# ChemComm

#### COMMUNICATION

## **RSC**Publishing

View Article Online View Journal | View Issue

Cite this: Chem. Commun., 2013, 49, 2195

Received 10th January 2013, Accepted 27th January 2013

DOI: 10.1039/c3cc00235g

www.rsc.org/chemcomm

### Bifunctional mesoporous silica nanoparticles as cooperative catalysts for the Tsuji–Trost reaction – tuning the reactivity of silica nanoparticles†

Arne T. Dickschat,<sup>a</sup> Frederik Behrends,<sup>b</sup> Sabrina Surmiak,<sup>a</sup> Mark Weiß,<sup>b</sup> Hellmut Eckert\*<sup>b</sup> and Armido Studer\*<sup>a</sup>

Bifunctional mesoporous silica nanoparticles (MSNs) bearing Pd-complexes and additional basic sites were prepared and tested as cooperative active catalysts in the Tsuji–Trost allylation of ethyl acetoacetate. Functionalization of the MSNs was realized by postmodification using clickchemistry. The selectivity of mono *versus* double allylation was achieved by control of reaction temperature and the nature of the catalyst.

Bi- or multifunctional mesoporous silica nanoparticles (MSNs) have been successfully used as catalysts in synthesis.<sup>1</sup> The large surface area and the immersive channels in mesoporous materials such as MCM-41 render them highly valuable as solid supports to conduct heterogeneous catalysis. Furthermore, spatial separation of different functionalities in these materials allows for bifunctional catalysis.<sup>1</sup> We recently introduced a new concept for preparation of bifunctional MSNs by late stage chemical functionalization starting with one 'mother'-particle **A** bearing two chemical orthogonal functionalities that are for example azides and alkoxyamines (Scheme 1).<sup>2</sup> The two functionalities were addressed selectively by orthogonal click-chemistry and the novel



Scheme 1 Late stage functionalization of bifunctional particle A.

Corrensstrasse 28/30, 48149 Münster, Germany. E-mail: eckerth@uni-muenster.de

 $\dagger$  Electronic supplementary information (ESI) available. See DOI: 10.1039/c3cc00235g

approach allowed for the synthesis of a small catalyst library  $\mathbf{B}_{1-n}$  containing organic acids and bases as cooperative active moieties in a short time from a single MSN of type **A**.

Herein we present first results on the application of this concept for the preparation of MSNs bearing amines along with Pd-complexes as cooperative active functionalities and their use as catalysts in the Tsuji–Trost reaction.<sup>3</sup> For these studies we chose azides and alkoxyamines as orthogonal addressable entities. The azide–alkyne cycloaddition is *the* standard click reaction<sup>4</sup> and the alkoxyamine moiety at the MSN is readily chemically modified by thermal nitroxide exchange.<sup>2,5</sup>

We first had to identify a route for late stage immobilization of a Pd-ligand *via* azide modification. To this end, we co-condensed tetraethyl orthosilicate (TEOS) **1** with the triethoxysilane **2** to obtain the azide functionalized material **3** (Scheme 2). Cu-catalyzed azide–alkyne click-reaction (CuAAC)<sup>4</sup> with 2-ethynylpyridine provided MSN **4** bearing triazole–pyridyl moieties serving as Pd-ligands (see 5).<sup>6,7</sup>

The success of these transformations was readily monitored *via* solid state <sup>13</sup>C CP/MAS NMR, elemental analysis and IR. The <sup>13</sup>C NMR spectra are shown in Fig. 1 (for further characterisation of 5, see ESI<sup>†</sup>). In comparison to the spectra of triethoxysilane 2 in solution and azide functionalized material 3, the <sup>13</sup>C CP/MAS NMR spectra of 4 and 5 clearly show three broad new carbon resonances in the aromatic region comprising the seven carbons of the formed ligand. The signal that can most likely be assigned to the carbon next to the newly



Scheme 2 Azide–alkyne cycloaddition and complexation.

