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Synthesis of Heterocycles and Fused Heterocycles Catalyzed by Nanomaterials

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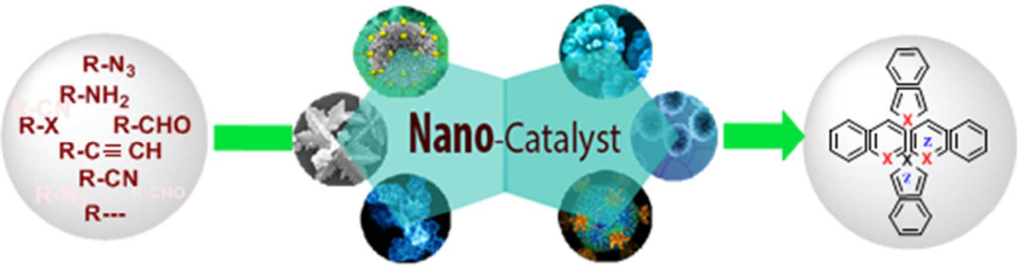

The application of nanomaterials as heterogeneous catalyst for the synthesis of different heterocyclic systems is reviewed.

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1. Introduction

Heterocycles are an important class of compounds, making up more than half of all known organic compounds. Heterocycles are present in a wide variety of drugs, most vitamins, many natural products, biomolecules, and biologically active compounds, including antitumor, antibiotic, anti-inflammatory, antidepressant, antimalarial, anti-HIV, antimicrobial, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, and insecticidal agents. They have also been frequently found as a key structural unit in synthetic pharmaceuticals and agrochemicals. Most of the heterocycles possess important applications in materials science such as dyestuff, fluorescent sensor, brightening agents, information storage, plastics, and analytical reagents. Heterocycles are also of considerable interest because of their synthetic utility as intermediates, protecting groups, chiral auxiliaries, organic catalysts, and metal ligands in asymmetric catalysts.[1-3]

The intellectual challenge to invent concise, elegant and conceptually novel synthetic routes to heterocyclic systems has become a steadily increasing driving force both in academia and industry. Therefore, extensive efforts have been directed to develop new and efficient synthetic strategies for these compounds. Among a variety of synthetic protocols, recent researches have been focused on establishment of catalytic approaches to synthesize heterocycles from easily accessible precursors under mild reaction conditions.

In this respect, chemists have made considerable achievements during the twentieth century in heterogeneous catalysis.[4] Heterogeneous catalysis have the advantage of easy removal of catalyst materials and possible use of high temperatures. Heterogeneous catalysts of metals are composed of two major components: the active metal particles and the support. Typical supports are Al_2O_3, SiO_2, MgO, Fe_2O_3, TiO_2, CeO_2, and many others.[5] The most widely used conventional method for preparing metal catalysts is the wet impregnation method.[6] One area of catalysis that is developing at a rapid pace is nano-catalysis.[7]

Nanomaterial-based catalysts are usually heterogeneous catalysts broken up into metal nanoparticles (NPs) in order to speed up the catalytic process. Metal nanoparticles have a higher surface area so there is increased catalytic activity because more catalytic reactions can occur at the same time. Nanoparticles catalysts can also be easily separated and recycled with more retention of catalytic activity than their bulk counterparts.[8] These catalysts can play two different roles in catalytic processes: they can be the site of catalysis or they can act as a support for catalytic processes.[9] They are typically used under mild conditions to prevent decomposition of the nanoparticles at extreme conditions.[10]

Many experimental studies on nanocatalysts have focused on correlating catalytic activity with particle size. In addition, many other factors such as geometry, composition, oxidation state, and chemical/physical environment can play a role in determining NP reactivity. There are many reviews on the multiple NP synthetic modes[11], and here we will not systematically detail this aspect per se.

In continuation of our interest in reviewing the different approaches for the synthesis of heterocyclic systems[12-16], this review focuses, on the application of nanomaterials as heterogeneous catalyst for the synthesis of heterocyclic systems. A number of other reviews[17,18] that have appeared, concerning this matter, did not pay special attention to the specific synthesis of such systems in an organized manner with respect to the type of the heterocyclic systems.

The fused heterocycles mentioned in this review are classified according to the type of the ring system. In order to prevent ambiguity, the fused ring systems are determined according to the following criteria:

a) The presence or the absence of bridgehead nitrogen.

b) Number of atoms in each ring (including carbon and hetero atoms) starting with the number of atoms in the ring taken as a prefix.

c) The number of heteroatoms in each ring. Yields of the target molecules reported in the review are those given in the last step in the reaction except when an overall yield was given.

2. Specific synthesis of heterocycles catalyzed by nanomaterials

2.1. Synthesis of five-membered heterocycles

2.1.1. Five-membered rings with one heteroatom

2.1.1.1. Furan

Cano *et al.* used commercially available nano-powder magnetite as an excellent catalyst for the addition of acid chlorides **1** to internal and terminal alkynes **2**, yielding the corresponding chlorovinyl ketones in good yields. The use of the iridium impregnated on magnetite catalyst permits the integration of the chloroacylation process with a second dehydrochlorination annulation process to yield, in one-pot, 3-aryl-2,5-dialkylfurans **3a-e** in good yields, independently of the nature of the starting reagents, and including the heteroaromatic ones (Scheme 1, Table 1).[19]

Scheme 1

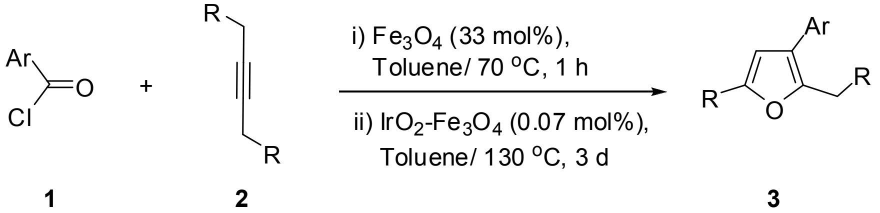


Table 1

Entry	Ar	R	Product	Yield (%)[a]
1	C_6H_5	^{n}Pr	**3a**	88
2	C_6H_5	Me	**3b**	91
3	4-ClC_6H_4	^{n}Pr	**3c**	76
4	4-$MeOC_6H_4$	^{n}Pr	**3d**	94
5	2-Thienyl	^{n}Pr	**3e**	74

[a] Isolated yield after column chromatography

Cao *et al*. reported the regioselective synthesis of α-carbonylfurans **6a-r** from a range of electron-deficient alkynes **4a-f** and 3-substituted 2-yn-ols **5a-h** The reaction proceeded using 10 mol% nano-Cu_2O in *N*,*N*-dimethylformamide at 50 °C (Scheme 2, Table 2, Method A).[20]

Furthermore, 2,4,5-trisubstituted 3-ynylfurans **6s-v** were obtained in 42–51% yield by nano-Cu_2O-catalyzed reaction of alkynes **4** and 5-arylpenta-2,4-diyn-1-ols **5** (Scheme 2, Table 2, entries 19-22, Method B).[20]

Scheme 2

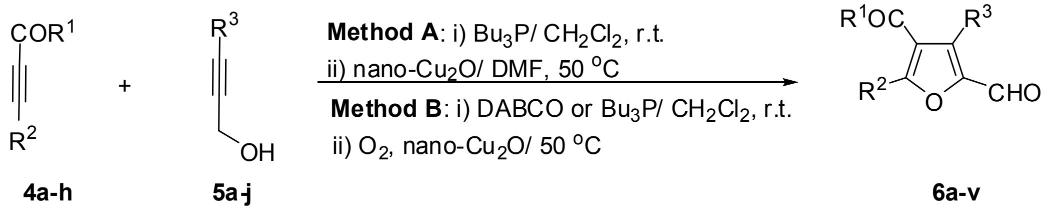
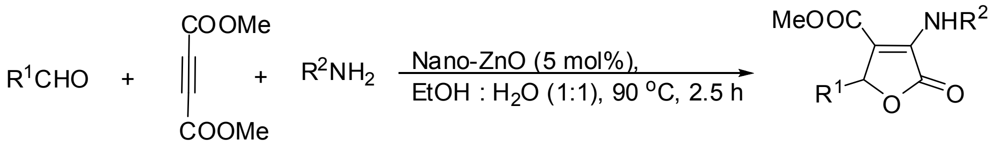


Table 2

Entry	R^1	R^2	R^3	Method	Product	Yield (%)
1	OEt	C_6H_5	H	A	**6a**	71
2	OEt	C_6H_5	Me	A	**6b**	67
3	OEt	C_6H_5	C_6H_5	A	**6c**	63
4	OEt	C_6H_5	3-MeC_6H_4	A	**6d**	68
5	OEt	C_6H_5	4-$MeOC_6H_4$	A	**6e**	65
6	OEt	C_6H_5	4-$O_2NC_6H_4$	A	**6f**	66
7	OEt	C_6H_5	2-Pyridyl	A	**6g**	69
8	4-MeC_6H_4	C_6H_5	2-Thienyl	A	**6h**	62
9	4-MeC_6H_4	4-MeC_6H_4	H	A	**6i**	67
10	4-MeC_6H_4	4-MeC_6H_4	Me	A	**6j**	73
11	OEt	4-MeC_6H_4	C_6H_5	A	**6k**	70
12	C_6H_5	Me	Me	A	**6l**	60
13	C_6H_5	C_6H_5	H	A	**6m**	68
14	C_6H_5	C_6H_5	C_6H_5	A	**6n**	73
15	C_6H_5	C_6H_5	Me	A	**6o**	71
16	C_6H_5	C_6H_5	4-$MeOC_6H_4$	A	**6p**	71
17	C_6H_5	C_6H_5	4-$O_2NC_6H_4$	A	**6q**	67
18	C_6H_5	C_6H_5	2-Thienyl	A	**6r**	61
19	OEt	C_6H_5	$C\equiv C\text{-}C_6H_5$	B	**6s**	42
20	C_6H_5	C_6H_5	$C\equiv C\text{-}C_6H_5$	B	**6t**	45
21	OEt	OEt	$C\equiv C\text{-}C_6H_4\text{-}5\text{-}Me$	B	**6u**	49
22	OMe	OMe	$C\equiv C\text{-}C_6H_5$	B	**6v**	51

Tekale *et al.* have successfully developed an efficient protocol for the one-pot three-component synthesis of 3,4,5-trisubstituted furan-2(5*H*)-ones **10a-l** from aldehydes **7a-h**, amines **9a-e** and dimethylacetylene dicarboxylate (DMAD) **8** using nano-crystalline ZnO as a reusable heterogeneous catalyst. The catalyst can be recycled several times with consistent catalytic activity (Scheme 3, Table 3).[21]

Scheme 3



7a-h **8** **9a-e** **10a-l**

Table 3

Entry	R^1	R^2	Product	Yield (%)
1	C_6H_5	C_6H_5	**10a**	94
2	C_6H_5	4-MeC_6H_4	**10b**	95
3	4-MeOC_6H_4	C_6H_5	**10c**	88
4	C_6H_5	4-FC_6H_4	**10d**	84
5	4-ClC_6H_4	C_6H_5	**10e**	89
6	2-ClC_6H_4	C_6H_5	**10f**	87
7	3-MeOC_6H_4	C_6H_5	**10g**	85
8	4-MeC_6H_4	C_6H_5	**10h**	84
9	C_6H_5	4-^{i}PrC_6H_4	**10i**	88
10	C_6H_5	2-FC_6H_4	**10j**	84
11	2,4-$Cl_2C_6H_3$	2-FC_6H_4	**10k**	85
12	2,4-$(MeO)_2C_6H_3$	C_6H_5	**10l**	83

The plausible mechanism for the ZnO nanoparticle catalyzed synthesis of furan 2(5*H*)-ones **10a-l** suggests initially the formation of enamine from amine **9** and DMAD by ZnO promotion. ZnO polarizes the carbonyl group of aldehyde **7** to form polarized adduct which reacts with the enamine followed by cyclization with the elimination of methanol molecule to afford the corresponding furan-2(5*H*)-ones **10a-l**.

2.1.1.2. Pyrrole

Hosseini-Sarvari *et al.* reported an environmentally benign method for the preparation of *N*-substituted pyrroles **12a-l** from one-pot condensation reaction of 2,5-dimethoxytetrahydrofuran **11** with amines **9** in the presence of nano sulfated titania (Fig. 1) under solvent-free conditions (Scheme 4, Table 4, Method A).[22]. As shown in Table 4, aromatic amines with electron-donating groups or electron-withdrawing groups are both effective in the Clauson-Kaas reaction, giving desired pyrroles **12a-l** in high yield.

There are many Lewis and Brønsted acid sites in the sulfated metallic oxides. The superacidity of these materials is attributed to the Brønsted acid sites, created or already existing, whose acidity is increased by the presence of neighboring strong Lewis acid sites. The strength of these Lewis acid sites is due to an inductive effect exercised by sulfate on the metallic cation, which becomes more deficient in electrons[23], as seen in the Fig. 1. Thus, nano sulfated titania represents a novel type of Lewis acid catalyst.

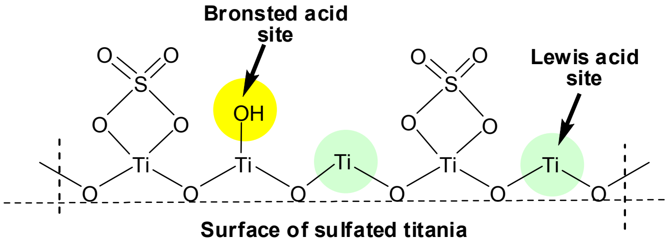


Fig. 1

Polshettiwar and Varma prepared nano-organocatalyst (Fig. 2) by supporting totally benign and naturally abundant glutathione on magnetic nanoparticles. The catalyst showed excellent activity for microwave-assisted synthesis of *N*-substituted pyrroles **12m-ab** by the reaction of a variety of amines **9** with tetrahydro-2,5-

dimethoxyfuran **11** (Scheme 4, Table 4, Method B). The rates were essentially the same for both the aliphatic or aromatic nature of the amines, showing the high activity of the catalyst.[24]

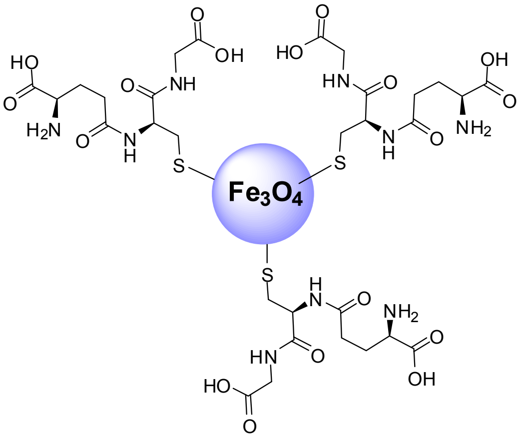
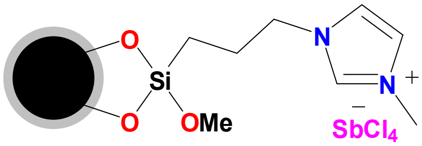


Fig. 2

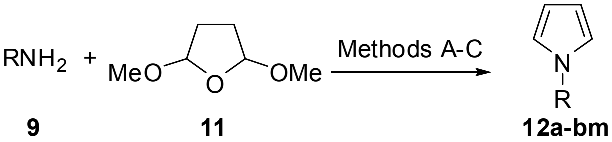
Ma *et al*. reported a facile approach to prepare magnetic nanoparticle-supported antimony catalyst (Fe_2O_3@SiO_2–Sb-IL, Fig. 3). This catalyst exhibited excellent catalytic efficiency in Clauson-Kaas reaction of amines **9** to 2,5-dimethoxytetrahydrofuran **11** in aqueous medium to afford the corresponding *N*-substituted pyrroles **12b, 12f, 12k, 12l, 12u** and **12ac-bm** (Scheme 4, Table 4, Method C).[25]



γ-Fe_2O_3@SiO_2-Sb-IL

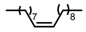
Fig. 3

Scheme 4



Method A[22]: Nano sulfated TiO_2/ Oil bath/ 120 °C
Method B[24]: Nano organocatalyst / H_2O/ MW/ 140 °C, 20 min
Method C[25]: γ-Fe_2O_3@SiO_2-Sb-IL/ H_2O/ Δ

Table 4

Entry	R	Method	Product	Yield (%)
1	3-MeC_6H_4	A	**12a**	98
2	4-MeC_6H_4	A	**12b**	90
3	2-EtC_6H_4	A	**12c**	98
4	3-$MeOC_6H_4$	A	**12d**	95
5	2-HOC_6H_4	A	**12e**	90
6	3-HOC_6H_4	A	**12f**	95
7	4-HOC_6H_4	A	**12g**	95
8	2-HO-5-MeC_6H_3	A	**12h**	95
9	4-NCC_6H_4	A	**12i**	95
10	2-$F_3CC_6H_4$	A	**12j**	95
11	4-BrC_6H_4	A	**12k**	95
12	4-$H_2NC_6H_4$	A	**12l**	90
13	-$CH_2C_6H_5$	B	**12m**	92
14	-$CH(Me)C_6H_5$ (*S*)	B	**12n**	90
15	-$CH(Me)C_6H_5$ (*R*)	B	**12o**	90
16	-$(CH_2)_3C_6H_5$	B	**12p**	86
17	C_6H_5	B	**12q**	88
18	3-$EtOOCC_6H_4$	B	**12r**	85
19	2-$MeOCC_6H_4$	B	**12s**	82
20	Pyridyl-CH_2-	B	**12t**	78
21	$NHOCC_6H_5$	B	**12u**	72
22	-OCC_6H_5	B	**12v**	NR
23	NH-4-$O_2NC_6H_4$	B	**12w**	NR
24	^{i}Bu	B	**12x**	90
25		B	**12y**	84
26	-$(CH_2)_3OH$	B	**12z**	86
27	-$(CH_2)_3NH_2$	B	**12aa**	85
28	-$(CH_2)_3NH_2$	B	**12ab**	72

Entry	R	Method	Product	Yield (%)
29	C_6H_5	C	**12ac**	95
30	3-HOC_6H_4	C	**12f**	93
31	2-$MeOC_6H_4$	C	**12ad**	85
32	4-$MeOC_6H_4$	C	**12ae**	96
33	4-$EtOC_6H_4$	C	**12af**	96
34	2-MeC_6H_4	C	**12ag**	89
35	4-MeC_6H_4	C	**12b**	94
36	3,4-$Me_2C_6H_3$	C	**12ah**	96
37	2,5-$Me_2C_6H_3$	C	**12ai**	90
38	2,6-$Me_2C_6H_3$	C	**12aj**	87
39	2,6-$^iPr_2C_6H_3$	C	**12ak**	75
40	4-$^tBuC_6H_4$	C	**12al**	92
41	2-FC_6H_4	C	**12am**	81
42	4-FC_6H_4	C	**12an**	82
43	2,4-$F_2C_6H_3$	C	**12ao**	85
44	3,4-$F_2C_6H_3$	C	**12ap**	90
45	3-ClC_6H_4	C	**12aq**	86
46	4-ClC_6H_4	C	**12ar**	87
47	3-Cl-4-MeC_6H_3	C	**12as**	92
48	3-Cl-4-FC_6H_3	C	**12at**	89
49	2,4,5-$Cl_3C_6H_2$	C	**12au**	88
50	2-BrC_6H_4	C	**12av**	82
51	3-BrC_6H_4	C	**12aw**	85
52	4-BrC_6H_4	C	**12k**	88
53	4-IC_6H_4	C	**12ax**	89
54	2-$O_2NC_6H_4$	C	**12ay**	80
55	4-$O_2NC_6H_4$	C	**12az**	85
56	4-AcC_6H_4	C	**12ba**	89
57	3-$F_3CC_6H_4$	C	**12bb**	84
58	4-$F_3CC_6H_4$	C	**12bc**	83
59	4-$EtOOCC_6H_4$	C	**12bd**	90
60	2-Naphthyl	C	**12be**	93
61	2-(4-Bromonaphthyl)	C	**12bf**	95
62	2-Fluorenyl	C	**12bg**	93
63	2-Pyridyl	C	**12bh**	71
64	6-Picolyl	C	**12bi**	70
65	2-Pyrimidyl	C	**12bj**	85
66	2-(5-Methylbenzthiazolyl)	C	**12bk**	80
67	NH-COC_6H_4	C	**12u**	90
68	CO-4-$H_2NC_6H_4$	C	**12bl**	92
69	4-$NH_2C_6H_4$	C	**12l**	94
70	2-(5-aminonaphthyl)	C	**12bm**	100

N-substituted pyrroles **14a-g** have also been prepared from one-pot Paal-Knorr condensation of 2,5-diketone **13** and the appropriate aromatic amine **9** using nano-crystalline sulfated zirconia (SZ) as the catalyst in ethanol at moderate temperature (Scheme 5, Table 5).[26]

Scheme 5

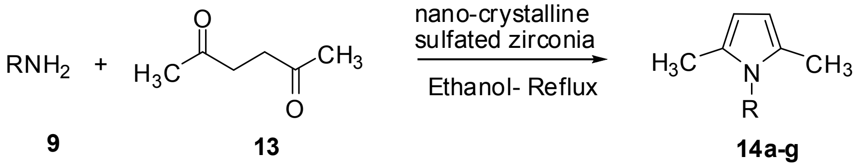


Table 5

Entry	R	Product	Yield (%)
1	C_6H_5	**14a**	94
2	$4\text{-}ClC_6H_4$	**14b**	90
3	$4\text{-}BrC_6H_4$	**14c**	85
4	$4\text{-}O_2NC_6H_4$	**14d**	90
5	$C_6H_5CH_2NH_2$	**14e**	81
6	$4\text{-}MeC_6H_4$	**14f**	90
7	$4\text{-}MeOC_6H_4$	**14g**	86

Li *et al*. reported one-pot three-component synthesis of multisubstituted pyrroles **17a-av** by the reaction of amines **9**, nitroolefins **16** and 1,3-dicarbonyl compounds **15** catalyzed by novel magnetic nano-$CoFe_2O_4$ supported Sb ([$CoFe_2O_4$@SiO_2–DABCO–Sb], Fig. 4), (Scheme 6, Table 6). The magnetic heterogeneous catalyst could be easily recovered using an external magnet and reused many times without significant loss of catalytic activity.[27]

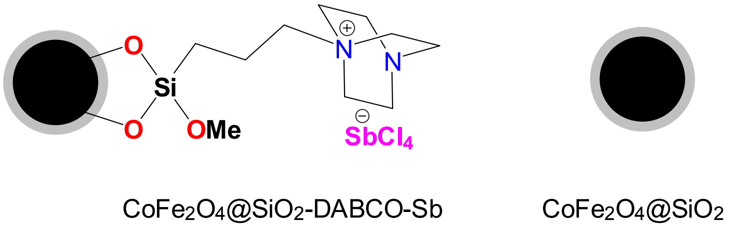
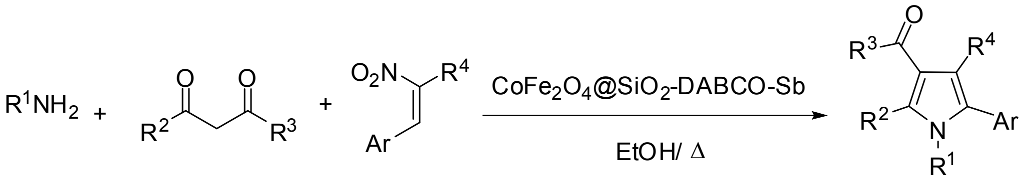


Fig. 4

Scheme 6



9 **15** **16** **17a-av**

Table 6

Entry	R^1	R^2	R^3	R^4	Ar	Product	Yield (%)
1	C_6H_5	Me	Me	H	C_6H_5	**17a**	93
2	C_6H_5	Me	Me	Me	C_6H_5	**17b**	80
3	C_6H_5	Me	Me	Me	4-MeC_6H_4	**17c**	87
4	C_6H_5	Me	Me	Me	4-FC_6H_4	**17d**	86
5	C_6H_5	Me	Me	Me	2-ClC_6H_4	**17e**	75
6	C_6H_5	Me	Me	Me	3-ClC_6H_4	**17f**	78
7	C_6H_5	Me	Me	Me	4-ClC_6H_4	**17g**	85
8	C_6H_5	Me	Me	Me	4-$O_2NC_6H_4$	**17h**	75
9	C_6H_5	Me	Me	Me	2-Furyl	**17i**	88
10	C_6H_5	Me	Me	Me	2-Thienyl	**17j**	82
11	C_6H_5	Me	Me	Me	2-Naphthyl	**17k**	47
12	C_6H_5	Me	Me	Et	C_6H_5	**17l**	80
13	C_6H_5	Me	Me	Et	4-MeC_6H_4	**17m**	80
14	C_6H_5	Me	Me	Et	2-Furyl	**17n**	76
15	C_6H_5	Me	Me	Et	2-Thienyl	**17o**	78
16	4-$^tBuC_6H_4$	Me	Me	H	C_6H_5	**17p**	92
17	2-Naphthyl	Me	Me	H	C_6H_5	**17q**	75
18	2-Fluorenyl	Me	Me	H	C_6H_5	**17r**	80
19	4-MeC_6H_4	Me	Me	Me	C_6H_5	**17s**	82
20	4-$MeOC_6H_4$	Me	Me	Me	C_6H_5	**17t**	88
21	4-FC_6H_4	Me	Me	Me	C_6H_5	**17u**	82
22	4-ClC_6H_4	Me	Me	Me	C_6H_5	**17v**	75
23	2-BrC_6H_4	Me	Me	Me	C_6H_5	**17w**	70
24	3-BrC_6H_4	Me	Me	Me	C_6H_5	**17x**	72
25	4-BrC_6H_4	Me	Me	Me	C_6H_5	**17y**	77
26	4-$F_3CC_6H_4$	Me	Me	Me	C_6H_5	**17z**	51
27	4-$F_3COC_6H_4$	Me	Me	Me	C_6H_5	**17aa**	85
28	2-Furyl-CH_2	Me	Me	Me	C_6H_5	**17ab**	90
29	2-Fluorenyl	Me	Me	Me	C_6H_5	**17ac**	73
30	Allyl	Me	Me	Me	C_6H_5	**17ad**	91
31	Bn	Me	Me	Me	C_6H_5	**17ae**	90
32	$C_6H_5CH_2CH_2$	Me	Me	Me	C_6H_5	**17af**	92
33	$C_6H_5CH(CH_3)$-	Me	Me	Me	C_6H_5	**17ag**	87
34	^cPr	Me	Me	Me	C_6H_5	**17ah**	89
35	^cPn	Me	Me	Me	C_6H_5	**17ai**	72
36	^nPr	Me	Me	Me	C_6H_5	**17aj**	88
37	^nBu	Me	Me	Me	C_6H_5	**17ak**	86
38	C_6H_5	Me	OMe	Me	C_6H_5	**17al**	82
39	C_6H_5	Me	OEt	Me	C_6H_5	**17am**	85
40	C_6H_5	Me	$O(CH_2)_2OMe$	Me	C_6H_5	**17an**	80
41	C_6H_5	41	O-allyl	Me	C_6H_5	**17ao**	78
42	C_6H_5	Et	OMe	Me	C_6H_5	**17ap**	76
43	C_6H_5	Me	$OCMe_3$	Me	C_6H_5	**17aq**	83
44	C_6H_5	Me	$OCH_2CH(CH_3)_2$	Me	C_6H_5	**17ar**	81
45	2-Furyl-CH_2	Me	Me	Et	C_6H_5	**17as**	89
46	Bn	Me	Me	Et	C_6H_5	**17at**	86
47	^cPr	Me	Me	Et	C_6H_5	**17au**	82
48	^nPr	Me	Me	Et	C_6H_5	**17av**	83

Sabbaghan and Ghalaei *et al*. reported a simple procedure for synthesis of polysubstituted pyrroles **20a-m** by the three-component reaction of amines **9**, phenacyl bromide **18** and dialkyl acetylenedicarboxylates **19** under solvent free conditions using nano structures of ZnO as catalyst (Scheme 7, Table 7).[28]

Scheme 7

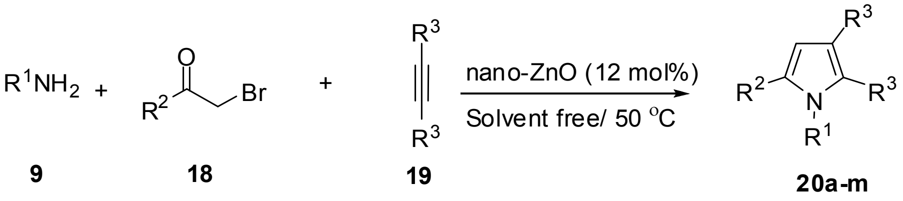


Table 7

Entry	R^1	R^2	R^3	Product	Yield (%)
1	Et	C_6H_5	COOMe	**20a**	90
2	Et	C_6H_5	COOEt	**20b**	88
3	Bn	C_6H_5	COOMe	**20c**	90
4	Bn	C_6H_5	COOEt	**20d**	94
5	$4\text{-}ClC_6H_2\text{-}CH_2\text{-}$	C_6H_5	COOEt	**20e**	92
6	$4\text{-}MeC_6H_2\text{-}CH_2\text{-}$	C_6H_5	COOEt	**20f**	86
7	^{n}Hexyl	C_6H_5	COOMe	**20g**	92
8	^{n}Hexyl	C_6H_5	COOEt	**20h**	86
9	Et	$4\text{-}MeOC_6H_4$	COOEt	**20i**	75
10	Et	$4\text{-}ClC_6H_4$	COOMe	**20j**	78
11	C_6H_5	C_6H_5	COOEt	**20k**	0
12	$4\text{-}MeOC_6H_5$	C_6H_5	COOEt	**20l**	0
13	^{n}Hexyl	COOEt	COOMe	**20m**	0

ZnO nano particles catalyze the reaction through its Lewis acid sites (Zn^{2+}) and Lewis basic sites (O^{2-}).[29,30] In this reaction, the Zn^{2+} sites are interacting with carbonyl groups in acetylenic compound and phenacyl bromide and Lewis basic sites [O^{2-}] taking up a proton from the generated enamine to give the pyrrole structure.

A magnetic nanoparticle $CoFe_2O_4$ supported molybdenum catalyst ([$CoFe_2O_4@SiO_2\text{-}PrNH_2\text{-}Mo(acac)_2$]), (Fig. 5), was prepared and found to be a highly active and efficient catalyst for a one-pot synthesis of polysubstituted pyrroles **22a-aq** *via* a four-component reaction of aldehydes **7**, amines **9**, 1,3-dicarbonyl compounds **15** and nitromethane **21** (Scheme 8, Table 8). The catalyst could be easily recovered by simple magnetic decantation and reused five times without significant loss of activity.[31]

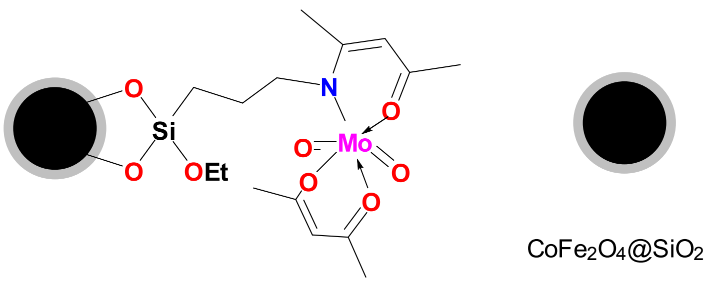
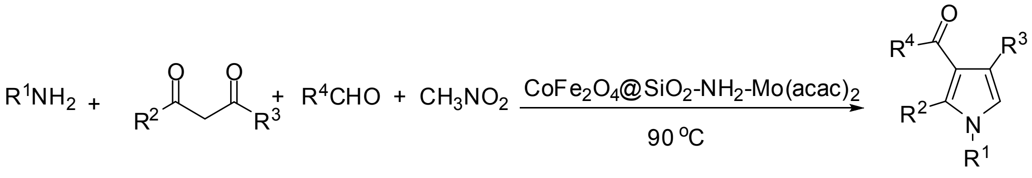


Fig. 5

Scheme 8



9 **15** **7** **21** **22a-aq**

Table 8

Entry	R^1	R^2	R^3	R^4	Product	Yield (%)
1	C_6H_5	Me	Me	C_6H_5	**22a**	90
2	4-$MeOC_6H_4$	Me	Me	C_6H_5	**22b**	86
3	4-MeC_6H_4	Me	Me	C_6H_5	**22c**	92
4	4-FC_6H_4	Me	Me	C_6H_5	**22d**	90
5	4-ClC_6H_4	Me	Me	C_6H_5	**22e**	80
6	4-BrC_6H_4	Me	Me	C_6H_5	**22f**	82
7	4-$O_2NC_6H_4$	Me	Me	C_6H_5	**22g**	50
8	4-$F_3COC_6H_4$	Me	Me	C_6H_5	**22h**	80
9	1-Naphthyl	Me	Me	C_6H_5	**22i**	48
10	2-Fluorenyl	Me	Me	C_6H_5	**22j**	83
11	Allyl	Me	Me	C_6H_5	**22k**	88
12	Bn	Me	Me	C_6H_5	**22l**	90
13	4-MeC_6H_4-CH_2-	Me	Me	C_6H_5	**22m**	91
14	4-FC_6H_4-CH_2-	Me	Me	C_6H_5	**22n**	87
15	C_6H_4-CH_2-CH_2-	Me	Me	C_6H_5	**22o**	91
16	4-HOC_6H_4-CH_2-CH_2-	Me	Me	C_6H_5	**22p**	90
17	^{c}Pr	Me	Me	C_6H_5	**22q**	90
18	^{c}Pn	Me	Me	C_6H_5	**22r**	86
19	^{n}Pr	Me	Me	4-FC_6H_4	**22s**	90
20	C_6H_5	Me	Me	4-$(Me_2)CHOC_6H_4$	**22t**	81
21	C_6H_5	Me	Me	4-FC_6H_4	**22u**	87
22	C_6H_5	Me	Me	4-ClC_6H_4	**22v**	86
23	C_6H_5	Me	Me	4-BrC_6H_4	**22w**	85
24	C_6H_5	Me	Me	4-$O_2NC_6H_4$	**22x**	83
25	C_6H_5	Me	Me	4-$F_3CC_6H_4$	**22y**	85
26	C_6H_5	Me	Me	2-Furyl	**22z**	60
27	C_6H_5	Me	Me	2-Thienyl	**22aa**	71
28	C_6H_5	Me	Me	1-Naphthyl	**22ab**	80
29	4-MeC_6H_4-CH_2-	Me	Me	2-Thienyl	**22ac**	80
30	4-FC_6H_4	Me	Me	2-Thienyl	**22ad**	75
31	4-FC_6H_4	Me	Me	2-(5-Methylthienyl)	**22ae**	78
32	4-ClC_6H_4	Me	Me	2-(5-Methylthienyl)	**22af**	70
33	2-Fluorenyl	Me	Me	2-(5-Methylthienyl)	**22ag**	80
34	Bn	Me	Me	2-Thienyl	**22ah**	80
35	C_6H_4-CH_2-CH_2-	Me	Me	4-MeC_6H_4	**22ai**	88
36	C_6H_4-CH_2-CH_2-	Me	Me	4-FC_6H_4	**22aj**	89
37	C_6H_4-CH_2-CH_2-	Me	Me	3-$F_3CC_6H_4$	**22ak**	85
38	^{c}Pr	Me	Me	4-^{t}BuC_6H_4	**22al**	88
39	C_6H_5	Me	OMe	C_6H_5	**22am**	80
40	C_6H_5	Me	OEt	C_6H_5	**22an**	82
41	C_6H_5	Me	$O(CH_2)_2OMe$	C_6H_5	**22ao**	80
42	C_6H_5	Me	O-allyl	C_6H_5	**22ap**	78
43	C_6H_5	Et	OMe	C_6H_5	**22aq**	80

2.1.2. Five-membered rings with two heteroatoms

2.1.2.1. Pyrazole

Emtiazi *et al.* developed a convenient and direct approach for the preparation of pyrazole derivatives **24a-q** in good yields by condensing 1,3-diketones **15** and hydrazines **23** in the presence of nano-silica sulfuric acid. Investigation was made of a series of aromatic hydrazines bearing either electron-donating or electron-withdrawing groups on the aromatic ring (Scheme 9, Table 9, Method A). The substitution group on the phenyl ring did not affect the reaction significantly neither in the product yield nor in the reaction rate.[32]

