**Sustainable Approach of Nanocatalyst for Organic Synthesis in Aqueous Hydrotropic Medium**

Suraj R. Attar, Aboli C. Sapkal, Santosh B. Kamble\*

*Department of Chemistry, Yashavantrao Chavan Institute of Science, Karmveer Bhaurao Patil University, Satara 415001, Maharashtra, India*

Email: [santosh.san143@gmail.com](mailto:santosh.san143@gmail.com)

Aboli Sapkal: Orcid Id: 0000-0002-4838-1266

Suraj Attar: Orcid Id: 0000-0002-1596-9696

Santosh Kamble: Orcid Id: 0000-0002-4668-1628

**Introduction:**

In recent times, Nanocatalyst is a rising field applicable to almost all types of catalytic organic transformations and an essential tool of green chemistry as it enables the development of less polluting chemical processes and opens up synthetic pathways to desired products using a sustainable approach.[1] Nanoparticles (NPs) play a crucial role in the organic transformation and are increasingly attractive in the field of catalysis as they show good catalytic activity in organic as well as aqueous medium.[2] Several forms of nanocatalyst such as metal NPs, metal oxide, magnetic nanocatalyst, nano-mixed metal oxide, core-shell nanocatalyst, and supported nano catalysts have been employed in the catalytic applications.[3] Nanocatalysts have a particle size in the nm scale, and thus have a large surface area, which enables the interaction of chemical reactants via cooperative activation to bring them in closer proximity with each other.On the other hand, The synthesis of heterocyclic as well as biologically active compound represent a broad class of compounds, which have received considerable attention due to their wide range of biological activities.

In parallel, According to green chemistry, nanoparticles catalyzed organic transformations are the safest reactions, which do not affect the environment. Most heterocyclic compounds synthesized in the laboratory as well as in industry need organic solvents as reaction media.[4] In spite of the fact that water is safe, environmentally friendly, benign and cheap compared with organic solvents. Today’s environmental consciousness imposes the use of water as a solvent in both industrial and academic chemists.[5] In essence, water is an interesting and beneficial solvent in organic synthesis, but the poor solubility of organic substances in water is the main obstacle. However, a variety of strategies have been investigated to solubilize organic compounds in water in order to expand the scope of water based organic synthesis. This problem is overcome by the addition of amiphiphiles for example, Phase Transfer Catalyst, Co-solvents, Hydrotropes and Surfactants. It performs as a greener reaction media alternative to organic solvent in organic synthesis with eco-friendly approach. Aqueous solution of hydrotropes represents clean and green protocol; it shows unique properties as an alternative reaction media for organic synthesis. Hydrotropes are cheap, non-toxic and environment friendly. The aqueous hydrotropic solutions possess physico-chemical characteristics which being an alternative greener solvents for organic synthesis. The number of different organic synthesis carried out in aqueous hydrotropic medium which includes Claisen-Schmidt reaction in hydrotropic aqueous solution [6], microwave-enhanced Hantzschdihydropyridine ester synthesis [7], Friedlander′s Heteroannulation method for synthesis of quinoline [8]. Along with organic synthesis hydrotrope also enhance the rate of multiphase reaction [9] which can lead to autocatalysis in the biphasic alkaline hydrolysis of aromatic esters [10]. The hydrotropes shows variety of applications other than organic synthesis such as, in formulation of pharmaceuticals [11-15], extraction and separation processes [16-18]and the most recent research of hydrotropic action has been performed on these above two processes. They show influence on oil-in-water (OW) for micro-emulsions [19-20] and related cleaning and washing processes. Their biological action has also received more attention [21].

Our goal is to develop a novel system that enables the use of water as a solvent for wide range of reactions of organic materials. It performs as a greener reaction media alternative to organic solvent in organic synthesis.

