFe$_2$O$_4$ supported Molybdenum as an efficient catalyst for a one-pot four component synthesis of functionalized pyrroles (37) (Scheme 11). In this work, the research group after carrying out almost complete characterization of synthesized catalyst by EDX, FT-IR, TEM, SEM, powder XRD, TGA, ICP-MS and VSM analyses applied it in the multi-component reaction of aldehydes (1), amines (34), 1,3-dicarbonyl compounds (35) and nitromethane (36). The reaction showed no positive result in absence of catalyst and showed the best result when 1 mol% of synthesized catalyst was used. Reaction was also carried out in presence of various solvents like THF, water, CH$_3$CN, methanol and toluene, but finest result was obtained under solvent-free condition at 90 $^\circ$C. Catalyst was easily magnetically separated from the reaction mixture by an external magnet and reused in five consecutive reactions. Other advantages of this methodology include excellent substrate variability and high yield of desired product.
J. Safari et al.\textsuperscript{34} reported rapid synthesis of amidoalkyl naphthols (4) by condensation of $\beta$-naphthol (2), aldehydes (1) and amides (3). For this one-pot MCR (Scheme 12), the research group applied carbon nanotubes functionalized magnetic nano-Fe$_3$O$_4$ (nano-Fe$_3$O$_4$-CNTs) as a reusable catalyst. After characterization of solid acid catalyst by EDX, TEM, XRD and VSM, authors had set up a model reaction and did a systematic standardization for various reaction parameters in order set up perfect experimental condition for it. 0.03g of nano-Fe$_3$O$_4$-CNTs was found to be good enough to catalyze the reaction in SFRC under microwave irradiation. Catalyst was recycled and reused in consecutive runs without much decrease in catalytic activity.

Ali Reza Kiasat and co-workers\textsuperscript{35} used nano-Fe$_3$O$_4$@silica sulfuric as an efficient reusable catalyst for one-pot solvent-free synthesis of indazolo[2,1-$b$] phthalazine-triones (40) and pyrazolo [1,2-$b$] phthalazine-diones (41) from aldehydes (1), 2,3-dihydrophthalazine-1,4-dione (38) and either dimedone (29) or acetylacetone (39) (Scheme 13). The advantages of the reaction are simple procedure, cleaner reaction, use of reusable catalyst, easy workup and solvent-free conditions.
Multi-walled carbon nanotubes supported nano-Fe$_3$O$_4$ (Fe$_3$O$_4$ NPs/MWCNTs) were synthesized by A. Fallah-Shojaei and co-workers$^{36}$ and its characterization was done by FT-IR, XRD, VSM, TEM and SEM. After synthesis and characterization was complete, it was applied for the synthesis of biologically important pyran derivatives (42) (Scheme 14). Aldehydes (1), malononitrile (14), 1,3-cyclic diketones (22) or ethylacetooacetate (10) were taken as the starting materials. Standardization of reaction parameters were also scrutinized and for that firstly it was carried out in presence of various solvents like EtOH, acetonitrile, n-hexane, water and also under solvent-free condition. Reaction was showing best positive result in presence of EtOH. A standardization of catalyst concentration was also carried out and it was found that 5 mg of Fe$_3$O$_4$ NPs/MWCNTs was the optimum concentration of catalyst required for formation of pyran derivatives from reactants. Temperature standardization was also carried out and reflux condition was chosen as the most favourable one. Other significant advantages of this procedure are easy work-up procedure, milder reaction condition, environmentally benign conditions and magnetically separable catalyst which can be reused easily in five consecutive cycles.
Benzoylthiourea Fe (II) complex supported on silica NPs (Fe(II)-BTU-SNPs) was synthesized, characterized and employed as an efficient, reusable heterogeneous catalyst for the one-pot multi-component synthesis of benzopyranopyrimidine derivatives (44) by S. Amirnejat et al.37 The prepared catalyst was characterized by FT-IR, SEM, EDX, TEM, TGA, BET, ICP and elemental analysis. For this reaction salicylaldehyde (1), malononitrile (14) and secondary amine (43) were used as starting materials in the molar ratio of 2:1:1 (Scheme 15). To appraise the effect of media reaction was carried out in presence of various solvents and the best result appeared in presence of EtOH at room temperature. 15 mg per mole of reactants was taken as desired catalyst amount for the reaction and after the reaction was complete it was separated from the reaction mixture by simple filtration and reused in five consecutive cycles without much decrease in catalytic amount. This reaction also offered high substrate scope.

