CHAPTER I

Ni Nanoparticles: Mild and efficient catalyst for the chemoselective synthesis of 2-arylbenzimidazoles, 2-arylbenzothiazoles and Schiff’s bases

Metal nanoparticles have witnessed a burst in research activities owing to their ease of preparation and remarkable applications in organic synthesis. Though metal nanoparticles of a variety of transition metals like Ni, Pd, Pt, Au, Ag and Cu have been prepared, nanoparticles of Ni and Pd have drawn special interest in organic synthesis. 2-arylbenzimidazoles, 2-arylbenzothiazoles and azomethines have found applications as antiulcers, antihypertensives, antivirals, antifungals, anticancers and antihistamines.

A new and efficient method has been developed for the synthesis of 2-arylbenzimidazoles, 2-arylbenzothiazoles and azomethines using recyclable and inexpensive polyvinyl pyrrolidone (PVP)–stabilized Ni nanoparticles in ethylene glycol at room temperature. The Ni nanoparticles were prepared from nickel chloride and sodium borohydride using PVP as the stabilizing agent and were characterized by different techniques. The dispersion was used as such for the reactions.

Reactions of 1,2-phenylenediamine with electron deficient aldehydes with substitution at para-position resulted in the formation of benzimidazoles whereas unsubstituted, electron-rich and heterocyclic aldehydes as well as electron deficient aldehydes with substitution at ortho- and meta- positions gave corresponding schiff’s bases (eq. 1).

\[
\text{ArCHO} + \text{PVP-Ni nps} \rightarrow \text{PVP-Ni nps} \rightarrow \text{ArNH}_2 \text{N} \equiv \text{Ar} \quad \text{...(1)}
\]

Reactions of 2-aminothiophenol with arylaldehydes yielded the corresponding benzothiazoles irrespective of the nature of substitution in aromatic aldehydes (eq. 2).
whereas reaction of 2-aminophenol with arylaldehydes gave the corresponding Schiff’s bases only and attempts to cyclize these subsequently have been unsuccessful (eq. 3). All the reactions were complete in 3-12 min. The reactions were carried out at in ethylene glycol using 2.0 mL of the dispersion per 0.1g of the aldehyde. The nickel nanoparticles could be recycled without significant loss in the yields of products for up to five cycles. The involvement of Ni nanoparticles has been confirmed by independent experiments.

\[
\text{R-CHO} + \begin{array}{c} \text{PVP-Ni nps} \\
\text{EG, r.t.} \end{array} \rightarrow \begin{array}{c} \text{OH} \\
\text{N} \end{array} \begin{array}{c} \text{R} \\
\text{..(2)} \end{array}
\]

\[
\text{R-CHO} + \begin{array}{c} \text{OH} \\
\text{N} \end{array} \begin{array}{c} \text{R} \\
\text{..(3)} \end{array}
\]

CHAPTER II

PEG-stabilized Ni nanoparticles: A proficient catalyst for synthesis of biologically important spiropyrans

Spiro compounds represent an important class of naturally occurring substances known for their biological properties. Among them, spiropyrans have attracted strong interest owing to their potential activity as hypertensive/analgesic agents and applications to industrial fields.

In this chapter, we have successfully synthesized spiropyrans via a one pot three component condensation of malononitrile, 1,3-dicarbonyl compounds and ninhydrin or acenaphthequinone or isatin catalyzed by highly dispersed and recyclable Ni nanoparticles stabilized by PEG in ethylene glycol (2.0 mL/0.1g of substrate) at room temperature in high yields. The condensations of ninhydrin (1 equiv.) and malononitrile (1 equiv.) with a variety of 1,3-dicarbolins (1 equiv.) like 5,5-dimethylcyclohexane-1,3-dione, 5-methylcyclohexane-1,3-dione, 4-hydroxy coumarin, 4-hydroxy-6-methyl pyran-2-one, 1,3-dimethyl barbituric acid, 1,3-diethyl-2-thiobarbituric acid, cyclopentane-1,
3-dione, indane-1,3-dione, 3-methyl-1\textit{H}-pyrazol-5(4\textit{H})-one, cyclohexane-1,3-dione, barbituric acid and ethyl acetoacetate could be achieved in 10-15 min in quantitative yields (Scheme I). Replacement of ninhydrin by acenaphthquinone also led to the successful condensations under otherwise similar conditions to give corresponding spiroacenaphthylenes in high yields (Scheme I). Similarly, reactions of isatin with malononitrile and 1,3-dicarbonyls yielded corresponding spirooxindoles in 8-12 min (Scheme I). The role of nickel nanoparticles in catalyzing the condensation was confirmed by blank reactions in the absence of Ni nanoparticles.

