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Article

Recyclable Cu-MOF-74 Catalyst for Ligand-Free O-Arylation Reaction of 4-Nitrobenzaldehyde and Phenol

Pedro Leo, Gisela Orcajo, David Briones, Guillermo Calleja and Fernando Martínez *

Department of Chemical and Energy Technology, ESCET. Rey Juan Carlos University, C/ Tulipan s/n, 28933 Mostoles, Spain; pedro.leo@urjc.es (P.L.); gisela.orcajo@urjc.es (G.O.); david.briones@urjc.es (D.B.); guillermo.calleja@urjc.es (G.C.)

* Correspondence: fernando.castillejo@urjc.es; Tel.: +34 91 488 7182

Abstract: The activity and cyclability of Cu-MOF-74 as catalyst was studied for the ligand-free C-O cross-coupling reaction of 4-nitrobenzaldehyde (NB) with phenol (Ph) to form 4-formyldiphenyl ether (FDE). Cu-MOF-74 is characterized by unsaturated copper sites in a highly porous metal-organic framework. The influence of solvent, reaction temperature, NB/Ph ratio, catalyst concentration and basic agent (type and concentration) were evaluated. High conversions were achieved at 120°C, 5 mol% of catalyst, NB/Ph ratio of 1:2, DMF as solvent and 1 equivalent of K2CO3 base. The activity of Cu-MOF-74 material was higher than other ligand-free copper catalytic systems tested in this study. This catalyst was easily separated and reused in five successive runs, achieving a remarkable performance without significant porous framework degradation. The leaching of copper species in the reaction medium was negligible. The O-arylation between NB and Ph took place only in the presence of Cu-MOF-74 material, being negligible without the solid catalyst.

Keywords: MOF; catalyst; recyclable Cu-MOF-74; ligand-free; O-arylation reaction; 4-nitrobenzaldehyde; phenol; 4-formyldiphenyl ether

1. Introduction

Diaryl ethers are very valuable organic compounds in the synthesis of biologically natural products and in the pharmacological and polymer fields [1, 2]. The traditional synthesis is based on the Ullmann cross-coupling reaction of phenols with aryl halides, catalyzed by copper salts [3]. However, homogeneous copper-mediated coupling reactions are limited by the large amount of catalyst needed and harsh reaction conditions [4-7]. The high concentration of the catalyst is an important environmental drawback, as large quantities of hazardous copper-based waste are produced. Additionally, it has been reported that additives or ligands are needed for promoting the ether formation at milder reaction conditions [8, 9]. The synthesis of diaryl ethers with palladium as catalyst has been also reported [10], but the need of expensive palladium amounts and complex ligands limit its feasibility. The development of copper heterogeneous catalysts for Ullmann C-O cross-coupling reactions is therefore a motivating challenge for a more sustainable process, as they could be easily recoverable and reusable and probably not requiring assisting ligands. Up to date, very few works have been addressed to this issue [11-12]. Magnetic $CuFe_2O_4$ nanoparticles showed remarkable performances for the C-O crossing reaction of phenols with aryl halides, although acetylacetone as ligand was necessary [13]. More recently, metal-organic framework (MOF) materials have been evaluated. MOF materials are porous crystalline solids with surface areas surpassing activated carbons and zeolites, composed by metal nodes connected by organic linkers through strong chemical bonds [14]. Although MOF materials have been originally used for gas separation and storage, their potential as active and selective catalysts in a wide range of chemical reactions are being lately demonstrated [15-19]. Phan and co-workers have paid attention on ligand-free copper-catalyzed coupling reactions of phenols with aryl iodines or nitroarenes [20] using MOF-199 and $Cu_2(BDC)_2(DABCO)$ (BDC = 1,4-bencene dicarboxylate and DABCO = 1,4-diazabicyclo[2,2,2]octane), respectively. T. Maity and coworkers have also investigated the O-arylation of aryl alcohols with aryl bromides using a Zn-based isoreticular metal organic framework (IRMOF-3) in which copper(II) was anchored following a post-synthetic modification method[21]. The most stimulating features of MOF materials for catalytic applications are their high surface area, tunable pore size, scaffold flexibility, and diversity of structural functional sites like the accessible metallic centers [22].

In this work, the Cu-MOF-74 material characterized by exhibiting unsaturated copper sites pointing to the pore channels, was studied as a catalyst of the free-ligand O-arylation of phenol with 4-nitrobenzladehyde reaction. This Cu-MOF-74 material was previously tested in the acylation of anisole with phenol, exhibiting a remarkable catalytic activity and structural stability[23]. The influence of different reaction variables such as temperature, type of solvent, catalyst concentration and type and concentration of base in the absence of assisting ligands was evaluated, in order to determine the best operation conditions for the synthesis of diaryl ethers. The cyclability of the catalyst was also studied along several successive catalytic runs, checking its resistance to activity loss.

