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Heterogeneous Hydrothiolation of Alkynes with Thiols Catalyzed by Diphosphino-Functionalized MCM-41 Anchored Rhodium Complex

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Abstract A novel diphosphino-functionalized MCM-41 anchored rhodium complex [MCM-41-2P-RhCl(PPh_3)] was conveniently synthesized by the reaction of diphosphino-functionalized MCM-41 (MCM-41-2P) with RhCl(PPh_3)$_3$. It was found that this rhodium complex is an efficient catalyst for the hydrothiolation of terminal alkynes with thiols and can be recovered and recycled by a simple filtration of the reaction solution and used for at least ten consecutive trials without any decreases in activity.

Keywords Supported catalyst · MCM-41 · Hydrothiolation · Phosphine rhodium complex · Heterogeneous catalysis

1 Introduction

Although, organic thiols have been widely employed as the sources of ligands for various transition metals [1, 2], the transition-metal-catalyzed reactions with thiols as substrates have been scarcely developed because organic sulfur compounds are often considered to be incompatible with metal-catalyzed reactions due to the fact that sulfur containing substrates can bind strongly to transition metals and often poison the catalysts [3–5]. Vinyl sulfides are important synthetic intermediates in total synthesis and are versatile building blocks for many functionalized molecules owing to the versatile reactivity of the sulfonyl group and the carbon–carbon double bond [6–9]. The addition of thiols to alkynes is one of the most straightforward routes to vinyl sulfides. Thiols are known to add to alkynes, in the presence of a radical initiator, to afford regioselectively the anti-Markovnikov products, usually as a stereoisomeric mixture [10]. The addition of thiols to alkynes catalyzed by transition metals has provided a straightforward and atom-efficient method for the formation of stereo- and regiodefined vinyl sulfides [11–20]. Among these transition metal complexes reported, rhodium complexes have attracted much attention, due to their high catalytic activity and regio- and stereoselectivity for either Markovnikov or anti-Markovnikov products under mild reaction conditions [12–14, 16–18]. Ogawa and Love groups [12, 16] have reported that Wilkinson's catalyst [RhCl(PPh_3)$_3$] exhibits excellent catalytic ability toward the anti-Markovnikov addition of thiols to terminal alkynes, which affords regio- and stereoselectively the corresponding (*E*)-vinyl sulfides. However, the problem with homogeneous catalysis is the difficulty to separate the catalyst from the reaction mixture and the impossibility to reuse it in consecutive reactions. In contrast, heterogeneous catalysts can be easily separated from the reaction mixture by simple filtration and reused in successive reactions provided that the active sites have not become deactivated. The high costs of the transition metal catalysts coupled with toxic effects associated with many transition metals has led to an increased interest in immobilizing catalysts onto a support. Heterogeneous catalysis also helps to minimize wastes derived from reaction workup, contributing to the development of green chemical processes [21, 22]. So far, supported palladium catalysts have successfully been used for the Heck reaction,

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the Suzuki–Miyaura reaction, the Sonogashira reaction, and the Stille reaction, etc. [23–25]. However, carbon–carbon bond or carbon-heteroatom bond formation reactions catalyzed by heterogeneized rhodium complexes have received less attention.

Developments on the mesoporous material MCM-41 provided a new possible candidate for a solid support for immobilization of homogeneous catalysts [26]. MCM-41 has a regular pore diameter of ca.5 nm and a specific surface area > 700 m^2g^{-1} [27]. Its large pore size allows passage of large molecules such as organic reactants and metal complexes through the pores to reach to the surface of the channel [28–30]. Shyu et al. [31] reported phosphinated MCM-41-supported rhodium complex for catalytic hydrogenation of olefins and found that it is an excellent hydrogenation catalyst with turnover frequency (TOF) three times higher than that of $RhCl(PPh_3)_3$ in the hydrogenation of cyclohexene. However, to the best of our knowledge, no hydrothiolation reaction of alkynes with thiols catalyzed by a heterogeneized rhodium complex has been reported until now. In this paper, we wish to report the synthesis of diphosphino-functionalized MCM-41 anchored rhodium complex [abbreviation: MCM-41-2P-$RhCl(PPh_3)$] and its catalytic properties in the hydrothiolation reaction of alkynes with thiols.

