Date: 12-06-12 18:14:06

Eurjoean Journal of Organic Chemistry 2 18:14:06 Pages: 8

DOI: 10.1002/ejoc.201200359

Practical Oxidative Homo- and Heterocoupling of Terminal Alkynes Catalyzed by Immobilized Copper in MCM-41

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Keywords: 1,3-Diynes / Supported catalysts / Copper / C-C coupling / Heterogeneous catalysis

A practical oxidative homo- and heterocoupling of terminal alkynes was achieved in CH_2Cl_2 at 25 °C by using a 3-(2-aminoethylamino)propyl-functionalized MCM-41-immobilized copper(I) complex (MCM-41–2N-CuI, 1 mol-%) as the catalyst, piperidine (0.1 or 3 equiv.) as the base, and air as the environmentally friendly co-oxidant, yielding a variety of

Introduction

Diynes and polyynes have been widely used as important building blocks in organic synthesis,^[1] and 1,3-conjugated diynes occur widely in numerous natural products, pharmaceuticals, and bioactive compounds with, for example, antiinflammatory, antifungal, anti-HIV, antibacterial, or anticancer activities.^[2] In addition, 1,3-conjugated divnes play an important role in the construction of a variety of functional polymeric materials, such as nonlinear-optical materials, electrically conductive plastics, high-density and highstrength fibers, and liquid crystals.^[3] Therefore, much attention has been devoted to the development of new and efficient methods for the synthesis of conjugated divnes since 1869.^[1a,1d,1e,4] Glaser oxidative coupling of terminal alkynes has been the main method of preparation of 1,3-diynes for over 50 years.^[1e,4a,5] The Glaser coupling reaction involves oxidative homocoupling of two terminal alkynes using Cu salts as reagents or catalysts to produce symmetrical 1,3diynes.^[6] Current research on the Glaser-type coupling reaction is mainly focused on modifications of Glaser's original conditions to promote oxidative alkyne-alkyne coupling more effectively. The homocoupling of terminal alkynes catalyzed by the bimetallic palladium/copper system represents one of the most attractive ways to synthesize symmetrical 1,3-divnes due to its efficiency and mildness.^[7] However, palladium reagents are expensive and often require air-sensitive and expensive phosphane ligands, and oxidants other than oxygen or air are required to regenerate the active palladium species. To avoid the use of expensive palladium catalysts, several methodologies using copper(I) or copper(II) salts as catalysts have been developed in recent years for the

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symmetrical and unsymmetrical 1,4-disubstituted 1,3-diynes in good to excellent yields. This heterogeneous copper catalyst showed a higher catalytic activity than CuI and can be recovered and recycled by a simple filtration of the reaction mixture and used for at least 10 consecutive runs without any decrease in activity.

oxidative homocoupling of terminal alkynes.^[8] Very recently, solvent-free systems mediated by copper have also been used for the synthesis of 1,3-diynes.^[9]

Although these copper-catalyzed homocouplings of terminal alkynes are highly efficient, the difficulty in separating the catalyst from the reaction mixture and the impossibility of reusing it in subsequent reactions are disadvantages of homogeneous catalysis. In addition, homogeneous catalysis might result in unacceptable copper contamination of the desired isolated product, which is a significant obstacle to its implementation in the pharmaceutical industry. In contrast, heterogeneous catalysts can be easily separated from the reaction mixture by a simple filtration and reused in successive reactions, provided that the active sites have not become deactivated. Heterogeneous catalysis also helps to minimize waste derived from reaction work-up, so contributing to the development of green chemical processes.^[10] From the standpoint of environmentally benign organic synthesis, the development of immobilized copper catalysts is challenging and important. In an ideal system, they can be recovered by simple filtration and reused indefinitely, and the contamination of products by copper is avoided. Recently, several copper-based heterogeneous catalytic systems for the homocoupling of terminal alkynes have been reported, including CuAl hydrotalcite,^[11] copper(I)-modified zeolites,^[8h] Cu(OH),/TiO₂,^[8e] and copper nanoparticles.^[8k,12] However, these catalytic systems generally suffer from some drawbacks such as a requirement for a stoichiometric amount of TMEDA and copper (110 mol-%),^[11] a higher reaction temperature (110 °C),^[8e,8h] and poor recyclability^[8h,8k] or a decrease in activity with repeated uses.^[8e,12] Therefore, the development of polymer-supported copper-complex catalysts having a high activity and excellent recyclability is a topic of enormous importance.

Polymer-supported palladium-complex catalysts have been used successfully in a variety of carbon-carbon or car-

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201200359.

Pages: 8

FULL PAPER

bon-heteroatom bond-forming reactions;[10d,10e,13] however, polymer-supported copper-complex catalysts for organic transformations have received less attention.^[14] To the best of our knowledge, no homocoupling of terminal alkynes catalyzed by polymer-supported copper complexes has been reported to date. The development of the mesoporous material MCM-41 provided a new possible candidate for a solid support for the immobilization of homogeneous catalysts.^[15] MCM-41 has a regular pore-diameter of ca. 5 nm and a specific surface area $>700 \text{ m}^2\text{g}^{-1}$.^[16] Its large poresize allows the passage of large molecules such as organic reactants and metal complexes through the pores to reach to the surface of the channel.^[17] It is generally believed that a high surface area of a heterogeneous catalyst results in a high catalytic activity. Considering the fact that the MCM-41 support has an extremely high surface area and the catalytic copper species would be anchored onto the inner surface of the mesopore of MCM-41, we expect that an MCM-41-supported copper catalyst will exhibit high activity and good reusability. As part of our continued effort to develop greener synthetic pathways for organic transformations, we wish to report herein the synthesis of a new 3-(2-aminoethylamino)propyl-functionalized MCM-41-immobilized copper-complex catalyst and to illustrate its application in the homo- and heterocoupling reactions of terminal alkynes using air as an environmentally friendly co-oxidant.

