

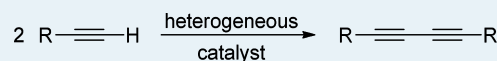
# Heterogeneous Catalytic Homocoupling of Terminal Alkynes

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**ABSTRACT:** The homocoupling of terminal alkynes under heterogeneous catalysis is tackled in this perspective. The performance of different unsupported and supported catalysts, primarily based on palladium and copper, is analyzed from a critical point of view. This type of coupling provides the most direct access to 1,3-diynes, which can be found in nature and are very important compounds in organic synthesis.

**KEYWORDS:** alkynes, coupling, palladium, copper, heterogeneous catalysis



## 1. INTRODUCTION

1,3-Diynes are widespread in nature, some of which possess prominent biological activities such as antibacterial, antimicrobial, antifungal, antitumor, anticancer, anti-HIV, or pesticidal properties (Scheme 1).<sup>1</sup> They have been isolated from varied natural sources including plants, fungi, bacteria, marine sponges, and corals. However, dihydromatricaria acid is the unique example of a conjugated diyne secreted by an insect (the soldier beetle). The 1,3-diyne moiety represents an important scaffold in supramolecular chemistry, especially for the construction of molecular boxes as high-efficiency hosts.<sup>2</sup> In addition, this structural motif plays an important role in the design of advanced materials such as conjugated polymers, liquid crystals, molecular wires or nonlinear optic materials, among others (Scheme 1).<sup>3,4</sup>

The metal-catalyzed homocoupling of terminal alkynes can be considered the most straightforward route to this type of compounds, though they can be also obtained by homocoupling of various preformed alkynyl organometallics (e.g., organolithium, organomagnesium, organoboron, organosilicon, organotin, or organolead compounds), iodoalkynes, or alkynyltellurides.<sup>5,6</sup> In particular, the oxidative dimerization of copper(I) acetylides, discovered in 1869 by Glaser,<sup>7–9</sup> has recently experienced an intense revival evolving into an array of methods which imply catalytic amounts of the metal.<sup>5,6,10–13</sup> There is a general upsurge of interest in maximizing the general efficiency of the process by seeking new catalytic systems which are simple (e.g., without palladium and additives such as oxidants or ligands), are environmentally benign (e.g., green solvents or solvent-free systems), minimize the amount of metal, and are recyclable. In this latter respect, heterogeneous catalysts are advantageous over the homogeneous counterparts, offering an easy recovery and recycling as well as enhanced stability.<sup>14,15</sup> In spite of the wide array of existing methods, the heterogeneously catalyzed homocoupling of terminal alkynes has been scarcely studied. The aim of this perspective is to survey the contributions to the field from a critical point of view, trying to point out the main advantages and disadvantages. To better compare the different methodologies reported, we will focus on those articles which involve heterogeneous catalysts, that is, the catalyst is in the solid

state in the reaction mixture. Some other reusable reaction systems with homogeneous catalysts,<sup>16–20</sup> though interesting, are out of the scope of this perspective. A recycling symbol accompanying every scheme represents the number of runs in which the catalyst was used in the homocoupling of phenylacetylene (unless otherwise stated).

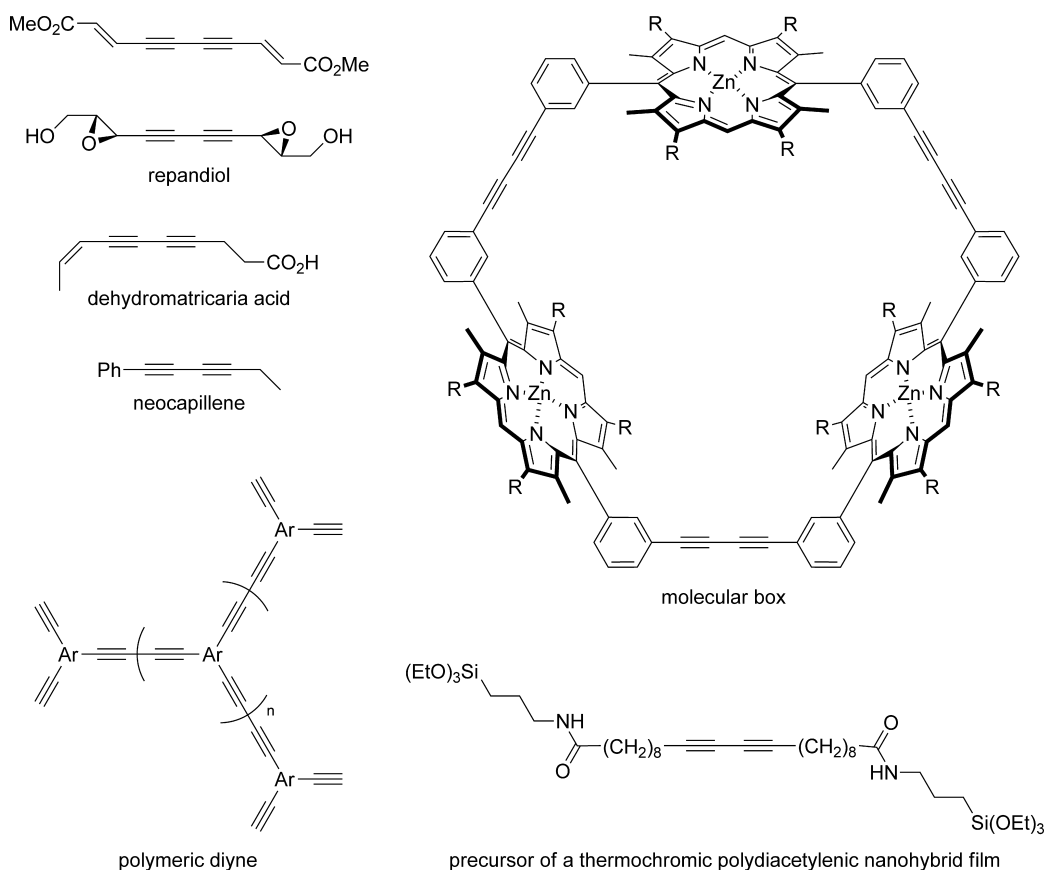
## 2. PALLADIUM-CATALYZED HOMOCOUPLING OF ALKYNES

Heterogeneous palladium catalysts have been widely used in coupling reactions because of their recycling properties which make processes more economical and efficient.<sup>21</sup> In 2005, while studying the Sonogashira reaction, Macquarrie et al. observed that palladium complexes anchored to mesoporous silica promoted the highly selective phenylacetylene homocoupling when 4-iodophenol was used as the Sonogashira partner compound.<sup>22</sup> Reactions were carried out in air with 1 mol % Pd in the presence of triethylamine (3 equiv) and undecane (1 equiv, as internal standard) at 70 °C for 12 h (Scheme 2). Interestingly, 2- and 3-iodophenol were unselective whereas the reaction failed with 4-iodoanisole. This unprecedented result was rationalized in terms of 4-iodophenol acting as an oxidizing agent of the intermediate Pd(0) adduct to the catalytically active Pd(II) complex (Scheme 2). The heterogeneous nature of the process was confirmed by the filtration test. The preparation of the catalyst seems rather tedious including the following: (a) preparation of aminopropyl silica, (b) reaction with 2-pyridinecarbaldehyde, (c) drying at 90 °C (overnight), (d) reaction with palladium(II) acetate in acetone (24 h), (e) filtration and washing with acetone, (f) drying in air at 90 °C (overnight), (g) refluxing in ethanol, toluene and then acetonitrile (27 h), and (h) drying in air at 90 °C (overnight). The reusability of the catalyst was only studied in a Sonogashira cross-coupling reaction but not in the alkyne homocoupling, with a partial loss of catalytic activity being observed in the third cycle (>99–53%).

