Grignard-type reaction of phenylacetylene with aldehydes was performed by Bimetallic Metal-Organic Frameworks (Ni/Fe-Base) catalyst in water

O T K Nguyen¹*, H. T. Vu², Q H Tran³, B T Hoang⁴, S. T. Do⁴

¹Center of Excellence for Green Energy and Environmental Nanomaterials, Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam.
²Faculty of Hydro-Meteorology, HCMC University of Natural Resources and Environment, Viet Nam
³Laboratory of Material and Environment Technology, Institute of Chemistry, Vietnam Academy of Science and Technology, Hanoi City, Viet Nam
⁴Institute of Natural Products Chemistry, Vietnam Academy of Science and Technology, Hanoi, Vietnam

*ntkoanh@ntt.edu.vn

Abstract. A Grignard-type reaction of terminal alkyls and aldehydes were grown via alkyl C–H activation under water media catalyzed by a bimetallic Ru–In system. Nevertheless, a mixture homogeneous catalyst was hardly recycled after carrying a reaction. In this research, we wish to show that by utilizing a bimetallic Ni/Fe-BDC catalytic system which was synthesized by the solvothermal method, it was suggested that an aqueous media Lewis acid catalyst is commanded to activate the carbonyl group. A crucial observation of those inspections showed that while the alkynes were changed into a scope of products (approx. 78% of yield), the aldehyde did not take part in the reaction. The feature of products was substantiated by utilizing NMR spectra and GC-MS. The shape of solid catalyst was confirmed by utilizing a variety of modern technologies, consisting of XRD (X-ray diffraction), TEM (Transmission Electron Microscopy), TGA (Thermogravimetric Analysis), FT-IR (Fourier Transform Infrared) and \( \text{N}_2 \) physisorption measurements BET (Brunauer-Emmett-Teller). The Ni/Fe-BDC material might be simply separated from the reaction compound and could be reused without a notable drop in catalytic activity.

1. Introduction
Recently, reactions to build carbon frames from simple molecules through transition metal catalysts have been attracting the attention of the scientific community for many years, widely used in the industry produces high-quality chemicals as well as high-performance technical materials. Reaction to form carbon-carbon bonds often uses transition metal catalysts in homogeneous or heterogeneous formations, in which heterogeneous catalysts are being considered due to easier separation and purification of the product, as well as heterogeneous catalysts will be able to recover and reuse better. Today, research groups are gradually reducing or eliminating the utilize or creation of toxic agents in the plan and production process, and these are significant efforts that have been made to develop chemical technologies and utilize of chemie products and green chemistry processes [1]. The creations of C–C bonds via metal mediated are among the best crucial reactions in organic synthesis [2].
development of Barbier-Grignard-type reactions in aqueous media has been significant recent consideration [3]. Those problems which were interested showed evidently in the figure of topical and fantabulous reviews that have explained the benefits of utilizing water organometallic reactions over those happening in an organic solvent, in synthesis [4]. Besides, the mixtures which diluted with water such as carbohydrates reaction may directly occur for lack of derivatization, and the catalyst which diluted in water can be reutilized for an elongated period [5]. Nevertheless, while the alkylation, arylation, and alkynylation of carbonyl mixtures, in company with the aldol kind reaction, have been flourishing with various metals in water, an high yield Barbier-Grignard-type carbonyl alkylation with no activated halides in water has still to be progressed [6].

Recently, Chao-Jun Li et al. represented a Grignard-type reaction of alkynes and aldehydes to create propargyl alcohols by catalyst C–H activation in aqueous media [1]. A similar crucial reaction is the appropriating supplement of alkynes and imines, to create propargyl amines [7]. In 2008, Zhi-Liang Shen et al. reported an efficient process for the Grignard-type alkylation reaction of aldehydes utilizing nonactivated alkyl halides in aqueous with the attendance of a catalyst compound including In/Cu/I2 or In/Ag/I2 [8]. Additionally, in 2002, Chao-Jun Li et al. and Chunmei Wei et al. have demonstrated that Grignard type reaction has highly efficient via C–H activation in aqueous media with the presence of the phenylacetylene and imines, or phenylacetylene and benzaldehyde.

In this study, we illustrated that the heterogeneous catalyst of Ni/Fe-BDC was catalyzed for Grignard type reaction between phenylacetylene and benzaldehyde in the water solvent, and the catalyst may be reused many times after performing the reaction.

2. Experimental section

2.1. Preparation of Ni/Fe-BDC catalyst

Materials Ni/Fe-BDC were synthesized by hydrothermal method, according to the calibrated process of Vinh Huu Nguyen et al. [11]. Accordingly, the mixture of terephthalic acid (H2BDC, 1.494 gram, 9 mmol), FeCl3·6H2O (1.244 gram, 4.6 mmol) and Ni(NO3)2·6H2O (0.407 gram, 1.4 mmol) were dissolved in the solvent of N,N-dimethylformamide (DMF, 60 mL). The compound was stirred about 30 minutes to create homogeneous mixtures. The mixture was added to the autoclave Teflon and heated at 100 °C within 3 days. Finally, the orange solid material collected and dried at 60 °C for 24 hours, yielding 0.8525 g of Ni/Fe-BDC material.