A. Maleki and research group38 synthesized chitosan supported super paramagnetic iron oxide NPs and applied that as an efficient catalyst for the synthesis of benzodiazepine derivatives (46). Authors used o-phenylenediamine (45), dimesone (29) and various aldehydes (1) (aromatic, heteroaromatic) as the starting materials and carried out the one-pot multi-component reaction at room temperature (Scheme 16). After carrying out a detailed standardization for reaction parameters authors concluded that reaction was giving the best result in presence of 0.03g of catalyst in presence of ethanol as solvent. After reaction concluded, the heterogenous catalyst was separated by an external magnet. After that the recycled catalyst was washed with ethanol or acetone and dried. After drying, this recycled catalyst was reused in five more cycles without much decrease in catalytic activities.
Scheme 16

One-pot three-component reaction for the synthesis of 1, 2, 3-triazoles (51, 52, 53) was also reported by J. Lu et al. In their work authors synthesized magnetic catalyst, characterized it by FT-IR, powder XRD, EDX, XPS, VSM etc. After successful characterization of synthesized catalyst it was applied for the synthesis of 1, 2, 3-triazoles by using epoxides (47) or benzyl chlorides (48) or phenyl boronic acids (49), acetylene (50) and azide (6) in water at room temperature. Analysis of different reaction parameters like kind of catalyst, catalyst concentration and solvent was also carried out and it was found in presence of 1 mol% of NiFe$_2$O$_4$-glutamate-Copper catalyst and water as solvent reaction was showing the best result (Scheme 17). Higher substrate variability, ambient reaction condition, high yields, easy separation of catalyst by using external magnet and its efficient recycling are the added advantages of this procedure.

Scheme 17

H. Eshghi reported a magnetic nano-organic-inorganic hybrid catalyst (Fe@Si-Gu-Prs) by anchoring Preyssler heteropolyacids (H$_{14}$[NaP$_5$W$_{30}$O$_{110}$]) on to nano-Fe$_3$O$_4$ coated with guanidine-propyl-trimethoxysilane linker. The synthesized green catalyst was characterized by FT-IR, SEM, TEM, EDX, VSM, TGA, XRD, BET and ICP. After successful characterization of catalyst its catalytic investigation for the one-pot multi-component synthesis of tetrahydropyridine (55) derivatives using aldehyde (1), aniline (54) and ethylacetoacetate (10) was carried out (Scheme 18). After carrying out total standardization of reaction parameters it was found that reaction was showing the best result in presence of 0.025g of Fe@Si-Gu-Prs at room temperature.
under SFRC. This synthesized surface modified nano catalyst was able to carry out reaction successfully within shorter period of time (45 min). Catalyst can be easily recycled by using an external magnet and can be reused in five consecutive reactions without much decrease in catalytic activity.

\[
\text{Fe@Si-Gu-Prs (0.025g)}
\]

SFRC, r.t., 20-45 min

Scheme 18

A series of spirooxiindole derivatives were synthesized by application of superparamagnetic MnFe\(_2\)O\(_4\)@NH\(_2\)@2AB-Ni catalyst (Scheme 19).\(^{41}\) In their synthetic approach of this novel catalyst authors synthesised manganese ferrite nanoparticles coated that with 3-aminopropyltriethoxysilane (APTES) then they attached isotoic anhydride on its surface which is used as a site for attachment of nickel. The synthesized catalyst was then characterized by using various techniques like FT-IR, powder XRD, SEM, TGA and VSM. After characterization, application of catalyst (10 mg) was carried out in MCR involving isatins (56), 1,3-cyclic diketones (22) and 2, 6-diaminopyrimid-4(3H)-one (57 or 58) was carried out for the synthesis of spiroindole derivatives (59 or 60) in presence of water as solvent. Magnetic nanoparticle can be separated from the reaction mixture and easily recycled in four consecutive fresh reactions.
SO$_3$H-functionalized mesoporous silica materials (SO$_3$H-FMSM) as solid acid nanocatalyst was applied for the synthesis of a series of $2H$–indazolo[2,1-$b$]phthalazine-1,6,11-trione derivatives (40) by A. A. Ameri and group. In order to determine optimum reaction parameters for this one-pot MCR, various reaction conditions were applied. Ball milling and ultrasonication techniques were also applied but they failed to show positive result and ultimately when the starting materials i.e. aldehydes (1), 2, 3-dihydropthalazine-1, 4-dione (38) and dimedone (29) was mixed together in molar ratio of 1:1:1 under SFRC at 110 °C in presence of 20 mg of synthesized solid acid, the reaction was showing the highest yield for the formation of desired product (Scheme 20). Synthesized catalyst before being applied in the reaction was characterized by various analytical techniques like FT-IR, SEM, EDX. After completion of reaction the recyclable capability of catalyst was also studied and it was found that the desired solid acid catalyst can be recycled and reused in four consecutive runs.

Ahmad Shaabani and co-workers reported synthesis and characterization of Cu/GA/Fe$_3$O$_4$@SiO$_2$ NPs catalyst. They obtained the catalyst by ultrasonic-assisted
grafting of guanidine acetic acid (GA) on modified Fe$_3$O$_4$@SiO$_2$ core shell followed by immobilization of Cu (II) on it. Catalyst after being characterized by XRD, FT-IR, VSM etc was applied in the MCR of (i) dimedone (29), o-phenylenediamine (45) and aldehydes (1) for the synthesis of benzodiazepines (46) and (ii) benzil (61) or benzoin (62), aldehydes (1) and ammonium acetate (19) for the synthesis of trisubstituted imidazoles (63) (Scheme 21). Synthesis of benzodiazepines was carried in presence of ethanol and synthesis of imidazoles was carried out under SFRC at 60 °C and at 90 °C respectively. In both the reactions 0.01g of Cu/GA/Fe$_3$O$_4$@SiO$_2$ NPs catalyst were used. Recyclability of the desired catalyst was also scrutinized in both the reactions discussed above. Recycling of catalyst was carried out by using an external magnet and after washing with ethanol and after drying under vacuum for 3h was reused in five more runs. Comparison between FT-IR, CHN and ICP-OES analyses results of freshly prepared catalyst and reused catalyst was also done to confirm the stability of the reused catalyst after five time reusability.