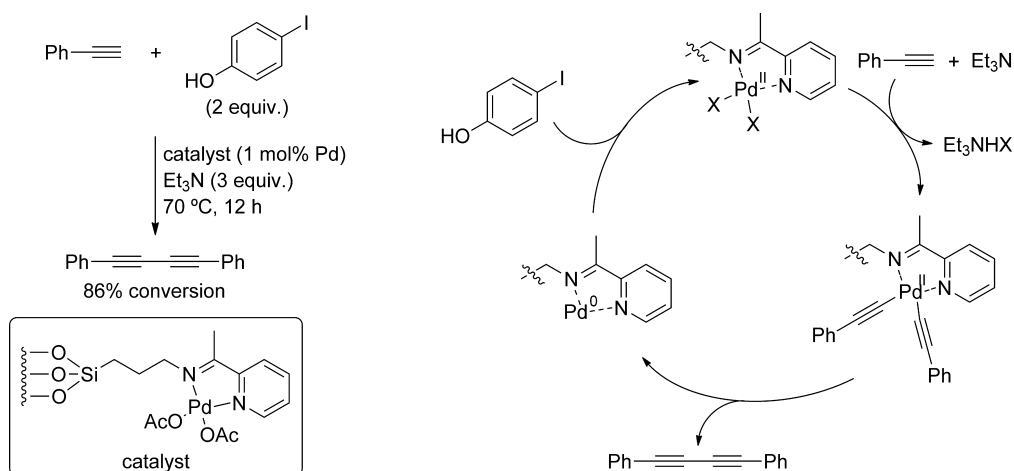
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Scheme 1. Some Examples of Natural and Synthetic 1,3-Diynes



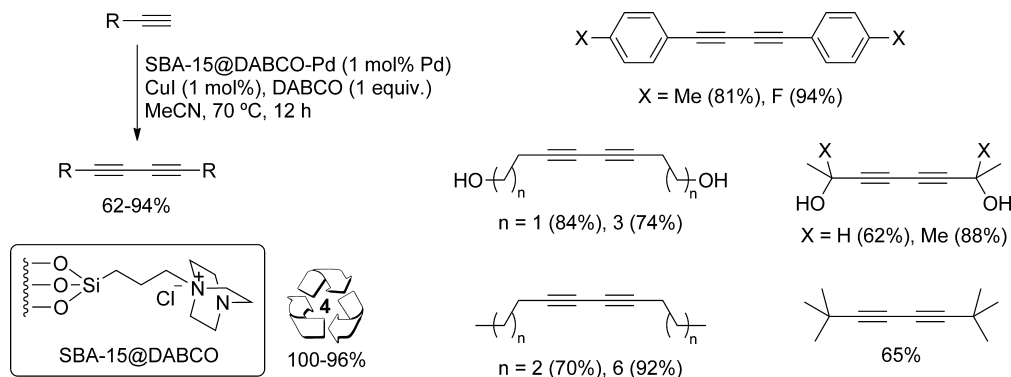
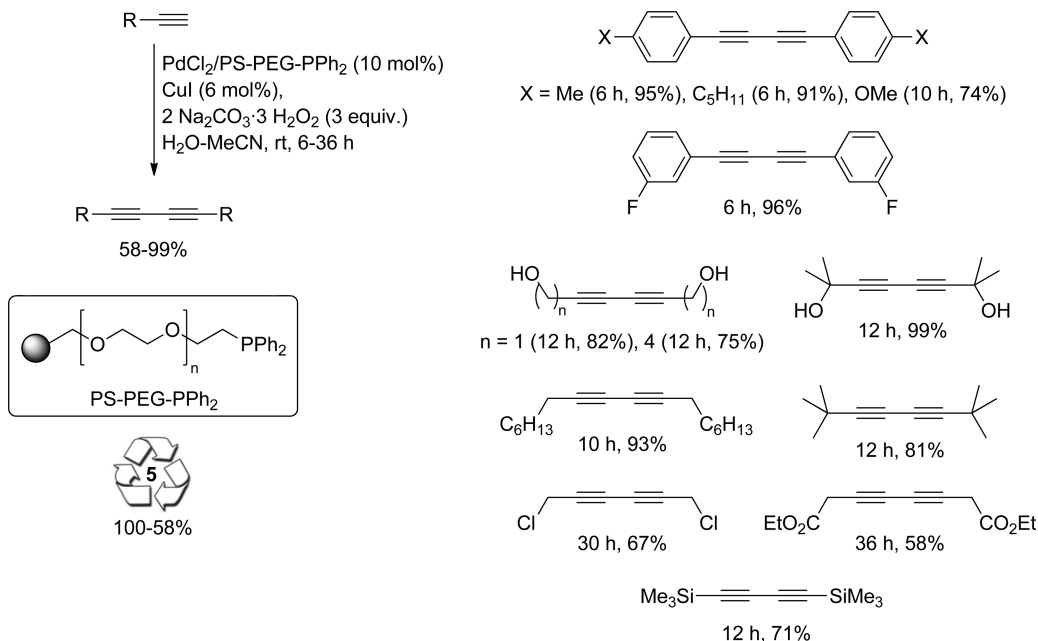
Scheme 2. Homocoupling of Phenylacetylene Catalyzed by Mesoporous-Silica Supported Palladium and the Proposed Catalytic Cycle



Very recently, the group of Yang and Pu prepared a catalyst based on palladium supported on a DABCO-functionalized SBA-15 mesoporous silica.<sup>23</sup> The catalyst, which was fully characterized, was composed of palladium nanoparticles (ca. 2–6 nm) in about 3.5:1 Pd(II)/Pd(0) ratio. A variety of aromatic and aliphatic alkynes, including hydroxyl-substituted alkynes, were transformed into the expected 1,3-diynes in moderate-to-high yields using 1 mol % of the SBA-15@DABCO-Pd complex (Scheme 3). The main feature of this article is the fact that reactions proceed at room temperature. However, the presence of stoichiometric DABCO (1 equiv) as a base and CuI (1 mol

%) as cocatalyst were found to be crucial to reach high conversions. It is noteworthy that this catalyst could be easily separated by centrifugation and filtration and reused over four cycles without any apparent loss of activity (100–96%). Moreover, additional reaction time (10 h) allowed further catalyst reutilization in a fifth run with quantitative product yield. The only unfavorable criticism to this work is the multistep and rather complex procedure required to obtain the definitive catalyst, including the following: (a) dispersion of SBA-15 in boiling toluene, reaction with (3-chloropropyl)-trimethoxysilane (24 h), filtration, Soxhlet extraction with 106

## Scheme 3. Homocoupling of Alkynes Catalyzed by SBA-15@DABCO-Pd and CuI

Scheme 4. Homocoupling of Alkynes Catalyzed by  $\text{PdCl}_2/\text{PS-PEG-PPh}_2$  and CuI

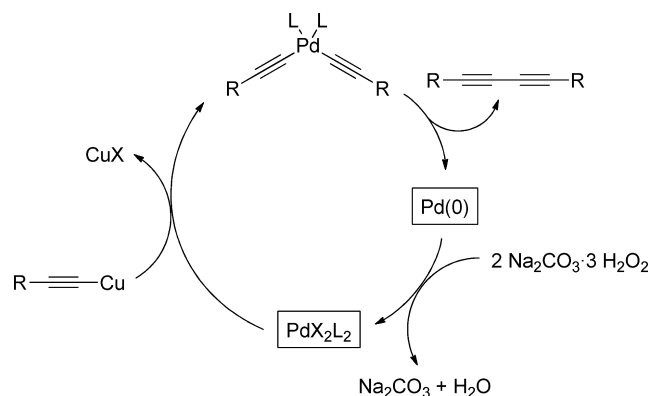
107  $\text{CH}_2\text{Cl}_2$ , and drying at 70 °C (5 h); (b) refluxing of the  
 108 resulting solid (SBA-15@Cl) with DABCO in acetone under  
 109 Ar (24 h), filtration, Soxhlet extraction with  $\text{CH}_2\text{Cl}_2$  (over-  
 110 night), and drying at 50 °C (4 h); (c) refluxing of the obtained  
 111 powder (SBA-15@DABCO) with  $\text{Pd}(\text{OAc})_2$  in acetone at 50  
 112 °C (5 h), filtration, washing three times with  $\text{Et}_2\text{O}$  and MeOH,  
 113 and drying under air.

