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Bridging homogeneous and heterogeneous catalysis with MOFs: “Click” reactions with Cu-MOF catalysts

I. Luz, F.X. Llabrés i Xamena, A. Corma *

Instituto de Tecnología Química (UPV-CSIC), Universidad Politécnica de Valencia, Consejo Superior de Investigaciones Científicas, Avenida de los Naranjos s/n, 46022 Valencia, Spain

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ABSTRACT

Various copper-containing MOF catalysts, i.e., [Cu(2-pymo)$_2$], [Cu(im)$_2$], [Cu$_3$(BTC)$_2$] and [Cu(BDC)] (2-pymo: 2-hydroxypyrimidinolate; im: imidazolate; BTC: benzene tricarboxylate; BDC: benzene dicarboxylate), have shown to be highly active and fully regioselective for “click” reactions (1,3-dipolar cycloaddition reactions). The activity of the best MOF catalyst is comparable to homogeneous Cu catalysts. It has been found that the activity of Cu changes with the organic linker in the MOF, being those containing CuN$_4$ more active than CuO$_4$ centers. The controlling step of the reaction is the formation of an adduct between Cu and phenylacetylene. When using MOF catalysts, the use of alcohol or alcohol–water solvents is not required, and the catalysts can be fully recovered and recycled. Finally, Cu-MOF catalysts allow to design a one-pot two-step process, where the azide is formed “in situ” and reacted immediately with phenylacetylene.

1. Introduction

Metals in solution, either as metal salts or transition metal complexes, have been widely used as homogeneous catalysts with extraordinary success. They are able to catalyze a large number of organic reactions, in many cases with extraordinary chemo, region and enantioselectivities. Homogeneous catalysts, however, are most of the times difficult to be recovered, and/or they decompose during the reaction. In an attempt to overcome those limitations, researchers have developed methods to heterogenize homogeneous catalysts. In some cases, the objective was simply to anchor it on a solid carrier to achieve well-isolated, uniform single sites that will not interact between them and decompose. However, in other cases the heterogeneization went further in such a way that the solid also intervenes in the catalytic process, either by stabilizing transition states or by introducing additional active sites [1,2]. Then, heterogeneization of homogeneous transition metal catalysts has been achieved by grafting and even impregnation on solid carriers, by intercalation within layered compounds, by introducing them in zeolite cavities by “ship in a bottle” technique or by forming structured or non-structured mesoporous organic–inorganic hybrid systems. More recently, heterogeneous catalysts have been developed based on metal organic frameworks where the active sites were the metal atoms located at the nodes of the crystalline structure, metal complexes that were part of the organic linkers or even supported metal nanoparticles [3–5]. When the catalysis is based on metal activity at the nodes or at the ligands forming the walls, the microporous MOF catalysts, also known as porous coordination polymers, appear directly as a solid counterpart of homogeneous catalysts.

The Huisgen 1,3-dipolar cycloaddition of alkynes and azides affords a means for the facile preparation of 1,2,3-triazoles derivatives, through the direct reaction of the two molecules (“click” chemistry). This reaction can be carried out either thermally or in the presence of a copper catalyst [6,7]. In this latter case, the reaction is known to be fully regioselective to the 1,4-substituted triazole. In this work, we show that different copper-containing MOFs can be used as efficient and regioselective heterogeneous catalysts for the “click” reaction between azides and alkynes.

2. Materials and methods

2.1. Preparation of the MOFs

Copper hydroxypyrimidinolate, [Cu(2-pymo)$_2$], copper imidazolate, [Cu(im)$_2$], copper trimesate, [Cu$_3$(BTC)$_2$], and copper terephthalate, [Cu(BDC)], were prepared according to the reported procedures [8–11]. X-ray diffraction (Phillips X’Pert diffractometer) showed good crystallinity for all materials.

[Cu(2-pymo)$_2$] is a distorted 3D sodalite framework, formed by α-cages accessible through hexagonal windows of about 8 Å. Copper ions are in square planar coordination, surrounded by 4 N atoms from four different 2-hydroxypyrimidine molecules. Similar to this structure, the “blue” copper imidazolate polymorph, [Cu(im)$_2$], is also related to a highly distorted *sod*-type framework,

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* Corresponding author. Fax: +34 963877809.
E-mail address: acorma@itq.upv.es (A. Corma).

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with pores accessible through similar hexagonal windows. In this material, copper ions are in a highly distorted four coordination, with trans N-Cu-N angles of ca. 140° and 155°. The well-known HKUST-1 copper trimesate, $[Cu_3(BTC)_2]$, forms a face-centered cubic crystal lattice with main pores of about 9 Å in diameter, as well as a set of additional tetrahedral pockets having windows of about 3.5 Å in diameter. Copper is coordinated to four O atoms from four trimesate molecules and an additional water molecule in the apical position, forming $Cu_2(COO)_4(H_2O)_2$ paddle wheel dimmers. Finally, copper terephthalate is a lamellar material featuring also the same copper paddle wheel dimmers but having an apical DMF molecule instead of water. These 2D sheets are stacked through weak interactions. DMF molecules can be eliminated through thermal treatments, leading to a porous desolvated structure, which is believed to possess square channels, similar to those found in copper *trans*-1,4-cyclohexanedicarboxylate [12].

