

Today

Manuscript Draft

Manuscript Number:

Title: DIRECT α -ARYLATION OF KETONES EFFICIENTLY CATALYZED BY Cu-MOF-74

Article Type: SI: CIS-8 Conference

Keywords: MOF; heterogeneous catalyst; recyclable Cu-MOF-74; α -aryl-ketones

Corresponding Author: Dr. Gisela Orcajo,

Corresponding Author's Institution: Universidad Rey Juan Carlos

First Author: PEDRO LEO

Order of Authors: PEDRO LEO; Gisela Orcajo; DAVID BRIONES; FERNANDO MARTÍNEZ; GUILLERMO CALLEJA

Abstract: The activity and reusability of Cu-MOF-74 as heterogeneous catalyst were studied in the Cu-catalyzed C-C cross-coupling reaction of 4-iodotoluene (4-IT) with acetylacetone (AcAc) to direct synthesis of α -aryl-ketones. Cu-MOF-74 is characterized by having unsaturated copper sites into its highly porous metal-organic framework that can play a crucial role in catalytic applications. The influence of critical reaction variables such as solvent, reaction temperature, AcAc/4-IT ratio, catalyst concentration and basic agent (type and concentration) were evaluated. High conversions were achieved at 140 °C, 5 mol % of catalyst, AcAc/4-IT ratio of 2:1, DMF as solvent and 1.5 equivalent of Cs₂CO₃ base. The C-arylation between 4-IT and AcAc proceeded only in the presence of Cu-MOF-74 material, being very low the transformation in absence of the solid catalyst. Cu-MOF-74 material displayed a remarkable structural stability, regarding its XRD patterns and solid recovery degree after several reaction cycles, which was also complemented by the negligible amount of copper leached in the reaction media. This catalyst showed promising results in comparison to other homogeneous and heterogeneous Cu-based catalysts. This work evidences the great potential of MOF materials as heterogeneous catalysts in fine chemistry applications.

Madrid, June 30th 2019

Dr. J.J. Spivey
Editor of *Catalysis Today*

Please, enclose you can find the manuscript that we would like to submit for its publication in *Catalysis Today*:

Title: "DIRECT α -ARYLATION OF KETONES EFFICIENTLY CATALYZED BY Cu-MOF-74"

Authors: P. Leo, G. Orcajo, D. Briones, F. Martínez, G. Calleja

Corresponding author: Gisela Orcajo, Chemical and Environmental Engineering Group, ESCET, Universidad Rey Juan Carlos, C/ Tulipán s/n, 28933 Móstoles, Madrid, Spain.

E-mail: gisela.orcajo@urjc.es

Manuscript type: Article

In the last years, the potential of metal-organic frameworks as heterogeneous catalysts is being widely explored. The crystalline hybrid organic-inorganic composition of these materials makes possible the incorporation of highly active catalytic sites into their structures for a myriad of chemical transformations. After the previous works in our research group related to the assessment of the catalytic activity of acid-base MOF-based catalysts (especially MOF-74 family) (G. Calleja, R. Sanz, G. Orcajo, D. Briones, P. Leo, F. Martínez, *Catalysis Today*, 227 (2014) 130-137; F. Martínez, G. Orcajo, D. Briones, P. Leo, G. Calleja, *Microporous and Mesoporous Materials* 246 (2017) 43-50; P. Leo, G. Orcajo, D. Briones, G. Calleja, M. Sánchez-Sánchez and F. Martínez, *Nanomaterials* 7, 149 (2017) 1-15), this work is focused on the evaluation of the catalytic activity of Cu-MOF-74 in the Cu-catalyzed C-C cross-coupling reaction to direct synthesis of α -aryl-ketones.

In this manuscript we report the activity and reusability of Cu-MOF-74 as heterogeneous catalyst in the Cu-catalyzed C-C cross-coupling reaction of 4-iodotoluene (4-IT) with acetylacetone (AcAc) to direct synthesis of α -aryl-ketones. Cu-MOF-74 is characterized by having unsaturated copper sites into its highly porous metal-organic framework that can play a crucial role in catalytic applications. We studied the influence of critical reaction variables such as solvent, reaction temperature, AcAc/4-IT ratio, catalyst concentration and basic agent (type and concentration), and we found high conversions at 140 °C, 5 mol % of catalyst, AcAc/4-IT ratio of 2:1, DMF as solvent and 1.5 equivalent of Cs₂CO₃ base. This copper-based MOF displayed a remarkable structural stability and promising performance in comparison to other homogeneous and heterogeneous Cu-based catalysts. This work evidences the great potential of MOF materials as heterogeneous catalysts in fine chemistry applications.

Looking forward to hearing from you. Sincerely yours,

Gisela Orcajo
Chemical and Environmental Engineering Group
ESCET, Rey Juan Carlos University.
C/Tulipán s/n, E-28933 Móstoles, Madrid, Spain
Tel: 34 91 488 70 06, Fax: 34 91 488 70 68, e-mail: gisela.orcajo@urjc.es



FACULTY OF SCIENCE
Charles University

Prague, April 18, 2019

Letter of invitation

Dr. Pedro Leo
Department of Chemical and Environmental Technology,
Rey Juan Carlos University,
Calle Tulipán s/n, 28933 Móstoles,
Spain.

Invitation to submit a manuscript for Catalysis Today: 8th Czech-Italian-Spanish Symposium on Catalysis

Dear Pedro,

I would like to invite you to submit a manuscript for a special issue of Catalysis Today dedicated to 8th Czech-Italian-Spanish Symposium on Catalysis.

DIRECT α -ARYLATION OF KETONES EFFICIENTLY CATALYZED BY Cu-MOF-74

P. Leo^a, G. Orcajo^b, D. Briones^a, F. Martínez^a, G. Calleja^b

Submission should be done via official website of Catalysis Today. Your manuscript will be reviewed according to the procedures of the journal.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Jiri Cejka'.