![Scheme 21](image)

Chitosan coated nano-Fe$_3$O$_4$ were prepared by Zohre Zarnegar and group by simple reported procedures and they applied it in one-pot MCR of 2,4,5-trisubstituted imidazoles (65) by using benzil derivatives (1 mmol) (64), aldehydes (1 mmol) (1) and ammonium acetate (5 mmol) (19) in ethanol (Scheme 22). This methodology offers several advantages compared to reported procedures like application of a magnetically recyclable heterogeneous catalyst in very less amount (0.05g), its high catalytic activity, simple and quick isolation of products, clean and milder conditions etc.

![Scheme 22](image)
Scheme 22

Magnetically recyclable L-arginine functionalized nano-Fe$_3$O$_4$ (Fe$_3$O$_4$@L-arginine) was synthesized, characterized (by FT-IR, powder XRD, TGA, SEM, TEM and VSM analyses) and applied for the one-pot synthesis of a series of chromene derivatives (67/68). Cyclocondensation of 1 or 2-naphthol (66/2), malononitrile (14) and aldehydes (1) in the molar ration of 1:1:1 in presence of 40 mg of Fe$_3$O$_4$@L-arginine lead to the formation of desired product in good yield after ultra-sonicating it for 1h under ambient conditions (Scheme 23). The catalyst can be easily recycled from the reaction mixture and reused in four consecutive runs.

Scheme 23

X. N. Zhao and research group reported synthesis of cobalt ferrite chitosan sulfonic acid magnetic NPs (CoFe$_2$O$_4$-CS-SO$_3$H) and applied this magnetically recyclable heterogeneous catalyst in one-pot MCR of phthalic anhydride (69), hydrazinium hydroxide (70), 1, 3-cyclohexanedione (22) and aldehydes (1) for the synthesis of 2H-indazolo [2,1-] phthalazine-trione derivatives (40) (Scheme 24). The reaction was carried out by using 10 mg of catalyst under SFRC at 80°C. After completion of reaction catalyst was separated easily by using an external magnetic field and the reused in five more cycles.
Superparamagnetic nano-Fe$_3$O$_4$ coated with ionic liquid 1-methyl-3-(3-trimethoxysilylpropyl) imidazolium chloride (IL-MNPs) was synthesized by J. Safari et al.\textsuperscript{47} Its characterization was carried out by various analytical techniques like FT-IR, powder XRD, SEM, VSM etc. After successful characterization, the surface modified NPs were applied in the one-pot MCR of benzil (61), ammonium acetate (19), aldehyde (1) and amines (34). 0.1g of IL-MNPs was enough to catalyze the reaction and provided maximum yield when stirred at 120 $^\circ$C or when irradiated under microwave at 100 W (Scheme 25). This method provided certain advantages like shorter reaction time, high yield of desired product, easy workup procedure, simple recyclability of magnetically separable catalyst, and high substrate variation.

Recently K. Debnath and co-workers\textsuperscript{48} reported proficient synthesis of spiro[indolo-3,100-indeno[1,2-b]quinolin]-2,4,110-triones (74) and indenoquinoline-spirooxindoles (75) under solvent-free reaction condition using magnetically separable Fe$_3$O$_4$-SO$_3$H nanoparticles. The nature of the N-substitution on the starting isatin played a major role on the type of product formed. Efficiency of this protocol was highlighted by the shorter reaction time, high yield of desired product, solvent-free reaction condition, and easy recyclability of catalyst (Scheme 26).
Pyrazole derivatives (77) were synthesized by J. Rakhtshah and co-workers\textsuperscript{49} by using dioxomolybdenum complex supported on silica coated magnetite NPs as an efficient catalyst. Catalyst was characterized by various analytical techniques like powder XRD, SEM, TEM, VSM, ICP-AES etc. Mixture of aldehyde (1), malononitrile (14), phenyl hydrazine (76) and catalyst (0.02g) was mixed in one-pot under SFRC and stirred at room temperature (Scheme 27).\textsuperscript{49} High yield of desire product, cleaner reaction profile, shorter reaction time, low cost and easy recyclability of this nano-catalyst are certain other advantages of this protocol.

Tetrasubstituted and trisubstituted imidazole derivatives were synthesized by the application of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-imid-PMA\textsuperscript{A} catalyst (Scheme 28).\textsuperscript{50} For synthesizing 1,2,4,5-tetrasubstituted imidazoles (71), benzil (61), ammonium acetate (19), aldehyde (1), amines (34) were mixed together and stirred at 110 °C or irradiated under microwave (100 W) in presence of 0.03g of catalyst. And for synthesizing 2,4,5-trisubstituted imidazoles (63) 1,2-diketones (61), ammonium acetate (19) and aldehyde (1) was mixed with 0.03 g of catalyst and was stirred under similar conditions. This methodology was bestowed with several other merits like simple work up and experimental procedures, excellent yield of desired product, high rate of reaction and application of magnetically recyclable catalyst which contributes significantly to the practice of green chemistry.
Scheme 28