Results and Discussion

А 3-(2-aminoethylamino)propyl-functionalized new MCM-41-immobilized copper complex catalyst (MCM-41-2N-CuI) was very conveniently synthesized starting from commercially available and cheap 3-(2-aminoethylamino)propyltrimethoxysilane and CuI according to Scheme 1. First, the MCM-41 support was treated with 3-(2-aminoethylamino)propyltrimethoxysilane in toluene at 100 °C for 24 h. This was followed by silvlation with Me₃SiCl in toluene at room temperature for 24 h to generate 3-(2-aminoethylamino)propyl-functionalized MCM-41 (MCM-41-2N). Then, MCM-41-2N was treated with CuI in DMF at room temperature for 7 h to generate the 3-(2-aminoethylamino)propyl-functionalized MCM-41-immobilized copper complex catalyst (MCM-41-2N-CuI) as a pale blue powder.

The copper content of the catalyst was found to be 0.45 mmol/g according to the ICP–AES measurements. X-ray powder diffraction (XRD) analysis of the new MCM-41-immobilized copper-complex catalyst (MCM-41–2N-CuI) showed, in addition to an intense diffraction peak (100), two higher order peaks (110) and (200) with lower intensities, indicating that the chemical bonding procedure did not reduce the structural ordering of the MCM-41.

In our initial screening experiments to optimize the reaction conditions, the homocoupling reaction of phenylacetylene was investigated, and the results are summarized in Table 1. Oxidative homocoupling of phenylacetylene was carried out using MCM-41-2N-CuI (1.0 mol-%) as catalyst in the presence of a base at room temperature in different solvents in air. No oxygen atmosphere, co-oxidants, or additives were utilized. First, the effect of solvent was examined, and a significant solvent effect was observed. Good to high yields were obtained when the reaction was performed in CH₂Cl₂, EtOH, or DMF (Table 1, entries 1–3), whereas CH₃CN, MeOH, and toluene afforded moderate yields (Table 1, entries 4-6), and 1,4-dioxane was ineffective (Table 1, entry 7). Hence, CH₂Cl₂ was selected as the solvent for subsequent reactions. Our next studies focused on the effect of base on the model reaction. Among the bases examined, piperidine was found to be the most effective (Table 1, entry 1). Pyrrolidine and Et₂NH also gave good yields (Table 1, entries 8 and 10), whereas other bases such as Et₃N, pyridine, NaHCO₃, K₃PO₄, K₂CO₃, Na₂CO₃, and NaOAc were ineffective (Table 1, entries 9, 11-16), and Cs₂CO₃ was substantially less effective (Table 1, entry 17). The amount of supported copper catalyst was also screened, and a 1.0 mol-% loading of copper was found to be optimal. A lower yield was observed when the amount of the catalyst was decreased (Table 1, entry 18). Increasing the amount of copper catalyst shortened the reaction time, but did not increase the yield of 1.4-diphenylbuta-1.3-diyne (Table 1, entry 19). Interestingly, the same result was obtained when 10 mol-% piperidine was used as had been seen with 1 equiv. piperidine (Table 1, entry 20). Thus, the optimized reaction conditions for this homocoupling reaction are the MCM-41-2N-CuI (1.0 mol-%) in CH₂Cl₂ using piperidine (10 mol-%) as base at 25 °C in air for 2 h (Table 1, entry 20).



Scheme 1. Preparation of the MCM-41-2N-CuI complex.

phenylacetylene.[a]

Pages: 8



Table 1. Screening of reaction conditions for the homocoupling of

Oxidative Coupling of Terminal Alkynes

	MCM-41-2 base, so	N-Cul (1.0 mol-%? Nvent, air, 25 °C)→ ⟨	
Entry	Solvent	Base	Time [h]	Yield [%] ^[b]
1	CH ₂ Cl ₂	piperidine	2	94
2	EtOH	piperidine	3	85
3	DMF	piperidine	3	83
4	CH ₃ CN	piperidine	5	76
5	toluene	piperidine	5	69
6	MeOH	piperidine	4	75
7	1,4-dioxane	piperidine	24	trace
8	CH_2Cl_2	pyrrolidine	3	84
9	CH_2Cl_2	Et ₃ N	24	trace
10	CH_2Cl_2	Et ₂ NH	3	80
11	CH_2Cl_2	pyridine	24	trace
12	CH_2Cl_2	NaHCO ₃	24	trace
13	CH_2Cl_2	K ₃ PO ₄	24	trace
14	CH_2Cl_2	K_2CO_3	24	trace
15	CH_2Cl_2	Na ₂ CO ₃	24	trace
16	CH_2Cl_2	NaOAc	24	trace
17	CH_2Cl_2	Cs_2CO_3	24	50
18 ^[c]	CH ₂ Cl ₂	piperidine	5	85
19 ^[d]	CH_2Cl_2	piperidine	1	93
20 ^[e]	CH_2Cl_2	piperidine	2	94

[a] Reaction conditions: phenylacetylene (1.0 mmol), copper catalyst (1.0 mol-%), base (1.0 mmol), solvent (2 mL), air, 25 °C. [b] Isolated yield. [c] 0.5 mol-% copper catalyst was used. [d] 2.5 mol-% copper catalyst was used. [e] 10 mol-% piperidine was used.