2 Experimental

The diphosphino-functionalized mesoporous material MCM-41-2P was prepared according to our previous procedure, the phosphine content was 1.44 mmol/g [32]. Other reagents were obtained from commercial suppliers and purified by distillation. All hydrothiolation products were characterized by comparison of their spectra and physical data with authentic samples. IR spectra were determined on a Perkin–Elmer 683 instrument. ^{1}H NMR spectra were recorded on a Bruker AC-P400 (400 MHz) spectrometer with TMS as an internal standard in $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded on a Bruker AC-P400 (100 MHz) spectrometer in $CDCl_3$ as solvent. X-ray powder diffraction patterns were obtained on Damx-rA (Rigaku). ^{31}P one-pulse experiments were performed on a Bruker AMX 400 spectrometer at a ^{31}P frequency of 161.98 MHz at room temperature. Chemical shifts were referenced to Na_2HPO_4 at 0 ppm. Microanalyses were obtained using a Perkin–Elmer 240 elemental analyzer.

2.1 Preparation of MCM-41-2P-$RhCl(PPh_3)$

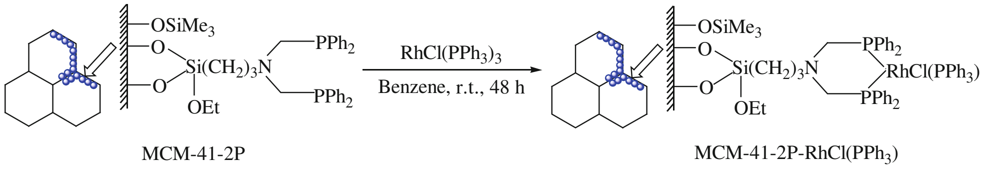
To a solution of $RhCl(PPh_3)_3$ (1.109 g, 1.2 mmol) in benzene (50 mL) was added MCM-41-2P (2.04 g). The mixture was stirred under an argon atmosphere at 25 °C for 48 h. The solid product was filtered by suction, washed with benzene (5 × 10 mL), and dried at 70 °C/26.7 Pa under an argon atmosphere for 3 h to give 2.34 g of the light yellow rhodium complex [MCM-41-2P-$RhCl(PPh_3)$]. The phosphine and rhodium content was 1.74 mmol/g and 0.39 mmol/g, respectively.

2.2 General Procedure for the Hydrothiolation of Alkynes with Thiols

In a 20 mL two-necked glass flask with a magnetic stirring bar under an argon atmosphere were placed MCM-41-2P-$RhCl(PPh_3)$ (77 mg, 0.03 mmol), EtOH (2 mL), and alkyne (1.0 mmol). Then thiol (1.1 mmol) was added dropwise to the solution over 1 h at 40 °C. The reaction was continued with magnetic stirring for 24 h at 40 °C. The mixture was diluted with Et_2O (30 mL). The MCM-41-2P-$RhCl(PPh_3)$ catalyst was separated from the mixture by filtration, washed with EtOH (2 × 10 mL), Et_2O (2 × 10 mL) and reused in the next run. The solvent was removed in vacuo, and the residue was purified by Flash chromatography on silica gel to give the desired product.