2. Results and Discussion

2.1. Characterization of Cu-MOF-74

Cu-MOF74 was synthesized by the solvothermal method previously described [24] with a yield of 74%. Conventional techniques were used for the physico-chemical characterization of Cu-MOF-74 material as shown in Figure 1. Powder X-ray diffraction (PXRD) pattern revealed the typical reflections of the MOF-74/CPO-27 phase [25], discarding the presence of secondary crystalline phases (Figure 1a). SEM micrographs also revealed the expected large needle-shaped crystals that have been previously reported for this Cu-MOF-74 material [24] (Figure 1b). Both, PXRD pattern and SEM pictures confirmed the crystallinity of Cu-MOF-74 material. Elemental analysis by using ICP-OES indicated a copper loading of 6.1 mmol/g, which is close to the theoretical content from the molecular structure (6.23 mmol/g). The porosity of the material was measured by nitrogen adsorption at -196 ºC (Figure 1c). The isotherms revealed a microporous material with a BET specific surface area around 1100 m^2/g, a pore volume of 0.57 cm^3/g and an average pore diameter of ca. 10.1 Å. Thermogravimetric analysis (TGA) under N2 atmosphere evidenced a first weight loss at ca. 100 ºC corresponding to the solvent removal from the porous framework as well as a high thermal stability until 370 °C, when the decomposition of the organic ligand takes place (Figure 1d).

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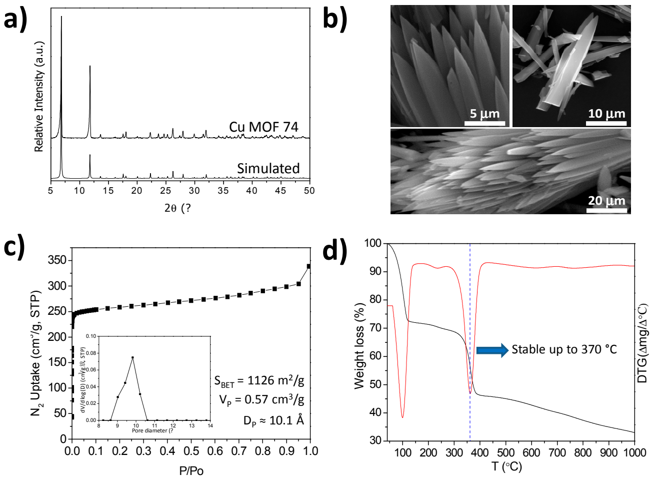

Figure 1. Catalyst characterization of Cu-MOF-74: a) PXRD patterns; b) SEM images c) Nitrogen adsorption-desorption isotherms at 77 K and d) TGA at inert atmosphere.

2.2. Catalytic study

2.2.1. Influence of temperature

The influence of the temperature on the O-arylation cross-coupling reaction of 4-nitrobenzaldehyde (NB) and phenol (Ph) to form 4-formyldiphenyl ether was evaluated at 60, 80, 100, 120 and 140 °C (Figure 2). These reactions were carried out in DMF with a NB/Ph molar ratio of 1/2, 2 equivalents of K_2CO_3 as a base and 5 mol % of catalyst, conditions that are similar to those previously published (Phan et al. [20]). A remarkable 88% conversion of NB was achieved after 6 minutes and 100% conversion after 1 hour for the highest reaction temperature (140 °C). The decrease of temperature reduced the catalytic activity of Cu-MOF-74, being less significant in the range of 140-120 °C. At the lowest temperature (60 °C), the NB conversion after 2 h was ca. 60%. At the reaction temperature of 100 °C, the Cu-MOF-74 showed a catalytic activity similar to another Cu-based MOF material ($Cu_2(BDC)_2(DABCO)$) reported in the literature[20]. However, $Cu_2(BDC)_2(DABCO)$ evidenced a stronger loss of activity at lower reaction temperatures as compared to Cu-MOF-74. This behavior is related to the average pore diameter and diffusional constraints of both materials when the temperature is decreased. The pore size diameter of Cu-MOF-74 (10.1 Å) is larger than that reported for $Cu_2(BDC)_2(DABCO)$ (6.4 Å), a difference that enables an easier diffusion of reactants within the porous structure of Cu-MOF-74, favoring its catalytic activity. On the other hand, the $Cu_2(BDC)_2(DABCO)$ material was not tested at temperatures above 100 °C, where the catalytic performance of Cu-MOF 74 is significantly enhanced[20]. Therefore, the Cu-MOF-74 is active at mild reaction temperatures (60 °C) and becoming extremely active at 120 °C, with a NB conversion close to 80% in few minutes.