Having achieved this promising result, we started to investigate the scope of this reaction under the optimized conditions. A variety of terminal alkynes were subjected to homocoupling using 1.0 mol-% MCM-41-2N-CuI and piperidine (0.1 equiv.) at room temperature under aerobic conditions, and the results are summarized in Table 2. Catalytic oxidative homocoupling of phenylacetylenes 1a-g, containing electron-donating or electron-withdrawing substituents, proceeded smoothly to afford the corresponding symmetrical 1,3-divnes (i.e., 2a-g) in 88-98% yield (Table 2, entries 1-7). This heterogeneous copper-complex catalyst showed a higher catalytic activity than CuI. For example, the oxidative homocoupling of phenylacetylene (1a) in the presence of only 1 mol-% MCM-41-2N-CuI in CH₂Cl₂ using piperidine (0.1 equiv.) as base at 25 °C in air for 2 h gave a 94% yield of homocoupling product 2a (Table 2, entry 1). The same reaction in the presence of CuI (10 mol-%) in CH₂Cl₂ using piperidine (1.0 equiv.) as base at 25 °C in air for 3 h gave 2a in 91% yield.^[8c] It is known that aliphatic terminal alkynes are less reactive towards Glaser dimerization, probably due to the lower acidity of the acetylenic protons.^[8d,8e,8g] Under the same reaction conditions as those used above (Table 2, entries 1–7), the oxidative homocoupling of aliphatic terminal alkynes such as 1-hexyne (1h), 1-octyne (1i), 3-methoxypropyne (1j), and cyclopropylacetylene (1k) proceeded readily to give 1,4-dialkyl-1,3divnes 2h-k in good yields (Table 2, entries 8-11). 1,4-Bis(trimethylsilyl)buta-1,3-diyne (21) was obtained from the dimerization of trimethylsilylacetylene (11) in 85% yield

(Table 2, entry 12). Alkynes based on propargylic alcohols also afforded the corresponding symmetrical 1,3-diynes (i.e., **2m** and **2n**) in good yields (Table 2, entries 13 and 14). This demonstrates that the hydroxy group does not exert any influence on the progress of dimerization. The reaction of heteroatom-containing alkynes **10** and **1p** also proceeded efficiently under same reaction conditions to give the desired coupled products (i.e., **20** and **2p**) in high yields (Table 2, entries 15 and 16). Propargyl acetate (**1q**) afforded 1,3-diyne **2q** in 89% yield (Table 2, entry 17). It is obvious that the homocoupling reaction catalyzed by the MCM-41– 2N-CuI complex tolerates several functional groups, including hydroxy, fluoro, silyl, methoxy, and ester groups.

Table 2. Homocoupling of terminal alkynes catalyzed by MCM-41–2N-CuI. $^{\left[a\right] }$

р —	MCM-41-2N-Cul (1.0	> P	р	
1	piperidine (10 mol-%), CH	°C	2 K K	
Entry	R	Time [h]	Product	Yield [%] ^[b]
1	Ph (1a)	2	2a	94
2	$4-CH_{3}C_{6}H_{4}$ (1b)	4	2b	91
3	$3-CH_{3}C_{6}H_{4}$ (1c)	4	2c	93
4	$4-C_2H_5C_6H_4$ (1d)	7	2d	89
5	$4-CH_{3}OC_{6}H_{4}$ (1e)	7	2e	88
6	$4 - FC_6H_4$ (1f)	4	2f	96
7	$3-FC_{6}H_{4}$ (1g)	3	2g	98
8	$n-C_{4}H_{9}$ (1h)	4	2h	83
9	$n-C_{6}H_{13}$ (1i)	4	2i	81
10	CH_3OCH_2 (1j)	4	2j	88
11	cyclopropyl (1k)	2	2k	86
12	(CH ₃) ₃ Si (11)	4	21	85
13	1-hydroxycyclohexyl (1m)	3	2m	78
14	$HOC(CH_3)_2$ (1n)	3	2n	82
15	thiophen-2-yl (10)	6	20	87
16	pyridin-3-yl (1p)	5	2р	90
17	$CH_3CO_2CH_2$ (1q)	4	2q	89

[[]a] Reaction conditions: terminal alkyne 1 (1.0 mmol), MCM-41–2N-CuI (1.0 mol-%), piperidine (0.1 mmol), CH_2Cl_2 (2 mL), air, 25 °C. [b] Isolated yield.

