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Synthesis of substituted acetylenes, aryl–alkyl ethers, 2-alkene-4-ynoates and nitriles using heterogeneous mesoporous Pd-MCM-48 as reusable catalyst

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ABSTRACT

Pd-MCM-48 has been employed as a heterogeneous catalyst for the synthesis of substituted acetylenes via Sonogashira reactions under copper and amine-free reaction conditions. In addition, the catalyst exhibited excellent regioselectivity for primary alcohols towards C–O coupling leading to formation of alkyl–aryl ethers in high yields. A green procedure for the stereoselective synthesis of 2-alkene-4-ynoates and nitriles from the reactions of *vic*-(*E*)-diiodoalkenes with activated alkenes has also been demonstrated using Pd-MCM-48 catalyst. The catalyst was easily recovered from the reaction mixture by filtration and reused for at least six times with minimal loss of activity.

1. Introduction

The carbon–carbon and carbon–heteroatom bond formation via palladium-catalyzed coupling reactions[1–3] plays a crucial role in the organic synthesis. Conventionally, reactive and soluble palladium complexes have been used as homogeneous catalysts for these coupling reactions. However, non-reusability of the homogeneous catalysts remains a scientific challenge due to economical and environmental concerns. As a result different strategies have been reported for heterogenization of the homogeneous catalysts, which enabled the easy separation of products from the reaction mixture as well as recycling of the catalysts. The ordered mesoporous siliceous material supported Pd catalysts[2m,4] have attracted much attention in recent years due to their unique physical characteristics. Among various classes of mesoporous materials, the cubic MCM-48 is attractive because its following features: (i) thermal stability (ii) large surface areas (1000–2500 $m^2\ g^{-1}$) enabling high dispersion of catalytic active sites, (iii) uniform pore sizes, (iv) easily tunable pore volume that allow for facile encapsulation of nanoparticles (NPs) and finally, (v) interpenetrating network of three-dimensional pores, which facilitate molecular transport of reactants and products more efficiently than the one-dimensional network of MCM-41.[4d] However, only a few studies have been reported in the literature using Pd-MCM-48 as catalyst[4m–p] because of the challenging preparative method of MCM-48 involving long reaction times (1–7 days) and/or hydrothermal reaction conditions.[5] The simple and room temperature procedure for preparation of MCM-48 reported by us[6a] has paved the way to the exploration of MCM-48-based catalysts for organic synthesis. As a part of our continued interest in the heterogeneous catalysis,[6] we have reported a simple protocol for the synthesis of a novel, heterogeneous, and versatile catalyst, Pd-MCM-48 at room temperature as well as its application for chemo- and region-selective hydrogenation and coupling (Heck and Suzuki) reactions under ligand-free aerobic conditions.[6j] Excellent activity and selectivity of the catalyst motivated us to better explore its potential in organic synthesis. In this paper, we report the use of Pd-MCM-48 catalyst for the synthesis of aryl–aryl or alkyl–aryl substituted acetylenes via Sonogashira cross-coupling of aryl halides with terminal alkynes, aryl–alkyl ethers and 2-alkene-4-ynoates and nitriles by a simple reaction of *vic*-(*E*)-diiodoalkenes with conjugated alkenes in water (Scheme 1).

2. Results and discussion

Two different methods namely, impregnation and deposition were designed to introduce Pd nanoparticles into MCM-48 support. In the impregnation method, aqueous solution of pre-formed Pd nanoparticles was added to the precursor mixture of MCM-48 using our recently published procedure for catalyst **1**.[6j] Two more catalysts were prepared in this manner, but with different amounts

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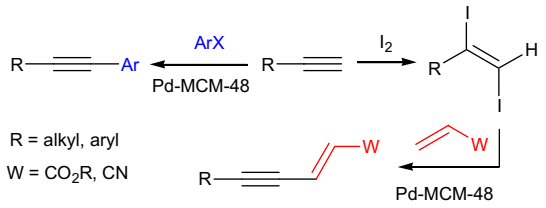


Scheme 1. Pd-MCM-48 catalyzed coupling reactions.

of the Pd nanoparticles. These catalysts are referred to as impregnated Pd-MCM-48 (catalysts **1**–**3**). Briefly, the required amount of Pd NPs[6j] was added to an appropriate molar composition of cetyltrimethylammonium bromide, NH_3 and tetraethyl orthosilicate in ethanol/water mixture and stirred at room temperature for 4 h. The mesoporous material was obtained through washing with water followed by drying, calcination at 550 °C in air and mild reduction with H_2 gas (see Experimental section for details). In the deposition method,[6j] a precursor Pd salt was deposited on the synthesized MCM-48 (referred to as deposited Pd-MCM-48) and then reduced by H_2 gas. The prepared catalysts were characterized by powder X-ray diffraction (XRD), transmission electron microscopy (TEM) imaging, nitrogen sorption, and chemisorption (CO-pulse) studies. The quantity of Pd in the catalyst has been determined from atomic absorption spectroscopic (AAS) study. The analytical and textural data of catalysts **1**–**3** are given in Table 1. The XRD studies revealed the formation of cubic mesoporous MCM-48 as evident from the small peak near 2θ 3.2° (Fig. 1).

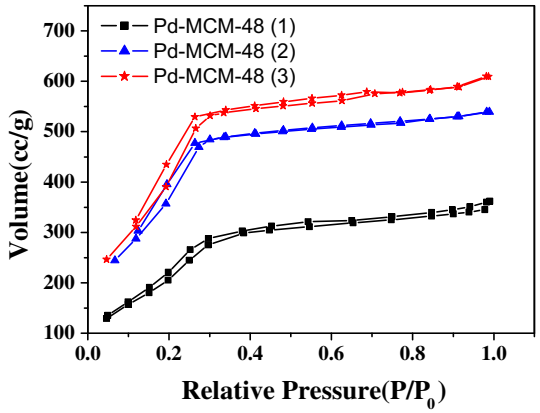


Fig. 2. Nitrogen adsorption–desorption isotherms of catalyst, **1**–**3**.

This result is also in accordance with the previously published results by Yasar et al.[4k] With increasing Pd loading, the chances of agglomeration increase, which led to the observed decrease in the Pd-surface area and Pd-dispersion. While most of small Pd NPs (<2 nm) were present inside the pores of MCM-48, some larger sized Pd NPs (average size ~6 nm) were detected on the surface of mesoporous material as observed in the TEM image (Fig. 4). The TEM image also indicates that the Pd NPs on the surface of the MCM-48 are well dispersed. The CO pulse (chemisorption) study revealed that the crystallite size of the Pd NPs was increased from 5.8 nm in catalyst **1** to 28 nm in catalyst **3** with increasing Pd content in the samples.