**Recent Research and Development**

Synthesis of important organic scaffolds via nanocatalyst is a significant aspect related to synthesis of bioactive compounds. Nanocatalysts have a particle size in the nm scale, and thus have a large surface area, which enables the interaction of chemical reactants via cooperative activation to bring them in closer proximity with each other.[4] This study more advantageous when the synthesis is carried out in aqueous medium and it follows the principals of green chemistry. So that many active research group are engaged in research field of organic synthesis in aqueous medium. The uses of hydrotropic medium for various organic transformations have been done due to the diverse applications of the hydrotrope in organic chemistry. Hydrotropic medium fulfill the many principles of green chemistry.There are large numbers of publications have been cited in the reputed international journals. Numbers of citations are also reported due to its valuable applications. These parts of synthesis have made significant contribution in this field at national and international level.

Alonso and co-workers recently reported Copper nanoparticles catalyzed click reaction**[Scheme 1]** in water[22]. On the other hand, Borah et al. collected Montmorillonitrile clay from west part of India and generated Cu (0) nanoparticles in the nanopores of modified Montmorillonite. Furthermore it was used as catalyst for Click reaction in aqueous medium.[23]



**[Scheme 1]**

Deng et al. developed magnetic Silica supported dodecyl benzene sulphonic acid catalyst for an efficient one pot three component reaction of Spirooxindole- pyrimidine derivatives [**Scheme 2**] in water.[24]



[**Scheme 2**]

Ghahremanzadeh also reported synthesis of spiroindoles derivatives via one pot three component system of isatins, dimedone and anilinolactones [**Scheme 3**] using Mn/Fe2O4 NPs.[25]

****

[**Scheme 3**]

After successful application of Mn/Fe2O4 NPs Naeimi and group reported synthesis of Pyrimidine derivative by using Cu/Fe2O4 NPs as a inverse structure [**Scheme 4**] as compared to Mn/Fe2O4 NPs.[26]



[**Scheme 4**]

Saha et al. demonstrated fluorescent tetragonal ZrO2 NPs catalyzed multicomponent synthesis of biological active 2-aminochromenes, dihydropyrano [3,2,c] chromene, Chromeno [4,3,b] chromene derivative **[Scheme 5]** in aqueous medium.[27]

****

**[Scheme 5]**

Shrestha et al. reported green and efficient protocol for the synthesis of Spirooxindole derivatives **[Scheme 4]** by using CeO2 as a nanocatalyst in aqueous medium.[28]

****

**[Scheme 6]**

Payra et al. reported synthesis of 3,4-dicarbonyl substituted furan derivatives **[Scheme 5]** via direct functionalization of α, β-unsaturated carbonyl compounds through conjugate addition initiated domino reactions by using CuO NPs in aqueous alcohol.[29]



**[Scheme 7]**

Naeimi and group reported synthesis of Pyrimidine derivative [**Scheme 6**] by using Cu/Fe2O4 NPs as a catalyst in aqueous medium.[30]

****

[**Scheme 8**]

In another report, Kale et al. designed novel γFe2O4 @ hydroxyapatite (HAP) catalyst and used for the synthesis of 1,2,3 Triazole **[Scheme 7]** in aqueous medium.[31]



**[Scheme 9]**

**Importance and current status of various nanocatlyst for organic synthesis**

Organic scaffold by nanocatalyst in aqueous medium has become a crucial and demanding research area in modern synthetic chemistry. In the year 1980, Breslow discovered that huge rate (i.e. 700 times faster reaction rate) accelerations occurred when the Diels-Alder reaction was performed in water. This observation increased the interest of synthetic organic chemists to analyze organic reactions in aqueous medium. To date, many more organic transformations have been carried out in water.

The use of environmentally benign solvents like aqueous hydrotropic medium represents very powerful green chemical technology from the economical and synthetic point of view. They not only reduce the burden of organic solvent disposal, but also enhance the rate of many organic reactions. It performs eco-efficient processes. It protects the environment, not by cleaning up, but by inventing new chemical processes that do not pollute the environment.

Recyclability with high efficiency is the most important factor for any catalyst in organic transformation. The most important aspect of this NPs heterogeneous nanocatalyst with respect to previously reported work is its recyclability. NPs (catalyst) were separated by a simple process after completion of the reaction and rerycled without loss of catalytic efficiency.

Naturaly abundant and eco-friendly nanocatalyst are not only easy to prepare but also highly sustainable in nature due to its recyclability. These all factors like aqueous medium, sustainable catalyst and reusability of the catalyst make this ptotocol most efficient and green.