2.2. The general process for the synthesis of 1,3-diphenylprop-2-yn-1-ol

The selected Ni/Fe-BDC material catalyzed the Grignard type reaction via C-H bond activation of benzaldehyde and phenylacetylene. In a typical reaction process, a compound of benzaldehyde (0.2 mmol, 0.0212g), phenylacetylene (0.3 mmol, 0.0306g) were dissolved in 1 mL of 5% aqueous K2CO3 (wt%) with the presence of 20 mol% of Ni/Fe-BDC material. Afterward, the compound was stirred and heated at 80 °C for 20 hours, until the absolute consumption of benzaldehyde as observed by TLC. After the reaction was finished, the compound was cooled to ambient temperature, and attenuated in ethylacetate and washed with water. The organic constituent which made to loss water over anhydrous Na2SO4, segregated and the solvent was evaporated under decrease pressure. The raw material was isolated by silica column chromatography (with the solvent compound of ethylacetate/ hexane = 1/3) to achieve the desired product and determined by 1H-NMR, 13C-NMR spectra.

Prepared as shown in the general experimental procedure and purified on silica gel (hexane/ethyl acetate = 1:2): white solid, 78% yield. 1H-NMR (500 MHz, CDCl3) δ 7.58 – 7.53 (m, 2H), 7.44-7.36 (m, 8H), 5.61 (s,1H), 3.70 (s, 1H); 13C-NMR (125 MHz, CDCl3) δ 139.9, 128.9, 128.4, 128.3, 127.6, 127.1, 122.7, 89.4, 86.4, 61.3.

3. Results and discussion

3.1. Characteristic of Ni/Fe-BDC catalyst
The synthesis of Ni/Fe-BDC material was characterized by some technologies, consisting of XRD, FT-IR, Raman, and SEM (Refer figure 1). Especially, X-ray diffraction is one of the essential methods to test the crystallinity of synthetic materials. The result of the powder X-ray diffraction of Ni/Fe-BDC is described in figure 1A. This result illustrated that a characteristic sharp peak at 20 = 7.6° and 9.2°, which proves that Ni/Fe-BDC has a stable crystalline and compatible with previous report [12][11]. FT-IR analyzed the result of Ni/Fe-BDC catalyst illustrated that it has a sharp peak at 1680 cm⁻¹ which is a characteristic peak of C=O group of carboxylate, compared with H₂BDC acid, this group is located at 1684 cm⁻¹ [13]. The wide ranges at 3500 – 3175 cm⁻¹ indicate the presence of moisture in the material block; the measurement results are shown in figure 1B. Figure 1C shows the Raman spectra of Ni/Fe-BDC material, which is an apparent characteristic peak at 1140 cm⁻¹. This result showed that is allocated to the vibration of C–C in the carboxylate group and the benzene ring. Besides, the vibrations around 1445 cm⁻¹ and 1501 cm⁻¹ can be to distribute the oscillation of COO⁻ bond in the carboxylate group. This result can additionally explain the material structure of Ni/Fe-BDC. In additionally, morphology, size, and regularity of catalyst sample were studied by SEM image (Refer figure 1D). The SEM micrograph indicated the formation of uniform micro-size hexagonal rods and applicable with the result of previous literature [14].

Figure 1. Shown in X-ray powder diffraction (A), FT-IR spectra (B), Raman spectra (C) and SEM photo (D) of Ni/Fe-BDC.

One of the outstanding features of MOFs material compared with many traditional inorganic materials is its high gas adsorption capacity base on its broad surface. The adsorption result of N₂ at 77K of Ni/Fe-BDC also shows in figure 2A at P/P₀ = 1, the maximum adsorption volume of the material is approximately 271 cm³/g. The specific surface calculated by the BET method (taking the calculated pressure interval P/P₀ = 0.05 - 0.3) is 247 m²/g. An accompanying result is equally
important to the pore distribution (Refer figure 2B). Based on the pore distribution line, the average pore diameter of Ni/Fe-BDC is 13 nm. Although the results show that the pore distribution of Ni/Fe-BDC is quite complicated, in which the distribution range extends from 2 nm to about 40 nm. This result is often seen with many traditional MOF materials.