3 Results and Discussion

The novel diphosphino-functionalized MCM-41 anchored rhodium complex [MCM-41-2P-$RhCl(PPh_3)$] was conveniently synthesized by the reaction of diphosphino-functionalized MCM-41 (MCM-41-2P) with $RhCl(PPh_3)_3$ (Scheme 1). Small angle X-ray powder diffraction (XRD) analysis of the MCM-41-2P-$RhCl(PPh_3)$ indicated that, the 100 reflection of MCM-41-2P-$RhCl(PPh_3)$ had lower intensity compared to that of the parent MCM-41, while the 110 and 200 reflections became weak and diffuse, which could be due to contrast matching between the silicate framework and organic moieties which are located inside the channels of MCM-41. Therefore, the basic structure of the parent MCM-41 was not damaged in the whole process of catalyst preparation. Elemental analyzes and solid state ^{31}P NMR were used to characterize the supported rhodium complex [MCM-41-2P-$RhCl(PPh_3)$]. The P:Rh mole ratio of the MCM-41-2P-$RhCl(PPh_3)$ was determined to be 4:5. Blumel et al. [33, 34] investigated the silica-supported phosphine rhodium complexes by solid state ^{31}P NMR spectroscopy. Solid state ^{31}P NMR of MCM-41-2P showed a signal at δ −23.1 ppm, which further indicates that the mesoporous material MCM-41-2P contains phosphorus. Solid state ^{31}P NMR of MCM-41-2P-$RhCl(PPh_3)$ showed three signals at δ −23.1, 12.2, and 31.3 ppm, respectively (Fig. 1b). One of these corresponds to the unreacted anchoring ligand while the other two are assigned to the anchoring ligand and triphenylphosphine ligand coordinated to the Rh complex since they are shifted



Scheme 1 Preparation of MCM-41-2P-RhCl(PPh$_3$) complex

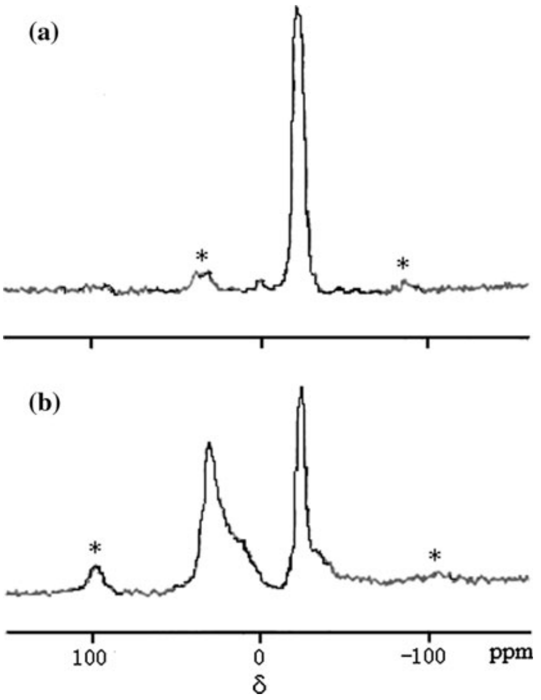
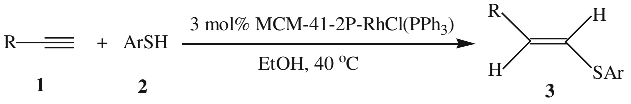


Fig. 1 Solid state ^{13}P NMR spectra of **a** MCM-41-2P and **b** MCM-41-2P- RhCl(PPh$_3$). Signals arising from side bands are marked with *asterisks*



Scheme 2 Stereoselective synthesis of (*E*)-vinyl sulfides

relative to the ^{31}P signal of RhCl(PPh$_3$)$_3$. However, exact assignments cannot be concluded. These observations indicate that Rh has been successfully immobilized on the mesoporous material MCM-41.