A new nano-organocatalyst based on 3,4-dihydroxypyridine (Fe$_3$O$_4$/Py) was synthesized and applied in one-pot MCR of 5-methylpyrazol-3-amine (78), aldehydes (1), meldrum’s acid (79) and barbituric acid (80), aldehyde (1), malononitrile (14) for the synthesis of 3-methyl-4-aryl-2,4,5,7-tetrahydropyrazolo[3,4-b]pyridine-6-ones (81) and 7-amino-2,4-dioxo-5-phenyl-2,3,4,5-tetrahydro-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile (82) respectively. M. Pirhayati and his group$^{51}$ in this work reported that the synthesized catalyst was very efficient and in both the reactions, only 40 mg of Fe$_3$O$_4$/Py was enough to form the desired product in good yield in presence of ethanol as solvent (Scheme 29). After completion of reaction the catalyst was separated by using external magnetic field and reused in six consecutive runs.

Scheme 29

Pyridoimidazoisoquinolines (86) was synthesized by A. Maleki and group$^{52}$ under ultrasonic irradiation in presence of catalytic amount of nano- Fe$_3$O$_4$@SiO$_2$-CO-C$_6$H$_4$-NH$_2$. Reaction of phthalaldehyde (83), trimethylsilylcyanide (84) and aminopyridine (85) was carried out in presence of 5 mol % of catalyst and 10 ml of ethanol (Scheme 30). Before being applied in the one-pot MCR, the synthesized catalyst was characterized by FT-IR, SEM, EDX, TGA/DTA, NMR, MS and CHN analyses. After completion of reaction the desired catalyst was magnetically separable and was reused in several runs with very less loss in catalytic activity.
Fe$_3$O$_4$@Si$_2$O$_2$(CH)$_3$Cl based magnetic NPs with cobalt phthalocyanine tag (ACoPc-MNPs) was synthesized by M. A. Zolfigol and group.$^{53}$ Synthesized catalyst was characterized by FT-IR, XRD, TGA, SEM, AFM, TEM, BET, XRF, EDX and VSM analyses. After successful characterization its catalytic activity was evaluated for one-pot multi-component synthesis of tetrahydrobenzo[b]pyran (87) derivatives. A mixture of dimesdone (29), malononitrile (14) and aldehydes (1) were stirred in presence of 0.02 g of catalyst at room temperature (Scheme 31). After completion of reaction (TLC) ethanol was added to the reaction mixture and the catalyst was collected by means of external magnet and reused in subsequent reactions. The obtained products were recrystalized in ethanol.

Copper NPS supported on Fe$_3$O$_4$-polyethylene glycol (Fe$_3$O$_4$-PEG-Cu) was characterized by various analytical techniques and was applied for the one-pot multi-component synthesis of 2,4,5-trisubstituted imidazoles (63) and 1,2,4,5-substituted imidazoles (71). Reaction was carried out under solvent-free reaction condition (SFRC) at 110 °C (Scheme 32).$^{54}$ The new catalyst was found to be active and the green catalyst displayed magnetic properties which allowed their fast separation from reaction mixture by using external magnet.
Magnetic NPs coated with tungstic acid (MNP-TA) was synthesized as novel catalytic system by A. K. Nezhad and group. The synthesized catalyst was characterized by using different microscopic and spectroscopic techniques like XRD, TEM, SEM and FT-IR. NPs were obtained with nearly spherical morphology and the tungsten (W) content was determined by ICP analysis. After characterization, catalyst (0.1g) was applied for the synthesis of spirooxindoles (91) via one-pot MCR of isatin (88), various malononitriles (90) and 6-amino-1,3-dimethyl uracil (89) in presence of water as solvent under refluxing condition (Scheme 33). After completion of reaction, catalyst were recycled magnetically and reused in five more cycles.

Behrooz Maleki and co-workers described an ultrasound promoted one-pot multicomponent strategy for the synthesis of highly substituted pyran derivatives (93-96) by using silica coated NiFe₂O₄ NPs supported Preyssler heteropolyacid (H₁₄[NaP₅W₃₀O₁₁₀]) (NFS-PRS) as a magnetically recyclable heterogeneous catalyst (Scheme 34). The reaction of active methylene compounds (29/10/92/10+70), aldehydes (1) and malononitrile (14) was carried under ultrasonic irradiation at room temperature in presence of ethanol as solvent. In comparison to other conventional methods this synthetic protocol provides certain advantages like shorter reaction time,
milder reaction condition, higher yield of desired product and application of a heterogeneous catalyst which can be easily separated from the reaction mixture by using an external magnet and can be reused four more times without much decrease in catalytic activities.

\[
\begin{align*}
R^1\text{CHO} + & \text{NCO} \rightarrow \text{NFS-PRS (0.02 g)} \\
\text{14} & \text{10} \\
\text{1} & \text{10} \\
\text{NH}_2\text{NH}_2\text{H}_2\text{O} & \text{92} \rightarrow \text{93} \\
\text{94} & \text{95} \rightarrow \text{96}
\end{align*}
\]