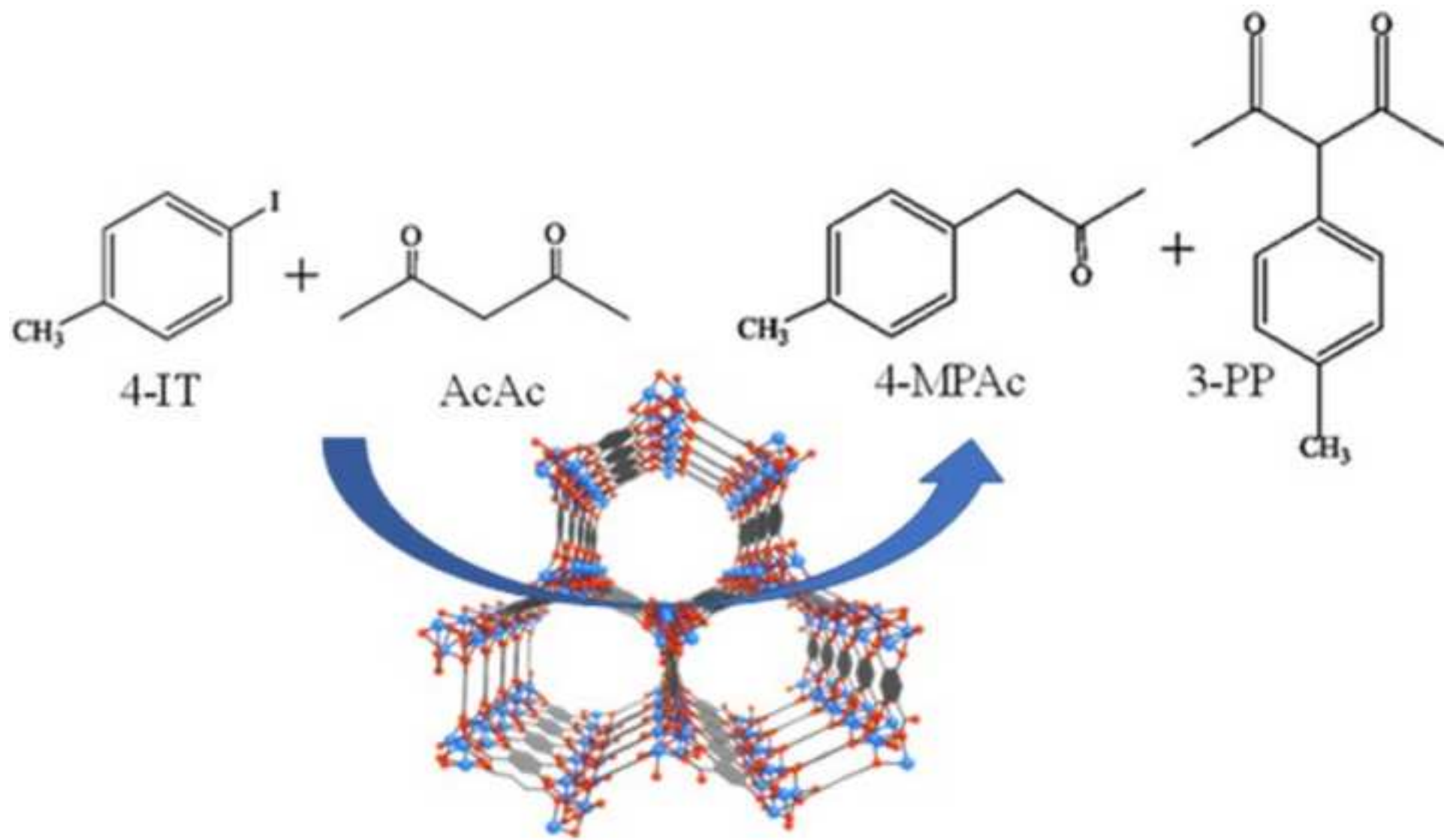
Jiří Čejka
Guest Editor

Highlights

Cu-MOF-74 catalyst showed efficient performance in a C-arylation reaction.

Cu-MOF-74 catalytically surpassed other homogeneous and heterogeneous Cu-catalysts.

Cu-MOF-74 was stable and reusable during several reaction cycles.



**DIRECT α -ARYLATION OF KETONES EFFICIENTLY
CATALYZED BY Cu-MOF-74**

P. Leo^a, G. Orcajo^{b*}, D. Briones^a, F. Martínez^a, G. Calleja^b

^a Department of Chemical and Environmental Technology, Rey Juan Carlos University, Calle Tulipán s/n, 28933 Móstoles, Spain.

^b Department of Chemical, Energy and Mechanical Technology, Rey Juan Carlos University, Calle Tulipán s/n, 28933 Móstoles, Spain.

***Corresponding author:** Tlf: +34 91 488 76 01, FAX: +34 91 488 70 68

E-mail address: gisela.orcajo@urjc.es

Abstract

The activity and reusability of Cu-MOF-74 as heterogeneous catalyst were studied in the Cu-catalyzed C-C cross-coupling reaction of 4-iodotoluene (4-IT) with acetylacetone (AcAc) to direct synthesis of α -aryl-ketones. Cu-MOF-74 is characterized by having unsaturated copper sites into its highly porous metal-organic framework that can play a crucial role in catalytic applications. The influence of critical reaction variables such as solvent, reaction temperature, AcAc/4-IT ratio, catalyst concentration and basic agent (type and concentration) were evaluated. High conversions were achieved at 140 °C, 5 mol % of catalyst, AcAc/4-IT ratio of 2:1, DMF as solvent and 1.5 equivalent of Cs₂CO₃ base. The C-arylation between 4-IT and AcAc proceeded only in the presence of Cu-MOF-74 material, being very low the transformation in absence of the solid catalyst. Cu-MOF-74 material displayed a remarkable structural stability, regarding its XRD patterns and solid recovery degree after several reaction cycles, which was also complemented by the negligible amount of copper leached in the reaction media. This catalyst showed promising results in comparison to other homogeneous and heterogeneous Cu-based catalysts. This work evidences the great potential of MOF materials as heterogeneous catalysts in fine chemistry applications.

Keywords: MOF; heterogeneous catalyst; recyclable Cu-MOF-74; α -aryl-ketones

1. Introduction

α -aryl ketones constitute an important class of organic molecules, since are crucial intermediates [1] and final products in the synthesis of natural products and pharmaceutical compounds [2] and accordingly their synthesis has gained attention during the last years. Buchwald and Hartwig pioneered the palladium-catalyzed arylation of several carbonyl compounds using aryl halides as electrophiles. In this process, an enolate is generated from a ketone and base in the presence of an aryl halide, and a palladium catalyst couples this enolate with the aryl halide [3, 4]. Despite the promising results obtained in those works, the high cost and relatively low availability of palladium, encouraged to explore other cheaper alternatives like homogeneous copper-based catalytic systems for synthesizing aryl carbonyls molecules [5, 6]. Besides, nowadays there is a strong incentive to replace homogeneous processes by green and efficient heterogeneous processes for economic and environmental reasons. In heterogeneous systems, not only the separation of the catalyst but also the reaction products also becomes easier, allowing the catalyst to be reused in consecutive reaction cycles [7]. Up to date, few works has been addressed to the use of Cu-based heterogeneous catalysts in this kind of reactions, two examples of them are CuO-nanoparticles and another one testing the MOF-199 material [8, 9].

Metal-organic framework (MOF) materials are porous crystalline solids with specific surface areas surpassing activated carbons and zeolites, composed of metal-containing nodes connected by organic linkers through coordination chemical bonds [10]. Recently, MOFs are being extensively tested in different catalytic system for a wide range of acid-base and redox reactions [11 - 14]. The most stimulating features of MOF materials for catalytic applications are their high surface area, tunable pore size, scaffold flexibility, and particularly, the great diversity of structural metallic and organic functional sites [15].

From the best of our knowledge, the only work where a copper-based MOF is used for this kind of C-C coupling reaction is the one reported by Phan and co-workers who tested MOF-199 (also called HKUST-1) in the coupling of aryl iodides with acetylacetone to form α -aryl ketones as principal products [8].