Cadiot-Chodkiewicz coupling and its variants have been widely used in the synthesis of unsymmetrical 1,3-diynes.^[18] The heterocoupling reactions of haloalkynes with terminal alkynes catalyzed by palladium are also reported for the preparation of unsymmetrical 1,3-diynes.^[19] Recently, Lei et al. described the synthesis of unsymmetrical 1,3-diynes via the oxidative heterocoupling of two different terminal alkynes catalyzed by NiCl₂/CuI.^[20] However, the copper-mediated oxidative heterocoupling of two different terminal alkynes has received less attention.^[8c,8n,9a] The cross-coupling of two different terminal alkynes was also investigated using our catalytic system, with an excess amount of one of the terminal alkyne substrates. Considering the fact that separation of heterocoupling products from homocoupling products would be difficult to achieve when two terminal alkynes of similar polarity were used as substrates, we selected one nonpolar and another polar terminal alkyne for cross-coupling reactions. The scope of terminal alkynes used for the synthesis of unsymmetrical 1,3-diynes was ex-

Pages: 8

FULL PAPER

plored, and the results are listed in Table 3. Since one of the alkynes was used in excess, the corresponding homocoupled 1,3-diynes were isolated in high yields. As shown in Table 3, all the heterocoupling reactions proceeded smoothly in the presence of 1 mol-% of MCM-41-2N-CuI under mild conditions, and a variety of unsymmetrical 1,3diynes were produced in 63-89% yields. An excess amount of phenylacetylene (5 mmol) was successfully cross-coupled with various terminal alkynes including propargylic alcohols, aliphatic alkynes, and 4-methoxyphenylacetylene in good to high yields (Table 3, entries 1-4). Substituted phenylacetylenes (5 mmol) such as 4-fluorophenylacetylene and 4-methylphenylacetylene could also be cross-coupled with aromatic acetylenes or propargylic alcohols in moderate to good yields (Table 3, entries 6 and 7). Excess amounts of cyclopropylacetylene (Table 3, entry 5) and homopropargyl alcohol (Table 3, entry 8) were treated with aromatic acetylenes to afford the corresponding unsymmetrical 1,3diynes (i.e., 3e and 3h) in moderate yields, respectively. Heterocoupling of terminal alkynes catalyzed by the MCM-41-2N-CuI complex avoids the use of a bimetallic catalysis, such as NiCl₂/CuI.^[20] Also, it does not suffer from low yields as is the case when copper(II) chloride is used.^[9a] This heterogeneous cross-coupling reaction of terminal alkynes also tolerates several functional groups, including hydroxy, methoxy, and fluoro groups.

Table 3. Heterocoupling of terminal alkynes catalyzed by MCM-41–2N-CuI. $^{\left[a\right] }$

R1Ξ	\equiv + \equiv R ²	MCM-41-2N-Cul (1 piperidine, CH ₂ Cl ₂ , a	.0 mol-%) air, 25 °C	→ R ¹ —=	=
Entry	\mathbb{R}^1	R ²	Time [h]	Product	Yield [%] ^[b]
1	Ph	HOCH ₂	6	3a	85
2	Ph	CH ₃ OCH ₂ CH ₂	8	3b	74
3	Ph	$HOC(CH_3)_2$	3	3c	89
4	Ph	4-CH ₃ OC ₆ H ₄	8	3d	75
5	cyclopropyl	4-CH ₃ OC ₆ H ₄	10	3e	68
6	$4\text{-FC}_6\text{H}_4$	4-CH ₃ OC ₆ H ₄	6	3f	81
7	$4-CH_3C_6H_4$	1-hydroxycyclo-	12	3g	68
		hexyl			
8	$\mathrm{HOCH}_2\mathrm{CH}_2$	$4-CH_3C_6H_4$	7	3h	63

[a] Reaction conditions: $R^1C \equiv CH$ (5.0 mmol), $R^2C \equiv CH$ (1.0 mmol), MCM-41–2N-CuI (1.0 mol-%), piperidine (3.0 mmol), CH₂Cl₂ (5 mL), air, 25 °C. [b] Isolated yield.

In order to determine whether the catalysis was due to the MCM-41–2N-CuI complex or to a homogeneous copper complex that is released from the support during the reaction and then returns to the support at the end, we performed a filtration test on the homocoupling reaction of phenylacetylene. We filtered off the MCM-41–2N-CuI complex after a reaction time of 0.5 h and allowed the filtrate to react further. We found that after this filtration, no further reaction was observed, and no copper could be detected by ICP–AES in the filtered solution. This result points to a process of a heterogeneous nature. For a heterogeneous transition metal catalyst, it is important to examine how easily it can be separated, how well it can be recovered, and its reusability. We also investigated the recyclability of the MCM-41-2N-CuI using the homocoupling reaction of 4-fluorophenylacetylene. After carrying out the reaction, the catalyst was separated by simple filtration and washed with diethyl ether. After being air-dried, it was reused directly without further purification. The recovered copper catalyst was used in the next run, and almost consistent activity was observed for 10 consecutive cycles (Table 4, entries 1-10). In addition, copper leaching from the supported catalyst was determined. The copper content of the catalyst was found by ICP analysis to be 0.45 mmol/g after 10 consecutive runs, which means that no copper had been lost from the MCM-41 support. The high stability and excellent reusability of the catalyst is expected to result from the chelating action of the bidentate 2-aminoethylamino ligand on copper, and from the mesoporous structure of the MCM-41 support. The result is important from a practical point of view. The high catalytic activity, excellent reusability and the easy accessibility of the MCM-41-2N-CuI make it a highly attractive heterogeneous copper catalyst for the parallel solution phase synthesis of diverse libraries of compounds.

Table 4. Homocoupling reaction of 4-fluorophenylacetylene catalyzed by recycled catalyst. $^{[a]}$

F-C	$ \begin{array}{c} 2N-Cul \\ \xrightarrow{II-\%)} \\ \hline CH_2Cl_2 \\ & \circ C \end{array} F - \swarrow F - \swarrow F - \swarrow F - \swarrow F - F - F - F -$
Cycle	Yield [%] ^[b]
1	96
2	96
3	95
4	95
5	94
6	95
7	94
8	93
9	94
10	93

[a] Reaction conditions: 4-fluorophenylacetylene (10 mmol), MCM-41–2N-CuI (0.1 mmol), piperidine (1.0 mmol), CH_2Cl_2 (20 mL), air, 25 °C, for 4 h. [b] Isolated yield.