In order to evaluate the catalytic activity of the novel diphosphino-functionalized MCM-41 anchored rhodium complex [MCM-41-2P-RhCl(PPh$_3$)], the hydrothiolation reaction of alkynes with thiols was studied under the conditions similar to those used in the corresponding homogeneous reactions (Scheme 2), ethanol was selected as solvent according to Ogawa's work [12]. The experimental results are summarized in the Table 1. As seen from the Table 1, the hydrothiolation reaction of phenylacetylene with PhSH proceeded very smoothly at 40 °C in the presence of 3 mol% MCM-41-2P-RhCl(PPh$_3$) complex in EtOH to give (*E*)-2-(phenylthio)styrene in excellent yield (entry 1). Substituted phenylacetylenes such as 4-methylphenylacetylene, 4-chlorophenylacetylene, 4-fluorophenylacetylene and, 4-methoxyphenylacetylene also reacted with PhSH to afford the corresponding (*E*)-vinyl sulfides in good to high yields (entries 2–5). The catalytic activity of MCM-41-2P-RhCl(PPh$_3$) is comparable to that of RhCl(PPh$_3$)$_3$ [12]. For example, the preparation of (*E*)-1-(4-methylphenyl)-2-phenylthioethene (**3b**) was successful using 3 mol% MCM-41-2P-RhCl(PPh$_3$) as catalyst in ethanol at 40 °C and gave a 93% yield after 24 h (entry 2), the same reaction catalyzed by 3 mol% RhCl(PPh$_3$)$_3$ gave a 94% yield after 20 h. The procedure can be applied to a variety of aliphatic alkynes, the corresponding (*E*)-vinyl sulfides **3h**–**r** was obtained in good yields (entries 8–18). Similarly, arenethiols bearing 4-methyl, 4-methoxy and 4-chloro groups can add to terminal alkynes regio- and stereoselectively, but the reactivity of arenethiols with electron-donating substituents was lower than that of arenethiols with electron-withdrawing substituents (entries 6, 7, 9, 10). In contrast, the hydrothiolation reaction of terminal alkynes with alkanethiols such as butanethiol and cyclohexanethiol did not occur at all under the same conditions and most of the starting materials were recovered unchanged. Functionalities such as chloro, fluoro, hydroxy, methyl, methoxy, and olefinic groups tolerate the reaction conditions (entries 2–7, 9, 10, 12–18). In all cases listed in Table 1, the addition reaction proceeded with excellent regio- and stereoselectivity to provide only the *E* isomer of the anti-Markovnikov adduct **3**. Although the solid supports such as H-Rho-Zeolite and Montmorillonite K 10 are known to catalyze regioselectively the addition of thiols to olefins in high yields in an anti-Markovnikov or a Markovnikov manner [35, 36], no the addition of thiols to alkynes catalyzed by the solid supports has been reported until now. We also found that the addition reaction of thiols to alkynes did not occur in the presence of MCM-41 or MCM-41-2P support without rhodium.

Compounds **3a**–**r** were characterized by their FT-IR, ^{1}H NMR, ^{13}C NMR and MS spectra. Investigation of the crude products **3** by ^{1}H NMR spectroscopy (400 MHz) showed their isomeric purities of more than 98% and no *Z*-isomer

Table 1 Regio- and stereoselective addition of thiols to terminal alkynes catalyzed by MCM-41-2P-RhCl(PPh_3)[a]

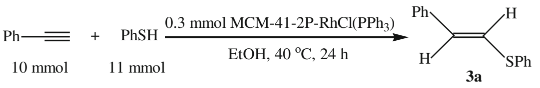
Entry	R	Ar	Product	Yield[b] (%)
1	Ph	Ph	**3a**	95
2	4-$CH_3C_6H_4$	Ph	**3b**	93
3	4-ClC_6H_4	Ph	**3c**	80
4	4-FC_6H_4	Ph	**3d**	74
5	4-$CH_3OC_6H_4$	Ph	**3e**	88
6	Ph	4-$CH_3C_6H_4$	**3f**	87
7	Ph	4-ClC_6H_4	**3g**	97
8	*n*-C_6H_{13}	Ph	**3h**	81
9	*n*-C_6H_{13}	4-ClC_6H_4	**3i**	85
10	*n*-C_6H_{13}	4-$CH_3OC_6H_4$	**3j**	70
11	*i*-C_5H_{11}	Ph	**3k**	69
12	*i*-C_5H_{11}	4-ClC_6H_4	**3l**	73
13	$PhCH_2CH_2$	4-ClC_6H_4	**3m**	76
14	1-Cyclohexenyl	Ph	**3n**	72
15	$HOCH_2CH_2CH_2$	Ph	**3o**	63
16	$CH_3OCH_2CH_2CH_2$	Ph	**3p**	67
17	$ClCH_2CH_2CH_2$	Ph	**3q**	70
18	$ClCH_2CH_2CH_2$	4-ClC_6H_4	**3r**	74