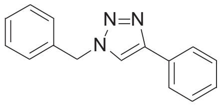
2.2. Computational details

Calculations were carried out by means of the Gaussian03 program package [13] using the density functional B3LYP method [14,15] and a LANL2DZ effective core potential basis set for Cu [16] and the standard 6-311G(d,p) basis set for C, O, N and H atoms [17]. Atomic charges were produced by natural bond orbital (NBO) methods [18]. The MOF materials were modeled by means of three clusters of atoms that were cut out from the experimental crystal structure and are depicted in Fig. S1 in Supplementary material.

2.3. Catalysis

The general reaction procedure for 1,3-dipolar cycloaddition of benzyl azide to phenylacetylene ("click" reaction) was as follows. Copper-MOF catalyst (0.1 mmol Cu) in ethanol (6 ml) was placed inside a round bottom flask connected to a reflux condenser, and the temperature was set to 70 °C under N_2 atmosphere. Benzyl azide (1 mmol) and phenylacetylene (1.2 mmol) were then added with a syringe. Aliquots were taken during the course of the reaction and analyzed by GC using hexadecane as external standard. The reaction was confirmed to be quantitatively regioselective to the 1,4-substituted triazole (**3a**) by means of ^1H and ^{13}C NMR analysis of the isolated product.

Compound **3a** (Table 1).



^1H NMR (300 MHz, [D_1] chloroform, 25 °C, TMS): δ 5.57 (s, 2H), 7.27–7.44 (m, 8H), 7.76–7.84 (m, 2H), 7.68 (s, 1H). ^{13}C NMR (75.5 MHz, [D_1] chloroform, 25 °C, TMS): δ 54.7, 120.1, 126.2, 128.6, 128.7, 129.3, 129.4, 129.7, 131.1, 135.3, 148.7.

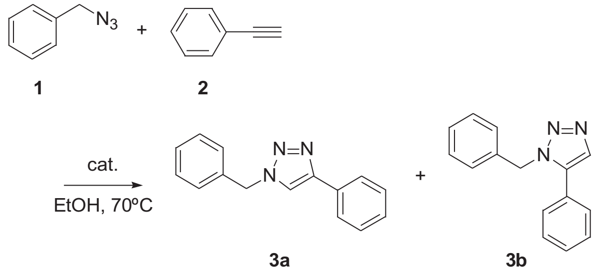
3. Results and discussion

3.1. 1,3-Dipolar cycloaddition reaction

Different copper-containing MOFs were found to be active catalysts for 1,3-dipolar cycloaddition reactions ("click" reaction). Thus, for instance, when benzyl azide (**1**) was contacted with phenylacetylene (**2**) in the presence of [Cu(2-pymo)$_2$] in ethanol at 70 °C, complete conversion of the benzyl azide was observed after 4 h (Table 1, entry 1). Meanwhile, the only product obtained was the 1,4-substituted triazole (**3a**), being the reaction regioselective, as expected for a copper-catalyzed 1,3-dipolar cycloaddition [6,19,20].

Table 1

Results obtained for the 1,3-dipolar cycloaddition reaction catalyzed by various copper-containing MOF catalysts



Entry	Catalyst	Yield of **3a**[b] (%)	Reaction time (h)
1	[Cu(2-pymo)$_2$]	>99	4
2	[Cu(im)$_2$]	>99	1
3	[Cu_3(BTC)$_2$]	37	8
4	[Cu(BDC)]	42	8

[a] Reaction conditions: benzyl azide (1 mmol) and phenylacetylene (1.2 mmol) in ethanol (6 ml), copper MOF (0.1 mol% Cu), 70 °C, N_2 atmospheric pressure.

[b] Determined by GC using hexadecane as external standard. The reaction is regioselective to product **3a**: no traces of **3b** were detected.

After the catalytic reaction, the solid MOF was recovered by filtration and thoroughly washed with ethanol. According to the X-ray diffraction patterns of [Cu(2-pymo)$_2$] before and after the catalytic reaction, (see Fig. S2 in Supplementary material), the crystalline structure of the material was preserved. The copper-containing MOF can be reused for at least six consecutive runs without loss of activity and selectivity.

The heterogeneous nature of the catalytic process was demonstrated by a hot filtration test. Thus, the reaction was stopped at partial conversion (~40%), and the catalyst was quickly removed by filtration at the reaction temperature, to avoid re-precipitation from the solution of eventually leached species. After filtration, the reaction filtrate was allowed to react at 70 °C, but the conversion did not increase further (see Fig. S3 in Supplementary material). According to chemical analysis (as determined by ICP-AES), the filtrate did not contain appreciable amounts of copper leached from the solid. Moreover, the contribution of the thermal 1,3-dipolar cycloaddition (i.e., uncatalyzed reaction) to the overall conversion was found to be negligible; i.e., less than 1–2% conversion after 12 h under the present reaction conditions.