Various hydrazines and hydrazides reacted also efficiently with 1,3-diketones in the presence of supported glutathione on magnetic nanoparticles (Fig. 2) under microwave irradiation to give the pyrazoles **24r-y** in good yields (Scheme 9, Table 9, Method B).[24]

Scheme 9

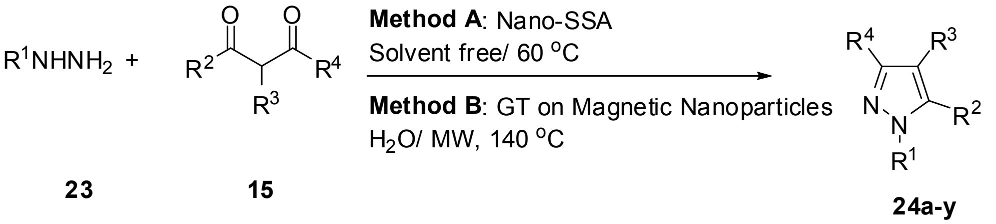


Table 9

Entry	R^1	R^2	R^3	R^4	Product	Method	Yield (%)
1	2,4-$(O_2N)_2$-C_6H_3	Me	H	Me	**24a**	A	85
2	2,4-$(O_2N)_2$-C_6H_3	C_6H_5	H	Me	**24b**	A	92
3	2,4-$(O_2N)_2$-C_6H_3	C_6H_5	H	C_6H_5	**24c**	A	92
4	2,4-$(O_2N)_2$-C_6H_3	Me	Cl	Me	**24d**	A	89
5	C_6H_5	C_6H_5	H	C_6H_5	**24e**	A	93
6	C_6H_5	Me	Cl	Me	**24f**	A	93
7	H	C_6H_5	H	Me	**24g**	A	87
8	4-BrC_6H_4	Me	Cl	Me	**24h**	A	94
9	4-BrC_6H_4	C_6H_5	H	C_6H_5	**24i**	A	90
10	4-BrC_6H_4	C_6H_5	H	Me	**24j**	A	92
11	4-MeC_6H_4	C_6H_5	H	C_6H_5	**24k**	A	87
12	4-MeC_6H_4	C_6H_5	H	Me	**24l**	A	89
13	4-$MeOC_6H_4$	C_6H_5	H	C_6H_5	**24m**	A	74
14	4-$MeOC_6H_4$	C_6H_5	H	Me	**24n**	A	88
15	4-$MeC_6H_4SO_2$	Me	H	Me	**24o**	A	83
16	4-$MeC_6H_4SO_2$	C_6H_5	H	C_6H_5	**24p**	A	83
17	4-$MeC_6H_4SO_2$	C_6H_5	H	Me	**24q**	A	84
18	C_6H_5	Me	H	Me	**24r**	B	96
19	C_6H_5	Me	Cl	Me	**24s**	B	80
20	C_6H_5	Me	Et	Me	**24t**	B	84
21	4-ClC_6H_4	Me	H	Me	**24u**	B	82
22	4-ClC_6H_4	Me	Cl	Me	**24v**	B	78
23	4-ClC_6H_4	Me	Et	Me	**24w**	B	84
24	C_6H_5CO	Me	H	Me	**24x**	B	88
25	2-Furoyl	Me	H	Me	**24y**	B	84

2.1.2.2. Imidazole

Nano-$SnCl_4 \cdot SiO_2$ as a solid Lewis acid has been synthesized by the reaction of nano-SiO_2 and $SnCl_4$. The catalyst has been found to be an extremely efficient catalyst for the preparation of 2,4,5-trisubstituted imidazoles **26** *via* three-component reactions of benzyl **25**, aldehydes **7** and ammonium acetate under mild conditions (Scheme 10, Table 10, Method A). Furthermore, the catalyst could be recovered conveniently and reused for at least three times.[33]

Safari and Zarnegar also synthesized trisubstituted imidazoles **26** in high yield in the presence of sulphamic acid functionalized magnetic Fe_3O_4 nanoparticles (SA–MNPs, Fig. 6) as a novel solid acid catalyst. The reaction proceeds *via* a three component reaction of benzil **25**, aromatic aldehyde **7** and ammonium acetate under solvent-free classical heating conditions or using microwave irradiation (Scheme 10, Table 10, Method B). The heterogeneous catalyst could be recovered easily and reused many times without significant loss of catalytic activity.[34]

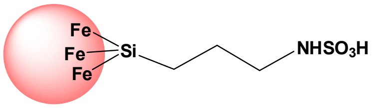
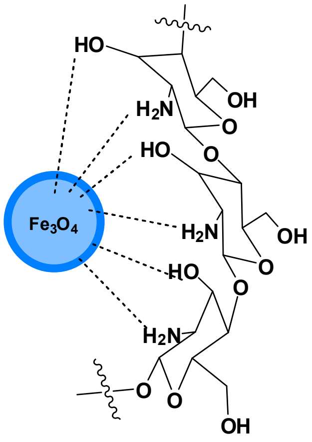


Fig.6

Nano-$TiCl_4 \cdot SiO_2$ has been found to be an extremely efficient catalyst for the preparation of 2,4,5-trisubstituted imidazoles **26** *via* similar three-component reactions (Scheme 10, Table 10, Method C). Nano-$TiCl_4 \cdot SiO_2$ as a solid Lewis acid has been synthesized by reaction of nano-SiO_2 and $TiCl_4$.[35]

Zarnegar and Safari prepared chitosan-coated Fe_3O_4 nanoparticles (Fe_3O_4@CS, Fig. 7) through in *situ* co-precipitation of Fe^{2+} and Fe^{3+} ions *via* NH_4OH in an aqueous solution of chitosan and investigated their catalytic activity in the synthesis of 2,4,5-trisubstituted imidazoles **26** by a similar one-pot reaction (Scheme 10, Table 10, Method D).[36]



Fe_3O_4@CS

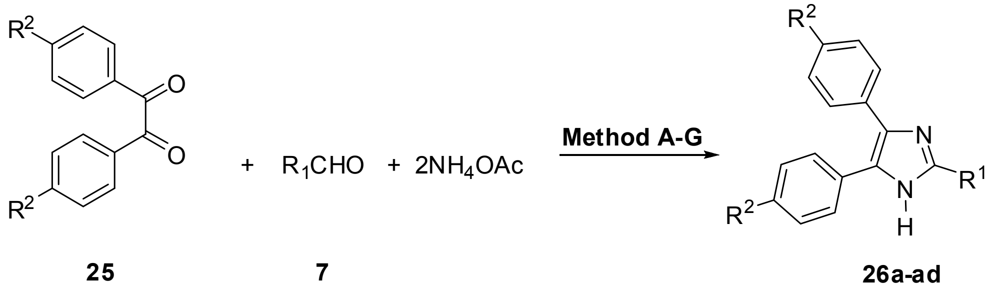
Fig. 7

Teimouri and Chermahini reported a synthesis of 2,4,5-trisubstituted imidazoles **26** by a similar three components cyclocondensation reaction using nano-crystalline sulfated zirconia (SZ) as catalyst in ethanol at moderate temperature (Scheme 10, Table 10, Method E). It can be seen that electron donating and electron withdrawing groups does not show any difference on the reaction yields.[37]

Sulfonic acid functionalized SBA-15 nanoporous material (SBA-Pr-SO_3H) with a pore size of 6 nm was found to be a green and effective solid acid catalyst in the one-pot synthesis of 2,4,5-trisubstituted imidazoles **26** under solvent-free conditions (Scheme 10, Table 10, Method F).[38]

Keivanloo *et al*. used boehmite nanoparticles (AlOOH NPs) as a highly active and green catalyst for the synthesis of highly substituted imidazoles **26** under solvent-free conditions (Scheme 10, Table 10, Method G).[39]

Scheme 10



Method A: Nano-$SnCl_4.SiO_2$/ solvent free, 130 °C
Method B: NH_4OAc/ SA-MNPs/ Δ, 100 °C or MW
Method C: Nano-$TiCl_4.SiO_2$/ solvent free, 110 °C
Method D: Nano-Fe_3O_4@CS/ EtOH, Δ
Method E: Nano-sulfated zirconia/ EtOH, Δ
Method F: Nano-SBA-Pr-SO_3H/ solvent free, 140 °C
Method G: AlOOH NPs/ solvent free, 120 °C

Table 10

Entry	R^1	R^2	Product	Method	Yield (%)
1	C_6H_5	H	**26a**	A	95
2	4-MeC_6H_4	H	**26b**	A	83
3	4-$O_2NC_6H_4$	H	**26c**	A	96
4	4-ClC_6H_4	H	**26d**	A	95
5	2-$MeOC_6H_4$	H	**26e**	A	80
6	4-$MeOC_6H_4$	H	**26f**	A	85
7	2-ClC_6H_4	H	**26g**	A	89
8	2,4-$Cl_2C_6H_4$	H	**26h**	A	91
9	4-BrC_6H_4	H	**26i**	A	92
10	2-$O_2NC_6H_4$	H	**26j**	A	87
11	3-$O_2NC_6H_4$	H	**26k**	A	93
12	2-BrC_6H_4	H	**26l**	A	90
13	C_6H_5	H	**26a**	B	85 (96)
14	4-MeC_6H_4	H	**26b**	B	87 (99)
15	3-MeC_6H_4	H	**26m**	B	76(95)
16	4-MeC_6H_4	H	**26b**	B	82(98)
17	4-ClC_6H_4	H	**26d**	B	78(95)
18	3-ClC_6H_4	H	**26n**	B	83(95)
19	4-BrC_6H_4	H	**26i**	B	88(93)
20	3-BrC_6H_4	H	**26o**	B	78(95)
21	2-Naphthyl	H	**26p**	B	77(94)
22	2,4-$Cl_2C_6H_3$	H	**26q**	B	79(94)
23	2-Thienyl	H	**26r**	B	75(95)
24	3-$O_2NC_6H_4$	H	**26k**	B	85(93)
25	4-$Me_2NC_6H_4$	H	**26s**	B	77(96)
26	2-HOC_6H_4	H	**26t**	B	85(93)
27	3-HOC_6H_4	H	**26u**	B	90(93)
28	C_6H_5	H	**26a**	C	90
29	4-$Me_2NC_6H_4$	H	**26s**	C	91
30	4-$MeOC_6H_4$	H	**26f**	C	92
31	2-$MeOC_6H_4$	H	**26e**	C	89
32	2-ClC_6H_4	H	**26g**	C	88
33	4-ClC_6H_4	H	**26d**	C	89
34	2,4-$Cl_2C_6H_3$	H	**26q**	C	84
35	4-BrC_6H_4	H	**26i**	C	89
36	2-$O_2NC_6H_4$	H	**26j**	C	85
37	3-$O_2NC_6H_4$	H	**26k**	C	87
38	4-$O_2NC_6H_4$	H	**26c**	C	89
39	4-MeC_6H_4	H	**26b**	C	-

* In Method B MW yields % were indicated between paranthes

Entry	R^1	R^2	Product	Method	Yield (%)
40	C_6H_5	H	**26a**	D	95
41	4-MeOC_6H_4	H	**26f**	D	90
42	3-MeOC_6H_4	H	**26v**	D	92
43	4-ClC_6H_4	H	**26d**	D	96
44	3-MeOC_6H_4	H	**26v**	D	98
45	2-Naphthyl	H	**26p**	D	98
46	3-MeOC_6H_4	H	**26v**	D	98
47	C_6H_5	OMe	**26w**	D	95
48	4-MeOC_6H_4	OMe	**26x**	D	90
49	2-Naphthyl	OMe	**26y**	D	95
50	3-MeOC_6H_4	F	**26vz**	D	98
51	2-Naphthyl	F	**26aa**	D	98
52	C_6H_5	H	**26a**	E	87
53	4-ClC_6H_4	H	**26d**	E	92
14	4-BrC_6H_4	H	**26i**	E	81
55	4-$O_2NC_6H_4$	H	**26c**	E	80
56	4-HOC_6H_4	H	**26ab**	E	82
57	4-MeC_6H_4	H	**26a**	E	93
58	4-MeOC_6H_4	H	**26f**	E	85
59	C_6H_5	H	**26a**	F	100
60	4-ClC_6H_4	H	**26d**	F	99
61	4-MeOC_6H_4	H	**26f**	F	98
62	4-HOC_6H_4	H	**26ac**	F	80
63	4-$Me_2NC_6H_4$	H	**26s**	F	93
64	3-$O_2NC_6H_4$	H	**26k**	F	87
65	2-HOC_6H_4	H	**26t**	F	80
66	C_6H_5	H	**26a**	G	98
67	3-$O_2NC_6H_4$	H	**26k**	G	79
68	4-MeC_6H_4	H	**26b**	G	88
69	2-ClC_6H_4	H	**26g**	G	95
70	4-ClC_6H_4	H	**26d**	G	86
71	3,4-$Cl_2C_6H_3$	H	**26ad**	G	83
72	4-MeOC_6H_4	H	**26f**	G	85
73	2-MeOC_6H_4	H	**26e**	G	78

Teimouri and Chermahinib reported a versatile and efficient synthesis of 1,2,4,5-tetrasubstituted imidazoles **27** in high yields by four component cyclocondensation of benzyl **25**, aniline **9**, ammonium acetate and various aromatic aldehydes **7** using nano-crystalline sulfated zirconia (SZ) as a catalyst in ethanol at moderate temperature (Scheme 11, Table 11, Method A).[37]

Ziarani *et al*. used sulfonic acid functionalized SBA-15 nanoporous material (SBA-Pr-SO_3H) with a pore size of 6 nm as an effective catalyst in the synthesis of a variety of tetrasubstituted imidazoles **27** (Scheme 11, Table 11, Method B).[38]

Montazeri *et al*. reported also a four-component synthesis of 1,2,4,5-tetrasubstituted imidazoles **27** using nano Fe_3O_4 as magnetically recyclable catalyst under solvent free conditions (Scheme 11, Table 11, Method C).[40]

Mirjalili *et al*. applied Nano-$TiCl_4$.SiO_2 (Fig. 8) as an efficient catalyst for synthesis of 1,2,4,5-triphenylimidazoles **27** with good to excellent yields *via* a similar four-component reaction (Scheme 11, Table 11, Method D).[41]

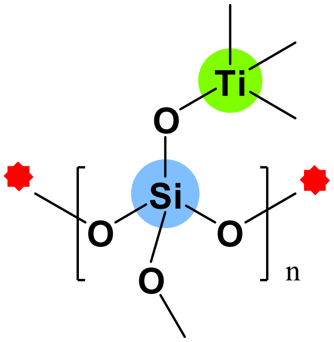


Fig. 8

Keivanloo *et al*. reported the synthesis of 1,2,4,5-tetrasubstituted imidazoles **27** catalyzed by oboehmite nanoparticles (AlOOH NPs) under solvent-free conditions (Scheme 11, Table 11, Method E). The results show that the reactions are equally facile with both electron donating and electron-withdrawing substituents present on both the aromatic aldehydes **7** and aromatic amines **9**, resulting in good-to high yields of the corresponding imidazoles **27**. Aliphatic amines also reacted efficiently, affording the desired products in 78–90% yield.[39]

Ray *et al*. prepared a porous silica nano particle (PSNP-CA, Fig. 9), by post synthesis grafting of COOH functionalized organosilane on porous silica nano particle by using surface hydroxyl groups as anchor point. This catalyst was found to promote the chemoselective synthesis of 1,2,4,5-tetrasubstituted imidazole **27** in water during a similar four multi-component reaction (Scheme 11, Table 11, Method F).[42]

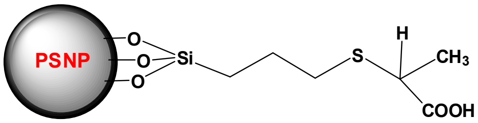
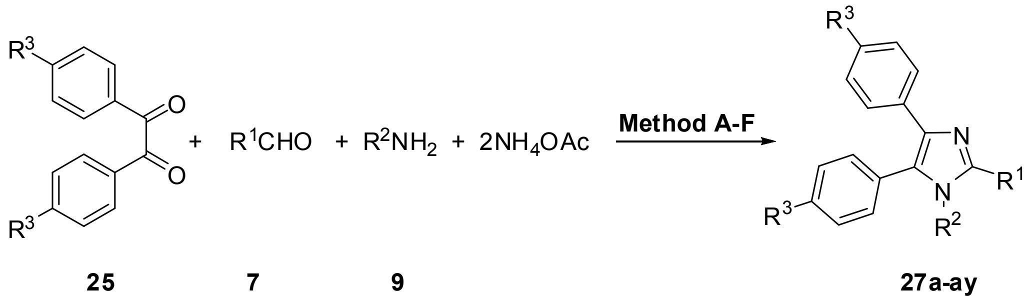


Fig.9

Scheme 11



Method A: Nano-crystaline SZ/ EtOH, Δ
Method B: Nano-SBA-Pr-SO_3H/ solvent free, 140 °C
Method C: Nano-Fe_3O_4/ solvent free
Method D: Nano-$TiCl_4$-SiO_2/ solvent free, 110 °C
Method E: AlOOH NPs/ solvent free, 120 °C
Method F: PSNP-CA/ H_2O, r.t.

Table 11

Entry	R^1	R^2	R3	Method	Product	Yield (%)
1	C_6H_5	C_6H_5	H	A	**27a**	87
2	4-ClC_6H_4	C_6H_5	H	A	**27b**	92
3	4-BrC_6H_4	C_6H_5	H	A	**27c**	85
4	4-$O_2NC_6H_4$	C_6H_5	H	A	**27d**	76
5	4-HOC_6H_4	C_6H_5	H	A	**27e**	85
6	4-MeC_6H_4	C_6H_5	H	A	**27f**	87
7	4-$MeOC_6H_4$	C_6H_5	H	A	**27g**	80
8	4-ClC_6H_4	C_6H_5	H	B	**27b**	100
9	4-ClC_6H_4	Bn	H	B	**27h**	100
10	4-$MeOC_6H_4$	C_6H_5	H	B	**27g**	97
11	4-MeC_6H_4	C_6H_5	H	B	**27f**	99
12	4-MeC_6H_4	Bn	H	B	**27i**	95
13	4-$Me_2NC_6H_4$	Bn	H	B	**27j**	99
14	3-$O_2NC_6H_4$	C_6H_5	H	B	**27k**	95
15	3-$MeOC_6H_4$	Bn	H	B	**27l**	84
16	C_6H_5	C_6H_5	H	C	**27a**	94
17	C_6H_5	Bn	H	C	**27m**	92
18	4-$O_2NC_6H_4$	4-MeC_6H_4	H	C	**27n**	80
19	4-ClC_6H_4	C_6H_5	H	C	**27b**	85
20	4-MeC_6H_4	Bn	H	C	**27i**	75
21	4-MeC_6H_4	C_6H_5	H	C	**27f**	91
22	4-ClC_6H_4	4-$O_2NC_6H_4$	H	C	**27o**	79
23	4-$O_2NC_6H_4$	Bn	H	C	**27p**	81
24	4-MeC_6H_4	Bn	H	C	**27i**	87
25	4-ClC_6H_4	Bn	H	C	**27h**	82
26	4-$MeOC_6H_4$	C_6H_5	H	C	**27g**	92
27	4-$MeOC_6H_4$	Bn	H	C	**27q**	93
28	C_6H_5	Me	H	C	**27r**	80

Entry	R^1	R^2	R^3	Method	Product	Yield (%)
29	C_6H_5	C_6H_5	H	D	**27a**	82
30	C_6H_5	Bn	H	D	**27m**	84
31	C_6H_5	^{c}Hexyl	H	D	**27s**	64
32	C_6H_5	Et	H	D	**27t**	70
33	4-ClC_6H_4	C_6H_5	H	D	**27b**	81
34	4-ClC_6H_4	Bn	H	D	**27h**	79
35	2-ClC_6H_4	Bn	H	D	**27u**	83
36	4-HOC_6H_4	Bn	H	D	**27v**	68
37	4-MeC_6H_4	C_6H_5	H	D	**27f**	73
38	4-MeC_6H_4	Bn	H	D	**27i**	91
39	4-MeC_6H_4	^{c}Hexyl	H	D	**27w**	75
40	3-$MeOC_6H_4$	Bn	H	D	**27l**	91
41	2-$O_2NC_6H_4$	Bn	H	D	**27x**	86
42	^{i}Pr	Bn	H	D	**27y**	60
43	C_6H_5	C_6H_5	H	E	**27a**	94
44	C_6H_5	Bn	H	E	**27m**	96
45	4-MeC_6H_4	C_6H_5	H	E	**27f**	86
46	4-ClC_6H_4	C_6H_5	H	E	**27b**	92
47	C_6H_5	3-ClC_6H_4	H	E	**27z**	93
48	4-$O_2NC_6H_4$	C_6H_5	H	E	**27d**	78
49	C_6H_5	^{c}Hexyl	H	E	**27s**	89
50	C_6H_5	4-$O_2NC_6H_4$	H	E	**27aa**	80
51	C_6H_5	^{n}Pr	H	E	**27ab**	88
52	C_6H_5	$MeOCH_2CH_2$-	H	E	**27ac**	90
53	C_6H_5	^{i}Pr	H	E	**27ad**	85
54	C_6H_5	^{n}Bu	H	E	**27ae**	86
55	C_6H_5	2-THF-CH_2-	H	E	**27af**	78

Entry	R^1	R^2	R^3	Method	Product	Yield (%)
56	$4\text{-}O_2NC_6H_4$	$3,4\text{-}Me_2C_6H_3$	H	F	**27ag**	96
57	$3\text{-}O_2NC_6H_4$	$3,4\text{-}Me_2C_6H_3$	H	F	**27ah**	96
58	$4\text{-}NCC_6H_4$	$3,4\text{-}Me_2C_6H_3$	H	F	**27ai**	94
59	$4\text{-}MeOC_6H_4$	$4\text{-}MeC_6H_4$	H	F	**27aj**	94
60	$3\text{-}O_2NC_6H_4$	$3\text{-}MeC_6H_4$	H	F	**27ak**	95
61	$4\text{-}BrC_6H_4$	$4\text{-}MeOC_6H_4$	H	F	**27al**	94
62	$3\text{-}O_2NC_6H_4$	$3\text{-}MeOC_6H_4$	H	F	**27am**	91
63	$4\text{-}NCC_6H_4$	$4\text{-}MeC_6H_4$	H	F	**27an**	92
64	$4\text{-}MeOC_6H_4$	$3,4\text{-}Me_2C_6H_3$	H	F	**27ao**	88
65	$4\text{-}O_2NC_6H_4$	Bn	Cl	F	**27ap**	96
66	$4\text{-}O_2NC_6H_4$	$3,4\text{-}Me_2C_6H_3$	Cl	F	**27aq**	97
67	$3\text{-}O_2NC_6H_4$	$3,4\text{-}Me_2C_6H_3$	Cl	F	**27ar**	97
68	$4\text{-}O_2NC_6H_4$	$3,4\text{-}Me_2C_6H_3$	Me	F	**27as**	85
69	^{n}Pr	^{c}Hexyl	H	F	**27at**	78
70	$4\text{-}BrC_6H_4$	^{c}Hexyl	H	F	**27au**	95
71	$4\text{-}MeOC_6H_4$	^{c}Hexyl	H	F	**27av**	89
72	4-Pyridyl	$3,4\text{-}Me_2C_6H_3$	H	F	**27aw**	83
73	$3\text{-}O_2NC_6H_4$	$3\text{-}O_2NC_6H_4$	H	F	**27ax**	91
74	$4\text{-}ClC_6H_4$	$3,4\text{-}Me_2C_6H_3$	H	F	**27ay**	97

Mitra *et al*. have explored the use of nano In_2O_3 as an effective and versatile catalyst for the synthesis of 4,5-unsymmetrically substituted 1-*H*-imidazoles **26ae-ap** in good yields. The reaction was performed by the reaction of varying amidines **28** with a wide range of structurally diverse nitroolefins **29** (Scheme 12, Table 12). As it is evident from Table 12, this procedure is uniformly effective for nitroolefins with different substituents on the benzene ring as well as for aliphatic nitroolefin.[43] Based on previous results, the indium (III) catalyst promotes Michael addition of amidine-nitroolefin by activating the double bond.[44]

Scheme 12

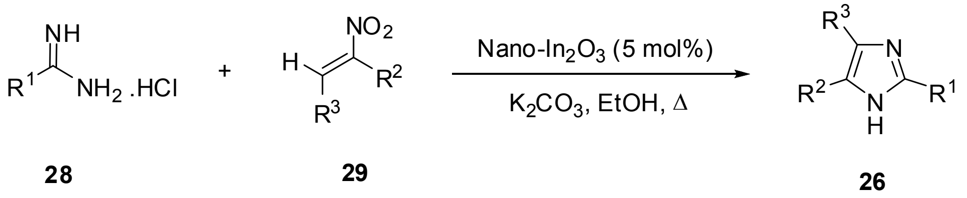


Table 12

Entry	R^1	R^2	R^3	Product	Yield (%)
1	C_6H_5	Me	C_6H_5	**26ae**	88
2	C_6H_5	Me	4-$MeOC_6H_4$	**26af**	80
3	C_6H_5	Me	4-ClC_6H_4	**26ag**	70
4	C_6H_5	Me	4-MeC_6H_4	**26ah**	80
5	C_6H_5	Me	4-BrC_6H_4	**26ai**	72
6	C_6H_5	Me	^{i}Pr	**26aj**	65
7	C_6H_5	Me	3,4-$CH_2O_2C_6H_3$	**26ak**	81
8	C_6H_5	Me	2-Furyl	**26al**	79
9	C_6H_5	Et	C_6H_5	**26am**	70
10	3-$O_2NC_6H_4$	Me	C_6H_5	**26an**	75
11	3-$O_2NC_6H_4$	Me	4-$MeOC_6H_4$	**26ao**	82
12	Me	Me	C_6H_5	**26ap**	55

2.1.2.3. Thiazole

A magnetically ionic liquid supported on Fe_3O_4@SiO_2 nanoparticles (MNPs@ SiO_2-IL, Fig. 10) was synthesized and evaluated as a recoverable catalyst for the one-pot synthesis of 1,3-thiazolidin-4-ones **31a-j** in high to excellent yield by the three-component condensation of arylaldehydes **7**, anilines **9** and thioglycolic acid **30** under solvent-free conditions (Scheme 13, Table 13).[45] It can be speculated that the methylimidazolium cation $[MIM]^+$ in the MNPs@SiO_2-IL favors the interact on oxygen atom of the carbonyl group of the aldehyde and facilitates the formation of imine intermediate by increasing the electrophilicity of the carbonyl group of the aldehyde.

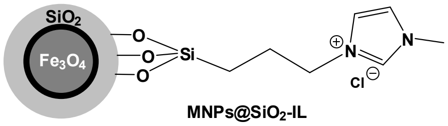


Fig. 10

Scheme 13

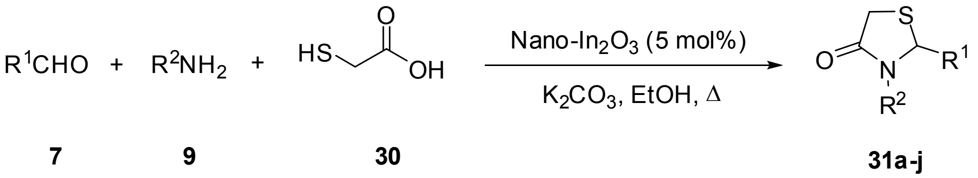


Table 13

Entry	R^1	R^2	Product	Yield (%)
1	C_6H_5	C_6H_5	**31a**	94
2	C_6H_5	4-MeC_6H_4	**31b**	90
3	C_6H_5	4-ClC_6H_4	**31c**	90
4	C_6H_5	4-$O_2NC_6H_4$	**31d**	86
5	4-MeC_6H_4	4-MeC_6H_4	**31e**	93
6	4-MeC_6H_4	C_6H_5	**31f**	88
7	4-ClC_6H_4	C_6H_5	**31g**	95
8	4-$O_2NC_6H_4$	C_6H_5	**31h**	92
9	4-$O_2NC_6H_4$	4-MeC_6H_4	**31i**	90
10	3-$O_2NC_6H_4$	C_6H_5	**31j**	89

2.1.3. Five-membered rings with three heteroatoms

2.1.3.1. Oxadiazole

4,5,6,7-Tetrahydro-6-((5-substituted-1,3,4-oxadiazol-2-yl)methyl)thieno[2,3-*c*]pyridi-nes **33a-m** have been prepared by subjecting hydrazide compound **32** and different aromatic aldehydes **7** to reflux in ethanol using combined nano (ZnO–TiO_2) (1 mmol each) as a catalyst (Scheme 14, Table 14).[46]

Scheme 14

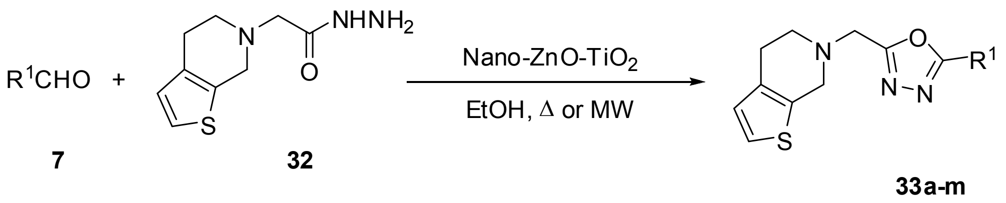


Table 14

Entry	R^1	Product	MW Yield (%)	Δ Yield (%)
1	4-ClC_6H_4	**33a**	96	91
2	C_6H_5	**33b**	91	88
3	4-$MeOC_6H_4$	**33c**	95	91
4	C_6H_5	**33d**	91	87
5	3,4-$(HO)_2C_6H_3$	**33e**	95	91
6	2,6-$Cl_2C_6H_4$	**33f**	91	88
7	2,4-$(MeO)_2C_6H_3$	**33g**	94	90
8	4-HOC_6H_4	**33h**	94	89
9	2-Pyrrolyl	**33i**	95	87
10	2-Thienyl	**33j**	94	88
11	4-FC_6H_4	**33k**	94	90
12	2,4-$Cl_2C_6H_4$	**33l**	92	89
13	2-Pyridyl	**33m**	95	87

2.1.3.2. 1,2,3-Triazole

Kaboudin *et al*. reported the synthesis of 1,2,3-triazoles **36a-q** *via* a one-pot reaction of arylboronic acids **34** with sodium azide in water at room temperature in the presence of Cu_2–β-CD (CD = Cyclodextrin) as a nanocatalyst followed by a click cyclization reaction with alkynes **35** (Scheme 15, Table 15).[47]

Scheme 15

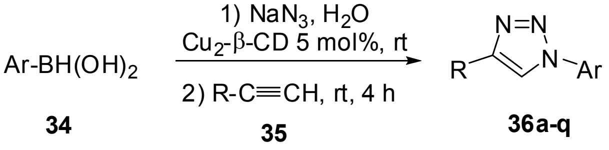


Table 15

Entry	Ar	R	Product	Yield (%)
1	C_6H_5	C_6H_5	**36a**	94
2	2-FC_6H_5	C_6H_5	**36b**	94
3	3-$O_2NC_6H_4$	C_6H_5	**36c**	95
4	3,5-$F_2C_6H_4$	C_6H_5	**36d**	96
5	4-MeC_6H_4	C_6H_5	**36e**	94
6	4-$MeOC_6H_4$	C_6H_5	**36f**	97
7	4-ClC_6H_5	C_6H_5	**36g**	96
8	4-HOC_6H_4	C_6H_5	**36h**	94
9	2-Naphthyl	C_6H_5	**36i**	94
10	C_6H_5	4-MeC_6H_4	**36j**	95
11	C_6H_5	3-$NH_2C_6H_4$	**36k**	95
12	C_6H_5	^{n}Pr	**36l**	93
13	C_6H_5	^{n}Bu	**36m**	89
14	C_6H_5	^{n}Pn	**36n**	91
15	C_6H_5	CH_2OH	**36o**	92
16	C_6H_5	$CH_3(CH_2)_3$-CH(OH-)	**36p**	90
17	C_6H_5	COOH	**36q**	94

The authors proposed mechanism for Cu_2–*β*-CD catalyzed in *situ* azidation of arylboronic acids **34** for the synthesis of 1,2,3-triazoles **36a-q**. The reaction is initiated by transmetallation of the aryl group from Boron to copper *via* the attack of the hydroxide ligand to the oxophilic boron center. The resulting arylcopper intermediate undergoes subsequent reductive azidation to the arylazide compound (Fig. 11). According to literature reports for the Cu-catalyzed azide-alkyne 1,3-dipolar cycloaddition,[48] the 1,2,3-triazole formation proceeds through attack of the hydroxido ligand of Cu_2-*β*-CD complex to the terminal hydrogen of acetylene to give copper acetylide. Continuing, coordination of the arylazide to the copper center of the acetylide initiates an azide–alkyne 1,3-dipolar cycloaddition.