\textbf{Scheme I}

Ni nanoparticles could be recycled and reused for up to four cycles without any significant loss of yield, after which a drop in yield was observed.
CHAPTER III

Chemoselective $N$-benzylation of 2-thiohydantoins and 2-thiobarbituric acids catalyzed by PEG-stabilized Ni nanoparticles and their anti-microbial activities

Thiohydantoins and their derivatives represent an important class of biologically active molecules having broad medicinal applications viz. anticancer, anticonvulsant, antidiabetic, antimicrobial, antiarrhythmic, hypolipidemic and hypotensive; and agrochemical (herbicidal and fungicidal) applications. 2-Thiobarbituric acid derivatives also possess a variety of biological activities.

In this chapter, we report the synthesis of new $N$-benzylated arylidene thiohydantoins viz. 3-benzyl-5-arylidene-2-thioxoimidazolidin-4-ones and $N,N$-dibenzylated arylidene thiobarbituates viz. 1,3-dibenzyl-5-arylidene-2-thioxodihydropyrimidine-4,6(1$H$,5$H$)-diones in presence of 2 mL of PEG-Ni nanoparticles dispersion in ethylene glycol (0.0235 wt% Ni/ 0.1 g of aldehyde) at 70°C. A variety of $N$-3 benzylated arylidene thiohydantoins were synthesized by carrying out reactions of aromatic aldehydes (n equiv.), 2-thiohydantoin (n equiv.) and benzyl bromide (n equiv.) in presence of Ni nps at 70°C (eq. 4). All our attempts to prepare dibenzylated product were unsuccessful.

\[
\text{ArCHO} + \text{HNHSO} + \text{Br} \overset{\text{Ni nps, EG} \ 70\degree C}{\longrightarrow} \text{HNAr} \quad \text{..(4)}
\]

Reactions of 2-thiobarbituric acid with benzyl bromide and a variety of aromatic aldehydes yielded the dibenzylated product 1,3-dibenzyl-5-(4-nitrobenzylidene)-2-thioxodihydropyrimidine-4,6(1$H$,5$H$)-dione in quantitative yields under otherwise similar conditions (eq. 5).

\[
\text{ArCHO} + \text{HNHSO} + \text{Br} \overset{\text{Ni nps, EG} \ 70\degree C}{\longrightarrow} \text{HNAr} \quad \text{..(5)}
\]
The role of Ni nanoparticles has been confirmed by control experiments. The \( N \)-benzylation could not be achieved with 2-thiohydantoin or 2-thiobarbituric acid and benzyl bromide in the absence of aldehydes. The synthesized compounds have been tested for their anti-microbial (anti-bacterial and anti-fungal) activities.

CHAPTER IV

*Cinnamomum tamala* leaf extract mediated green synthesis of Ag nanoparticles and its application in the synthesis of pyranopyrazoles

Ag nps have been known to have strong anti-bacterial and anti-inflammatory properties. Ag nps have been used as catalysts for oxidations and reductions, A\(^3\) coupling reactions, synthesis of \( \beta \)-enaminones, Diels-Alder cycloadditions and hydrogenation of chloronitrobenzenes.

In this chapter, we have reported a green approach for the synthesis of Ag nps by reduction of AgNO\(_3\) using *Cinnamomum tamala* aqueous leaf extract, commonly known as Tejpat in India, as reducing and stabilizing agent to synthesize silver nanoparticles and their application as a catalyst for the synthesis of pyranopyrazoles. The Ag nps so prepared have been characterized by UV-Vis spectrum, HRTEM, EDAX and XRD analysis and were found to be in the range of 7-10 nm which is smaller or comparable to other biochemical reported methods.