Conclusions

In summary, we have successfully developed a novel, practical, and environmentally friendly catalyst system for the homo- and heterocoupling reactions of terminal alkynes by using a 3-(2-aminoethylamino)propyl-functionalized MCM-41-immobilized copper complex as catalyst and air as co-oxidant under mild reaction conditions. The reactions generated the corresponding symmetrical or unsymmetrical 1,4-disubstituted 1,3-diynes in good to excellent yields and were applicable to various terminal alkynes. This novel heterogeneous copper catalyst can be conveniently prepared by a simple two-step procedure from commercially available and cheap reagents, it shows a higher activity than CuI, and it can be reused at least 10 times without any decrease in activity. Although high yields of homocoupling products

Date: 12-06-12 18:14:06

Pages: 8



Oxidative Coupling of Terminal Alkynes

were achieved using CuI (10 mol-%) as catalyst and piperidine (1.0 equiv.) as base in dichloromethane at 25 °C in air,^[8c] the amount of catalyst used is larger and the homogeneous copper catalyst is not recyclable. Some attractive advantages of our methodology are the low copper loading (1 mol-%), the use of a catalytic amount of piperidine (10 mol-%), and the excellent recyclability of the catalyst. The homo- and heterocoupling reactions of terminal alkynes catalyzed by the MCM-41–2N-CuI complex provide a better and more practical procedure for the synthesis of a variety of 1,4-disubstituted 1,3-diynes.

Experimental Section

General: All chemicals were reagent grade and were used as purchased. All solvents were dried and distilled before use. The products were purified by flash chromatography on silica gel. A mixture of EtOAc and hexane was generally used as eluent. All coupled products were characterized by comparison of their spectra and physical data with authentic samples. IR spectra were recorded with a Perkin-Elmer 683 instrument. ¹H NMR spectra were recorded with a Bruker Avance (400 MHz) spectrometer in CDCl₃ as solvent, with TMS as an internal standard. ¹³C NMR spectra were recorded with a Bruker Avance (100 MHz) spectrometer in CDCl₃ as solvent. Copper content was determined using an Atomscan16 inductively coupled plasma atomic emission spectrometer (ICP-AES, TJA Corporation). X-ray powder diffraction data was obtained with a Damx-rA (Rigaka) instrument. Microanalyses were measured using a Yanaco MT-3 CHN microelemental analyzer. The mesoporous material MCM-41 was easily prepared according to a literature procedure.^[21]

Synthesis of 3-(2-Aminoethylamino)propyl-functionalized MCM-41-Immobilized Copper Complex (MCM-41–2N-CuI): A solution of 3-(2-aminoethylamino)propyltrimethoxysilane (1.54 g, 6.94 mmol) in dry chloroform (18 mL) was added to a suspension of MCM-41 (2.2 g) in dry toluene (180 mL). The mixture was stirred for 24 h at 100 °C. The solid was filtered and washed with CHCl₃ (2×20 mL) and then dried in vacuo at 160 °C for 5 h. The dried white solid was then soaked in a solution of Me₃SiCl (3.1 g, 28.57 mmol) in dry toluene (100 mL) at room temperature whilst stirring for 24 h. Then the solid was filtered, washed with acetone (3×20 mL) and diethyl ether (3×20 mL), and dried in vacuo at 120 °C for 5 h to obtain hybrid material MCM-41–2N (3.49 g). The nitrogen content was found to be 1.84 mmol/g by elemental analysis.

In a small Schlenk tube, the above-functionalized MCM-41 (MCM-41–2N; 1.0 g) was mixed with CuI (0.1 g, 0.52 mmol) in dry DMF (10 mL). The mixture was stirred at room temperature for 7 h under an argon atmosphere. The solid product was filtered by suction, washed with DMF and acetone, and dried at 40 °C/26.7 Pa under Ar for 5 h to give a pale blue copper complex (MCM-41–2N-CuI; 1.066 g). The nitrogen and copper contents were found to be 1.67 and 0.45 mmol/g, respectively.

Typical Procedure for the Homocoupling Reaction of Terminal Alkynes: A mixture of terminal alkyne 1 (1 mmol), piperidine (1 mmol), and MCM-41–2N-CuI (1 mol-%) in CH₂Cl₂ (2 mL) was stirred open to atmospheric air at 25 °C with TLC monitoring for 2–7 h. The mixture was then diluted with dichloromethane and filtered. The catalyst was washed with diethyl ether (2×5 mL) and reused in the next run. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to afford coupled products 2.

1,4-Diphenylbuta-1,3-diyne (2a): Yield: 0.095 g, 94%. White solid, m.p. 86–87 °C (ref.^[8n] m.p. 88–89 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.54–7.52 (m, 4 H), 7.38–7.32 (m, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 132.51, 129.21, 128.45, 121.81, 81.56, 73.91 ppm. IR (KBr): \tilde{v} = 3050, 2980, 2140, 1570, 920, 753 cm⁻¹.