<sup>&</sup>lt;sup>a</sup> Westfälische Wilhelms-Universität, Organisch-Chemisches Institut, Corrensstrasse 40, 48149 Münster, Germany. E-mail: studer@uni-muenster.de; Fax: +49 251-833-6523

<sup>&</sup>lt;sup>b</sup> Westfälische Wilhelms-Universität, Physikalisch-Chemisches Institut,



**Fig. 1** (a) <sup>13</sup>C NMR of **2** in CDCl<sub>3</sub> and <sup>13</sup>C CP/MAS NMR of (b) azide functionalized material **3**, (c) triazole **4** and (d) Pd-loaded particles **5**. The marked signals are due to residual solvents diethyl ether and methanol.

formed triazole ring shifts from 51.4 ppm in 2 (carbon next to the azide) to 52.3 ppm in 4 and 53.8 ppm in 5, respectively. For the MSN 5 only minor changes in the NMR spectra can be detected compared to MSN 4 (see also the ESI<sup>†</sup>) but the broadening of the aromatic resonances could indicate a coordination of the ligands to Pd. The <sup>13</sup>C NMR spectra give clear evidence for the successful synthesis and functionalization of the materials investigated. Encouraged by these initial experiments we prepared bifunctional MSNs 7 by co-condensation of azide 2, alkoxyamine 6 and TEOS in a 1:1:8 ratio (Scheme 3).

CuAAC reaction of 7 with 2-ethynylpyridine provided 8 which was analysed using  $^{13}$ C CP/MAS NMR spectroscopy (Fig. 2).

Resonances that can be clearly attributed to the alkoxyamine moiety in the solid material are the peak near 91 ppm, assigned to the  $\alpha$ -carbon of the alkoxyamine heterocycle and the signal near 70 ppm attributed to the two oxygen-bonded C-atoms. In the aromatic



**Scheme 3** Co-condensation of **2**, **6** and TEOS to give **7** and formation of **8** *via* azide–alkyne reaction.



Fig. 2 (a)  $^{13}$ C NMR of 6 in CDCl<sub>3</sub> and (b)  $^{13}$ C CP/MAS MAS NMR of 8.



region, the signals of the triazole pyridine moiety and those of the phenyl rings associated with the alkoxyamine ligand closely overlap, precluding their individual resolution. Altogether, the comparison of the signals of **8** with those of **6** and **4** clearly indicates the successful synthesis of **8**. MSN **8** was then subjected to nitroxide exchange reactions using various nitroxides containing different amino groups to provide MSNs bearing basic amino functionalities. Treatment with PdCl<sub>2</sub> finally afforded MSNs **9–12** (Fig. 3; for synthesis and characterisation of the various nitroxides and MSNs, as well as their BJH plots,<sup>8</sup> see the ESI<sup>†</sup>). Hence, four different catalysts were readily prepared starting with one mother system **8** documenting the power of our late stage functionalization approach.

The MSNs **9–12** (2–5 mol%)<sup>9</sup> were successfully applied as catalysts in the Tsuji–Trost allylation of allyl methyl carbonate **13** with ethyl acetoacetate **14** in THF using  $K_2CO_3$  as an external base (Scheme 4 and Table 1). Near quantitative yield of monoallylated product **15** resulted with catalyst **9** (entry 1). The amino functionalities in **9** influenced the reaction outcome<sup>10</sup> since MSN **10** bearing aminoamide groups instead showed a higher activity and bisallylated product **16** was obtained in 96% yield (entry 2).

