Copper Ferrite Superparamagnetic Nanoparticle-Catalyzed Cross-coupling Reaction to Form Diindolylmethane (DIM): Effect of Experimental Parameters

Oanh T.K. Nguyen1,2,3,*, Ha Trong Pha1,2, Huynh Dang Khoa1,2, Duy Chinh Nguyen3,4, Nguyen Thi Hong Tham3,4

1Department of Chemical Engineering, Ho Chi Minh City University of Technology (HCMUT), 268 Ly Thuong Kiet Street, District 10, Ho Chi Minh City 700000, Vietnam
2Vietnam National University Ho Chi Minh City, Linh Trung Ward, Thu Duc District, Ho Chi Minh City 700000, Vietnam
3NTT Hi-Tech Institute, Nguyen Tat Thanh University, Ho Chi Minh City 700000, Vietnam
4Center of Excellence for Green Energy and Environmental Nanomaterials (CE@GrEEN), Nguyen Tat Thanh University, Ho Chi Minh City 700000, Vietnam.

Received: 22nd June 2020; Revised: 23rd July 2020; Accepted: 31st July 2020; Available online: 14th August 2020; Published regularly: December 2020

Abstract

Superparamagnetic copper ferrite (CuFe2O4) nanoparticles were utilized as a heterogenous catalyst for the cross-coupling reaction of indole to form 3,3'-diindolylmethane (DIM) as the desirable product. High reaction yield, at around 82%, was achieved under optimal conditions. The CuFe2O4 material could be easily separated from the reaction mixture by an external magnetic field and could be reutilized several times without a significant decrease in catalytic activity. We also showed that no sites of catalyst material leached into reaction solution was detected. To our best knowledge, the above cross-coupling reaction was not previously conducted under catalysis of superparamagnetic nanoparticles. Copyright © 2020 BCREC Group. All rights reserved

Keywords: CuFe2O4; superparamagnetic nanoparticles; heterogeneous catalyst; cross-coupling reaction; 3,3'-diindolylmethane (DIM)

How to Cite: Nguyen, O.T.K., Pha, H.T., Khoa, H.D., Nguyen, D.C., Tham, N.T.H. (2020). Copper Ferrite Superparamagnetic Nanoparticle-Catalyzed Cross-coupling Reaction to Form Diindolylmethane (DIM): Effect of Experimental Parameters. Bulletin of Chemical Reaction Engineering & Catalysis, 15(3), 631-640 (doi:10.9767/bcrec.15.3.8228.631-640)

Permalink/DOI: https://doi.org/10.9767/bcrec.15.3.8228.631-640

1. Introduction

3,3'-Diindolylmethane (DIM) is a dimeric product of 3-indolemethanol, generated from acidic medium and consists of bis-indole moiety [1]. DIM has been shown to hold potential applications in treatment of thyroid proliferative disease via promotion of estrogen metabolism [2] and in induction of apoptosis of prostate cancer cells in mouse model [3]. DIM is also an important metabolite that exhibits potential anticancer properties and is produced from the consumption of indole-3-carbinol, a compound cre-
activated from the glycoside glucobrassicin, which widely exists in cruciferous vegetables such as broccoli, brussel sprouts, and cauliflower [4]. In addition, DIM was shown to possess multiple useful bioactivities including antioxidant [5], anti-inflammatory [6], antiangiogenic [7], and anticancer activities [8].

DIM was previously synthesized using different routines and catalysts. Chen et al. [9] and Qi et al. [10] reported the production of DIM from indole in methanol solvent with the presence of homogeneous catalyst (Ir) in the air. Similarly, Zhang et al. [11] demonstrated that the derivative of DIM can be synthesized by using tetramethylthlenediamine (TMEDA) as a methane corner supplier with Cu(II) catalyst reaction at 120 °C, reflux module and MeCN solvent. Pu et al. [12] reported an efficient synthesis procedure in which indole ice DIM was produced with solvent of N,N-dimethylformamide (DMF), 10 mol% CuCl catalyst, temperature of 140 °C for 14 hours in the presence of tert-butyl hydroperoxide (TBHP) as an oxidant. Despite the high reaction efficiency and selectivity, all aforementioned studies utilized homogeneous catalysts in DIM production, presenting difficulty in catalyst recovery and going against the emergent trend of green chemistry.