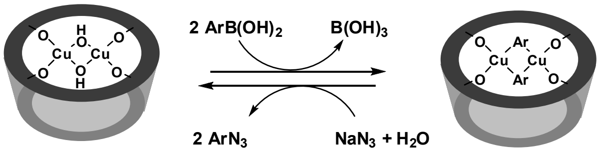
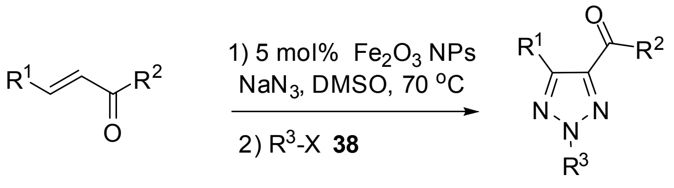


Fig. 11

Kamal and Swapna developed a new Fe_2O_3 nanoparticle catalyzed three-component reaction for the construction of 2,4,5-trisubstituted-1,2,3-triazoles **39a-x** from chalcones **37**, sodium azide and aryl halides **38.** This tandem three-component reaction involves an oxidative 1,3-dipolar cycloaddition of the chalcone and azide and subsequent regioselective *N*-2-arylation (Scheme 16, Table 16). Control experiments suggest that atmospheric oxygen acts as the sacrificial oxidant in the reaction. The reaction has good substrate scope and furnishes the products in very good yields. Importantly, the catalyst is easily recoverable and may be reused without any significant loss in catalytic activity.[49]

Scheme 16



37 **39a-x**

Table 16

Entry	R^1	R^2	R^3	X	Product	Yield (%)
1	2-FC_6H_4	2-FC_6H_4	2-$O_2NC_6H_4$	F	**39a**	92
2	4-FC_6H_4	3-$CF_3C_6H_4$	2-$O_2NC_6H_4$	F	**39b**	90
3	4-$O_2NC_6H_4$	C_6H_5	2-$O_2NC_6H_4$	F	**39c**	89
4	3-F-4-ClC_6H_3	4-FC_6H_4	2-$O_2NC_6H_4$	F	**39d**	80
5	4-$CF_3C_6H_4$	4-FC_6H_4	2-$O_2NC_6H_4$	F	**39e**	80
6	4-MeC_6H_4	C_6H_5	2-$O_2NC_6H_4$	F	**39f**	75
7	C_6H_5	4-$MeOC_6H_4$	2-$O_2NC_6H_4$	F	**39g**	65
8	4-MeC_6H_4	3-ClC_6H_4	2-$O_2NC_6H_4$	F	**39h**	70
9	4-$MeOC_6H_4$	4-FC_6H_4	2-$O_2NC_6H_4$	F	**39i**	75
10	3-MeO-4-FC_6H_3	4-FC_6H_4	2-$O_2NC_6H_4$	F	**39j**	72
11	4-$MeOC_6H_4$	4-FC_6H_4	2-F-4-$O_2NC_6H_3$	F	**39k**	62
12	4-MeC_6H_4	3-ClC_6H_4	2-F-4-$O_2NC_6H_3$	F	**39l**	59
13	4-$MeOC_6H_4$	4-FC_6H_4	2,4-$(O_2N)2C_6H_3$	Cl	**39m**	70
14	4-MeC_6H_4	3-ClC_6H_4	2-$O_2NC_6H_4$	Cl	**39n**	68
15	4-$^iPrC_6H_4$	C_6H_5	2-$O_2NC_6H_4$	F	**39o**	62
16	2-MeC_6H_4	C_6H_5	2-F-4-$O_2NC_6H_3$	F	**39p**	69
17	2-MeC_6H_4	C_6H_5	2-F-4-$O_2NC_6H_3$	F	**39q**	65
18	4-$O_2NC_6H_4$	C_6H_5	2-F-4-$O_2NC_6H_3$	F	**39r**	86
19	4-FC_6H_4	4-FC_6H_4	2-F-2,4-$(O_2N)_2C_6H_2$	F	**39s**	93
20	2-Thienyl	C_6H_5	2-$O_2NC_6H_4$	F	**39t**	-
21	2-Pyrrolyl	C_6H_5	2-$O_2NC_6H_4$	F	**39u**	-
22	2-MeC_6H_4	C_6H_5	2-$O_2NC_6H_4$	Cl	**39v**	-
23	4-FC_6H_4	4-FC_6H_4	4-O_2NPyridyl	Cl	**39w**	-
24	2-MeC_6H_4	C_6H_5	2-MeC_6H_4	Cl	**39x**	-

Wang *et al*. prepared nanoparticle-supported tris(triazolyl)–CuBr (Fig. 12), with a diameter of approximately 25 nm and evaluated its catalytic activity in the copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction (Scheme 17, Table 17, Method A). It was found that the procedure can be successfully extended to various organic azides and alkynes to afford the corresponding 1*H*-1,2,3-triazoles **41a-q**. [50]

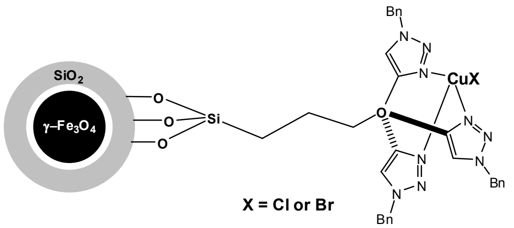


Fig. 12

Rad *et al.* reported that the 1,3-dipolar cycloaddition of organic azides with terminal alkynes **35** can be catalyzed by doped nano-sized Cu_2O on melamine formaldehyde resin (nano-Cu_2O MFR) to furnish the corresponding 1,4-disubstituted 1*H*-1,2,3-triazole adducts **41s–ag** in good to excellent yields at room temperature (Scheme 17, Table 17, Method B).[51]

Nano copper-doped silica cuprous sulfate (CDSCS), proved also to be a highly efficient heterogeneous catalyst for the regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles derivatives **41g** and **41ah-bj**. In this synthetic methodology, CDSCS catalyzes 1,3-dipolar Huisgen cycloaddition of different functionalized β-azido alcohols and alkynes in a (1:1, v/v) solution of THF/H_2O at room temperature (Scheme 17, Table 17, Method C). The catalyst can be easily prepared and reused for many consecutive runs without a significant decrease in its catalytic reactivity.[52]

Veerakumar *et al.* used highly dispersed SiO_2 supported CuNPs (copper nanoparticles, Fig. 13) as a recyclable heterogeneous nanocatalyst to employ the synthesis of 1,4-disubstituted-1,2,3-triazoles **41az-bi** *via* Huisgen 1,3-dipolar cycloaddition reactions of halides **38**, alkynes **35**, and sodium azide using DMSO as the solvent (Scheme 17, Table 17, Method D). All the reactions proceed smoothly to give **41** in high yield.[53]

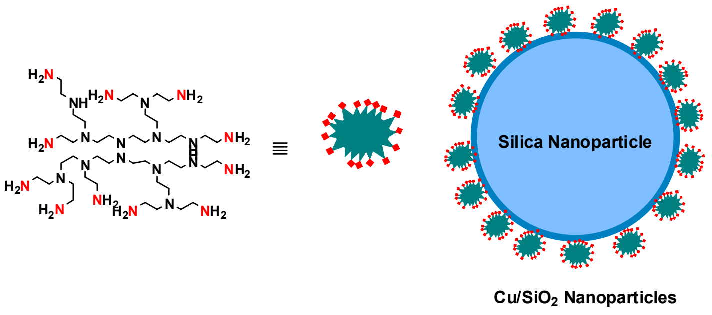
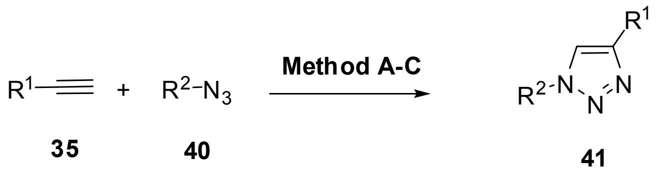


Fig. 13

Scheme 17

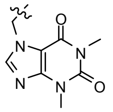


Method A: Tris(triazolyl)-CuBr-NPs 0.5 mol%/ H_2O, rt.
Method B: nano-Cu_2O MFR/ THF/ H_2O, rt.
Method C: CDSCS/ THF/ H_2O, rt.
Method D: Cu-SiO_2 NPs/ DMSO, rt.

Table 17

Entry	R^1	R^2	Method	Product	Yield (%)
1	C_6H_5	C_6H_{13}	A	**41a**	95
2	C_6H_5	C_8H_{17}	A	**41b**	91
3	C_6H_5	$C_{18}H_{32}$	A	**41c**	82
4	C_6H_5	C_6H_5	A	**41d**	92
5	C_6H_5	$4\text{-}MeOC_6H_4$	A	**41e**	83
6	C_6H_5	$4\text{-}IC_6H_4$	A	**41f**	81
7	C_6H_5	Bn	A	**41g**	96
8	$4\text{-}CHOC_6H_4$	Bn	A	**41h**	96
9	$4\text{-}MeOC_6H_4$	Bn	A	**41i**	94
10	$4\text{-}NH_2OC_6H_4$	Bn	A	**41j**	92
11	2-Pyridyl	Bn	A	**41k**	86
12	3-Pyridyl	Bn	A	**41l**	92
13	C_4H_9	Bn	A	**41m**	99
14	C_5H_{11}	Bn	A	**41n**	93
15	$HO\text{-}C(CH_3)$	Bn	A	**41o**	89
16	$HO\text{-}C(C_6H_5)$	Bn	A	**41p**	93
17	Ferrocenyl	Bn	A	**41q**	96
18	C_6H_5	$PhOCH_2CH(OH)CH_2\text{-}$	B	**41r**	93
19	C_6H_5	$2\text{-}HOC_6H_{10}\text{-}$	B	**41s**	92
20	C_6H_5	$CH_2{=}C(Me)COOCH_2CH(OH)CH_2\text{-}$	B	**41t**	83
21	$4\text{-}ClC_6H_4OCH_2$	$2,4\text{-}Cl_2C_6H_3OCH_2CH(OH)CH_2\text{-}$	B	**41u**	80
22	$4\text{-}ClC_6H_4OCH_2$	$4\text{-}BnC_6H_4OCH_2CH(OH)CH_2\text{-}$	B	**41v**	81
23	$Me_2C(OH)$	$4\text{-}MeOC_6H_4OCH_2CH(OH)CH_2\text{-}$	B	**41w**	85
24	$Me_2C(OH)$	$PhOCH_2CH(OH)CH_2\text{-}$	B	**41x**	91
25	$Me_2C(OH)$	$4\text{-}MeOC_6H_4OCH_2CH(OH)CH_2\text{-}$	B	**41y**	93
26	$HOCH_2$	$PhOCH_2CH(OH)CH_2\text{-}$	B	**41z**	88
27	$BrCH_2$	$4\text{-}ClC_6H_4OCH_2CH(OH)CH_2\text{-}$	B	**41aa**	86
28	-A	$4\text{-}MeOC_6H_4OCH_2CH(OH)CH_2\text{-}$	B	**41ab**	90
29	-A	$MeCH_2CH(OH)CH_2\text{-}$	B	**41ac**	88
30	-B	$4\text{-}MeOC_6H_4OCH_2CH(OH)CH_2\text{-}$	B	**41ad**	93
31	-B	$2\text{-}C_{10}H_7CH_2CH(OH)CH_2\text{-}$	B	**41ae**	92
32	-B	$2\text{-}HOC_6H_{10}\text{-}$	B	**41af**	83
33	$Ph\text{-}C{\equiv}CPh$	$2\text{-}HOC_6H_{10}\text{-}$	B	**41ag**	-

A =



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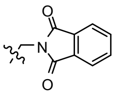
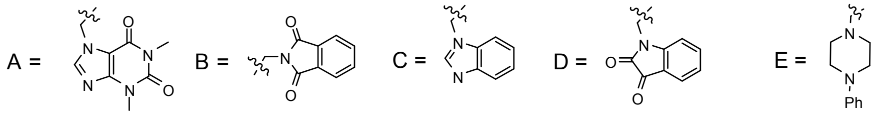


Entry	R^1	R^2	Method	Product	Yield (%)
34	-B	$C_{10}H_7OCH_2CH(OH)CH_2$-	C	**41ah**	93
35	-B	4-Me$OC_6H_4OCH_2CH(OH)CH_2$-	C	**41ai**	92
36	-A	4-Me$OC_6H_4OCH_2CH(OH)CH_2$-	C	**41aj**	83
37	-A	4-Cl-3-Me$C_6H_3OCH_2CH(OH)CH_2$-	C	**41ak**	80
38	-A	Me$CH_2CH(OH)CH_2$-	C	**41al**	81
39	-C	Ph$OCH_2CH(OH)CH_2$-	C	**41am**	85
40	-D	^{n}Bu$OCH_2CH(OH)CH_2$-	C	**41an**	91
41	-D	Allyl$OCH_2CH(OH)CH_2$-	C	**41ao**	93
42	4-Cl$C_6H_4OCH_2$	2,4-$Cl_2C_6H_3OCH_2CH(OH)CH_2$-	C	**41ap**	88
43	4-Cl$C_6H_4OCH_2$	4-Bn$C_6H_4OCH_2CH(OH)CH_2$-	C	**41aq**	86
44	4-$O_2NC_6H_4OCH_2$	2-HOC_6H_{10}-	C	**41ar**	90
45	C_6H_5	Ph$OCH_2CH(OH)CH_2$-	C	**41as**	88
46	C_6H_5	Allyl$OCH_2CH(OH)CH_2$-	C	**41at**	87
47	$Me_2C(OH)$	4-Bn$C_6H_4OCH_2CH(OH)CH_2$-	C	**41au**	91
48	$Me_2C(OH)$	Ph$OCH_2CH(OH)CH_2$-	C	**41av**	90
49	-E	4-Cl-3-Me$C_6H_3OCH_2CH(OH)CH_2$-	C	**41aw**	-
50	C_6H_5	Bn	D	**41g**	98
51	C_6H_5	C_6H_5	D	**41ax**	97
52	C_6H_5	Me	D	**41ay**	92
53	C_6H_5	C_3H_7	D	**41az**	83
54	C_6H_5	C_6H_{13}	D	**41ba**	95
55	C_6H_5	$C_{10}H_{24}$	D	**41bb**	95
56	C_6H_5	$C_{12}H_{25}$	D	**41bc**	65
57	C_6H_5	$C_{16}H_{33}$	D	**41bd**	62
58	C_6H_5	$C_{10}H_{20}N_3$	D	**41be**	60
59	$Me_2C(OH)$	Bn	D	**41bf**	65
60	$Me_2C(OH)$	C_6H_5	D	**41bg**	95
61	$Me_2C(OH)$	C_3H_7	D	**41bh**	90
62	$Me_2C(OH)$	C_6H_{13}	D	**41bi**	94



* The dimeric acetylene was the main product

Nanoparticle-supported tris(triazolyl)–CuBr, with a diameter of approximately 25 nm has been easily prepared, and its catalytic activity was evaluated in the copper-catalyzed azide–alkyne cycloaddition (CuAAC) reaction. The catalyst has been applied for the one-pot synthesis of triazoles **41**, through a cascade reaction involving benzyl bromides **38**, alkynes **35**, and sodium azide (Scheme 18, Table 18, Method A).[54]

A graphene based composite material with c-Fe_2O_3 (Fig. 14) nanoparticles has been synthesized *via* a simple chemical route and can also serves as an efficient catalyst for one-pot synthesis of a series of 1,4-disubstituted-1,2,3 triazoles **41** *via* reaction of halides **38**, sodium azide and the corresponding alkynes **35** (Scheme 18, Table 18, Method B). It is noticeable that increase of electronic effect in the benzyl moiety increases the yield whereas it decreases with substrates containing electron deficient aromatic halides. The same observation is found when different alkynes are studied.[55]

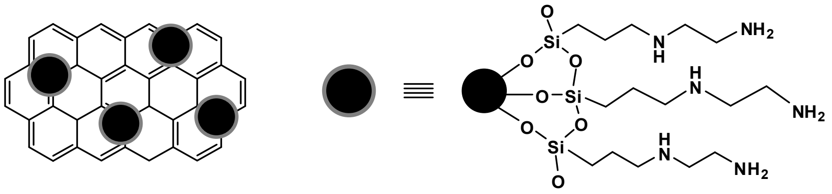
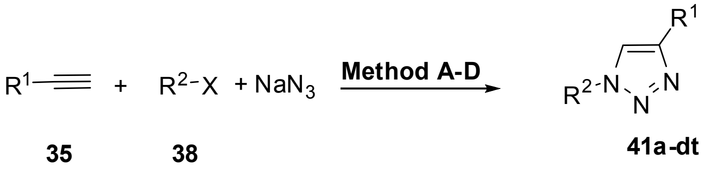


Fig. 14

Alonso *et al.* found that copper nanoparticles on activated carbon CuNPs/C can also effectively catalyze the multicomponent synthesis of 1,2,3-triazoles **41** from the reaction of different halides, diazonium salts or amines, with sodium azide and alkynes in water at a low copper loading (Scheme 18, Table 18, Method C).[56,57]

The same group used CuNPs/C, at a low catalyst loading (0.5 mol%), to promote the multicomponent synthesis of 1,2,3-triazoles from phenylacetylene, sodium azide and epoxides (Scheme 18, Table 18, Method D, entry 78).[56,57]

Scheme 18



Method A: Tris(triazolyl)-CuBr-NPs 0.5 mol%/ H_2O, rt.
Method B: Nano-Fe_3O_4 composite/ H_2O, 60 °C/Ar atmosphere
Method C: CuNPs/C/ H_2O, 70 °C
Method D: CuNPs/C/ ^{t}BuONO, H_2O, Δ

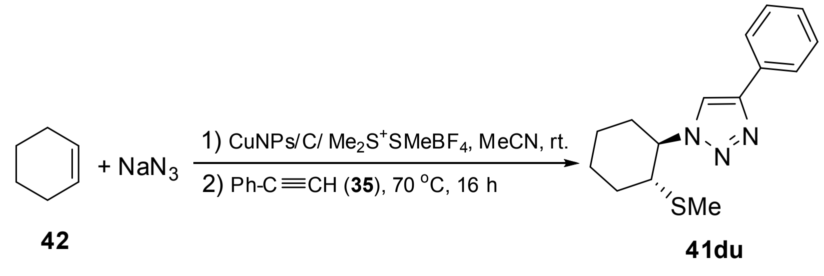
Table 18

Entry	R^1	R^2	X	Method	Product	Yield (%)
1	C_6H_5	2-Br$C_6H_4CH_2$-	Br	A	**41bj**	88
2	C_6H_5	3-I$C_6H_4CH_2$-	Br	A	**41bk**	87
3	C_6H_5	4-CN$C_6H_4CH_2$-	Br	A	**41bl**	72
4	C_6H_5	4-$O_2NC_6H_4CH_2$-	Br	A	**41bm**	90
5	C_6H_5	3-Me$C_6H_4CH_2$-	Br	A	**41bn**	98
6	C_6H_5	1-Me-4-C_6H_4triazolyl-	Br	A	**41bo**	83
7	C_6H_5	$C_6H_4CH_2$-	Br	B	**41bp**	92
8	C_6H_5	4-HO$C_6H_4CH_2$-	Br	B	**41bq**	93
9	C_6H_5	4-MeO$C_6H_4CH_2$-	Br	B	**41br**	91
10	C_6H_5	3-$O_2NC_6H_4$	Br	B	**41bs**	89
11	C_6H_5	$C_6H_4CH_2CH_2$-	Br	B	**41bt**	81
12	^{n}Hexyl	$C_6H_4CH_2$-	Br	B	**41bu**	72
13	COOEt	$C_6H_4CH_2$-	Br	B	**41bv**	84
14	4-MeOC_6H_4	$C_6H_4CH_2$-	Br	B	**41i**	91
15	4-MeC_6H_4	$C_6H_4CH_2$-	Br	B	**41bw**	85
16	4-BrC_6H_4	$C_6H_4CH_2$-	Br	B	**41bx**	78
17	C_6H_5	^{c}Hexyl	Br	B	**41by**	70
18	C_6H_5	$C_6H_4CH_2$-	Cl	B	**41a**	88
19	^{c}Hexyl	4-MeO$C_6H_4CH_2$-	Cl	B	**41bz**	80
20	C_6H_5	$C_6H_4CH_2$-	Br	C	**41bp**	98
21	C_6H_5	$C_6H_4CH_2$-	Cl	C	**41ca**	99
22	C_6H_5	4-NC$C_6H_4CH_2$-	Br	C	**41bp**	99
23	C_6H_5	3,5-(MeO)2$C_6H_3CH_2$-	Br	C	**41bp**	98
24	C_6H_5	$C_6H_5CH{=}CHCH_2$-	Br	C	**41cb**	94
25	C_6H_5	$C_6H_4COCH_2$-	Cl	C	**41cc**	82
26	C_6H_5	EtOOCCH_2-	Br	C	**41cd**	98
27	C_6H_5	$CH_3(CH_2)_8$-	I	C	**41ce**	98
28	C_6H_5	$CH_3(CH_2)_8$-	Cl	C	**41cf**	94
29	C_6H_5	^{c}Hexyl	Br	C	**41cg**	93
30	C_6H_5	Indol-3-yl-CH_2CH_2-	Br	C	**41a**	89
31	$C_6H_5OCH_2$	$C_6H_4CH_2$-	Br	C	**41ch**	76
32	N-Phthalimidyl-CH_2	$C_6H_4CH_2$-	Br	C	**41ci**	84
33	$SiMe_3$	$C_6H_4CH_2$-	Br	C	**41cj**	82
34	$CH_2CH_2CH_2C{\equiv}CH$	$C_6H_4CH_2$-	Br	C	**41ck**	87

Entry	R^1	R^2	X	Method	Product	Yield (%)
35	C_6H_5	$C_6H_4CH_2$-	Br	C	**41g**	98
36	C_6H_5	$C_6H_4CH_2$-	Cl	C	**41g**	99
37	C_6H_5	4-$NCC_6H_4CH_2$-	Br	C	**41cbl**	99
38	C_6H_5	3,5-(MeO)2$C_6H_3CH_2$-	Br	C	**41cm**	98
39	C_6H_5	9-Anthracenyl-CH_2-	Br	C	**41cn**	90
40	C_6H_5	$C_6H_5CH{=}CHCH_2$-	Br	C	**41co**	94
41	C_6H_5	$C_6H_4COCH_2$-	Cl	C	**41cp**	82
42	C_6H_5	$EtOOCCH_2$-	Br	C	**41cq**	98
43	C_6H_5	$CH_3(CH_2)_8$-	I	C	**41cr**	98
44	C_6H_5	$CH_3(CH_2)_8$-	Cl	C	**41cs**	91
45	C_6H_5	^{c}Hexyl	Br	C	**41a**	93
46	C_6H_5	Indol-3-yl-CH_2CH_2-	Br	C	**41ct**	89
47	$C_6H_5OCH_2$	$C_6H_4CH_2$-	Br	C	**41cu**	76
48	4-$MeOC_6H_4$	$C_6H_4CH_2$-	Br	C	**41i**	90
49	Pyrid-2-yl	$C_6H_4CH_2$-	Br	C	**41k**	92
50	N-Phthalimidyl-CH_2	$C_6H_4CH_2$-	Br	C	**41cv**	84
51	$SiMe_3$	$C_6H_4CH_2$-	Br	C	**41cw**	82
52	$(CH_2)_5CH_3$	$CH_3(CH_2)_8$-	I	C	**41cx**	92
53	$(CH_2)_8CH_3$	^{c}Hexyl	Br	C	**41cy**	89
54	3-$(HC{\equiv}C)C_6H_4$	$C_6H_4CH_2$-	Br	C	**41cz**	92
55	$(CH_2)_3C{\equiv}CH$	$C_6H_4CH_2$-	Br	C	**41da**	87
56	None	$HC{\equiv}C$-$(CH_2)_4$-	Cl	C	**41db**	89
57	C_6H_5	C_6H_5	$N_2^+BF_4$-	C	**41d**	85
58	C_6H_5	4-$MeOC_6H_4$	$N_2^+BF_4$-	C	**41e**	75
59	C_6H_5	4-$MeOCC_6H_4$	$N_2^+BF_4$-	C	**41de**	71
60	C_6H_5	4-NCC_6H_4-	$N_2^+BF_4$-	C	**41df**	78
61	C_6H_5	4-$O_2NC_6H_4$-	$N_2^+BF_4$-	C	**41dg**	92
62	4-$MeOC_6H_4$	4-$O_2NC_6H_4$-	$N_2^+BF_4$-	C	**41dh**	88
63	Pyrid-2-yl	4-$O_2NC_6H_4$-	$N_2^+BF_4$-	C	**41di**	91
64	4-$F_3CC_6H_4$	4-$O_2NC_6H_4$-	$N_2^+BF_4$-	C	**41dj**	90
65	$SiMe_3$	4-$O_2NC_6H_4$-	$N_2^+BF_4$-	C	**41dk**	83
66	C_6H_5	C_6H_5	$N_2^+BF_4$-	C	**41d**	85
67	C_6H_5	C_6H_5	NH_2	D	**41d**	90
68	C_6H_5	4-$MeOC_6H_4$	NH_2	D	**41dl**	95
69	C_6H_5	2-ClC_6H_4	NH_2	D	**41dm**	64
70	C_6H_5	3-ClC_6H_4	NH_2	D	**41dn**	80
71	C_6H_5	4-ClC_6H_4	NH_2	D	**41do**	78
72	C_6H_5	4-MeC_6H_4	NH_2	D	**41dp**	90
73	C_6H_5	4-$F_3CC_6H_4$	NH_2	D	**41dq**	66
74	C_6H_5	1-Naphthyl	NH_2	D	**41dr**	70
75	$(CH_2)_3CH_3$	C_6H_5	NH_2	D	**41ds**	93
76	^{c}Hexyl	C_6H_5	NH_2	D	**41dt**	89
77	C_6H_5	C_6H_5	NH_2	D	**41d**	92
78	C_6H_5	C_6H_5	Oxiranyl	C	**41d**	92

Alonso *et al*. applied also a new strategy in which the alkene **42** was directly mixed with the CuNPs/C, dimethyl(methylthio)-sulfonium tetrafluoroborate DMTSF, and NaN_3 in MeCN to produce the corresponding methylsulfanyl azide in only 1 h at room temperature. The subsequent reaction with the alkyne **35** afforded the triazole **41du** which represent its synthesis from an alkene **42** in one pot for the first time (Scheme 19).[56]

Scheme 19



42

41du

Yield 81%

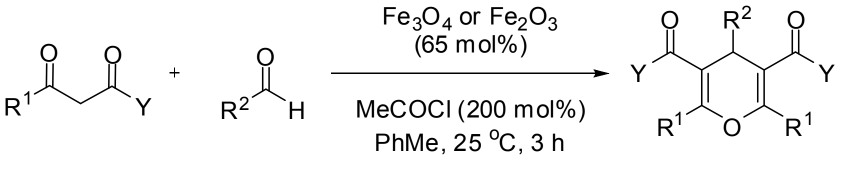
2.2. Synthesis of six-membered heterocycles

2.2.1. Six-membered rings with one heteroatom

2.2.1.1. 4*H*-Pyran

Commercially available nano-power magnetite or iron(III) oxide have been used as a catalyst in the construction of 4-substituted-4*H*-pyrans **43a-l** from reaction of β-keto esters or other 1,3-dicarbonyl compound **15** with the corresponding aldehyde **7** (Scheme 20, Table 19). The reaction implies a tandem process, involving an aldol condensation, a Michael-type addition, and a dehydrating annulation. The isolated yields of pyrans **43a-l** were similar independently of the aromatic aldehyde used, with electron-withdrawing groups, unsubstituted rings, or electron-donating groups being well tolerated.[58]

Scheme 20



15 **7** **43a-l**

Table 19

Entry	R^1	Y	R^2	Product[a]	Yield (%)
1	Me	OMe	4-BrC_6H_4	**43a**	96 (94)
2	Me	OMe	4-NCC_6H_4	**43b**	79
3	Me	OMe	Ph	**43c**	85 (82)
4	Me	OMe	4-$MeOC_6H_4$	**43d**	83
5	Me	OMe	4-HOC_6H_4	**43e**	68
6	Me	OMe	2-naphthyl	**43f**	57
7	Me	OMe	$(CH_2)_5CH$	**43g**	80 (79)
8	Me	OMe	*i*-Pr	**43h**	72 (67)
9	Me	OEt	4-BrC_6H_4	**43i**	95
10	Me	OEt	4-$MeOC_6H_4$	**43j**	63
11	Me	Me	4-$MeOC_6H_4$	**43k**	75 (64)
12	Me	OMe	4-BrC_6H_4	**43l**	91 (79)

[a] Reaction carried out using compound**15** (2.5 mmol), **7** (1 mmol), in 3 mL of toluene during 3 h, unless otherwise stated. Yields obtained by Fe_2O_3 catalysis appeared in paranthesis.

2.2.1.2. Dihydropyridine

1,4-Dihydropyridine derivatives **44a-o** have been prepared efficiently in a one-pot synthesis *via* Hantzsch condensation using nanosized titanium dioxide as a heterogeneous catalyst. Thus, various aliphatic, aromatic, and heterocyclic aldehydes **7** underwent smooth cyclocondensation with ethyl acetoacetate and ammonium acetate to give **44a-o** in good yields (Scheme 21, Table 20, Method A). The present methodology offers several advantages such as excellent yields, short reaction times (30–120 min) environmentally benign, and mild reaction conditions. The catalyst can be readily separated from the reaction products and recovered in excellent purity for direct reuse.[59]

Mirzaei and Davoodnia used a microwave-assisted sol-gel method to synthesize nano-sized MgO particles using $Mg(NO_3)_2{\cdot}6H_2O$ as precursor and deionized water as solvent. The catalytic behavior of the catalyst was investigated in the one-pot synthesis of Hantzsch 1,4-dihydropyridines **44a-c, 44f-h, and 44p,q** (Scheme 21, Table 20, Method B). The reaction proceeded in good to high yields from the reaction of aromatic aldehydes, ethylacetoacetate, and ammonium acetate.[60]

A reaction mechanism is proposed and postulated that in MgO nanoparticles, there are acid-base bifunctional sites where Mg and O act as a weak Lewis acidic site and relatively high strength Brönsted basic site, respectively. These acid-base bifunctional sites facilitate the formation of arylidene and enamine intermediates that then react to give the final products.

Scheme 21

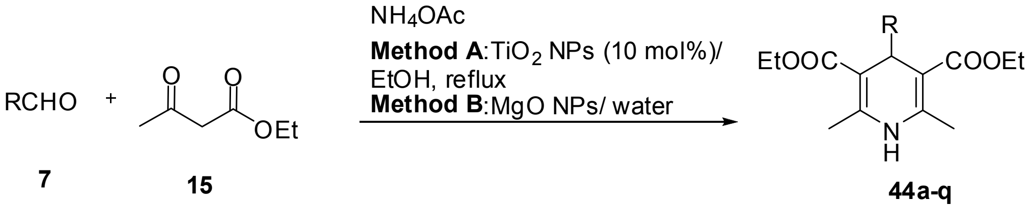


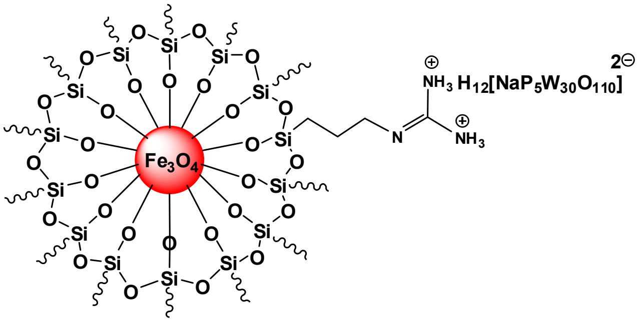
Table 20

Entry	Ar	Products	Method	Yield[a] (%)
1	C_6H_5	**44a**	A	92
2	4-BrC_6H_4	**44b**	A	89
3	4-ClC_6H_4	**44c**	A	90
4	3-ClC_6H_4	**44d**	A	86
5	2-ClC_6H_4	**44e**	A	80
6	4-$O_2NC_6H_4$	**44f**	A	87
7	4-$MeOC_6H_4$	**44g**	A	81
8	4-HOC_6H_4	**44h**	A	93
9	4-$CH_3C_6H_4$	**44i**	A	90
10	4-NCC_6H_4	**44j**	A	90
11	C_6H_5-CH=CH	**44k**	A	86
12	C_7H_5O	**44l**	A	92
13	2-Furyl	**44m**	A	50
14	2-Thienyl	**44n**	A	90
15	$C_6H_{12}O$	**44o**	A	95
16	C_6H_5	**44a**	B	85
17	4-BrC_6H_4	**44b**	B	88
18	4-ClC_6H_4	**44c**	B	90
19	4-HOC_6H_4	**44h**	B	83
20	4-$MeOC_6H_4$	**44g**	B	90
21	4-MeC_6H_4	**44p**	B	92
22	3-$O_2NC_6H_4$	**44q**	B	78
23	4-$O_2NC_6H_4$	**44f**	B	73

[a] Isolated yield of the pure product based on aryl aldehyde.

2.2.1.3. Tetrahydropyridine

Eshghi *et al*. prepared a nanomagnetic organic-inorganic hybrid catalyst (Fe@Si-Gu-Prs, Fig. 15) by the chemical anchoring of Preyssler heteropolyacid ($H_{14}[NaP_5W_{30}O_{110}]$) onto the surface of modified Fe_3O_4 magnetic nanoparticles with guanidine-propyl-trimethoxysilane linker. The catalytical activity of this catalyst in the synthesis of tetrahydropyridine **45a-u** was investigated. Thus, reaction of aldehydes **7**, amines **9**, and ethyl acetoacetate **15** using 0.025 g Fe@Si-GuPrs at room temperature and under solvent-free conditions afforded **45a-u** in high yield (Scheme 22, Table 21). The results shown in Table 22 showed that aldehyde **7** and amine **9** compounds with substituents carrying either electron donating or electron-withdrawing groups reacted successfully and gave the expected products in excellent yields following short reaction times.[61]



Fe@Si-Gu-Prs

Fig. 15

Scheme 22

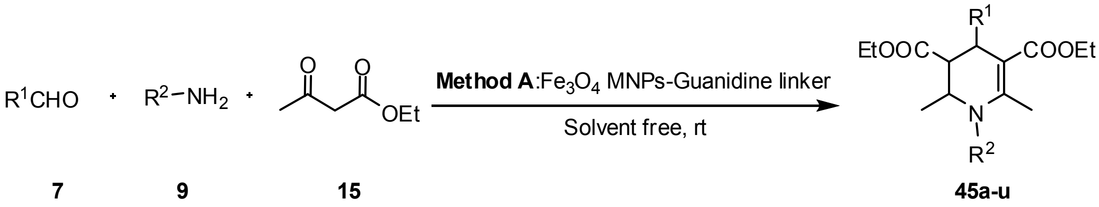


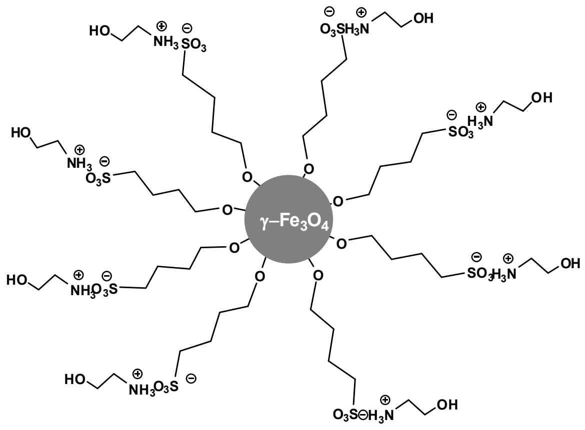
Table 21

Entry	R^1	R^2	Products	Yield (%)
1	C_6H_5	C_6H_5	**45a**	96
2	C_6H_5	4-BrC_6H_4	**45b**	94
3	C_6H_5	4-ClC_6H_4	**45c**	91
4	4-NCC_6H_4	C_6H_5	**45d**	92
5	4-NCC_6H_4	4-ClC_6H_4	**45e**	95
6	4-MeC_6H_4	4-MeC_6H_4	**45f**	95
7	4-MeC_6H_4	C_6H_5	**45g**	91
8	4-MeC_6H_4	4-BrC_6H_4	**45h**	92
9	4-MeC_6H_4	4-$O_2NC_6H_4$	**45i**	95
10	4-MeC_6H_4	4-MeC_6H_4	**45j**	92
11	3-$O_2NC_6H_4$	C_6H_5	**45k**	90
12	4-MeOC_6H_4	4-ClC_6H_4	**45l**	93
13	4-ClC_6H_4	4-BrC_6H_4	**45m**	90
14	4-ClC_6H_4	4-MeC_6H_4	**45n**	93
15	4-ClC_6H_4	C_6H_5	**45o**	91
16	4-MeOC_6H_4	4-MeC_6H_4	**45p**	92
17	4-MeOC_6H_4	C_6H_5	**45q**	90
18	4-MeOC_6H_4	4-BrC_6H_4	**45r**	94
19	C_6H_5	4-IC_6H_4	**45s**	91
20	4-ClC_6H_4	4-BrC_6H_4	**45t**	92
21	4-NCC_6H_4	4-BrC_6H_4	**45u**	91

2.2.1.4. Pyridine

Pyridine dicarbonitriles **47** have been synthesized in good yields *via* a one-pot multi–component reaction of aldehydes **7**, malononitrile **46**, and thiols **30** in the presence of nano-TiO_2 as a catalyst in ethanol (Scheme 23, Table 22, Method A).[62]

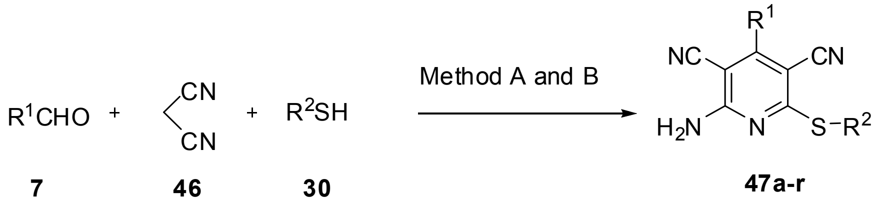
2-Hydroxyethylammonium sulphonate immobilized on-Fe_2O_3 nanoparticles (-Fe_2O_3-2-HEAS, Fig. 16) was synthesized as a new supported ionic liquid by the reaction of *n*-butylsulfonated-Fe_2O_3 with ethanolamine. This catalyst also efficiently promoted the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines **47** in good to high yields under solvent-free conditions (Scheme 23, Table 22, Method B+). The catalyst was easily isolated from the reaction mixture by magnetic decantation using an external magnet and reused at least five times without significant degradation in the activity.[63]