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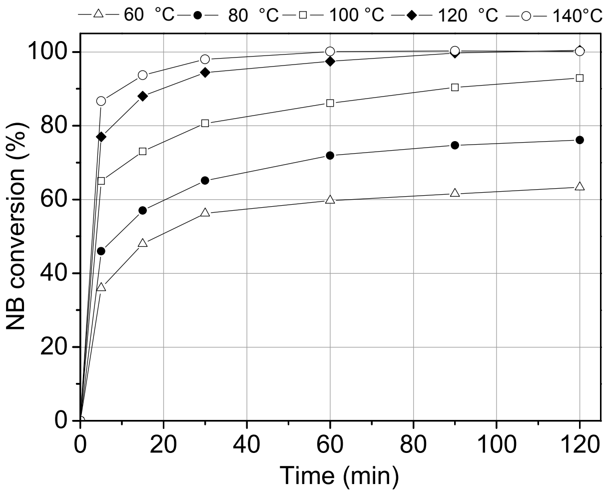

Figure 2. Influence of reaction temperature on the catalytic activity of Cu-MOF-74.

In order to evaluate the contribution of homogeneous catalysis by possible leached copper species of Cu-MOF-74, an additional catalytic run at 120ºC was carried out, removing the solid catalyst from the mixture by hot filtration after 5 minutes of reaction. In these conditions, the reaction mixture was still maintained 2 hours. Figure 3 shows the NB conversion profiles with the solid Cu-MOF-74 catalyst present all the time (called "best conditions") and the so-called "leaching experiment" with the Cu-MOF74 catalyst removed after 5 minutes. The active role of the heterogeneous Cu-MOF-74 catalyst in the O-arylation cross-coupling reaction is clearly proven when comparing both profiles. No further conversion of NB was detected once the solid catalyst was removed from the reaction mixture, which demonstrates a null contribution of homogeneous catalysis by plausible copper leaching. In fact, dissolved copper species were not detected in the reaction mixture by ICP-OES analyses.

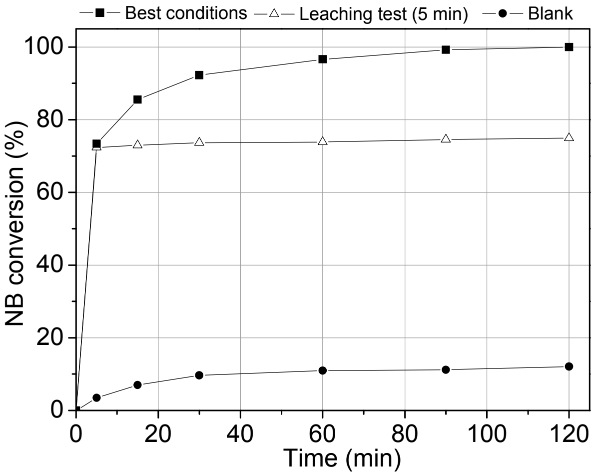

Figure 3. Influence of homogeneous catalysis on the O-arylation cross-coupling reaction of phenol and 4-nitrobenzaldehyde

2.2.2. Influence of 4-nitrobenzaldehyde/phenol molar ratio

The influence of the reactants ratio in the cross-coupling reaction was also investigated for NB/Ph molar ratio of 1/1, 1/1.5, 1/2 and 1/3 (Figure 4). These reactions were carried out at 120 °C with DMF and 2 equivalents of K_2CO_3 in the presence of 5 mol % of Cu-MOF-74 catalyst. It is clearly observed a significant effect of the NB/Ph ratio on the conversion. The increase of phenol proportion

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until NB/Ph = 1/2 produced a significant enhancement of the NB conversion. It must be noted that similar results were reported using other copper-based MOF materials, like $Cu_2(BDC)_2(DABCO)$, being the best NB/Ph molar ratio 1/1.5 [20]. This result can be explained by the role of phenol as a ligand in the catalytic mechanism, which accelerates the coupling with aryl halides, as observed in homogeneous copper catalytic systems [26]. In the case of heterogeneous Cu-MOF materials, the benefit of using phenol in excess is also probably related to the primary interaction of phenolates with available copper sites followed by coupling with NB, instead of complexation of NB as electrophilic reactant and later coupling with phenolate as nucleophilic agent.