Like MSN 9, catalysts 11 and 12 afforded exclusively the monoallylated product 15 in high yields (entries 3 and 4) further documenting the role of the amine as a cooperative active unit. Reaction with 10 using 1 equiv. of K<sub>2</sub>CO<sub>3</sub> did not change the outcome (compare entries 2 and 5). However, in the absence of K<sub>2</sub>CO<sub>3</sub> the allylation did not proceed (entry 6). Interestingly, clean monoallylation was also achieved with the most active catalyst 10 upon running the allylation at 30 °C (compare entries 2 and 7). Hence, product control was possible by simple temperature adjustment. Even with the less reactive catalysts 9 and 11 reactions could be conducted at lower temperature, but reaction time had to be increased and yields were lower (compare entries 1 and 3 with entries 8 and 9). In both cases the reaction only proceeded to give the monoallylated product in good yields. To evaluate the effect of the additional amine (cooperativity) on the reaction we tested catalyst 5 lacking the amine moiety and noted a significantly lower degree of conversion to the monoallylation product 15 at longer reaction time under otherwise identical conditions



Table 1 Results of Pd-catalyzed Tsuji–Trost allylation

				Yield	eld [%]	
Entry	Catalyst	Temperature [°C]	Reaction time [h]	15	16	
1	9	70	18	99	0	
2	10	70	18	0	96	
3	11	70	12	99	0	
4	12	70	18	93	0	
5	10	70	18	0	93 <sup>a</sup>	
6	10	70	18	0	$0^b$	
7	10	30	18	91	0	
8	9	rt	24	62	$0^c$	
9	11	rt	24	52	$0^c$	
10	5	70	24	77	$0^{c}$	
11	5, $NEt_3$	70	24	77	$0^{c}$	
12	9	70	18	0	$99^{c,d}$	
13	9	70	18	85	$15^{c,e}$	

Table 2 Pd-catalyzed Tsuji–Trost allylation with MSNs 17–19

				Yield <sup>a</sup> [%]	
Entry	Catalyst	Temperature [°C]	Reaction time [h]	15	16
1	17	70	24	99	0
2	18	70	24	93	0
3	19	70	24	33	66
4	17	rt	24	0	0
5	18	rt	24	0	0
6	19	rt	24	0	0
<sup>a</sup> GC-c	onversion.				

 $^a$  1 eq.  $K_2CO_3$  was used.  $^b$  0 eq.  $K_2CO_3$  was used.  $^c$  GC-conversion.  $^d$  Pd(OAc)\_2 was used as a Pd-source.  $^e$  Pd\_2(dba)\_3 was used as a Pd-source.

(entry 10). Addition of external NEt<sub>3</sub> to 5 did not improve the result (entry 11) which clearly shows the beneficial effect of immobilized amine bases on the allylation. To exclude that reactions are catalysed by Pd-compounds that leached out of the MSN, we ran the reaction with MSN 9 to obtain around 75% conversion and carefully filtered off the particles. The filtrate was then kept at 70 °C for another 18 h and no further conversion was noted which gives evidence that catalysis occurs exclusively at the MSN particles. We tested different Pd-sources and noted a similar reactivity upon starting with  $Pd(OAc)_2$  (entry 12), whereas particles derived from Pd<sub>2</sub>(dba)<sub>3</sub> were significantly less reactive (entry 13). In addition, we also tested catalyst 9 in a recycling experiment and the reactivity remained high for 4 runs. However, in the 5th run high conversion was observed but a mixture of mono- and bisallylated product was formed.<sup>11</sup> Finally, we also tested the effect of the structure of the Pd-ligand on the allylation. To this end, we prepared a bipyridyl type ligand, which was then attached to the surface via CuAAC chemistry. Nitroxide exchange reaction provided MSNs 17, 18 and 19 (Fig. 4).

The results of the allylations with catalysts **17–19** are presented in Table 2. With **17** the reaction proceeded smoothly and the monoallylated product **15** was obtained in quantitative yield (entry **1**). The aminoamide functionality, which in combination



Fig. 4 MSNs 17–19 bearing bipyridyl complexed Pd.

with the triazole ligand gave the most active catalyst **10**, showed a slightly lower activity in combination with the bipyridyl ligand (entry 2). The most active system in this series was found to be **19** which provided a 1 : 2 mixture of mono- and bisallylated product (entry 3). In contrast to the pyridyltriazole based catalysts, **17–19** were not active at room temperature.