Table 1
Analytical and textural data of Pd-MCM-48 catalysts

Pd-MCM-48 Catalysts	Surface area [$m^2\ g^{-1}$]	Pore diameter [nm]	Pd-surface area [$m^2\ g^{-1}$]	Pd-dispersion [%]	Pd-content [%]
1	1357	2.2	95.3	20	0.6
2	1697	1.9	35.4	8	1.6
3	1788	1.8	17.7	4	2.6

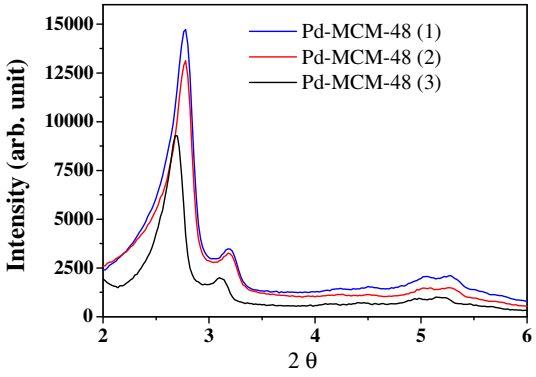


Fig. 1. Powder XRD pattern of Pd-MCM-48 catalyst, **1**–**3**.

The pore size distribution of the catalysts was calculated from the Barrett–Joyner–Halenda (BJH) equations using the nitrogen desorption isotherm (Fig. 2), and surface area was calculated using Brunauer–Emmett–Teller (BET) equation (Table 1).

The data in Table 1 indicate that all three catalysts have narrow pore size distribution (Fig. 3) with pore diameters ranging from 1.8 to 2.2 nm (See Table 1) and large surface area (1355–1788 $m^2\ g^{-1}$).

However, the pore diameter, metal surface area and dispersion of the Pd NPs were found to decrease with increasing Pd content in the sample. The decrease in pore diameter may be ascribed to the presence of Pd species within the pores of the mesoporous material.

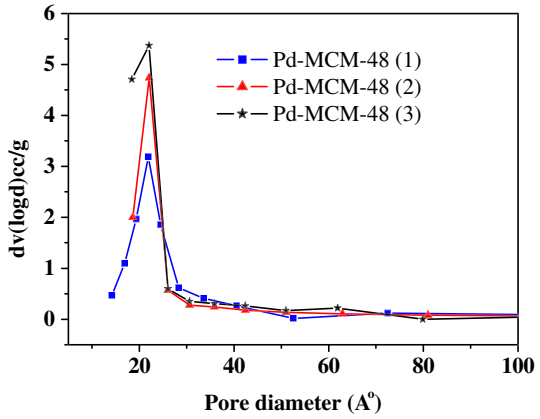


Fig. 3. Pore size distribution of catalyst, **1**–**3**.

The synthesized Pd-MCM-48 catalysts have been employed for the synthesis of substituted acetylenes via Sonogashira cross-coupling (sp^2–sp) of aryl halides with terminal alkynes. We observed that the Pd-MCM-48 efficiently catalyzed this reaction under copper-amine-free reaction conditions. It was observed that the presence of copper always leads to unwanted dimerization of alkyne, which often happens in presence of air or other oxidizing agents.[7]

Moreover, amines often have a pungent smell that curtails practicality of the process. The reaction conditions were optimized,

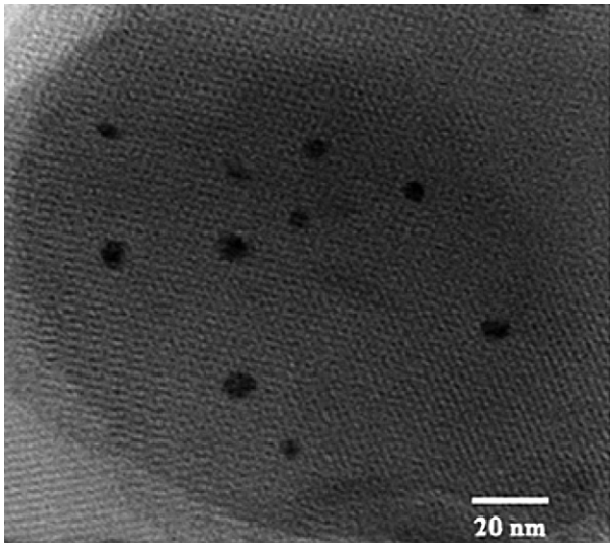


Fig. 4. TEM images of Pd-MCM-48 catalyst **1**.

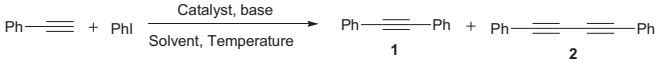
and their synthetic outcome is summarized in Table 2. Addition of copper (I) iodide as a co-catalyst always produced diyne 2 as major product (entry 1–4, 7–8, Table 2) in aerobic conditions. The Pd-MCM-48(**1**)/EtOH/K_2CO_3 reagent system was found to be the best. It was also observed that the yield of the product did not increase significantly for the increased amount of Pd over 0.6%.

conditions. In some cases, the yields of these reactions are better than reported Pd-salts or supported Pd catalysts (references were given in Table 3). The comparison has been shown in the Table 3. Most importantly, it is worth mentioning here, whereas Pd-MCM-48 smoothly catalyzes Sonogashira coupling of bromobenzene derivatives with terminal alkynes (Table 3, entries 3, 8, 13–17), Pd-MCM-41 was not able initiate these reactions.[2m] However, chlorobenzene did not react, and starting materials were recovered. Most of the reactions (entries 1–12, 14–16) in Table 3 have been carried out using ethanol and no ether formation was observed. However, for nitro and cyano-substituted bromobenzene, ether was formed at the yield ~40%. The formation of ether was avoided by using DMF as solvent (entries 13 and 17, Table 3).

Interestingly, reaction of some nitro-substituted aryl iodides and bromides with ethanol always exclusively led to C–O coupling products (Scheme 2). Various nitro-substituted aryl iodides and bromides were found to be reactive under these conditions. Very recently, Beller et al.[8] reported a procedure for $Pd(OAc)_2$-catalyzed C–O coupling in presence of the bulky di-1-adamantyl-substituted bipyrazolylphosphine ligand.