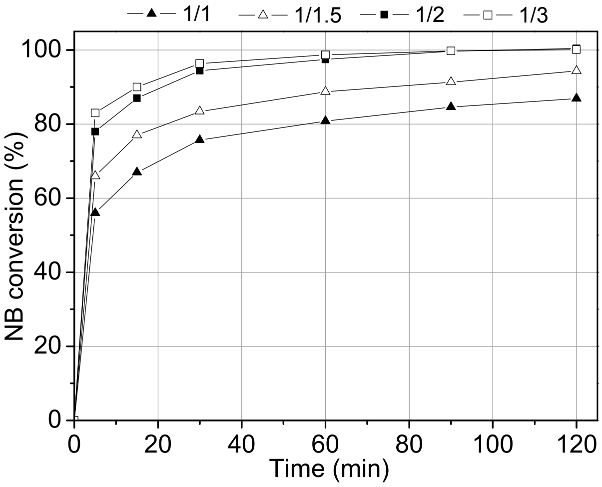

Figure 4. Influence of NB/Ph molar ratio on the catalytic activity of Cu-MOF-74.

2.2.3. Influence of catalyst concentration

In order to assess the influence of the catalyst concentration, a new reaction run was performed with DMF at 120 °C, NB/Ph molar ratio of 2, two equivalents of K_2CO_3 and catalyst concentrations of 0, 1, 3, 5, 7 mol % (Figure 5). Catalyst concentration was calculated based on the Cu/NB molar ratio values. A low NB conversion (ca. 10 %) was achieved in the absence of solid catalyst (blank). The presence of Cu-MOF-74 catalyst provided a remarkable initial rate in hardly 10 minutes of reaction, with values of NB conversion from 58% (1% catalyst concentration) to 81% (7% of catalyst concentration). In 2 h reaction time and catalyst concentration of 1 and 3%, yields of NB conversion were 84 and 94%, respectively. An increase of catalyst concentration up to 5% led to 100% conversion in 90 minutes, but interestingly, an increase beyond 5% did not produce any significant improvement. Similar results were reported by Chen et al., for NB conversion when using 5 mol % of ($Cu(OAc)_2.H_2O$) as a catalyst and similar reaction conditions [12]. However, it must be pointed out that Cu content for reaching a complete conversion of NB as shown before is significantly lower compared to conventional Ullman reactions, where an average value of 10 mol % Cu-catalyst concentration is needed [27, 28].

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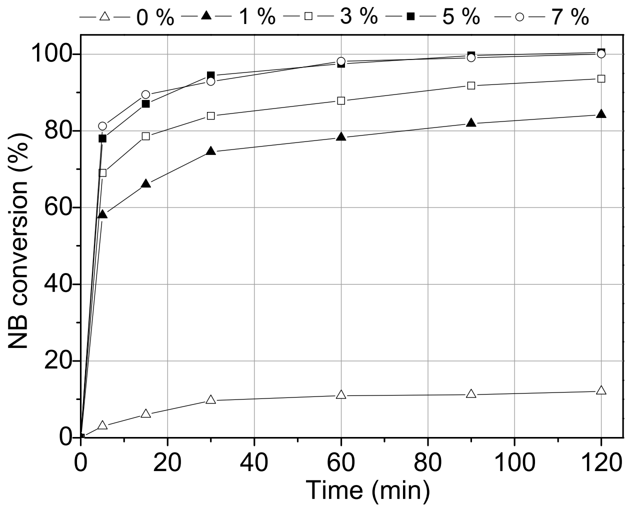

Figure 5. Influence of Cu-MOF-74 concentration on the catalytic activity of Cu-MOF-74.

2.2.4. Influence of solvent

The type of solvent can be crucial in coupling Ullmann reactions due to its influence on the reaction mechanism and solubility of reactants. So, the O-arylation reaction of Ph with NB was tested not only with DMF as solvent, but also with nitrobenzene, toluene and acetonitrile, keeping constant the temperature (120 °C), the NB/Ph molar ratio (1/2), 2 equivalents of K_2CO_3 as a base and 5 molar % of catalyst concentration. As shown in Figure 6, toluene was the worst solvent, with only 20% of NB conversion after 2h of reaction. For the same reaction time, nitrobenzene also showed a relatively low conversion (around 43%), whereas acetonitrile led to a much higher conversion (75%), although still lower than the 100 % attained with DMF in hardly 1.5 h of reaction. These results are in good agreement with the literature when using other MOF materials [20], homogeneous catalysts [12] and different Ullman reactions [4, 29, 30]. The solvent has also an important effect on homogeneous Ullmann O-arylation reactions of phenol with aryl chlorides using copper bromide in the presence 1,10-phenantroline as ancillary ligand (L) [31]. In this case, the halogen atom transfer based mechanism is sometimes proposed but other are also suggested based on oxidative addition, σ-bond, methathesis or single electron transfer mechanisms. Hartwig et al. [32] described an equilibrium between neutral LCu–OAr (Cu(I)-phenoxide complex as consequence of the base neutralization) and ionic forms of the $Cu(L)_2^+$ cation and $Cu(OAr)_2^-$ anion, as result of disproportionation of LCu–OAr species. This equilibrium is controlled by the solvent polarity. Thus, the use of polar solvents favors the formation of ionic complexes, suggesting that ionic forms lead to the halogen atom transfer of aryl chlorides for the formation of diaryl ethers [33].