γ–Fe_2O_3-2-HEAS

Fig. 16

Scheme 23



Method A: nano-TiO_2
Method B:γ-Fe_2O_3 MNPs-2-HEAS

Table 22

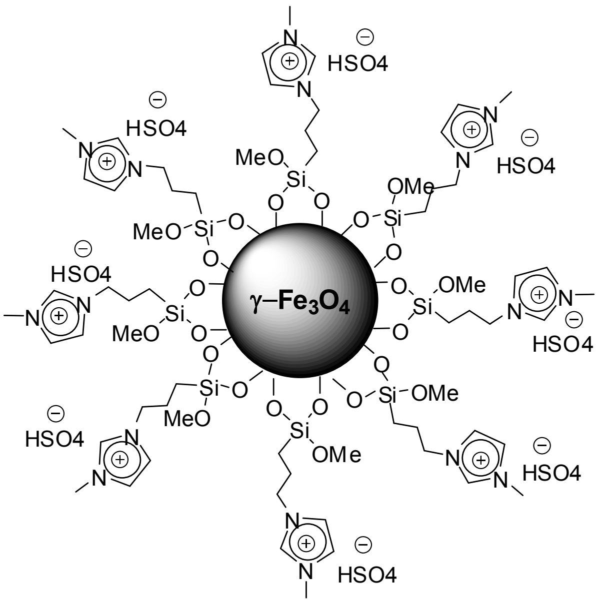
Entry	R^1	R^2	Method	Product	Yield[a,b] (%)
1	C_6H_5	4-MeC_6H_4	A	**47a**	82
2	4-ClC_6H_4	4-MeC_6H_4	A	**47b**	87
3	3-ClC_6H_4	4-MeC_6H_4	A	**47c**	85
4	4-BrC_6H_4	4-MeC_6H_4	A	**47d**	83
5	3-BrC_6H_4	4-MeC_6H_4	A	**47e**	83
6	3-$O_2NC_6H_4$	4-MeC_6H_4	A	**47f**	81
7	4-$O_2NC_6H_4$	4-MeC_6H_4	A	**47g**	82
8	4-$MeOC_6H_4$	4-MeC_6H_4	A	**47h**	85
9	C_6H_5	C_6H_5	B	**47i**	91
10	C_6H_5	4-ClC_6H_4	B	**47j**	81
11	C_6H_5	4-$MeOC_6H_4$	B	**47k**	79
12	C_6H_5	4-MeC_6H_4	B	**47a**	84
13	4-MeC_6H_4	C_6H_5	B	**47l**	81
14	4-ClC_6H_4	C_6H_5	B	**47m**	87
15	4-ClC_6H_4	4-MeC_6H_4	B	**47b**	80
16	2-Naphthyl	C_6H_5	B	**47n**	79
17	2-Pyridinyl	C_6H_5	B	**47o**	89
18	2-Phenylpropanal	C_6H_5	B	**47p**	88
19	Me	C_6H_5	B	**47q**	90
20	C_6H_5	*n*-Bu	B	**47r**	83

[a] Method A Yields were analyzed by GC, [b] Method B yield refer to those of pure isolated products

2.2.2. Six-membered rings with two heteroatoms

2.2.2.1. Dihydropyrimidine

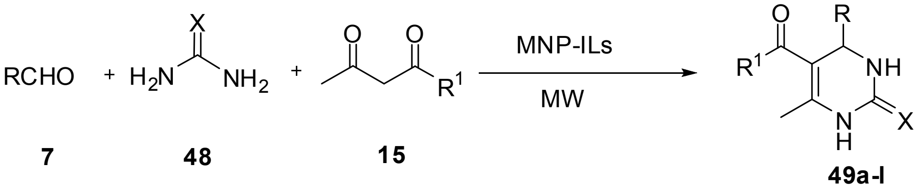
The magnetic Fe_3O_4 nanoparticles supported imidazolium-based ionic liquids (MNPs–IILs, Fig. 17), were used as efficient new catalysts for the one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones(thiones) **49a-l.** The reaction proceeded *via* a one-pot cyclocondensation of an aromatic aldehydes **7**, β-dicarbonyl compound **15**, urea or thiourea **48** in the presence of the magnetic nanocatalysts under microwave irradiation and solvent-free conditions (Scheme 24, Table 23).[64]



MNP-IIL-HSO4

Fig. 17

Scheme 24



7 48 15 49a-l

Table 23

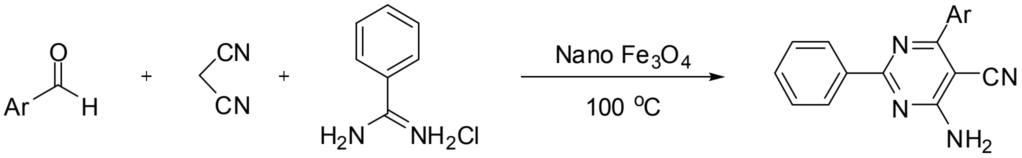
Entry	R	X	R^1	Product	Time /Yield (%) MW[a]	Time /Yield (%) Δ[b]
1	Ph	O	OEt	**49a**	4/97	30/95
2	3-ClC_6H_4	O	OEt	**49b**	4/98	25/97
3	$4\text{-O}_2NC_6H_4$	O	OEt	**49c**	4/98	30/97
4	2-Thienyl	O	OEt	**49d**	4/98	25/98
5	2-FC_6H_4	O	OEt	**49e**	4/97	35/92
6	$3,4\text{-(OMe)}_2C_6H_3$	O	OEt	**49f**	4/99	20/98
7	4-MeC_6H_4	S	OEt	**49g**	4/95	40/90
8	Ph	S	OEt	**49h**	4/97	35/96
9	2-Thienyl	S	OEt	**49i**	4/95	25/95
10	Ph	O	Me	**49j**	4/97	30/95
11	Ph	S	Me	**49k**	4/96	30/93
12	4-MeC_6H_4	S	Me	**49l**	4/95	35/92

[a] Using microwave irradiation
[b] Under classical heating conditions

2.2.2.2. Pyrimidine

4-Amino-6-aryl-2-phenyl pyrimidine-5-carbonitrile derivatives **50a-m** were synthesized through a one-pot, three-component reaction of an aldehydes **7**, malononitrile **46** and benzamidine hydrochloride **28**, in the presence of magnetic nano Fe_3O_4 particles as a catalyst under solvent-free conditions (Scheme 25, Table 24). The products **50a-m** were all prepared with excellent yields at 100 ^{O}C in 1–1.5 h. Both aromatic aldehydes with electron donating substituents and electron-withdrawing substituents showed significant reactivity in this process.[65]

Scheme 25



7 **46** **28** **50a-m**

Table 24

Entry	Ar	Product	Yield[a] (%)
1	Ph	**50a**	98
2	4-ClC$_6$H$_4$	**50b**	96
3	4-BrC$_6$H$_4$	**50c**	94
4	2,3-diClC$_6$H$_3$	**50d**	96
5	2-ClC$_6$H$_4$	**50e**	96
6	4-NCC$_6$H$_4$	**50f**	98
7	4-MeC$_6$H$_4$	**50g**	96
8	2,4-diClC$_6$H$_3$	**50h**	96
9	3-O$_2$NC$_6$H$_4$	**50i**	96
10	4-O$_2$NC$_6$H$_4$	**50j**	96
11	3-Indolyl	**50k**	90
12	4-MeCONHC$_6$H$_4$	**50l**	95
13	4-MeOC$_6$H$_4$	**50m**	95

[a] Isolated yields.

2.2.2.3. Pyrazine

An iron Schiff base complex was encapsulated in SBA-15 mesoporous silica to afford a Fe(III)-Schiff base/SBA-15 heterogeneous nanocatalyst (Fig. 18) for the synthesis of pyrazines **52a-d** from the reaction of the appropriate diamines **51a,b** with the corresponding 1,2-diketone **25**. These reactions proceeded in water with excellent yields (Scheme 26).[66]

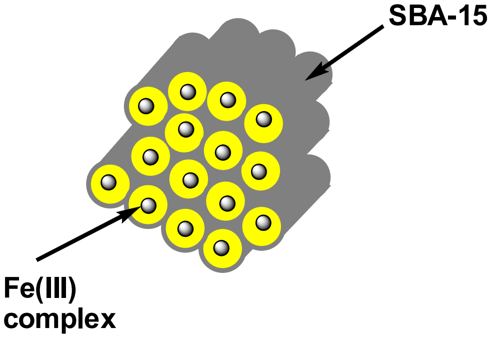
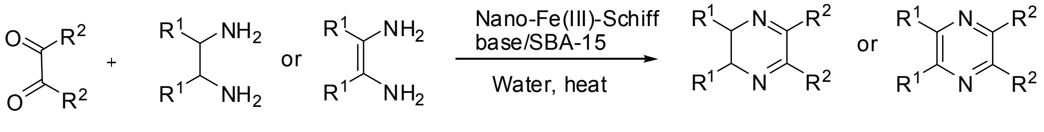


Fig. 18

Scheme 26



25 **51a** **51b** **52a,b** **52c,d**

R^1 = H, R^2 = Ph yield = 99%
R^1 = CN, R^2 = Me yield = 96%

2.3. Synthesis of fused bicyclic systems

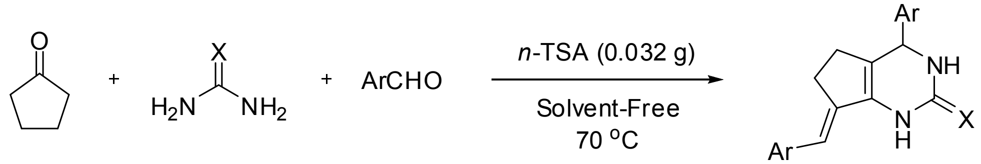
2.3.1. Carbocyclic fused heterocycles

2.3.1.1. Five-membered carbocyclic fused with 6-membered heterocyclic ring: two heteroatoms

2.3.1.1.1. Cyclopenta[*d*]pyrimidine

Nano titania-supported sulfonic acid (*n*-TSA) has been easily prepared from the reaction of nano titania (titanium oxide) with chlorosulfonic acid as sulfonating agent. This catalyst was efficiently used as a heterogeneous catalyst for synthesis of pyrimidinones **54a-s**, *via* three component reaction of aromatic aldehydes **7**, cylopentanone **53**, urea or thiourea **49a,b** in solvent-free at 70 °C (Scheme 27, Table 25).[67]

Scheme 27



53 **49a**: X=O **49b**: X=S **7** **54a-s**

Table 25

Entry	Ar	X	Product	Time (h)	Yield^b (%)
1	C_6H_5	O	**54a**	0.75	95
2	2-ClC_6H_4	O	**54b**	1.5	86
3	4-ClC_6H_4	O	**54c**	1.25	84
4	4-FC_6H_4	O	**54d**	1.25	83
5	4-BrC_6H_4	O	**54e**	1.25	89
6	4-MeC_6H_4	O	**54f**	1	94
7	4-$MeOC_6H_4$	O	**54g**	1	93
8	3-$O_2NC_6H_4$	O	**54h**	2.5	83
9	2-Naphthyl	O	**54i**	1.5	82
10	C_6H_5	S	**54j**	1	96
11	2-ClC_6H_4	S	**54k**	2	86
12	4-ClC_6H_4	S	**54l**	1.5	92
13	4-FC_6H_4	S	**54m**	1.6	86
14	4-BrC_6H_4	S	**54n**	1.4	89
15	4-MeC_6H_4	S	**54o**	1	91
16	4-$MeOC_6H_4$	S	**54p**	1	93
17	3-$O_2NC_6H_4$	S	**54q**	3.5	79
18	4-$O_2NC_6H_4$	S	**54r**	3	91
19	2-Naphthyl	S	**54s**	1.5	87

[a] Reaction conditions: aromatic aldehyde (1 mmol), cyclopentanone (1 mmol), urea or thiourea (1.2 mmol) in solvent-free at 70 °C.
[b] Isolated yield.

2.3.1.2. Six-membered carbocyclic fused with 6-membered heterocyclic ring: one heteroatom

2.3.1.2.1. Tetrahydro-4*H*-chromene

Nano magnetic complex lanthanum strontium magnesium oxide $La_{0.7}Sr_{0.3}MnO_3$ (LSMO) has been explored as an efficient and recyclable catalyst to effect the one-pot three-component synthesis of 2-amino-5-oxo-5,6,7,8-tetrahydro-4*H*-chromenes **56** by condensation reactions between aromatic aldehydes **7**, malononitrile **46** and 5,5-dimethyl-cyclohexane-1,3-dione **55** in EtOH under ultrasound irradiation conditions (Scheme 28, Table 26, Method A).[68]

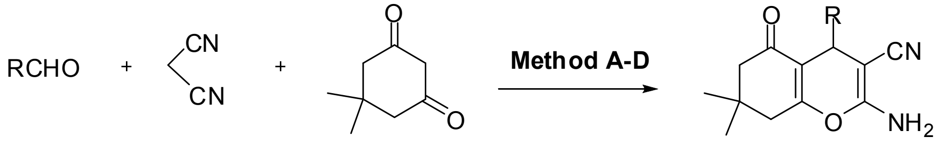
Azarifar *et al.* used nano-titania-supported Preyssler-type heteropolyacid, *n*-$TiO_2/H_{14}[NaP_5W_{30}O_{110}]$ as an efficient and reusable heterogeneous catalyst for the synthesis of highly functionalized 4*H*-chromenes **56** under ultrasound irradiation conditions. (Scheme 28, Table 26, Method B).[69]

The same group reported also the synthesis of highly functionalized 4*H*-chromenes **56** in the presence of nano-titania sulfuric acid (15-nm TSA) as a heterogeneous catalyst. (Scheme 28, Table 26, Method C).[70]

As shown in Table 26, the ease of the reaction is directly related to the substituents attached to the benzene ring and the spatial accessibility of aldehyde **7** as well. The electron withdrawing groups were found to activate the aldehyde toward nucleophilic attack and increase the reaction rate (entry 10, 11).

Sarrafi *et al.* demonstrated a similar approach for the synthesis of 4*H*-chromene derivatives **56** in excellent yields using mesoporous silica nanoparticles as a bio-compatible, and recoverable catalyst (Scheme 28, Table 26, Method D).[71]

Scheme 28



7 **46** **55** **56a-aa**

Method A: LMSO-MNPs/)))), EtOH, rt.
Method B: *n*-$TiO_2/H_{14}[NaP_5W_{30}O_{110}]$ /)))), EtOH, 40 °C
Method C: *n*-TSA /)))), EtOH, 40 °C
Method D: MSNs/EtOH, 60 °C

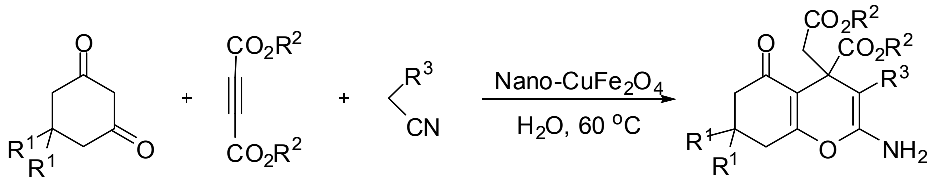
Table 26

Entry	R	Product	Method	Yield (%)
1	C_6H_5	**56a**	A	92
2	4-FC_6H_4	**56b**	A	96
3	4-ClC_6H_4	**56c**	A	97
4	3-$O_2NC_6H_4$	**56d**	A	98
5	4-$O_2NC_6H_4$	**56e**	A	88
6	4-$MeOC_6H_4$	**56f**	A	5
7	4-MeC_6H_4	**56g**	A	87
8	2-ClC_6H_4	**56h**	A	83
9	4-HOC_6H_4	**56i**	A	92
10	2-$O_2NC_6H_4$	**56j**	A	77
11	$CH=CHC_6H_4$	**56k**	A	Trace
12	$CH_2CH_2C_6H_4$	**56l**	A	Trace
13	C_6H_5	**56a**	B	98
14	4-$MeOC_6H_4$	**56f**	B	73
15	4-MeC_6H_4	**56g**	B	93
16	4-$Me_2NC_6H_4$	**56m**	B	90
17	2-ClC_6H_4	**56h**	B	86
18	4-ClC_6H_4	**56c**	B	94
19	4-BrC_6H_4	**56n**	B	90
20	2-$O_2NC_6H_4$	**56j**	B	83
21	3-$O_2NC_6H_4$	**56d**	B	98
22	4-$O_2NC_6H_4$	**56e**	B	97
23	2-FC_6H_4	**56o**	B	90
24	$CH_3CH_2CH_2$	**56p**	B	70
25	Furan-2-yl	**56q**	B	93
26	$CH=CHC_6H_5$	**56k**	B	71
27	C_6H_5	**56a**	C	97
28	4-$MeOC_6H_4$	**56f**	C	89
29	4-MeC_6H_4	**56g**	C	93
30	4-$Me_2NC_6H_4$	**56m**	C	95
31	2-ClC_6H_4	**56h**	C	86
32	4-ClC_6H_4	**56c**	C	94
33	4-BrC_6H_4	**56n**	C	93
34	2-$O_2NC_6H_4$	**56j**	C	88
35	3-$O_2NC_6H_4$	**56d**	C	95
36	4-$O_2NC_6H_4$	**56e**	C	94

Entry	R	Product	Method	Yield (%)
37	C_6H_5	**56a**	D	94
38	2-ClC_6H_4	**56h**	D	97
39	2-BrC_6H_4	**56r**	D	94
40	4-ClC_6H_4	**56c**	D	98
41	4-BrC_6H_4	**56n**	D	96
42	3-$ClOC_6H_4$	**56s**	D	96
43	4-FC_6H_4	**56b**	D	98
44	2-ClC_6H_4	**56h**	D	96
25	2-$O_2NC_6H_4$	**56j**	D	95
46	4-$O_2NC_6H_4$	**56e**	D	93
47	4-$NCOC_6H_4$	**56t**	D	95
48	3-HOC_6H_4	**56u**	D	90
49	2-Naphthyl	**56v**	D	97
50	1-Naphthyl	**56w**	D	92
51	2-Furyl	**56x**	D	94
52	2-Thienyl	**56y**	D	96
53	4-$OHCC_6H_4$	**56i**	D	98
54	4-$OHCC_6H_4$	**56i**	D	98
55	Et	**56z**	D	88
56	^{n}Pr	**56aa**	D	86

$CuFe_2O_4$ magnetic nanoparticles were synthesized and recognized as an efficient catalyst for the one-pot synthesis of 4*H*-chromene derivatives **57** in aqueous medium at mild conditions and in excellent yields. The reaction proceeds *via* MCR's of dimedone or cyclohexane-1,3-dione, **55** dialkyl acetylenedicarboxylates **8** and malononitrile or ethyl cyanoacetate **46** (Scheme 29, Table 27).[72]

Scheme 29



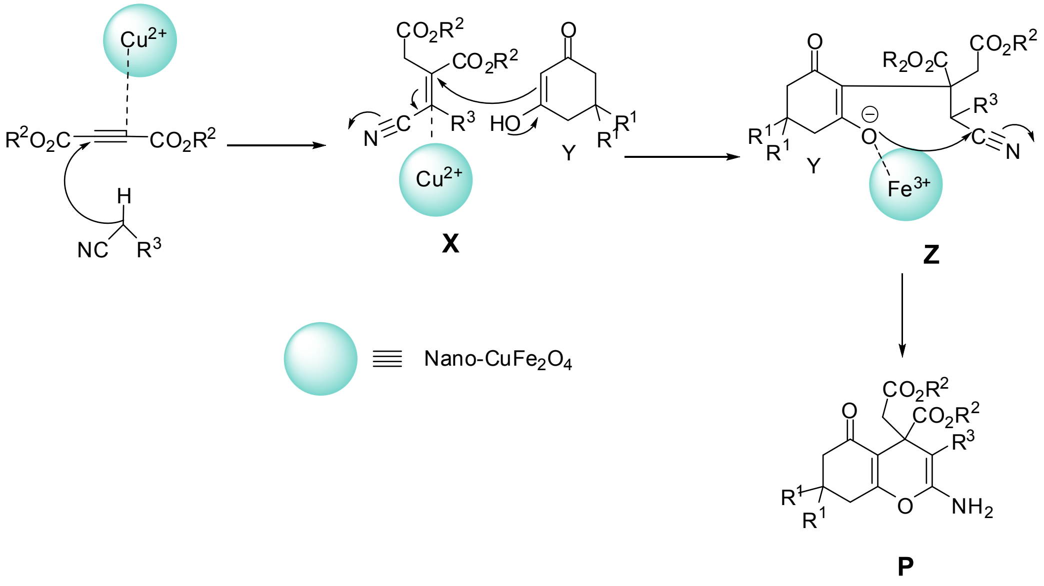
55 **8** **46** **57a-h**

Table 27

Entry	R^1	R^2	R^3	Product	Time (h)	Yield (%)
1	Me	Et	CN	**57a**	2	92
2	Me	Et	CO_2Et	**57b**	2.5	88
3	Me	Me	CN	**57c**	2	91
4	Me	Me	CO_2Et	**57d**	2.5	86
5	H	Et	CN	**57e**	2	94
6	H	Et	CO_2Et	**57f**	2.5	89
7	H	Me	CN	**57g**	2	92
8	H	Me	CO_2Et	**57h**	2.5	86

Pradhan *et al.* proposed a possible mechanism (Scheme 3) for this 3 CRs. Thus, Cu^{2+} of $CuFe_2O_4$ catalyzed the Michael addition reaction of dialkyl acetylene dicarboxylate with alkyl nitrile derivatives (malononitrile and ethyl cyanoacetate) during the formation of the intermediate X. The nucleophilic attack by the intermediate Y at the β position (with respect to nitrile group) of the intermediate X was enhanced by Cu^{2+} may be due to the polarization of the π-electron cloud. Finally, the Lewis acidic Fe^{3+} interacted with enolate intermediate Z which in turn facilitates intramolecular electrophilic cyclization with the formation of the six member ring (P). (Scheme 30).[72]

Scheme 30

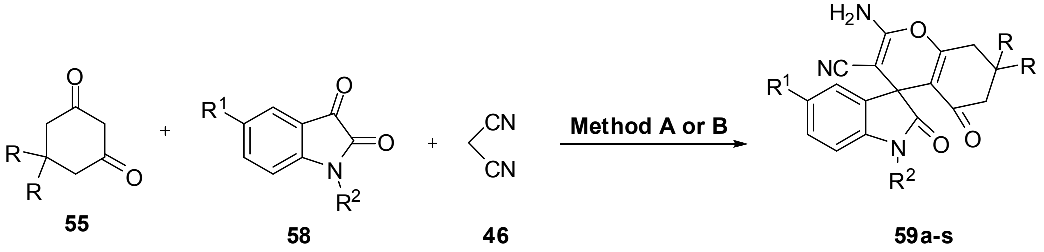


Sarrafi *et al*. investigated the synthesis of spiro[(4*H*-chromene)-4,3'-oxindoles] **59a-s** by three component reaction of an isatin, malononitrile, and cyclic 1,3-diketones in ethanol at 60 °C using mesoporous silica nanoparticles as a catalyst (Scheme 31, Table 28, Method A).[71]

Hosseini-Sarvari and Tavakolian also synthesized spirooxindole derivatives **59** by a one-pot, three-component reaction of **55**, **58** and **46** in excellent yield at room temperature under solvent-free conditions in the presence of 10 mol % ZnO nano-rods catalyst by a very simple procedure (using a mortar and the mixture was ground by a pestle at room temperature) (Scheme 31, Table 28, Method B). All of the reactions provided the desired spirooxindole products in excellent yields employing both electron-deficient (entries 2, 4, and 5) and electron-rich (entry 3) isatins as substrates.[73]

The nano ZnO has Lewis acid (Zn^{2+}) and Lewis basic (O^{2-}) sites.[74] In the first step (i) a Lewis acid site (Zn^{2+}) is coordinated to O-atom of the C=O group of isatin, resulting in the increase of its reactivity.[75]

Scheme 31



Method A: MSNs/EtOH, 60 °C
Method B: ZnO nano-rodes/solvent free, rt

Table 28

Entry	R^1	R^2	R	Product	Method	Yield (%)
1	H	H	Me	**59a**	A	98
2	H	H	H	**59b**	A	97
3	H	H	Me	**59c**	A	95
4	H	H	H	**59d**	A	96
5	H	Bn	Me	**59e**	A	93
6	H	Bn	H	**59f**	A	95
7	5-Br	H	Me	**59g**	A	97
8	5-Br	H	H	**59h**	A	98
9	5-Me	H	Me	**59i**	A	95
10	5-Me	H	H	**59j**	A	94
11	5-O_2N	H	Me	**59k**	A	96
12	5-O_2N	H	H	**59l**	A	97
13	5-Br	H	Me	**59e**	A	96
14	5-Br	H	H	**59h**	B	96
15	H	H	H	**59d**	B	98
16	H	NO_2	H	**59m**	B	94
17	H	Me	H	**59n**	B	92
18	H	Cl	H	**59o**	B	97
19	H	Br	H	**59p**	B	91
20	Me	H	H	**59q**	B	96
21	H	H	Me	**59a**	B	97
22	H	NO_2	Me	**59r**	B	93
23	H	Cl	Me	**59s**	B	90

2.3.1.3.2. Hexahydroquinoline

Tajbakhsh *et al*. reported four component reaction of dimedone **55**, aldehyde **7**, acetoacetic ester **15**, and ammonium acetate using a catalytic amount of titanium dioxide nanoparticles to prepare the polyhydroquinoline derivatives **60** in high yields (Scheme 32, table 29). It can be seen that both electron-rich and electron-deficient aldehydes as well as heterocyclic ones worked well, giving good to excellent yields of the substituted polyhydroquinoline derivatives.[76]

Scheme 32

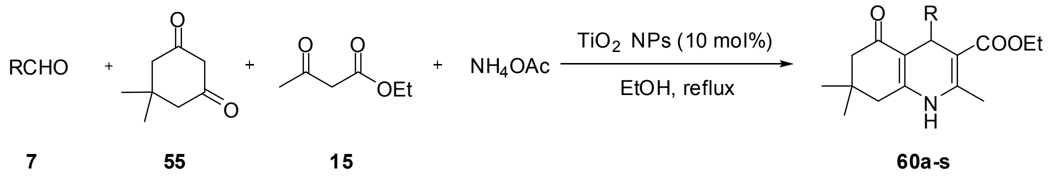


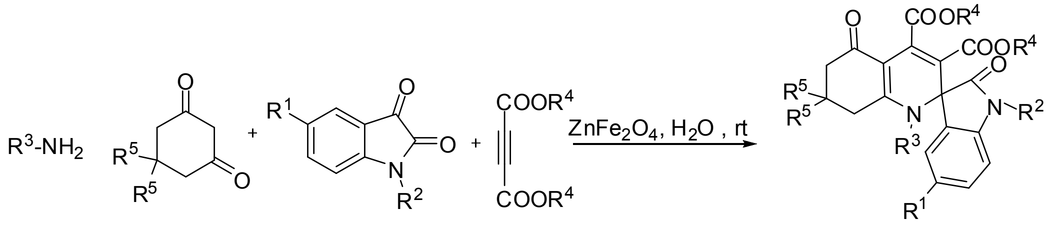
Table 29

Entry	R	Product	Yield (%)[a]
1	C_6H_5	**60a**	96
2	4-BrC_6H_4	**60b**	94
3	3-BrC_6H_4	**60c**	90
4	4-ClC_6H_4	**60d**	92
5	2-ClC_6H_4	**60e**	90
6	3-ClC_6H_4	**60f**	90
7	4-$(CH_3)_2NC_6H_4$	**60g**	80
8	2-MeOC_6H_4	**60h**	93
9	2-FC_6H_4	**60i**	90
10	4-$NO_2C_6H_4$	**60j**	88
11	2-$NO_2C_6H_4$	**60k**	82
12	4-MeC_6H_5	**60l**	92
13	4-OHC_6H_5	**60m**	86
14	$C_6H_5CH{=}CH$	**60n**	90
15	2-Thienyl	**60o**	89
16	3-Thienyl	**60p**	91
17	2-Furyl	**60q**	90
18	3-Pyridyl	**60r**	89
19	C_4H_8O	**60s**	84

[a]Yield refers to isolated products.

The bimetallic $ZnFe_2O_4$ nanopowder, a dual Lewis acid–base combined catalyst, is found to efficiently catalyze a four component reaction for the synthesis of functionalized tetrahydrospiro[indoline-3,2'-quinoline] derivatives **61a-ae**. Thus, reaction of arylamines **9**, dialkyl acetylene dicarboxylates **8**, isatin derivatives **58** and cyclohexane-1,3-diones **55** in water medium at room temperature afforded **61** in good yields (Scheme 33, Table 30).[77] A probable mechanism for the formation of **61** depends on the dual role of $ZnFe_2O_4$ as a Lewis acidic site, as well as basic site.[78]

Scheme 33



9 **55** **58** **8** **61a-ae**

Table 30

Entry	R^1	R^2	R^3	R^4	R^5	Product	Yield (%)
1	H	H	4-MeC_6H_4	Me	Me	**61a**	77
2	H	H	4-MeOC_6H_4	Et	Me	**61b**	75
3	H	H	4-BrC_6H_4	Me	Me	**61c**	72
4	H	H	4-BrC_6H_4	Et	Me	**61d**	73
5	Et	H	4-MeOC_6H_4	Me	Me	**61e**	80
6	Et	H	4-ClC_6H_4	Me	Me	**61f**	78
7	H	Br	4-MeOC_6H_4	Me	Me	**61g**	71
8	Et	Cl	4-MeOC_6H_4	Et	H	**61h**	77
9	H	Cl	4-BrC_6H_4	Me	Me	**61i**	69
10	Pr	H	4-MeOC_6H_4	Me	Me	**61j**	72
11	H	Cl	4-ClC_6H_4	Et	Me	**61k**	76
12	Pr	Cl	4-MeOC_6H_4	Me	Me	**61l**	81
13	Pr	Cl	4-MeC_6H_4	Et	Me	**61m**	72
14	Pr	H	4-ClC_6H_4	Me	H	**61n**	70
15	H	H	4-MeOC_6H_4	Et	H	**61o**	74
16	Pr	Cl	4-ClC_6H_4	Me	H	**61p**	76
17	H	F	4-MeOC_6H_4	Et	H	**61q**	78
18	H	Br	4-ClC_6H_4	Et	Me	**61r**	73
19	Et	Cl	4-FC_6H_4	Et	H	**61s**	79
20	H	Cl	4-MeC_6H_4	Et	Me	**61t**	82
21	H	H	3-ClC_6H_4	Et	Me	**61u**	67
22	H	H	3-MeOC_6H_4	Et	Me	**61v**	70
23	H	Cl	3-ClC_6H_4	Et	Me	**61w**	69
24	H	H	4-ClC_6H_4	Me	Me	**61x**	77
25	H	Cl	4-MeOC_6H_4	Me	Me	**61y**	73
26	H	Cl	C_6H_5	Me	Me	**61z**	67
27	H	Cl	4-MeOC_6H_4	Et	Me	**61a**	78
28	H	H	4-MeOC_6H_4	Me	Me	**61b**	78
29	H	H	C_6H_5	Me	Me	**61c**	73
30	H	H	4-ClC_6H_4	Et	Me	**61d**	79
31	H	H	4-MeC_6H_4	Et	Me	**61e**	82

2.3.2. Benzo fused heterocycles

2.3.2.1. Benzo fused with 5-membered heterocyclic ring: two heteroatoms

2.3.2.1.1. Benzoxazole

Sarode *et al*. reported a green and sustainable approach for the synthesis of 2-substituted benzoxazole **63** by using a one pot redox cascade condensation reaction of benzyl amine derivatives **9** and 2-nitrophenols **62**, catalyzed by Cu Ferrite NPs (Scheme 34, Table 31).[79] Cu Ferrite NPs are magnetically separable, air stable and can be recycled up to fifth cycle without a significant loss in catalytic activity.

Scheme 34

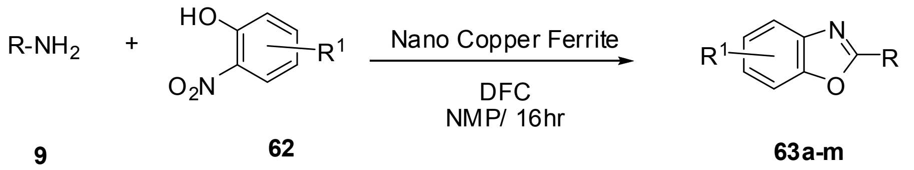
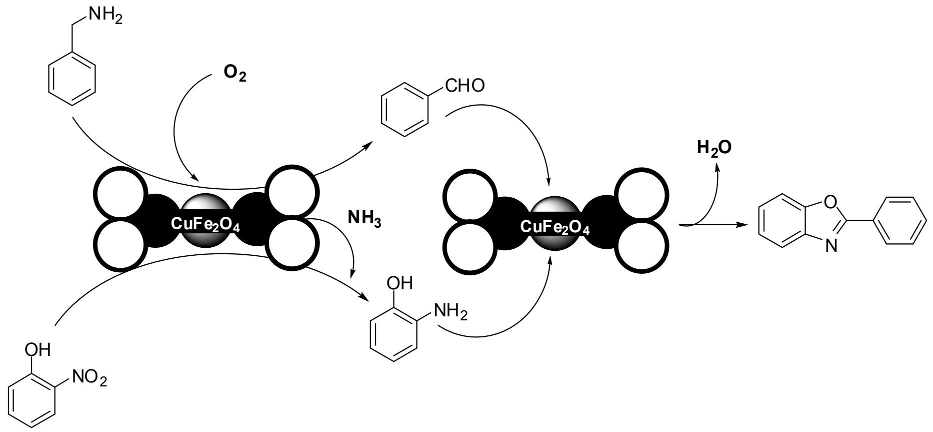


Table 31

Entry	R-NH$_2$	R^1	Product	R	Yield (%)^b
1	$C_6H_5CH_2$-	H	**63a**	C_6H_5	92
2	3-$HOC_6H_4CH_2$-	H	**63b**	3-HOC_6H_4	84
3	4-$MeOC_6H_4CH_2$-	H	**63c**	4-$MeOC_6H_4$	89
4	4-$FC_6H_4CH_2$-	H	**63d**	4-FC_6H_4	85
5	4-$BrC_6H_4CH_2$-	H	**63e**	4-BrC_6H_4	78
6	2-Naphthyl-CH_2-	H	**63f**	2-Naphthyl	90
7	3-Pyridyl-CH_2-	H	**63g**	3-Pyridyl	87
8	3,5-$(MeO)_2C_6H_3CH_2$-	H	**63h**	3,5-$(MeO)_2C_6H_3$	81
9	$C_6H_5CH_2$-	2-Me	**63i**	C_6H_5	84
10	$C_6H_5CH_2$-	3-Cl	**63j**	C_6H_5	80
11	$C_6H_5CH_2$-	3,4-Me_2	**63k**	C_6H_5	90
12	$C_6H_5CH_2$-	3-Cl	**63l**	C_6H_5	86
13	$C_6H_5CH_2$-	2-Me-3-Cl	**63m**	C_6H_5	83

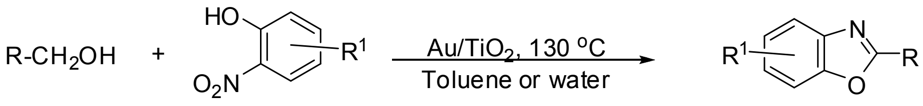
The plausible reaction mechanism depends on the basis that Cu Ferrite NPs provide the surface for the simultaneous oxidation and reduction of the reactants.[80] Benzyl amine on autoxidation forms corresponding benzaldehyde and releases the ammonia which was confirmed by the litmus paper test after the workup of the reaction. Here ammonia acts as a hydrogen source for the reduction of the nitro group of the *o*-nitro phenol. It reduces to 2-amino phenol which was then condensed with the benzaldehyde and gives the 2-phenylbenzo[*d*]oxazole (Scheme 35).