Over the last years, research on nanoparticles of metal based materials has attracted much consideration due to their interesting properties, such as: superparamagnetism and ease of separability, and potential applications in a wide range of fields [13–15]. In the field of catalysis, copper ferrite nanoparticles have been used as a catalyst for a wide range of organic transformations [16–18]. Among these heterogeneous catalysts, functionalized metal oxide-based catalysts were used in most cases [19–21]. One notable application of copper ferrite has been reported by Prakash et al., in which CuFe$_2$O$_4$ nanoparticles were assembled on carbon nanotubes, affirming a nanohybrid catalyst that facilely promoted the Huisgen 1,3-cycloaddition of terminal alkynes with in situ generated organic azide under very mild operating conditions [22]. In another application, copper ferrite was doped with cerium to produce a nanocrystalline catalyst that was capable of inducing strong photodegradation of methyl orange under UV light [23]. It has been recently reported that unfunctionalized CuFe$_2$O$_4$ superparamagnetic nanoparticles could be also active in organic reactions with high catalytic activity and selectivity [24–26]. In our previous study, we developed a copper ferrite-catalyzed cross-coupling reaction that used TBHP as oxidant to form DIM and investigated the effects of various indole substituents on the reaction yield [27]. Continuing this research pathway, in this study, we wish to report a similar DIM-forming dimeric reaction of indole and determined optimal experimental conditions (temperature, catalyst amount, solvent type, solvent amount, oxidant type and oxidant amount) that gave highest reaction yield.

## 2. Materials and methods

### 2.1 Materials and Instrumentation

Chemicals used in this study were commercially obtained and used as received without further purification. X-ray diffraction method (XRD) was measured on D8 advance device (Bruker) using Cu-Kα emission source (λ = 1.54 Å). Recording of transmission electron microscopy images was carried out utilizing JEOL-JEM-1400 device at 80 kV.

Samples taken from reaction mixture were analyzed on Shimadzu GC 2010-Plus chromatograph using flame ionization detector (FID). The column used for analysis is SPB-5 column (length 30m × internal diameter 0.25 mm x film thickness 0.25 µm). The temperature program for gas chromatographic analysis is as follows: the initial temperature was held at 100 °C for 1 minute, subsequently heated from 100 °C to 280 °C at 30 °C/min and then held again for 15 minutes. The injection chamber temperature was kept fixed at 280 °C. Diphenyl ether is used as an internal standard. NMR spectra (1H and 13C) were measured using Bruker AV 500 equipment operating at 500 MHz when measuring 1H and at 125 MHz when measuring 13C. The standard is Tetramethylsilane.

### 2.2 Catalytic Studies

In a typical experiment, the reaction is carried out in the reaction flask (special glass vial with a volume of 8 mL). The mixture includes: CuFe$_2$O$_4$ catalyst (0.05 mmol), indole (0.5 mmol), internal standard diphenyl ether (0.025 mmol), TBHP (1.5 mmol) as an oxidant, and N,N-dimethylacetamide (DMAC) (1.5 mL) as solvent. The flask was sealed in air and heated at 140 °C for 24 hours. The efficiency of the reaction was monitored by taking 0.1 mL of the reaction mixture after the reaction had completed and dissolving it with a mixture of solution including distilled water (1 mL) and ethyl acetate (2 mL). The ethyl acetate soluble fraction was anhydrous with Na$_2$SO$_4$ salt and ana-
lyzed by GC. The structure of the product was characterized by GC-MS, 1H-NMR, and 13C-NMR. The recyclability of CuFe2O4 was examined by removing the liquid phase of reaction mixture by an external magnetic field. The catalytic material was washed with large amounts of distilled water, ethanol, ethyl acetate, and acetone, separated by an external magnetic field, and dried under a vacuum at 150 °C for 180 min. For investigation of leaching test, the synthesis reaction was stopped after one hour, analyzed by GC, and had catalytic material removed. The reaction mixture was then carried out for a further 7 hours. Reaction proceeding, if any, was controlled by GC analysis.