1,4-Bis(4-methylphenyl)buta-1,3-diyne (2b): Yield: 0.105 g, 91%. White solid, m.p. 183–185 °C (ref.^[8n] m.p. 182–183 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.42 (d, J = 8.0 Hz, 4 H), 7.14 (d, J = 8.0 Hz, 4 H), 2.36 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 139.49, 132.39, 129.21, 118.80, 81.54, 73.44, 21.62 ppm. IR (KBr): \tilde{v} = 3052, 2990, 2130, 1502, 1265, 802 cm⁻¹.

1,4-Bis(3-methylphenyl)buta-1,3-diyne (2c): Yield: 0.107 g, 93%. White solid, m.p. 75–76 °C (ref.^[7a] m.p. 74–75 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.33 (d, *J* = 8.0 Hz, 2 H), 7.24–7.16 (m, 6 H), 2.34 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 138.17, 132.99, 130.12, 129.62, 128.33, 121.66, 81.62, 73.65, 21.21 ppm. IR (KBr): \tilde{v} = 3052, 2918, 2142, 1502, 1265, 802, 785 cm⁻¹.

1,4-Bis(4-ethylphenyl)buta-1,3-diyne (2d): Yield: 0.115 g, 89%. White solid, m.p. 97–98 °C (ref.^[8d] m.p. 97–98 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.44 (d, J = 8.4 Hz, 4 H), 7.17 (d, J = 8.0 Hz, 4 H), 2.66 (q, J = 7.6 Hz, 4 H), 1.23 (t, J = 7.6 Hz, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 145.75, 132.49, 128.03, 119.00, 81.55, 73.42, 28.92, 15.26 ppm. IR (KBr): \tilde{v} = 2960, 2930, 1650, 1430, 820 cm⁻¹.

1,4-Bis(4-methoxyphenyl)buta-1,3-diyne (2e): Yield: 0.115 g, 88%. White solid, m.p. 143–144 °C (ref.^[8n] m.p. 140–141 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.46 (d, J = 8.4 Hz, 4 H), 6.85 (d, J = 8.4 Hz, 4 H), 3.82 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 160.26, 134.04, 114.15, 113.98, 81.23, 72.97, 55.34 ppm. IR (KBr): \tilde{v} = 3055, 2980, 2140, 1585, 1560, 1250, 1220, 1140, 1058, 840, 798 cm⁻¹.

1,4-Bis(4-fluorophenyl)buta-1,3-diyne (2f): Yield: 0.114 g, 96%. White solid, m.p. 192–193 °C (ref.^[8n] m.p. 194–195 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.53–7.50 (m, 4 H), 7.06–7.02 (m, 4 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.05 (d, ¹*J*_{CF} = 250 Hz), 134.54 (d, ³*J*_{CF} = 8 Hz), 117.80 (d, ⁴*J*_{CF} = 4 Hz), 115.92 (d, ²*J*_{CF} = 23 Hz), 80.41, 73.53 ppm. IR (KBr): \tilde{v} = 2344, 1594, 1499, 1215, 1157, 1093, 824, 695 cm⁻¹.

1,4-Bis(3-fluorophenyl)buta-1,3-diyne (2g): Yield: 0.117 g, 98%. White solid,^[81] m.p. 121–122 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.33–7.31 (m, 4 H), 7.26–7.21 (m, 2 H), 7.12–7.07 (m, 2 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 162.26 (d, ¹*J*_{CF} = 245 Hz), 130.15 (d, ³*J*_{CF} = 8 Hz), 128.49 (d, ⁴*J*_{CF} = 3 Hz), 123.36 (d, ³*J*_{CF} = 10 Hz), 119.24 (d, ²*J*_{CF} = 23 Hz), 116.93 (d, ²*J*_{CF} = 21 Hz), 80.63 (d, ⁴*J*_{CF} = 3 Hz), 74.41 ppm. IR (KBr): \tilde{v} = 2345, 1604, 1499, 1215, 1157, 1093, 824, 675 cm⁻¹.

Dodeca-5,7-diyne (2h): Yield: 0.067 g, 83%. Light yellow oil.^[8c] ¹H NMR (400 MHz, CDCl₃): δ = 2.25 (t, *J* = 6.8 Hz, 4 H), 1.55–1.48 (m, 4 H), 1.47–1.38 (m, 4 H), 0.90 (t, *J* = 7.2 Hz, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 77.49, 65.25, 30.40, 21.93, 18.90, 13.54 ppm. IR (neat): \tilde{v} = 2929, 2858, 1458, 1322, 725 cm⁻¹.

Hexadeca-7,9-diyne (2i): Yield: 0.088 g, 81%. Light yellow oil.^[8n] ¹H NMR (400 MHz, CDCl₃): δ = 2.24 (t, *J* = 6.8 Hz, 4 H), 1.53– 1.48 (m, 4 H), 1.40–1.35 (m, 4 H), 1.34–1.26 (m, 8 H), 0.89 (t, *J* = 6.4 Hz, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 77.52, 65.27, 31.30, 28.53, 28.33, 22.50, 19.21, 14.01 ppm. IR (neat): \tilde{v} = 2929, 2858, 1458, 1322, 725 cm⁻¹.

1,6-Dimethoxyhexa-2,4-diyne (2j): Yield: 0.061 g, 88%. Light yellow oil.^[22] ¹H NMR (400 MHz, CDCl₃): δ = 4.18 (s, 4 H), 3.40 (s,

FULL PAPER

6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 75.19, 70.47, 60.13, 57.85 ppm. IR (neat): \tilde{v} = 2994, 2825, 2255, 1450, 903 cm⁻¹.