Importantly, the authors reported excellent and uncommon chemoselectivity for a primary alcohol versus its secondary and tertiary counterparts. Motivated by their results; we investigated the selectivity of our mesoporous Pd-MCM-48 catalyst **1** towards C–O coupling reactions and found by far higher reactivity of primary alcohol (Scheme 2). Thus, when a mixture of ethanol (primary), *iso*-propanol (secondary) and *tert*-butanol (tertiary) was refluxed with 4-nitroiodobenzene in presence of Pd-MCM-48 **1** (40 mg, 0.6%) only ethanol was consumed (forming 1-ethoxy-4-

Table 2
Optimization of reaction conditions for the Sonogashira cross-coupling reaction



Entry	Catalyst	Base	Solvent	Temp (°C)	Time (h)	Products ratio (%)[a]		Yield (%)[a]
						1	**2**	
1	Pd-MCM-48[b]/CuI[c]	Et_3N	EtOH	80	12	0	100	70
2	Pd-MCM-48[b]/CuI[c]	Piperidine	DMF	120	12	0	100	74
3	Pd-MCM-48[b]	Piperidine	DMF	100	10	0	100	82
4	Pd/Cu-MCM-48	Piperidine	DMF	120	10	0	100	90
5	Pd-MCM-48[b]	NaOH	EtOH/H_2O	80	24	0	0	0
6	Pd-MCM-48[b]/CuI[c]	NaOAc	EtOH/H_2O	100	24	0	0	0
7	Pd-MCM-48[b]/CuI[c]	K_2CO_3	DMF	100	10	20	80	86
8	Pd-MCM-48[b]/CuI[c]	K_2CO_3	EtOH	80	10	25	75	90
9	Pd-MCM-48[b]	K_2CO_3	DMF	120	10	55	45	80
10	**Pd-MCM-48 (1)** [b]	**K_2CO_3**	**EtOH**	**80**	**10**	**100**	**0**	**85**
11	Pd-MCM-48 (2) (1.6%)	K_2CO_3	EtOH	80	10	100	0	88
12	Pd-MCM-48 (3) (2.6%)	K_2CO_3	EtOH	80	10	100	0	83
13	Pd-MCM-48 (Deposited)[d]	K_2CO_3	EtOH	80	10	100	0	75

Bold font shows the optimum reaction condition, which was used to carry out all the reactions listed within this Table.
[a] The yields and ratio of the products was determined from the ^1H NMR spectra.
[b] Pd-MCM-48 (30 mg) was used for 1 mmol of phenylacetylene.
[c] CuI (5 mol %) was used for 1 mmol of phenylacetylene.
[d] Catalyst was prepared by depositing Pd-precursor on synthesized MCM-48.

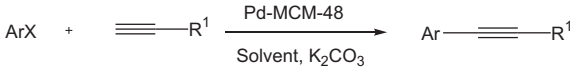
The scope and general applicability of the Pd-MCM-48 (**1**) (0.6%) catalyst have been investigated under optimized reaction conditions (Table 2, entry 10). A series of alkyl and aryl-substituted terminal alkynes were coupled with different aryl halides in presence of Pd-MCM-48 (30 mg, 0.6%, 1.7×10^{-3} mmol of Pd) and K_2CO_3 (2 mmol) in ethanol at 80 °C to produce alkyl–aryl or aryl–aryl substituted acetylenes in good yields. The results are summarized in Table 3. The reactions were very selective and always produced the target disubstituted acetylenes under these reaction conditions with no diynes observed.

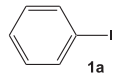
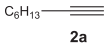
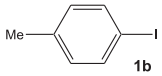
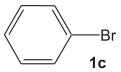
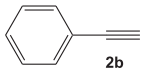
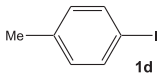
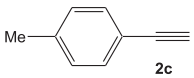
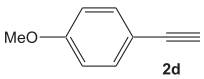
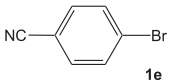
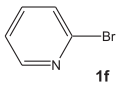
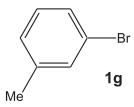
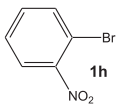
Aryl iodides and bromides with either an electron donating or withdrawing substituent readily reacted under this reaction nitro-benzene as the product) while the secondary and tertiary alcohols remained intact under the ligand-free and aerobic reaction conditions (Scheme 3).

The catalyst recyclability has been investigated for the synthesis of diphenylacetylene (Table 3, entry 4). The catalytic material was recovered from the reaction mixture by filtration, washed with ethanol, dried in air, and reused for subsequent runs. It was observed that the catalyst can be used for six times with minimal loss of activity. The results are presented in Table 6.

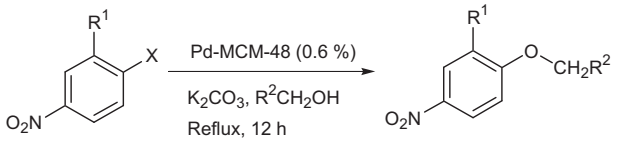
After the successful application of the Pd-MCM-48 catalyst for the Sonogashira and C–O coupling reactions, we explored its potential for the synthesis of organic molecules with valuable

Table 3
Pd-MCM-48 (**1**) catalyzed Sonogashira cross-coupling reaction



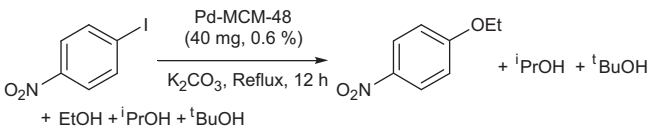
Entry	ArX	R^1	Time (h)	Yield (%)[a]	Ref
1	 **1a**	 **2a**	10	78	4h
2	 **1b**	**2a**	12	75	4h
3	 **1c**	 **2b**	12	72 (43)[b] (18)[c] (16)[d,e] (0)[f]	2f
4	**1a**	**2b**	8	85	2f
5	**1b**	**2b**	8	82	2f
6	 **1d**	**2b**	10	80	2f
7	**1a**	 **2c**	10	90	2f
8	**1c**	**2c**	12	70 (0)[f]	2f
9	**1b**	**2c**	12	85 (30)[d,e]	2f
10	**1d**	**2c**	12	78	2f
11	**1a**	 **2d**	8	84	2f
12	**1b**	**2d**	12	75	2f
13	 **1e**	**2a**	7	85	2i
14	 **1f**	**2a**	10	65	2i
15	**1f**	**2b**	12	70	2i
16	 **1g**	**2b**	12	70 (57)[b]	2i
17	 **1h**	**2b**	10	80 (60)[b]	2i

[a] Yields refers to those of pure and isolated products characterized by ^1H and ^{13}C NMR. 30 mg (0.6%) of Pd-MCM-48 was used per 1 mmol of alkyne.
[b] Catalyst=$PdCl_2/PPh_3/K_2CO_3$.[2i]
[c] Using $Pd(PPh_3)_4/CuI$.[2j]
[d] Catalyst is Pd–SiO_2.[2k]
[e] Yield obtained from Pd-Zeolite.[2l]
[f] Using Pd-MCM-41[2m].The reactions listed in entries 1–12 and 14–15 have been carried out using ethanol and for entries 13 and 17 DMF was used.



