

Cite this article: D. Saha, Potential of solid supported copper catalyst in sustainable organic synthesis, *RP Cur. Tr. Appl. Sci.* **3** (2024) 10–13.

Original Research Article

Potential of solid supported copper catalyst in sustainable organic synthesis

Debasree Saha

Department of Chemistry, Raidighi College (Under University of Calcutta), 24 Parganas (South), West Bengal, India

*Corresponding author, E-mail: debasree27@gmail.com

ARTICLE HISTORY

Received: 01 Dec. 2023

Revised: 19 Jan. 2024

Accepted: 23 Jan 2024

Published online: 25 Jan. 2024

KEYWORDS

Copper; Heterogeneous;
Sustainable; Organic
synthesis; Reusability.

ABSTRACT

Heterogeneous metal catalysis has gained importance in the last decade as it offers advantages like reusability of the catalyst, ease of separation, minimum metal contamination in product and economical as well as environmental sustainability. Heterogeneous copper catalyst has been developed with an aim to study the efficiency of supported copper on synthetic organic reactions leading to useful molecules which are important components in pharmaceutical chemistry. The methodologies involving heterogeneous copper catalysis leads to sustainable alternative pathways to the synthesis of drug molecules as well as other biologically relevant moieties. This review will include the synthesis and application of copper catalysts supported on several different solid supports like hydroxyapatite, titanium dioxide, silica etc. The review will highlight the use of these solid supported copper catalysts in useful organic reactions. The aim of this article is to develop a platform which will guide future organic chemists towards developing newer methods of heterogeneous catalysis for sustainable organic synthesis.

1. Introduction

Transition metal catalysed organic synthesis has gained tremendous attention since the last few decades [1-7] and the trend of developing newer and more improved methodologies of transition metal catalysed reactions are still on the rise. In today's world where we are constantly striving to achieve sustainability, heterogeneous metal catalysis has become a popular mode for the transition metal catalysed synthesis of organic molecules [8-11]. Heterogeneous catalysis leads to reuse of metal salts, thus ensuring economical as well as environmental sustainability. Since the solid supported metal catalyst can be separated from the organic medium most of the times by simple filtration, the product has minimum risk of metal contamination, thus reducing the toxic metallic side effects which is highly desirable in medicinal chemistry.

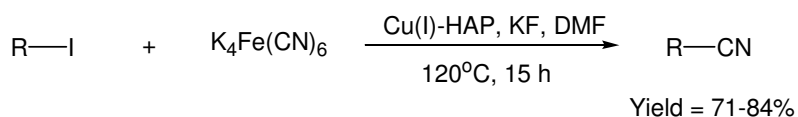
Copper has gained tremendous importance as transition metal catalyst employed in the synthesis of a variety of organic molecules [12]. Versatility, abundance, low cost and low toxicity make copper a very efficient catalyst for organic synthesis. Quite a few reviews have already been published about the effectiveness of copper as a catalyst in synthetic organic reactions [11, 13, 14]. However, there is scope for covering the recent important developments of solid supported copper catalysts employed for catalysing organic reactions. It will be the aim of this review to highlight useful organic reactions catalysed by copper supported on easily available solid supports like hydroxyapatite and titanium dioxide.

2. Hydroxyapatite supported copper catalysed cyanation of styrenyl and aryl halides

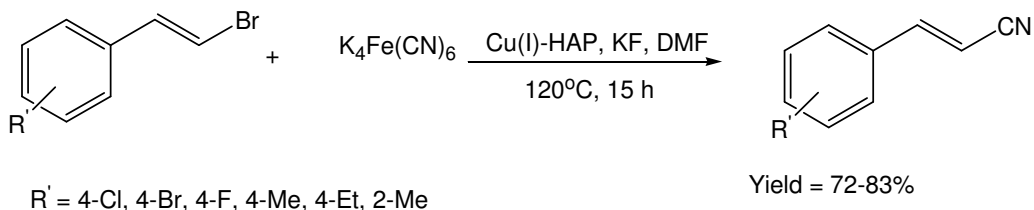
Hydroxyapatite serves as a good support for cations and anions as the apatite system can incorporate a large number of ions owing to their high ion exchange capacity. Ranu and his group [15] developed Cu(I) catalyst supported on hydroxyapatite, starting from easily available starting materials like calcium nitrate, diammonium hydrogen phosphate and cuprous iodide. The resultant catalyst was characterised by SEM, EDS, AFM, XPS and ICP-MS analysis. The copper content as determined by ICP-MS analysis was found to be 0.3237 mmol/g. The EDS (Energy Dispersive Spectra) confirmed the presence of copper and calcium in the catalyst system. XPS (X-ray Photoelectron Spectroscopy) showed a peak corresponding to Cu 2p_{3/2} at 934.2 eV with no satellite peak, thus indicating the oxidation state of copper as +1 in the catalyst system. FESEM and AFM studies showed the morphology of the catalyst system.