**Scheme 34**

Magnetic nanoparticles coated with chitosan (Fe$_3$O$_4$@chitosan) was synthesized by a simple and eco-friendly procedure by A. Maleki and co-workers.$^{57}$ Synthesized surface modified NPs were characterized by SEM, EDX, FT-IR and powder XRD. After successful characterization, catalyst was employed for the synthesis of tetrahydrobenzoxanthenones (97). The one-pot MCR of 2-naphthol (2), aldehydes (1) and dimedone (29) was carried out in presence of 30 mg of Fe$_3$O$_4$@chitosan using ethanol as solvent at 40 °C (Scheme 35). The magnetic biopolymer catalyst after being separated from reaction mixture by an external magnet was washed with ethanol and reused in subsequent runs (5 times). Pure benzoxanthenones were afforded by recrystallization from ethanol.
L. Q. Wu\textsuperscript{58} reported synthesis of nano n-propylsulfonated $\gamma$-Al$_2$O$_3$ catalyst and explored its catalytic activity for the synthesis of spiro[indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine]dione derivatives (100) in aqueous medium. Reaction was carried out by taking 3-aminocrotononitrile (98), phenylhydrazine (76), thioacid (99) and isatin (88) in the molar ratio of 1:1:1:1 under reflux condition using water as solvent (Scheme 36). Amount of catalyst used in the reaction is 100 mg. Synthesized catalyst before being applied in the reaction was characterized by FT-IR, TEM, SEM, powder XRD, TGA etc. Reusability of desired catalyst was also checked and it was found that catalyst can be effectively applied in seven more subsequent reactions without much decrease in catalytic activities.

Rostamizadeh and co-workers\textsuperscript{59} reported synthesis of 8-dioxo-octahydroxanthenes (101) by mixing dimedone (29) and aldehydes (1) in the molar ratio of 2:1 using nano-MCM41-SO$_3$H (0.05 g) as recyclable catalyst under ultrasonic irradiation in aqueous media (Scheme 37). Comparison of catalytic activity of desired catalyst was also compared with other Lewis acids like NaHSO$_4$/SiO$_2$, ZrOCl$_2$/K 10 etc. but they lead to the formation of only intermediate.

J. Safari and group\textsuperscript{60} reported ultrasound mediated one-pot synthesis of amidoalkyl naphthols (4) by using 2-naphthol (2), aldehydes (1) and various amides (3) in presence of nanoparticles modified by ionic liquid (MNP-IL-OAc) (0.04 g) (Scheme 37).
The novel heterogeneous nanocatalyst was prepared by immobilization of the ionic liquid 1-methyl-3-(3-trimethoxysilylpropyl) imidazolium acetate. After synthesis the catalyst was characterized by FT-IR, powder XRD, SEM and VSM analyses. After completion of reaction, catalyst was recycled by using an external magnet and reused in corresponding seven runs without much decrease in catalytic activities.

Scheme 38
A sulfonated magnetic cellulose based nanomaterial (MCSA) catalyst was synthesized and characterized by using SEM, EDX, powder XRD, FT-IR spectroscopy. Synthesized green nano-catalyst was then used for the synthesis of α-aminonitriles (104) via one-pot MCR of aldehydes or ketones (102), trimethylsilylcyanide (103) and amines (35). Reaction was carried out in presence of ethanol at room temperature and amount of catalyst taken was 40 mg (Scheme 39). The new Fe₃O₄@cellulose-OSO₃H (MCSA) bio-polymer based heterogeneous catalyst was easily separable from the reaction mixture by external magnetic field and was reused in six more reactions without much decrease in catalytic activity.

Scheme 39
J. Safari et al. reported a procedure in which they synthesized nano-Fe₃O₄@chitosan and applied that for the one-pot multi-component synthesis of pyran derivatives (106) via addition of aldehydes (1), resorcinol (105) and malononitrile (14). Reaction showed excellent result in presence of water as solvent, 0.15g of catalyst under ultrasonication at 50 °C (Scheme 40). After completion of reaction the magnetically separable nano heterogeneous catalyst was recycled and reused in 5 new cycles.
A biological-based nanomagnetic catalyst, \{Fe_3O_4@SiO_2 @(CH_2)_3-thiourea dioxide-SO_3H/HCl\} was first synthesized and employed in one-pot MCR for the synthesis of \textit{bis}-pyrazols (107) and pyrano[3,2-\textit{c}]pyrazoles (95) (Scheme 41). For synthesis of \textit{bis}-pyrazols 1 mmol of aldehydes (1), and 2 mmol of 3-methyl-1-phenyl-1\textit{H}-pyrazol-5(4\textit{H})-one (92) were added in the reaction mixture with 7 mg of catalyst and for synthesizing pyrano[3,2-\textit{c}]pyrazoles, aldehydes (1), 3-methyl-1-phenyl-1\textit{H}-pyrazol-5(4\textit{H})-one (92) and malononitrile (14) was added in the molar ratio of 1:1:1 and stirred under SFRC at 90 °C in presence of 7 mg of desired catalyst. The recycling possibility of synthesized catalyst was investigated in both the reaction schemes for eight times.