3. Results and Discussions

3.1 Characterization of CuFe2O4 Catalyst

The CuFe2O4 superparamagnetic nanoparticles were determined by various techniques. Figure 1 showed that XRD patterns of the CuFe2O4 are consistent with the standard XRD patterns JCPDS 01-077-0010 [28]. Transmission electron microscopy (TEM) revealed that most of the particles are spherical and have the size that is uniform and in the range of 20-50 nm (Figure 2).

3.2 The Synthesis of 3,3'-diindolylmethane

In the following optimization studies, the catalytic activity of CuFe2O4 material was determined in the cross-coupling reaction of indole in the DMAC solvent to form 3,3'-diindolylmethane as the major product (Scheme 1). Its structure was determined by 1H NMR, and 13C NMR. In this reaction, TBHP could be used as an oxidant.

Temperature is the first important factor that determines reaction yield. The reaction was performed in 1.5 mL DMAC solvent with

Figure 1. XRD diagram of the CuFe2O4.

Figure 2. TEM micrograph of the CuFe2O4.

Figure 3. Effect of temperature on the reaction conversion.

Scheme 1. The cross-coupling reaction of indole in N,N-dimethylacetamide solvent using CuFe2O4 catalyst.
indole (0.5 mmol), utilizing 3 equivalents TBHP as a oxidant for 24 hours, with 10 mol% CuFe$_2$O$_4$ catalyst at varying temperatures including room temperature, 60, 80, 100, 120, and 140 °C. From the Figure 3, it was shown that the reaction did not take place at temperature lower than 60 °C. At 80 °C and 100 °C, the reaction seemed to be relatively inefficient, resulting in reaction yields of around 45% after 24 hours. However, as the temperature was elevated to 140 °C, an outstanding enhancement in reaction yield was observed, achieving around 77% yield after 24 hours. The temperature at which this reaction was previously carried out varied depending on the catalytic nature, ligand as well as the used substances. In particular, lower reaction temperature seemed to necessitate longer reaction time, which could be more than 48 hours [29]. Therefore, this reaction is considered as a high temperature reaction, usually performed in the temperature range of 110 °C to 160 °C for many different catalytic systems [12,30,31].

For an organic transformation utilizing a heterogenous catalyst, the amount of used catalyst is an important determinant of yield. The reaction was performed in 1.5 mL DMAC solvent with indole (0.5 mmol), utilizing 3 equivalents TBHP as an oxidant at 140 °C for 24 hours, with the presence of varying amounts of CuFe$_2$O$_4$ catalyst of 2.5, 5, 7.5, 10, 12.5 and 15 mol% (Figure 4). It was observed that the catalyst quantity of 7.5 mol% could afford 70% reaction yield, while up to 82% reaction yield was obtained with 15 mol% of catalyst after 24 hours. The control experiment was performed without copper ferrite nanoparticles, resulting the reaction yield of around 7%. Therefore, the amount of catalyst of 15 mol% was selected as optimal. In fact, the used catalyst quantity of 15 mol% is not very substantial and is very common for oxide-type catalysts. For example, copper-iron and copper oxide catalysts were previously used in organic synthesis with the amount ranging from 10 to 20 mol% [17,32,33]. Furthermore, the catalyst quantity of 15 mol% is not considerably higher than those of studies that aim to form 3.3-Diindolylmethane compound with indole derivatives, including those involving homogeneous catalyst systems with complex ligands where a catalyst amount of 10 mol% was still used [34,35].

The amount of used solvent is another crucial factor that also significantly affect the conversion and determination of optimal solvent use is essential to justify the economic efficiency of the reaction. The reaction was conducted at 140 °C in 24 hours, with the presence of 15 mol% CuFe$_2$O$_4$ catalyst using 3 equivalents of TBHP.
TBHP as an oxidant and in the different solvent ratios of DMAC including 1, 1.5, 2, 2.5 and 3 mL (Figure 5). The results show that the solvent volume of 1.5 mL gave the highest efficiency of 82%. Afterwards, increasing the volume of used solvent seemed to reduce the reaction yield. This suggests that 1.5 mL of solvent is optimal to efficiently convert 0.5 mmol of indole through this reaction. The trend could be obviously explained by the reduced interaction of substances containing in the diluted reaction medium, which greatly affects the reaction efficiency. The reported solvent use in this study is consistent with results of most other studies on the synthesis of DIM compounds where the maximum quantity of the used solvent was 3 mL [35,36].