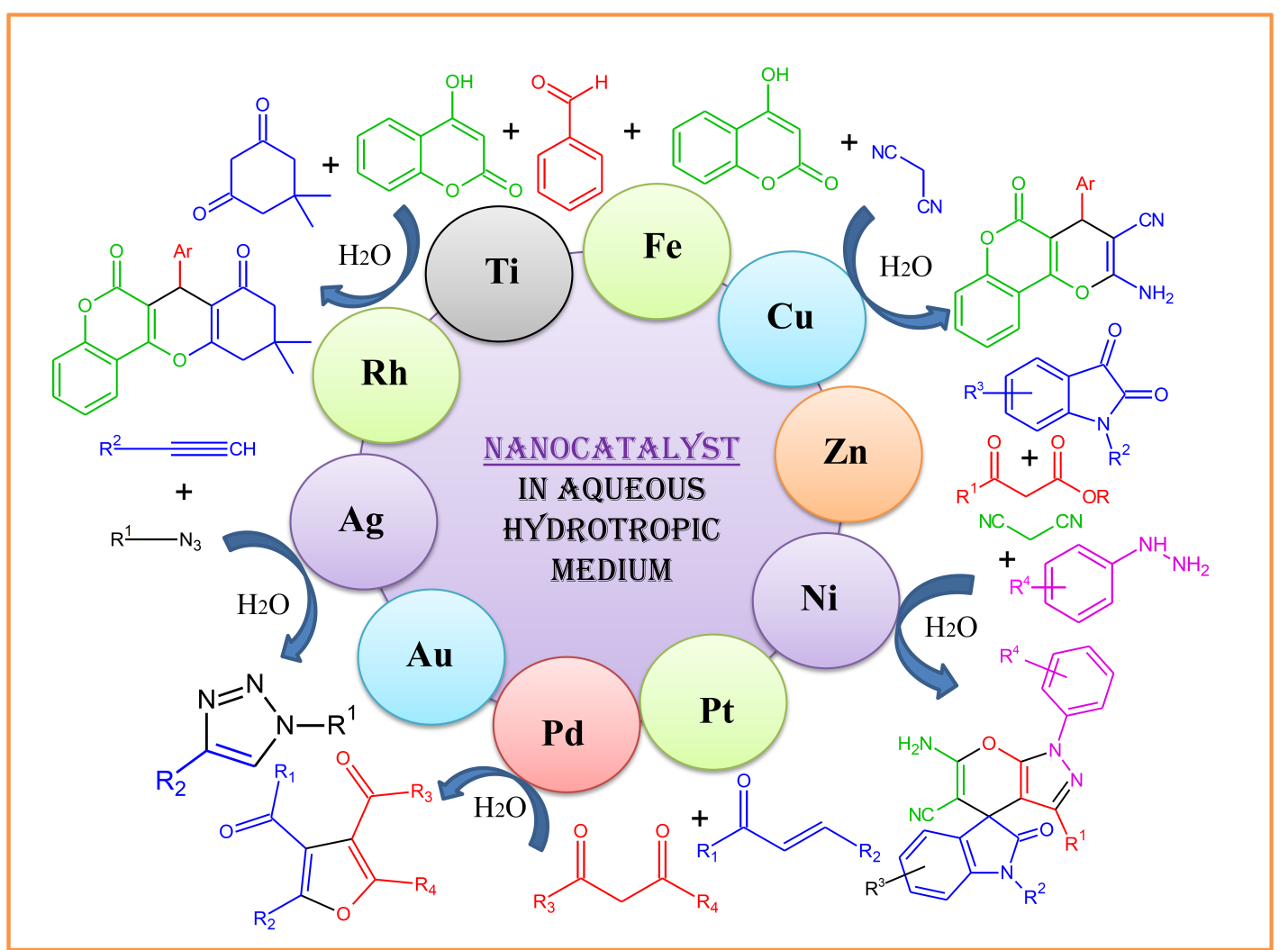


Fig. 1 Applications of nanocatalysts for various organic transformations.