114 Jiang et al. developed another palladium–copper cocatalyzed  
 115 homocoupling of terminal alkynes involving a palladium  
 116 complex immobilized on a PS-PEG<sub>400</sub>-PPh<sub>2</sub> resin.<sup>24</sup> Sodium  
 117 percarbonate (3 equiv) was used as the oxidant in aqueous  
 118 acetonitrile, with the latter playing a key role for the reaction to  
 119 succeed. Reactions were performed at room temperature with  
 120 relatively high catalyst loading (10 mol % Pd and 6 mol % CuI)  
 121 and were compatible with the presence of hydroxyl, chloro,  
 122 trimethylsilyl, and ester functionalities (Scheme 4). Some other  
 123 more sensitive functional groups (e.g., carbon–carbon double  
 124 bonds, carbonyl, amino, cyano, thioether groups, etc.) are  
 125 expected to be oxidized by sodium percarbonate.<sup>25,26</sup> The  
 126 catalyst was reused in five runs for the homocoupling of 2-  
 127 methyl-3-butyn-2-ol, with a decline in activity (100–58%)  
 128 which was ascribed to palladium leaching from the resin and/or  
 129 physical destruction of the polymer matrix by stirring. In the

proposed mechanism, the in situ generated copper acetylide is  
 130 transmetalated into a dialkynyl palladium(II) intermediate  
 131 which, eventually, undergoes reductive elimination to the diyne  
 132 and Pd(0). Sodium percarbonate was suggested to act both as a  
 133 base, in the generation of the acetylide, and as a reoxidizing  
 134 agent for the Pd(0) species to Pd(II) (Scheme 5). We must  
 135 underline that the PS-PEG<sub>400</sub>-PPh<sub>2</sub> resin is not commercially  
 136 available, but must be synthesized from PS-PEG-NH<sub>2</sub> resin  
 137 through (a) conditioning with solvents (MeCN and  $\text{CH}_2\text{Cl}_2$ );  
 138 (b) reaction with paraformaldehyde and diethylphosphane (65  
 139 °C under argon in toluene); (c) successive washing with  
 140 MeOH, MeCN, and  $\text{CH}_2\text{Cl}_2$ ; and (d) drying.<sup>27</sup>

A more environmentally benign protocol was introduced by  
 142 the group of Sajiki in which, symmetrical 1,3-diynes were  
 143 synthesized by oxidative dimerization of terminal alkynes with  
 144 heterogeneous Pd/C–CuI.<sup>28</sup> Low palladium loadings were  
 145 generally used (0.01 mol % for aromatic alkynes, 0.03 mol % for  
 146 aliphatic alkynes), together with CuI (3 mol %) in  
 147 dimethylsulfoxide (DMSO) at room temperature, under an  
 148 atmosphere of molecular oxygen (balloon) (Scheme 6). Under  
 149 these conditions, high yields of the corresponding diynes were  
 150 obtained, though the reaction of phenyl propargyl sulfide  
 151 required an extra amount of palladium (0.5 mol %) to  
 152

**Scheme 5. Proposed Catalytic Cycle for the Homocoupling of Alkynes Catalyzed by  $\text{PdCl}_2/\text{PS-PEG-PPh}_2$  and  $\text{CuI}$**



overcome the poisoning effect of sulfur. A modified method, involving air instead of molecular oxygen, was shown to be equally effective in the presence of higher amounts of palladium (0.05–0.3 mol %). Moreover, this method was applicable to a larger-scale reaction of 50 mmol of the alkyne. Apparently, reutilization of supported palladium was not attempted, but it would be recommended to study this possibility for those reactions carried out with larger amounts of catalyst.

### 3. COPPER-CATALYZED HOMOCOUPLING OF ALKYNES

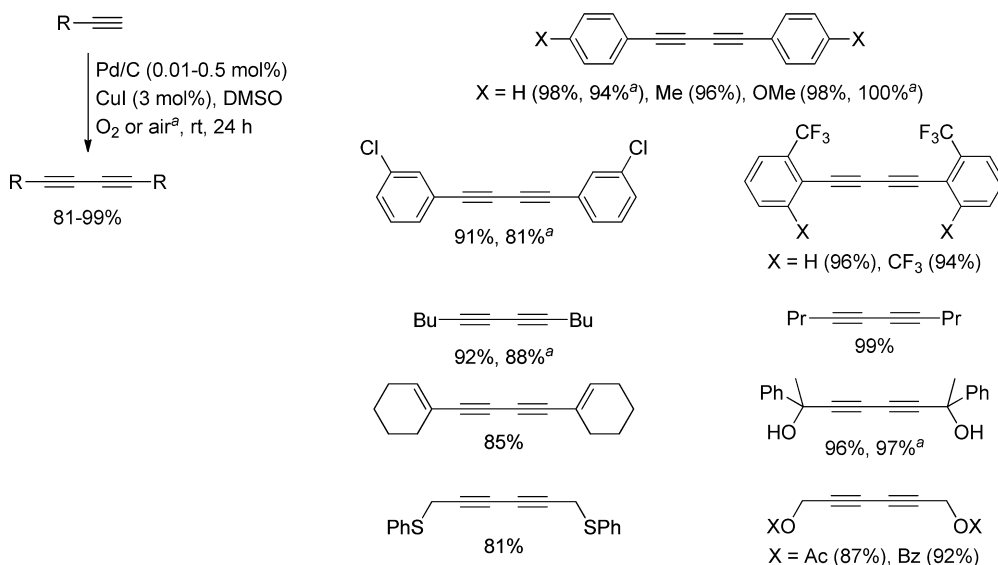
The development of catalysts that do not require precious metals should be a priority in modern research because (a) nonprecious metals are about 100 to 1000 fold cheaper than precious metals, because of their higher abundance; (b) the use of specialized and expensive organic ligands can be often avoided, and (c) in some cases, the environmental and toxicological impact can be minimal.<sup>29</sup> In this sense, copper has demonstrated to supplant noble metals in diverse organic reactions, with a notable success in coupling reactions.<sup>30–33</sup> The application of copper nanoparticles in coupling reactions is an emerging area which benefits from the advantageous features of metal nanoparticles.<sup>34</sup> Additional advantages of the nano-

catalysis can be obtained by immobilization of metal nanoparticles on high-surface-area inorganic supports, allowing a higher stability and dispersion of the particles as well as a further exploitation of the special activity and recycling properties of the catalyst.<sup>35–39</sup>