In the following survey, the amount of oxidant was examined with respect to reaction yield. The reaction was performed at 140 °C for 24 hours, with 15 mol% CuFe\textsubscript{2}O\textsubscript{3} catalyst, utilizing the various oxidant amounts of 0.5 equiv, 1 equiv, 2 equiv, 3 equiv, and 4 equiv (Figure 6). Noticeable improvement in yield was observed when increasing the TBHP amount from 0.5 to 1 equiv. However, increasing the amount of TBHP from 1 equiv to 2 equiv only caused the reaction yield to slightly improve by approximately 2%. Therefore, the amount of oxidant used in the cross-coupling reaction was selected at around 1 equiv. This result is relatively consistent with some previous studies on DIM compounds [30,37]. In addition, the use of oxidant at a ratio of 1:1 compared to indole was able to achieve almost complete conversion and selectivity up to 82% after 24 hours, so the investigation of the use of oxidant at larger concentrations is not strictly necessary.

To gain further insights into feasibility of the use of TBHP in this reaction, we compared the yields obtained using different oxidants in the following survey (Figure 7). The results showed that the reaction yield achieved when using TBHP, at 82%, far surpassed that obtained using DTBP or 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO). Additionally, the reaction did not seem to occur with O\textsubscript{2}, Ar or no oxidant. This is consistent with results of previous studies which indicated that the reaction only occurs with the presence of radicals as reaction intermediates [12,34,36].
The effect of used solvent was examined by comparing yields obtained with different solvents. The synthetic reaction of DIM product was conducted at 140 °C in 1.5 mL of solvent for 24 hours, with 15 mol% CuFe₂O₄ catalyst using 1 equivalent of TBHP as an oxidant, with various solvents (Figure 8). The results showed that the performance varied greatly between different types of solvents. In general, polar solvents, such as: DMAC, DMF and γ-alumina (NMA), produced much higher efficiencies compared to less polar solvents, such as: 1,4-dioxane, m-xylene and p-xylene. The DMAC solvent gave the highest reaction efficiency of around 82% yield.

To justify the use of CuFe₂O₄ superparamagnetic nanoparticles in the reaction, we carried out the reaction at 140 °C in 1.5 mL of solvent for 24 hours, with the presence of various homogenous and heterogenous catalysts. The results shown in Figure 9 illustrated that among homogenous catalysts, Cu(CH₃COO)₂.H₂O gave the highest efficiency of 76%. However, comparing with results of heterogeneous catalysts, this yield was still lower than that achieved with CuFe₂O₄ catalyst, at 82%. The results shown in Figure 10 also illustrated that other types of magnetic nanoparticle are not as effective as CuFe₂O₄ superparamagnetic nanoparticle in catalyzing the cross-coupling reaction. It is worth noting that all examined metal–organic framework (MOF) materials resulted in very high yields in which the outstanding efficiency, at 91%, was achieved when using MOF-199. However, the use of MOFs is not in line with the objective of this study, which is to identify a catalyst that is environmentally friendly, re-recyclable, highly heat-resistant and easily recoverable with an external magnetic field. Moreover, it is speculated that MOF materials often exhibit poorer thermal stability than magnetic materials. As such, as the reaction was carried out under elevated temperatures, part of the material core and ligand existing in the reaction media may impair the reaction efficiency. Based on the heterogeneous catalyst property, CuFe₂O₄ material is a suitable catalyst for reaction in this study.

The dissolution of active sites on the heterogeneous catalyst into the solution occurring during the reaction might affect recoverability, selectivity and reusability of the used catalyst. To determine whether the dissolution of active sites of the CuFe₂O₄ catalyst contributed to the generation of desired product, an experiment under optimal conditions was performed with the magnetic separation of catalyst (leaching test). The reaction was carried out at 140 °C in DMAC solvent for 24 hours, utilizing indole (0.5 mmol) with one equivalent of TBHP as oxidant and the presence of 15 mol% CuFe₂O₄ catalyst. After 60 minutes reaction time, the DMAC phase was separated from the reaction solution by an external magnetic field, transferred to a new round bottom flask, which was heated for 7 hours at 140 °C. As indicated in the graph (Figure 11), generation of 3,3’-diindolylmethane ceased after the CuFe₂O₄ catalyst had been removed from the reaction.