The family of MOF-74 materials are quite interesting since they are robust, enough porous (~ 1000 m²/g), with one of the highest concentration of metal sites per volume among MOF materials, and can be prepared with Zn, Ni, Co, Mg, Mn and Cu [16, 17]. They provide non-coordinated metal sites after removing the synthesis solvent, leading to the so-called Open Metal Sites (OMS). This fact is of a valuable interest for catalytic applications offering active sites for accessible substrates. Particularly, Cu-MOF-74 was developed in our research group [17] and it could be a good candidate to catalyze C-C cross-coupling reactions. This Cu-MOF-74 material was previously tested in the C-O coupling reaction of phenol with 4-nitrobenzaldehyde, exhibiting a remarkable catalytic activity and structural stability under consecutive reaction cycles [18].

For those reasons, in the present work, the Cu-MOF-74 material was studied as a heterogeneous catalyst for C-arylation reaction of acetylacetone and 4-iodotoluene. The influence of different variables such as reaction temperature, solvent, catalyst concentration and the type and concentration of base will be evaluated in order to determine the best reaction conditions for the synthesis of α -aryl ketones using a recoverable and reusable catalyst.

2. Experimental

2.1. Catalysts preparation

Cu-MOF-74 was solvothermally synthesized basically following the procedure previously published [17], in which a mixture of 2.2g of 2,5 dihydroxyterephthalic acid

(H₂dhtp, 11.2 mmol, Aldrich) and trihydrated copper nitrate(II) (5.9 g, 24.6 mmol, Aldrich) were dissolved in 250 mL solution of N,N-dimethylformamide (DMF) and 2-propanol (20:1 (v/v)) using a 500 mL screw cap bottle. Then, the resultant solution was placed in an oven at 80 °C during 18 h. Thereafter, it was cooled down to room temperature and the reddish needle-shaped crystals were separated from the mother liquor by vacuum filtration. Afterwards, the solid 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. For comparison purposes, other heterogeneous catalysts such as copper oxide (CuO) or copper-containing MOF materials (URJC-1 and HKUST-1) and homogeneous copper salts (CuCl₂ and Cu(NO₃)₂) were used. URJC-1 was synthesized in our laboratory according to the procedure described in the literature [19]. The other materials (CuO y HKUST-1) and copper salts were purchased to Sigma-Aldrich.

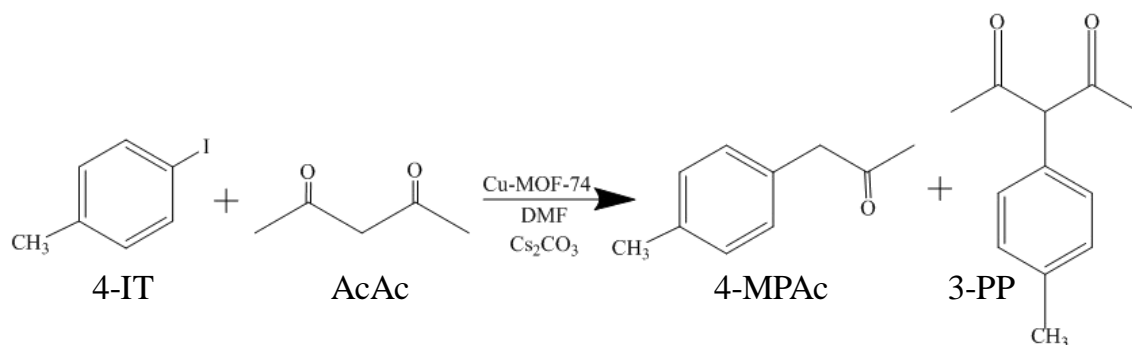
2.2. Catalyst characterization

X-ray powder diffraction (XRD) patterns were acquired on a PHILIPS X'PERT diffractometer using Cu K α radiation. The data were recorded from 5 to 50° (2 θ) 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 specific surface area was calculated by using the Brunauer–Emmett–Teller (BET) model [20]. The pore volume and diameter were estimated by non-local DFT calculations, assuming a kernel model of N₂ at -196 °C on carbon (cylindrical pores, NLDFT equilibrium model) [21]. Simultaneous thermogravimetry and derivative thermogravimetric analyses (TGA/DTG) were carried

out under nitrogen atmosphere with an N₂ 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.

2.3. Reaction procedure

Cu-MOF-74 material was tested in the C-arylation cross coupling reaction of acetylacetone (AcAc) and 4-iodotoluene (4-IT) to form 4-methylphenylacetone (4-MPAC) as a principal product and 3-phenyl-2,4-pentanedione (3-PP) as side byproduct (Scheme 1). All the catalytic experiments were carried out in a round bottom flask placed in a silicone bath under N₂ atmosphere. The influence of temperature, molar ratio between substrates (AcAc/4-IT), catalyst concentration, type of solvent, type of base and base concentration was evaluated, starting with the conditions found in literature [8]. The required amounts of substrates (AcAc and 4-IT) were added to 12 mL of DMF. The base and Cu-MOF-74 catalyst concentrations were adjusted according to molar ratios of base/AcAc and Cu/4-IT, respectively. The reaction was monitored by withdrawing aliquots from the reaction medium at different times ranging from 0 to 300 min. All reactants and products concentrations in the reaction were 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 temperature were set to 300°C and the oven temperature program starts at 80°C to further heating until 300°C at 40°C/min⁻¹ and then it was kept at 300°C during 0.6 min. Hexadecane was used as internal standard and all samples were analyzed by duplicate.



Scheme 1. C-C cross-coupling reaction of acetylacetone with 4-iodotoluene.

3. Results and discussion

3.1 Characterization of Cu-MOF-74

The most relevant characterization data of the Cu-MOF74 synthesized by solvothermal method is depicted in Figure 1. Powder X-ray diffraction (PXRD) pattern revealed the location and intensity of the main reflections of the MOF-74 phase [22], discarding the presence of secondary crystalline phases when comparing with the simulated pattern from the crystallographic data (Figure 1a). SEM micrographs of the as-synthesized material revealed the expected large needle-shaped crystals with a size of 20 μm that have been previously reported for this Cu-MOF-74 material [17] (Figure 1b). Elemental analysis by using ICP-OES indicated a copper loading of 6.1 mmol/g, which is quite close to the theoretical content from the molecular structure (6.2 mmol/g). The porosity of the material was measured by nitrogen adsorption at $-196\text{ }^\circ\text{C}$ (Figure 1c). The basically type I adsorption/desorption isotherm revealed a permanent microporosity with a BET specific surface area around $1100\text{ m}^2/\text{g}$, a pore volume of $0.57\text{ cm}^3/\text{g}$ and an average pore diameter of ca. 10 \AA . Thermogravimetric analysis (TGA) under N_2 atmosphere evidenced a significant loss of weight at ca. $100\text{ }^\circ\text{C}$ which was attributed to the methanol used for the removal of original DMF solvent. The decomposition of the structural organic ligand at ca. $370\text{ }^\circ\text{C}$, evidences a remarkable thermal stability (Figure 1d).