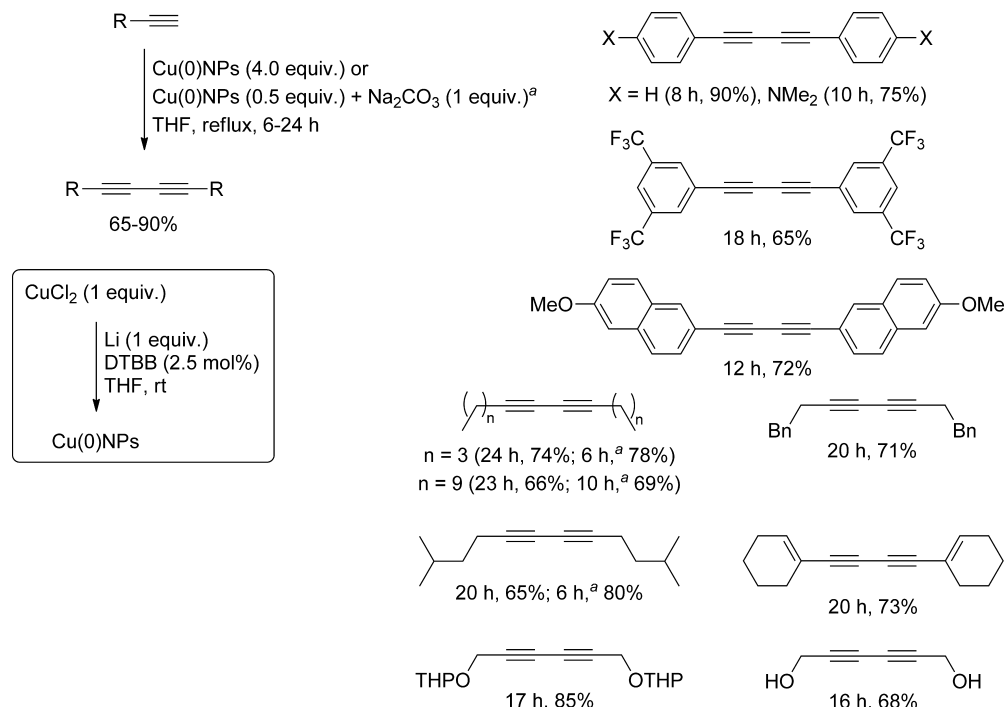
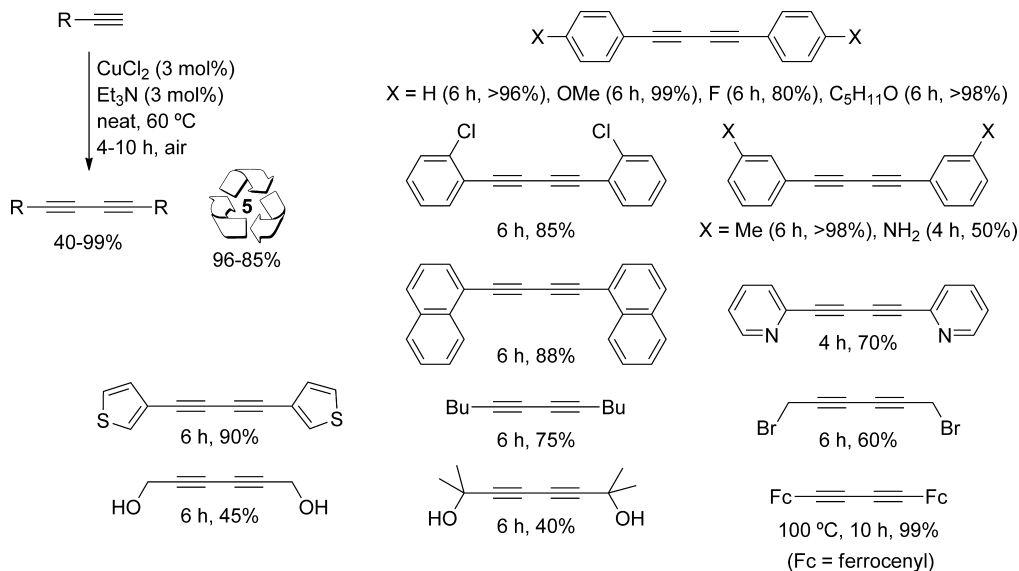
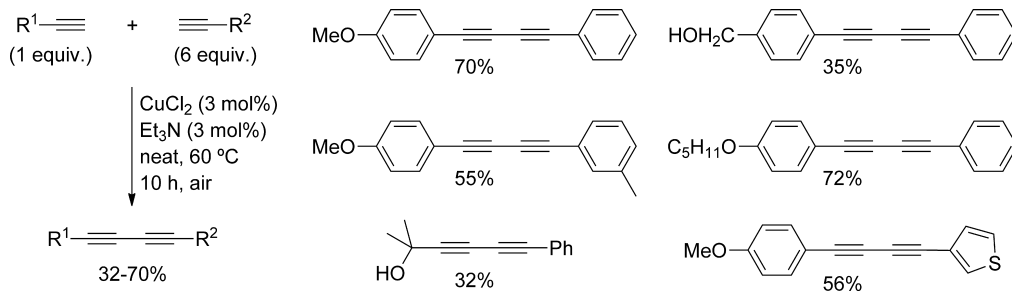
**3.1. Unsupported Copper Catalysts.** To the best of our knowledge, Radivoy et al. reported the first homocoupling of terminal alkynes promoted by copper nanoparticles.<sup>40</sup> The copper(0) nanoparticles ( $3.0 \pm 1.5$  nm) were readily generated from anhydrous copper(II) chloride, lithium metal, and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB, 2.5 mol %) as electron carrier, in tetrahydrofuran (THF) at room temperature. The homocoupling reaction was conducted with a large excess of copper nanoparticles (4 equiv) in refluxing THF under a nitrogen atmosphere, furnishing a wide range of diaryl- and dialkyl-substituted 1,3-diynes in moderate-to-high yields (Scheme 7). The generally longer reaction times required for alkyl-substituted alkynes, in comparison with the aryl counterparts, was attributed to partial agglomeration of the nanoparticles (15–30 nm) upon prolonged heating. It is worth noting that the addition of sodium carbonate (1.0 equiv) improved the reaction rate while allowing the use of a substoichiometric amount of CuNPs (0.5 equiv). The presence of the base was related to the deprotonation of the alkyne prior to the formation of alkynyl-CuNPs species, in a similar manner as suggested by Rothenberg and co-workers in Sonogashira-type reactions.<sup>41</sup> The CuNPs were not recovered, and it remains ill-defined whether Cu(0) or some other species are the true catalyst since half of the required amount of reductant for  $\text{CuCl}_2$  was employed.

An efficient and simple approach to the homocoupling of terminal alkynes was presented by Chen et al. using  $\text{CuCl}_2$  (3 mol %) and  $\text{Et}_3\text{N}$  (3 mol %) in air, at 60 °C under solvent-free conditions.<sup>42</sup> A variety of functional groups were resistant to these conditions, though modest yields were recorded for propargyl alcohol derivatives (Scheme 8). The reaction crudes could be purified by reduced pressure distillation, with this method being more environmentally benign than column chromatography. Furthermore, this methodology was extended to the cross-coupling of two different terminal alkynes by using

**Scheme 6. Homocoupling of Alkynes Catalyzed by  $\text{Pd/C}$ – $\text{CuI}$**



## Scheme 7. Homocoupling of Alkynes Promoted by Unsupported Copper Nanoparticles

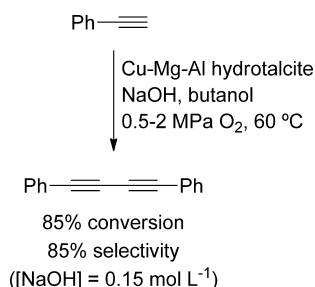
Scheme 8. Homocoupling of Alkynes Catalyzed by CuCl<sub>2</sub>Scheme 9. Cross-Coupling of Different Alkynes Catalyzed by CuCl<sub>2</sub>



under vacuum. Some decrease in the activity was observed after five cycles, with an average catalyst recovery of about 80%.

**3.2. Supported Copper Catalysts.** In 1995, Baiker and co-workers presented a copper-containing hydrotalcite as a heterogeneous catalyst for the homocoupling of phenylacetylene.<sup>43</sup> The Cu–Mg–Al hydrotalcite-derived catalyst was prepared by the coprecipitation method from Cu(NO<sub>3</sub>)<sub>2</sub>, Mg(NO<sub>3</sub>)<sub>2</sub>, and Al(NO<sub>3</sub>)<sub>3</sub> at 60 °C, in the presence of Na<sub>2</sub>CO<sub>3</sub>. The precipitate was successively subjected to filtration, washing with water, drying at 90 °C (48 h), and calcination at 400 °C (under vacuum, 4 h). The homocoupling of phenylacetylene was effected in a stainless steel autoclave containing dry NaOH dissolved in butanol under 0.5–2 MPa oxygen pressure at 60 °C (Scheme 10). No conversion was

**Scheme 10. Homocoupling of Phenylacetylene Catalyzed by a Cu–Mg–Al Hydrotalcite**



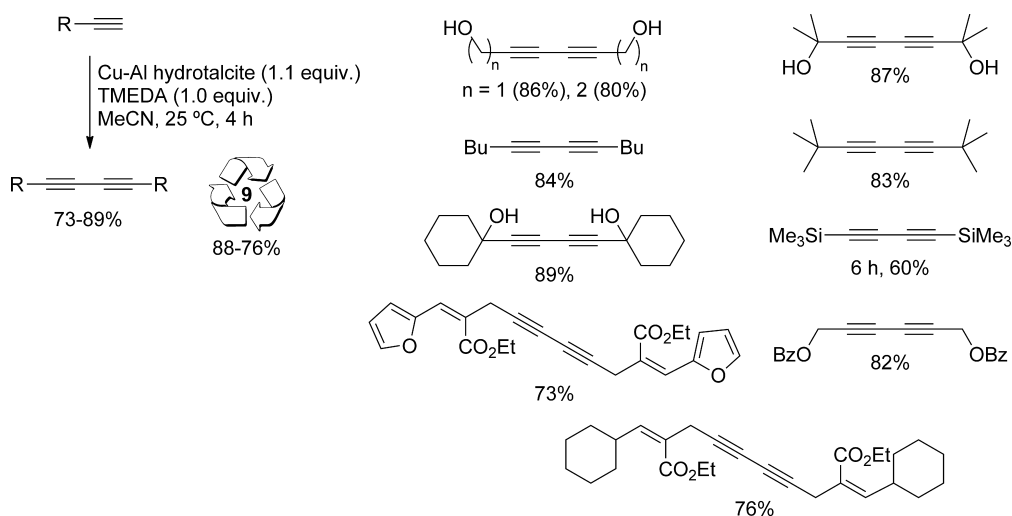
observed in the absence of the base, with the intrinsic basicity of the hydrotalcite being insufficient for deprotonating phenylacetylene. An optimum 85% conversion-selectivity was reached at a about [NaOH] = 0.15 mol L<sup>−1</sup>, whereas higher concentrations led to an increase in the formation of soluble copper hydroxide species. A prominent rise in the conversion was caused by increasing the oxygen pressure from 0.5 to 1.0 MPa. However, when compared with other heterogeneous methodologies, the whole procedure and equipment required is rather sophisticated. The substrate scope was limited to phenylacetylene and, though presented as a heterogeneous catalyst, no comment was made about its reutilization capability.