**Synthesis of Nanocatalyst:**

**Synthesis of Nanocatalyst from plant extract for Sustainable Development**

In the scenario of nanotechnology numerous methods have been employed to develop sustainable synthetic methods for preparation of nanocatalyst. To control size and shape with desired functional property further efforts are necessary. Plant extract contains organic compounds like alkaloids and terpenoids which are act as reducing agents, capping agents, and/or complexing agents to control size and shape of Nanocatalyst.

**Synthesis of supported Nanocatalysts:**

Recently, Supported nanoparticles are of great interest due to its numerous applications. In recent years supported metallic nanoparticles and their applications is one of the fastest growing research field. When metal nanoparticles deposited onto the surface of mono porous material it forms supporting metal nanoparticles.[32] While formation of nanocatalyst particle size decreases to nanoscale dimensions due to which aggregation of the particles into small clusters were formed. This aggregation degrades the catalytic efficiency. To achieve the aim of nanoparticles size, shape it is necessary to terminate aggregation and partial growth addition of organic ligands, inorganic capping materials, metal salts and polymer plays vital role.[33] The porous material is normally solid like silica gel,[34]zeolites,[35] metal oxides,[36] activated charcoal,[37] and graphite materials[38] can be considered as porous media. Naturally occurring clay and rocks[39] also used as porous media. The support can be either a powder or pre-shaped cheap solid with a porous environment that usually not only inhibits particle growth to a particular size but also reduces particle aggregation.

**Applications of Nanocatalyst in organic transformations:**

**Scheme 1**: Reaction of o-phenylenediamines and ketone in aqueous medium by efficient recyclable heterogeneousnanocatalyst.



**Scheme-1**

**Scheme 2**: Nanoparticle catalysedFriedel-Crafts alkylation of indole with different α,β-unsaturated Nitroalkenes.

**Scheme-2**

**Scheme 3**: Synthesis of 2-substituted quinazoline using nanocatalyst.



**Scheme-3**

**Scheme 4:**Synthesis of 2-amino-5-cyno-6-hydroxy-4-arylpyrimidines by using nanocatalyst.

**Scheme-4**

**Scheme 5:**Synthesis of quinoxaline from 1,2-Diamine and 1,2-Diketone by using nanocatalyst.

**Scheme-5**

.

**References:**

[1] V. Polshettiwar and R. S. Varma, “Green chemistry by nano-catalysis,” p. 12, 2010.

[2] M. B. Gawande, Y. Monga, R. Zboril, and R. K. Sharma, “Silica-decorated magnetic nanocomposites for catalytic applications,” *Coord. Chem. Rev.*, vol. 288, pp. 118–143, 2015.

[3] R. Breslow, “Determining the geometries of transition states by use of antihydrophobic additives in water,” *Acc. Chem. Res.*, vol. 37, no. 7, pp. 471–478, 2004.

[4] T. M. Dhameliya *et al.*, “A decennary update on applications of metal nanoparticles (MNPs) in the synthesis of nitrogen- and oxygen-containing heterocyclic scaffolds,” *RSC Adv.*, vol. 10, no. 54, pp. 32740–32820, 2020, doi: 10.1039/D0RA02272A.

[5] T. Kitanosono, K. Masuda, P. Xu, and S. Kobayashi, “Catalytic Organic Reactions in Water toward Sustainable Society,” *Chem. Rev.*, vol. 118, no. 2, pp. 679–746, Jan. 2018, doi: 10.1021/acs.chemrev.7b00417.

[6] V.G.Sadvilkar, S.D.Samant, V.G.Gaikar, J.Chem.Technol. Biotechnol., 1995, 62, 405.

[7] B. M. Khadilkar, V. R. Madyar, Org. Process Research and Devlopment., 2001, 5, 452.

[8] S. J. Chandratre, Z. A. Filmwala, J. of Dispersion Science and Technology, 2007, 28, 279.

[9] B. Janakiraman, M. M. Sharma, Chem. Eng. Sci., 1985, 40, 2156.

[10] X. N. Chen, J. C. Micheau, Colloid Interface Sci., 2002, 249, 172.

[11]G. D. Gupta, S. Jain, N. K. Jain, Pharmazie, 1997, 52, 709.