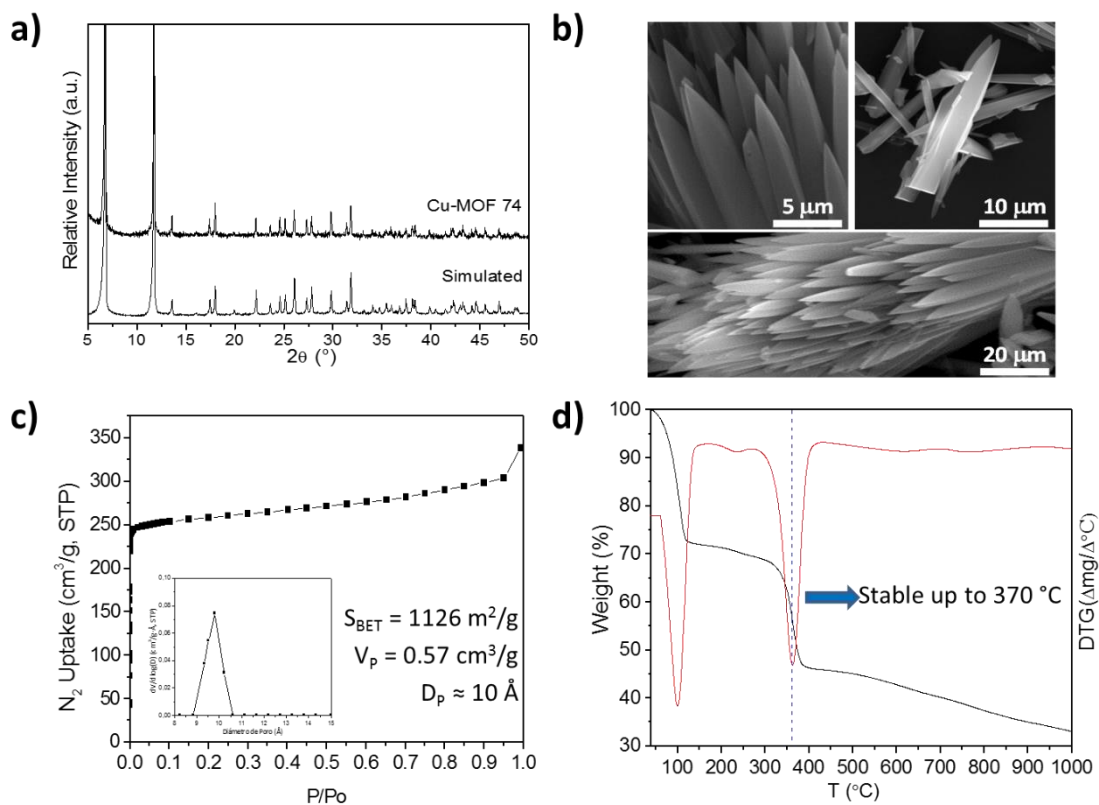


Figure 1. Catalyst characterization of Cu-MOF-74: a) PXRD patterns; b) SEM images c) Nitrogen adsorption-desorption isotherms at $-196\text{ }^{\circ}\text{C}$ (inset of micropore size distribution curve generated by NL-DFT method), and d) TGA at inert atmosphere.

3.2. Catalytic study

Influence of temperature

The influence of the temperature on the C-arylation cross-coupling reaction of 4-iodotoluene (4-IT) and acetylacetone (AcAc) to form α -aryl ketones was evaluated at 80, 100, 120 and 140 $^{\circ}\text{C}$ (Figure 2). These reactions were carried out in DMF as solvent, an AcAc/4-IT molar ratio of 3:1, 1.5 equivalents of Cs_2CO_3 as base and 10 mol % of catalyst, which are similar conditions to those published by Phan et al. [8]. The increase of temperature improved the catalytic performance of Cu-MOF-74 material. A remarkable 72 % of 4-iodotoluene (4-IT) conversion and 57 % of 4-methylphenylacetone

(4-MPAC) yield were achieved in only 30 min at 140 °C. For longer reaction times until 6 h, a moderate increase of both, 4-IT conversion and 4-MPAC yield, was obtained (almost 90 % of conversion and product yield). It must be also pointed out that the increase of temperature evidenced a significant enhancement of the 4-MPAC yield. In this Ullmann coupling reaction, other side by-products such as, 3-phenyl-2,4-pentanedione (3-PP) can appear. Thus, the increase of temperature seems to prompt the breakdown of acetylacetone to react with the toluene-based intermediates, increasing the 4-MPAC yield.

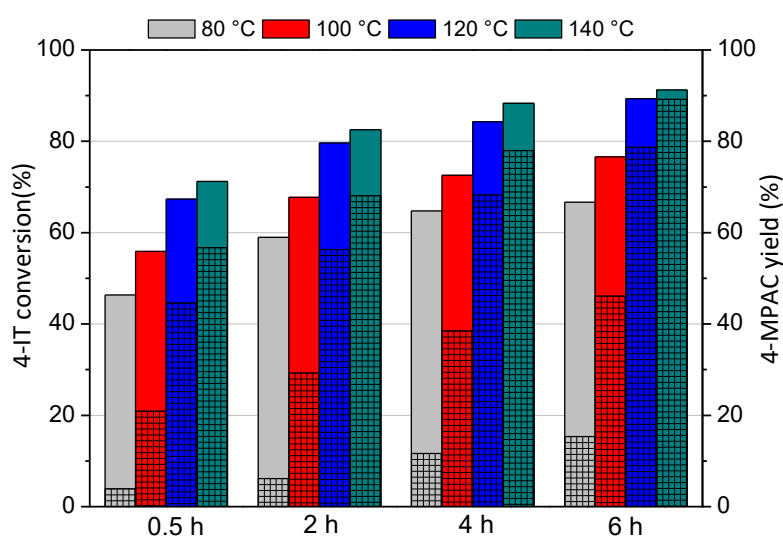


Figure 2. Influence of temperature on the catalytic performance of Cu-MOF-74.

Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield.

In order to evaluate the contribution of homogeneous catalysis from possible leached copper species of Cu-MOF-74, an additional experiment at 140 °C was carried out, that is shown in Figure 3. For that purpose, the solid catalyst was separated after the first 30 minutes from the reaction medium by hot filtration, and the reaction continued up to 6 hours (catalyst removal). The figure shows the comparison of 4-IT conversion profiles of this experiment with the typical experiment keeping the solid Cu-MOF-74 catalyst for the complete reaction time of 6 hours (with catalyst). The active role of the solid Cu-MOF-

74 in the C-arylation cross-coupling reaction is clearly proven when comparing both profiles. No further conversion of 4-IT was detected once the solid catalyst was removed from the reaction mixture, which demonstrates a null contribution of homogeneous catalysis by plausible copper leaching. Moreover, ICP-OES analyses revealed that copper species were not detected in the reaction medium.

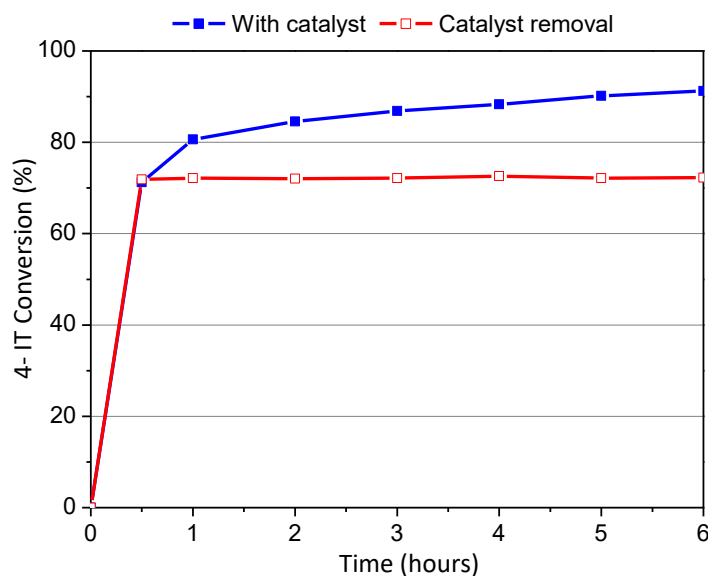


Figure 3. Evaluation of homogeneous catalytic contribution of Cu-MOF-74 for C-arylation cross-coupling reaction of AcAc and 4-IT.