In contrast with the aforementioned report, the group of Jiang prepared a highly recyclable hydrotalcite for the homocoupling of alkynes at room temperature.<sup>44</sup> In this case, a Cu–Al hydrotalcite was obtained similarly as above, with the catalyst being finally dried overnight at 80 °C in air without calcination. Alkyne homocoupling was accomplished with stoichiometric amounts of TMEDA (1 equiv) and catalyst (1.1 equiv) in MeCN at 25 °C for 4 h (Scheme 11). Good yields of the corresponding diynes were attained in all cases, including the presence of hydroxyl, silane, or conjugate ester functionalities. The catalyst was recovered by filtration and exhibited excellent recyclability, with a slight decrease in the yield being observed only after the eight cycle (88–86% in 8 cycles, 76% ninth cycle). The recovered catalyst must be dried at 80 °C before each run, though the main challenge for this methodology should be to diminish the amount of catalyst.

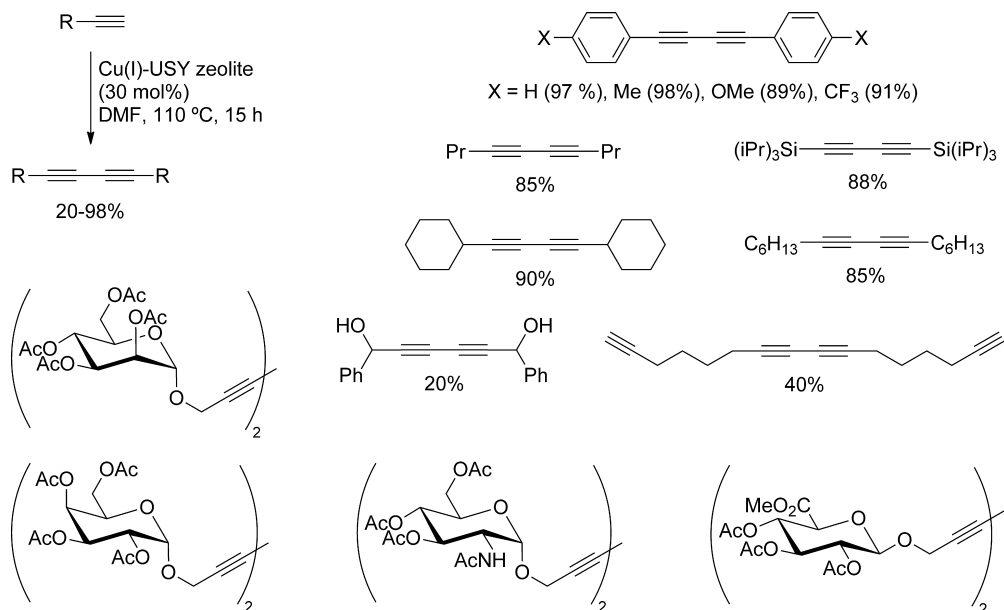
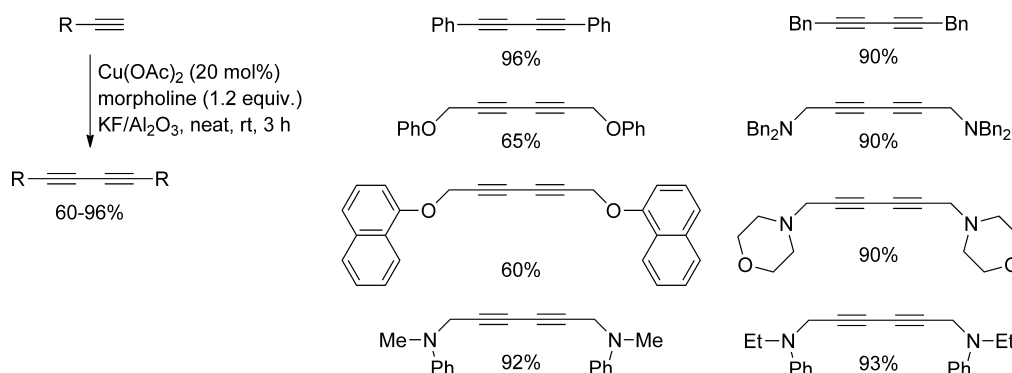
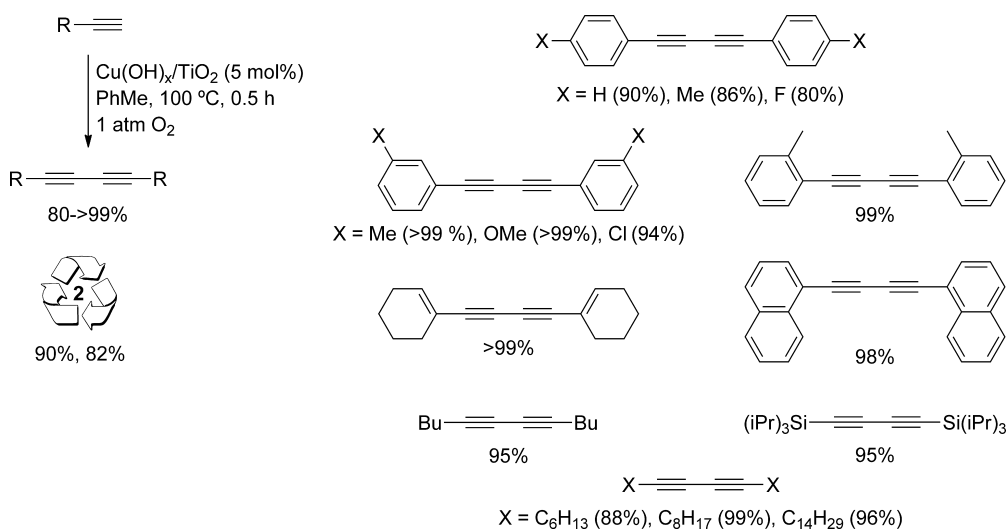
The group of Pale and Sommer prepared a variety of copper(I)-modified zeolites with which the title reaction was tested.<sup>45,46</sup> The authors concluded that Cu(I)-USY was the most efficient catalyst, behaving as an acidic Glaser-type catalyst [i.e., the rate increased with increasing copper(I) concentration]. The reaction efficiency could be directly correlated with the pore size of the zeolite (the larger the pore size, the higher the yield) as well as with the Si/Al ratio (the higher the Si/Al ratio, the higher the yield). Alkyne homocoupling was performed with 30 mol % copper loading in dimethylformamide (DMF) at 110 °C and was successfully accomplished, not only for common substrates but also for some carbohydrate derivatives with a pendant propargyl moiety (Scheme 12). Good-to-excellent yields of the expected diynes were recorded (74–98%), with the exception of two examples which underwent decomposition or oligomerization. One main advantage of this methodology is that the process proceeds in the absence of base; the reaction temperature and catalyst loading are, however, relatively high. Although it was confirmed that no leaching occurred during the reaction, no comment was made with regard to the possibility of catalyst recycling.

Kabalka et al. reported in 2001 the microwave enhanced, solvent free, Glaser coupling reaction on potassium fluoride-alumina in the presence of copper(II) chloride.<sup>47</sup> Although this method benefited from the solvent-free conditions and rapidness of the microwave irradiation (8 min), a large excess