[12]R. M. Khalil, Pharmazie, 1997, 52, 866.

[13]G. D. Gupta, S. Jain, N. K. Jain, Pharmazie, 1997, 52, 621.

[14]S. A. ElNahhas, Pharmazie, Pharmazie, 1997, 52, 624.

[15]N. K. Jain, S, Jain, A. K. Singhai, Pharmazie, 1997, 52, 942.

[16]G. K. Poochiikian, J. C. Cradock, Pharm. Sci., 1979, 68, 728.

[17]N. S. Tavare, E. J. Colonia, J. Eng. Data, 1997, 42, 631.

[18]J. E. Colonia, A. B. Dixit, N. S. Tavare, Ind. Eng. Chem. Res., 1998, 37,1956.

[19]S. E. Friberg, C. Brancewicz, D. S. Morrison, Langmuir, 1994, 10, 2945.

[20]G. Horvath-Szabo, J. H. Masliyah, J. J. Czarnecki, J. Colloid Interface Sci., 2001, 242,

274.

[21] R. H. McKee, Use of hydrotropic solutions in industy, Ind. Eng. Chem., 1946, 38, 382.

[22] F. Alonso, Y. Moglie, and G. Radivoy, “Copper Nanoparticles in Click Chemistry,”

*Acc. Chem. Res.*, vol. 48, no. 9, pp. 2516–2528, Sep. 2015, doi:

10.1021/acs.accounts.5b00293.

[23]B. J. Borah, D. Dutta, P. P. Saikia, N. C. Barua, and D. K. Dutta, “Stabilization of Cu(0)-nanoparticles into the nanopores of modified montmorillonite: An implication on the catalytic approach for ‘Click’ reaction between azides and terminal alkynes,” *Green Chem.*, vol. 13, no. 12, p. 3453, 2011, doi: 10.1039/c1gc16021d.

[24]J. Deng, L.-P. Mo, F.-Y. Zhao, Z.-H. Zhang, and S.-X. Liu, “One-pot, three-component synthesis of a library of spirooxindole-pyrimidines catalyzed by magnetic nanoparticle supported dodecyl benzenesulfonic acid in aqueous media,” *ACS Comb. Sci.*, vol. 14, no. 5, pp. 335–341, 2012.

[25]R. Ghahremanzadeh, Z. Rashid, A. H. Zarnani, and H. Naeimi, “Synthesis of novel spirooxindoles in water by using MnFe2O4 nanoparticles as an efficient magnetically recoverable and reusable catalyst,” *Appl. Catal. Gen.*, vol. 467, pp. 270–278, 2013.

[26]H. Naeimi and A. Didar, “Efficient sonochemical green reaction of aldehyde, thiobarbituric acid and ammonium acetate using magnetically recyclable nanocatalyst in water,” *Ultrason. Sonochem.*, vol. 34, pp. 889–895, Jan. 2017, doi: 10.1016/j.ultsonch.2016.07.021.

[27] A. Saha, S. Payra, and S. Banerjee, “On water synthesis of pyran–chromenes via a multicomponent reactions catalyzed by fluorescent t-ZrO 2 nanoparticles,” *RSC Adv.*, vol. 5, no. 123, pp. 101664–101671, 2015.

[28] R. Shrestha, K. Sharma, Y. R. Lee, and Y.-J. Wee, “Cerium oxide-catalyzed multicomponent condensation approach to spirooxindoles in water,” *Mol. Divers.*, vol. 20, no. 4, pp. 847–858, 2016.

[29] S. Payra, A. Saha, S. Guchhait, and S. Banerjee, “Direct CuO nanoparticle-catalyzed synthesis of poly-substituted furans via oxidative C–H/C–H functionalization in aqueous medium,” RSC Adv., vol. 6, no. 40, pp. 33462–33467, 2016.

[30]H. Naeimi and A. Didar, “Efficient sonochemical green reaction of aldehyde,

thiobarbituric acid and ammonium acetate using magnetically recyclable nanocatalyst in

water,” Ultrason. Sonochem., vol. 34, pp. 889–895, Jan. 2017.