Influence of catalyst concentration

In order to assess the influence of the catalyst concentration over the reaction evolution, the reaction was carried out in DMF at 140 °C, AcAc/4-IT molar ratio of 3:1, one and half equivalents of Cs_2CO_3 as base and catalyst concentrations of 0, 2.5, 5, 7.5, 10 mol % (Figure 4), regarding the copper/4-iodotoluene molar ratio.

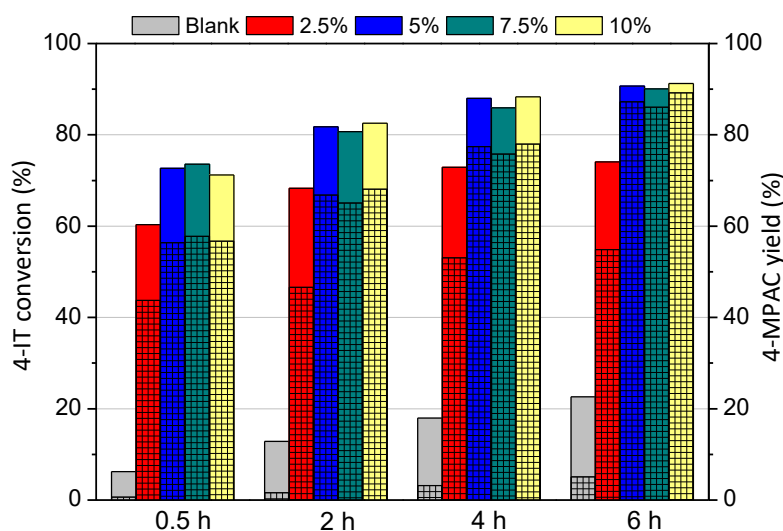


Figure 4. Influence of the Cu-MOF-74 concentration on the reaction performance. Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield.

A low 4-IT conversion of ca. 20% and poor 4-MPAC yield were achieved after 6 hours of reaction in absence of the solid catalyst. The presence of Cu-MOF-74 catalyst provided a remarkable initial rate for the initial 30 min of reaction, with values of 4-IT conversion ranging from ca. 60% (for 2.5 mol % of catalyst) to 72 (from 5 to 10 mol % of catalyst). It is remarkable that higher concentrations of catalyst than 5 mol % in the reaction medium do not improve the 4-IT conversion. Similar behavior was observed for the results of the 4-MPAC yield with values around 55-57% at 30 minutes and 86-90 % after 6 hours of reaction for catalyst concentrations between 5 and 10 mol %. It should be noted that the commonly used copper concentration for this kind of reactions in homogeneous systems is around 10% [23], occasionally reporting up to 20 % [24, 25]. Regarding the only heterogeneous catalysts tested to date, MOF-199 material and CuO nanoparticles [8, 9], a concentration of 10 % was employed, which is the double to that required in the case of Cu MOF-74. In this work, Cu-MOF-74 catalyst achieved 4-IT conversions of around 90 % and 4-MPAC yields close to 90 % after 6 hours of reaction with only 5 mol % of copper with respect to 4-iodotoluene substrate.

Influence of solvent

The effect of the solvent can be decisive in coupling Ullmann-type reactions due to its impact on the reaction mechanism and solubility of reactants and products [26]. It has been observed that the polarity of the solvent is the critical parameter and it can be measured by their dielectric constant. Therefore, the C-arylation reaction of 4-iodotoluene with acetylacetone was carried out in different common solvents as dimethyl sulfoxide (DMSO), N,N-dimethylformamide (DMF), nitrobenzene, N-Methyl-2-pyrrolidone (NMP) and toluene, with different dielectric constants of 47, 37, 35, 32 and 2.4, respectively. For the rest of variables the AcAc/4-IT molar ratio was kept at 3:1, 1.5 equivalents of Cs_2CO_3 as base and 5 molar % of catalyst concentration. As shown in Figure 5, a poor performance was evidenced for the solvent with the lowest dielectric constant (toluene), obtaining only 20 % of 4-IT conversion after 6 h of reaction. Under the same conditions, nitrobenzene led to a much higher conversion (78 %), although still lower than the 91 % conversion attained with DMF. This is not surprising since the reaction intermediate is a carbanion that would have greater stability in polar solvents [9]. So, these results are in good agreement with previous works found in literature using other homogeneous and heterogeneous catalysts such as copper iodide and CuO nanoparticles, respectively [8, 9, 27]. Both NMP and DMSO were found to be unsuitable for this reaction using Cu-MOF-74 catalyst, since the MOF structure collapsed in these solvents at 140 °C. Special attention is paid to the results obtained for nitrobenzene referred to the high conversion values but very low yields, evidencing a poor selectivity towards 4-MPAC product, which denotes possible low solubility of the products in nitrobenzene. In order to confirm this assumption, an extra experiment was done by adding the product 4-methylphenylacetone in nitrobenzene at 140 °C and vigorous

stirring during 20 min. The results evidenced that the product was not dissolved. Apart from the importance of the solubility of reactants and products in the solvent, it has been reported that polar solvents favor the formation of ionic complexes, suggesting that ionic forms promote the halogen atom transfer of aryl chlorides for the formation of α -aryl ketones [28].

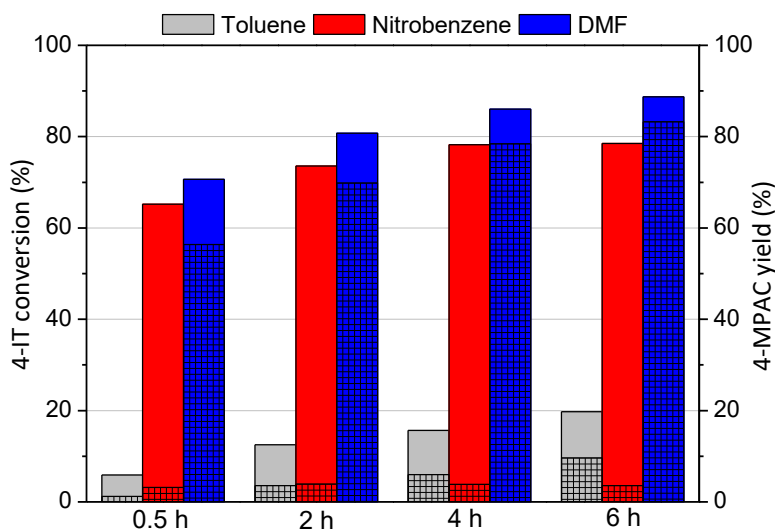


Figure 5. Influence of the solvent reaction on the catalytic performance of Cu-MOF-74. Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield.