\textbf{Scheme 40}

\textbf{Scheme 41}

B. Asadi and group\textsuperscript{64} reported microwave assisted one-pot regioselective synthesis of quinolines (112) and \textit{bis}-quinolines (113/114/115) catalyzed by Bi (III) immobilized on triazine dendimer stabilized Fe_3O_4 magnetic NPS [nano-Fe_3O_4-TDSN-Bi(III)]. The reaction for the synthesis of quinolines was accomplished by taking aryl amine (108/109/110), aldehyde (1) and methyl propiolate (111) using 133 mg of nano-Fe_3O_4-TDSN-Bi(III). Additionally, the catalytic system was applied for the synthesis of symmetric and unsymmetric \textit{bis}-quinolines by replacing either aldehydes or amines with dialdehyde or diamine or by application of two different diamines (Scheme 42). Other significant advantages of this procedure includes excellent yield of desired
products, high reaction rate, SFRC, application of microwave (MW) as energy source easy recovery of catalyst and simple working procedure.

\[
\begin{align*}
X & \quad \text{NH}_2 \\
\text{CHO} & \quad \text{CH}_3 \\
Y & \quad \text{COOCH}_3
\end{align*}
\]

nanofe_3O_4-TDSN-Bi(III) (133 mg)
MW (360 W, 85 °C)

\[
\begin{align*}
\text{CHO} & \quad \text{CHO} \\
\text{NH}_2 & \quad \text{NH}_2 \\
\text{CHO} & \quad \text{CHO} \\
\text{H}_3\text{COOC} & \quad \text{H}_3\text{COOC}
\end{align*}
\]

Scheme 42

A. Maleki and group reported synthesis of ultrasound mediated one-pot synthesis of polycyclic imidazo (thiazolo)pyrimidine derivatives (117). Authors carried out MCR between 2-aminobenzothiazole (116) or 2-aminobenzimidazole (21), dimedone (29) and aldehydes (1) in presence of nano-Fe_3O_4@clay as a magnetically recyclable heterogeneous catalyst. Reaction mixture was stirred in presence of 5 mg of catalyst and 5 ml of water at room temperature (Scheme 43). After completion of reaction catalyst was recovered by external magnetic field and reused in several runs without much decrease in catalytic activity.
J Safaei-Ghomi et al.\textsuperscript{66} carried out one-pot ultrasound mediated synthesis of benzo[g]chromenes (119) by the application of nano-Fe\(_3\)O\(_4\)/polyethylene glycol (PEG) core/shell. A mixture of aldehyde (1), 2-hydroxy-1,4-naphthoquinone (118) and malononitrile (14) was sonicated (60 W) for 15-20 min in presence of 12 mg of nano-Fe\(_3\)O\(_4\)@PEG and ethanol as solvent (Scheme 44). After completion of reaction, catalyst was separated by external magnet and reused in five more consecutive runs.

Polysubstituted pyrrolidine derivatives (122) were synthesized by using a novel 7-Aminonaphthalene-1,3,-disulfonic acid (ANDS\(_\text{A}\)) functionalized magnetic nano-Fe\(_3\)O\(_4\). First step in the synthesis of nano-Fe\(_3\)O\(_4\)@SiO\(_2\)@Propyl-ANDS\(_\text{A}\) involves preparation of nano-Fe\(_3\)O\(_4\) followed by coating its surface with SiO\(_2\), (3-Chloropropyl)triethoxysilane and ANDS\(_\text{A}\). After synthesis and characterization of synthesized catalyst by FT-IR, EDX, XRD, SEM, TEM, TGA, VSM and XPS analyses 0.05g of nano-Fe\(_3\)O\(_4\)@SiO\(_2\)@Propyl-ANDS\(_\text{A}\) was employed in one-pot MCR of aldehydes (1), amines (120) and acetylenedicarboxylate (121) at room temperature in presence of ethanol as solvent (Scheme 45).\textsuperscript{67}
D. Saberi and co-workers\textsuperscript{68} reported synthesis of \(\alpha\)-aminonitriles and \(\alpha\)-aminophosphonates by using dehydroascorbic acid (DHAA) capped magnetite NPs as an efficient magnetically recoverable nano-organocatalyst. For synthesizing \(\alpha\)-aminonitriles (104), 1 mmol of aldehyde or ketones (1 or 102), 1.2 mmol of TMSCN (103) and 1.2 mmol of amine (35) were added in a one-pot followed by addition of ethanol and 20 mg of catalyst (DHAA-Fe\(_3\)O\(_4\)) and stirred at room temperature. And for synthesizing \(\alpha\)-aminophosphonates (124), aldehydes or ketones (1 or 102), amines (35) and dimethyl phosphite (123) in presence of 20 mg of catalyst was stirred under SFRC at 40 °C in the molar ratio of 1:1:1 (\textbf{Scheme 46}). Reusability of DHAA-Fe\(_3\)O\(_4\) was also checked and it was found that the catalyst can be easily recycled in 6 consecutive runs.