The application of Ag nps was investigated for the synthesis of pyranopyrazoles by carrying out the reactions of aromatic aldehydes (n equiv.), malononitrile (n equiv.), ethyl acetoacetate (n equiv.) and hydrazine hydrate (n equiv.) in water in the presence of Ag nps (0.5 wt% of Ag / 0.1 g of aldehyde) at room temperature. All the aldehydes gave quantitative yields of corresponding dihydropyran[2,3-c]pyrazoles in short reaction time (eq. 6). Similarly, reactions of aldehydes, ethyl acetoacetate and malononitrile with phenyl hydrazine, in place of hydrazine hydrate, yielded the corresponding pyranopyrazoles in presence of Ag nps in water at 60°C (eq. 7).
Chapter VI

$$\text{ArCHO} + \text{CN} + \text{N}_2\text{H}_4\text{H}_2\text{O} \quad \text{Ag nps, H}_2\text{O} \quad \text{r.t.} \quad \text{Ar-CN}$$

$$\text{ArCHO} + \text{PhNH-NH}_2 + \text{CN} \quad \text{Ag nps, H}_2\text{O} \quad 60^\circ\text{C}$$

The Ag nps could be recycled up to four cycles. A probable pathway has been reported.

CHAPTER V


Ionic liquids offer several advantages such as extremely low vapor pressure, excellent thermal stability, reusability, ability to dissolve many organic and inorganic substrates. There is growing interest in using ionic liquids as green media in organic synthesis. Xanthenes and benzoxanthenes are important components of biologically active heterocycles and display activities such as antibacterial, anti-inflammatory and antiviral, etc.

In this chapter, we report the synthesis of novel 2-hydroxy-12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones by cyclocondensation of aldehydes, 2,7-dihydroxynaphthalene and dimedone or cyclohexane-1,3-dione in [bmim]BF$_4$ in presence of pTSA. Synthesis of 3-hydroxy-12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones and 5,13-diaryl-2,2,10,10-tetramethyl-2,3,9,10,11,13-hexahydroxantheno[2,1-a]xanthene-4,12(1H,5H)-diones has been achieved by cyclocondensation of aldehydes, 2,6-dihydroxynaphthalene and dimedone in [bmim]BF$_4$ in presence of pTSA by changing the molar ratios and temperature. After optimizing the reaction conditions by using different ionic liquids and varying amounts of pTSA and temperature, the reactions of aromatic aldehydes (1.0 mmol), 2,7-dihydroxynaphthalene (1.0 mmol) and dimedone/ cyclohexane-1,3-dione (1.1 mmol) were carried out in in [bmim]BF$_4$ in presence of 2 mol% pTSA at 50°C to give the corresponding 2-hydroxy-12-aryl-
8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones (eq. 8). Reactions using double molar ratio of aldehyde and dimedone failed to give the desired bis-condensation product.

![Chemical structure](image)

Similarly, condensation of aldehydes (1.0 mmol), dimedone (1.0 mmol) and 2,6-dihydroxynaphthalene (1.1 mmol) in [bmim]BF₄ in presence of 2 mol% pTSA at 60°C (eq. 9) gave the corresponding 3-hydroxy-12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones in quantitative yields.

![Chemical structure](image)

The reaction of 2,6-dihydroxynaphthalene with double molar ratios of aldehyde and dimedone in [bmim]BF₄ in presence of 5 mol% pTSA at 90°C gave the desired bis-condensation product. A variety of aromatic aldehydes underwent the reaction under otherwise similar conditions to produce the corresponding 5,13-diaryl-2,2,10,10-tetramethyl-2,3,9,10,11,13-hexahydroxantheno[2,1-a]xanthene-4,12(1H,5H)-diones (eq. 10).

![Chemical structure](image)

The ionic liquid could be easily recycled and reused for upto four cycles.