R^1 = H; R^2 = Me; X = I : Yield = 90 %
R^1 = NO_2; R^2 = Me; X = I : Yield = 95 %
R^1 = NO_2; R^2 = ^{n}Pr; X = Br : Yield = 88 %

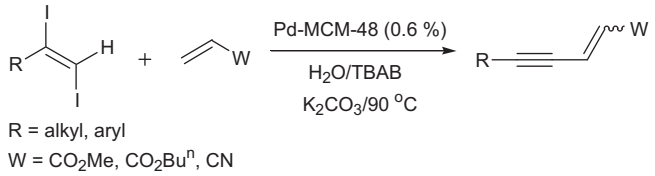
Scheme 2. Pd-MCM-48 catalyzed C–O coupling.



Scheme 3. Pd-MCM-48 catalyzed selective C–O coupling.

biological and optical properties. Thus, formation of the 1,3-enyne unit opens a practical synthetic approach to molecules with vast applications in biology,[9] electronics and photonics.[10] Generally,

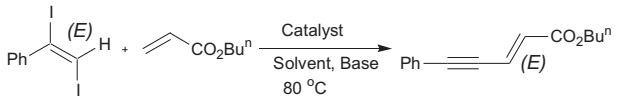
these compounds are synthesized by homogeneous Pd- or Cu-catalyzed coupling of alkynes or organometallic alkynes and vinyl halides.[11] Recently, Ranu et al.[12a] synthesized (*E*)-and (*Z*)-2-ene-4-ynoates and nitriles by Pd NPs-catalyzed coupling of *vic*-diiodoalkenes with conjugated alkenes. However, none of these catalysts are reusable. To overcome this limitation, later on Ranu et al.[12b] applied hydroxyapatite-supported Pd (Pd-HAP) as reusable catalyst for the construction of the 2-ene-4-ynoate unit. However, this material has not reported to catalyze coupling of *vic*-diiodoalkenes with conjugated nitriles.[12b] Therefore, a heterogeneous catalyst with wider applicability was long awaited. We found that Pd-MCM-48 efficiently catalyzes the coupling of *vic*-diiodoalkenes with conjugated esters or nitriles, leading to (*E*)- and (*Z*)-2-alkene-4-ynoates and 2-ene-4-yne-nitriles in good yields in presence of K_2CO_3 and tetra-butyl ammonium bromide (TBAB) in water (Scheme 4).



Scheme 4. Pd-MCM-48 catalyzed coupling of *vic*-diiodoalkenes with conjugated alkenes.

In order to optimize the reaction of *vic*-(*E*)-diiodostyrene and *n*-butyl acrylate (Table 4), we have screened several bases (K_2CO_3, Na_2CO_3 and NaOH) in various solvents (DMF, EtOH, *N*-methyl pyrrolidone (NMP), H_2O, etc.).

Table 4
Optimization of reaction conditions for the synthesis of butyl 5-phenylpent-2-en-4-ynoate



Entry	Catalyst	Base	Solvent	Time (h)	Yield (%)[a]
1	Pd-MCM-48	K_2CO_3	EtOH	12	15
2	Pd-MCM-48	Na_2CO_3	EtOH	12	10
3	Pd-MCM-48	K_2CO_3	DMF	4	75
4	Pd-MCM-48	K_2CO_3	H_2O	24	0
5	Pd-MCM-48	K_2CO_3	TBAB[b]/H_2O	4	85
6	Pd-MCM-48	Na_2CO_3	TBAB[b]/H_2O	6	60
7	Pd-MCM-48	NaOH	TBAB[b]/H_2O	12	0
8	Pd-MCM-48	K_2CO_3	NMP[c]	6	45
9	Pd–C (10%)	K_2CO_3	EtOH	6	0
10	Pd-MCM-48 (deposited)[d]	K_2CO_3	EtOH	6	0

[a] Yields refer to those of pure and isolated products.
[b] 1.5 mmol of tetrabutyl ammonium bromide (TBAB) was used for 1 mmol of diiodostyrene.
[c] NMP is *N*-methyl pyrrolidine.
[d] Catalyst was prepared by depositing Pd-precursor on synthesized MCM-48.

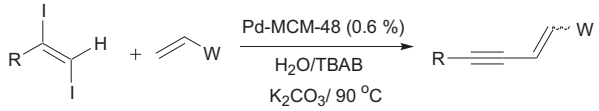
The reaction was inefficient (15% yield) with Pd-MCM-48 (**1**) and K_2CO_3 in ethanol (Table 4, entry 1) and failed in water without TBAB (Table 4, entry 4). However, the use of TBAB along with water led to the desired product, butyl 5-phenylpent-2-en-4-ynoate in high yield (Table 4, entry 5). The reaction in DMF proved to be successful as well (Table 4, entry 3). However, to avoid tedious workup process, we have replaced DMF solvent with H_2O. The commercially available Pd/C (10%) (Table 4, entry 9) and Pd-MCM-48 (deposited) (Table 4, entry 10) lead to the formation of an unidentified product in both cases. The Pd-MCM-48(**1**)/K_2CO_3/H_2O/TBAB system exhibited the best catalytic performance (Table 4, entry 5) for this coupling reaction. Therefore, this reagent has been selected to explore its scope of applicability. Both alkyl- and aryl-substituted alkenes produced 1,3-eneyne esters and nitriles in good yields (70–92%) within practical reaction time (4–6 h). The coupling is highly stereoselective, thus only (*E*)-isomer was isolated in case of acrylic esters. However, (*Z*)-stereoisomer was obtained as a major product when acrylonitrile was used. Only 30 mg of Pd-MCM-48 (**1**) catalyst containing 1.7×10^{-3} mmol of Pd were sufficient to perform the reactions smoothly in presence of K_2CO_3 and TBAB in water with no involvement of hazardous organic solvents.