Besides [Cu(2-pymo)$_2$], other copper-containing MOFs were also found to be active, regioselective and reusable [21] for 1,3-dipolar cycloaddition reactions, although different performances were observed for each material. Copper trimesate, [Cu_3(BTC)$_2$], and copper terephthalate, [Cu(BDC)] (Table 1, entries 3 and 4), showed lower activities than [Cu(2-pymo)$_2$] and copper imidazolate, [Cu(im)$_2$] (entries 1 and 2). Kinetic curves for the reaction over the four catalysts are shown in Fig. S4 in Supplementary material. Thus, our findings indicate that Cu-MOFs are active and selective catalysts for "click" reaction. Moreover, MOFs featuring copper(II) sites surrounded by four diazaheterocyclic nitrogen atoms (CuN_4) are generally more active catalysts than those having copper centers surrounded by four carboxylate oxygen atoms (CuO_4). The differences in activity cannot be explained based on pore dimensions, since all the MOFs tested have channel dimensions larger than the substrates and products of the "click" reaction. So, diffusion limitations can, in principle, be ruled out. Nevertheless, when the kinetic evolution of products was closely analyzed, a clear reaction induction period could be observed with all MOF catalysts, being the

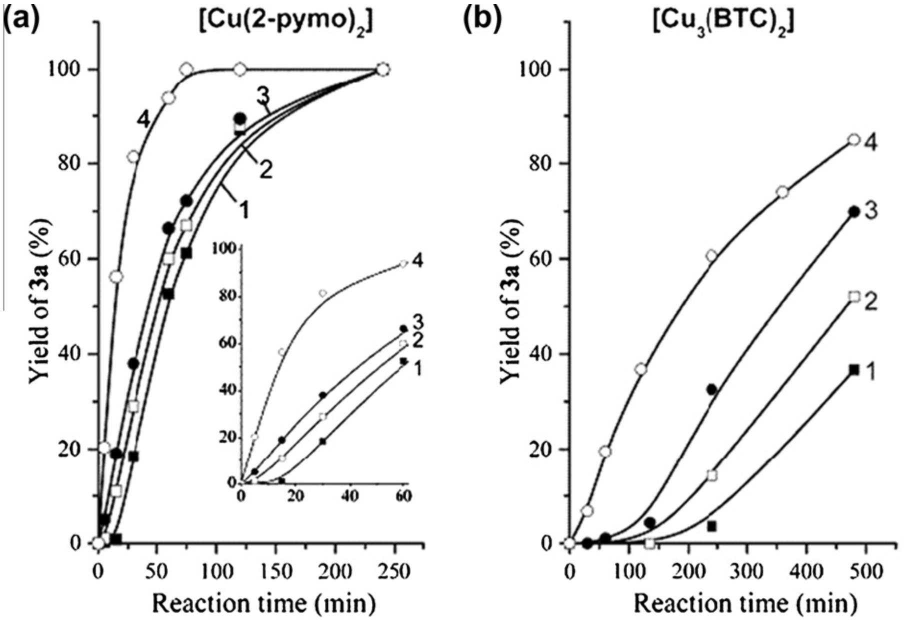


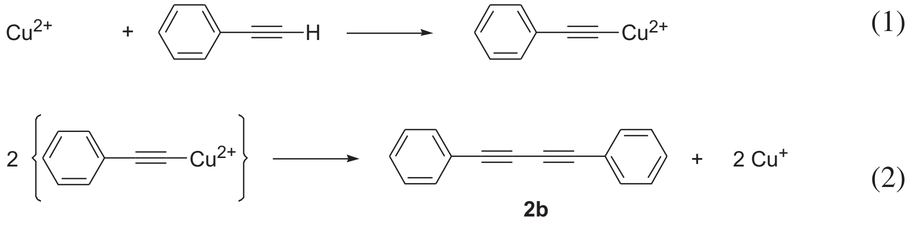
Fig. 1. Time–conversion plots of benzyl azide (**1**) over (a) [Cu(2-pymo)$_2$] and (b) [Cu$_3$(BTC)$_2$]. In both parts, the numbers of each curve indicate the time of pre-treatment with phenylacetylene before adding benzyl azide. Curve 1: no pre-treatment; curve 2: 15 min; curve 3: 30 min; curve 4: 4 h. The inset in part (a) shows an expanded view of the first 60 min of reaction to appreciate better the induction period.

induction period much longer for MOFs containing CuO$_4$ centers; i.e., [Cu$_3$(BTC)$_2$] and [Cu(BDC)]. We also observed that when the catalysts were pre-treated with the alkyne for a certain time period (up to 4 h) before adding the azide, the induction period gradually disappeared in all cases. To illustrate this point, Fig. 1 shows the results obtained for [Cu(2-pymo)$_2$] and [Cu$_3$(BTC)$_2$], while analogous results were obtained for the other two MOFs, [Cu(im)$_2$] and [Cu(BDC)].

The marked differences observed between MOFs containing CuN$_4$ and CuO$_4$ centers prompted us to analyze in detail the coordination environment around copper in different materials as a possible cause for the differences in reactivity observed. Reactivity differences could be related to a different electron donation ability of the diazaheterocyclic N atoms with respect to the carboxylate O atoms, thus resulting in different charge densities on the central copper ions. However, this hypothesis was discarded at the light of first principle calculations performed on MOF cluster models, which in all cases evidenced almost identical charge densities on the copper ion: +1.28 for [Cu(2-pymo)$_2$]; +1.27 for [Cu(im)$_2$] and +1.30 for [Cu$_3$(BTC)$_2$] and [Cu(BDC)]. Alternatively, a feasible explanation for the observed differences could be the accessibility of the reaction substrates to the catalytic center. The interaction of the copper sites with water molecules adsorbed in the pore system of the solid is stronger in the case of MOFs having CuO$_4$ centers. For instance, the Cu–O$_{water}$ distance in the case of [Cu$_3$(BTC)$_2$] is 2.165 Å [10], while it is larger than 2.5 Å for [Cu(2-pymo)$_2$] [22]. Furthermore, the higher catalytic activity of [Cu(im)$_2$] with respect to [Cu(2-pymo)$_2$] (compare entries 1 and 2 in Table 1) could be related to the fact that in the latter material, copper ions are in square planar coordination, while in the former, copper ions are displaced out of the plain, in a highly distorted tetrahedral coordination (trans N–Cu–N angles of ca. 140° and 155° [9]). Thus, the deformation energy necessary to allow the interaction between the copper site and the reaction substrate is probably lower in the case of [Cu(im)$_2$]. Further theoretical calculations with periodic models for both materials are currently underway to evaluate this point.