In the case of the O-arylation of phenol with nitrobenzaldehyde instead of aryl chlorides, this mechanism can be also responsible of the formation of ionic species over the unsaturated copper metal sites of the Cu-MOF-74, which promotes the coupling reaction with NB. Besides, it is also very important to point out the solvent influence on the solubility of reactants, based of its polarity. The solubility of NB in the reaction conditions was ranged from 0.5 to 1.7 M for toluene and DMF, respectively. These results are in agreement with their polarity indexes, ranging from 2.3 to 6.4 for these both solvents. It is then concluded that the effect of solvent on the solubility of NB could be also affecting the catalytic performance of the heterogeneous Cu-MOF-74 catalyst [31].

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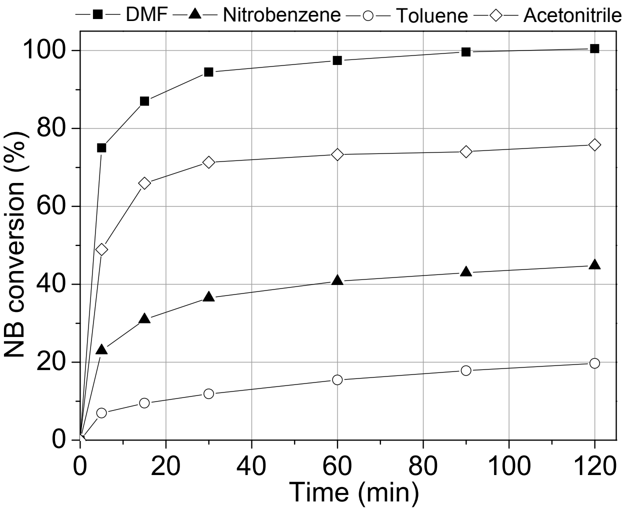

Figure 6. Influence of solvent reaction on the catalytic activity of Cu-MOF-74.

2.2.5. Influence of the base

The influence of the base on the catalytic activity of Cu-MOF-74 was also studied. Chen a co-workers proved that Cs_2CO_3 is more efficient than other bases for the coupling reaction between phenol and 4-nitrobenzaldehyde. However, due to the relatively high cost of Cs_2CO_3, other more readily available and inexpensive bases such as K_2CO_3, Na_2CO_3, K_3PO_4 and Na_3PO_4 were tested in the usual conditions: DMF solvent, 120 °C, NB/Ph molar ratio of 2, one equivalent of base and 5 molar % of catalyst. Figure 7 shows the NB conversion obtained for the different bases. An additional blank experiment with no base is also included. As observed, a significant NB conversion of 60 % was achieved in absence on base, but much higher values were obtained when the base was present. The catalytic activity of Cu-MOF-74 is quite influenced by the type of base (carbonate or phosphate) and the counter-balanced cation. Carbonates evidenced a better catalytic performance than phosphates when they are counter-balanced with the same cation (sodium or potassium). The higher kinetic diameter of phosphate anions is probably affecting the catalytic process of deprotonation of phenol inside the porous structure of the Cu-MOF-74 framework. Additionally, the use of potassium instead of sodium salts also showed a remarkable effect on the catalytic performance of Cu-MOF-74. This effect has been related to the lower electronegativity of potassium cations. A higher electronegativity promotes a stronger affinity to deprotonated phenoxide anions, which would hinder the formation of Cu-phenoxide complexes and consequently the following transmetallation step for the formation of the diaryl ether compound.

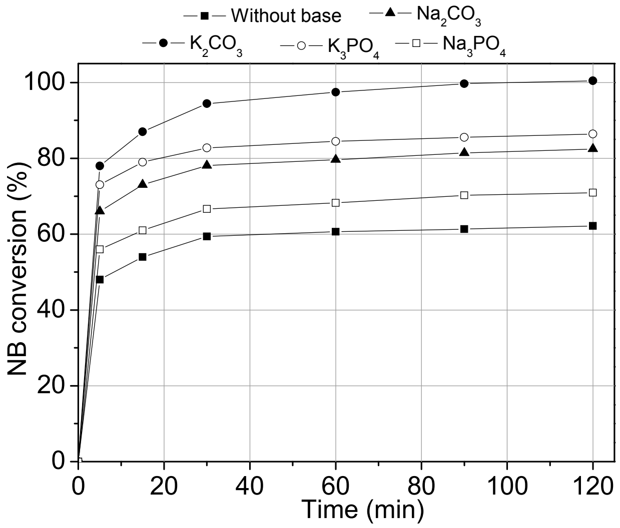

Figure 7. Influence of the type of base on the catalytic activity of Cu-MOF-74.