Scheme 35



Tang *et al*. described a one-pot direct synthesis of benzoxazoles **63** using *o*-nitrophenols **62** and alcohols **64** as the starting materials catalyzed by gold nanoparticles supported on titanium dioxide (Au/TiO_2) (Scheme 36). The products were obtained in good yields and yields are summarized in Table 32 The electronic properties of a series of benzylic alcohols were found to have little influence on the reaction. Reactions with benzylic alcohols bearing both electron-donating groups (Table 32, entries 2–5) and electron-withdrawing groups (Table 32, entries 8–10) in the aromatic ring could effectively afford the desired products in excellent yields. However, the steric hindrance of the substituents had a negative influence on the reaction. Relatively low yields of the corresponding products were obtained when the substituent groups appeared in the *ortho*-position of the benzene ring (Table 32, entries 6 and 7).[81]

Scheme 36



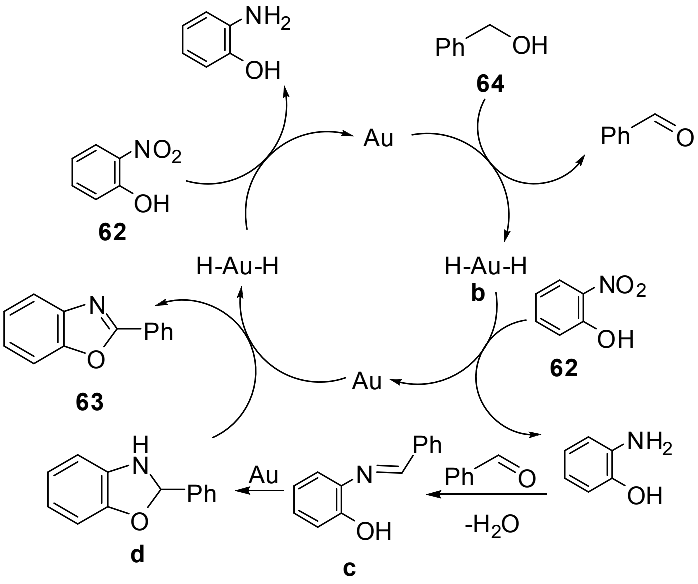
64 **62** **63**

Table 32

Entry	R	R^1	Product	Yield (%)
1	C_6H_5	H	**63a**	99(90)
2	4-MeC_6H_4	H	**63n**	98
3	3-MeC_6H_4	H	**63o**	97
4	4-MeOC_6H_4	H	**63p**	99(91)
5	3-MeOC_6H_4	H	**63q**	91
6	2-MeC_6H_4	H	**63r**	81
7	2-MeOC_6H_4	H	**63s**	85
8	4-FC_6H_4	H	**63d**	95(85)
9	3-FC_6H_4	H	**63t**	94
10	4-ClC_6H_4	H	**63u**	98
11	4-BrC_6H_4	H	**63e**	63/17
12	4-$CF_3C_6H_4$-	H	**63v**	70
13	1-Naphthyl	H	**63w**	95
14	Me	H	**63x**	52
15	^{t}Bu	H	**63y**	63(55)
16	$^nC_5H_{11}$	H	**63z**	56
17	Cyclohexyl	H	**63aa**	60
18	C_6H_5	4-Me	**63ab**	96
19	C_6H_5	5-Me	**63ac**	95(84)
20	C_6H_5	4-MeO	**63ad**	97
21	C_6H_5	5-F	**63ae**	98
22	C_6H_5	4-F	**63af**	99
23	C_6H_5	4-Cl	**63ag**	95
24	C_6H_5	H	**63a**	80(75)

The authors suggested a possible mechanism for the reaction as depicted in Scheme 37 First of all, dehydrogenative oxidation of the alcohol **64** to its corresponding carbonyl compound generates the gold-hydride species (**b**) and 2-nitrophenol (**62**) is reduced to 2-aminophenol in *situ* by **b**. This is the first hydrogen-transfer process. Then, the aldehyde can readily react with 2-aminophenol to afford the corresponding imine (**c**). **c** is selectively converted to the intermediate 2-phenyl-2,3-dihydrobenzoxazole (**d**) under the catalysis of a gold catalyst. Subsequently, **d** can be rapidly oxidized to the product **63** in the presence of a gold catalyst accompanied by the generation of **b** and 2-nitrophenol (**62**) is reduced to 2-aminopheno by **b**. This is the second hydrogen-transfer process. In the whole catalytic cycle, the alcohol and the intermediate 2-phenyl-2,3-dihydrobenzoxazole are used as reductants (hydrogen donor) once and 2-nitrophenol is used as the oxidant (hydrogen acceptor) twice.[81]

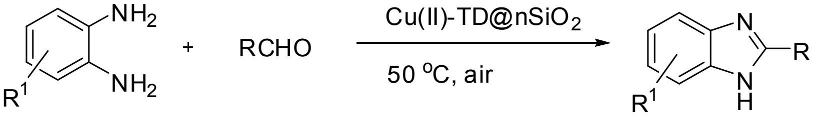
Scheme 37



2.3.2.1.2. Benzimidazole

Nasr-Esfahani *et al*. reported the synthesis of a stable heterogeneous catalyst, Cu(II) containing nanosilica triazine dendrimer (Cu(II)-TD@nSiO$_2$). This catalyst has been successfully applied for the synthesis of benzimidazoles **65**a-k *via* the condensation of 1,2-phenylenediamines **9** with a wide variety of aromatic, polycyclic and heteroaromatic aldehydes at ambient atmosphere under conventional conditions (Scheme 38, Table 33).[82]

Scheme 38



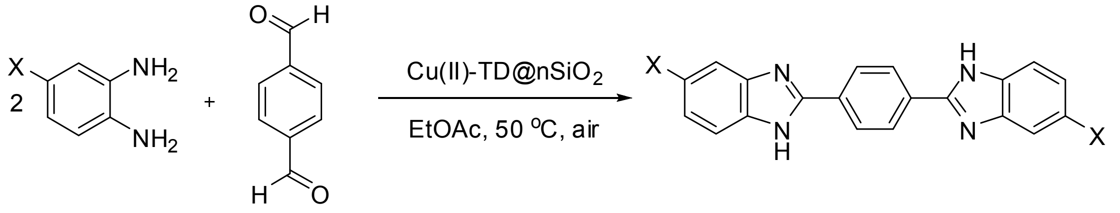
9 **7** **65a-k**

Table 33

Entry	R	R^1	Product	Yield (%)
1	C_6H_5	H	**65a**	95
2	4-ClC_6H_4	H	**65b**	97
3	2-BrC_6H_4	H	**65c**	97
4	4-MeC_6H_4	H	**65d**	95
5	$3\text{-O}_2NC_6H_4$	4-Me	**65e**	89
6	1-Naphthyl	4-Me	**65f**	93
7	1-Naphthyl	4-Cl	**65g**	88
8	9-Anthryl	H	**65h**	92
9	3-Pyridyl	H	**65i**	91
10	3-Indolyl	4-Me	**65j**	92
11	2-Thienyl	H	**65k**	92

The same authors has also achieved an efficient synthesis of bis-benzimidazoles **66**, from terephthaldialdehyde using this catalytic system (Scheme 39).[82]

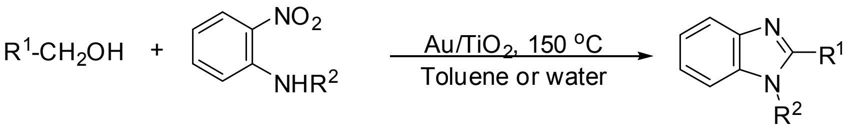
Scheme 39



9 **7** **66** X = H, yield = 92% (120 min)
X = Cl, yield = 87% (120 min)

A highly efficient and selective reaction for the synthesis of 2-substituted benzimidazoles **68** using *o*-nitroanilines **67** and alcohols **64** as the starting materials catalyzed by Au/TiO_2 has been developed *via* two hydrogen-transfer processes (Scheme 40, Table 34). This reaction has a good tolerance to air and water, a wide substrate scope, and represents a new avenue for practical C–N and C–O bond formation. More importantly, no additional additives, oxidants and reductants are required for the reaction and the catalyst can be recovered and reused readily.[81]

Scheme 40



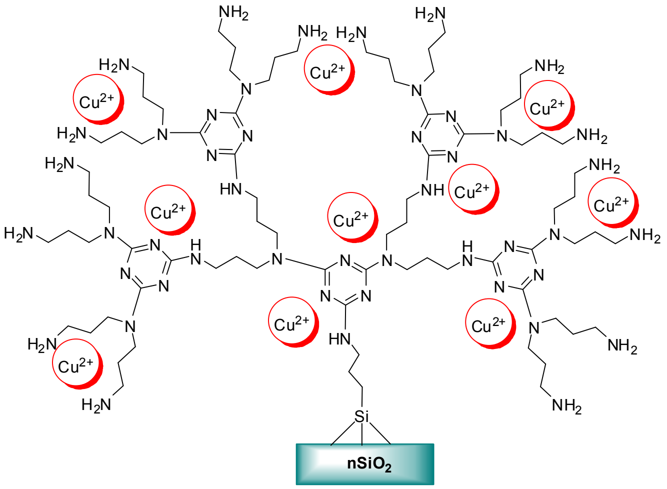
64 **67** **68a-f**

Table 34

Entry	R^1	R^2	Product	Yield (%)
1	C_6H_5	H	**68a**	78(70)
2	C_6H_5	Me	**68b**	84
3	4-MeC_6H_4	Me	**68c**	83
4	4-$MeOC_6H_4$	Me	**68d**	86(81)
5	4-FC_6H_4	Me	**68e**	86
6	4-ClC_6H_4	Me	**68f**	79(70)

2.3.2.1.3. Benzothiazole

The Cu(II) containing nanosilica triazine dendrimer (Cu(II)-TD@nSiO_2, Fig. 19) can also be used as an efficient catalyst for the preparation of various benzothiazoles under mild conditions. The reaction proceeded by reaction of the appropriate aromatic aldehydes **7** with 2-aminothiophenol **9** in the presence of a catalytic amount of Cu(II)-TD@nSiO_2 (Scheme 41, Table 35, Method A).[82]

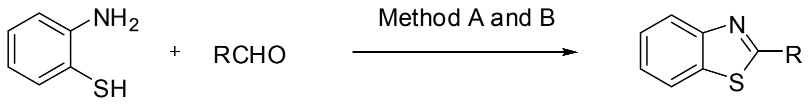


Cu(II)-TD@nSiO2

Fig. 19

Rahmani *et al.* prepared nano titania-supported sulfonic acid (*n*-TSA) from the reaction of nano titania (titanium oxide) with chlorosulfonic acid as sulfonating agent. This was efficiently used as a heterogeneous catalyst for synthesis of 2-arylbenzothiazoles **69**, *via* reaction of aromatic aldehyde with 2-aminothiophenol in solvent-free at 70 °C (Scheme 41, Table 35, Method B).[67]

Scheme 41



9 **7** **69a-u**

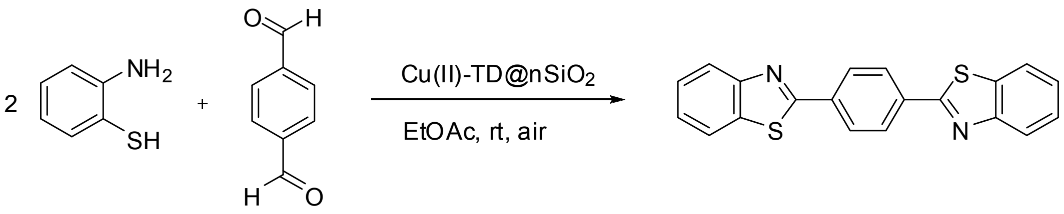
Method A: Cu(II),TD@*n*-SiO_2,rt or 50 °C
Method B: *n*-TSA/Solvent-Free, 70 °C

Table 35

Entry	Ar	Product	Method	Yield (%)
1	4-ClC_6H_5	**69a**	A	97
2	2,4-$Cl_2C_6H_3$	**69b**	A	96
3	3,4-$(MeO)_2C_6H_3$	**69c**	A	93
4	4-MeC_6H_4	**69d**	A	98
5	3-$MeOC_6H_4$	**69e**	A	96
6	3-$O_2NC_6H_4$	**69f**	A	87
7	1-Naphthyl	**69g**	A	93
8	3-Pyridyl	**69h**	A	92
9	3-indolyl	**69i**	A	94
10	2-Thienyl	**69j**	A	92
11	C_6H_5	**69k**	B	90
12	2-ClC_6H_4	**69l**	B	84
13	4-ClC_6H_4	**69a**	B	86
14	2-HOC_6H_4	**69m**	B	82
15	4-HOC_6H_4	**69n**	B	83
16	4-FC_6H_4	**69o**	B	86
17	4-BrC_6H_4	**69p**	B	86
18	4-MeC_6H_4	**69d**	B	90
19	4-$MeOC_6H_4$	**69q**	B	93
20	2-$O_2NC_6H_4$	**69r**	B	81
21	3-$O_2NC_6H_4$	**69f**	B	86
22	4-$O_2NC_6H_4$	**69s**	B	89
23	2-Naphthyl	**69t**	B	90
24	Furyl	**69u**	B	79

Nasr-Esfahani *et al*. prepared symmetrical bis-benzothiazole **70** in high yield by the reaction of terephthaldialdehyde **7** with two equivalents of 2-aminothiophenol **9** in the presence of a catalytic amount of Cu(II)-TD@nSiO_2 under conventional conditions (Scheme 42).[82]

Scheme 42



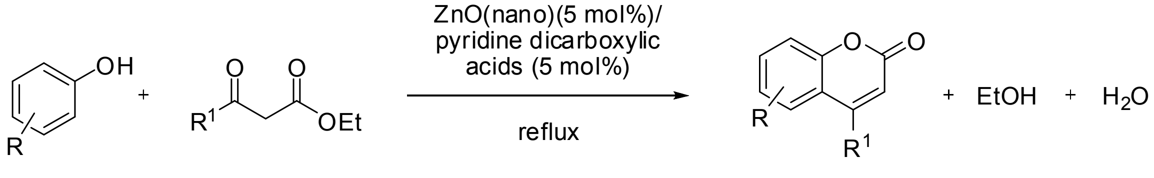
9 **7** **70** 87% (150 min)

2.3.2.2. Benzo fused with 6-membered heterocyclic ring: one heteroatom

2.3.2.2.1. 2*H*-Chromene

A wide range of substituted coumarin derivatives **71a-l** were synthesized by refluxing in acetonitrile, ethyl acetoacetate, and ethyl benzoyl acetate **15** with a wide range of structurally diverse phenol derivatives **62** within a short reaction time with a catalytic combination of pyridine dicarboxylic acid as organocatalyst and nanocrystalline ZnO (Scheme 43, Table 36).[83]

Scheme 43



62 **15** **71a-l**

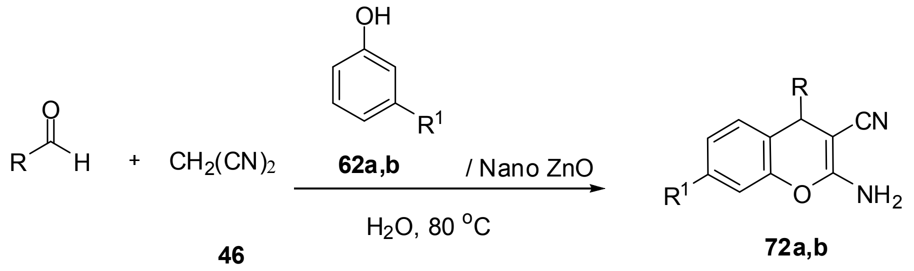
Table 36

Entry	R	R^1	Product	Yield (%)
1	H	Me	**71a**	90
2	3-OH	Me	**71b**	93
3	3,5-$(OH)_2$	Me	**71c**	89
4	3-MeO	Me	**71d**	93
5	3-OH-2-Me	Me	**71e**	86
6	3-NH_2	Me	**71f**	89
7	4-O_2N	Me	**71g**	92
8	4-Cl	Me	**71h**	73
9	3-OH	Ph	**71i**	88
10	3,5-$(OH)_2$	Ph	**71j**	85
11	3-MeO	Ph	**71k**	87
12	3,5-$(Me)_2$	Ph	**71l**	85

2.3.2.2.2. 4*H*-Chromene

Nano ZnO can serve as an efficient catalyst for the synthesis of 2-amino-4*H*-benzopyrans **72a,b** in good yields from methylenemalononitrile, generated *in situ* from aldehyde **7** and malononitrile **46** and phenols **62a,b** (Scheme 44).[84]

Scheme 44



72a, R^1 = H, R = 4-ClC_6H_4, yield 30%
72b, R^1 = OH,R = 4-ClC_6H_4, yield 65%

Mohammad and Kassaee reported the use of sulfochitosan-coated Fe_3O_4 magnetic nanoparticles (Fe_3O_4@CS-SO_3H NPs, Fig. 20) as a "green" heterogeneous catalyst for preparation of 2-amino-4*H*-chromen-4-yl phosphonates **72c-k** through one-pot, three-component reactions of salicylaldehydes **7**, malononitrile **46**, and triethyl phosphite in water at room temperature (Scheme 45, Table 37).[85]

Scheme 45

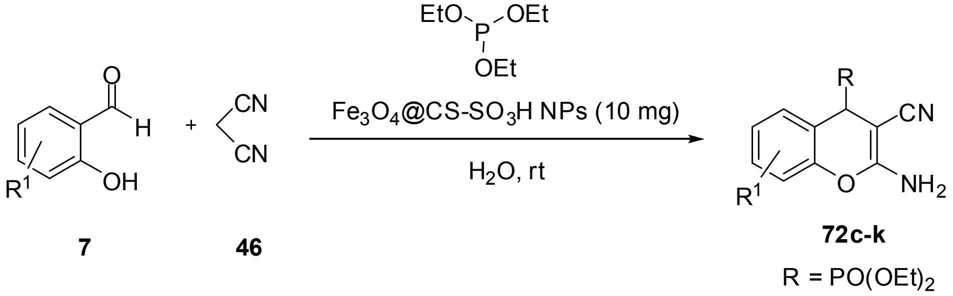
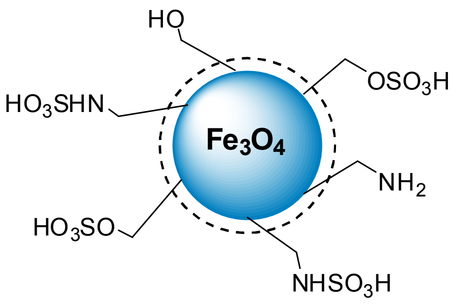


Table 37

Entry	R^1	Product	Yield (%)
1	H	**72c**	93
2	6-Cl	**72d**	96
3	6-O_2N	**72e**	92
4	6-Me	**72f**	95
5	6-Br	**72g**	97
6	7-MeO	**72h**	93
7	6,8-Br_2	**72i**	97
8	6,8-Br_2	**72j**	94
9	6-MeO	**72k**	88



Fe$_3$O$_4$@CS-SO$_3$H NPs

Fig. 20

2.3.2.3. Benzo fused with 6-membered heterocyclic ring: two heteroatoms

2.3.2.3.1. Quinoxaline

An iron Schiff base complex was encapsulated in SBA-15 (Santa BArbara No. 15), the most interesting mesoporous silica, to afford a Fe(III)-Schiff base/SBA-15 heterogeneous nanocatalyst (Fig. 21). The latter catalyzed the synthesis of quinoxalines **73a-d** with excellent yields from the reaction of *o*-phenylenediamine with the appropriate 1,2-diketone **25** in water (Scheme 46, Table 38).[66]

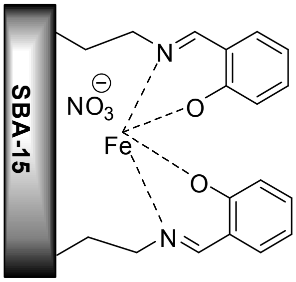
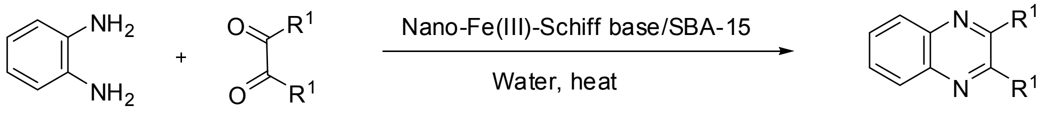


Fig. 21

Scheme 46



9 **25** **73a-d**

Table 38

Entry	R^1	Product	Yield (%)
1	C_6H_5	**73a**	99
2	4-FC_6H_4	**73b**	99
3	4-$MeOC_6H_4$	**73c**	98
4	Me	**73d**	99

2.3.2.3.2. Quinazoline

Zhang *et al*. prepared a new heterogeneous catalyst consisting of CuO NPs supported on kaolin and studied its catalytic activity for the synthesis of quinazolines **75**. Thus, a series of quinazoline derivatives **75** were synthesized from 2-aminobenzophenones **74** and benzylic amines **9** under mild conditions in good to excellent yields (Scheme 47, Table 39). The employment of a suitable supporting material can not only increase the catalytic activity of CuO NPs but also facilitate the separation between the catalyst and the product.[86]

Scheme 47

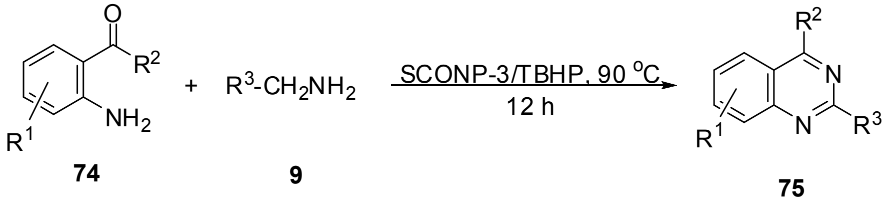
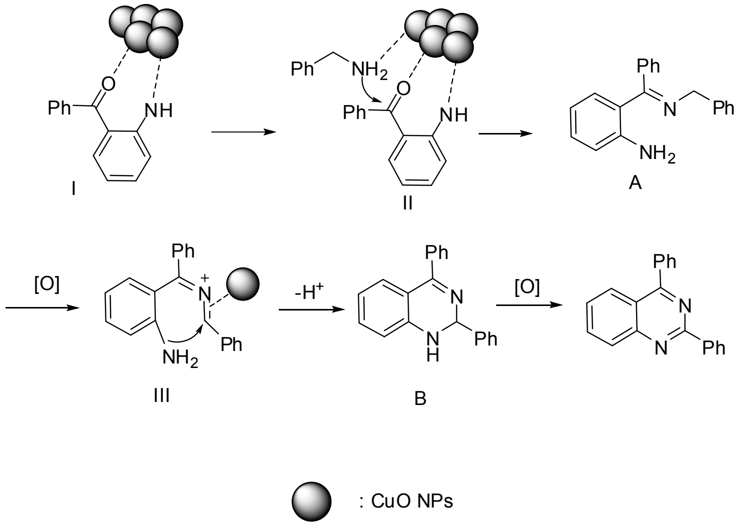


Table 39

Entry	R^1	R^2	R^3	Product	Yield (%)
1	H	C_6H_5	C_6H_5	**75a**	90
2	H	4-Fluorophenyl	C_6H_5	**75b**	88
3	H	4-Bromophenyl	C_6H_5	**75c**	83
4	H	*p*-Tolyl	C_6H_5	**75d**	82
5	H	2,5-diMephenyl	C_6H_5	**75e**	71
6	H	Mesityl	C_6H_5	**75f**	0
7	H	Et	C_6H_5	**75g**	84
8	H	^{n}Bu	C_6H_5	**75h**	95
9	H	Hexadecyl	C_6H_5	**75i**	78
10	H	^{i}Pr	C_6H_5	**75j**	90
11	H	^{t}Bu	C_6H_5	**75k**	89
12	H	Cyclopropyl	C_6H_5	**75l**	90
13	H	Cyclopropyl	C_6H_5	**75l**	74
14	H	C_6H_5	C_6H_5	**75m**	73
15	6-Cl	C_6H_5	C_6H_5	**75a**	85
16	6-Br	C_6H_5	C_6H_5	**75n**	93
17	6,7-diMe	C_6H_5	C_6H_5	**75o**	63
18	6-Cl	C_6H_5	C_6H_5	**75p**	45
19	H	C_6H_5	p-Tolyl	**75q**	89
20	H	C_6H_5	m-Tolyl	**75r**	86
21	H	C_6H_5	o-Tolyl	**75s**	94
22	H	C_6H_5	4-Methoxyphenyl	**75t**	88
23	H	C_6H_5	Benzo[1,3]dioxol-5-yl	**75u**	58
24	H	C_6H_5	4-Chlorophenyl	**75v**	87
25	H	C_6H_5	4-Fluorophenyl	**75w**	91
26	H	C_6H_5	4-(Trifluoromethyl)phenyl	**75x**	92
27	H	C_6H_5	1-Naphthyl	**75y**	86
28	H	C_6H_5	2-Furyl	**75z**	51

A postulated reaction pathway is proposed, as shown in Scheme 8 Firstly, CuO NPs may activate 2-aminobenzophenone to generate intermediate I. Meanwhile, benzylic amine can attach to the surface of the CuO NPs to form intermediate II. In the intermediate II, the distance between 2-aminobenzophenone and benzylic amine may be shortened, facilitating the attack of benzylic amine to 2-aminobenzophenone. After attacked by benzylic amine, imine A is formed. A subsequently undergoes an oxidation process and is stabilized by CuO NPs (intermediate III). Intramolecular attack of the amino-group to the imine cation results in intermediate B. Further oxidation of intermediate B gives the quinazoline product.[86]

Scheme 48



Tang *et al*. developed a highly efficient and selective nitrogen source-promoted reaction for the synthesis of 2,4-disubstituted quinazolines **75** from *o*-nitroacetophenones **76** and alcohols **64** catalyzed by Au/TiO$_2$ *via* a hydrogen-transfer strategy (Scheme 49, Table 40). This reaction has good tolerance to air and water, a wide substrate scope, and represents a new avenue for practical multiple C–N bond formation. More importantly, no additional additive, oxidant and reductant are required in the reaction and the catalyst can be recovered and reused readily. The electronic properties of a series of aromatic alcohols were found to have little influence on the reaction. The reactions could be carried out effectively to afford the desired products with good yields regardless of the electron-donating groups or electron-withdrawing groups at the benzene ring of benzylic alcohols. However, the steric hindrance of the substituents had a negative influence on the reaction.[87]

Scheme 49

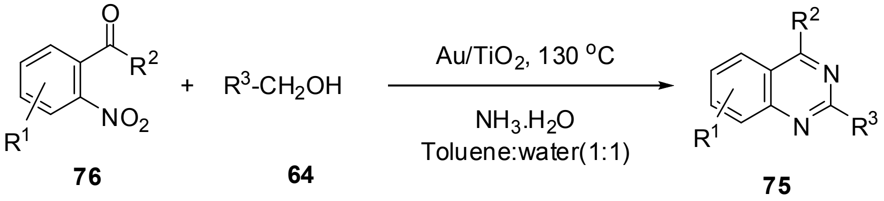


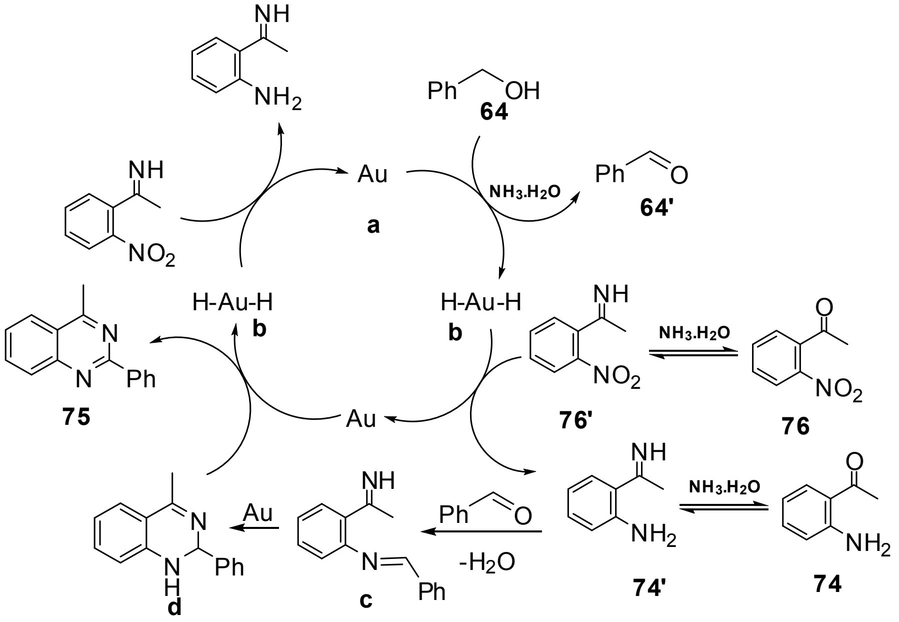
Table 40

Entry	R^1	R^2	R^3	Yield (%)
1	H	Me	C_6H_5	99(83)[a]
2	H	Me	4-MeC_6H_4	97(80)[a]
3	H	Me	4-MeOC_6H_4	95
4	H	Me	2-MeOC_6H_4	54(84)[b]
5	H	Me	3,4-$(MeO)_2C_6H_3$	97
6	H	Me	4-FC_6H_4	91(81)[a]
7	H	Me	3-FC_6H_4	70
8	H	Me	4-ClC_6H_4	96
9	H	Me	2-ClC_6H_4	63(86)[b]
10	H	Me	4-BrC_6H_4	94(85)[a]
11	H	Me	4-MeOOCC_6H_4	36(94)[b]
12	H	Me	4-$CF_3C_6H_4$	31(87)[b]
13	H	Me	1-Naphthyl	89
14	H	Me	Me	85(74)[a]
15	H	Me	^{n}Pr	76
16	H	Me	^{t}Bu	58
17	H	Me	Cyclohexyl	73
18	H	C_6H_5	C_6H_5	74
19	H	4-MeC_6H_4	C_6H_5	71
20	H	4-FC_6H_4	C_6H_5	76
21	H	4-ClC_6H_4	C_6H_5	73
22	H	4-BrC_6H_4	C_6H_5	68
23	H	2,4,6-$(Me)_3C_6H_2$	C_6H_5	0
24	6-Cl	C_6H_5	C_6H_5	73
25	6-Me	Me	C_6H_5	92
26	6-F	Me	C_6H_5	94(97)[a]
27	7-Cl	Me	C_6H_5	91
28	H	H	C_6H_5	53
29	H	^{n}Bu	C_6H_5	56
30	H	^{c}Pn	C_6H_5	71
31	H	Hexadecyl	C_6H_5	68

[a] Under air, [b] 150 °C

The possible mechanism is depicted in Scheme 50. First of all, dehydrogenative oxidation of the alcohol (**64**) into the corresponding carbonyl compound (**64′**) promoted by ammonia, generates the gold-hydride species (**b**) and **76a′** is reduced into **76b** in *situ* by **b**. This is the first hydrogen-transfer process and also the rate-limiting step of the reaction. Then, **76b** can readily react with **64a′** to afford the corresponding imine **(c)**. Compound **c** is converted to the intermediate **(d)** under the catalysis of gold. Subsequently, **d** can be rapidly oxidized to the product of **75** in the presence of the gold catalyst accompanied with the generation of **b**. And **76a′** is again reduced into **76b** by **b**. This is the second hydrogen-transfer process. In the whole catalytic cycle, the alcohol **64** and the intermediate **d** are used as the reductant (hydrogen donor) once and the nitro compound **76a′** is used as the oxidant (hydrogen acceptor) twice.[87]

Scheme 50



2.3.3.Two fused heterocycles

2.3.3.1. Fused [5-5] systems: two bridgehead nitrogens and one extra heteroatom

2.3.3.1.1. Pyrazolo[1,2-*a*][1,2,4]triazole

Azarifar *et al.* explored the catalytic activity of nano-structured ZnO in the synthesis of pyrazolo[1,2-*a*][1,2,4]triazole-1,3-dione derivatives **78** *via* a three-component coupling reaction between aromatic aldehydes **7**, malononitrile **46**, and 4-aryltriazoles **77** under solvent-free conditions (Scheme 51, Table 41, Method A).[88]

Naeimi *et al.* also developed an efficient clean method for the synthesis of pyrazolo[1,2-a][1,2,4]triazole derivatives **75** *via* a one-pot three-component reaction of aromatic aldehydes **7**, **77** and **46** in the presence of a catalytic amount of nanocrystalline (NC) magnesium oxide (Scheme 51, Table 41, Method B).[89]

Shaterian and Moradi used a similar approach for the synthesis of 7-amino-1,3-dioxo-1,2,3,5-tetrahydropyrazolo[1,2-*a*][1,2,4]triazole derivatives **78** by employing magnetic Fe_3O_4 nanoparticles coated by (3-aminopropyl)-triethoxysilane (Fig. 22) as a catalyst for a similar reaction (Scheme 51, Table 41, Method C).[90]

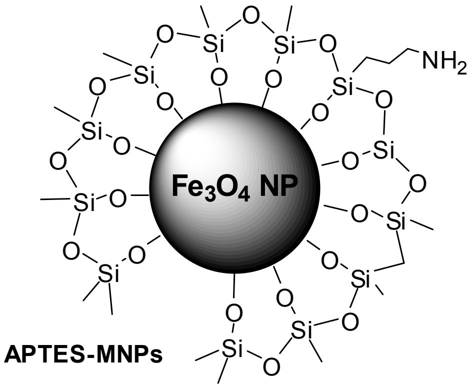
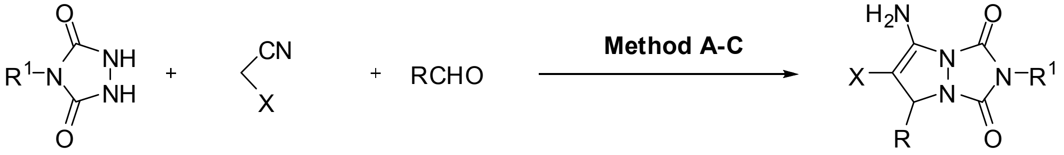


Fig. 22

Scheme 51



77 **46** **7** **78a-ai**

Method A: Nano-ZnO/ solvent free, reflux
Method B: NC MgO(10 mol%)/EtOH, reflux
Method C: APTES-MNPs/solvent free, 80 ^{o}C

Table 41

Entry	R	X	R^1	Product	Method	Yield (%)
1	C_6H_5	CN	C_6H_5	**78a**	A	90
2	4-ClC_6H_4	CN	C_6H_5	**78b**	A	88
3	C_6H_5	CN	4-ClC_6H_4	**78c**	A	91
4	4-ClC_6H_4	CN	4-ClC_6H_4	**78d**	A	91
5	4-$O_2NC_6H_4$	CN	4-ClC_6H_4	**78e**	A	90
6	4-$O_2NC_6H_4$	CN	2,4-$Cl_2C_6H_4$	**78f**	A	86
7	4-$O_2NC_6H_4$	CN	4-$O_2NC_6H_4$	**78g**	A	71
8	C_6H_5	CN	4-$MeOC_6H_4$	**78h**	A	84
9	4-$O_2NC_6H_4$	CN	4-$MeOC_6H_4$	**78i**	A	81
10	C_6H_5	CN	4-$^tBuC_6H_4$	**78j**	A	80
11	4-$O_2NC_6H_4$	CN	4-$^tBuC_6H_4$	**78k**	A	75
12	4-Cl-3$O_2NC_6H_3$	CN	C_6H_5	**78l**	A	86
13	2,4,6-$(MeO)_3C_6H_2$	CN	C_6H_5	**78m**	A	78
14	2,3-$Cl_2C_6H_4$	CN	C_6H_5	**78n**	A	91
15	C_6H_5	CN	C_6H_5	**78a**	A	-
16	C_6H_5	CN	C_6H_5	**78a**	B	89
17	4-BrC_6H_4	CN	C_6H_5	**78o**	B	88
18	3-$O_2NC_6H_4$	CN	C_6H_5	**78p**	B	91
19	4-ClC_6H_4	CN	C_6H_5	**78q**	B	86
20	3-BrC_6H_4	CN	C_6H_5	**78r**	B	81
21	2-BrC_6H_4	CN	C_6H_5	**78s**	B	87
22	4-MeC_6H_4	CN	C_6H_5	**78t**	B	90
23	C_6H_5	COOMe	C_6H_5	**78u**	B	83
24	3-$O_2NC_6H_4$	COOMe	C_6H_5	**78v**	B	84
25	4-ClC_6H_4	COOMe	C_6H_5	**78w**	B	85
26	4-$O_2NC_6H_4$	COOMe	C_6H_5	**78x**	B	92
27	4-ClC_6H_4	COOEt	C_6H_5	**78y**	B	82
28	4-$O_2NC_6H_4$	COOEt	C_6H_5	**78z**	B	86
29	4-MeC_6H_4	COOEt	C_6H_5	**78aa**	B	89
30	Ferrocenyl	CN	C_6H_5	**78ab**	B	-
31	C_6H_5	CN	C_6H_5	**78a**	C	92
32	4-ClC_6H_4	CN	C_6H_5	**78b**	C	90
33	4-FC_6H_4	CN	C_6H_5	**78ac**	C	92
34	2-ClC_6H_4	CN	C_6H_5	**78ad**	C	88
35	3-ClC_6H_4	CN	C_6H_5	**78ae**	C	94
36	2-$O_2NC_6H_4$	CN	C_6H_5	**78af**	C	88
37	4-$O_2NC_6H_4$	CN	C_6H_5	**78ag**	C	89
38	2,4-$Cl_2C_6H_3$	CN	C_6H_5	**78ah**	C	90
39	3-$O_2NC_6H_4$	CN	C_6H_5	**78p**	C	90
40	4-MeC_6H_4	CN	C_6H_5	**78t**	C	89
41	3-BrC_6H_4	CN	C_6H_5	**78r**	C	93
42	2-BrC_6H_4	CN	C_6H_5	**78s**	C	92
43	4-BrC_6H_4	CN	C_6H_5	**78o**	C	89
44	*n*-Heptanal	CN	C_6H_5	**78ai**	C	-