![Figure 10](image1.png)

**Figure 10.** Effect of heterogenous catalysts on the reaction yield.

![Figure 11](image2.png)

**Figure 11.** Leaching test showing no contribution from homogeneous catalyst of active species leaching into reaction solution.
mixture at the one-hour mark. These results indicated that presence of the CuFe₂O₄ catalyst is a prerequisite for this reaction to take place and the leaching of active copper species into the solution was almost nonexistent, thus making no significant contribution to the yield.

To justify organic reactions utilizing heterogeneous catalysts in development of more environmentally benign processes, the facileness of separation as well as the recoverability and reusability of the catalysts should be taken into account. The CuFe₂O₄ was therefore studied for the recoverability and reusability in the cross-coupling reaction. The reaction was performed at 140 °C in DMAC solvent for 24 hours, using indole (0.5 mmol) with one equivalent of TBHP as an oxidant, with 15 mol% CuFe₂O₄ catalyst. After the first run, the CuFe₂O₄ catalyst was removed from the reaction solution by an external magnetic field, washed with large amounts of distilled water, ethanol, ethyl acetate, and acetone to remove any physisorbed reagents, dried at 140 °C under vacuum in 180 min, and reutilized in further reactions with conditions identical to those of the first run. It was illustrated that the CuFe₂O₄ catalyst could be recovered and reutilized nine times in the cross-coupling reaction without significant compromise of catalytic activity. Evidently, the yield of 3,3'-diindolylmethane still reached 74% after eight runs, which is 8 percent point lower than the yield achieved at the first run (Figure 12). The recoverability of the CuFe₂O₄ catalysts before and after nine runs was illustrated by XRD diffractograms (Figure 13), indicating that crystal morphology of the CuFe₂O₄ material was almost unchanged after eight times of reuse.

4. Conclusion

In this study, the CuFe₂O₄ nanoparticles were used as heterogeneous catalyst for the cross-coupling reaction of indole to create 3,3'-diindolylmethane as the major product. The optimal conditions that gave the highest yield consisted of TBHP as oxidant in DMAC solvent, temperature of 140 °C, reaction time of 24 hours and catalyst quantity of 15 mol%. The CuFe₂O₄ demonstrated higher catalytic activity in the cross-coupling reaction than other magnetic heterogeneous catalysts, such as: CoFe₂O₄, NiFe₂O₄, Fe₃O₄, and Fe₂O₃. We also further confirmed that the reaction could only proceed to create 3,3'-diindolylmethane in the presence of the CuFe₂O₄ catalyst and that the contribution from leached active sites of the CuFe₂O₄ catalyst was negligible. Furthermore, the CuFe₂O₄ nanoparticles could be easily removed from the reaction solution by an external magnetic field and could be reutilized for nine times with only minor loss of catalytic activity.

Acknowledgement

We would like to give my sincerest thank to Department of Chemical Engineering, Ho Chi Minh City University of Technology for providing us with facilities and chemicals to carry out experiments.

Author Contributions

Investigation, Oanh Nguyen T. K., Trong Pha Ha, Dang Khoa Huynh and Hong Tham Nguyen Thi; Supervision, Van Tan Lam; Writing – original draft, Oanh Nguyen T. K.; Writing – review & editing, Duy Chinh Nguyen.

Figure 12. Catalyst recycling studies.

Figure 13. X-ray powder diffractograms of the CuFe₂O₄ fresh (red) and CuFe₂O₄ reutilizing (black).
References

[1] Roy, S., Gajbhiye, R., Mandal, M., Pal, C., Meyyapan, A., Mukherjee, J., Jaisankar, P. (2014). Synthesis and antibacterial evaluation of 3,3′-diindolylmethane derivatives. Medicinal Chemistry Research, 23(3), 1371–1377. DOI: 10.1007/s00044-013-0737-7

[2] Rajoria, S., Suriano, R., Parmar, P.S., Wilson, Y.L., Megwulu, U., Moscatello, A., Bradlow, H.L., Sepkovic, D.W., Geliebter, J., Schantz, S.P., Tiwari, R.K. (2011). 3,3′-diindolylmethane modulates estrogen metabolism in patients with thyroid proliferative disease: A pilot study. Thyroid, 21(3), 299–304. DOI: 10.1089/thy.2010.0245

