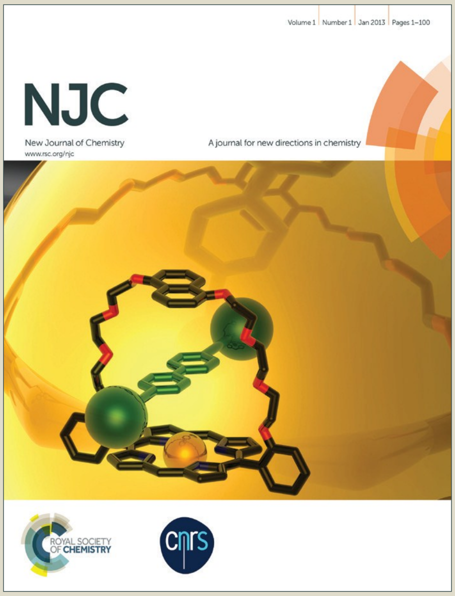
NJC

Accepted Manuscript



Volume 1 | Number 1 | Jan 2013 | Pages 1–100

NJC

New Journal of Chemistry

www.rsc.org/njc

A journal for new directions in chemistry

ROYAL SOCIETY
OF CHEMISTRY

www.rsc.org/njc

NJC

RSCPublishing

LETTER

PMoA/MCM-41 catalyze aza-Michael: Special effects of mesoporous nanoreactor on chemical equilibrium and reaction rate through surface energy transform

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Kui Fan,[a] Yonghai Hui,[*,a] Xinmei Hu,[a] Wei Shi,[b] Haixia Pang,[a] Zhengfeng Xie[*,b]

PMoA/MCM-41, a heterogeneous catalyst, acts as a nanoreactor to catalyze the aza-Michael reaction of nitro-olefins with hydrazides. Experiments showed that this mesoporous nanoreactor could affect the chemical equilibrium and kinetics. The possible mechanisms were thoroughly studied, and the surface energy of PMoA/MCM-41 was demonstrated to promote the aza-Michael reaction.

Heterogeneous catalysts often present more advantages than homogeneous catalysts. Li *et al.* found that the confinement effect of carbon nanotubes favors asymmetric catalysis.[1] Yang and Liu designed an innovative nanoreactor that simulates natural biological processes to guide cascade reaction.[2] Considering these previous studies, our group has worked on a similar study with the aim of designing functional nanoreactors that can be recycled as heterogeneous catalysts.[3] A nanoreactor is not a special or peculiar apparatus; rather, it is a microstructure that restricts chemical reactions in extremely narrow nanoscale environments, which is likely to affect reaction kinetics and mechanisms.[4] As a result, several studies have been conducted in this area.[5]

The results presented by Uozumi have greatly inspired and motivated us to study and prepare unique catalyst that may affect chemical equilibrium. Chemical equilibrium is generally affected only by temperature, not by the catalyst used. For this reason, large amounts of excess reactants or dehydrating agents are required to obtain even quantitative yields of esters.[6] However, some esterification reactions have challenged this notion.[7] Uozumi *et al.* notably proposed that esterification could be catalyzed by macroporous polymeric acids via phase separation under non-equilibrium conditions;[8] the catalysts for these esterification reactions were all nanoreactors or similar catalyst.[9] We believe that nanoreactors could be applied to other reactions and affect their chemical equilibrium. Thus, we examined whether the mesoporous heterogeneous nanoreactor PMoA/MCM-41 (Phosphomolybdic acid/Mobil Composition of Matter No. 41) affects the chemical equilibrium of aza-Michael reaction of nitro-olefins with hydrazides and found that the extent of the reaction is facilitated by the surface energy of the nanoreactor.

First, potential nanoreactors were designed and synthesized. MCM-41 is a classic mesoporous nanoreactor[10] with a catalytic activity that can be further promoted via physical adsorption[11] or grafting of other chemical catalysts.[12] PMoA/MCM-41 is a mesoporous nanoreactor created from MCM-41. By comparing the data of the two nanoreactors, the preparation of PMoA/MCM-41 was shown to be successful. Differences between the nanoreactors were evident in their transmission electron micrographs, which showed that the surface of PMoA/MCM-41 became noticeably rougher than that of MCM-41 (Figure 1b).[13]

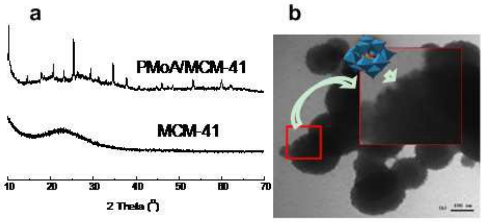
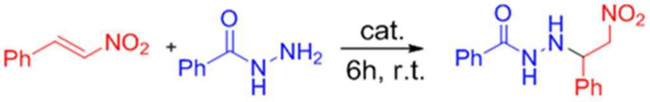