2.3.3.2. Fused [5-5] systems: four heteroatoms [2:2]

2.3.3.2.1. Imidazo[4,5-*d*]imidazole

Nano-sized HZSM-5 zeolite have been used by Vessally *et al*. as a mild and efficient catalyst for the synthesis of tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)dione derivatives **79a-f** through reaction between urea **49** and the appropriate dicarbonyl compound **25**. The yield of the reaction increases when the time of the reaction reaches 72 h. The amount of catalyst was also reported to increase the reaction yields. HZSM-5 was prepared by ion exchange of ZSM-5 nanozeolite with NH_4Cl, followed by drying and calcination (Scheme 52, Table 42).[91]

Scheme 52

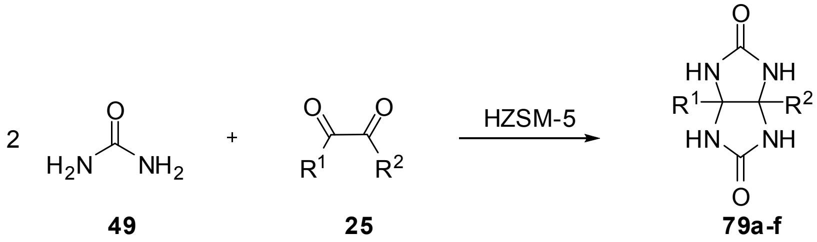


Table 42

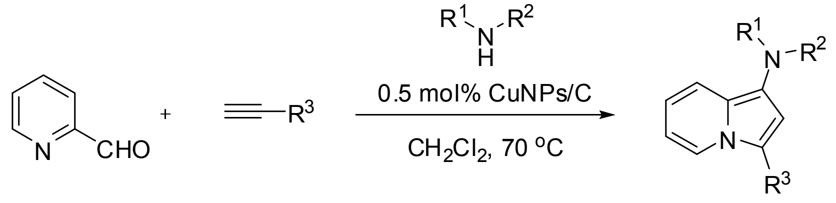
Entry	R^1	R^2	Product	Yield (%)
1	H	H	**79a**	56
2	Me	Et	**79b**	67
3	C_6H_5	C_6H_5	**79c**	71
4	4-MeOC_6H_4	4-MeOC_6H_4	**79d**	70
5	Me	Me	**79e**	67
6	Et	Et	**79f**	70

2.3.3.3. Fused [5-6] systems: one bridgehead nitrogen

2.3.3.3.1. Indolizine

Albaladejo *et al*. reported the synthesis of a wide range of indolizines **80a-m** in moderate-to-high yields (59–93%) by the reaction of pyridine-2-carbaldehyde **7** secondary amines and arylacetylenes **35** using low catalyst loading (0.5 mol%) of Cu NPs/C (Cu NPs on activated carbon) (Scheme 53, Table 43).[92]

Scheme 53



7 **35** **80a-m**

Table 43

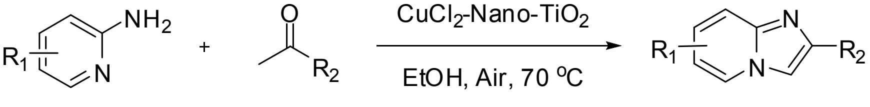
Entry	R^1 R^2	R^3	Yield (%)
1	$-CH_2)_5$	C_6H_5	86
2	$-CH_2)_2-O-CH_2)_2-$	C_6H_5	74
3	Bu,Bu	C_6H_5	91
4	Me,Bn	C_6H_5	80
5	Bn,Bn	C_6H_5	93
6	$-CH_2)_5$	$4-MeC_6H_4$	69
7	$-CH_2)_5$	$4-F_3CC_6H_4$	76
8	$-CH_2)_5$	$4-MeOOCC_6H_4$	59
9	$-CH_2)_5$	$4-Me_2NC_6H_4$	93
10	$-CH_2)_5$	$4-MeOC_6H_4$	86
11	$-CH_2)_5$	$4-BrC_6H_4$	73
12	Bn,Bn	$4-MeC_6H_4$	91
13	Bu,Bu	^{n}Decyl	64

2.3.3.4. Fused [5-6] systems: one bridgehead nitrogen and one extra heteroatom

2.3.3.4.1. Imidazo[1,2-*a*]pyridine

Meng *et al*. developed an efficient and mild heterogeneously $CuCl_2$/nano-TiO_2-catalyzed aerobic synthesis of imidazo[1,2-*a*]pyridines **82a-d** in good yields with low catalyst loading (0.8 mol%) from 2-aminopyridines **9** and ketones **81** using air as the oxidant in the absence of any ligands and additives. This strategy was compatible with a large range of substrates, including unactivated aryl ketones and unsaturated ketones and went through the C–H bond functionalization mechanism (Scheme 54, Table 44).[93]

Scheme 54

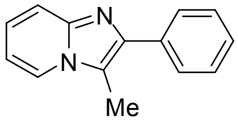


9 **81** **82a-ad**

Table 44

Entry	R^1	R^2	Product	Yield (%)
1	H	4-MeOC_6H_4	**82a**	85
2	H	3-MeOC_6H_4	**82b**	84
3	H	2-MeOC_6H_4	**82c**	69
4	H	4-MeC_6H_4	**82d**	88
5	H	3-MeC_6H_4	**82e**	82
6	H	2-MeC_6H_4	**82f**	91
7	H	4-ClC_6H_4	**82g**	92
8	H	3-ClC_6H_4	**82h**	88
9	H	2-ClC_6H_4	**82i**	70
10	H	4-BrC_6H_4	**82j**	85
11	H	4-$Me_2NC_6H_4$	**82k**	72
12	H	4-$F_3CC_6H_4$	**82l**	65
13	H	3-$F_3CC_6H_4$	**82m**	86
14	H	2-$F_3C_6H_4$	**82n**	72
15	H	4-MeOOCC_6H_4	**82o**	64
16	H	3-$O_2NC_6H_4$	**82p**	81
17	H	4-NCC_6H_4	**82q**	90
18	H	2-Furyl	**82r**	78
19	H	2-Thienyl	**82s**	86
20	H	2-Pyridyl	**82t**	74
21	H	2-Thiazolyl	**82u**	71
22	H	2-Styryl	**82v**	78
23	H	*	**82w**	84
24	3-Me	C_6H_5	**82x**	83
25	4-Me	C_6H_5	**82y**	80
26	4-Me	4-BrC_6H_4	**82z**	78
27	4-CF_3	C_6H_5	**82aa**	75
28	3-Br-2-Me	C_6H_5	**82ab**	61
29	2,4-Br_2-6-Me	C_6H_5	**82ac**	55
30	3-O_2N	C_6H_5	**82ad**	-

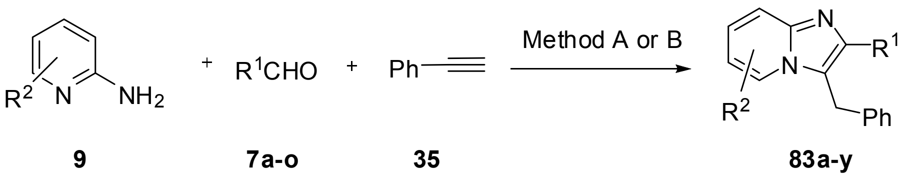
* methylphenylketone is used and the product is



Guntreddi *et al*. demonstrated the catalytic use of magnetic nano-Fe_3O_4–$KHSO_4$·SiO_2 for an efficient one pot synthesis of imidazo[1,2-*a*]pyridines **83** by one pot three-component reaction of 2-aminopyridine **9**, aldehyde **7**, and alkyne **35** (Scheme 55, Table 45, Method A).[94]

Tajbakhsh *et al*. synthesized a magnetically recoverable nano-catalyst based on a biimidazole Cu(I) complex by covalent grafting of biimidazole on chloride-functionalized silica@magnetite nanoparticles, followed by metalation with CuI. The prepared nanocatalyst was also shown to have excellent and green catalytic activity in the synthesis of imidazo[1,2-*a*]pyridines **83a-y** *via* the one-pot reaction of 2-aminopyridines **9**, aldehydes **7** and phenylacetylene **35** in aqueous media (Scheme 55, Table 45, Method B).[95]

Scheme 55



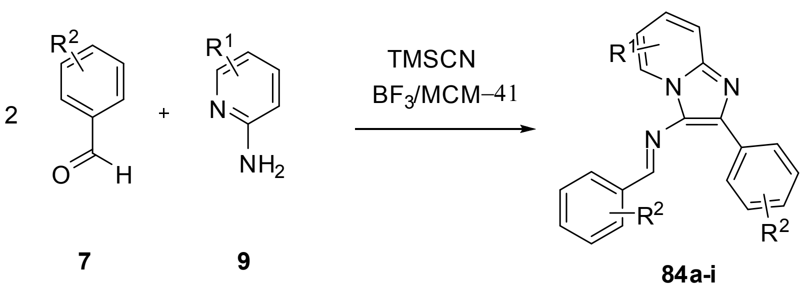
Method A: Fe_3O_4-$KHSO_4.SiO_2$-MNPs/110 °C, toluene, 17-24 h
Method B:MNP@BiimCu(1.2 mol%)/CTAB(5 mg)/H_2O, reflux

Table 45

Entry	R^1	R^2	Method	Product	Yield (%)
1	H	C_6H_5	A	**83a**	89
2	H	4-ClC_6H_4	A	**83b**	86
3	H	3-ClC_6H_4	A	**83c**	84
4	H	4-BrC_6H_4	A	**83d**	83
5	H	3-BrC_6H_4	A	**83e**	82
6	H	2-BrC_6H_4	A	**83f**	83
7	H	4-$MeOC_6H_4$	A	**83g**	75
8	H	4-$Me_2NC_6H_4$	A	**83h**	-
9	H	4-MeC_6H_4	A	**83i**	79
10	H	4-$O_2NC_6H_4$	A	**83j**	69
11	H	2-$O_2NC_6H_4$	A	**83k**	65
12	H	Et	A	**83l**	70
13	H	2-Furyl	A	**83m**	72
14	H	3-MeO-4-OHC_6H_4	A	**83n**	55
15	H	4-ClC_6H_4	B	**83b**	90
16	H	C_6H_5	B	**83b**	92
17	H	4-$MeOC_6H_4$	B	**83g**	85
18	H	4-BrC_6H_4	B	**83d**	90
19	H	4-MeC_6H_4	B	**83i**	78
20	H	4-NCC_6H_4	B	**83o**	95
21	H	4-$F_3CC_6H_4$	B	**83p**	90
22	H	4-FC_6H_4	B	**83q**	95
23	H	2-MeC_6H_4	B	**83r**	80
24	H	2-ClC_6H_4	B	**83s**	87
25	H	3-BrC_6H_4	B	**83e**	82
26	H	3-ClC_6H_4	B	**83c**	85
27	H	1-Naphthyl	B	**83t**	78
28	H	2-Furyl	B	**83u**	90
29	H	^{n}Pr	B	**83v**	65
30	H	^{i}Pr	B	**83w**	76
31	3-Me	C_6H_5	B	**83x**	82
32	3-Me	C_6H_5	B	**83y**	78

Multi-component reaction of various types of aldehydes **7**, 2-aminopyridines **9** and trimethylsilyl cyanide was carried out in the presence of MCM-41 supported boron trifluoride (BF_3/MCM-41) as a nanostructured solid acid catalyst for the synthesis of 3-iminoaryl-imidazo[1,2-*a*]pyridine derivatives **84a-i** (Scheme 56, Table 46). MCM-41 nanoparticles were synthesized by a sol–gel method and BF_3/MCM-41 samples with various loading amounts of BF_3 and different calcination temperatures were prepared and characterized by XRD, SEM and FT-IR techniques.[96]

Scheme 56



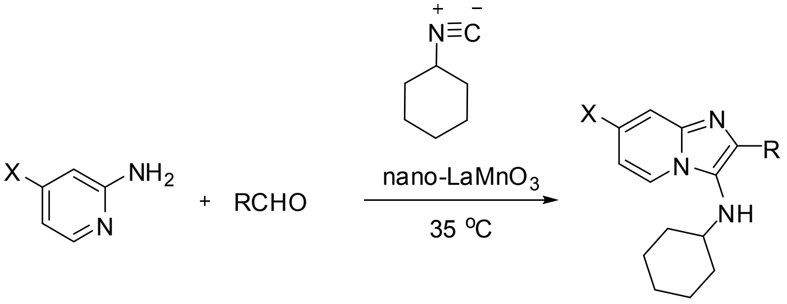
R^1 = H, 4-Me, 6-Me R^1 = H, 2-OH, 6-Me, 4-OMe, 4-Me, 4-F

Table 46

Entry	R^1	R^2	Product	Yield (%)
1	H	H	**84a**	95
2	H	6-Me	**84b**	75
3	3-Pyridyl	H	**84c**	85
4	4-Me	H	**84d**	80
5	4-MeO	H	**84e**	80
6	4-F	H	**84f**	80
7	4-Me	6-Me	**84g**	85
8	2-OH	4-Me	**84h**	80
9	4-F	6-Me	**84i**	75

Sanaeishoar *et al*. prepared $LaMnO_3$ perovskit nanoparticles using a sol–gel method. This perovskite-type oxide as a green and reusable catalyst for the synthesis of imidazo[1,2-*a*]pyridines **85a-o** by the reaction between 2-aminopyridine **9**, benzaldehydes **7**, and cyclohexyl isocyanide under solvent-free conditions within 1.5 h at 35 °C (Scheme 57, Table 47). The products **85a-o** were prepared under solvent free conditions without any additives.[97]

Scheme 57



9 **7** **85a-o**

Table 47

Entry	X	R	Product	Yield (%)
1	H	C_6H_5	**85a**	96
2	H	$4\text{-}MeC_6H_4$	**85b**	95
3	H	$4\text{-}ClC_6H_4$	**85c**	99
4	H	$4\text{-}Me_2NC_6H_4$	**85d**	94
5	H	2-Fluorenyl	**85e**	95
6	H	$4\text{-}MeOC_6H_4$	**85f**	91
7	H	$4\text{-}BrC_6H_4$	**85g**	99
8	H	2-Thiophen	**85h**	97
9	Me	C_6H_5	**85i**	95
10	Me	$4\text{-}MeC_6H_4$	**85j**	94
11	Me	$2,4\text{-}Me_2C_6H_3$	**85k**	91
12	Me	$4\text{-}ClC_6H_4$	**85l**	98
13	Me	$4\text{-}Me_2NC_6H_4$	**85m**	94
14	Me	2-Fluorenyl	**85n**	94
15	Me	$4\text{-}BrC_6H_4$	**85o**	99

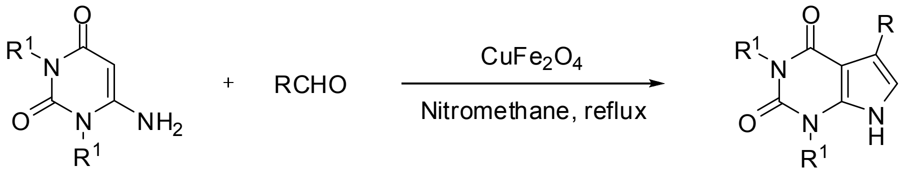
2.3.3.5. Fused [5-6] systems: three heteroatoms [1:2]

2.3.3.5.1. Pyrrolo[2,3-*d*]pyrimidine

Paul *et al*. developed a highly convergent, efficient and practical heteroannulation protocol for the synthesis of a library of uracil fused pyrrole derivatives **87a-i** by reactions involving the $CuFe_2O_4$ nanoparticles catalyzed one-pot three-component domino coupling of 6-aminouracil **86**, aldehydes **7** and nitromethane (Scheme 58, Table 48).[98]

The Fe^{3+} of the magnetic nanoparticles ($CuFe_2O_4$) has shown excellent catalytic activity in promoting the Knoevenagel condensation reaction by enhancing the electrophilicity of the aromatic aldehydes **7**. The Cu^{2+} of $CuFe_2O_4$ catalyzes the subsequent Michael addition reaction of the 6-aminouracil **86** to the α,β-unsaturated nitroalkene.

Scheme 58



86 **7** **87a-i**

Table 48

Entry	R	R^1	Product	Yield %
1	C_6H_5	Me	**87a**	89
2	4-MeOC_6H_4	Me	**87b**	92
3	4-FC_6H_4	Me	**87c**	88
4	4-MeC_6H_4	Me	**87d**	92
5	C_6H_5	H	**87e**	91
6	4-MeOC_6H_4	H	**87f**	91
7	4-FC_6H_4	H	**87g**	86
8	4-MeC_6H_4	H	**87h**	88
9	2-Furyl	H	**87i**	78

2.3.3.6. Fused [5-6] systems: three heteroatoms [2:1]

2.3.3.6.1. Pyrazolo[3,4-*c*]pyridine

MCM-41 (Mobil Composition of Matter No. 41) embedded magnetic nanoparticles which was prepared through the formation of MCM-41 in the presence of Fe_3O_4 nanoparticles has been used as a magnetically recoverable catalyst for the synthesis of new series of pyrazolo[3,4-*c*]pyridine derivatives **89a-p**. The reaction proceeded by the reaction of 3,5-dibenzylidenepiperidin-4-one **88** with methylhydrazine, hydrazine hydrate or hydrazine hydrate and subsequent acylation of the bicyclic compounds with acetic anhydride (Scheme 59, Table 49).[99]

It is worth mentioning that 3,5-dibenzylidenepiperidin-4-one with electron-withdrawing groups on the phenyl rings induce greater electronic positive charge on the corresponding β-atoms and reacted rapidly whereas electron-rich groups on the phenyl rings require longer reaction times.

Scheme 59

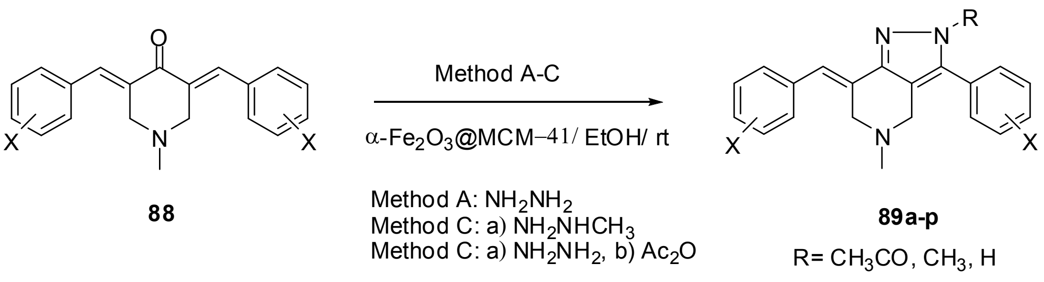
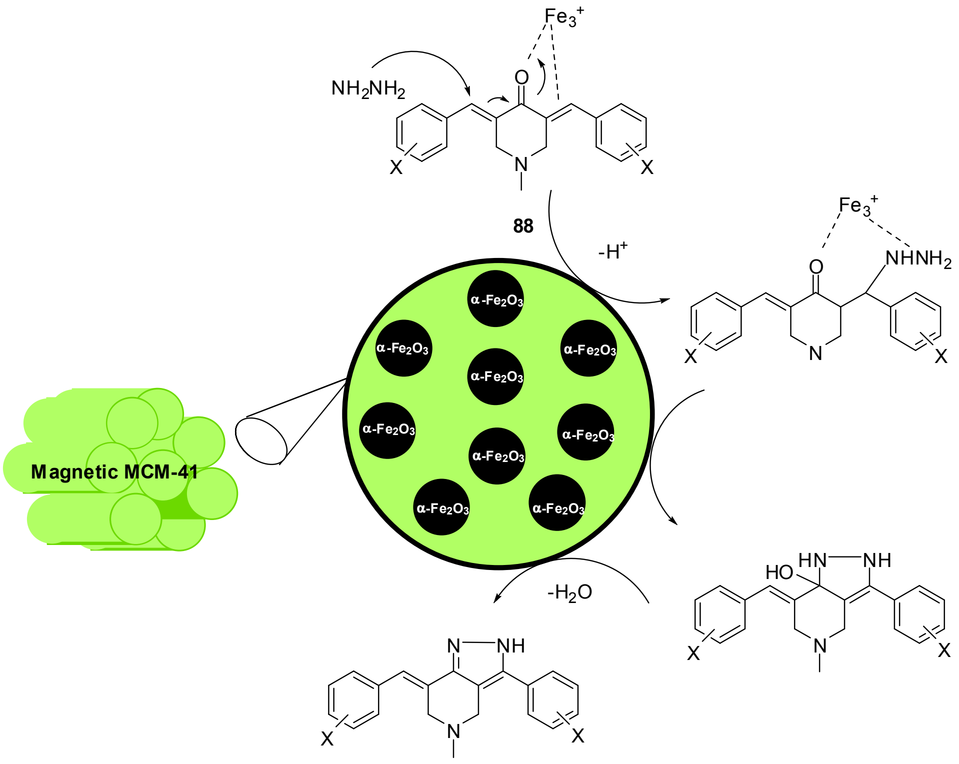


Table 49

Entry	X	R	Product	Yield (%)
1	4-Me	Me	**89a**	97
2	2,4-Cl_2	Me	**89b**	98
3	4-Br	Me	**89c**	90
4	4-$PhCH_2O$	Me	**89d**	95
5	2,3-Cl_2	Me	**89e**	98
6	4-Cl	Me	**89f**	98
7	4-MeO	Me	**89g**	90
8	4-F	Me	**89h**	98
9	4-Me	Me	**89i**	98
10	4-CN	Me	**89j**	96
11	4-Cl	COMe	**89k**	90
12	4-$PhCH_2O$	COMe	**89l**	90
13	4-CN	COMe	**89m**	95
14	2,3-Cl_2	H	**89n**	95
15	3-O_2N	H	**89o**	96
16	2,4-Cl_2	H	**89p**	98

A plausible mechanism for the formation of pyrazolo[4,3-*c*]pyridines **89a-p** is shown in Scheme 60. Because of the Lewis acidity property of the Fe^{3+}, the intermediate 88 can be formed through the reaction of hydrazine hydrate with activated C=C double bond of 3,5-dibenzylidenepiperidin-4-one **88**. Then, the nucleophilic attack of the other NH_2 group on the carbonyl (C=O) moiety gives intermediate (4). Finally, the expected product (5) is afforded by water elimination.

Scheme 60



2.3.3.6.2. Imidazo[4,5-*b*]pyridine

Rai *et al*. reported unprecedented version of the Ugi three-component coupling reaction, in which isocyanides **91** react with unprotected aldoses **90** as biorenewable aldehyde components **7** and acyclic amidines **28** as amine components. The reaction proceeds through [4+1] cycloaddition of a conjugated imine intermediate with the isocyanide **91** followed by dehydrative ring transformation of the resulting 4-amino-5-(polyhydroxyalkyl)imidazole to afford imino sugarannulated imidazoles **92a-f** and **93a-f** in excellent yields (86–95%). The procedure is performed in one pot in the presence of a nanoclay (K-10) catalyst, and can be expeditiously effected under solvent-free microwave-irradiation conditions (Scheme 61, Table 50).[100]

Scheme 61

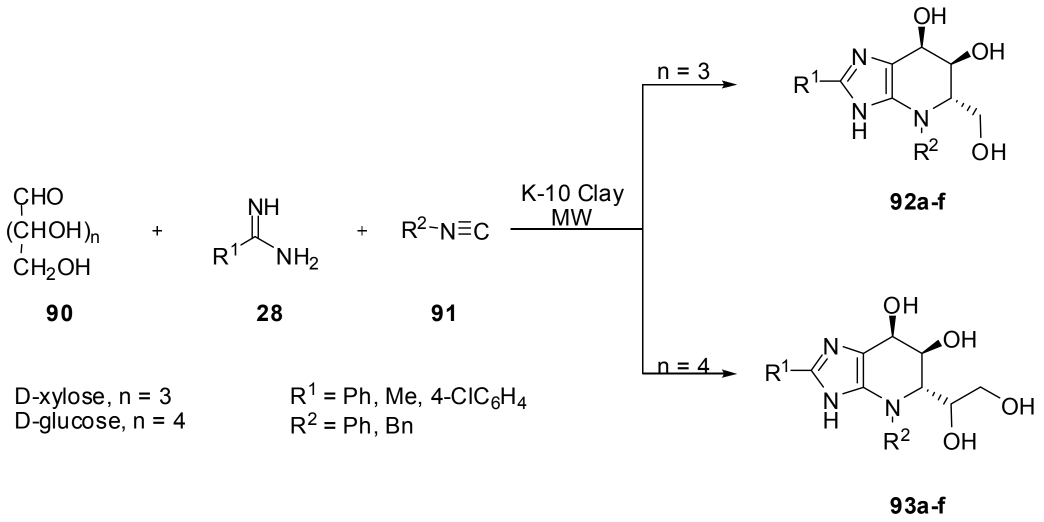


Table 50

Entry	R^1	R^2	Product	Time (min)[a]	Yield (%)[b]
1	Ph	Ph	**92a**	12	91
2	Ph	Bn	**92b**	15	88
3	Me	Ph	**92c**	12	90
4	Me	Bn	**92d**	12	89
5	4-ClC_6H_4	Ph	**92e**	14	94
6	4-ClC_6H_4	Bn	**92f**	12	92
7	Ph	Ph	**93a**	15	91
8	Ph	Bn	**93b**	15	90
9	Me	Ph	**93c**	15	90
10	Me	Bn	**93d**	12	86
11	4-ClC_6H_4	Ph	**93e**	13	92
12	4-ClC_6H_4	Bn	**93f**	12	95

[a] Time required for completion of the reaction as indicated by by TLC.
[b] Yield of isolated and purified products.

2.3.3.7. Fused [6-5] systems: three heteroatoms [1:2]

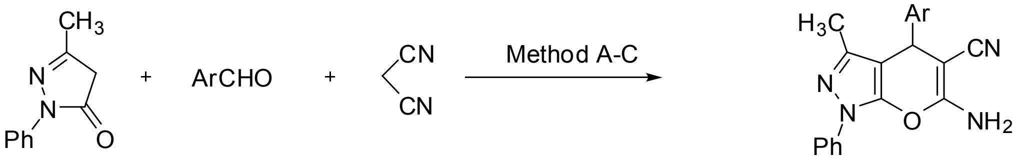
2.3.3.7.1. Dihydropyrano[2,3-*c*]pyrazole

Nano magnetic complex lanthanum strontium magnesium oxide $La_{0.7}Sr_{0.3}MnO_3$ (LSMO) has been explored as an efficient and recyclable catalyst to effect the one-pot three-component synthesis of 1,4-dihydropyrano[2,3-*c*]pyrazol-5-yl cyanide **95** by condensation reactions between aromatic aldehydes **7**, malononitrile **46** and 3-methyl-1-phenyl-2-pyrazolin-5-one **94** in EtOH under ultrasound irradiation conditions (Scheme 62, Table 51, Method A).[68]

Azarifar *et al*. reported also the synthesis of highly functionalized 1,4-dihydropyrano[2,3-*c*]pyrazole derivatives **95** from the ultrasound promoted reactions between **7**, **45** and **94** in the presence of nano-titania-supported Preyssler-type heteropolyacid (*n*-$TiO_2/H_{14}[NaP_5W_{30}O_{110}]$) as an efficient and reusable heterogeneous catalyst. (Scheme 62, Table 51, Method B).[69]

Nano-titania sulfuric acid (15-nm TSA) was also used as an efficient and reusable heterogeneous catalyst to furnish the synthesis of **95** in high to excellent yields by a similar ultrasound promoted reactions (Scheme 62, Table 51, Method C).[70]

Scheme 62



94 **7** **46** **95a-r**

Method A: LSMO-np (20 + 2 nm)/)))) / EtOH / rt
Method B:Nano-$TiO_2/H_{14}[NaP_5W_{30}O_{110}]$/EtOH/)))/ 40 °C
Method C:Nano-TSA/EtOH/)))/ 40 °C

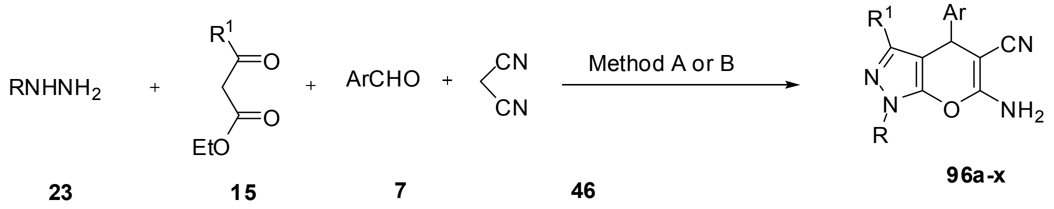
Table 51

Entry	Ar	Product	Method	Time (min)	Yield (%)
1	Ph	**95a**	A	11	89
2	4-FC$_6$H$_4$	**95b**	A	5	95
3	4-ClC$_6$H$_4$	**95c**	A	6	92
4	3-ClC$_6$H$_4$	**95d**	A	8	88
5	4-BrC$_6$H$_4$	**95e**	A	11	87
6	3-O$_2$NC$_6$H$_4$	**95f**	A	5	90
7	4-O$_2$NC$_6$H$_4$	**95g**	A	6	91
8	2,4-Cl$_2$C$_6$H$_3$	**95h**	A	11	88
9	3-EtO-4-HOC$_6$H$_3$	**95i**	A	14	86
10	4-PhC$_6$H$_4$	**95j**	A	9	91
11	2-Naphthyl	**95k**	A	11	90
12	4-HOCC$_6$H$_4$	**95l**	A	10	86
13	PhCH = CH	**95m**	A	80	Trace
14	PhCH$_2$CH$_2$	**95n**	A	80	Trace
15	Ph	**95a**	B	15	97
16	4-MeOC$_6$H$_4$	**95o**	B	30	83
17	4-MeC$_6$H$_4$	**95p**	B	20	93
18	2-ClC$_6$H$_4$	**95q**	B	30	86
19	3-ClC$_6$H$_4$	**95d**	B	15	91
20	4-ClC$_6$H$_4$	**95c**	B	15	95
21	4-BrC$_6$H$_4$	**95e**	B	20	90
22	4-PhC$_6$H$_4$	**95j**	B	15	90
23	4-OHCC$_6$H$_4$	**95l**	B	10	83
24	3-O$_2$NC$_6$H$_4$	**95f**	B	10	98
25	4-O$_2$NC$_6$H$_4$	**95g**	B	10	97
26	2-FC$_6$H$_4$	**95r**	B	10	90
27	2-Naphthyl	**95k**	B	12	92
28	Ph	**95a**	C	15	96
29	4-MeOC$_6$H$_4$	**95o**	C	25	85
30	4-MeC$_6$H$_4$	**95p**	C	15	92
31	2-ClC$_6$H$_4$	**95q**	C	20	88
32	3-ClC$_6$H$_4$	**95d**	C	15	96
33	4-ClC$_6$H$_4$	**95c**	C	10	95
34	4-BrC$_6$H$_4$	**95e**	C	15	92
35	4-PhC$_6$H$_4$	**95j**	C	15	87
36	4-OHCC$_6$H$_4$	**95l**	C	10	87
37	3-O$_2$NC$_6$H$_4$	**95f**	C	10	97
38	4-O$_2$NC$_6$H$_4$	**95g**	C	5	97
39	2-FC$_6$H$_4$	**95r**	C	5	91

A four-component reaction of hydrazine hydrate or phenyl hydrazine **23**, ethyl 3-alkyl-3-oxo propanoate **15**, aldehydes **7** and malononitrile **46** has been performed in the presence of nanosized magnesium oxide as a highly effective heterogeneous base catalyst to produce of 6-amino-3-alkyl-4-aryl-5-cyano-1,4-dihydropyrano[2,3-*c*]pyrazole derivatives **96** in excellent yields and in a short experimental time. This method is simple and rapid for focusing a pyrano ring with a pyrazole ring (Scheme 63, Table 52, Method A).[101]

Shaterian and Azizi *et al*. reported also a convenient and efficient solvent-free procedure for preparation of 6-amino-4-aryl-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitriles **96** by a similar four component reaction in the presence of a catalytic amount of titanium dioxide nano-sized particles (Scheme 63, Table 52, Method B).[102]

Scheme 63



23a: R = H
23b: R = Ph

Method A: MgO(comm or Nano)/ solvent
Method B: TiO_2 NPs

Table 52

Entry	R	R^1	Ar	Product	Method	Yield (%)
1	H	Me	C_6H_5	**96a**	A	97
2	H	Me	$2\text{-}ClC_6H_4$	**96b**	A	93
3	H	Me	$4\text{-}ClC_6H_4$	**96c**	A	97
4	H	Me	$3\text{-}BrC_6H_4$	**96d**	A	90
5	H	Me	$4\text{-}O_2NC_6H_4$	**96e**	A	90
6	H	Me	$4\text{-}MeOC_6H_4$	**96f**	A	89
7	Ph	Me	C_6H_5	**96g**	A	95
8	Ph	Me	$4\text{-}MeC_6H_4$	**96h**	A	93
9	Ph	Me	$4\text{-}MeOC_6H_4$	**96i**	A	90
10	Ph	Me	$4\text{-}ClC_6H_4$	**96j**	A	96
11	Ph	Me	$2,4\text{-}Cl_2C_6H_3$	**96k**	A	92
12	Ph	Me	$4\text{-}BrC_6H_4$	**96l**	A	88
13	Ph	Pr	$4\text{-}ClC_6H_4$	**96m**	A	92
14	Ph	*i*pr	$4\text{-}ClC_6H_4$	**96n**	A	93
15	Ph	*i*pr	$2,4\text{-}Cl_2C_6H_3$	**96o**	A	95
16	H	Me	C_6H_5	**96a**	B	96
17	H	Me	$3\text{-}MeO\text{-}4\text{-}HOC_6H_3$	**96p**	B	81
18	H	Me	$4\text{-}ClC_6H_4$	**96j**	B	93
19	H	Me	$4\text{-}MeOC_6H_4$	**96i**	B	89
20	H	Me	$4\text{-}O_2NC_6H_4$	**96e**	B	87
21	H	Me	$2,4\text{-}Cl_2C_6H_3$	**96k**	B	85
22	H	Me	$4\text{-}BrC_6H_4$	**96l**	B	86
23	H	Me	$3\text{-}BrC_6H_4$	**96d**	B	86
24	H	Me	$2\text{-}ClC_6H_4$	**96b**	B	85
25	H	Me	$2\text{-}O_2NC_6H_4$	**96q**	B	82
26	H	Me	$2,4\text{-}Cl_2C_6H_3$	**96k**	B	87
27	H	Me	$4\text{-}FC_6H_4$	**96r**	B	87
28	H	Me	$4\text{-}MeC_6H_4$	**96h**	B	85
29	H	Me	$2,5\text{-}(MeO)_2C_6H_3$	**96s**	B	85
30	H	Me	$3,4\text{-}(MeO)_2C_6H_3$	**96t**	B	82
31	H	Me	$3,4,5\text{-}(MeO)_3C_6H_2$	**96u**	B	84
32	H	Me	$4\text{-}HOC_6H_4$	**96v**	B	81
33	H	Me	$4\text{-}Me_2NC_6H_4$	**96w**	B	81
34	H	Me	$3\text{-}O_2NC_6H_4$	**96x**	B	92

Pradhan *et al.* synthesized $CuFe_2O_4$ magnetic nanoparticles and reported their use as an efficient catalyst for the one-pot synthesis of dihydropyrano[2,3-*c*]pyrazole derivatives **97a-k** at mild conditions and in excellent yields. The four component reaction (4CRs) of a wide variety of substituted hydrazine derivatives **23**, ethyl acetoacetate **15**, dialkyl acetylenedicarboxylates **8** and alkyl nitrile derivatives **46** (malononitrile and ethyl cyanoacetate) gave the targeted dihydropyrano[2,3-*c*]pyrazoles **97a-k** in good yield (Scheme 64, Table 53).[72]