[3] Cho, H.J., Park, S.Y., Kim, E.J., Kim, J.-K., Park, J.H.Y. (2011). 3,3′-diindolylmethane inhibits prostate cancer development in the transgenic adenocarcinoma mouse prostate model. Molecular Carcinogenesis, 50(2), 100–112. DOI: 10.1002/mc.20698

[4] Zhang, W. W., Feng, Z., Narod, S.A. (2014). Multiple therapeutic and preventive effects of 3,39-diindolylmethane on cancers including prostate cancer and high grade prostatic intraepithelial neoplasia. Journal of Biomedical Research, 28(5), 339–348. DOI: 10.7555/JBR.28.20140008

[5] Jayakumar, P., Pugalendi, K.V., Sankaran, M. (2014). Attenuation of hyperglycemia-mediated oxidative stress by indole-3-carbinol and its metabolite 3,3′-diindolylmethane in C57BL/6J mice. Journal of Physiology and Biochemistry, 70(2), 525–534. DOI: 10.1007/s13105-014-0332-5

[6] Cho, H.J., Seon, M.R., Lee, Y.M., Kim, J., Kim, J.-K., Kim, S.G., Park, J.H.Y. (2008). 3,3′-diindolylmethane suppresses the inflammatory response to lipopolysaccharide in murine macrophages. The Journal of Nutrition, 138(1), 17–23. DOI: 10.1093/jn/138.1.17

[7] Kunimasa, K., Kobayashi, T., Kaji, K., Ohta, T. (2010). Antiangiogenic effects of indole-3-carbinol and 3,3′-diindolylmethane are associated with their differential regulation of erk1/2 and akt in tube-forming hucce. The Journal of Nutrition, 140(1), 1–6. DOI: 10.3945/jn.109.112359

[8] Zong, J., Wu, Q.-Q., Zhou, H., Zhang, J.-Y., Yuan, Y., Bian, Z.-Y., Deng, W., Dai, J., Li, F.-F., Xu, M., Fang, Y., Tung, Q.-Z. (2015). 3,3′-Diindolylmethane attenuates cardiac H9c2 cell hypertrophy through 5′-adenosine monophosphate-activated protein kinase. Molecular Medicine Reports, 12(1), 1247–1252. DOI: 10.3892/mmr.2015.3523

[9] Chen, S.-J., Lu, G.-P., Cai, C. (2015). Iridium-catalyzed methylation of indoles and pyrroles using methanol as feedstock. RSC Advances, 5(86), 70329–70332. DOI: 10.1039/C5RA15822B

[10] Qiang, W., Liu, X., Loh, T.-P. (2019). Supported iridium catalyst for the green synthesis of 3,3′-bis(indolyl)methanes using methanol as the bridging methane source. ACS Sustainable Chemistry & Engineering, 7(9), 8429–8439. DOI: 10.1021/acsuschemeng.9b00094

[11] Zhang, L., Peng, C., Zhao, D., Wang, Y., Fu, H.-J., Shen, Q., Li, J.-X. (2012). Cu(i)-catalyzed C–H (sp3) oxidation and C–N cleavage: Base-switched methylation and formylation using tetramethylethlenediamine as a carbon source. Chemical Communications, 48(47), 5928–5930. DOI: 10.1039/c2cc32009f

[12] Pu, F., Li, Y., Song, Y.-H., Xiao, J., Liu, Z.-W., Wang, C., Liu, Z.-T., Chen, J.-G., Lu, J. (2016). Copper-catalyzed coupling of indoles with dimethylformamide as a methylenating reagent. Advanced Synthesis & Catalysis, 538(4), 53–90–542. DOI: 10.1002/ads.201500874

[13] Phan, N.T.S., Gill, C.S., Nguyen, J.V., Zhang, Z.J., Jones, C.W. (2006). Expanding the utility of one-pot multistep reaction networks through compartmentation and recovery of the catalyst. Angewandte Chemie International Edition, 45(14), 2209–2212. DOI: 10.1002/anie.200503445