Ranu and his group employed this Cu(I) supported on hydroxyapatite (Cu-HAP) as catalyst for the cyanation of styrenyl bromides and aryl iodides (Figure 1). Potassium hexacyanoferrate served as sustainable alternative cyanating agent to the conventional toxic alkali metal cyanides. The authors used potassium fluoride as the base and dimethyl formamide as solvent. A variety of differently substituted aryl bromides and styryl bromides participated in the reaction leading to significantly high yields of products. In case of styryl bromides, the reaction was found to be stereoselective except in the case of (Z)-2-methylstyrenyl bromide.

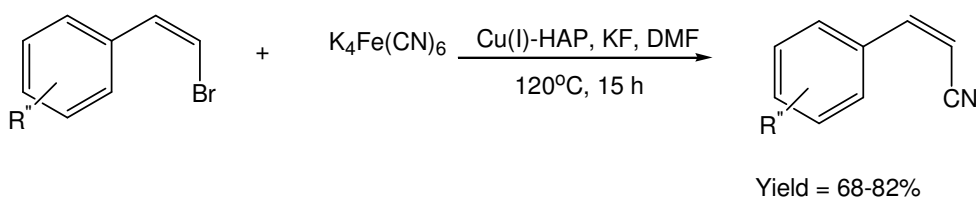




R = C₆H₅, 2-Br-C₆H₄, 4-Br-C₆H₄, 3-F-C₆H₄, 4-Cl-C₆H₄, 3-CF₃-C₆H₄, 3-O₂N-C₆H₄, 4-Me-C₆H₄, 3-Me-C₆H₄, 3-MeO-C₆H₄, 4-MeO-C₆H₄, 4-EtOOC-C₆H₄, 1-naphthyl, 2-naphthyl, 2-thienyl



R' = 4-Cl, 4-Br, 4-F, 4-Me, 4-Et, 2-Me



R'' = 4-Cl, 4-Br, 4-F, 4-Me, 4-Et

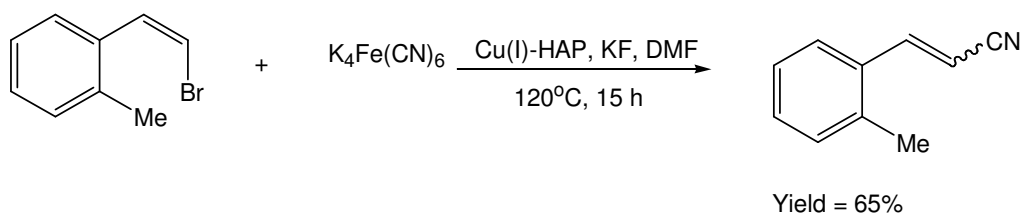
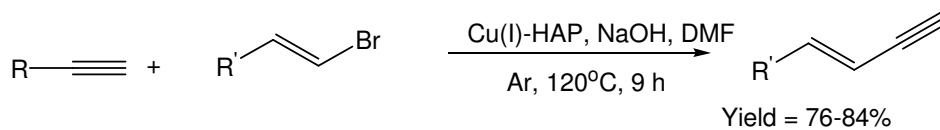
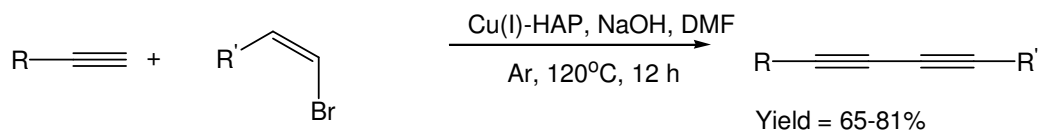


Figure 1: Copper hydroxyapatite catalysed cyanation of aryl and styrenyl halides.