Scheme 64

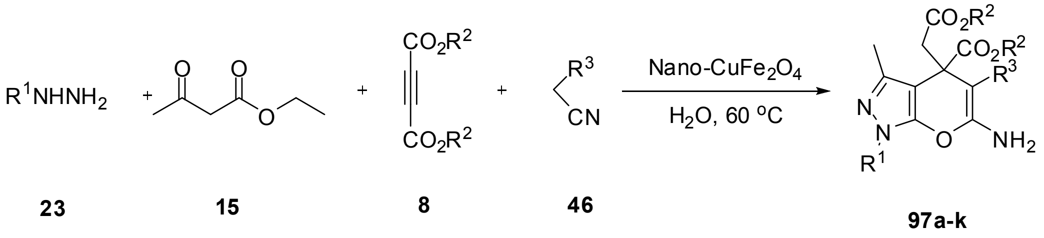


Table 53

Entry	R^1	R^2	R^3	Product	Yield (%)
1	C_6H_5	Et	CN	**97a**	95
2	$4\text{-}O_2NC_6H_4$	Et	CN	**97b**	90
3	$4\text{-}BrC_6H_4$	Et	CN	**97c**	94
4	$4\text{-}NCC_6H_4$	Et	CN	**97d**	94
5	H	Et	CN	**97e**	97
6	C_6H_5	Me	COOEt	**97f**	93
7	$4\text{-}O_2NC_6H_4$	Me	COOEt	**97g**	98
8	$4\text{-}BrC_6H_4$	Me	COOEt	**97h**	92
9	$4\text{-}NCC_6H_4$	Me	COOEt	**97i**	92
10	H	Me	COOEt	**97j**	96
11	H	Et	COOEt	**97k**	85

2.3.3.8. Fused [5-7] systems: four heteroatoms [2:2]

2.3.3.8.1. Pyrazolo[3,4-*e*][1,4]thiazepine

Nano *n*-propylsulfonated γ-Al_2O_3 is easily prepared by the reaction of nano γ-Al_2O_3 with 1,3-propanesultone. This reagent can be used as an efficient catalyst for the synthesis of spiro[indoline-3,4-pyrazolo[3,4-*e*][1,4]thiazepine]diones **100a-p** by a four-component condensation reaction of 3-aminocrotononitrile **98**, phenylhydrazine **23**, isatin **58** and 2-mercaptoacetic acid **99** in aqueous media (Scheme 65, Table 54). This method consistently has the advantages of excellent yields and short reaction times. Further, the catalyst can be reused and recovered several times.[103]

Scheme 65

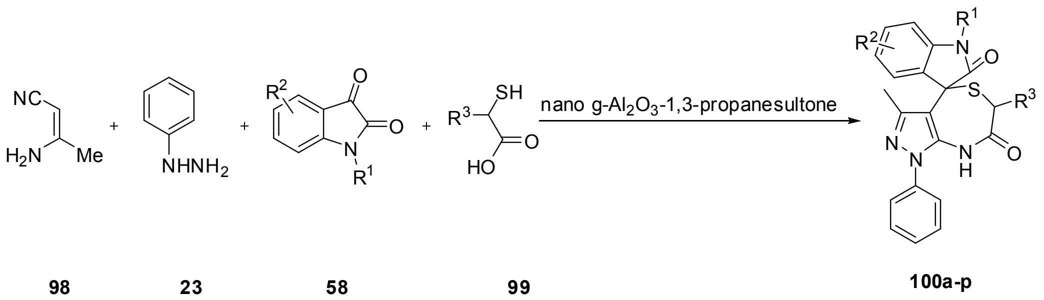


Table 54

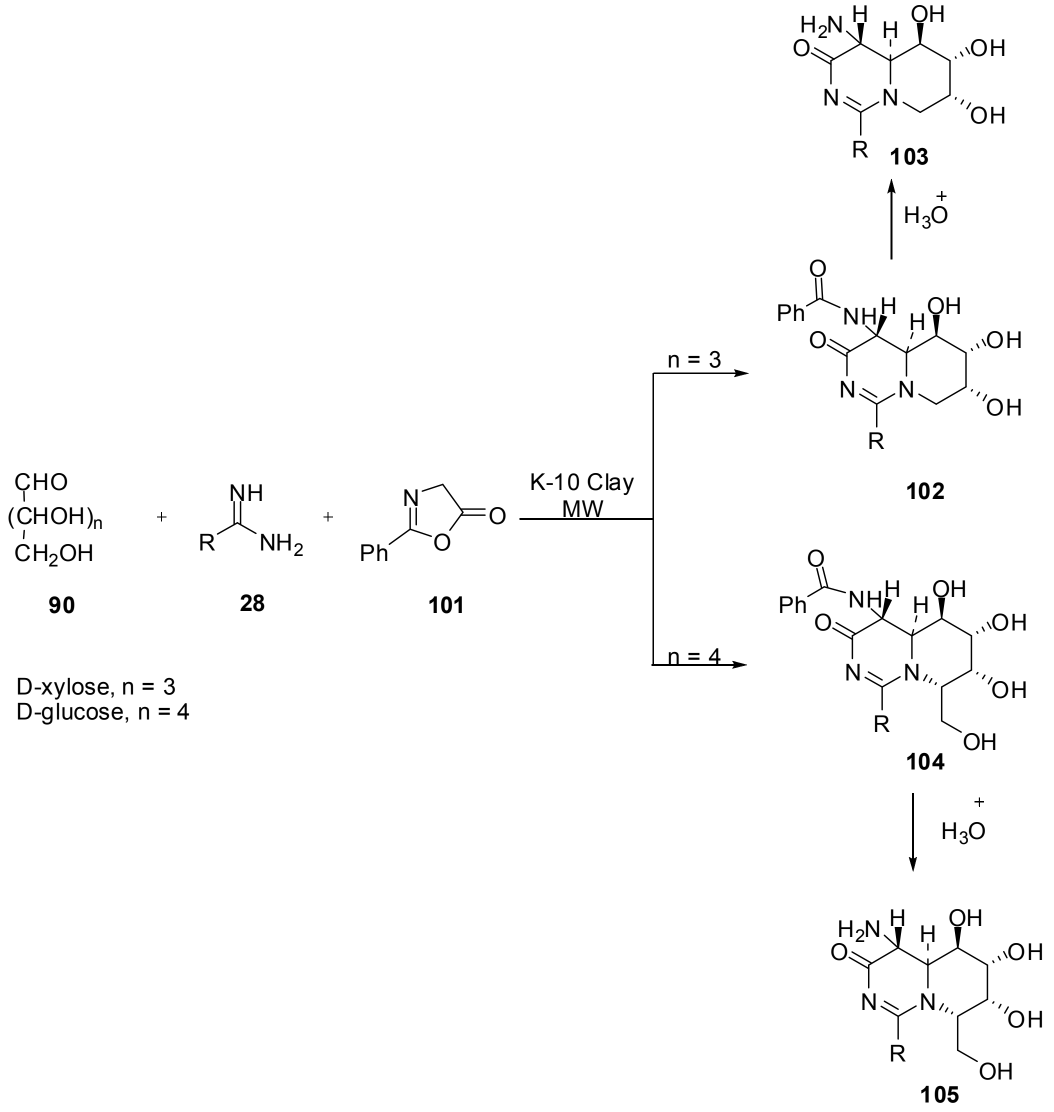
Entry	R^1	R^2	R^3	Product	Time (h)	Yield (%)
1	H	H	H	**100a**	5	91
2	H	H	Me	**100b**	5	92
3	H	5-Cl	Me	**100c**	8	88
4	H	5-Br	H	**100d**	8	87
5	H	5-F	H	**100e**	5	90
6	H	5-F	Me	**100f**	5	93
7	H	5-Me	H	**100g**	7	87
8	H	5-Me	Me	**100h**	7	86
9	Me	H	H	**100i**	6	90
10	Me	H	Me	**100j**	6	92
11	H	5-O_2N	H	**100k**	10	Trace
12	H	5-O_2N	Me	**100l**	10	Trace
13	H	6-Cl	H	**100m**	7	91
14	H	6-Cl	Me	**100n**	8	88
15	H	6-Br	H	**100o**	7	88
16	H	6-Br	Me	**100p**	8	90

2.3.3.9. Fused [6-6] systems: one bridgehead heteroatom and one extra atom

2.3.3.9.1. Pyrido[1,2-*c*]pyrimidine

Yadav and Rai have developed nanoclay-catalyzed unprecedented three component [3+2+1] coupling protocol for an expeditious synthesis of pharmaceutically relevant multifunctionalized fused pyrimidines **103**, **105** in excellent yields (79–92%) with high trans-diastereoselectivity (>94%) using unprotected aldoses as a biorenewable aldehyde component **7**, an active methylene building block 2-phenyl-1,3-oxazol-5-one (**101**), and amidines/guanidine **28** (Scheme 66, Table 55). The reaction proceeds under solvent-free MW irradiation conditions *via* initial formation of the protected benzoylamine derivatives **102** and **104,** respectively, followed by acid hydrolysis.[104]

Scheme 66



D-xylose, n = 3
D-glucose, n = 4

Table 55

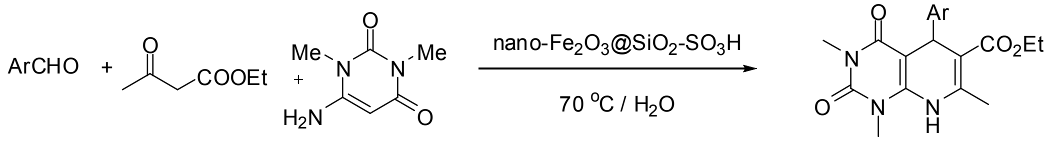
Entry	R	Product	Time (min)	Yield (%)	trans/cis ratio
1	Me	**103a**	10	89	98:2
2	NH_2	**103b**	10	79	95:5
3	H	**103c**	12	88	97:3
4	Ph	**103d**	10	92	96:4
5	4-$O_2NC_6H_4$	**103e**	11	90	96:4
6	4-$H_2NC_6H_4$	**103f**	10	83	98:2
7	Me	**105a**	11	86	96:4
8	NH_2	**105b**	12	89	95:5
9	H	**105c**	10	91	97:3
10	Ph	**105d**	12	89	95:5
11	4-$O_2NC_6H_4$	**105e**	10	82	98:2
12	4-$H_2NC_6H_4$	**105f**	10	90	96:4
13	Me	**103a**	4	45	95:5
14	Me	**105a**	6	52	95:5

2.3.3.10. Fused [6-6] systems: three heteroatoms [1:2]

2.3.3.10.1. Pyrido[2,3-*d*]pyrimidine

The magnetic nanoparticles supported silica sulfuric acid (Fe_3O_4@SiO_2–SO_3H) was used as an efficient catalyst for the synthesis of pyrido[2,3-*d*]pyrimidines **106a,b** by reacting 6-amino-1,3-dimethyl uracil **86** with ethylacetoacetate **15** and various substituent benzaldehydes **7** in water (Scheme 67). The desired products **106a,b** were obtained in excellent yields irrespective of the presence of an electron withdrawing or releasing substituent. The catalyst was readily recovered using an external magnet and could be reused several times without significant loss of reactivity.[105]

Scheme 67



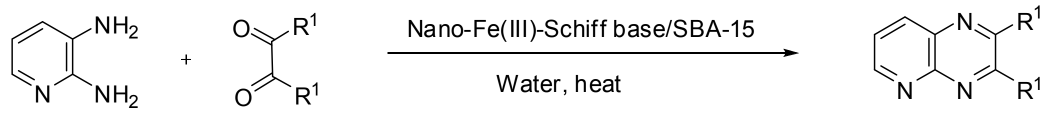
7 **15** **86** **106a,b**

Product	Ar	Yield (%)
106a	Ph	92
106b	4-$MeOC_6H_4$	87

2.3.3.10.2. Pyrido[2,3-*b*]pyrazine

Malakooti reported the synthesis of pyrido[2,3-*b*]pyrazines **108a-c** catalyzed by a heterogeneous nanocatalyst Fe(III)-Schiff base/SBA-15 from the reaction of 2,3-diaminopyridine **107** with the appropriate 1,2-diketone **25** (Scheme 68). These reactions proceeded in water with excellent yields.[66]

Scheme 68



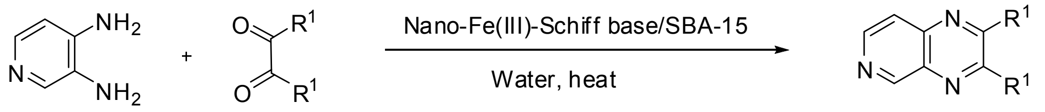
107 **25** **108a-c**

Product	R^1	Yield (%)
108a	C_6H_5	97
108b	4-FC_6H_4	97
108c	4-$MeOC_6H_4$	95

2.3.3.10.3. Pyrido[3,4-*b*]pyrazine

The same authors reported the synthesis of pyrido[3,4-*b*]pyrazines **110a-c** from the reaction of 3,4-diaminopyridine **109** with the appropriate 1,2-diketone **25** under similar reaction conditions and using the same nano-catalyst (Scheme 69).[66]

Scheme 69



109 **25** **110a-c**

Product	R^1	Yield (%)
110a	C_6H_5	96
110b	4-FC_6H_4	95
110c	4-$MeOC_6H_4$	95

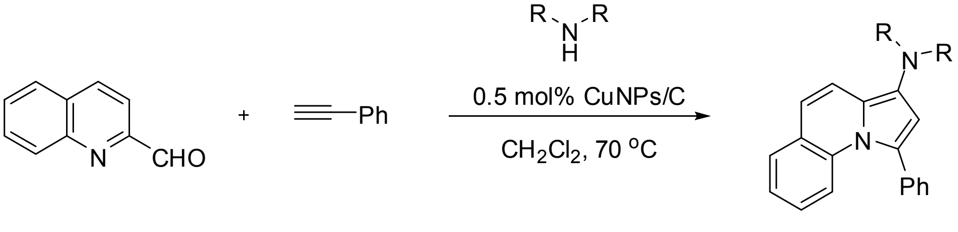
2.4. Synthesis of Fused tricyclic systems

2.4.1. Fused [5-6-6] system: one bridgehead heteroatom

2.4.1.1. Pyrrolo[1,2-*a*]quinoline

Albaladejo *et al*. reported the synthesis of a wide range of pyrrolo[1,2-*a*]quinolines in moderate-to-high yields (59–93 %) by the reaction of quinoline-2-carbaldehyde (**111**) secondary amines and phenylacetylene (**35**) using low catalyst loading (0.5 mol%) of Cu NPs/C (Cu NPs on activated carbon) (Scheme 70, Table 56).[92]

Scheme 70



111 **35** **112a-f**

Table 56

Entry	R	Product	Yield (%)
1	C_6H_5	**112a**	82
2	C_6H_5	**112b**	92
3	4-MeC_6H_4	**112c**	84
4	4-$CF_3C_6H_4$	**112d**	79
5	4-$MeOC_6H_4$	**112e**	84
6	4-BrC_6H_4	**112f**	72

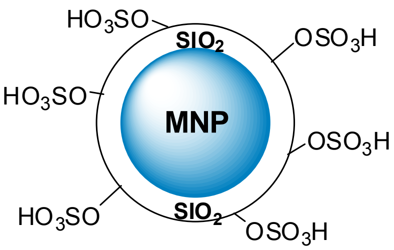
2.4.2. Fused [5-6-6] system: Two bridgehead heteroatoms

2.4.2.1. Pyrazolo[2,1-*b*]phthalazine

Kiasat *et al*. developed an efficient, and high yielding one-pot protocol for the synthesis of 2*H*-pyrazolo[2,1-*b*]phthalazinedione derivatives **115** by three-component coupling of phthalhydrazide **113**, acetylacetone **15** and some aromatic aldehydes **7** in ecofriendly neat conditions promoted by nano-γ-alumina sulforic acid (Scheme 71, Table 57, Method A).[106]

The catalytic activity of nano-structured ZnO has also been explored in the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones **114** *via* a three-component coupling reaction between **113**, **15**, and **7** (Scheme 71, Table 57, Method B).[88] Almost all the reactions proceeded smoothly in relatively short reaction times (8–20 min) to afford the respective 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones **4a–n** in high yields (86–93 %).

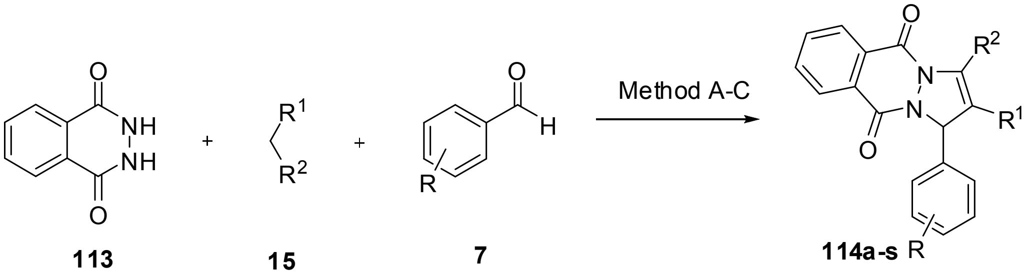
Kiasat and Davarpanah prepared Fe_3O_4@silica sulfuric acid core–shell nanocomposite (Fig. 23) and investigated its catalytic activity in the synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives **114** (Scheme 71, Table 57, Method C). The attractive features of this method are simple procedure, cleaner reaction, use of reusable catalyst, easy workup and performing multicomponent reaction under solvent free conditions.[107]



Fe_3O_4@Silica sulfuric acid

Fig. 23

Scheme 71

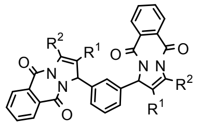


Method A: nano-ASA/neat / 110 °C
Method B: nano-ZnO/ solvent free / 80-100 °C
Method C: nano-Fe_3O_4@SSA

Table 57

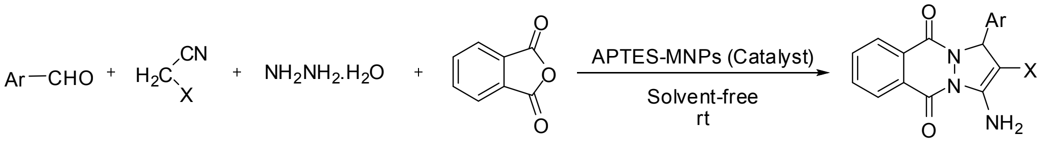
Entry	R	R^1	R^2	Product	Method	Yield (%)
1	C_6H_5	COMe	Me	**114a**	A	88
2	4-ClC_6H_4	COMe	Me	**114b**	A	60
3	4-$MeOC_6H_4$	COMe	Me	**114c**	A	81
4	4-$O_2NC_6H_4$	COMe	Me	**114d**	A	77
5	4-NCC_6H_4	COMe	Me	**114e**	A	70
6	2-ClC_6H_4	COMe	Me	**114f**	A	67
7	C_6H_5	CN	NH_2	**114g**	B	90
8	2-ClC_6H_4	CN	NH_2	**114h**	B	89
9	3-ClC_6H_4	CN	NH_2	**114i**	B	91
10	4-$O_2NC_6H_4$	CN	NH_2	**114j**	B	87
11	4-FC_6H_4	CN	NH_2	**114k**	B	93
12	4-MeC_6H_4	CN	NH_2	**114l**	B	86
13	2-BrC_6H_4	CN	NH_2	**114m**	B	90
14	3-$MeOC_6H_4$	CN	NH_2	**114n**	B	87
15	4-Pyridyl	CN	NH_2	**114o**	B	86
16	3-Pyridyl	CN	NH_2	**114p**	B	90
17	2-Naphthyl	CN	NH_2	**114q**	B	91
18	3-OHC-C_6H_4	CN	NH_2	**114r**	B	88*
19	2,4-$Cl_2C_6H_3$	CN	NH_2	**114s**	B	92
20	2,3-$Cl_2C_6H_3$	CN	NH_2	**114t**	B	91
21	C_6H_5	COMe	Me	**114a**	C	85
22	4-$O_2NC_6H_4$	COMe	Me	**114d**	C	88
23	4-NCC_6H_4	COMe	Me	**114e**	C	87
24	4-ClC_6H_4	COMe	Me	**114f**	C	84

* Product is the bis-derivative:



Shaterian and Mohammadnia reported an efficient, one-pot procedure for preparation of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives **116a-ab** from four-component condensation reaction of hydrazine monohydrate **23**, phthalic anhydride **115**, malononitrile or ethyl cyanoacetate **46** and aromatic aldehydes **7** in the presence of magnetic Fe_3O_4 nanoparticles coated by (3-aminopropyl)-triethoxysilane (Fig. 24) as catalyst under mild, ambient, and solvent-free conditions (Scheme 72, Table 58). The magnetic Fe_3O_4 nanoparticles coated by (3-aminopropyl)-triethoxysilane can be recovered and reused several times without loss of activity.[108]

Scheme 72



7 46 23 115 116a-ab

Table 58

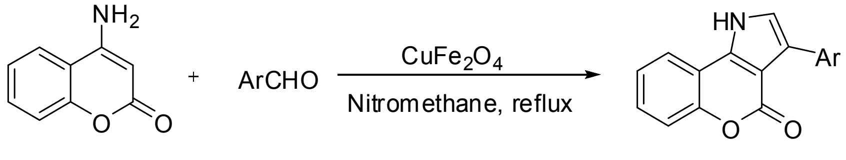
Entry	ArCHO	X	Product	Time (min)	Yield (%)
1	C_6H_5CHO	CN	**116a**	19	92
2	2-ClC_6H_4CHO	CN	**116b**	15	93
3	3-ClC_6H_4CHO	CN	**116c**	16	90
4	4-ClC_6H_4CHO	CN	**116d**	15	93
5	4-FC_6H_4CHO	CN	**116e**	17	89
6	2-$O_2NC_6H_4CHO$	CN	**116f**	14	91
7	4-BrC_6H_4CHO	CN	**116g**	15	92
8	3-BrC_6H_4CHO	CN	**116h**	16	89
9	3-ClC_6H_4CHO	CO_2Et	**116i**	23	88
10	2-$O_2NC_6H_4CHO$	CO_2Et	**116j**	21	89
11	3-$O_2NC_6H_4CHO$	CO_2Et	**116k**	22	91
12	4-$O_2NC_6H_4CHO$	CO_2Et	**116l**	21	89
13	4-BrC_6H_4CHO	CO_2Et	**116m**	22	90
14	2,6-$Cl_2C_6H_3CHO$	CN	**116n**	14	92
15	2,4-$Cl_2C_6H_3CHO$	CN	**116o**	15	91
16	2,3-$Cl_2C_6H_3CHO$	CN	**116p**	16	93
17	2-$MeOC_6H_4CHO$	CN	**116q**	14	90
18	3-$MeOC_6H_4CHO$	CN	**116r**	16	92
19	2,4,6-$(MeO)_3C_6H_2CHO$	CN	**116s**	17	91
20	2,6-$(MeO)_2C_6H_3CHO$	CN	**116t**	16	93
21	5-MeC_6H_4CHO	CN	**116u**	16	92
22	4-$F_3CC_6H_4CHO$	CN	**116v**	16	90
23	2,6-$Cl_2C_6H_3CHO$	CO_2Et	**116w**	22	89
24	2,4-$Cl_2C_6H_3CHO$	CO_2Et	**116x**	21	88
25	2,3-$Cl_2C_6H_3CHO$	CO_2Et	**116y**	23	89
26	2-$MeOC_6H_4CHO$	CO_2Et	**116z**	22	90
27	4-$F_3CC_6H_4CHO$	CO_2Et	**116aa**	22	89
28	*n*-Heptanal	CN	**116ab**	10 h	Trace

2.4.3. Fused [6-6-5] system: two heteroatoms [1:1]

2.4.3.1. Chromeno[4,3-*b*]pyrrole

Paul *et al*. reported a highly convergent, efficient and practical heteroannulation protocol for the synthesis of a library of coumarin fused pyrrole derivatives **118a-k** Thus, one-pot three-component domino coupling of 4-aminocoumarin **117**, aldehydes **7** and nitromethane catalyzed by $CuFe_2O_4$ magnetic nano particles resulted in highly substituted of **118** in good yields (Scheme 73, Table 59).[98]

Scheme 73



117 **7** **118a-k**

Table 59

Entry	R	Product	Yield (%)
1	C_6H_5	**118a**	87
2	4-MeO	**118b**	95
3	4-F	**118c**	85
4	4-Me	**118d**	87
5	3-O_2N	**118e**	80
6	4-Cl	**118f**	85
7	3-HO-4-MeO	**118g**	84
8	4-O_2N	**118h**	85
9	2,4-Cl_2	**118i**	90
10	4-Br	**118j**	87
11	2-Thienyl	**118k**	81

2.4.4. Fused [6-6-6] systems: one heteroatoms

2.4.4.1. Octahydro-1*H*-xanthene

Poly(4-vinylpyridine)-supported nanoparticles of copper(I) iodide(P4VPy–CuI) have been reported as a new, efficient and recyclable catalyst for the synthesis of 1,8-dioxooctahydroxanthenes **119a-t** from the reaction of cyclic 1,3-dicarbonyl compounds **55** (dimedone and 1,3-cyclohexadione) with aldehydes **7** under solvent-free conditions (Scheme 74, Table 60).[109] This catalyst can be recovered by simple filtration and recycled up to 10 consecutive runs without losing of its efficiency.

Scheme 74

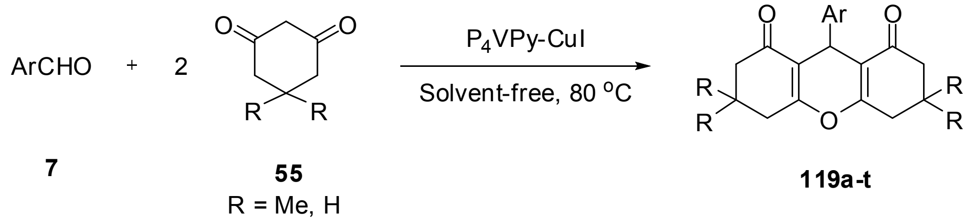


Table 60

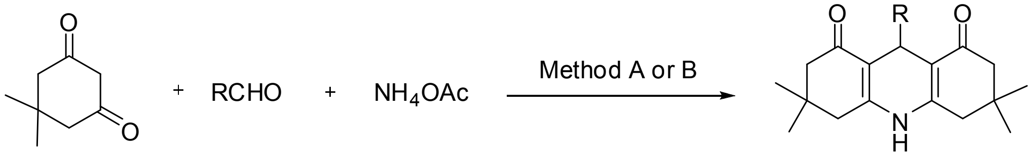
Entry	ArCHO	R	Time (min)	Product	Yield (%)
1	C_6H_5CHO	Me	13	**119a**	88
2	2-$O_2NC_6H_4CHO$	Me	15	**119b**	89
3	3-$O_2NC_6H_4CHO$	Me	10	**119c**	89
4	4-$O_2NC_6H_4CHO$	Me	7	**119d**	90
5	2-ClC_6H_4CHO	Me	10	**119e**	90
6	4-ClC_6H_4CHO	Me	8	**119f**	90
7	4-FC_6H_4CHO	Me	10	**119g**	88
8	4-MeC_6H_4CHO	Me	12	**119h**	87
9	2-$MeOC_6H_4CHO$	Me	25	**119i**	87
10	4-$MeOC_6H_4CHO$	Me	28	**119j**	85
11	3,4-$(MeO)_2C_6H_3CHO$	Me	36	**119k**	86
12	4-NCC_6H_4CHO	Me	14	**119l**	85
13	4-HOC_6H_4CHO	Me	35	**119m**	86
14	C_6H_5CHO	H	12	**119n**	90
15	4-BrC_6H_4CHO	H	9	**119o**	90
16	4-ClC_6H_4CHO	H	8	**119p**	91
17	4-$MeOC_6H_4CHO$	H	30	**119q**	86
18	4-NCC_6H_4CHO	H	12	**119r**	90
19	3-BrC_6H_4CHO	H	8	**119s**	87
20	3-$MeOC_6H_4CHO$	H	30	**119t**	88

2.4.4.2. Decahydroacridine

Dam *et al*. developed an efficient, high yielding, expeditious method for the synthesis of decahydroacridine derivatives **120a-n** *via* an one-pot multi-component condensation of dimedone **55**, aldehydes **7**, and ammonium acetate in water using Fe_3O_4@SiO_2 nanoparticles as a recyclable heterogeneous catalyst. This method takes advantage of the fact that water, a green solvent is used in combination with Fe_3O_4@SiO_2 nanoparticles as catalyst which can be easily recovered magnetically and reused for further runs (Scheme 75, Table 61, Method A).[110] The nature and position of substitution in the aromatic ring did not affect the reactions much. The reaction was tried with aliphatic aldehydes, ketones, and furfuraldehyde but no desired product **120a-n** was formed after 5 h of refluxing.

Fekri *et al*. reported also an efficient, three component synthesis of novel class of decahydroacridine derivatives **120a-n** from reaction between the appropriate aldehydes **7**, dimedone **55** and ammonium acetate in the presence of nano Fe_3O_4 as a recyclable catalyst under ultrasonic irradiation (Scheme 74, Table 61, Method B).[111]

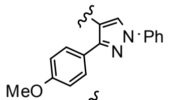
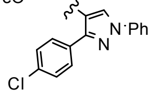
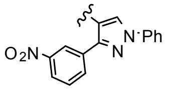
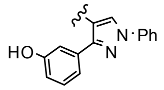
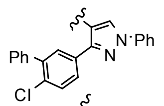
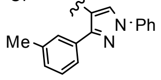
Scheme 75



55 **7** **120a-n**

Method A: $Fe_3O_4@SiO_2$ nanoparticles/ on water, reflux
Method B: Nano-Fe_3O_4/))))

Table 61

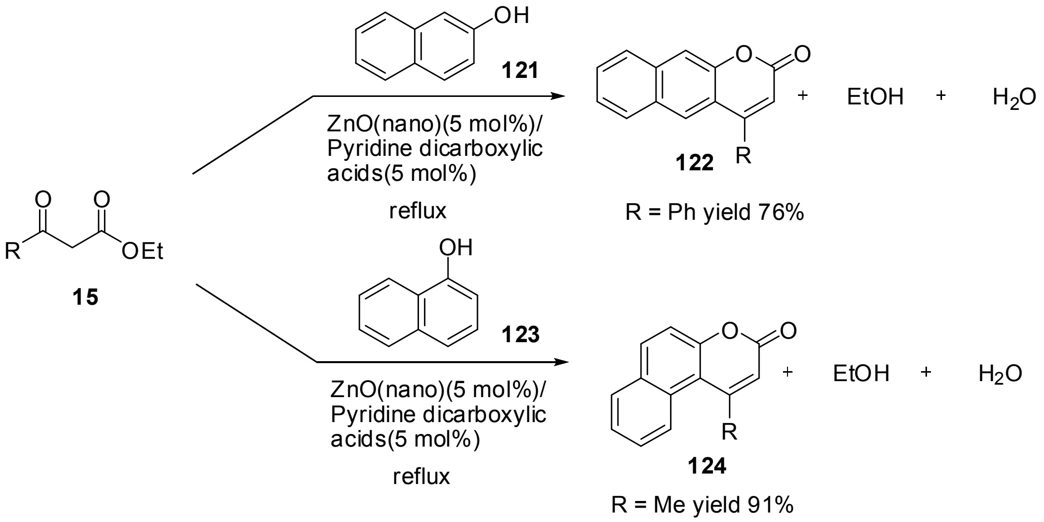
Entry	Ar	Product	Method	Yield (%)
1	4-ClC_6H_4	**120a**	A	92
2	4-BrC_6H_4	**120b**	A	89
3	4-NCC_6H_4	**120c**	A	93
4	4-$O_2NC_6H_4$	**120d**	A	95
5	2-$O_2NC_6H_4$	**120e**	A	94
6	2-ClC_6H_4	**120f**	A	90
7	4-$MeOC_6H_4$	**120g**	A	85
8	4-MeC_6H_4	**120h**	A	82
9		**120i**	B	90
10		**120j**	B	87
11		**120k**	B	81
12		**120l**	B	78
13		**120m**	B	83
14		**120n**	B	86

2.4.4.3. 3*H*-Benzo[*f*]chromene

2.4.4.4. 2*H*-Benzo[*g*]chromene

2*H*-Benzo[*h*]chromen-2-one **122** and 2*H*-benzo[*g*]chromen-2-one derivatives **124** were synthesized by refluxing in acetonitrile of ethyl acetoacetate or ethyl benzoyl acetate **15**, with each of α-naphthol **123** and β-naphthol **121** with a catalytic combination of pyridine dicarboxylic acid as organocatalyst and nanocrystallin ZnO (Scheme 76).[83]

Scheme 76



4*H*-Benzo[*h*]chromene

1*H*-benzo[*f*]chromene

Kumar *et al.* found that nanosized magnesium oxide can easily catalyze three-component condensation reaction of aldehydes **7**, malononitrile **46**, and α-naphthol **123** in water–PEG to afford the corresponding 4*H*-Benzo[*h*]chromenene **125a-f** in high yields at room temperature (Scheme 77, Table 62, Method A). The greener protocol was found to be fairly general and the catalyst was reused in subsequent reactions with consistent activity.[112]

Hosseini-Sarvari *et al.* used nano ZnO as an efficient catalyst for the synthesis of 2-amino-4*H*-chromenes **125a,b,e,f, g-k** from methylenemalononitrile, generated in *situ* from aldehyde **7** and malononitrile **46** and naphthol **123** (Scheme 77, Table 62, Method B).[84]

Scheme 77

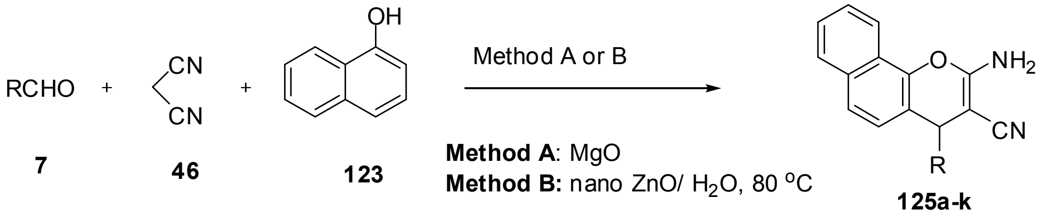


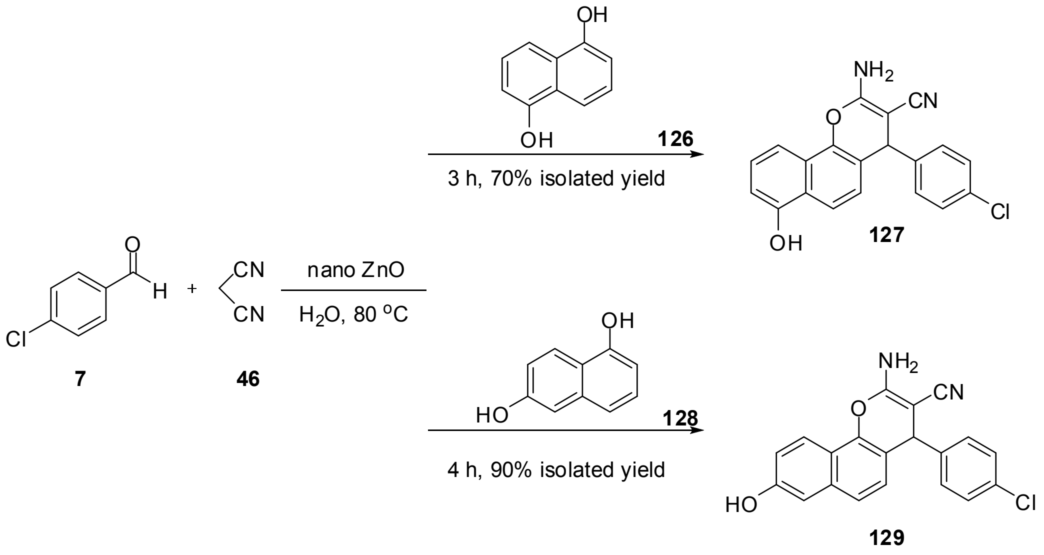
Table 62

Entry	R	Method	Product	Yield %*
1	Ph	A	**125a**	86(96)
2	4-MeOC$_6$H$_4$	A	**125b**	85(95)
3	3-O$_2$NC$_6$H$_4$	A	**125c**	92(96)
4	4-O$_2$NC$_6$H$_4$	A	**125d**	93(97)
5	4-ClC$_6$H$_4$	A	**125e**	86(89)
6	2-Furyl	A	**125f**	84(87)
7	4-O$_2$NC$_6$H$_4$	B	**125g**	98
8	Ph	B	**125a**	85
9	4-HOC$_6$H$_4$	B	**125h**	85
10	4-MeOC$_6$H$_4$	B	**125b**	50
11	4-ClC$_6$H$_4$	B	**125e**	95
12	3-ClC$_6$H$_4$	B	**125i**	75
13	2-ClC$_6$H$_4$	B	**125j**	80
14	2-Thiophenyl	B	**125k**	90
15	2-Furyl	B	**125f**	60