Further, the catalyst was recovered from the reaction mixture simply by filtration, washed with ethanol, dried, and reused for subsequent runs.

In one example, (reaction of *vic*-(*E*) diiodostyrene and *n*-butyl acrylate) we determined that the catalyst can be reused up to six times with minimal loss of activity (See Table 6). Only after the fourth cycle, the yield dropped to 58%. This could be due to the blockage of the pores of the mesoporous MCM-48 with organic compounds involved in the reaction.

For comparison, the most representative reported results for the synthesis of the 1,3-enyne unit via coupling of *vic*-(*E*) diiodoalkenes with conjugated alkenes on different Pd catalysts are summarized in Table 7. It is evident from the data outlined in Tables 5 and 6, that the Pd-MCM-48 catalyst is superior in terms of reaction time (4–6 h), general applicability for conjugated alkenes (both CO_2R- and CN-substituted), and reusability versus the most common $PdCl_2$/TBAB/K_2CO_3[12a] and Pd-HAP systems reported previously.[12b] Further, the new catalyst has proven to be a better alternative to the existing catalysts for the construction of the 1,3-enyne unit via coupling of *vic*-diiodoalkenes with conjugated alkenes.

Table 5
Pd-MCM-48 catalyzed coupling of *vic*-diiodoalkenes with conjugated alkenes



Entry	R	W	Time (h)	Yield (%)[a]	*E*:*Z*[b]
1	C_4H_9	CO_2Me	5	75	100:00
2	C_4H_9	$CO_2{}^nBu$	5	70	100:00
3	C_6H_{13}	$CO_2{}^nBu$	6	72	100:00
4	C_6H_5	CO_2Me	4	80	100:00
5	C_6H_5	$CO_2{}^nBu$	4	85	100:00
6	C_6H_5	CN	6	73	14:86
7	*p*-Me–C_6H_4	CO_2Me	5	78	100:00
8	*p*-Me–C_6H_4	$CO_2{}^nBu$	4.5	92	100:00
7	*p*-Me–C_6H_4	CN	6	70	30:70
9	*p*-Cl–C_6H_4	$CO_2{}^nBu$	4	76	100:00
10	*m*-OMe–C_6H_4	$CO_2{}^nBu$	4	89	100:00

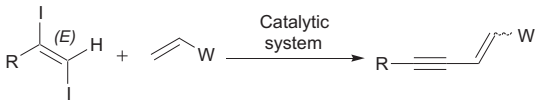
[a] Yields refer to those of pure and isolated products characterized by ^1H and ^{13}C NMR data.
[b] *E*/*Z* ratio was determined from analysis of ^1H NMR spectra. 30 mg of Pd-MCM-48 (**1**) and 1.5 mmol of TBAB was used per 1 mmol of alkene. All the products were known.

Table 6
Recyclability of Pd-MCM-48 for coupling reactions

Number of times the catalyst was reused	Yield (%)[a]	
	Diphenylacetylene (entry 4, Table 3)	Butyl 5-phenylpent-2-ene-4-ynoate (entry 5, Table 5)
1	85	85
2	85	84
3	82	76
4	80	65
5	75	58
6	75	45

[a] Yield refer to pure and isolated products.

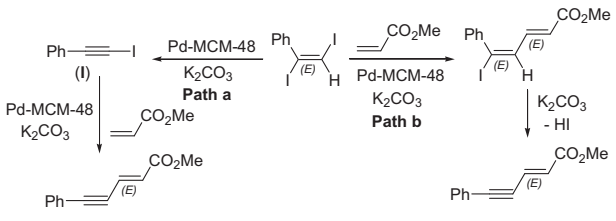
Table 7
Comparative results for the synthesis of 1,3-enyne unit using different Pd catalysts



Entry	Catalytic system	R	W	Time (h)	Yield (%)[a]	Recycle times	Ref
1	$PdCl_2$, TBAB/H_2O Na_2CO_3, 80 °C	Alkyl/aryl	CO_2R, CN	6–24	65–82	2	12a
2	Pd-HAP, NMP K_2CO_3, 90 °C	Alkyl/aryl	CO_2R	5–7	67–90	3	12b
3	Pd-MCM-48, TBAB K_2CO_3, H_2O/90 °C	Alkyl/aryl	CO_2R, CN	4–6	70–92	6	Present

[a] Yield refer to those of pure products.

In accordance with Ranu et al.,[12b] the coupling reactions are likely to proceed by two alternating pathways (Scheme 5). In path a, the final product, 2-ene-4-yonate was produced via intermediate iodoalkyne (**I**); we proved in a separate experiment, that this product (**I**) is exclusively produced as an intermediate from *vic*-diiodostyrene in presence of Pd-MCM-48/K_2CO_3. Treatment of this intermediate (**I**) with butyl acrylate under the reaction conditions produces the final enyne carboxylic ester through Heck coupling. The possibility of path b has also been documented by Ranu et al., where initially Heck reaction took place followed by HI elimination.[12b]



Scheme 5. Possible mechanism for the synthesis of 1,3-eneyne unit.

The high *E*-selectivity for CO_2R compared to the relatively small CN group and also the conversion to higher energy *Z*-isomer for CN group has been well addressed in Heck coupling.[1g]

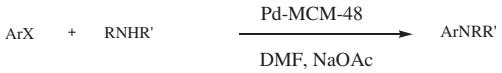
In earlier communication, we have presented two examples for the carbon-nitrogen (C–N) bond formation (Buchwald–Hartwig cross-coupling reaction) via cross-coupling reaction of 4-nitroiodobenzene and pyrrolidine using our Pd-MCM-48 catalyst.[6j] In this study, we have extended its scope for the C–N bond formation reactions and results are presented in Table 8. Various nitro and cyano-substituted aryl bromides and iodides were reacted with aliphatic amines in presence of Pd-MCM-48 catalyst and a base, NaOAc to yield C–N coupled products in good yields (75–95%).