3.2. Nature of the active sites

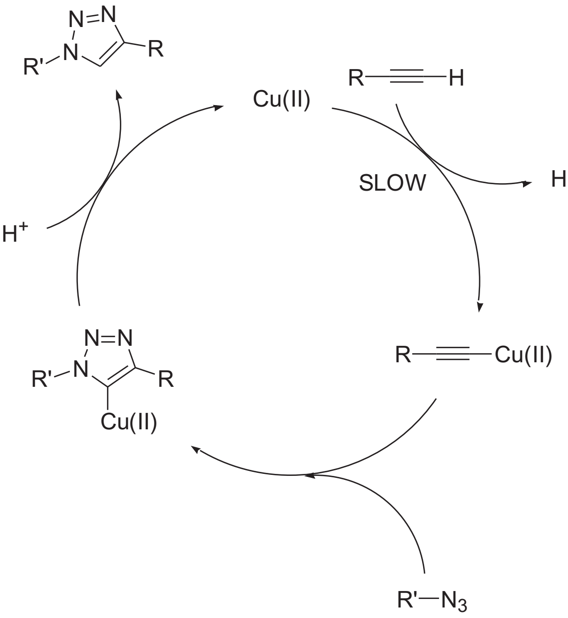
It is interesting to see that Cu(II) MOFs were active for this reaction, while it is generally accepted, with the sole exception of the report by Reddy et al. [23], that the active species for the "click" reaction between azides and terminal acetylenes are Cu(I) species. In the case of homogeneous catalysts, Cu(I) species are either added directly or formed in situ from Cu(II) salts by the action of a reducing agent, such as ascorbate [6]. In the case of solid catalysts, there is a widespread use of Cu(I) salts anchored on different solid supports [7,24–32], along with other materials having copper in a different oxidation state. For instance, when copper was in metallic Cu(0) state, such as metallic copper turnings [6] or in the form of supported copper metallic nanoparticles [33], the reaction was assumed to be mediated by Cu(I) ions present on the surface of the metal [33]. In the case of Cu(II)-containing solid catalysts, Yamaguchi et al. [34] have reported the existence of an induction period during the reaction between benzyl azide and phenylacetylene when using Cu(II) hydroxide particles supported on alumina and titania. The authors observed that the induction period disappeared when the catalyst was pre-treated with the acetylene before adding the azide. From these results, the authors concluded that the induction period corresponds to the time required for the formation of Cu(I) by reduction of the starting Cu(II) ions. During the pre-treatment of the catalyst with the acetylene, formation of the alkyne–alkyne homocoupling product (**2b**) was observed, almost in stoichiometric amounts with respect to the copper content of the catalyst. This was accompanied by the reduction of Cu(II) to Cu(I) following the process shown in Eqs. (1) and (2) in Scheme 1 [34]. According to this mechanism, an unstable derivative of Cu(II) acetylide would initially form, which would decompose into the phenylacetylene radical and a Cu(I) species. This would be followed by condensation of the two phenylacetylene radical species (the well-known Glaser reaction [35]). The resulting Cu(I) species formed in this process were proposed as the active catalytic sites for the ensuing 1,3-dipolar cycloaddition. Overall, the process consisted in the in situ generation of Cu(I) spe-



Scheme 1.

cies by the alkyne, without the need of adding external (sacrificial) reducing agents, such as ascorbate.