**Scheme 11. Homocoupling of Alkynes Catalyzed by a Cu–Al Hydrotalcite**

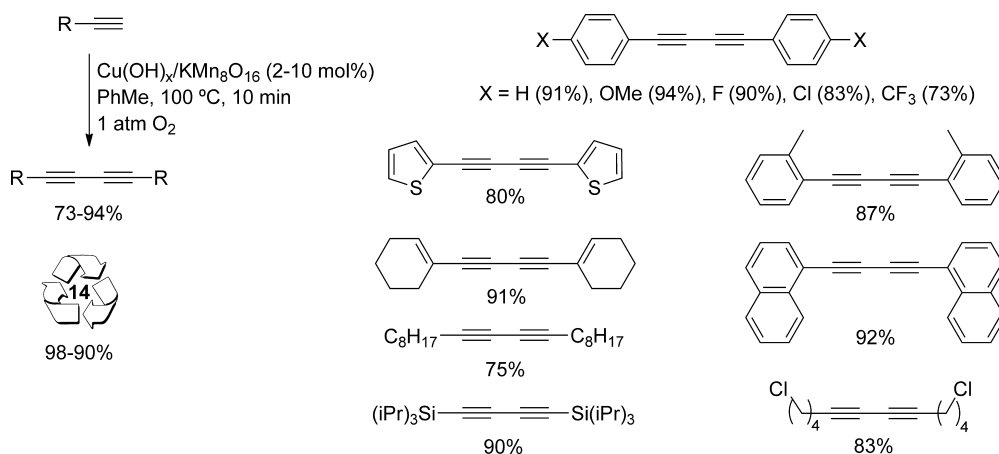


## Scheme 12. Homocoupling of Alkynes Catalyzed by Cu(I)-USY Zeolite

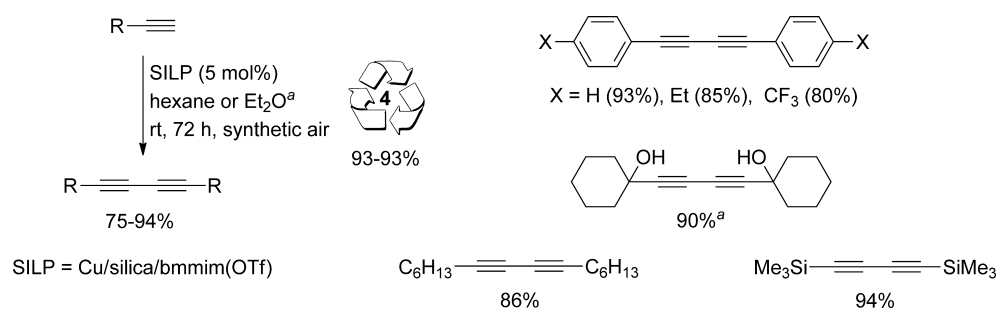
Scheme 13. Homocoupling of Alkynes Catalyzed by  $\text{Cu}(\text{OAc})_2\text{-KF/Al}_2\text{O}_3$ Scheme 14. Homocoupling of Alkynes Catalyzed by  $\text{Cu}(\text{OH})_x/\text{TiO}_2$ 

287 of the copper salt was utilized (3.7 equiv) to reach yields of up  
 288 to 75%. Soon after the group of Sharifi and Naimi-Jamal,  
 289 modified this method by using catalytic amounts of a copper  
 290 halide and alumina under microwave irradiation, getting

moderate yields of products.<sup>48</sup> More recently, this group  
 notably improved the methodology by grinding in a mortar a  
 mixture of the terminal acetylene with  $\text{KF/Al}_2\text{O}_3$  in the  
 presence of  $\text{Cu}(\text{OAc})_2\cdot\text{H}_2\text{O}$  (20 mol %) and morpholine (1.2

Scheme 15. Homocoupling of Alkynes Catalyzed by  $\text{Cu}(\text{OH})_x/\text{KMn}_8\text{O}_{16}$ 

Scheme 16. Homocoupling of Alkynes Catalyzed by SILP



equiv).<sup>49</sup> Under these conditions, the homocoupling was effected at room temperature, leading to the expected diynes in moderate-to-excellent yields (Scheme 13). The substrate scope studied was rather limited, and the reaction time was not clearly specified in every case. Another aspect which remains unclear is whether the copper(II) salt gets adsorbed on  $\text{KF}/\text{Al}_2\text{O}_3$  or both components operate independently. At any rate, no comment was made regarding the recovery and reusability of the catalyst.

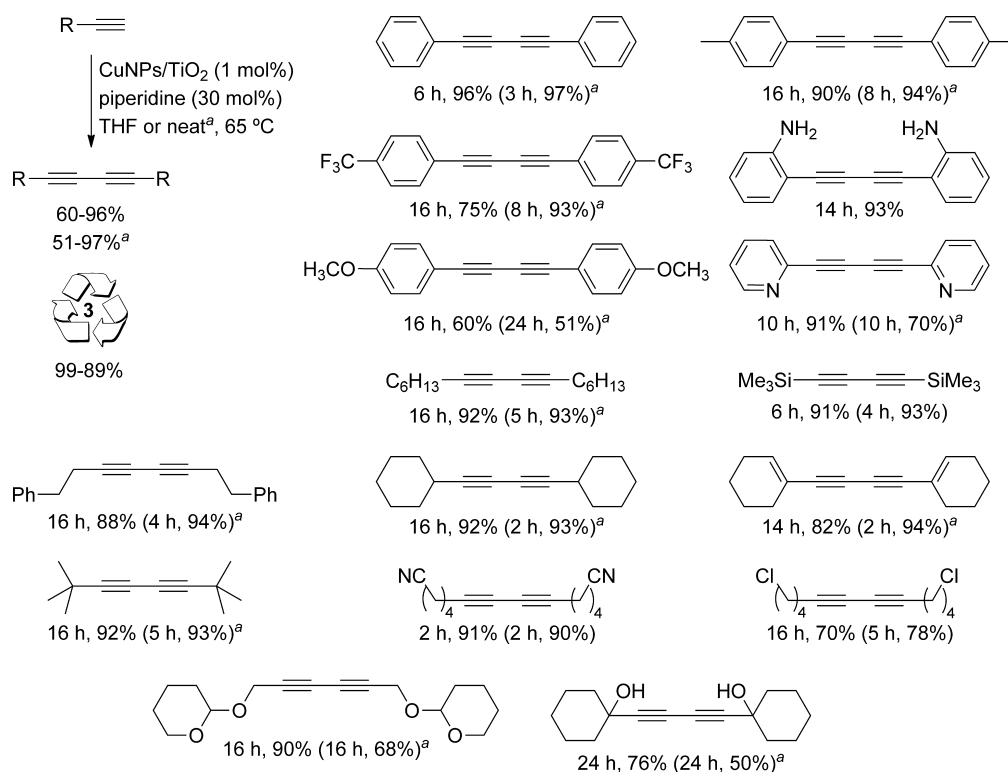
Mizuno et al. described a catalyst for the alkyne homocoupling consisting of copper hydroxide on titania [ $\text{Cu}(\text{OH})_x/\text{TiO}_2$ , 5 mol % Cu] which did not require the presence of a base and showed good catalytic activity (0.5 h) in toluene at 100 °C under 1 atm of molecular oxygen.<sup>50</sup> The catalyst was easily prepared by the impregnation method (calcined titania with an aqueous solution of  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ), involving the following: pH adjustment to 12 with NaOH, stirring for 24 h, filtration, washing with water, and drying in vacuo. The XPS peaks pointed to +2 as the most probable oxidation state of copper. The base treatment was found indispensable for a high catalytic performance, with the authors suggesting that copper hydroxide species form alkynyl species by abstraction of the alkyne acidic hydrogen. The substrate scope mostly covered hydrocarbon-based alkynes (11 examples), whereas the tolerance toward more reactive functional groups was not studied (Scheme 14). All yields were >80%, albeit they were determined by gas chromatography; isolated yields are preferable to GC yields to assess the practical utility of a given methodology. Different experiments ruled out the participation in the process of leached copper species or free-radical intermediates. Unfortunately, only one recycling experiment was presented in this article, showing a slight decrease in

yield (from 90 to 82%). In view of the above data, it is difficult to gauge the potential application of this catalytic system which, in addition, requires rather high temperature in toluene and an atmosphere of molecular oxygen.

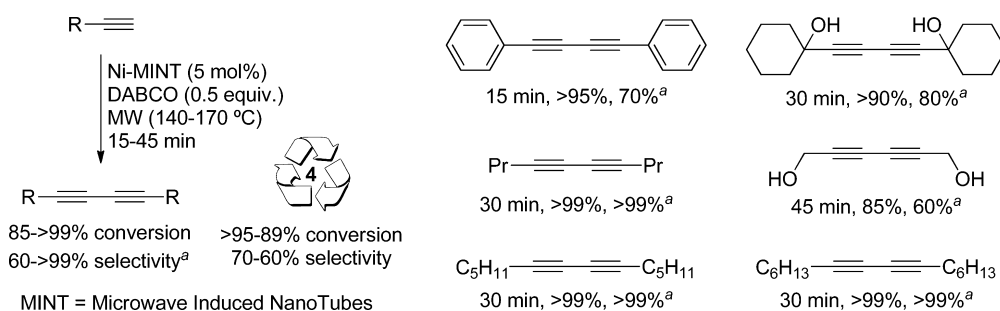
The same group above obtained a much more efficient catalyst following the same procedure but changing the  $\text{TiO}_2$  support into a manganese oxide-based octahedral molecular sieve ( $\text{KMn}_8\text{O}_{16}$ ).<sup>51</sup> The original idea was to use the manganese oxide as an electron mediator for the reoxidation of the copper(I) species. The catalyst reached high values of turnover frequency (TOF) and turnover number (TON) in comparison with other heterogeneous catalysts and could be reused in 14 runs with an excellent performance (98–90%). Reactions were very fast (10 min) and high yielding (73–94%) in toluene at 100 °C under 1 atm of molecular oxygen (Scheme 15). Longer reaction time was required under an air atmosphere, with the homocoupling of phenylacetylene being quantitative (40 min, >99%). Unfortunately, only this example was reported and, therefore, it is difficult to estimate if other substrates (especially aliphatic alkynes) would behave similarly. The process with molecular oxygen was successfully scaled to one gram of phenylacetylene (94% yield). A difficulty encountered while studying the substrate scope was the variable amounts of catalyst required for different alkynes, including 2, 3, 5, and 10 mol % Cu.