[31] S. R. Kale, S. S. Kahandal, M. B. Gawande, and R. V. Jayaram, “Magnetically recyclable γ-Fe 2 O 3–HAP nanoparticles for the cycloaddition reaction of alkynes, halides and azides in aqueous media,” *RSC Adv.*, vol. 3, no. 22, pp. 8184–8192, 2013.

[32] R. J. White, R. Luque, V. L. Budarin, J. H. Clark, and D. J. Macquarrie, “Supported metal nanoparticles on porous materials. Methods and applications,” *Chem Soc Rev*, vol. 38, no. 2, pp. 481–494, 2009, doi: 10.1039/B802654H.

[33] M. J. Ndolomingo, N. Bingwa, and R. Meijboom, “Review of supported metal nanoparticles: synthesis methodologies, advantages and application as catalysts,” *J. Mater. Sci.*, vol. 55, no. 15, pp. 6195–6241, 2020.

[34] S. D. Karande, S. A. Jadhav, H. B. Garud, V. A. Kalantre, S. H. Burungale, and P. S. Patil, “Green and sustainable synthesis of silica nanoparticles,” *Nanotechnol. Environ. Eng.*, vol. 6, no. 2, pp. 1–14, 2021.

[35] B. K. Singh, S. Lee, and K. Na, “An overview on metal-related catalysts: metal oxides, nanoporous metals and supported metal nanoparticles on metal organic frameworks and zeolites,” *Rare Met.*, vol. 39, no. 7, pp. 751–766, 2020.

[36] E. A. Monyoncho, S. Ntais, N. Brazeau, J.-J. Wu, C.-L. Sun, and E. A. Baranova, “Role of the metal-oxide support in the catalytic activity of Pd nanoparticles for ethanol electrooxidation in alkaline media,” *ChemElectroChem*, vol. 3, no. 2, pp. 218–227, 2016.

[37] J. L. Santos, C. Megías-Sayago, S. Ivanova, M. Á. Centeno, and J. A. Odriozola, “Structure-sensitivity of formic acid dehydrogenation reaction over additive-free Pd NPs supported on activated carbon,” *Chem. Eng. J.*, vol. 420, p. 127641, 2021.

[38] M. d’Halluin *et al.*, “Graphite-supported ultra-small copper nanoparticles–Preparation, characterization and catalysis applications,” *Carbon*, vol. 93, pp. 974–983, 2015.

[39] V. Shah *et al.*, “Fate and impact of zero-valent copper nanoparticles on geographically-distinct soils,” *Sci. Total Environ.*, vol. 573, pp. 661–670, 2016.

[40][Bipin Shinde](https://link.springer.com/article/10.1007/s11164-018-3295-2" \l "auth-Bipin-Shinde), [Santosh Kamble](https://link.springer.com/article/10.1007/s11164-018-3295-2#auth-Santosh-Kamble), [Pramod  
 Gaikwad](https://link.springer.com/article/10.1007/s11164-018-3295-2#auth-Pramod-Gaikwad), [VishvanathG hanwat](https://link.springer.com/article/10.1007/s11164-018-3295-2" \l "auth-Vishvanath-Ghanwat), [Sagar Tanpure](https://link.springer.com/article/10.1007/s11164-018-3295-2#auth-Sagar-Tanpure), [Pavan Pagare](https://link.springer.com/article/10.1007/s11164-018-3295-2#auth-Pavan-Pagare), [Bhausaheb  
 Karale](https://link.springer.com/article/10.1007/s11164-018-3295-2#auth-Bhausaheb-Karale) & [Arvind Burungale](https://link.springer.com/article/10.1007/s11164-018-3295-2" \l "auth-Arvind-Burungale),Novel catalytic application of Ni@ZnO nanoparticles and

ZnOnanoflakes in aqueous   
 solution of NaPTS hydrotrope at room temperature via a green synthesis of 3,4-  
 dihydropyrimidin-2(1H)-ones. Research on Chemical Intermediate, 2018, 44, 3097-  
 3113.