Given the similarities between the report by Yamaguchi et al. and our present results, concerning the presence of an induction period and the effect of acetylene pre-treatments, a similar mechanism can be thought for the Cu-MOF catalysts; i.e., in situ generation of Cu(I) sites mediated by the acetylene. However, all our attempts to detect the Cu(I) species eventually generated during this process failed. First of all, traces of the phenylacetylene homocoupling product (**2b**), which would indicate that reactions (1) and (2) are operating, were not detected. When EPR spectroscopy was used to study both the pre-treatment of the copper MOFs with phenylacetylene and the overall 1,3-dipolar cycloaddition reaction, it was not possible to detect any decrease in the signal due to Cu(II). Since formation of Cu(I) sites through reaction (2) implies the homolytic cleavage of the Cu(II)—C bond, the reaction was also carried out in the presence of a radical scavenger (TEMPO), but we failed to detect formation of radical species during the "click" reaction. Finally, the attempts to detect by UV–Vis spectroscopy the disappearance of the corresponding d–d transition bands of Cu(II) sites of the MOF, or the formation of Cu(I) phenylacetylide species [34], do not allow us to gather any evidence in favor of the formation of Cu(I). Therefore, although we cannot completely exclude generation of Cu(I) in our MOF systems, we did not observe any of the expected spectroscopic features or side product formation that, unambiguously, would confirm the formation and reactivity of Cu(I) as active sites [34]. Given the lack of direct or indirect evidences for Cu(I) formation, we thus must hypothesize that the active species for the 1,3-dipolar cycloaddition reaction over the copper-containing MOFs studied here consist of Cu(II) sites. If this is so, then we can better think on a reaction mechanism for Cu-MOFs, analogous to that proposed by Sharpless [19], but being the active species Cu(II) instead of Cu(I), as shown in Scheme 2. In that mechanism, formation of Cu(II) acetylide species would be the rate-determining step of the reaction, and this would explain the observed effect of catalyst pre-treatment with acetylene on the disappearance of the induction period. In order to check this possibility, the "click" reaction was carried out at different initial concentrations of phenylacetylene, and the results obtained are given in Fig. 2a. It can be seen there that the induction period decreases upon increasing phenylacetylene concentration. The result supports the reaction mechanism given in Scheme 2, where the controlling step should be the formation of the Cu(II)–phenylacetylide adduct. Indeed, when the concentration of phenylacetylene was kept constant and the initial concentration of the azide was varied (see Fig. 2b), changes in the induction period were practically negligible.



Scheme 2.

3.3. Comparison with homogeneous catalysts

In order to study the potential of copper-containing MOFs as heterogeneous catalysts for 1,3-dipolar cycloaddition reactions, their activity has been compared with that obtained with different Cu(II) and Cu(I) homogeneous catalysts, such as $\mathrm{CuCl_2}$, CuI, Cu(II)–phthalocyanine and $\mathrm{Cu(CH_3COO)_2}$. Among the different homogeneous catalysts, the best results were obtained with copper(II) acetate, which was found to be only slightly more active than $[\mathrm{Cu(im)_2}]$ under the same experimental conditions (see curves 1 and 2 in Fig. 3). The catalytic activity of copper acetate for the click reaction has already been described by Reddy et al. [23]. However, we noticed that during the course of the reaction in the presence of copper acetate, an insoluble yellow solid was formed. This corresponds to the well-known copper(I)–phenylacetylide coordination polymer, $[\mathrm{Cu(C{\equiv}C{-}Ph)}]$, as confirmed by X-ray diffraction [36] (see Fig. S5 in Supplementary material). Formation of this Cu(I) coordination polymer indicates that reactions 1 and 2 of Scheme 1 take place when phenylacetylene reacts with copper acetate and, indeed, it was possible to detect the formation of the phenylacetylene coupling product, **2b**. This is a completely different behavior with respect to copper MOFs, for which we did not detect any reduction of copper or concomitant formation of product **2b**. Nevertheless, the yellow solid poly-copper(I)–phenylacetylide, which irreversibly formed from copper acetate, was recovered and reused as catalyst in a successive run. This polymer was also found to be active for the "click" reaction (see curve 3 in Fig. 3), although it was considerably less active than the copper acetate precursor or $[\mathrm{Cu(im)_2}]$ MOF.

3.4. Solvent-free 1,3-dipolar cycloadditions with $[\mathrm{Cu(2\text{-}pymo)_2}]$ and $[\mathrm{Cu(im)_2}]$

Since MOFs containing $\mathrm{CuN_4}$ centers were solid and stable catalysts, they offer the possibility to perform the "click" reaction in

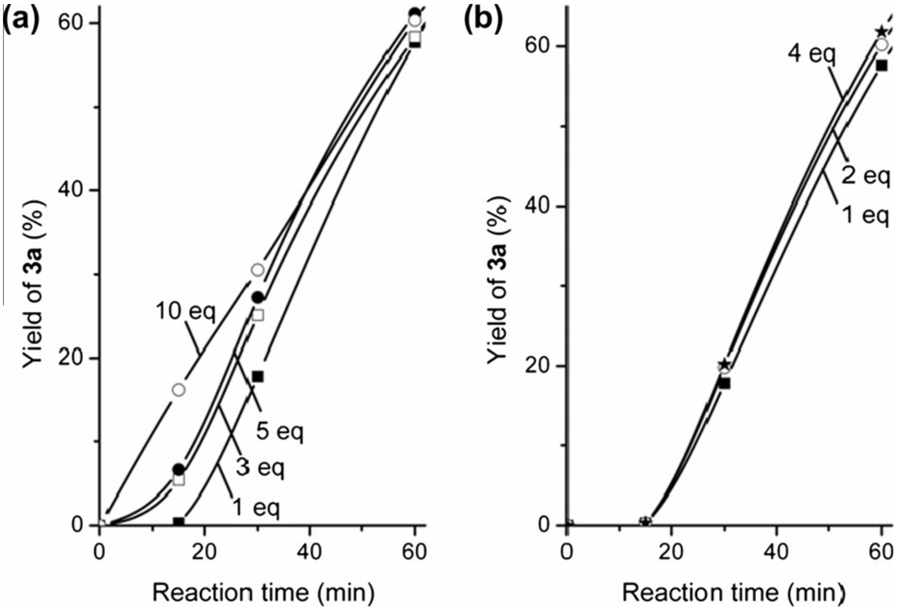


Fig. 2. Comparative time–conversion plots of benzyl azide over [Cu(2-pymo)$_2$]. In (a), the reaction was carried out at different initial concentration of phenylacetylene: 1, 3, 5 and 10 equivalents (with respect to benzyl azide). In (b), the amount of phenylacetylene was kept constant, and the initial concentration of benzyl azide was varied: 1, 2 and 4 equivalents (with respect to phenylacetylene). In all cases, the amount of Cu used was 0.1 equivalents with respect to the limiting substrate.