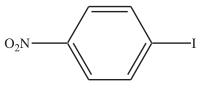
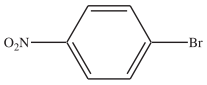
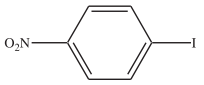
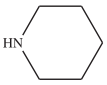
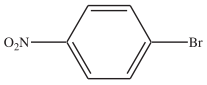
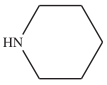
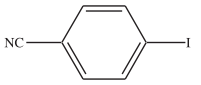
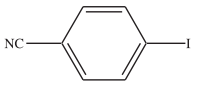
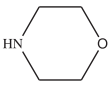
The heterogeneity of the Pd-MCM-48 catalyst was checked for the synthesis of diphenylacetylene (Table 3, entry 4) as a model reaction using the hot filtration method.[4p] Briefly, the hot reaction mixture was filtered through a fritted funnel after 2 h (~25% conversion by ^1H NMR), and the filtrate was refluxed for additional 10 h. However, only an insignificant 3% increase in yield was observed. This result proved that the reaction was catalyzed heterogeneously and Pd NPs did not leach from the mesoporous MCM-48 matrix during the course of the reaction.

3. Conclusions

In conclusion, mesoporous heterogeneous Pd-MCM-48 has been introduced as an efficient reusable catalyst for the synthesis of aryl–aryl or aryl–alkyl substituted acetylenes, aryl–alkyl ethers, (*E*)-and (*Z*)-2-alkene-4-ynoates, and nitriles under ligand-free and aerobic reaction conditions. The Sonogashira reaction has been carried out under copper- and amine-free conditions with high isolated yields. The excellent selectivity was observed for primary alcohols towards C–O coupling, leading to aryl–alkyl ethers in excellent yields (88–95%) under ligand-free conditions using Pd-MCM-48. Moreover, the impregnated catalyst showed excellent activity for the construction of 1,3-enyne units, whereas only unidentified products were produced on the deposited Pd-MCM-48 catalyst. To the best of our knowledge, selective C–O coupling and reactions of *vic*-diiodoalkenes with conjugated alkenes, documented in this study, have not been reported using Pd-mesoporous materials. Sonogashira coupling has never been reported using Pd-MCM-48. This body of work provides new knowledge regarding the applicability of mesoporous materials for those reactions.

Table 8
Pd-MCM-48 catalyzed C–N coupling reaction



Entry	ArX	Amine	Time (h)	Yield (%)[a]
1			12	80
2			15	75
3			8	95
4			8	80
5		PhNHMe	10	75
6			12	78

[a] Yields refer to those of pure products. All of the products gave ^1H and ^{13}C NMR data consistent with the structures and data in the literature.

4. Experimental section

4.1. Chemicals and reagents used

Hexadecyltrimethylammoniumbromide (CTAB, 99+%, Acros), ethanol (absolute 200 Proof, AAPER), aqueous ammonia (Fisher),

tetraethoxysilane (99%, Alfa Aesar), palladium(II) 2,4-pentanedionate (Alfa Aesar), and sodium terachloropalladate(II) ($Na_2[PdCl_4]$) (Pressure Chemicals) were used for the synthesis of Pd-MCM-48 catalysts. Dimethylaminopyridine (DMAP, 99%, Acros), sodium borohydride (98% Acros), toluene (Acros), tetra-*n*-octylammoniumbromide (TOAB, 98+% Alfa Aesar), and sodium sulfate anhydrous powder (Fisher) were used for the synthesis of Pd nanoparticles. All the chemicals, reagents and solvents used for the Sonogashira, C–O coupling, and synthesis of the enyne system were purchased from either Sigma–Aldrich and (or) Alfa Aesar, and used as received without any further purification. (*E*)-*vic*-Diiodoalkenes were synthesized from corresponding alkenes using molecular iodine in water–ethanol mixture at room temperature and were characterized by ^{1}H NMR spectroscopy data before use for reactions.

4.2. Synthesis of Pd(0) nanoparticles

Pd(0) Nanoparticles were synthesized by a published procedure, which involves reduction of Na_2PdCl_4 with $NaBH_4$, and stabilized by tetra-octylammonium bromide (TOAB) as a capping agent. Briefly, 9.6 mL of a 47 mM aqueous solution of Na_2PdCl_4 (yellow colour) was mixed with 40 mL of a 50 mM solution of TOAB dissolved in toluene and magnetically stirred at 300 rpm for 15 min. A red-brown organic solution and the colourless aqueous phase were formed due to the complete transfer of $PdCl_4^{2-}$ to the organic phase. The colourless aqueous phase was separated and the toluene phase was dried with Na_2SO_4. Then, 11.4 mL of a freshly prepared 0.1–1.0 M of $NaBH_4$ aqueous solution were added drop wise for a period of 2 h under vigorous magnetic stirring. The mixture was stirred overnight, consecutively washed with 40 mL of a 0.1 M H_2SO_4, 40 mL of a 0.1 M aqueous NaOH and 40 mL of water. Finally, the organic solution was dried over anhydrous Na_2SO_4. Then we transferred the Pd(0) nanoparticles to the aqueous phase. For that a solution (10 mL) of 4-dimethylaminopyridine (DMAP) (0.1 M) was used as a phase transfer agent and prepared by dissolving 0.1 g of DMAP in 10 mL of deionized water. Then, aqueous DMAP solution was added to 40 mL of the as-synthesized Pd nanoparticles in toluene. The mixture was stirred for 2 h to complete transfer of the Pd nanoparticles to the aqueous phase.

4.3. Representative experimental procedure for the synthesis of Pd-MCM-48 (1)

The Pd-MCM-48 (**1**) catalyst has been synthesized by impregnating Pd nanoparticles into the cubic phase of MCM-48 matrix following our previously published procedure.[6j] Pd nanoparticles were synthesized according to the published procedure by the reduction of Na_2PdCl_4 with $NaBH_4$ in the presence of tetra-*n*-octylammoniumbromide (TOAB) as a capping as well as stabilizing agent. In a typical experimental procedure, 1 mL of the Pd nanoparticles solution (the concentration was adjusted to the required loading), 25 mL ethanol, 1.2 g (3.3 mmol) of CTAB, 6 mL of aq NH_3 (0.09 mol) and 1.8 mL (8 mmol) of TEOS were sequentially added to a 125 mL polypropylene bottle, and stirred for 4 h at 300 rpm. The molar composition of the formed siliceous gel is 0.41 CTAB:11 aq NH_3:1.0 TEOS:53 EtOH:344H_2O. After 4 h, the mesoporous material was washed extensively with deionized water, and dried overnight at 100 °C. The dried material was finely ground with a mortar and pestle and calcined in air at 550 °C (ramp rate of 3 °C per min.) for 6 h in an alumina crucible to remove the surfactant molecules. Since the calcined Pd-MCM-48 may contain Pd in the +2 oxidation state, after calcinations this calcined material was reduced in hydrogen-gas flow (20 mL/min) at 300 °C for 2 h in a tubular furnace to improve consistency of the composition of the catalyst. The content of palladium in the synthesized catalyst was determined by atomic absorption spectroscopy and found to be 0.6 wt %.