\textbf{Scheme 45}

E. Kolvari and his research group\textsuperscript{69} employed nano-magnetic supported sulfonic acid (nano-\(\gamma\)-Fe\(_2\)O\(_3\)@SO\(_3\)H) in the multi-component reaction of aldehydes (1), ethylacetoacetate (10) or methylacetoacetate (18) and urea (11) for the synthesis of 3,4-dihydropyrimidin-2-(1H)-one derivatives (125). Nano-\(\gamma\)-Fe\(_2\)O\(_3\)@SO\(_3\)H (0.1g) was sufficient enough to catalyze the reaction both under thermal stirring as well as a microwave irradiation condition (\textbf{Scheme 47}). After completion of reaction catalyst was separated magnetically and reused in five more runs.
Silica-supported Fe₃O₄ nanoparticles (SMMNPs), a magnetically retrievable catalyst was employed for green and efficient synthesis of diazepine derivatives (128) and diazepine carboxamide (129) derivatives by A. maleki (Scheme 48). In this work authors reported synthesis of diazepine derivatives from diaminies (126), aryl alkynes (127) in the molar ration of 1:2. 5 mol % of S-MMNPs as catalyst was applied in reaction, and EtOH was used as solvent. Due to the high reactivity of imine site in the diazepine product (128), authors further explored possibility of performing another additional reaction in the same pot with isocyanides (31) to furnish the diazepine carboxamides (129). In presence of unsymmetrical substituted diamines, inseparable regioisomers were obtained. S-MMNPs catalyst could be easily separated from reaction mixture due to its magnetic nature by an external magnet after completion of reaction and was reused in five consecutive five runs.

Scheme 48
Nano γ-Fe₂O₃-supported fluroboric acid (γ-Fe₂O₃-HBF₄) was synthesized as a novel magnetically recyclable catalyst. Nanoparticle obtained was successfully applied for synthesis of 12-substituted –benzo[h][1,3]dioxolo[4,5-b]acridine-10,11-diones (131). For synthesizing (131), 3,4-methylenedioxyaniline (130), aldehyde (1) and 2-hydroxy-1,4-naphthoquinone (118) were mixed together in an one-pot in presence of DMF (10 ml). γ-Fe₂O₃-HBF₄ (0.1 mmol) was added to the reaction mixture and stirred at 130 °C (Scheme 49).
Scheme 49

J. Deng and co-workers\textsuperscript{72} reported a robust dodecyl benzenesulphonic acid functionalized silica coated ferrite nanoparticles and applied that in one-pot MCR of isatins (88), barbituric acid (80) and cyclohexane-1,3-diones (22) for the synthesis of a library of spirooxindole-pyrimidine derivatives (132) (Scheme 50). The desired catalyst could be easily recovered by simple application of an external magnet and reused for six consecutive runs without loss in catalytic activity. Further, very less amount of leaching of the catalyst was detected by ICP-AES analysis. Easy recovery, recycling, high yield, mild reaction condition and application of water as solvent are some of the economic and inherent environmental advantages of this methodology.

Scheme 50

R. Nongrum and her research group\textsuperscript{73} carried out synthesis, characterization and application of vitamin B\textsubscript{1} functionalized Fe\textsubscript{2}O\textsubscript{3}@SiO\textsubscript{2} NPs (Fe\textsubscript{2}O\textsubscript{3}@SiO\textsubscript{2}@VB\textsubscript{1}). The nano-organocatalyst after synthesis, was characterized by various analytical techniques like FT-IR, powder XRD, SEM etc. Following that the catalyst was applied in the diversity oriented one-pot multi-component syntheses of pyran derivatives. Pyran derivatives were synthesized starting from 1,3-diketone (29/134/135) (1.5 mmol), malononitrile/ethylcyanoacetate (14/133) (1.5 mmol) and aldehydes (1) (1.5 mmol). Aqueous ethanol mixture (4:1) was chosen as the reaction medium and 8 mg of Fe\textsubscript{2}O\textsubscript{3}@SiO\textsubscript{2}@VB\textsubscript{1} was added to it (Scheme 51). Reaction was carried out under ultrasonication at 50/80 °C. After completion of reaction scope of catalyst recyclability was also investigated and it was found that, the nano-organocatalyst can be easily reused in six consecutive runs without much decrease in catalytic activities.
Recently application of ionic liquid has attracted much interest in organic synthesis, as they tend to provide green and efficient media. A. Khalafi-Nezhad and co-workers\(^7\) combined the advantages of both magnetic NPs and ionic liquid to develop a magnetically supported acidic ionic liquid (MSAIL). The synthesized nanocatalyst (MSAIL) was found to be highly efficient for one-pot three component synthesis of novel spirooxindole derivatives (141) in water medium using isatin (57), active methylene compounds (140) and (89) at ambient temperature (Scheme 52). Catalyst was easily recuperated by an external magnet after completion of reaction and reused in five consecutive runs. Few inherent features of this protocol are easy recovery of the catalyst, operational simplicity, high yield of desired product, environmentally benign conditions and low cost.

N. Esfandiary and co-workers\(^7\) reported synthesis of glucose coated superparamagnetic NPs (Glu@Fe\(_3\)O\(_4\) NPs) and carried out its complete characterization by using various analytical techniques like FT-IR, powder XRD, TGA, VSM etc. Synthesized catalyst was then applied to achieve highly efficient, cheap, environment friendly and easy to handle protocol for one-pot multi-component
synthesis of substituted pyrazole (77) and chromene (67) derivatives from aldehydes (1), malononitrile (14) and phenylhydrazine (76) or aldehydes (1), malononitrile (14) and 2-naphthol (2) respectively (Scheme 53). Application of lower amount of catalyst (35 mg), room temperature, ultrasonic-irradiation, application of water as solvent, reusability of catalyst in four consecutive reactions are the added advantages of this procedure.