[14] Hudson, R., Ishikawa, S., Li, C.-J., Moores, A. (2013). Magnetically recoverable cufe2o4 nanoparticles as highly active catalysts for csp3-csp and csp3-csp3 oxidative cross-dehydrogenative coupling. Synlett, 24(13), 1637–1642. DOI: 10.1055/s-0033-1339278

[15] Sivakami, R., Babu, S.G., Dhanuskodi, S., Karvembu, R. (2015). Magnetically retrievable lepidocrocite supported copper oxide nanoparticles as highly active catalysts for the bridging methylene source. RSC Advances, 5(12), 8571–8578. DOI: 10.1039/C4RA13256D

[16] Polshettiwar, V., Luque, R., Fihri, A., Zhu, H., Bouhrara, M., Basset, J.-M. (2011). Magnetically recoverable nanocatalysts. Chemical Reviews, 111(5), 3036–3075. DOI: 10.1021/cr100230z

[17] Yang, D., Zhu, X., Wei, W., Jiang, M., Zhang, N., Ren, D., You, J., Wang, H. (2014). Magnetic copper ferrite nanoparticles: An inexpensive, efficient, recyclable catalyst for the synthesis of substituted benzoxazoles via Ullmann-type coupling under ligand-free conditions. Synlett., 25(05), 729–735. DOI: 10.1055/s-0033-1340599
Satisf, G., Reddy, K.H.V., Ramesh, K., Kumar, B.S.P.A., Nageswar, Y.V.D. (2014). An elegant protocol for the synthesis of N-substituted pyrroles through C–N cross coupling/aromatization process using CuFe2O4 nanoparticles as catalyst under ligand-free conditions. Tetrahedron Letters, 55(16), 2596–2599. DOI: 10.1016/j.tetlet.2014.01.075

Lu, A.-H., Salabas, E.-L., Schüth, F. (2007). Magnetic nanoparticles: Synthesis, protection, functionalization, and application. Angewandte Chemie International Edition, 46(8), 1222–1244. DOI: 10.1002/anie.200602866

Vásquez-Céspedes, S., Holtkamp, M., Karst, U., Glorius, F. (2017). Reusable and magnetic palladium and copper oxide catalysts in direct ortho and meta arylation of aniline derivatives. Synlett, 28(20), 2758–2764. DOI: 10.1055/s-0036-1589007

Zhang, W., Tian, Y., Zhao, N., Wang, Y., Li, J., Wang, Z. (2014). Nano CuO-catalyzed C–H functionalization of 1,3-azoles with bromo arenes and bromo alkenes. Tetrahedron, 70(36), 6120–6126. DOI: 10.1016/j.tet.2014.04.065

Prakash, P., Kumar, R.A., Miserque, F., Geertsen, V., Gravel, E., Doris, E. (2018). Carbon nanotube–copper ferrite-catalyzed aqueous 1,3-dipolar cycloaddition of in situ generated organic azides with alkanes. Chemical Communications, 54(29), 3644–3647. DOI: 10.1039/C8CC00231B

Rahimi-Nasrabadi, M., Behpour, M., Sobhani-Nasab, A., Jedd, M.R. (2016). Nanocrystalline Ce-doped copper ferrite: Synthesis, characterization, and its photocatalyst application. Journal of Materials Science: Materials in Electronics, 27(11), 11691–11697. DOI: 10.1007/s10854-016-5305-8

Al-Hunaiti, A., Al-Said, N., Halawani, L., Haija, M.A., Baqien, R., Taher, D. (2020). Synthesis of magnetic CuFe2O4 nanoparticles as green catalyst for toluene oxidation under solvent-free conditions. Arabian Journal of Chemistry, 13(4), 4945–4953. DOI: 10.1016/j.arabjc.2020.01.017

Nguyen, O.T.K., Nguyen, L.T., Truong, N.K., Nguyen, V.D., Nguyen, A.T., Le, N.T.H., Le, D.T., Phan, N.T.S. (2017). Synthesis of triphenylamines via ligand-free selective ring-opening of benzoazoles or benzothiazoles under superparamagnetic nanoparticle catalysis. RSC Advances, 7(65), 40929–40939. DOI: 10.1039/C7RA06168D