R = C₆H₅, 4-MeO-C₆H₄, Me(CH₂)₅

R' = C₆H₅, 4-F-C₆H₄, 4-Cl-C₆H₄, 4-Me-C₆H₄, 4-Et-C₆H₄



R = C₆H₅, 4-MeO-C₆H₄

R' = C₆H₅, 4-F-C₆H₄, 4-Cl-C₆H₄, 4-Me-C₆H₄, 4-Et-C₆H₄, Me(CH₂)₈

Figure 2: Copper hydroxyapatite catalysed Sonogashira reaction of styrenyl bromides.

The catalyst could be reused for four cycles. However, significant loss in yield of product was observed, possibly due to the formation of contaminant coating on the catalyst surface. The authors proposed a reaction mechanism involving the usual oxidative addition, transmetalation and reductive elimination steps. The XPS analysis of the recycled catalyst was found to contain copper in the +1 oxidation state, thus supporting the proposed mechanism.

3. Hydroxyapatite supported copper catalysed Sonogashira reaction of Styrenyl bromides

In 2012, Ranu and his group [16] employed the hydroxyapatite supported copper catalyst for Sonogashira

4. Titanium dioxide supported copper catalysed C-2 amination of azoles

In 2018 Sen, Saha and coworkers developed a nano structured copper catalyst supported on titanium dioxide [17]. The catalyst was prepared from tetraethylene glycol, titanium(IV)isopropoxide and copper(I) iodide via a sol gel method. The catalyst was characterised by SEM, TEM, EDS, ICP-MS and XPS analyses. ICP-MS analysis indicated 0.77 wt% of Cu in the catalyst system. XPS analysis showed Cu 2p_{3/2} peak with the absence of any satellite peak, thus

reaction of styrenyl bromides. The trans styrenyl bromides produced the usual trans-ene-yne product but the cis styrenyl bromides produced unsymmetrical 1,3-diynes via cross coupling of alkyne starting material and the alkyne generated from the styrenyl bromide (Figure 2). This reaction of cis styrenyl bromides to produce cross 1,3- diynes was found to be unique in literature. The reactions proceeded in argon atmosphere with sodium hydroxide as base. No use of toxic ligand or additive was needed in the protocol. The catalyst could be reused but after each cycle the catalytic activity decreased. A single electron transfer mechanism was proposed for the reaction of cis styrenyl bromides leading to the formation of unsymmetrical 1,3-diynes.

indicating the oxidation state of Cu to be +1 in the catalyst system.

The authors employed the catalyst for the regioselective C-2 amination of benzoxazole, benzothiazole and thiazole in a ligand and solvent free process (Figure 3). Several substituted amides and amines successfully participated in the reaction yielding the aminated azoles in high yields. Potassium tert-butoxide served as the base and silver acetate served as the additive in the methodology. The catalyst could be recycled four times. The authors extended the protocol towards gram scale synthesis of bioactive small molecule having anti tumour and anti HIV properties.

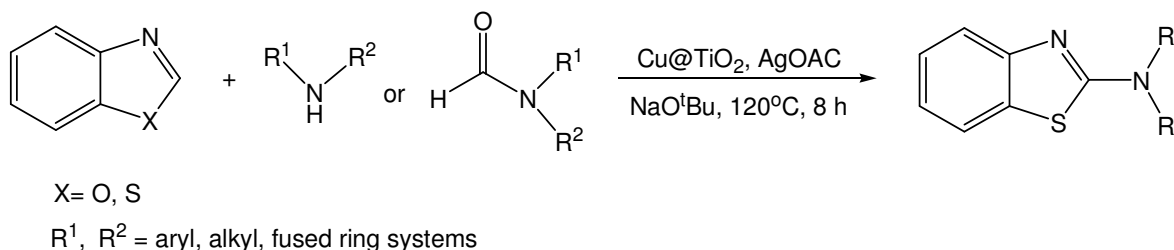


Figure 3: Titanium dioxide supported copper catalysed C-2 amination of azoles.