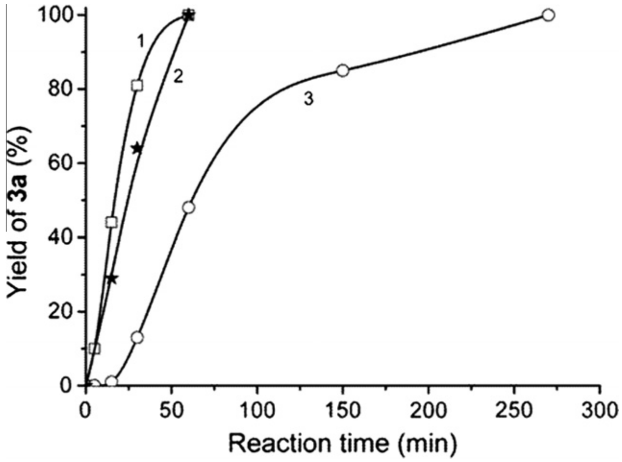


Fig. 3. Comparative time–conversion plots of benzyl azide (**1**) over: (1) copper acetate; (2) [Cu(im)$_2$] and (3) poly-copper(I) phenylacetylide, [Cu(C≡C—Ph)] (see text for details).

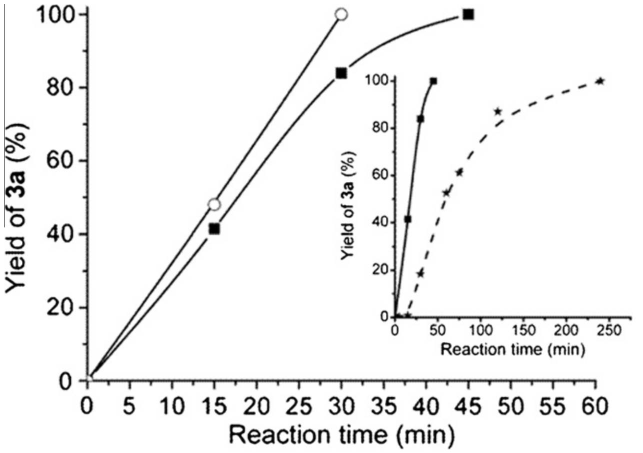
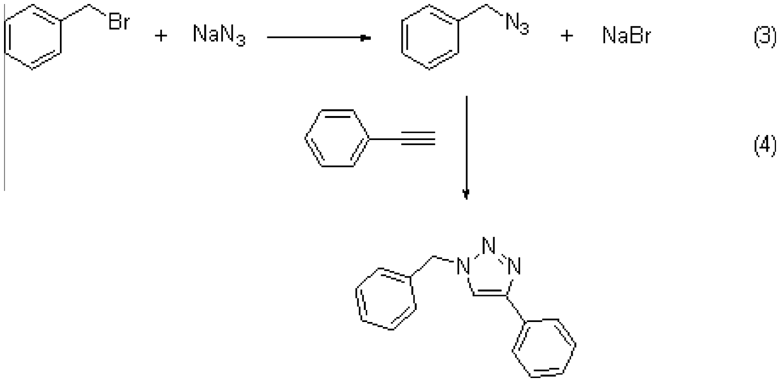


Fig. 4. Time–conversion plots of benzyl azide (**1**) over [Cu(2-pymo)$_2$] under solvent-free conditions. Square symbols correspond to the fresh catalyst, while open circles correspond to the second run. The inset shows a comparison of the kinetic data obtained with (start symbols) or without (square symbols) solvent.

absence of ethanol solvent and even could be used in fixed bed continuous reactors, if required. Therefore, we also studied here the possibility of performing "click" reactions without any extra solvent. Since the triazole product is a solid, we performed the reaction using an excess of phenylacetylide. These experimental conditions have, a priori, a number of advantages with respect to the conventional "click" reaction in alcoholic (or water/alcoholic) media reported so far: (1) The use of solvents and the necessity to treat additional wastes are avoided; (2) Continuous operation is very feasible. In fact, the reaction product can be separated at the end of reaction by simple filtration, since we observed that triazole crystallizes in phenylacetylene when the reaction medium is cooled to room temperature. Then, the excess phenylacetylene can be recycled and fed again to the reactor. Nevertheless, working in solventless conditions can also introduce additional problems (such as instability of the MOF under these new conditions or occurrence of unwanted side reactions), which have to be carefully examined. To check this point and to analyze the possibility of using the cooper MOFs as solvent-free "click" catalysts, we performed the reaction in a batch reactor under the following conditions: benzyl azide (131 mg, 1 mmol), phenylacetylene (1320 µl, 12 mmol) and [Cu(2-pymo)$_2$] (24 mg, 0.1 mmol Cu) at 70 °C. After the reaction, the catalyst was quickly recovered by filtration at the reaction temperature, and the filtrate was allowed to cool to room temperature, and then crystallization of the triazole product occurs. After recovering the triazole by filtration, the MOF and the excess of phenylacetylene were introduced again in the batch reactor, and 1 mmol of fresh benzylazide was added to start a second catalytic cycle. The results obtained are shown in Fig. 4. As it can be observed, when no solvent was used the reaction was much faster and the induction period was much shorter, when compared to the reaction performed in ethanol (see inset in Fig 4). This is not surprising, given the large excess of phenylacetylene used in the reaction. When the catalyst was reused in a second cycle, a decrease in activity was not observed, but rather a small increase in the initial



Scheme 3.

reaction rate (compare open circles and squares in Fig. 4). This probably indicates that the recovered catalyst contains some remaining phenylacetylide species adsorbed on the copper sites, which accelerate the reaction in the second catalytic run.