Nguyen, O.T.K., Ha, P.T., Dang, H.V., Vo, Y.H., Nguyen, T.T., Le, N.T.H., Phan, N.T.S. (2019). Superparamagnetic nanoparticle-catalyzed coupling of 2-amino pyridines/pyrimidines with trans-chalcones. RSC Advances, 9(10), 5501–5511. DOI: 10.1039/C9RA00097F

Ha, P., Nguyen, O., Huynh, K., Nguyen, T., Phan, N. (2018). Synthesis of unnatural arunines using a magnetically reusable copper ferrite catalyst. Synlett, 29(15), 2031–2034. DOI: 10.1055/s-0037-1610227

Tasca, J.E., Ponzinibbio, A., Diaz, G., Bravo, R.D., Lavat, A., González, M.G. (2010). CuFe2O4 nanoparticles: A magnetically recoverable catalyst for selective deacetylation of carbohydrate derivatives. Topics in Catalysis, 53(15–18), 1087–1090. DOI: 10.1007/s11244-010-9538-0

Pillaiyar, T., Gorska, E., Schnakenburg, G., Müller, C.E. (2018). General Synthesis of Unsymmetrical 3,3’-(Aza)diindolylmethane Derivatives. The Journal of Organic Chemistry, 83(17), 9902–9913. DOI: 10.1021/acs.joc.8b01349

Kaswan, P., Nandwana, N.K., DeBoe, B., Kumar, A. (2016). Vanadyl acetylacetonate catalyzed methylenation of imidazo[1,2-\alpyridines by using dimethylacetamide as a methane source: Direct access to bis[imidazo[1,2-\alpyridin-3-yl]methanes. Advanced Synthesis & Catalysis, 358(13), 2108–2115. DOI: 10.1002/adsc.201600225

Deb, M.L., Borpatra, P.J., Pegu, C.D., Thakuria, R., Saikia, P.J., Baruah, P.K. (2017). Indole/ tert -butyl hydroperoxide-mediated reaction of indoles with dimethylformamide/dimethylacetamide to synthesize bis- and tri(Nindolyl)methanes. ChemistrySelect, 2(1), 140–146. DOI: 10.1002/slct.201601857

Panda, N., Jena, A.K., Mohapatra, S., Rout, S.R. (2011). Copper ferrite nanoparticle-mediated N-arylation of heterocycles: A ligand-free reaction. Tetrahedron Letters, 52(16), 1924–1927. DOI: 10.1016/j.tetlet.2011.02.050

Rosario, A.R., Casola, K.K., Oliveira, C.E.S., Zeni, G. (2013). Copper oxide nanoparticle-catalyzed chalcogenation of the carbon-hydrogen bond in thiazoles: Synthesis of 2-(Organochalcogen)thiazoles. Advanced Synthesis & Catalysis, 355(14–15), 2960–2966. DOI: 10.1002/adsc.201300497

Deb, M.L., Borpatra, P.J., Saikia, P.J., Baruah, P.K. (2017). Introducing tetra-methylene as a new methylene precursor: A microwave-assisted RuCl3-catalyzed cross dehydrogenative coupling approach to bis(Indolyl)methanes. Organic & Biomolecular Chemistry, 15(6), 1435–1443. DOI: 10.1039/C6OB02671K
[35] Modi, A., Ali, W., Patel, B.K. (2016). N,n-dimethylacetamide (DMA) as a methylene synthon for regioselective linkage of imidazo[1,2-α]pyridine. *Advanced Synthesis & Catalysis, 358*(13), 2100–2107. DOI: 10.1002/adsc.201600067

[36] Mondal, S., Samanta, S., Santra, S., Bagdi, A. K., Hajra, A. (2016). n,n-dimethylformamide as a methylenating reagent: Synthesis of heterodiarylmethanes via copper-catalyzed coupling between imidazo[1,2-α]pyridines and indoles/n,n-dimethylaniline. *Advanced Synthesis & Catalysis, 358*(22), 3633–3641. DOI: 10.1002/adsc.201600674

[37] Srivastava, A., Agarwal, A., Gupta, S.K., Jain, N. (2016). Graphene oxide decorated with Cu(I)Br nanoparticles: A reusable catalyst for the synthesis of potent bisme(Indolyl)thane based anti HIV drugs. *RSC Advances, 6*(27), 23008–23011. DOI: 10.1039/C6RA02458K