1,4-Dicyclopropylbuta-1,3-diyne (2k): Yield: 0.056 g, 86%. Colorless oil.^[8n] ¹H NMR (400 MHz, CDCl₃): δ = 1.31–1.25 (m, 2 H), 0.82–0.72 (m, 8 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 80.01, 60.79, 8.69, 0.00 ppm. IR (neat): \tilde{v} = 3094, 3012, 2157, 1425, 1185, 938 cm⁻¹.

1,4-Bis(trimethylsilyl)-1,3-butadiyne (2l): Yield: 0.083 g, 85%. White solid, m.p. 110–112 °C (ref.^[11] m.p. 110–113 °C). ¹H NMR (400 MHz, CDCl₃): δ = 0.00 (s, 18 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 87.81, 85.66, -0.70 ppm. IR (KBr): \tilde{v} = 2942, 1731, 1599, 1425, 1367, 1259, 1087, 924, 708, 683 cm⁻¹.

1,4-Bis(1-hydroxycyclohexyl)buta-1,3-diyne (2m): Yield: 0.096 g, 78%. White solid, m.p. 174–175 °C (ref.^[8n] m.p. 178–179 °C). ¹H NMR (400 MHz, [D₆]DMSO): δ = 5.56 (s, 2 H), 1.73–1.21 (m, 20 H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 85.07, 67.52, 67.43, 39.69, 25.14, 22.99 ppm. IR (KBr): \tilde{v} = 3240, 2850, 1420, 1312, 1250, 1068, 950 cm⁻¹.

2,7-Dimethylocta-3,5-diyne-2,7-diol (2n): Yield: 0.068 g, 82%. White solid, m.p. 132–134 °C (ref.^[8n] m.p. 131–132 °C). ¹H NMR (400 MHz, CDCl₃): δ = 2.02 (s, 2 H), 1.54 (s, 12 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 84.05, 66.38, 65.60, 31.08 ppm. IR (KBr): \tilde{v} = 3220, 2982, 2514, 2256, 1685, 1449, 1364, 1211, 1170, 954, 889, 732 cm⁻¹.

1,4-Bis(thiophen-2-yl)buta-1,3-diyne (20): Yield: 0.093 g, 87%. White solid, m.p. 91–92 °C (ref.^[8n] m.p. 92–93 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.31–7.24 (m, 4 H), 7.02–7.00 (m, 2 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 132.14, 127.66, 127.19, 122.93, 86.23 ppm. IR (KBr): \tilde{v} = 3116, 1817, 1416, 843, 710 cm⁻¹.

1,4-Bis(pyridin-3-yl)buta-1,3-diyne (2p): Yield: 0.092 g, 90%. White solid, m.p. 145–146 °C (ref.^[8n] m.p. 144–146 °C). ¹H NMR (400 MHz, CDCl₃): $\delta = 8.78$ (s, 2 H), 8.61 (d, J = 4.4 Hz, 2 H), 7.84 (d, J = 8.0 Hz, 2 H), 7.32 (t, J = 4.8 Hz, 2 H) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 153.05$, 149.41, 139.52, 123.17, 118.91, 79.15 ppm. IR (KBr): $\tilde{v} = 2151$, 1638, 1579, 1413, 1022, 804, 699 cm⁻¹.

Hexa-2,4-diyne-1,6-diyl Diacetate (2q): Yield: 0.086 g, 89%. Colorless oil.^[8n] ¹H NMR (400 MHz, CDCl₃): δ = 4.74 (s, 4 H), 2.11 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 169.91, 73.60, 70.18, 52.14, 20.53 ppm. IR (neat): \tilde{v} = 2149, 1778, 1427, 828, 730 cm⁻¹.

Typical Procedure for the Heterocoupling Reaction of Two Different Terminal Alkynes: A mixture of R¹C=CH (5 mmol), R²C=CH (1 mmol), piperidine (3 mmol), and MCM-41–2N-CuI (1 mol-%) in CH₂Cl₂ (5 mL) was stirred open to atmospheric air at 25 °C with TLC monitoring for 3–12 h. The mixture was diluted with dichloromethane and filtered. The catalyst was washed with diethyl ether (2×5 mL) and reused in the next run. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to afford cross-coupled products **3**.

5-Phenylpenta-2,4-diyn-1-ol (3a): Yield: 0.133 g, 85%. Colorless oil.^[8n] ¹H NMR (400 MHz, CDCl₃): δ = 7.48 (d, *J* = 7.2 Hz, 2 H), 7.36–7.29 (m, 3 H), 4.41 (s, 2 H), 1.87 (s, 1 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 132.61, 129.37, 128.44, 121.35, 80.49, 78.56, 73.19, 70.39, 51.61 ppm. IR (neat): \tilde{v} = 3350, 2927, 2869, 1721, 1678, 1447, 1284, 753 cm⁻¹.

(6-Methoxyhexa-1,3-diynyl)benzene (3b): Yield: 0.136 g, 74%. Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.48–7.46 (m, 2 H), 7.32–7.26 (m, 3 H), 3.56 (t, *J* = 6.0 Hz, 2 H), 3.39 (s, 3 H), 2.64 (t, *J* = 6.0 Hz, 2 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 132.53,

128.94, 128.35, 121.90, 81.14, 75.16, 74.15, 70.20, 66.04, 58.79, 20.88 ppm. IR (neat): $\tilde{\nu}$ = 2928, 2246, 1595, 1490, 1442, 1185, 999, 755, 689 cm^{-1}. C_{13}H_{12}O (184.24): calcd. C 84.75, H 6.57; found C 84.47, H 6.42.