It is worth noticing that we did not observe side products, such as phenylacteylene polymerization or homocoupling products, and the reaction under solvent-free conditions is also completely selective to the 1,4-triazole regiosiomer, **3a**. The MOF recovered after two catalytic runs maintained the original crystallinity.

3.5. One-pot formation of the azide followed by "click" reaction through a cascade reaction

Process intensification by performing multistep reactions in a one-pot system is of economical and environmental interest, since it avoids costly separation and purification of intermediate products, while involving lower process investment and energy consumption [37]. Taking this into account, we explored here the possibility to form in situ the azide from the corresponding halogenated compounds and sodium azide, which will be successively reacted with the acetylene to form the 1,4-triazole. This can be considered a one-pot two-step domino reaction [38], as shown in Scheme 3.

The advantage of this method is the larger commercial availability and generally lower cost of the halo compounds with respect to the azido compounds. Additionally, the procedure avoids isolating the organic azides which, in certain cases, can be potentially unstable. We then studied the process in the presence of [Cu(2-pymo)$_2$] (or [Cu(im)$_2$]) in one-pot batch reactor. In a typical reaction, benzyl bromide (119 µl, 1 mmol), phenylacetylene (132 µl, 1.2 mmol) and sodium azide (71 mg, 1.1 mmol, dissolved in the minimum amount of water) were dissolved in ethanol (6 ml), and [Cu(2-pymo)$_2$] (24 mg, 0.1 mmol Cu) was added at 70 °C. When the reaction was completed, the solids (containing the MOF and NaBr) were separated by filtration and washed with water to eliminate NaBr. The recovered catalyst was used in a second catalytic cycle. The kinetic data are shown in Fig. 5. As it can be seen, the reaction with the fresh catalyst proceeds smoothly, at a rate comparable with the case in which the azide was directly used. However, the observed induction period was longer than when reacting the azido compound. Nevertheless, the catalytic activity of the recovered [Cu(2-pymo)$_2$] was maintained (full conversion of benzyl bromide was achieved after 4 h), and the X-ray diffractogram of the solid recovered after two catalytic cycles showed no evidences of crystallinity loss. This demonstrates the suitability of using [Cu(2-pymo)$_2$] as a catalyst for "click" reaction, even when the azide is formed in situ from the corresponding halo derivative. Also in this case, the results with [Cu(im)$_2$] were completely analogous to those obtained with [Cu(2-pymo)$_2$].

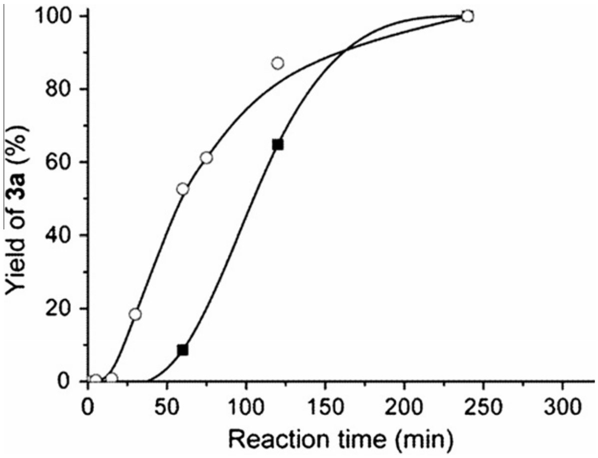


Fig. 5. Yield of 1,4-triazole (**3a**) over [Cu(2-pymo)$_2$] when benzyl azide (**1**) was formed in situ from benzyl bromide and sodium azide (square symbols), in comparison with the reaction starting directly from benzyl azide (open circles).

4. Conclusions

We have shown for the first time that Cu-MOFs are active and regioselective catalysts for "click" reactions (1,3-dipolar cycloaddition reactions) with activities and selectivities as high as when using homogeneous catalysts.

The organic component of the hybrid material can play an important role on the final activity, and it is shown that MOFs containing CuN_4 are more active than those with CuO_4 centers.

In the case of MOF catalysts, we were not able to detect the formation of Cu(I) species, which are believed to be the active ones for "click" reactions.

Cu-MOFs allow to propose a new process that does not require ethanol or water–alcohol solvent. Working in an excess of the alkyne, the reaction is highly effective, catalyst and products can be easily separated, and the excess of alkyne can be recycled.

Finally, the Cu-MOF catalysts are effective for the one-pot two-step domino reaction that forms first the azide that reacts with the acetylene to form the 1,4-triazole.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jcat.2010.09.010.