On the other hand, the thermal analysis result showed that Ni/Fe-BDC is stable to 400 °C temperature (Refer figure 2C). The results also once again showed that the activation process did not eliminate residual solvent molecules after the MOFs synthesis and washing process. There are two critical temperature jumps 150 to 370 °C is the mass loss corresponding to the breakdown of terephthalic acid group and from 370 to 530 °C corresponding to linkage destruction of Ni$^{2+}$, Fe$^{3+}$ and terephthalic acid simultaneously with the decomposition process of remaining organic substances.

![Figure 2. Shown in N$_2$ adsorption-desorption isotherms (A), pore size distributions (B) and TGA curve (C) of Ni/Fe-BDC sample.](image)

3.2. Catalyst studies
The Grignard-like reaction via C-H bond activation of benzaldehyde and phenylacetylene was performed with the Ni/Fe-BDC as a heterogeneous catalyst to form 1,3-diphenylprop-2-yn-1-ol as desire product (scheme 1).
Effects of many factors on reaction conversion have been investigated. Original studies solved the effects of temperatures, reagents molar ratios, catalyst concentrations, and various solvents on the reaction conversion to create of 1,3-diphenylprop-2-yn-1-ol. After that, reactions on a variety kind of catalysts were also conducted to compare the catalytic activity with Ni/Fe-BDC. Besides, the recyclability and reutilize of the Ni/Fe-BDC were then tested. The initial reaction factor to be studied was the temperatures. The reaction was carried out in 5% aqueous K$_2$CO$_3$, at the reagent molar ratio of 1:1.5, with the attendance of 20 mol% Ni/Fe-BDC as catalyst at the temperature ranging from room temperature to 100 °C. In figure 3A, it was found that the reaction occurred fastest when the temperature reached 80 °C. At about 80 °C, an efficiency of 78% was obtained after 20 hours. As looked for, when we decreased the temperature, the isolated yield in a considerable reducing in the reaction rate. At room temperature, a slight conversion of 3% was attained after 20 hours. Hence, 80 °C was advisable temperature.

The next important factor to be studied was the reactants molar ratio. The reaction was performed at 80 °C in water as a solvent, utilizing 20 mol% of Ni/Fe-BDC as a catalyst with benzaldehyde and phenylacetylene molar ratio of 1:1, 1:1.5, 1:2, 1:2.5, and 2:1, respectively (Refer figure 3B). Apparently, it illustrated that the change of reagent molar ratio did not affect too much on reaction conversion. When the reagents molar ratio was increased from 1:1 to 2:1 led to a notable drop in reaction rate of 62%, and 46%, respectively. The highest reaction rate was at the reactants molar ratio of 1:1.5, which gave the reaction conversion of 78% after 24 hours. In case of this reaction, the molar ratio of 1:1.5, affording the highest conversion, was chosen as the optimum ratio for further investigation. With these results in mind, the consequence of catalyst loading on reaction changeover was then investigated. The catalyst loading, with appreciation to the copper content in the Ni/Fe-BDC was researched in the scope of 0 mol% to 25 mol% relative to benzaldehyde. The reaction was carried out in water, at 80 °C, and at the reactants molar ratio of 1:1.5 (Refer table 1, entries 1-6). It was found that the highest yield of 78% was reached at 20 mol% of catalyst. When the catalyst loading was reduced to leads to a considerable reducing in the reaction rate, 55% and 37% of yield at 15% and
10% of catalyst after 20 hours, respectively. It should be noted that the catalyst loading was a significant advantage when using the Ni/Fe-BDC catalyst for this reaction.

Table 1. Optimal conditions on catalyzed between benzaldehyde and phenylacetylene in the aqueous solvent.

| Entry | Catalyst   | % catalyst | Solvent      | Isolated yield (%) |
|-------|------------|------------|--------------|--------------------|
| 1     | Ni/Fe-BDC  | 0          | 5% aq. K₂CO₃ | 5                  |
| 2     | Ni/Fe-BDC  | 5          | 5% aq. K₂CO₃ | 26                 |
| 3     | Ni/Fe-BDC  | 10         | 5% aq. K₂CO₃ | 37                 |
| 4     | Ni/Fe-BDC  | 15         | 5% aq. K₂CO₃ | 55                 |
| 5     | Ni/Fe-BDC  | 20         | 5% aq. K₂CO₃ | 78                 |
| 6     | Ni/Fe-BDC  | 25         | 5% aq. K₂CO₃ | 81                 |
| 7     | Ni(NO₃)₂.6H₂O | 20   | 5% aq. K₂CO₃ | 22                 |
| 8     | FeCl₃.6H₂O | 20         | 5% aq. K₂CO₃ | 45                 |
| 9     | Ni/Fe-BDC  | 20         | 5% aq. K₂CO₃ | 78                 |
| 10    | NiBDC      | 20         | 5% aq. K₂CO₃ | 57                 |
| 11    | FeBDC      | 20         | 5% aq. K₂CO₃ | 71                 |
| 12    | Ni/Fe-BDC  | 20         | 5% aq. Cs₂CO₃ | 61                |
| 13    | Ni/Fe-BDC  | 20         | 5% aq. Na₂CO₃ | 67                |
| 14    | Ni/Fe-BDC  | 20         | 5% aq. KHCO₃ | 54                 |
| 15    | Ni/Fe-BDC  | 20         | H₂O          | 47                 |