5. Conclusions

Supported metal catalysts serve as useful sustainable alternatives to homogeneous ones. In this review, the importance of a few solid supported copper catalytic systems that played useful catalytic role in synthetic organic reactions, have been highlighted. This article will hopefully be useful to scientists working in the area of heterogeneous catalysis.

References

- [1] T.-Y. Luh, M. Leung, K. -T. Wong, Transition metal-catalyzed activation of aliphatic C–X bonds in carbon–carbon bond formation, *Chem. Rev.* **100** (2000) 3187.
- [2] M. Beller, C. Bolm, Eds. *Transition Metals for Organic Synthesis*, Wiley-VCH, Weinheim (2004).
- [3] L.S. Hegedus, B.C.G. Söderberg, *Transition Metals in the Synthesis of Complex Organic Molecules*, University Science Books, Sausalito, 3rd Edn. (2009).
- [4] J. Magano, J.R. Dunetz, Large-scale applications of transition metal-catalyzed couplings for the synthesis of pharmaceuticals, *Chem. Rev.* **111** (2011) 2177-2250.
- [5] M. Ouchi, T. Terashima, M. Sawamoto, Transition metal-catalyzed living radical polymerization: Toward perfection in catalysis and precision polymer synthesis, *Chem. Rev.* **109** (2009) 4963-5050.
- [6] M. Yang, J. Li, P.R. Chen, Transition metal mediated bioorthogonal protein chemistry in living cells, *Chem. Soc. Rev.* **43** (2014) 6511-6526.
- [7] W.-M., Cheng, X. Lu, J. Shi, L. Liu, Selective modification of natural nucleophilic residues in peptides and proteins using arylpalladium complexes, *Org. Chem. Front.* **5** (2018) 3186-3193.
- [8] B.C. Ranu, S. Bhadra, D. Saha, Green recyclable supported-metal catalyst for useful organic transformations, *Curr. Org. Synth.* **8** (2011) 146-171.
- [9] L. Yin, J. Liebscher, Carbon–carbon coupling reactions catalyzed by heterogeneous palladium catalysts, *Chem. Rev.* **107** (2007) 133-173.
- [10] V. Polshethiwar, C. Len, A. Fihri, Silica-supported palladium: Sustainable catalysts for cross-coupling reactions, *Coord. Chem. Rev.* **253** (2009) 2599-2626.
- [11] N. Aflak, H.B.E. Ayouchia, L. Bahsis, H. Anane, M. Julve, S.-E. Stiriba, Recent advances in copper-based solid heterogeneous catalysts for azide–alkyne cycloaddition reactions, *Int. J. Mol. Sci.* **23** (2022) 2383.
- [12] S.R. Chemler, Copper catalysis in organic synthesis, *Beilstein J. Organic Chem.* **11** (2015) 2252-2253.
- [13] J., Fairoosa, M. Neetha, G. Anilkumar. Recent developments and perspectives in the copper-catalyzed multicomponent synthesis of heterocycles, *RSC Adv.* **11** (2021) 3452-3469.

- [14] D. Mulugeta, A review on recent trends in copper-catalyzed organic synthesis, *J. Environ. Chem. Eng.* **6** (2022) 24-33.
- [15] D. Saha, L. Adak, M. Mukherjee, B.C. Ranu, Hydroxyapatite-supported Cu(I)-catalysed cyanation of styrenyl bromides with $K_4[Fe(CN)_6]$: an easy access to cinnamitriles, *Org. Biomol. Chem.* **10** (2012) 952-957.
- [16] D. Saha, T. Chatterjee, M. Mukherjee, B.C. Ranu, Copper(I) hydroxyapatite catalyzed sonogashira reaction of alkynes with styrenyl bromides reaction of cis-styrenyl bromides forming unsymmetric diynes, *J. Organic Chem.* **77** (2012) 9379-9383.
- [17] P.K. Dutta, S. Sen, D. Saha, B. Dhar, Solid supported nano structured Cu-catalyst for solvent/ligand free C_2 amination of azoles, *Eur. J. Org. Chem.* (2018) 657-665.

Publisher's Note: Research Plateau Publishers stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.