The above procedure was used for the synthesis of other two catalysts; catalyst **2** and catalyst **3** by varying the amount of Pd NPs (3 mL of Pd NPs solution for catalyst **2**, and 5 mL of Pd NPs for catalyst **3**). Characterization data for all three catalysts are presented either in the main text or in Supplementary data.

4.4. General experimental procedure for the Sonogashira coupling of iodobenzene with phenylacetylene (Table 3, entry 4)

Iodobenzene (204 mg, 1 mmol), phenylacetylene (102 mg, 1 mmol), K_2CO_3 (276 mg, 2 equiv, 2 mmol) and Pd-MCM-48 (25 mg) were mixed in 5 mL of ethanol and refluxed for 12 h with stirring. The reaction progress was monitored by TLC. The reaction mixture was cooled to room temperature, and solvent was removed under vacuum. The residue was extracted with 100 mL of ethyl acetate and organic layer was washed with water (2×5 mL). The organic layer was dried over Na_2SO_4, and solvent was evaporated to provide diphenylacetylene as a white solid (151 mg, 85%). The ^{1}H NMR and ^{13}C NMR spectroscopic data of the product were in good agreement with previously reported data.[2f] This procedure was followed for all the reactions listed in Table 3. All the products listed in Table 3 are known and all of the products gave ^{1}H and ^{13}C NMR data consistent with the structures and data in the literature. The reference for each compound is provided in Table 3.

4.5. General experimental procedure for synthesis of butyl 5-phenylpent-2-ene-4-ynoate via coupling of 1,2-diiodovinylbenzene with butyl acrylate (Table 5, entry 5)

A mixture of 1,2-diiodovinylbenzene (356 mg, 1 mmol), *n*-butyl acrylate (192 mg, 1.5 mmol), K_2CO_3 (276 mg, 2 equiv, 2 mmol), and tetra-butyl ammonium bromide (TBAB) (483 mg, 1.5 mmol) in H_2O (5 mL) was stirred at 90 °C for 4 h. Progress of the reaction was monitored by TLC. The reaction mixture was extracted with ethyl acetate (2×5 mL). The organic layer was dried over anhydrous Na_2SO_4 the solvent was evaporated to yield the crude product, which was purified by flash chromatography over silica gel (eluted by 5% ethyl acetate in hexane) to afford pure butyl 5-phenylpent-2-en-4-ynoate (194 mg, 85%) as a yellow oil. The spectroscopic data (^{1}H NMR and ^{13}C NMR) are in good agreement with reported in the literature.[12a] This reaction procedure was followed for all the reactions listed in Table 5. All the products listed in Table 5 are known in the literature and were characterized by ^{1}H NMR and ^{13}C NMR spectroscopic data, which are in good agreement with reported values. The reference for each compound is given in Table 5.

4.6. General experimental procedure for synthesis of 1-(4-nitro-phenyl)-pyrrolidine via cross-coupling of 1-iodo-4-nitro-benzene and pyrrolidine (Table 8, entry 1)

A mixture of 1-iodo-4-nitro-benzene (1 mmol, 249 mg), pyrrolidine (2 mmol, 142 mg), Pd-MCM-48 (30 mg) and NaOAc (2 mmol, 164 mg) was heated at 130 °C in DMF (5 mL) for 12 h till completion of reaction (TLC). The reaction mixture was cooled to room temperature and catalyst was separated by filtration. The filtrate was extracted with ethyl acetate (20 mL), washed with water (5×1 mL), dried over Na_2SO_4. The solvent was evaporated to leave the crude product, which was purified by column chromatography over silica-gel (2% ethyl acetate in hexane) to provide pure 1-(4-nitro-phenyl)-pyrrolidine (153 mg, 80%). All the products listed in Table 3 are known in the literature and gave ^{1}H and

^{13}C NMR data consistent with the structures and data in the literature.