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The influence of the K_2CO_3 base concentration was also studied by varying the base concentration from 1 to 0.5 and 2 equivalents. Figure 8 shows the NB conversion for the three catalytic runs in the usual conditions (DMF, 120 °C, NB/Ph = 2 and 5 molar % catalyst). The increase of the K_2CO_3 concentration from 0.5 to 1 equivalents enhances the catalytic activity of Cu-MOF-74. However, the increase up to 2 equivalents does not produce further conversion improvement, revealing that one equivalent (base/Ph molar ratio of 0.5) is able to promote an efficient deprotonation of phenol for the formation of phenoxide complexes with the Cu containing sites of Cu-MOF-74 material.

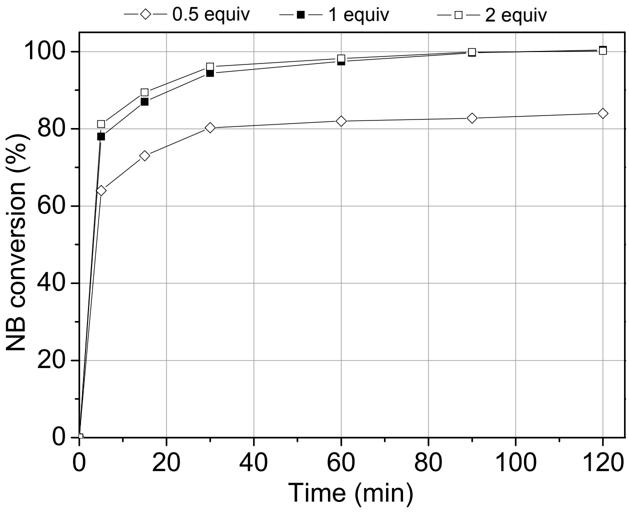

Figure 8. Influence of K_2CO_3 concentration on the catalytic activity of Cu-MOF-74.

2.2.6. Comparison with other Cu-catalysts

The catalytic performance of Cu-MOF-74 in the cross-coupling reaction of phenol with 4-nitrobenzaldehyde was also compared with other Cu-based heterogeneous catalysts (CuO and HKUST-1) and homogeneous catalysts (CuCl and $CuNO_3$ salts). The catalyst concentration was always set to copper contents of 5 mol %. The experiments were carried out using DMF at 120°C, NB/Ph molar ratio of 1/2 and 2 equivalents of K2CO3. Figure 9 shows the best catalytic performance of Cu-MOF-74 (100% conversion at 2 h) compared to the other CU-materials. The homogeneous catalytic systems based on CuCl and CuNO3 salts still show high NB conversions after 2 hours, but below 100%. This decrease of activity was attributed to possible negative effects of Cl^- and NO^{3-} anions in the O-arylation cross-coupling reaction. This was confirmed by additional experiments performed with extra amount of Cl- and NO3- (provided by potassium-based salts). These experiments showed a significant decrease of NB conversion until 62 and 76 % for CuCl and $CuNO_3$, respectively, demonstrating the strong interference of the anions in the reaction course. On the other hand, CuO particles showed the worst catalytic performance (65 % conversion), which indicates the crucial role of the microporous structure of Cu-MOF-74, which provides a higher availability of copper sites compared to the very low porosity of CuO (34 m^2/g). In the case of HKUST-1 (a well-known Cu-based MOF material), the catalytic performance was slightly lower than for Cu-MOF-74. The lower activity is probably due to the higher specific surface area of Cu-MOF-74 (1126 m^2/g) as compared to HKUST-1 (708 m^2/g) and the better accessibility of the open metal sites of MOF-74 structure.

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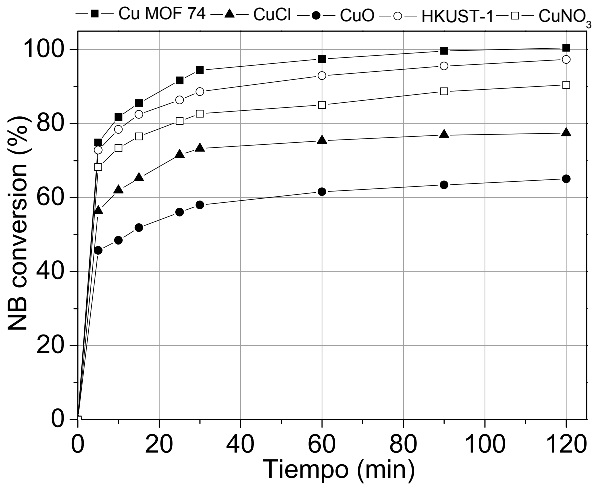

Figure 9. Comparison of different Cu-based catalysts for the O-arylation cross coupling reaction of 4-nitrobenzaldehyde and phenol.