References

[1] A. Corma, Catal. Rev. Sci. Eng. 46 (2004) 369.

[2] A. Comas-Vives, C. Gonzalez-Arellano, M. Boronat, A. Corma, M. Iglesias, F. Sanchez, G. Ujaque, J. Catal. 254 (2008) 226.

[3] D. Farrusseng, S. Aguado, C. Pinel, Angew. Chem., Int. Ed. 48 (2009) 7502.

[4] J.Y. Lee, O.K. Farha, J. Roberts, K.A. Scheidt, S.T. Nguyen, J.T. Hupp, Chem. Soc. Rev. 38 (2009) 1450.

[5] A. Corma, H. Garcia, F.X. Llabrés i Xamena, Chem. Rev. 110 (2010) 4606.

[6] V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless, Angew. Chem., Int. Ed. 41 (2002) 2596.

[7] C.W. Tornøe, C. Christensen, M. Meldal, J. Org. Chem. 67 (2002) 3057.

[8] L.C. Tabares, J.A.R. Navarro, J.M. Salas, J. Am. Chem. Soc. 123 (2001) 383.

[9] N. Masciocchi, S. Bruni, E. Cariati, F. Cariati, S. Galli, A. Sironi, Inorg. Chem. 40 (2001) 5897.

[10] S.S.Y. Chui, S.M.F. Lo, J.P.H. Charmant, A.G. Orpen, I.D. Williams, Science 283 (1999) 1148.

[11] C.G. Carson, K. Hardcastle, J. Schartz, X. Liu, C. Hoffmann, R.A. Gerhardt, R. Tannenbaum, Eur. J. Inorg. Chem. (2009) 2338.

[12] C.N. Kato, M. Hasegawa, T. Sato, A. Yoshizawa, T. Inoue, W. Mori, J. Catal. 230 (2005) 226.

[13] M.J. Frisch, G.W. Trucks, H.B. Schlegel, Gaussian 03, Revision B.04, Gaussian, Inc., Pittsburgh, PA, 2003.

[14] A.D. Becke, J. Chem. Phys. 98 (1993) 5648.

[15] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785.

[16] P.J. Hay, W.R. Wadt, J. Chem. Phys. 82 (1985) 270.

[17] P.C. Hariharan, J.A. Pople, Theor. Chim. Acta 28 (1973) 213.

[18] E. Glendening, A.E. Reed, J.E. Carpenter, F. Weinhold, NBO, Version 3.1, Theoretical Chemistry Institute, University of Wisconsin, Madison, WI, 1993.

[19] F. Himo, T. Lovell, R. Hilgraf, V.V. Rostovtsev, L. Noodleman, K.B. Sharpless, V.V. Fokin, J. Am. Chem. Soc. 127 (2005) 210.

[20] M. Meldal, C.W. Tornøe, Chem. Rev. 108 (2008) 2952.

[21] Note in Fig. S2 of supplementary material that there are important differences between the diffractograms of fresh and used [Cu(BDC)]. However, these changes are not due to collapse of the crystalline structure, but they rather indicate that partial replacement of DMF by EtOH molecules has taken place, as already observed by Carson et al. [11].

[22] J.A.R. Navarro, personal communication.

[23] K.R. Reddy, K. Rajgopal, M.L. Kantam, Synlett (2006) 957.

[24] C. Girard, E. Onen, M. Aufort, S. Beauviere, A. Samson, J. Herscovici, Org. Lett. 8 (2006) 1689.

[25] U. Sirion, Y.J. Bae, B.S. Lee, D.Y. Chi, Synlett (2008) 2326.

[26] L. Bonami, W. van Camp, D. van Rijckegen, F.E. Du Prez, Macromol. Rapid. Commun. 30 (2009) 34.

[27] T. Katayama, K. Kamata, K. Yamaguchi, N. Mizuno, ChemSusChem 2 (2009) 59.

[28] S. Chassaing, M. Kumarraja, A. Sani Souda Sido, P. Pale, J. Sommer, Org. Lett. 9 (2007) 883.

[29] A. Alix, S. Chassaing, P. Pale, J. Sommer, Tetrahedron 64 (2008) 8922.

[30] S. Chassaing, A. Sani Souda Sido, A. Alix, M. Kumarraja, P. Pale, J. Sommer, Chem. Eur. J 14 (2008) 6713.

[31] B.H. Lipshutz, B.R. Taft, Angew. Chem., Int. Ed. 45 (2006) 8235.

[32] M. Chtchigrovsky, A. Primo, P. Gonzalez, K. Molvinger, M. Robitzer, F. Quignard, F. Taran, Angew. Chem., Int. Ed. 48 (2009) 5916.

[33] L. Durán Pachón, J.H. Van Maarseveen, G. Rothenberg, Adv. Synth. Catal. 347 (2005) 811.

[34] K. Yamaguchi, T. Oishi, T. Katayama, N. Mizuno, Chem. Eur. J. 15 (2009) 10464.

[35] C. Glaser, Berichte 2 (1869) 422.

[36] S.S.Y. Chui, M.F.Y. Ng, C.M. Che, Chem. Eur. J. 11 (2005) 1739.

[37] M.J. Climent, A. Corma, S. Iborra, ChemSusChem 2 (2009) 500.

[38] A.K. Feldman, B. Colasson, V.V. Fokin, Org. Lett. 6 (2004) 3897.