Supported ionic liquid phase (SILP) catalysts consist of homogeneous catalysts or catalyst precursors immobilized in a thin film of an ionic liquid on the surface of a porous carrier material by physisorption, ionic or covalent anchoring.<sup>52–54</sup> Very recently, the group of Szesni prepared a wide range of SILP catalysts by immobilization of  $[\text{Cu}(\text{TMEDA})(\text{OH})]\text{Cl}$  in a nanometric film of an ionic liquid on various supports.<sup>55</sup> The



Scheme 17. Homocoupling of Alkynes Catalyzed by CuNPs/TiO<sub>2</sub>

## Scheme 18. Homocoupling of Alkynes Catalyzed by Ni-MINT



homocoupling of phenylacetylene was studied for catalyst screening, using 5 mol % Cu in hexane at room temperature for 72 h under synthetic air. A gradual increase in the activity of the tested catalysts was shown with decreasing surface area of the parent support material, reaching a maximum for medium surface areas (80–180 m<sup>2</sup> g<sup>−1</sup>). Thus, the catalytic systems based on silica and bmmim(OTf) (1-butyl-2,3-dimethylimidazolium triflate) successfully accomplished the homocoupling of several alkynes and could be reused for at least four times with no appreciable loss of activity (Scheme 16). The filtration test confirmed the process being heterogeneous in nature. The synthesis of the catalyst, thought not a direct one, seems easy despite the fact that the starting copper complex is not commercially available. The methodology is advantageous in the sense that reactions proceed at room temperature. However, the reaction time is excessive (72 h) and the substrate scope covered rather narrow. Finally, the previously reported methodology based on copper nanoparticles<sup>40</sup> was substantially upgraded by the group of Alonso and Yus with the introduction of supported nanoparticles.<sup>56</sup> A variety of copper catalysts were obtained

by simply adding the support to a suspension of the CuNPs, with the latter being readily generated from anhydrous copper(II) chloride, lithium metal, and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB, 10 mol %) in THF at room temperature.<sup>57–61</sup> In addition, the supported catalysts did not require any kind of treatment prior to use. The catalyst composed of ultrafine CuNPs/TiO<sub>2</sub> (ca. 1.0 ± 0.4 nm, mainly as Cu<sub>2</sub>O, 1 mol % Cu) exhibited the best performance either in THF or without any solvent at 65 °C in the presence of piperidine (30 mol %), producing a series of 1,3-diynes in high yields (Scheme 17). In general, reactions under solvent-free conditions were faster. This catalyst was found to be much more efficient than other commercially available catalysts based on copper, such as metal copper or the copper chlorides and oxides. Moreover, the catalyst, at low metal loading, could be reused over three cycles with negligible leaching. Different experiments conducted to gain an insight into the reaction mechanism allowed to conclude that alkynyl radicals were not involved in a process which was operationally simple (solvent and oxygen atmosphere were not required) and which, surprisingly, also gave high yields of product in an inert

401 atmosphere.<sup>62</sup> Although a higher reuse capability would be  
402 desirable, we must take into account that the amounts of both  
403 catalyst and copper loading utilized were low.

#### 4. OTHER CATALYSTS

404 The nickel-catalyzed homocoupling of alkynes has been barely  
405 reported, normally in the presence of CuI as cocatalyst.<sup>63,64</sup>  
406 Recently, Luque and co-workers prepared metal-containing  
407 tubular silica-based nanostructures from tetraethoxyorthosili-  
408 cate in the presence of a metal salt and dodecylamine in water-  
409 acetonitrile under microwave irradiation (1–15 min, 80–110  
410 °C).<sup>65</sup> Among the metals tested, Ni-MINT (Ni-Microwave  
411 Induced NanoTubes) was shown to be the most active catalyst  
412 in the homocoupling of phenylacetylene. Six terminal alkynes  
413 were subjected to the homocoupling reaction using 5 mol % Ni  
414 and 0.5 equiv of DABCO under microwave heating (300 W,  
415 140–170 °C, 15–45 min) (Scheme 18). The conversions and  
416 selectivities were high for alkyl-substituted alkynes, whereas the  
417 selectivities decreased to 60–80% for phenylacetylene and  
418 hydroxyl-substituted alkynes. The catalyst could be reused over  
419 four consecutive cycles (>95–89% conversion) maintaining  
420 good activity with a decline in the selectivity (70–60%).  
421 Although the reaction times are relatively short, some more  
422 sensitive functional groups might not tolerate the high  
423 temperatures applied, giving undesired side reactions. Indeed,  
424 it is our belief that the moderate selectivity attained in half of  
425 the examples studied could be attributable to partial cyclo-  
426 trimerization of the alkyne, given that nickel can promote this  
427 type of reaction. This side reaction might hamper the  
428 applicability of the catalytic system since the separation of  
429 such a hydrocarbon mixture would be troublesome.

#### 5. CONCLUDING REMARKS

430 The homocoupling of alkynes under heterogeneous catalysis  
431 offers easy recovery and reuse of the catalyst as major  
432 advantages with respect to the homogeneous counterpart. In  
433 this context, some heterogeneous palladium catalysts have been  
434 devised, mostly as immobilized complexes. Although low  
435 palladium loading is generally used, the high price of this  
436 precious metal and the need for copper cocatalysis has led to  
437 the displacement of palladium in favor of copper as the metal of  
438 choice. The long and tedious procedures required for palladium  
439 immobilization, together with the large amounts of solvents  
440 utilized during the catalyst preparation, are additional  
441 inconveniences that curtail the practical application of these  
442 methodologies. Certainly, copper catalysts are much more  
443 attractive because they can provide similar or even superior  
444 performance at a lower cost with simpler protocols. In  
445 particular, the supported copper catalysts are especially  
446 interesting because the separation from the reaction mixture  
447 is easier and they can be highly effective at low metal loading.  
448 Notwithstanding these advantages, the following general  
449 guidelines might be considered to design more efficient  
450 heterogeneous catalytic systems for the alkyne homocoupling,  
451 namely, (a) easy to implement and cost-effective methods for  
452 catalyst preparation; (b) relatively low catalyst loadings,  
453 preferably <5 mol %; (c) use of ecofriendly solvents or  
454 solvent-free reactions; (d) air as the natural oxidant instead of  
455 molecular oxygen or other chemical oxidants; (e) the absence  
456 of base or use of substoichiometric amounts of base; (f)  
457 reactions at room temperature or below 100 °C at least; and  
458 (g) scalable reactions. In addition, the cross-coupling of two

different terminal alkynes is a challenging issue not properly  
addressed yet which, together with the aforementioned  
requirements, leaves enough play for originality and creativity  
in the field.