In conclusion, we prepared various bifunctional mesoporous nanoparticles by co-condensation of TEOS and triethoxysilanes bearing azides and alkoxyamines at their termini. Late stage functionalization by orthogonal click chemistry and subsequent palladation provided different catalysts which were successfully used in a Tsuji–Trost allylation. The successful synthesis of these MSNs was ensured by solid state NMR. We showed that the structure of the amine functionalities heavily influences reaction which shows that they act as cooperative active entities.

This work was funded by the DFG *via* project SFB858. F.B. thanks the Fonds der Chemischen Industrie for a doctoral fellowship.

#### Notes and references

- For recent development see: (a) K. Motokura, M. Tomita, M. Tada and Y. Iwasawa, Chem.-Eur. J., 2008, 14, 4017–4027; (b) Y. Huang, S. Xu and V. S. Y. Lin, Angew. Chem., 2011, 123, 687–690; (c) E. L. Margelefsky, R. K. Zeidan, V. Dufaud and M. E. Davis, J. Am. Chem. Soc., 2007, 129, 13691–13697; (d) N. R. Shiju, A. H. Alberts, S. Khalid, D. R. Brown and G. Rothenberg, Angew. Chem., 2011, 123, 9789–9793; (e) S. Shylesh, A. Wagner, A. Seifert, S. Ernst and W. R. Thiel, ChemCatChem, 2010, 2, 1231–1234; (f) S. Shylesh, A. Wagner, A. Seifert, S. Ernst and W. R. Thiel, Angew. Chem., 2010, 122, 188–191; (g) H. Noda, K. Motokura, A. Miyaji and T. Baba, Angew. Chem., 2012, 124, 8141–8144; (h) K. K. Sharma, A. V. Biradar, S. Das and T. Asefa, Eur. J. Inorg. Chem., 2011, 3174–3182.
- 2 A. T. Dickschat, F. Behrends, M. Bühner, J. Ren, M. Weiß, H. Eckert and A. Studer, *Chem.-Eur. J.*, 2012, **18**, 16689–16697.
- 3 B. M. Trost, Chem. Rev., 1996, 96, 395-422.
- 4 (a) H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem.*, 2001, 113, 2056–2075; (b) C. Barner-Kowollik, F. E. Du Prez, P. Espeel, C. J. Hawker, T. Junkers, H. Schlaad and W. Van Camp, *Angew. Chem.*, 2011, 123, 61–64.
- 5 (a) H. Wagner, M. K. Brinks, M. Hirtz, A. Schäfer, L. Chi and A. Studer, *Chem.-Eur. J.*, 2011, 17, 9107–9112; (b) B. Schulte, M. Tsotsalas, M. Becker, A. Studer and L. De Cola, *Angew. Chem.*, 2010, 122, 7033–7036; (c) M. Becker, L. De Cola and A. Studer, *Chem. Commun.*, 2011, 47, 3392–3394.
- 6 "Click to chelate" approach: (a) H. Struthers, T. L. Mindt and R. Schibli, Dalton Trans., 2010, 39, 675–696, see also: (b) G. Zhang, Y. Wang, X. Wen, C. Ding and Y. Li, Chem. Commun., 2012, 48, 2979–2981.
- 7 Pd-catalysts immobilized into MSNs: (*a*) K. Komura, H. Nakamura and Y. Sugi, *J. Mol. Catal. A: Chem.*, 2008, **293**, 72–78; (*b*) G. Lv, W. Mai, R. Jin and L. Gao, *Synlett*, 2008, 1418–1422; (*c*) K. K. Sharma, A. V. Birandar, S. Das and T. Asefa, *Eur. J. Inorg. Chem.*, 2011, 3174–3182.
- 8 The surface area found for this type of material is around 20 m<sup>2</sup> g<sup>-1</sup>.
- 9 Catalyst loading was estimated based on elemental analysis.
- 10 Similar observation: H. Noda, K. Motokura, A. Miyaji and T. Baba, Angew. Chem., Int. Ed., 2012, 51, 8017–8020.
- 11 Due to the rather harsh conditions, some decomposition of the particles was observed. This is likely the reason for the loss of activity.