2-Methyl-6-phenylhexa-3,5-diyn-2-ol (3c): Yield: 0.164 g, 89%. White solid,^[8c] m.p. 59–61 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.48 (d, J = 7.2 Hz, 2 H), 7.37–7.32 (m, 3 H), 2.08 (s, 1 H), 1.58 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 132.52, 129.26, 128.43, 121.51, 86.67, 78.79, 73.12, 67.05, 65.76, 31.11 ppm. IR (KBr): \tilde{v} = 3428, 2981, 2446, 1642, 1570, 1165, 954, 860, 757 cm⁻¹.

1-Methoxy-4-(phenylbuta-1,3-diynyl)benzene (3d): Yield: 0.174 g, 75%. White solid, m.p. 97–98 °C (ref.^[8n] m.p. 95–96 °C). ¹H NMR (400 MHz, CDCl₃): δ = 7.53–7.50 (m, 3 H), 7.47 (d, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 6.85 (d, *J* = 8.0 Hz, 2 H), 3.81 (s, 3 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 160.40, 134.16, 132.46, 129.06, 128.45, 122.03, 114.19, 113.71, 81.87, 81.06, 74.22, 72.78, 55.36 ppm. IR (KBr): \tilde{v} = 3129, 2991, 2217, 1599, 1567, 1507, 1069, 954 cm⁻¹.

1-Methoxy-4-(cyclopropylbuta-1,3-diynyl)benzene (3e): Yield: 0.133 g, 68%. Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.40 (d, J = 8.0 Hz, 2 H), 6.81 (d, J = 8.0 Hz, 2 H), 3.80 (s, 3 H), 1.43–1.36 (m, 1 H), 0.89–0.81 (m, 4 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 160.04, 134.09, 114.06, 87.17, 74.32, 73.34, 60.59, 55.31, 9.02, 0.39 ppm. IR (neat): \tilde{v} = 3094, 2958, 2838, 2539, 2148, 1603, 1567, 1509, 1425, 1185, 938 cm⁻¹. C₁₄H₁₂O (196.25): C 85.68, H 6.16; found C 85.44, H 6.32.

1-Methoxy-4-(4-fluorophenylbuta-1,3-diynyl)benzene (3f): Yield: 0.203 g, 81%. White solid,^[23] m.p. 122–124 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.51–7.45 (m, 4 H), 7.02 (d, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.8 Hz, 2 H), 3.81 (s, 3 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 162.93 (d, ¹*J*_{CF} = 250 Hz), 160.45, 134.44 (d, ³*J*_{CF} = 8 Hz), 134.15, 118.17 (d, ⁴*J*_{CF} = 3 Hz), 115.85 (d, ²*J*_{CF} = 22 Hz), 114.20, 113.61, 81.84, 79.93, 74.00, 72.61, 55.34 ppm. IR (KBr): \tilde{v} = 3409, 2961, 2208, 1617, 1502, 1293, 1251, 1069, 954 cm⁻¹.

1-(*p***-Tolylbuta-1,3-diynyl)cyclohexan-1-ol (3g):** Yield: 0.162 g, 68%. White solid,^[24] m.p. 57–59 °C. ¹H NMR (400 MHz, [D₆]DMSO): δ = 7.62 (d, *J* = 8.0 Hz, 2 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 5.83 (s, 1 H), 2.50 (s, 3 H), 1.98–1.39 (m, 10 H) ppm. ¹³C NMR (100 MHz, [D₆]DMSO): δ = 140.19, 132.71, 129.91, 118.06, 88.99, 78.45, 73.46, 67.73, 67.63, 39.70, 25.17, 23.03, 21.57 ppm. IR (KBr): \tilde{v} = 3421, 2930, 2342, 1640, 1564, 1255, 1120, 967, 768, 619 cm⁻¹.

6-Tolylhexa-3,5-diyn-1-ol (3h): Yield: 0.116 g, 63%. Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.30 (d, *J* = 8.0 Hz, 2 H), 7.04 (d, *J* = 8.0 Hz, 2 H), 3.72 (t, *J* = 6.2 Hz, 2 H), 2.57 (t, *J* = 6.2 Hz, 2 H), 2.28 (s, 3 H), 1.80 (s, 1 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 139.43, 132.47, 129.18, 118.60, 80.58, 75.68, 73.31, 67.01, 60.83, 24.03, 21.60 ppm. IR (neat): \tilde{v} = 3352, 3030, 2924, 2246, 1605, 1508, 1415, 1045, 908 cm⁻¹. C₁₃H₁₂O (184.24): calcd. C 84.75, H 6.57; found C 84.54, H 6.31.

Supporting Information (see footnote on the first page of this article): ¹H NMR and ¹³C NMR spectra of compounds 2a-q and 3a-h.

Acknowledgments

We thank the National Natural Science Foundation of China (Project No. 20862008) and the Natural Science Foundation of Jiangxi Province in China (2010GZH0062) for financial support.

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Pages: 8



Oxidative Coupling of Terminal Alkynes

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Received: March 21, 2012

Published Online:

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Coupling of Terminal Alkynes

R. Xiao, R. Yao, M. Cai* 1-8

Practical Oxidative Homo- and Heterocoupling of Terminal Alkynes Catalyzed by Immobilized Copper in MCM-41

Keywords: 1,3-Diynes / Supported catalysts / Copper / C-C coupling / Heterogeneous catalysis