Influence of acetylacetone /4-iodotoluene molar ratio

The influence of the reactants ratio in the cross-coupling reaction was also investigated for AcAc/4-IT molar ratio of 1:1, 2:1, 3:1 and 4:1 (Figure 6). These reactions were carried out at 140 °C with DMF and one and half equivalents of Cs_2CO_3 as base in the presence of 5 mol % of Cu-MOF-74 catalyst.

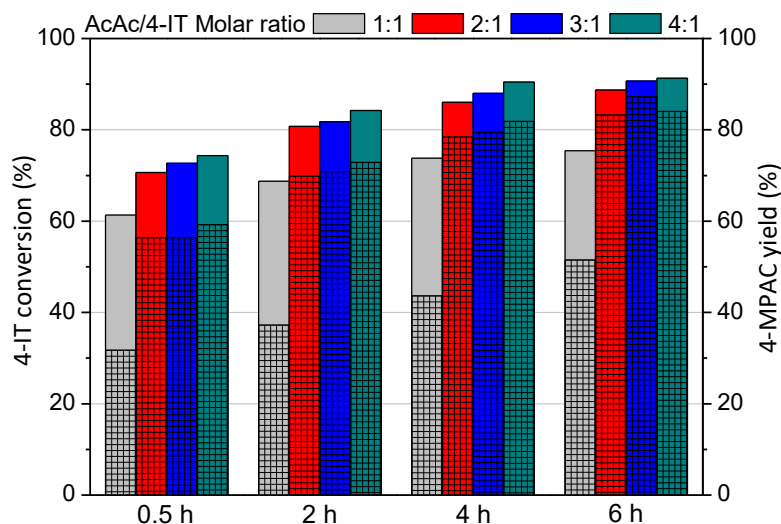


Figure 6. Influence of AcAc/4-IT molar ratio on catalytic performance of Cu-MOF-74. Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield.

Equimolar conditions of reactants allow reaching a conversion from 62 to 75% after 6 hours and a 4-MPAC yield from 32 to 51 %, which suggests a fast kinetic reaction during the first 30 min, and then, evolving slower until reaching the chemical equilibrium at 6 hours. It is also evidenced the enhancement of 4-IT conversion when acetylacetone is increased up to AcAc/4-IT of 2:1, attaining 89 % of 4-IT conversion and 82 % of 4-MPAC yield after 6 hours of reaction. From AcAc/4-IT molar ratio of 2:1 to 4:1, the enhancement in the catalytic activity is not significant. It must be noted that similar results were reported using other copper-based MOF material, being the optimal AcAc/4-IT molar ratio of 2:1 [8]. This result can be explained by the role of acetylacetone in increasing the formation of the copper intermediate that leads to the product without carbon-carbon cleavage [9], but limited by the stoichiometry of this reaction.

Influence of base

The influence of the base nature on the catalytic activity of Cu-MOF-74 was also studied. In order to accelerate the transmetalation step in the catalytic mechanism, different bases have been used in transition-metal catalyzed reactions [26, 29, 30, 31]. In this work, some

easy-available and inexpensive bases have been selected to be evaluated like Cs_2CO_3 , K_2CO_3 , Na_2CO_3 , K_3PO_4 , Na_3PO_4 in the performance of the reaction using one and half equivalent of base, AcAc/4-IT molar ratio 2:1, DMF, 140 °C and 5 molar % of catalyst. The results are shown in Figure 7.

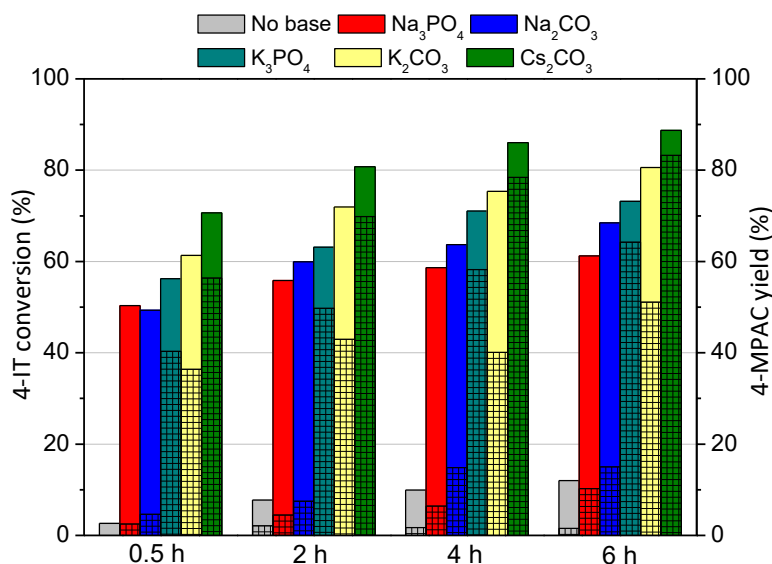


Figure 7. Influence of the base agent on catalytic performance of Cu-MOF-74. Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield.

Insignificant 4-IT conversion of 12% was achieved in absence of base after 6 hours of reaction time, meanwhile higher values of conversion and yield were obtained when the base was added to the reaction media. The catalytic activity of Cu-MOF-74 is quite influenced by the type of anion of the used salt (carbonate or phosphate) and its counter-cation. Carbonates evidenced a better catalytic performance than phosphates for the same counter-cation. The higher kinetic diameter of phosphate anions is probably affecting the catalytic process of deprotonation of the acetylacetone inside the porous structure of Cu-MOF-74. Additionally, the use of cesium with a lower electronegativity (0.7) than potassium (0.8) or sodium (0.9), marks an enhancement of the catalytic performance of Cu-MOF-74. This fact suggests that higher electronegativity promotes stronger affinity

to deprotonated anions, consequently hindering the transmetallation step for the formation of α -aryl ketones compound [18].

Since the most suitable base was Cs_2CO_3 , its concentration was also studied by varying the base equivalents from 0.5 to 2 equivalents. Figure 8 shows the 4-IT conversion and 4-MPAC yield for four catalytic experiments of 0.5, 1, 1.5 and 2 equivalents, using DMF at 140 °C, AcAc/4-IT molar ratio of 2:1 and 5 molar % of catalyst.

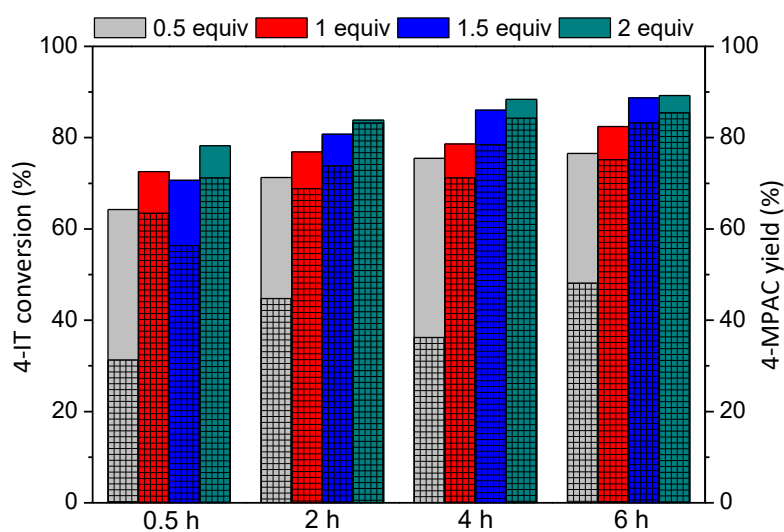


Figure 8. Influence of Cs_2CO_3 concentration on catalytic performance of Cu-MOF-74.

Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield.

The increase of the Cs_2CO_3 concentration from 0.5 to 1 equivalent enhances the catalytic activity of Cu-MOF-74, especially in terms of 4-MPAC yield. However, the increase beyond 1.5 equivalents does not produce further improvement, revealing that one and half equivalents are enough to promote an efficient deprotonation of the acetylacetone substrate.

3.3 Comparative with other Cu-catalyst

The catalytic performance of Cu-MOF-74 in the cross-coupling reaction of acetylacetone with 4-iodotoluene was also compared with other Cu-based heterogeneous (CuO, URJC-

1 and HKUST-1) and homogeneous (CuCl and Cu(NO₃)₂ salts) catalysts. It is important to note that CuO is a common heterogeneous catalyst used in this kind of reactions, but also it has also a similar chemical nature than the inorganic clusters of Cu-MOF-74. The catalyst concentration was always set to copper contents of 5 mol %. The experiments were carried out using DMF at 140°C, AcAc/4-IT molar ratio of 2:1 and 1.5 equivalents of Cs₂CO₃ as base. As it is displayed in Figure 9, the Cu-MOF-74 catalyst exhibited the best catalytic performance, in terms of 4-IT conversion and 4-MPAC yield, among all tested copper catalysts, particularly from 2h of reaction times.

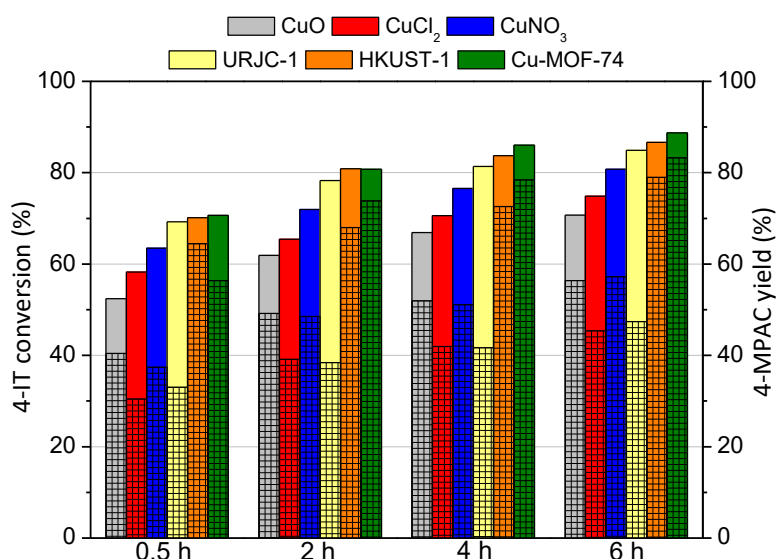


Figure 9. Catalytic performance for different Cu-based catalysts in the C-arylation cross coupling reaction of 4-iodotoluene and acetylacetone.

The homogeneous catalytic systems based on CuCl₂ and Cu(NO₃)₂ salts show high 4-IT conversions after 6 hours of reaction (ca. 75 % and 81 %, respectively), but in general, they are worse than the results of heterogeneous catalysts. This could be attributed to possible negative effects of Cl⁻ and NO₃⁻ anions in the C-arylation cross-coupling reaction. This was confirmed by additional experiments performed with extra amount (1.39 mg/mL) of Cl⁻ and NO₃⁻, provided by potassium-based salts. These experiments

showed a significant decrease in 4-IT conversion to 59% and 68% for CuCl and Cu(NO₃)₂, respectively, after 6h of reaction, demonstrating the strong interference of the anions in the reaction course.

Concerning the results obtained for heterogeneous Cu catalysts, the performance of CuO was the poorest in terms of 4-IT conversion. The three porous MOF materials tested (Cu-MOF-74, URJC-1 and HKUST-1) are characterized by exhibiting unsaturated copper sites, which would favor the interaction with the reaction species. The 4-IT conversion found for them was very similar for all the times; however, important differences in 4-MPAC yield were observed. The selectivity to any specific product, and consequently the yield of the reaction, is strongly dependent on the porous properties of the materials, where active sites are accessible to catalyze the reaction. So, it is reasonable that URJC-1, with a surface area of 408 m²/g and the narrowest pore size, shows a much lower value of 4-MPAC yield compared to those obtained for Cu-MOF-74 and HKUST-1, which have similar specific surface areas, of 1126 m²/g and 1008 m²/g, respectively, indicating that there are diffusion limitations in this material. Thus, the catalytic performance is limited by the pore size instead of the amount of copper active sites.

3.4. Reuse of Cu-MOF-74

An important issue of chemical processes based on organic reactions from the environmental point of view, is the reusability of the catalyst in several reaction cycles. Therefore, the recyclability of the catalyst was also studied in the C-arylation cross-coupling reaction for four successive catalytic runs. Prior to each catalytic run, the catalyst was recovered and washed with methanol several times and dried at 150°C for 18 h. The 4-IT conversion and the XRD patterns of the catalyst after the four reaction cycles are shown in the Figure 10a and Figure 10b, respectively. The catalytic performance was

above 84 % for the four cycles although a very slight decrease of activity was observed in the last cycle (Figure 10a). The XRD patterns of the catalyst after each cycle evidenced the maintenance of the crystalline phase of Cu-MOF-74 (Figure 10b), demonstrating the robustness of the MOF structure. Likewise, the copper leaching in the reaction medium was negligible and the catalyst recovery after each cycle was above 98 %. These results demonstrate the remarkable structure stability of the MOF material under the studied conditions. Thus, the slight catalyst deactivation could be attributed to possible chemisorbed by-products along the reaction cycles, that are not effectively removed through the regeneration process.