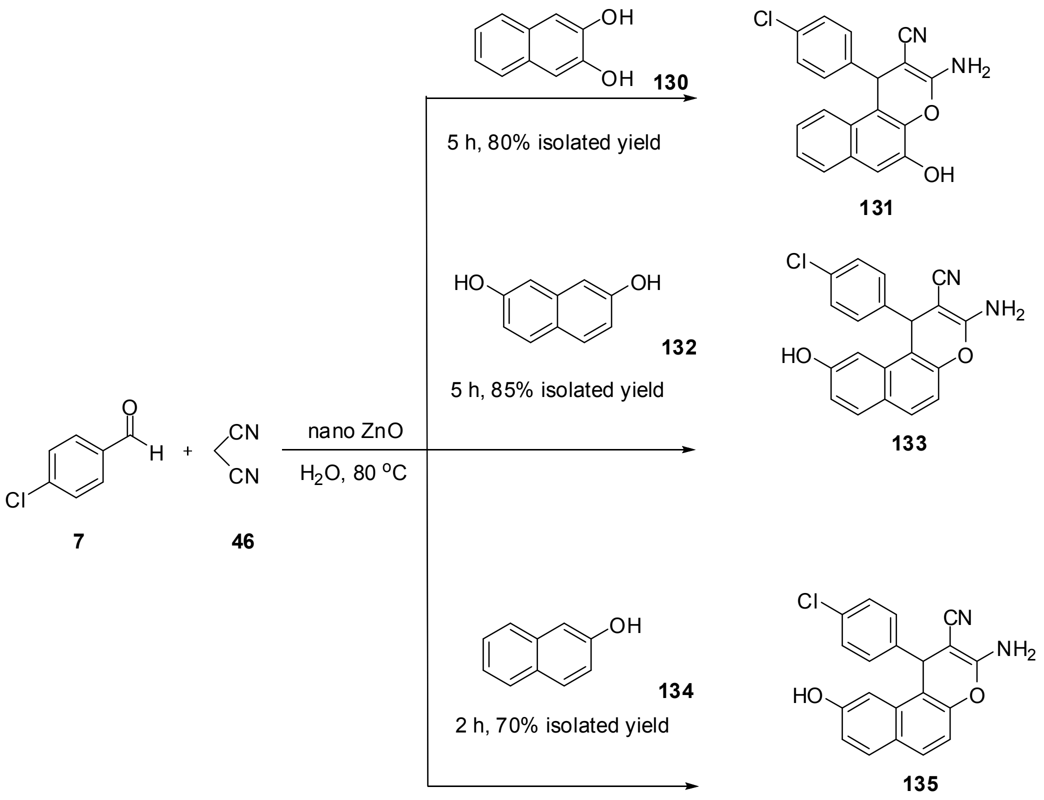
* yield in methanol between paranthes

Hosseini-Sarvari *et al.* also used nano ZnO to catalyze the reaction of various naphthalenediols **126, 128, 130, 132, 134** with aldehydes **7** and malononitrile **46** to produce 4*H*-benzo[*h*]chromene **127** and **129** (Scheme 78) and 1*H*-benzo[*f*]chromene **131**, **133**, and **135** (Scheme 79).[84]

Scheme 78



Scheme 79



2.4.5. Fused [6-6-6] system: Two heteroatoms [1:1]

2.4.5.1. Dihydropyrano[3,2-*c*]chromene

$CuFe_2O_4$ magnetic nanoparticles were synthesized and recognized as an efficient catalyst for the one-pot synthesis of pyrano[3,2-*c*]coumarin derivatives **137a-d** in aqueous medium at mild conditions and in excellent yields. The reaction proceeds *via* MCR's of 4-hydroxycoumarin **136**, dialkyl acetylenedicarboxylates **8** and malononitrile or ethyl cyanoacetate **46** (Scheme 80, Table 63).[72]

Scheme 80

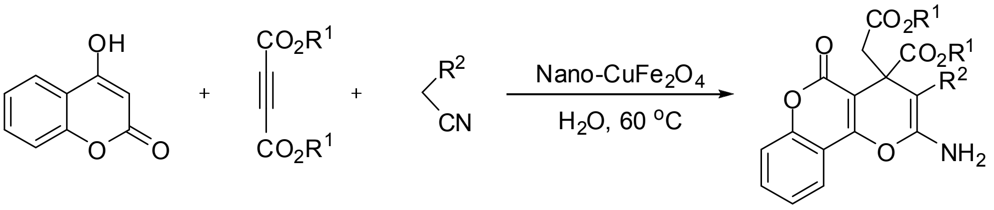
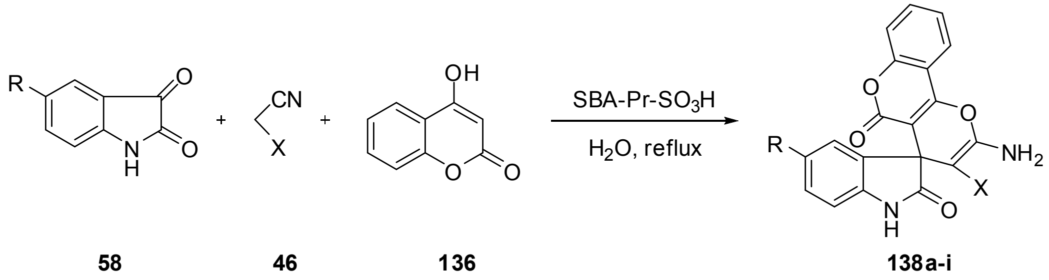


Table 63

Entry	R^1	R^2	Product	Yield (%)
1	Et	CN	**137a**	90
2	Et	CO_2Et	**137b**	87
3	Me	CN	**137c**	88
4	Me	CO_2Et	**137d**	84

Lashgari *et al*. applied sulfonic acid functionalized SBA-15 (SBA-Pr-SO_3H) as a new nanoporous solid acid catalyst in the green one-pot three-component synthesis of spirooxindole-4*H*-pyrans **138a-i** *via* condensation of isatins **58**, malononitrile or methyl cyanoacetate or ethyl cyanoacetate **46**, and 4-hydroxycoumarin **136** in water solvent (Scheme 81, Table 64).[113]

Scheme 81



R = H, Cl, Br

X = CN, CO_2Me, CO_2Et

Table 64

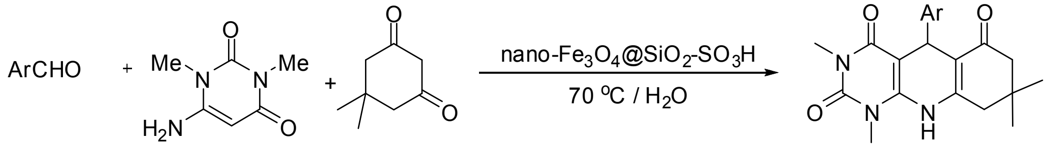
Entry	R	X	Product	Time (min)	Yield (%)
1	H	CN	**138a**	15	90
2	Cl	CN	**138b**	20	85
3	Br	CN	**138c**	20	78
4	H	CO_2Me	**138d**	20	75
5	Cl	CO_2Me	**138e**	20	78
6	Br	CO_2Me	**138f**	35	75
7	H	CO_2Et	**138g**	30	83
8	Cl	CO_2Et	**138h**	30	91
9	Br	CO_2Et	**138i**	35	84

2.4.6. Fused [6-6-6] system: Three heteroatoms [2:1]

2.4.6.1. Tetrahydropyrimido[4,5-*b*]quinoline

Nemati and Saeedirad used magnetic nanoparticles supported silica sulfuric acid (Fe_3O_4@SiO_2–SO_3H) as an efficient catalyst for the synthesis of pyrimido[4,5-*b*]quinolines **139a-i** by reacting 6-amino-1,3-dimethyl uracil **86** with dimedone **55** and various substituent benzaldehydes **7** in water (Scheme 82, Table 65).[105] The desired products were obtained in excellent yields irrespective of the presence of an electron withdrawing or releasing substituent. The catalyst was readily recovered using an external magnet and could be reused several times without significant loss of reactivity.

Scheme 82



7 **86** **55** **139a-i**

Table 65

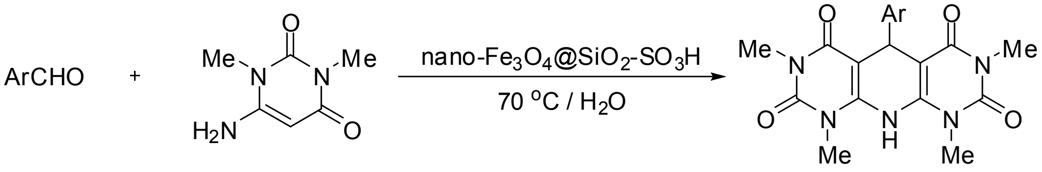
Entry	Ar	Product	Time (min)	Yield (%)
1	Ph	**139a**	30	92
2	4-MeOC$_6$H$_4$	**139b**	40	86
3	3-BrC$_6$H$_4$	**139c**	35	90
4	4-O$_2$NC$_6$H$_4$	**139d**	25	92
5	3-O$_2$NC$_6$H$_4$	**139e**	30	90
6	2-ClC$_6$H$_4$	**139f**	35	81
7	4-ClC$_6$H$_4$	**139g**	25	92
8	4-FC$_6$H$_4$	**139h**	30	89
9	2-Thiophene	**139i**	35	87

2.4.7. Fused [6-6-6] system: Five heteroatoms [2:1:2]

2.4.7.1. Pyrimido[5',4':5,6]pyrido[2,3-*d*]pyrimidine

The magnetic nanoparticles supported silica sulfuric acid ($Fe_3O_4@SiO_2–SO_3H$) was successfully used as an efficient catalyst for the synthesis of pyrimido[5',4':5,6]pyrido[2,3-*d*]pyrimidine **140** by reacting 6-amino-1,3-dimethyl uracil **86** with 6-amino-1,3-dimethylbarbituric acid and various substituent benzaldehydes **7** in water (Scheme 83).[105] The desired products were obtained in excellent yields irrespective of the presence of an electron withdrawing or releasing substituent.

Scheme 83



7 **86** **140**

Ar = 4-MeC$_6$H$_4$, Yield = 95%

2.4.8. Fused [6-6-7] system: Two heteroatoms

2.4.8.1. Tetrahydro-1*H*-dibenzo[*b*,*e*][1,4]diazepine

Maleki and Kamalzare *et al.* developed a new efficient, and green procedure for the synthesis of benzodiazepine derivatives **141a-l** in high yields *via* a one-pot, three-component reaction of *o*-phenylenediamine **9**, dimedone **55**, and different aldehydes **7** at room temperature by using a magnetic recyclable Fe_3O_4@chitosan composite nanocatalyst (Scheme 84, Table 66). [114]

Scheme 84

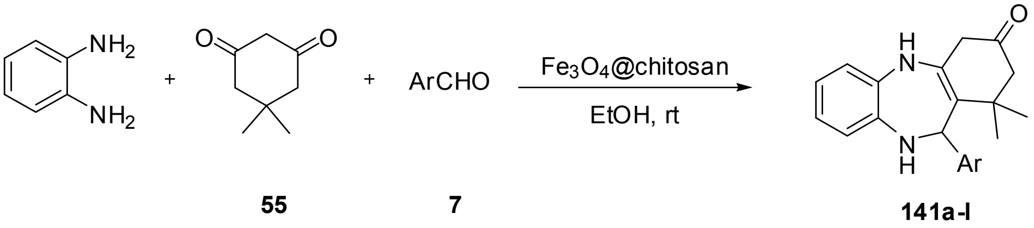


Table 66

Entry	Ar	Product	Yield (%)
1	4-$O_2NC_6H_4$	**141a**	94
2	3-$O_2NC_6H_4$	**141b**	89
3	4-ClC_6H_4	**141c**	91
4	2-ClC_6H_4	**141d**	90
5	2,4-$Cl_2C_6H_3$	**141e**	96
6	4-HOC_6H_4	**141f**	88
7	2-HOC_6H_4	**141g**	85
8	4-MeC_6H_4	**141h**	91
9	4-$Me_2NC_6H_4$	**141i**	94
10	2-Thienyl	**141j**	85
11	2-Furyl	**141k**	87
12	2-Pyridyl	**141l**	84

2.5. Synthesis of fused tetracyclic systems

2.5.1. Fused [6-5-5-6] systems: three heteroatoms [1:2]

2.5.1.1. Tetrahydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine

Mohammad *et al.* reported the synthesis of fused azo-linked pyrazolo[4,3-*e*]pyridines **144a-f**, and **145a-c** from indan-1,3-dione **142** and 3-amino-5-methylpyrazole **143**, using nano-Fe_3O_4 in water as an effective and reusable catalyst (Scheme 85, Table 67).[115] It is important to point out the fact that when 3-amino-5-methylpyrazole (**143**), indan-1,3-dione (**142**) and azo-linked benzaldehyde containing electron releasing substituents **7g-i** were refluxed for required reaction time, the reaction leads to the formation of the aromatized pyrazolopyridine **145g-i**, but in the case of using azo-linked aldehydes containing electron withdrawing substituents **7a-f**, just pyrazolopyridine **144a-f** were observed.

Scheme 85

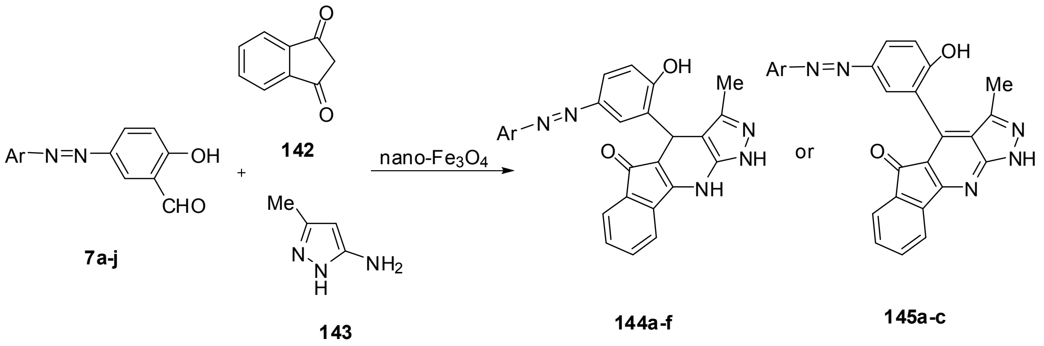


Table 67

Entry	Ar	Product	Time (min)	Yield (%)
1	4-IC_6H_4	**144a**	5	75
2	4-$O_2NC_6H_4$	**144b**	8	83
3	2-Me-4-$O_2NC_6H_4$	**144c**	8	75
4	2-ClC_6H_4	**144d**	5	83
5	3-ClC_6H_4	**144e**	5	95
6	4-ClC_6H_4	**144f**	5	84
7	Ph	**145a**	2	86
8	4-MeC_6H_4	**145b**	1	79
9	4-$MeOC_6H_4$	**145c**	1	87

2.5.2. Fused [6-5-6-6] systems: two bridgehead heteroatoms

2.5.2.1. Dihydro-2*H*-indazolo[2,1-*b*]phthalazine

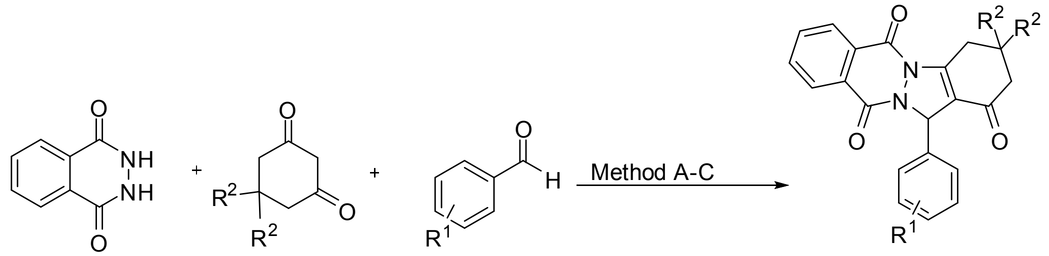
Kiasat *et al*. developed a simple and efficient one-pot protocol for the synthesis of 2*H*-indazolo[2,1-*b*]phthalazinetrione derivatives **146** by three-component coupling of phthalhydrazide **113**, dimedone **55** and some aromatic aldehydes **7** in ecofriendly neat conditions promoted by nano-γ-alumina sulfuric acid (Scheme 86, Table 68, Method A).[106]

Kiasat and Davarpanah prepared Fe_3O_4@silica sulfuric acid core–shell nanocomposite and investigated its catalytic activity also in the synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives **146** by a similar one-pot three component reaction. (Scheme 86, Table 68, Method B).[107]

Rostami *et al*. also applied *N*-propylsulfamic acid supported onto magnetic Fe_3O_4 nanoparticles (MNPs-PSA) as an efficient and magnetically recoverable catalyst for the synthesis of 2*H*-Indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **146** from a similar one-pot three-component reaction (Scheme 86, Table 68, Method C).[116]

The same authors have developed this synthetic method for the preparation of bis-2*H*-indazolo[2,1-*b*]phthalazine-trione **146** derivative in a 2:1.1:2 molar ratio of phthalhydrazide to isophthaladehyde and dimedone (Table 68, entry 32).[116]

Scheme 86



113 **55** **7** **146a-ab**

Method A: nano-Fe_3O_4@SSA/ solvent free
Method B: Fe_3O_4-MNPS-SPA/ solvent free / 100 °C
Method C: nano-ASA/ solvent free / 110 °C

Table 68

Entry	R^1	R^2	Method	Product	Yield (%)
1	C_6H_5	Me	A	**146a**	88
2	4-ClC_6H_4	Me	A	**146b**	90
3	4-$O_2NC_6H_4$	Me	A	**146c**	94
4	4-HOC_6H_4	Me	A	**146d**	85
5	4-NCC_6H_4	Me	A	**146e**	92
6	3-FC_6H_4	Me	A	**146f**	90
7	3-ClC_6H_4	Me	A	**146g**	90
8	3-MeC_6H_4	Me	A	**146h**	88
9	4-MeC_6H_4	Me	A	**146i**	86
10	4-$MeOC_6H_4$	Me	A	**146j**	85
11	2-$O_2NC_6H_4$	Me	A	**146k**	90
12	C_6H_5	Me	B	**146a**	93
13	2-MeC_6H_4	Me	B	**146l**	91
14	4-MeC_6H_4	Me	B	**146i**	90
15	3-$MeOC_6H_4$	Me	B	**146h**	87
16	4-$MeOC_6H_4$	Me	B	**146j**	89
17	3,4-$(MeO)_2C_6H_3$	Me	B	**146m**	88
18	3-BrC_6H_4	Me	B	**146n**	85
19	2-ClC_6H_4	Me	B	**146o**	87
20	4-ClC_6H_4	Me	B	**146b**	93
21	2,4-$(Cl)_2C_6H_3$	Me	B	**146p**	91
22	4-FC_6H_4	Me	B	**146q**	90
23	2-$O_2NC_6H_4$	Me	B	**146k**	82
24	3-$O_2NC_6H_4$	Me	B	**146r**	86
25	4-$O_2NC_6H_4$	Me	B	**146c**	83
26	2-Naphthyl	Me	B	**146s**	84
27	C_6H_5	H	B	**146t**	86
28	4-Me	H	B	**146u**	88
29	4-$MeOC_6H_4$	H	B	**146v**	90
30	4-$O_2NC_6H_4$	H	B	**146w**	83
31	4-FC_6H_4	H	B	**146x**	89
32	3-$HOCC_6H_4$	Me	B	**146y**	80*
33	C_6H_5	Me	C	**146a**	85
34	4-ClC_6H_4	Me	C	**146b**	98
35	4-$MeOC_6H_4$	Me	C	**146j**	94
36	4-$O_2NC_6H_4$	Me	C	**146c**	72
37	4-MeC_6H_4	Me	C	**146i**	70
38	4-CC_6H_4	Me	C	**146e**	89
39	4-$F_3CC_6H_4$	Me	C	**146z**	78
40	4-$NO_2NC_6H_4$	Me	C	**146c**	87
41	4-ClC_6H_4	Me	C	**146b**	70
42	3-$O_2NC_6H_4$	Me	C	**146r**	83
43	4-BrC_6H_4	Me	C	**146aa**	80
44	4-$EtOC_6H_4$	Me	C	**146ab**	70

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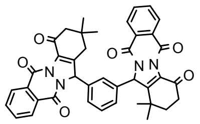
* the product was:

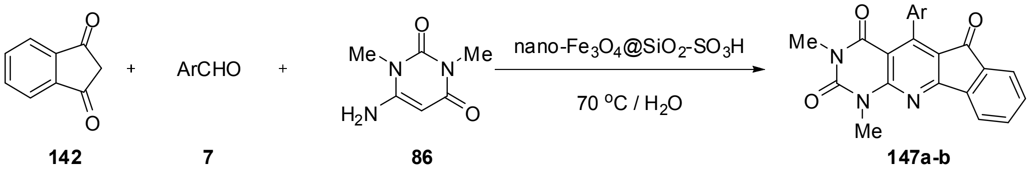


2.5.3. Fused [6-5-6-6] systems: three heteroatoms [1:2]

2.5.3.1. Indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine

Nemati and Saeedirad used magnetic nanoparticles supported silica sulfuric acid ($Fe_3O_4@SiO_2–SO_3H$) as an efficient catalyst for the synthesis of indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine **147a,b** by reacting 6-amino-1,3-dimethyl uracil **86** with 1,3-indanedione **142** and various substituent benzaldehydes **7** in water (Scheme 87).[105]

Scheme 87



Ar = C_6H_5, yield = 90%

Ar = 4-$O_2NC_6H_4$, yield = 94%

2.6. Synthesis of fused pentaacyclic systems

2.6.1. Fused [6-6-6-6-6] systems: one heteroatom

2.6.1.1. 14*H*-Dibenzo[*a,j*]xanthene

Novel magnetite–sulfuric acid ($Fe_3O_4·SO_3H$) magnetic nanoparticles MSA-MNP 1 and MSA-MNP 2 catalysts (Fig. 24) were prepared by the direct reaction of chlorosulfonic acid with magnetite nanoparticles and were shown to exhibit remarkable catalytic performance in the solvent-free synthesis of mono-, bis-, and tris-14*H*-dibenzo[*a,j*]xanthen-14-ylarenes **148a-g, 149, 150**, and **152a,b**. The reactions were performed by the reaction of 2-naphthol with benzaldehyde derivatives (Scheme 88), terephthalaldehyde, isophthalaldehyde (Scheme 89) or trialdehydes **151a** and **151b** (Scheme 90), respectively, in the presence of 0.1 g MSA-MNP 2 under solvent-free conditions.[117]

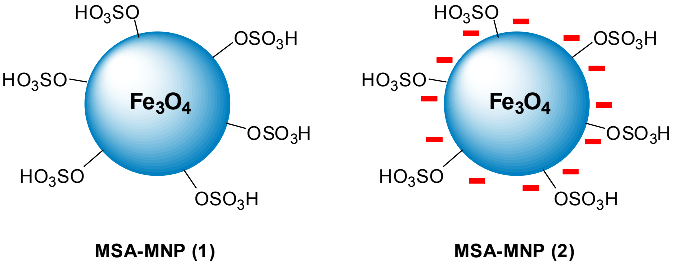
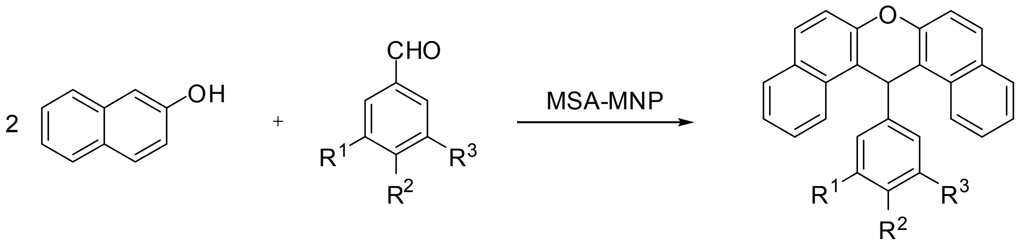


Fig. 24

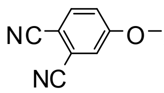
Scheme 88



121 **7a-g** **148a-g**

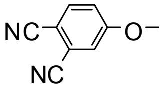
7a: R^1 = H, R^2 = H, R^3 = H
7b: R^1 = H, R^2 = 4-Me, R^3 = H
7c: R^1 = H, R^2 = 4-Cl, R^3 = H
7d: R^1 = H, R^2 = 4-NO_2, R^3 = H
7e: R^1 = MeO, R^2 = MeO, R^3 = MeO

7f: R^1 = H, R^2 =



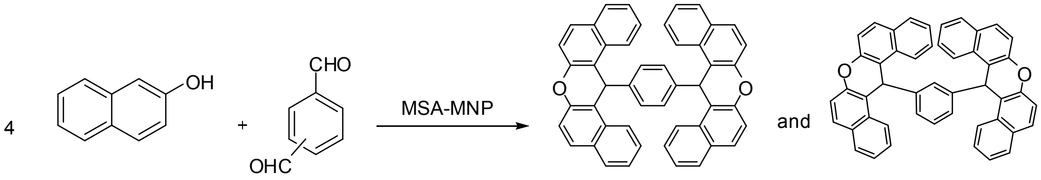
, R^3 = H

7g: R^1 = H, R^2 =

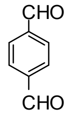


, R^3 = MeO

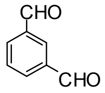
Scheme 89



121 **7a,b** **149a** **150b**

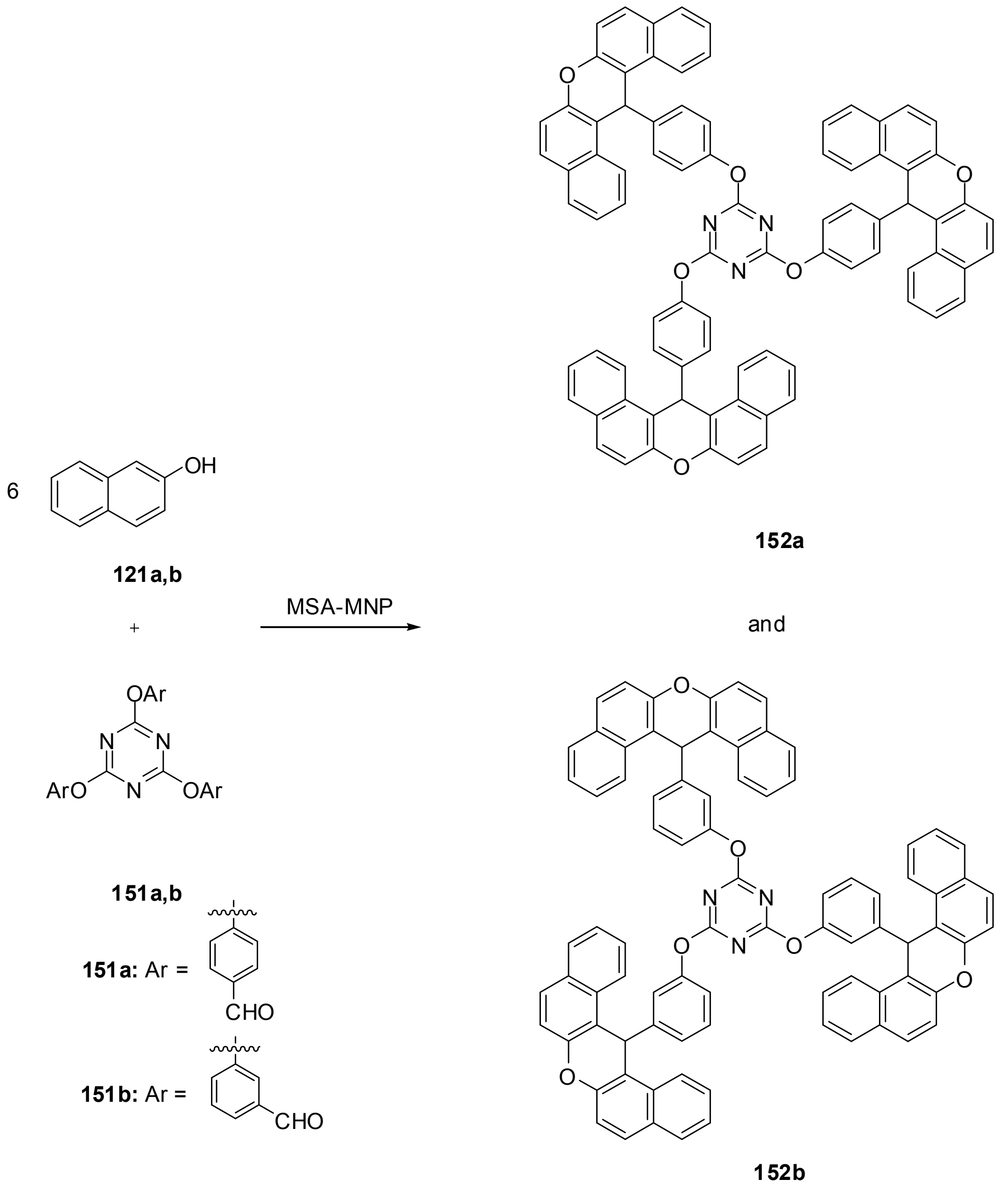


7a



7b

Scheme 90

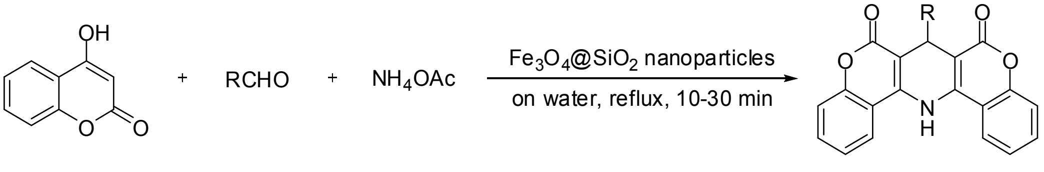


2.6.2. Fused [6-6-6-6-6] systems: Three heteroatoms [1:1:1]

2.6.2.1. Dichromeno[4,3-*b*:3',4'-*e*]pyridine

Dam *et al*. reported an efficient, high yielding method for the synthesis of dichromeno[4,3-*b*:3',4'-*e*]pyridine derivatives **153a-g** *via* an one-pot multi-component condensation of 4-hydroxycoumarine **136**, aldehydes **7**, and ammonium acetate in water using $Fe_3O_4@SiO_2$ nanoparticles as a recyclable heterogeneous catalyst (Scheme 91, Table 69).[110] The nature and position of substitution in the aromatic ring did not affect the reactions much.

Scheme 91



136 **7** **153a-g**

Table 69

Entry	Ar	Product	Yield (%)
1	4-ClC_6H_4	**153a**	88
2	4-BrC_6H_4	**153b**	86
3	4-NCC_6H_4	**153c**	90
4	4-FC_6H_4	**153d**	87
5	2-ClC_6H_4	**153e**	88
6	2-BrC_6H_4	**153f**	88
7	4-MeC_6H_4	**153g**	82

2.7. Synthesis of miscellaneous fused systems

2.7.1. 8,9-Dihydroacenaphtho[1,2-*b*]pyrazine

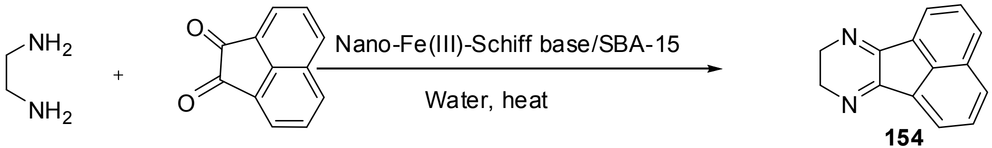
2.7.2. Acenaphtho[1,2-*e*]pyrido[3,4-*b*]pyrazine

2.7.3. Acenaphtho[1,2-*e*]pyrido[2,3-*b*]pyrazine

2.7.4. Dibenzo[*f*,*h*]pyrido[3,4-*b*]quinoxaline

Malakooti *et al*. reported the synthesis of fused pyrazines and fused pyrido[2,3-*b*]pyrazines **154-157** from the reaction of the diaminopyridines with the appropriate 1,2-diketone **25** in the presence of an iron Schiff base complex encapsulated in SBA-15 mesoporous silica [Fe(III)-Schiff base/SBA-15] as heterogeneous nanocatalyst (Scheme 92-95). These reactions proceeded in water with excellent yields.[66]

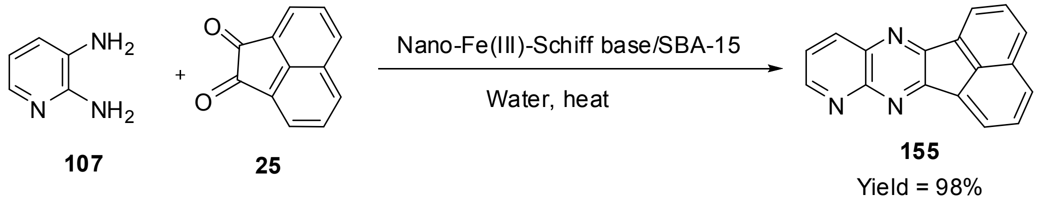
Scheme 92



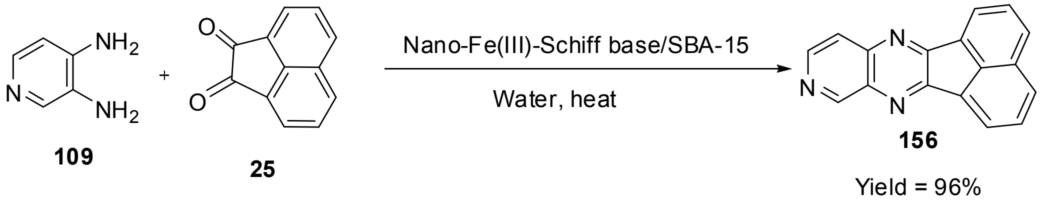
53 **25** **154**

Yield = 97%

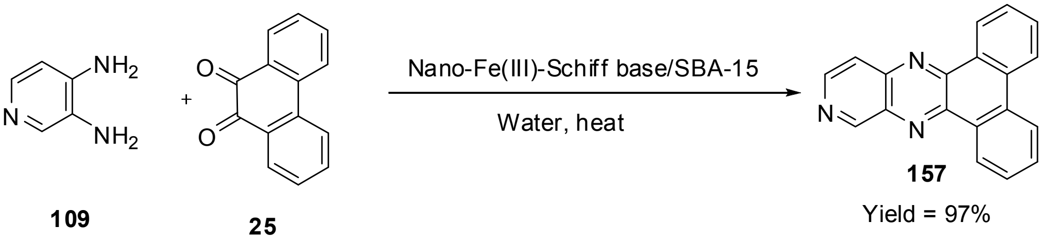
Scheme 93



Scheme 94



Scheme 95



3. Conclusions

Heterocycles are found in many natural products, pharmaceuticals, organic materials, and in numerous functional molecules. They are especially important in chemical and pharmaceutical industries. Therefore, the ongoing interest for developing new versatile and efficient syntheses of heterocyclic systems has always been a challenge in the synthetic community. They can be synthesized by a variety of synthetic approaches.

This review compiles the literatures on the application of nanomaterials in heterocyclic synthesis. The fused heterocycles mentioned in this review are arranged in an organized manner with respect to the type of heterocyclic systems.

In most of the reactions the spent catalyst can be easily separated from the reaction mixture. It can also be reused without noticeable change in its catalytic activity. Magnetic nanomaterials can be easily recovered by simple magnet, therefore it makes the catalyst more efficient.

We hope that this review will be useful not only for organic synthetic and organometallic chemists, but also for heterocyclic and natural product synthetic chemists.

Acknowledgements

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