The advantage of Ni/Fe-BDC catalyst is also demonstrated when compared with several other catalysts such as Ni(NO₃)₂.6H₂O, FeCl₃.6H₂O, NiBDC, FeBDC (Table 1, entries 7-11). These result showed that the Ni/Fe-BDC material gave the highest reaction efficiency (approx. 78%) compare with the metal single MOFs, and homogeneous catalyst. For liquid-phase organic transmutations utilizing solid catalysts, it is necessary to consider the result of various solvents on the reaction rate [15]. This reaction used water as a green solvent with 5% weight of other bases (Table 1, entries 12-15). It is clear that the solvent with 5% aqueous K₂CO₃ gave the highest yield compared with 5% aq.Cs₂CO₃, 5% aq. Na₂CO₃, and 5% aq. KHCO₃ of 61%, 67%, and 54%, respectively.

When using MOFs for heterogeneously catalyzed reaction, it is necessary to assure that the catalytic activation metal site might not be released from the MOFs structure into the liquid phase during the route of the reaction. Because the dissolve metal types, if happened, might show catalytic activity, and the reaction could not process under truly heterogeneous conditions. Hence, to confirm whether the activation copper types migrated from the Ni/Fe-BDC to the reaction environment or not, a monitor experiment was performed. The reaction was conducted at 80 °C in water, at the molar ratio of 1:1.5, in the presence of 20 mol% Ni/Fe-BDC as the catalyst. After 4 hours reaction time with 16% yield being followed, the solid catalyst was segregated from the reaction mixture by centrifugation. The reaction solution was then moved into a new reactor vessel and stirred for an additional 16 hours at 80 °C with aliquots being sampled at different time intervals, and analyzed by GC. As expected, it was established that the reaction stopped immediately after separating the catalyst, with the efficiency remaining almost unchanged after 20 hours. The fact that no further conversion from benzaldehyde to 1,3-diphenylprop-2-yn-1-ol was observed after catalyst separation would confirm that no catalytically metal site could dissolve from the catalyst to the liquid phase of the reaction (Refer figure 4A).
According to the conception of green chemistry, the requirements when utilizing solid catalyst in organic transformation are easy of catalyst withdrawing after the reaction, the similar of the ability to recover and reuse the solid catalyst. The ideal heterogeneous catalyst is the one could be simply segregated from the reaction mixture, and reutilized for some times until it deactivates finish (Refer figure 4B). As mentioned before in section, the Ni/Fe-BDC was proved to be completely removed from the reaction between banaldehyde and phenylacteylene. Thus, the experiments to test the recyclability and reusability of the Ni/Fe-BDC were also conducted. It was inspected that an efficiency of 70% was yet obtained after the 7th run. It indicated that Ni/Fe-BDC catalyst might be recycled and reutilized for seven times without considerable loss of catalyst performance.

Furthermore, to assure the ability to recycle and reuse the Ni/Fe-BDC as the catalyst, the recuperated Ni/Fe-BDC was also analyzed by XRD and FT-IR (Refer figure 5). The structure data of the recycled Ni/Fe-BDC was compared with that of the fresh Ni/Fe-BDC. In figure 5A, the XRD patterns showed that the recycled catalyst still exhibited the same sharp peaks compared with the fresh Ni/Fe-BDC. It proved that the Ni/Fe-BDC might retain crystallinity highly within the route of the
reaction. Besides, The FT-IR spectrum of the recycled Ni/Fe-BDC also revealed the same absorption compared with the fresh catalyst (Refer figure 5B).

4. Conclusion
The preparation of the Ni/Fe-BDC containing highly catalytically active sites was successfully achieved by the solvothermal method in high yield. The structure characteristic of the Ni/Fe-BDC was analyzed by different kinds of techniques, including XRD, FT-IR, SEM, Raman, BET, and TGA. To figure out the potential catalytic applicability, the Ni/Fe-BDC was utilized as a heterogeneous catalyst for the Grignard reaction between benzaldehyde and phenylacetylene to obtain the 1,3-diphenylprop-2-yn-1-ol with high efficiency after 20 hours. When using the Ni/Fe-BDC as the catalyst for this reaction showed that had many advantages over other kinds of catalysts, including highly reaction conversion and selectivity, remarkably reducing in catalyst loading, and in reaction time. Especially, the ease of recyclability and reusability of the Ni/Fe-BDC proved it as a convincing heterogeneous catalyst, satisfying the green chemistry requirements.

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