Bold values represent different structures of compounds **3a**–**3r** according to Scheme 1

[a] Reaction conditions: Terminal alkyne (1 mmol), ArSH (1.1 mmol), rhodium catalyst (0.03 mmol), EtOH (2 mL), 40 °C, 24 h

[b] Isolated yield based on the terminal alkyne used

Table 2 Hydrothiolation reaction of phenylacetylene with PhSH catalyzed by recycled catalyst



Entry	Catalyst cycle	Isolated yield (%)	TON
1	1st	95	31.7
2	10th	93	31
3	1st to 10th consecutive	av. 94	Total of 313.3

was isolated. The stereochemistry of the addition was readily apparent from the ^1H NMR spectra of compounds **3** which showed a doublet at $\delta = 6.04–6.94$ with a coupling constant of 15.6–16.4 Hz, fully in accord with an *E* geometry and overall *cis* addition of S–H bond to acetylenes.

A further objective of our studies was to determine whether the catalysis was due to the MCM-41-2P-RhCl(PPh_3) complex or to a homogeneous rhodium complex that comes off the support during the reaction and then returns to the support at the end. To test this, we focused on the hydrothiolation reaction of phenylacetylene with PhSH. We filtered off the MCM-41-2P-RhCl(PPh_3) complex after 2 h of reaction time and allowed the filtrate to react further. The catalyst filtration was performed at the reaction temperature (40 °C) in order to avoid possible recoordination or precipitation of soluble rhodium upon cooling. We found that, after this filtration, no further reaction was observed in the filtrate.

The MCM-41-2P-RhCl(PPh_3) complex can be easily recovered by a simple filtration of the reaction solution. We also investigated the possibility to reuse of the catalyst by using the hydrothiolation reaction of phenylacetylene with PhSH. In general, the continuous recycle of resin-supported transition-metal catalysts is difficult owing to leaching of the metal species from the polymer supports, which often reduces their activity within five recycles. However, when the reaction of phenylacetylene with PhSH was performed even with 3 mol% of MCM-41-2P-RhCl(PPh_3), the catalyst could be recycled 10 times without any loss of activity. The reaction promoted by the 10th recycled catalyst gave **3a** in 93% yield (entry 2, Table 2). The average yield of **3a** in consecutive reactions promoted by the first through the tenth recycled catalyst was 94% (entry 3, Table 2). The high stability and excellent reusability of the catalyst result from the chelating action of the bidentate phosphine ligand on rhodium and 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-41-2P-RhCl(PPh_3)

complex make them a highly attractive supported rhodium catalyst for the parallel solution phase synthesis of diverse libraries of compounds.

4 Conclusions

We have successfully developed a novel, practical and environmentally friendly method for the synthesis of (*E*)-vinyl sulfides through the addition reaction of thiols to terminal alkynes by using diphosphino-functionalized MCM-41 anchored rhodium complex [MCM-41-2P-RhCl (PPh_3)] as catalyst under mild reaction conditions. The reactions generated the corresponding (*E*)-vinyl sulfides regio- and stereoselectively in good to high yields. In addition, the catalyst could be easily recovered and reused for ten cycles without significant loss of activity or selectivity, thus making this procedure environmentally more acceptable.

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