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#### REFERENCES

- (1) For a review on naturally occurring polyyne, see: Tykwinski, R. R.; Shi Shun, A. L. K. *Angew. Chem., Int. Ed.* **2006**, *45*, 1034.
- (2) Whitlock, B. J.; Whitlock, J. W. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Eds.; Pergamon: Oxford, U.K., 1996; Vol. 2, Chapter 10.
- (3) Diederich, F.; Stang, P. J.; Tykwinski, R. R. *Acetylene Chemistry: Chemistry, Biology, and Materials Science*; Wiley-VCH: Weinheim, Germany, 2005.
- (4) Liu, J.; Lam, J. W. Y.; Tang, B. Z. *Chem. Rev.* **2009**, *109*, S799.
- (5) For a review, see: Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632.
- (6) For a review, see: Stefani, H. A.; Guarezemini, A. S.; Cella, R. *Tetrahedron* **2010**, *66*, 7871.
- (7) Glaser, C. *Ber. Dtsch. Chem. Ges.* **1869**, *2*, 422.
- (8) Glaser, C. *Ann. Chem. Pharm.* **1870**, *154*, 137.
- (9) Brandsma, L. *Synthesis of Acetylenes, Allenes and Cumulenes*; Elsevier Academic Press: Amsterdam, The Netherlands, 2004; Chapter 15.
- (10) For a recent contribution, see: Zheng, Q.; Hua, R.; Wan, Y. *Appl. Organomet. Chem.* **2010**, *24*, 314.
- (11) For a recent contribution, see: Wang, D.; Li, J.; Li, N.; Gao, T.; Hou, S.; Chen, B. *Green Chem.* **2010**, *12*, 45.
- (12) For a recent contribution, see: Meng, X.; Li, C.; Han, B.; Wang, T.; Chen, B. *Tetrahedron* **2010**, *66*, 4029.
- (13) For a recent contribution, see: Balaraman, K.; Kesavan, V. *Synthesis* **2010**, 3461.
- (14) *Supported Metals in Catalysis*; Anderson, J. A., Fernández García, M., Eds.; Imperial College Press: London, U.K., 2005.
- (15) For a review, see: Kaneda, K.; Ebitani, K.; Mizugaki, T.; Mori, K. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 981.
- (16) Yadav, J. S.; Reddy, B. V. S.; Bhaskar Reddy, K.; Uma Gayathri, K.; Prasad, A. R. *Tetrahedron Lett.* **2003**, *44*, 6493.
- (17) Lu, X.; Zhang, Y.; Luo, C.; Wang, Y. *Synth. Commun.* **2006**, *36*, 2503.
- (18) Kamata, K.; Yamaguchi, S.; Kotani, M.; Yamaguchi, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 2407.
- (19) Yamaguchi, K.; Kamata, K.; Yamaguchi, S.; Kotani, M.; Mizuno, N. *J. Catal.* **2008**, *258*, 121.
- (20) Chen, S.-N.; Wu, W.-Y.; Tsai, F.-Y. *Green Chem.* **2009**, *11*, 269.
- (21) Molnár, A. *Chem. Rev.* **2011**, *111*, 2251.
- (22) Bandini, M.; Luque, R.; Budarin, V.; Macquarrie, D. J. *Tetrahedron* **2005**, *61*, 9860.
- (23) Li, H.; Yang, M.; Pu, Q. *Microporous Mesoporous Mater.* **2012**, *148*, 166.
- (24) Zhou, L.; Zhang, H.-Y.; Liu, H.-L.; Jiang, H.-F. *Chin. J. Chem.* **2007**, *25*, 1413.

- (25) For a review, see: Muzart, J. *Synthesis* **1995**, 1325.
- (26) For a review, see: McKillop, A.; Sanderson, W. R. *Tetrahedron* **1995**, *51*, 6145.
- (27) Yoshihito, K.; Yoshiki, S.; Takao, L. *Adv. Synth. Catal.* **2003**, *345*, 175.
- (28) Kurita, T.; Abe, M.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Synlett* **2007**, 2521.
- (29) *Catalysis Without Precious Metals*; Morris Bullock, R., Ed.; Wiley-VCH: Weinheim, Germany, 2010.
- (30) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.
- (31) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054.
- (32) For a review, see: Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954.
- (33) Jiang, Y.; Ma, D. In *Catalysis Without Precious Metals*; Morris Bullock, R., Ed.; Wiley-VCH: Weinheim, Germany, 2010; Chapter 9.
- (34) For a review, see: Ranu, B. C.; Dey, R.; Chatterjee, T.; Ahammed, S. *ChemSusChem* **2012**, *5*, 22.
- (35) Armelao, L.; Barreca, D.; Bottaro, G.; Gasparotto, A.; Gross, S.; Maragno, C.; Tondello, E. *Coord. Chem. Rev.* **2006**, *250*, 1294.
- (36) For a review, see: Sun, J.; Bao, X. *Chem.—Eur. J.* **2008**, *14*, 7478.
- (37) White, R. J.; Luque, R.; Budarin, V. L.; Clark, J. H.; Macquarrie, D. J. *Chem. Soc. Rev.* **2009**, *38*, 481.
- (38) For a review, see: Campelo, J. M.; Luna, D.; Luque, F.; Marinas, J. M.; Romero, A. A. *ChemSusChem* **2009**, *2*, 18.
- (39) For a review, see: De Rogatis, L.; Cargnello, M.; Gombac, V.; Lorenzut, B.; Montini, T.; Fornasiero, P. *ChemSusChem* **2010**, *3*, 24.
- (40) Nador, F.; Fortunato, L.; Moglie, Y.; Vitale, C.; Radivoy, G. *Synthesis* **2009**, 4027.
- (41) Thathagar, M. B.; Beckers, J.; Rothenberg, G. *Green Chem.* **2004**, *6*, 215.
- (42) Wang, D.; Li, J.; Li, N.; Gao, T.; Hou, S.; Chen, B. *Green Chem.* **2010**, *12*, 45.
- (43) Auer, S. M.; Schneider, M.; Baiker, A. *J. Chem. Soc., Chem. Commun.* **1995**, 2057.
- (44) Zhu, B. C.; Jiang, X. Z. *Appl. Organomet. Chem.* **2007**, *21*, 345.
- (45) Kuhn, P.; Alix, A.; Kumarraja, M.; Louis, B.; Pale, P.; Sommer, J. *Eur. J. Org. Chem.* **2009**, 423.
- (46) Kuhn, P.; Pale, P.; Sommer, J.; Louis, B. *J. Phys. Chem. C* **2009**, *113*, 2903.
- (47) Kabalka, G. W.; Wang, L.; Pagni, R. M. *Synlett* **2001**, 108.
- (48) Sharifi, A.; Mirzaei, M.; Naimi-Jamal, M. R. *J. Chem. Res. (S)* **2002**, 628.
- (49) Sharifi, A.; Mirzaei, M.; Naimi-Jamal, M. R. *Monatsh. Chem.* **2006**, *137*, 213.
- (50) Oishi, T.; Katayama, T.; Yamaguchi, K.; Mizuno, N. *Chem.—Eur. J.* **2009**, *15*, 7539.
- (51) Oishi, T.; Yamaguchi, K.; Mizuno, N. *ACS Catal.* **2011**, *1*, 1351.
- (52) For a review, see: Riisager, A.; Fehrmann, R.; Haumann, M.; Wasserscheid, P. *Eur. J. Inorg. Chem.* **2006**, 695.
- (53) For a review, see: Wasserscheid, P. *J. Ind. Eng. Chem.* **2007**, *13*, 325.
- (54) For a review, see: Riisager, A.; Fehrmann, R.; Haumann, M.; Wasserscheid, P. *Top. Organomet. Chem.* **2008**, *23*, 149.
- (55) Szesni, N.; Kaiser, M.; Putzien, S.; Fischer, R. W. *Comb. Chem. High Throughput Screening* **2012**, *15*, 170.
- (56) Alonso, F.; Melkonian, T.; Moglie, Y.; Yus, M. *Eur. J. Org. Chem.* **2011**, 2524.
- (57) For some other applications of supported copper nanoparticles from this group, see: Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Adv. Synth. Catal.* **2010**, *352*, 3208, and references 58–61.
- (58) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Org. Biomol. Chem.* **2011**, *9*, 6385.
- (59) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *J. Org. Chem.* **2011**, *76*, 8394.
- (60) Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. *Heterocycles* **2012**, *84*, 1033.
- (61) Albaladejo, M. J.; Alonso, F.; Moglie, Y.; Yus, M. *Eur. J. Org. Chem.* **2012**, 3093.
- (62) The mechanism of the oxidative homocoupling of alkynes has been a subject of intense debate, with proposals ranging from the formation of alkynyl radicals, through the dimerization of Cu(II) or Cu(I)- $\pi$  complexes, to the involvement of three copper ions [two Cu(I) and one Cu(II)] per alkyne unit in the rate-limiting stage.<sup>5</sup> Certainly, further research is needed to upgrade the understanding of this complex mechanism.
- (63) Yin, W. Y.; He, C.; Zhang, H.; Lei, A. W. *Org. Lett.* **2009**, *11*, 709.
- (64) Crowley, J. D.; Goldup, S. M.; Gowans, N. D.; Leigh, D. A.; Ronaldson, V. E.; Slawin, A. M. Z. *J. Am. Chem. Soc.* **2010**, *132*, 6243.
- (65) González Arellano, C.; Balu, A. M.; Luque, R.; Macquarrie, D. J. *Green Chem.* **2010**, *12*, 1995.