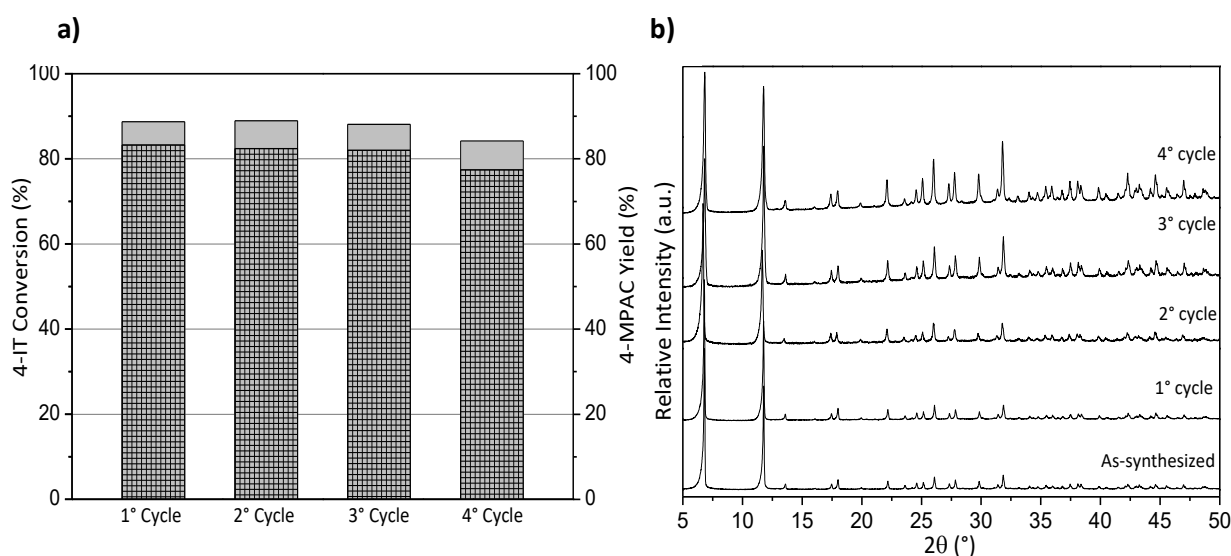


Figure 10. (a) Catalytic activity of Cu-MOF-74 catalyst after several reaction cycles. Normal columns indicate 4-IT conversion; fill columns indicate 4-MPAC product yield. (b) XRD patterns of Cu-MOF-74 catalyst after several reaction cycles.

4. Conclusions

The activity of Cu-MOF-74 and the influence of different critical variables on the performance of C-arylation of 4-IT and AcAc has been proven. This C-arylation reaction only proceeds in the presence of Cu-MOF-74 heterogeneous catalyst, discarding copper leaching from the MOF structure. The increase of temperature promoted a higher 4-

MPAC yield and the solvent polarity played an important role in the catalytic performance of Cu-MOF-74. The optimal conditions using this catalyst were 4-IT:AcAc ratio of 1:2, DMF as solvent and Cs₂CO₃ base. A catalyst concentration of 5 mol % allowed a high 4-iodotoluene conversion (ca. 90%) with a 4-methylphenylacetone product yield of 83% after 6 hours of reaction at 140 °C. The catalytic activity of Cu-MOF-74 was higher than those shown by homogeneous (CuCl and Cu(NO₃)₂) and heterogeneous (CuO, URJC-1HKUST-1) Cu-based catalysts in terms of 4-IT conversion and 4-MPAC product yield. Finally, the catalyst was stable and reusable during several reaction cycles. This work evidences the enormous potential of MOF materials as heterogeneous catalysts for many applications, particularly in fine chemistry.

ACKNOWLEDGMENTS

The authors wish to thank Spanish Ministry of Science and Innovation for the financial support to the CICYT Projects (CTQ2015-64526-P and PGC2018-099296-B-I00).

REFERENCES

- [1] M. Wisser F., Mohr Y., Quadrelli E.A., Farrusseng D., Canivet J., *ChemCatChem* 10 (2018) 1778 – 1782.
- [2] Edmondson S., Danishefsky S. J., Sepp-Lorenzino L., Rosen N., *J. Am. Chem. Soc.*, 121 (1999) 2147–2155.
- [3] Palucki M., Buchwald S. L., *J. Am. Chem. Soc.*, 119 (1997) 11108 –11109.
- [4] Hartwig J. F., *Angew. Chem.*, 37 (1998) 2154 – 2177.
- [5] Colacot T. J., Johansson C. C., *Angew. Chem. Int.*, 49 (2010) 676 – 707.
- [6] He C., Guo S., Huang L., Lei A., *J. Am. Chem. Soc.*, 132 (2010) 8273-8275.
- [7] Kantam M. L., Laha S., Yadav J., Jha S., *Tetrahedron Lett.*, 50 (2009) 4467 – 4469.
- [8] Phan N., Nguyen T., Ho P., Nguyen K., *ChemCatChem*, 5 (2013) 1822-1831.
- [9] Kidwai M., Bhardwaj S., Poddar R., *Beilstein Journal of Organic Chemistry*, 6 (2010) 35-40.

- [10] Zhou H., Long J., Yaghi O., *Chem.Rev.*, 112 (2012) 673-674.
- [11] Neogi S., Sharma M.K., Bharadwaj P.K., *J. Mol. Catal. A: Chem.*, 299 (2009) 1-4.
- [12] Gándara F., Gómez-Lor B., Gutiérrez-Puebla E., Iglesias M., Monge M.A., Proserpio D.M., Snejkoal N., *Chem. Mater.*, 20 (2008) 72-76.
- [13] Alkordi M.H., Liu Y.L., Larsen R.W., Eubank J.F., Eddaoudi M., *J. Am. Chem. Soc.*, 130 (2008) 12639-12641.
- [14] Schröder F., Esken D., Cokoja M., van den Berg M.W.E., Lebedev O.I., van Tendeloo G., Walaszek B., *J. Am. Chem. Soc.*, 130 (2008) 6119-6130.
- [15] Llabres i Xamena F., Gascón J., *Real Society of Chemistry*, 12 (2013) 406-424.
- [16] Caskey S., Wong-Foy A., Matzger A., *Journal of American Chemical Society*, 130 (2008) 10870-10871.
- [17] Sanz R., Martínez F., Orcajo G., Wojtas L., Briones D., *Dalton Trans.*, 42 (2013) 2392-2398.
- [18] Leo P., Orcajo G., Briones D., Calleja G., Sánchez-Sánchez M., Martínez F., *Nanomaterials*, 7 (2017) 149-163.
- [19] Leo P., Martínez G., Calleja G., Briones D., Wojtas L., Orcajo G., *Polymers*, 8 (2016) 1-12.
- [20] Brunauer S., Emmett P., Teller E., *J. Am. Chem. Soc.*, 60 (1938) 309-314.
- [21] Jagiello J., Thommes M., *Carbon* 42 (2004) 1227.
- [22] Rosi N., Kim J., Eddaoudi M., Chen B., O’Keeffe M., Yaghi O., *J. Am. Chem. Soc.*, 127 (2005) 1504-1518.
- [23] Tanabe K.K., Cohen S.M., *Inorganic Chemistry*. 49 (2010) 6766-6774.
- [24] Xie X., Chen Y., Ma D., *J. Am. Chem. Soc.*, 128 (2006) 16050-16051.
- [25] Xie X., Cai G., Ma D., *Org. Lett.*, 7 (2005) 4693- 4695.
- [26] Johansson C., Colacot T. J., *Angew. Chem. Int. Ed.*, 49 (2010) 676 – 707.
- [27] Zeevaart J.G., Parkinson C.J., de Koning C.B, *Tetrahedron Lett.*, 48 (2007) 3289-3293.
- [28] Wang, M., Fan, T., Lin, Z., *Organometallics*, 31 (2012) 560-569.
- [29] Klapars A., Huang X., Buchwald S.L., *J. Am. Chem. Soc.*, 124 (2002) 7421-7428.

[30] Zeevaart J. G., Parkinson C. J., de Koning C. B., *Tetrahedron Lett.*, 45 (2004) 4261–4264.

[31] Ozdemir I., Yigit M., Cetinkaya E., Cetinkaya B., *Tetrahedron Lett.*, 45 (2004) 5823–5825.