Acknowledgements

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References and notes

1. For review of Heck reaction see: (a) de Meijere, A.; Meyer, F. E. *Chem. Int. Ed. Engl.* **1994**, *33*, 2379; (b) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427; (c) Polshettiwar, V.; Lenb, C.; Fihri, A. *Coord. Chem. Rev.* **2009**, *253*, 2599; (d) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2010**, *39*, 2447; (e) Alonso, D. A.; Nájera, C. *Chem. Soc. Rev.* **2010**, *39*, 2891; (f) Karimi, B.; Behzadnia, H.; Elhamifar, D.; Akhavan, P. F.; Esfahani, F. K.; Zamani, A. *Synthesis* **2010**, 1399; (g) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.
2. For Book and review of Sonogashira reaction, see: (a) Sonogashira, K. In *Handbock of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., de Meijere, A., Eds.; Wiley-Interscience: New York, NY, 2002; Vol 1, p 493; (b) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46; (c) Tykwinski, R. R. *Angew. Chem., Int. Ed.* **2003**, *42*, 1566; (d) Negishi, E.-I.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979; (e) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874; (f) Thakur, K. G.; Jaseer, E. A.; Naidu, A. B.; Sekar, G. *Tetrahedron Lett.* **2009**, *50*, 2865; (g) Li, P.-H.; Wang, L. *Adv. Synth. Catal.* **2006**, *348*, 681; (h) Lamblin, M.; Nassar-Hardy, L.; Hierso, J.-C.; Fouquet, E.; Felpinb, F.-X. *Adv. Synth. Catal.* **2010**, *352*, 33; (i) Guan, J. T.; Weng, T. Q.; Yu, G.-A.; Liu, S. H. *Tetrahedron Lett.* **2007**, *48*, 7129; (j) Bhattacharyaa, S.; Sengupta, S. *Tetrahedron Lett.* **2004**, *45*, 8733; (k) Rollet, P.; Kleist, W.; Dufaud, V.; Djakovitch, L. *J. Mol. Catal. A: Chem.* **2005**, *241*, 39; (l) Djakovitch, L.; Rollet, P. *Tetrahedron Lett.* **2004**, *45*, 1367; (m) Komura, K.; Nakamura, H.; Sugi, Y. *J. Mol. Catal. A: Chem.* **2008**, *293*, 72.
3. For review of Suzuki cross-coupling, see: (a) Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213; (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (c) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147; (d) Suzuki, A. *Chem. Commun.* **2005**, 4759; (e) Phan, N. T. S.; Van der Sluys, M.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609; (f) Pigge, F. C. *Synthesis* **2010**, 1745.
4. (a) Kresge, C. T.; Leonowicz, M. E.; Roth, W. J.; Vartuli, J. C.; Beck, J. S. *Nature* **1992**, *359*, 710; (b) Ying, J. Y.; Mehnert, C. P.; Wong, M. S. *Angew. Chem., Int. Ed.* **1999**, *38*, 56; (c) Yeung, L. K.; Crooks, R. M. *Nano Lett.* **2001**, *1*, 14; (d) Fraile, J. M.; García, J. I.; Mayoral, J. A.; Vispe, E.; Brown, D. R.; Naderi, M. *Chem. Commun.* **2001**, 1510; (e) Tsai, F.-Y.; Wu, C.-L.; Mou, C.-Y.; Chao, M.-C.; Linc, H.-P.; Liua, S.-T. *Tetrahedron Lett.* **2004**, *45*, 7503; (f) Panpranot, J.; Pattamakomsan, K.; Goodwin, J. G.; Praserthdam, P. *Catal. Commun.* **2004**, *5*, 583; (g) Papp, A.; Galbács, G.; Molnár, A. *Tetrahedron Lett.* **2005**, *46*, 7725 and references cited therein; (h) He, C.; Li, J.; Cheng, J.; Li, L.; Li, P.; Hao, Z. P.; Xu, Z. *Ind. Eng. Chem. Res.* **2009**, *48*, 6930; (i) Jana, S.; Haldar, S.; Koner, S. *Tetrahedron Lett.* **2009**, *50*, 4820; (j) Chen, J.-Y.; Lin, T.-C.; Chen, S.-C.; Chen, A.-J.; Moub, C.-Y.; Tsai, F.-Y. *Tetrahedron* **2009**, *65*, 10134; (k) Gürbüj, N.; Vural, S.; Yasar, S.; Özdemir, I.; Seckin, T. *J. Inorg. Orgnaomet. Polym.* **2010**, *20*, 19; (l) Garcia-Martinez, J.; Linares, N.; Sinibaldi, S.; Coronado, E.; Ribera, A. *Micropor. Mesopor. Mater.* **2009**, *117*, 170; (m) Mukhopadhyay, K.; Sarkar, B. R.; Chaudhari, R. V. *J. Am. Chem. Soc.* **2002**, *124*, 9692; (n) Lee, H.-Y.; Ryu, S.; Kang, H.; Junb, Y.-W.; Cheon, J. *Chem. Commun.* **2006**, 1325; (o) Wang, L.-C.; Huang, C.-Y.; Chang, C.-Y.; Lin, W.-C.; Chao, K. J. *Micropor. Mesopor. Mater.* **2008**, *110*, 451; (p) Bhunia, S.; Sen, R.; Koner, S. *Inorg. Chim. Acta* **2010**, *363*, 3993.
5. (a) Czechura, K.; Sayari, A. *Chem. Mater.* **2006**, *18*, 4147; (b) Kim, S.; Marand, E.; Ida, J.; Guliants, V. V. *Chem. Mater.* **2006**, *18*, 1149; (c) Chao, K. J.; Chang, Y. P.; Chen, Y. C.; Lo, A. S.; Phan, T. H. *J. Phys. Chem. B* **2006**, *110*, 1638; (d) Wang, T.; Kaper, H.; Antonietti, M.; Smarsly, B. *Langmuir* **2007**, *23*, 1489; (e) Bronkema, J. L.; Bell, A. T. *J. Phys. Chem. C* **2007**, *111*, 420.
6. (a) Boote, B.; Subramanian, H.; Ranjit, K. T. *Chem. Commun.* **2007**, 4543; (b) Subramanian, H.; Koodali, R. T. *React. Kinet. Catal. Lett.* **2008**, *95*, 239; (c) Banerjee, S.; Das, J.; Santra, S. *Tetrahedron Lett.* **2009**, *50*, 124; (d) Banerjee, S.; Sereda, G. *Tetrahedron Lett.* **2009**, *50*, 6959; (e) Banerjee, S.; Santra, S. *Tetrahedron Lett.* **2009**, *50*, 2037; (f) Zhao, D.; Budhi, S.; Rodriguez, A.; Koodali, R. T. *Int. J. Hydrogen Energy* **2010**, *35*, 5276; (g) Banerjee, S.; Das, J.; Alvarez, R. P.; Santra, S. *New J. Chem.* **2010**, *34*, 302; (h) Rajpara, V.; Banerjee, S.; Sereda, G. *Synthesis* **2010**, *16*, 2835; (i) Zhao, D.; Rodriguez, A.; Dimitrijevic, N. M.; Rajh, T.; Koodali, R. T. *J. Phys. Chem. C* **2010**, *114*, 15728; (j) Banerjee, S.; Balasanthiran, V.; Koodali, R. T.; Sereda, G. A. *Org. Biomol. Chem.* **2010**, *8*, 4316; (k) Banerjee, S.; Horn, A.; Khatri, H.; Sereda, G. *Tetrahedron Lett.* **2011**, *52*, 1878.
7. Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632.
8. Gowrisankar, S.; Sergeev, A. G.; Anbarasan, P.; Spannenberg, A.; Neumann, H.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 11592.
9. (a) Zein, N.; Sinha, A. M.; McGahren, W. J.; Ellestad, G. A. *Science* **1988**, *240*, 1198; (b) Rudi, A.; Schleyer, M.; Kashman, Y. *J. Nat. Prod.* **2000**, *63*, 1434; (c) Iverson, S. L.; Uetrecht, J. P. *Chem. Res. Toxicol.* **2001**, *14*, 175.
10. Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1350.
11. (a) Nishimura, T.; Araki, H.; Maeda, Y.; Uemura, S. *Org. Lett.* **2003**, *5*, 2997; (b) Jeffery, T. *Synthesis* **1987**, 70; (c) Takeuchi, R.; Tanabe, K.; Tanaka, S. *J. Org. Chem.* **2000**, *65*, 1558; (d) Bates, C. G.; Saejueng, P.; Venkataraman, D. *Org. Lett.* **2004**, *6*, 1441; (e) Hoshi, M.; Shirakawa, K. *Synlett* **2002**, 1101.
12. (a) Ranu, B. C.; Chattopadhyay, K. *Org. Lett.* **2007**, *9*, 2409; (b) Ranu, B. C.; Adak, L.; Chattopadhyay, K. *J. Org. Chem.* **2008**, *73*, 5609.