2.2.7. Reuse of Cu-MOF-74

An important feature of chemical processes based on organic reactions from the environmental point of view is the reusability of the catalyst in a number of reaction cycles. Therefore, the cyclability of the catalyst was also studied in the O-arylation cross-coupling reaction for 5 successive catalytic runs. Prior to each catalytic run, the catalyst was recovered and washed several times with methanol and dried at 150 °C for 18 h. The NB conversion and the XRD patterns of the catalyst along the 5 cycles are shown in Figures 10 and 11, respectively. The catalytic performance was above 90% after the 5 cycles, although a slight decrease of activity was observed after the third one (Figure 10). XRD measurements of Figure 11 show that the crystalline phase of Cu-MOF-74 keeps unaltered, meaning that the catalyst structure is stable. The copper leaching was negligible, as commented, the MOF phase was also stable and the catalyst recovery after each cycle was above 97% as well. All these results demonstrate that the crystalline framework of Cu-MOF-74 material is stable in the reaction conditions, being the slight deactivation observed possible due to chemisorbed by-products along the reaction cycles that were not completely removed during the regeneration process.

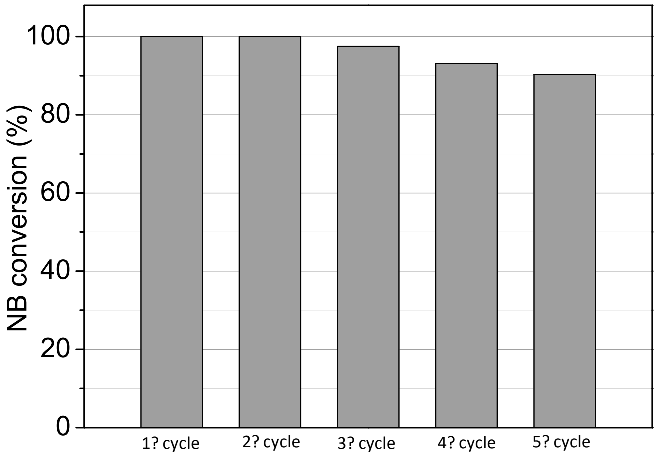

Figure 10. Catalytic activity of Cu-MOF-74 catalyst after several reaction cycles.

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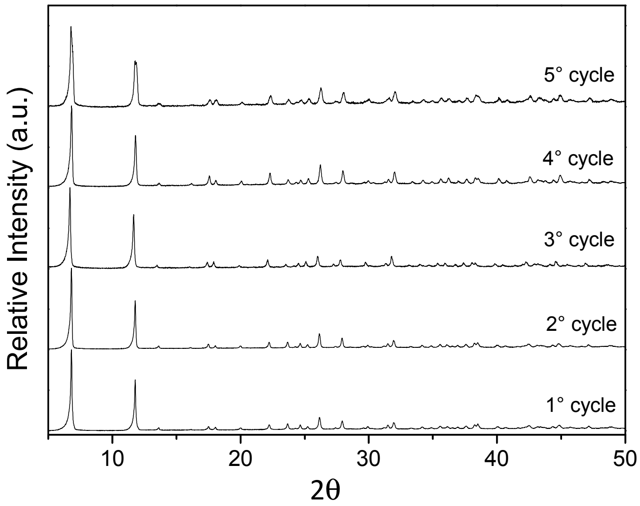

Figure 11. XRD patterns of Cu-MOF-74 catalyst after several reaction cycles.

4. Materials and Methods

Catalysts preparation

Cu-MOF-74 was synthesized basically following the procedure previously published [24], in which a mixture of 2.2g of 2,5 dihydroxyterephthalic acid (H_2dhtp, 11.2 mmol, Aldrich) and trihydrated copper nitrate(II) (5.9 g, 24.6 mmol, Aldrich) were added to 250 mL solution of N,N-dimethylformamide (DMF) and 2-propanol (20:1 (v/v)) in a 500 mL screw cap bottle. The suspension was stirred until homogeneous solution. Then, the resultant solution was placed in an oven at 80 °C for 18 h. Thereafter, the sample was cooled down to room temperature and the mother liquor was separated from reddish needle-shaped crystals by vacuum filtration. Afterwards, the crystalline solid sample was washed with DMF and immersed in 100 mL of methanol for four 4 days, renewing it by fresh methanol every 24 h. Prior to the catalytic runs, the solid material was dried at 150 °C under vacuum (10–3 bar) for 5 h and stored under inert atmosphere. Other powdered materials used in this study with the purpose of comparison were HKUST-1 (Sigma-Aldrich) as copper MOF material and CuO. Likewise, homogeneous copper salts such as $CuCl_2$ and $Cu(NO_3)_2$ were used as homogeneous catalysts (Sigma-Aldrich).