[41] Bipin Shinde, Santosh B. Kamble, Dattaprasad M.   
 Pore, Prasad Gosavi, AmolGaikwad, Harsharaj S. Jadhav, Bhausaheb K. Karale, and   
 Arvind S. Burungale, pH-TransformedZnO-NPs /NaPTS: The First Room-Temperature

Brisk Synthesis of   
 Flavanones in Aqueous Medium. Chemistry Select 2018, 3, 13197– 13206.

[42] BipinShinde, Santosh B. Kamble, Harsharaj S. Jadhav, Bhausaheb K. Karale,

Kaluram G. Kanade, and Arvind S. Burungale The Calotropisprocera Transformed

Green NiO and Fe-NiO Nanoparticles for Diaryl  
 Pyrimidinones Synthesis in Hydrotropic Medium at Room Temperature., Chemistry

Select, 2018, 3, 13140– 13153.

[43] Bipin Shinde, Santosh Kamble, Harsharaj Jadhav, Prasad Mane, Kalpesh Khude,

Hern Kim, Bhausaheb Karale, Arvind Burungale, ‘In water’ exploration

of Alpiniazerumbet‑fabricated CuO NPs in the presence of NaPTS at room

temperature: green synthesis of 1,8‑dioxooctahydroxanthene derivatives. Research on

Chemical Intermediates, 2021, 47, 121-1237.

[44] [Suraj R. Attar](https://link.springer.com/article/10.1007/s11164-020-04233-5#auth-Suraj_R_-Attar), [BipinShinde](https://link.springer.com/article/10.1007/s11164-020-04233-5#auth-Bipin-Shinde) & [Santosh B. Kamble](https://link.springer.com/article/10.1007/s11164-020-04233-5#auth-Santosh_B_-Kamble)Enhanced catalytic activity of bio-

fabricated ZnO NPs prepared by ultrasound- assisted route for the synthesis of

tetraketone and benzylidenemalonitrile in hydrotropic aqueous medium. Research

on Chemical Intermediates, 2020, 46, 4723-4748.

[45] Pramod Gaikwad, Santosh Kamble, Microwave Enhanced Green and Convenient

Synthesis of 2-amino-4H-chromenes inAqueous Hydrotropic Medium. Current

Research in Green and Sustainable Chemistry, 2020.

[46] Aboli Sapkal, Santosh Kamble Sodium toluene‐4‐sulfonate as a reusable and

ecofriendly catalyst for Greener Synthesis of 5‐aminopyrazole‐4‐carbonitrile in

aqueous medium, Journal of Heterocyclic Chemistry,2020.

[47] Aboli Sapkal, Santosh Kamble ,Greener and Environmentally Benign Methodology

for the Synthesis of Pyrazole Derivatives, Journal of Chemistry Select, 5, 2020,

12971-13026

[48] ArjunKumbhar, Santosh Kamble, Siddharth Kamat, Yashovardhan Indi, An aqueous

hydrotropic solution as environmentally benign reaction medium for organic

transformations , Research on Chemical Intermediates, 6(17),2022.

[49] S.R. Attar, S.B. Kamble, Recent Advances of Nanoparticles towards Sustainability

and their Application for Organic Transformation in Aqueous Medium, Nanoscale

2022, **14**, 16761-16786.

[50] S.R. Attar, A.C. Sapkal, C. S. Bagade, S. H. Mujawar, S.B. Kamble, Gel Entrapped

ZnO Nanorods: an efficient and sustainable catalyst for the Claisen-Schmidt

Condensation Reaction in Aqueous Hydrotropic Medium, Molecular Catalysis 542

(2023) 113120

[51] S.R. Attar, A.C. Sapkal, N.S. Dhane, S.B. Kamble, Agar Supported NiO NPs: A

Sustainable Approach for synthesis of 3, 4‑dihydropyrimidin‑2(1H)‑ones in Aqueous

Hydrotropic Media, Catal Lett (2023). https://doi.org/10.1007/s10562-023-04375-2

[52] Attar, S.R., Sapkal, A.C., Bagade, C.S. Kamble, S.B., Biogenic CuO NPs for synthesis of coumarin derivatives in hydrotropic aqueous medium, Res Chem Intermed (2023). https://doi.org/10.1007/s11164-023-05034-2