![Scheme 53](image)

M. M. Hosseini and co-workers\textsuperscript{76} recently reported nano-ZrO\textsubscript{2} coated sulphuric acid [n-ZrO\textsubscript{2}-SO\textsubscript{3}H (n-ZrSA)] as an efficient catalyst, carried out characterisation by various analytical techniques like FT-IR, XRD, TGA, FESEM, TEM, EDX, BET, BJX, ICP and pH analysis. After successful characterization, the catalyst was applied as an efficient heterogeneous solid acid nanocatalyst (0.034 g) in Biginelli reaction (a three component MCR) under SFRC for the synthesis of dihydropyrimidinones (127/143). After completion of reaction, the nanocatalyst was separated by centrifugation and reused in five consecutive runs without much decrease in catalytic activities.

![Scheme 54](image)

R. Jamatia et. al.\textsuperscript{77} reported nano-ferrite coated glutathione as an efficient catalyst for the synthesis of spiro derivatives (147). Reaction was carried out in presence of water as solvent and was stirred at 80 °C. After completion of reaction, catalyst was recycled by using an external magnet and reused in eight consecutive runs without much decrease in catalytic activities. 1 mmol of 1,2-diketone (144), 1 mmol of malonates (145) and 1 mmol of enolizable C-H activated compounds (146) were stirred in presence of 8 mg of catalyst to form the desired product. (Scheme 55)
A. Gupta and his research group reported synthesis of pyran derivatives via one-pot multi-component reaction of malononitrile, aromatic aldehydes and C-H activated compounds by using nano-FGT (nano-ferrite coated with glutathione) as an efficient catalyst. Reaction was carried out by using water as solvent. After completion of reaction, catalyst was recycled by using an external magnet and reused in five consecutive reactions.
Scheme 56
Supported copper bromide on graphene oxide/Fe$_3$O$_4$ NPs was synthesized and applied as a magnetically separable catalyst for multi-gram scale one-pot multi-component synthesis of 1,2,3-triazoles (152). Catalyst after being characterized by TGA, TEM, powder XRD, XPS etc. was applied as a semi-heterogeneous catalyst in the reaction of primary halide (150), sodium azide (6) and terminal alkyne (151). Reaction was carried out under microwave irradiation using water as solvent (Scheme 57).

Scheme 57
Highly monodisperse platinum NPs (Pt NPs@rGO) supported with reduced graphene oxide was employed in one-pot, efficient and greener synthesis of acridinedione derivatives (153) by B. Aday and group. Dimedone (29), aldehyde (1) and various anilines (54) were added in the molar ratio of 2:1:1. Catalyst (8 mg) was applied in the reaction using water:ethanol (2:1) solution mixture as the solvent at 90 °C for 60 min. After completion of reaction, it was observed that Pt NPs@rGO can be successfully reused for five times and gave satisfactory yields (Scheme 58).
Highly monodisperse PdRuNi NPs furnished with graphene oxide (PdRuNi@GO NPs) was developed and applied as stable, novel, exceptional, efficient and reusable heterogeneous catalyst for the synthesis of 1,4-dihydropyridine derivatives (154/155) by T. Demirci and group (Scheme 59). It was observed that only 6 mg of desired catalyst was sufficient enough to carry out the desired one-pot multi-component reaction of ammonium acetate (19) (2 mmol), ethylacetoacetate (10) (2 mmol) or ethylacetoacetate (10) (1 mmol)-dimedone (29) (1 mmol) and aldehyde (1) (1 mmol). After completion of reaction, catalyst was removed from the reaction mixture by centrifugation, washed with methanol, water, dried and reused in five more runs.

Molybdenum supported on graphene oxide/ Fe₃O₄ was applied as an efficient, magnetically separable catalyst for one-pot multi-component construction of spiro-oxindole dihydropyridine derivatives (157) in deep eutectic solvent under microwave irradiation. Isatin (88), malononitrile (14) and anilinolactones (156) are added in the molar ratio of 1:1:1 and Fe₃O₄/GO-Mo (20 mg) in deep eutectic solvent like choline chloride (ChCl) was stirred under microwave irradiation at 90 °C (Scheme 60). After completion of reaction catalyst was separated by external magnet, washed with acetone followed by water, dried and reused in following reaction.
Magnetically recyclable copper oxide NPs supported on graphene oxide (Fe$_3$O$_4$ NPs/GO-CuO NPs) was synthesized, characterized and applied in one-pot multi-component reaction of propargylamines (160) by M. Mirabedini and group. 20 mg of Fe$_3$O$_4$ NPs/GO-CuO NPs was reported to possess efficient catalytic activity in presence of ethanol as solvent at r.t. Various aldehydes (1), secondary amines (158) and alkynes (159) were mixed in a one-pot to yield a wide range of propargyl amines (160) in good to excellent yields (Scheme 61).

Recently a newer approach for the synthesis of biologically important heterocycles by using graphite oxide as reusable heterogeneous catalyst was reported by Jamatia et al. In their work, authors reported one-pot multi-component synthesis of 1, 5-benzodiazepine derivatives (162) by using 20 mg graphite oxide as an efficient catalyst (Scheme 62). Reaction advanced smoothly and the catalyst was recycled back after completion of reaction by simple centrifugation and filtration and reused in nine consecutive runs without much decrease in catalytic activity.
1.2. References:


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