Catalyst characterization

X-ray powder diffraction (XRD) patterns were acquired on a PHILIPS X'PERT diffractometer using Cu K radiation. The data were recorded from 5 to 50° (2θ) with a resolution of 0.01°. Scanning electron microscopy (SEM) micrographs were obtained on a PHILIPS XL30 ESEM electronic microscope operating at 200 kV. Nitrogen adsorption–desorption isotherms at −196 °C were measured using an AutoSorb equipment (Quantachrome Instruments). The micropore surface area was calculated by using the Brunauer–Emmett–Teller (BET) model [34]. The pore volume and diameter were estimated by non-local DFT calculations, assuming a kernel model of N_2 at -196 °C on carbon (cylindrical pores, NLDFT equilibrium model)[35]. Simultaneous thermogravimetry and derivative thermogravimetric analyses (TGA/DTG) were carried out under a nitrogen atmosphere with an N_2 flow of 100 mL min^{-1} at a heating rate of 5 °C/min up to 700 °C, using a TA Instruments SDT 2860 apparatus.

Reaction procedure

Cu-MOF-74 material was tested in the O-arylation cross coupling reaction of phenol (Ph) and 4-nitrobenzaldehyde (NB) to form 4-formyldiphenyl ether (FDE) (Scheme 1). All the catalytic experiments were carried out in a round bottom flask placed in a silicone bath under N_2 atmosphere. The influence of the temperature, the molar ratio of reactants (NB/Ph), the catalyst concentration, the type of solvent and base and the base concentration was evaluated according to preliminary

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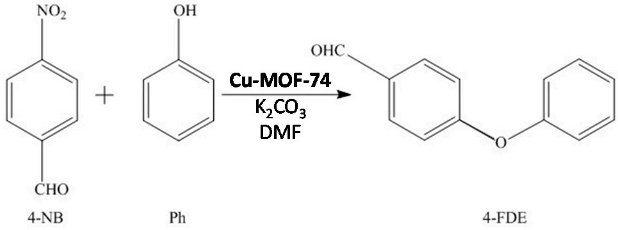
conditions found in the literature [20]. The required amounts of reactants (Ph and NB) were added to 20 mL of DMF. The base and catalyst concentrations were adjusted according to molar ratios of base/Ph and Cu/NB, respectively. The reaction was monitored by withdrawing aliquots from the reaction medium at different times ranging from 0 to 120 min. The NB and FDE were identified and quantified by gas chromatography, using a GC-3900 Varian chromatograph equipped with a CPSIL 8 CB capillary column (30 m × 0.25 mm, film thickness 0.25 μm) and a flame ionization detector (FID). The injector and FID temperatures were set to 280ºC and the oven temperature program starts a 120 °C for 1 min to further heating until 280ºC at 40°C/min-1 and 3 min at 280 °C. Hexadecane was used as an internal standard and all samples were analyzed by duplicate.



Scheme 1. C-O cross-coupling reaction of phenol with 4-nitrobenzaldehyde.

The relative NB conversion was calculated taking into account the maximum theoretical NB conversion, which depends on the 4-NP/Ph ratio of each catalytic run. The selectivity to diaryl ether FDE was considered of 100% as no other byproducts were detected. Similar assumption was observed in literature for this reaction [20].

5. Conclusions

The catalytic activity of Cu-MOF-74 has been demonstrated for the O-arylation cross-coupling reaction of 4-nitrobenzaldehyde and phenol. A catalyst concentration of 5 mol% exhibits a total conversion of NB after 2 hours at 120 °C, whereas only 10% is achieved in the absence of catalyst. This O-arylation reaction only proceeds in the presence of Cu-MOF-74 catalyst, discarding a possible contribution of homogeneous catalysis due to active leached species in the liquid phase. The excess of phenol as well as a high polarity of the solvent plays an important role in the catalytic performance of Cu-MOF-74. Best conditions for the reaction are NB/Ph ratio of 1/2, DMF as solvent and a non-expensive K_2CO_3 base. The catalytic activity of Cu-MOF-74 (above 90%) is the highest compared to other homogeneous and heterogeneous Cu-based catalysts, and the material is stable and also reusable during several reaction cycles.

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Author Contributions: Pedro Leo performed all the synthesis and catalytic experiments. David Briones performed samples characterization. Gisela Orcajo analyzed the samples characterization data and wrote the manuscript. Fernando Martínez and Guillermo Calleja designed and analyzed the catalytic tests data and assisted in the manuscript preparation. All the listed authors have contributed substantially to this work.

Conflicts of Interest: The authors declare no conflict of interest.

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