Figure 1. (a) Wide-angle XRD image of PMoA/MCM-41. (b) TEM image of PMoA/MCM-41 (bar scale: 100 μm)

Next, the catalytic activity of PMoA/MCM-41 in the aza-Michael reaction of 2-nitrovinylbenzene with benzohydrazide was tested. Heteropoly acid/MCM-41 exhibited better catalytic activity as a complete catalyst than heteropoly acids (Entry 4 and Entry 5, Table 1), MCM-41 (Entry 3, Table 1) or Heteropoly acid + MCM-41 (Entry 8 - Entry 9, Table 1). Comparative experiments indicated that the pores indeed facilitated the aza-Michael reaction (Entry 2 and Entry 3, Table 1). Finally, PMoA/MCM-41 can be confirmed to catalyze the aza-Michael reaction, the mechanism of which is worth exploring.

Table 1. The effects of catalysts and their surface polarity[a]



Entry	Catalyst	Solvent	Yield (%)[b]
1	no	CH_2Cl_2	-
2	MCM-41[c]	CH_2Cl_2	13
3	MCM-41	CH_2Cl_2	35
4	PMoA	CH_2Cl_2	40
5	PWA	CH_2Cl_2	38
6	PMoA/MCM-41[d]	CH_2Cl_2	60
7	PWA/MCM-41[d]	CH_2Cl_2	42
8	PMoA+MCM-41[e]	CH_2Cl_2	39
9	PWA+MCM-41[e]	CH_2Cl_2	34

[a] Reaction conditions (unless noted otherwise): nitroolefins (0.1 mmol), hydrazide (0.1 mmol), catalyst (0.0050 g or 10 mol %) in solvent (0.5 mL) at r.t. for 6 h. [b] Isolated yield. [c] Pores are blocked. [d] Adsorbed heteropoly acids. [e] Unadsorbed heteropoly acids.

Our results led us to further experiments. The catalytic processes of heteropoly acids were greatly altered after adsorption onto the surface of MCM-41. As can be seen from Figure 2, the pores on the catalyst surface play a critical role in the reaction. Such a result demonstrates that the aza-Michael reaction is further promoted by the nanoreactor.

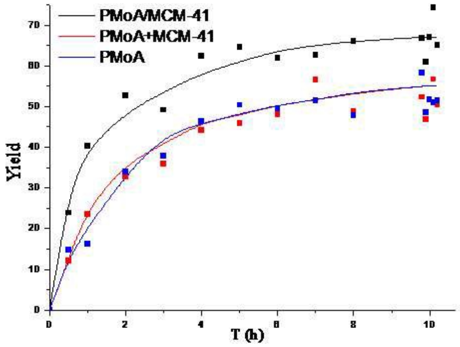


Figure 2. Yield-time curve in various situations

Further experimentation revealed that the chemical equilibrium the reaction may be also affected by the catalytic process. Reactions catalyzed by PMoA were carried out for 20 days, but the reaction yields did not exceed 60%. This result implies that yields were limited by the chemical equilibrium constant. By contrast, reactions catalyzed by PMoA/MCM-41 provided yields of over 60%. The validity of the results was demonstrated through trial and error. Herein, we two explanations for the phenomena observed. Moreover, we designed experiments to test the performance of various carriers.[13]

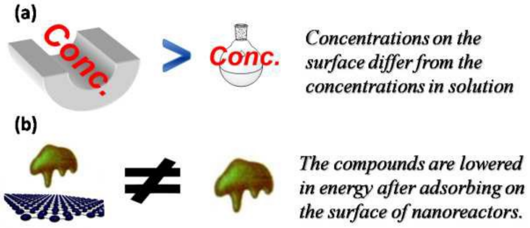


Figure 3. (a) The pores of nanoreactors cause the concentrations to change. (b) The surface of nanoreactors leads to energy change

(i) The adsorption and confinement effect of the pores enrich the compounds and alter the reaction results (Figure 3a). A higher concentration of compounds in the pores of mesoporous should accelerate the reaction.

(ii) Adsorption may change the entropy of the compounds (Figure 3b). The results of our experiments suggest a decrease in Gibbs free energy.

The concentration inside the nanoreactor is difficult to detect, but changes in the solvent can be measured by UV spectrophotometry. Our experiments showed that the concentration decreased after addition of the nanoreactors (Figure 4). The volume of the catalyst was so small that the concentration within the pores is considerably higher than that within the solvent.

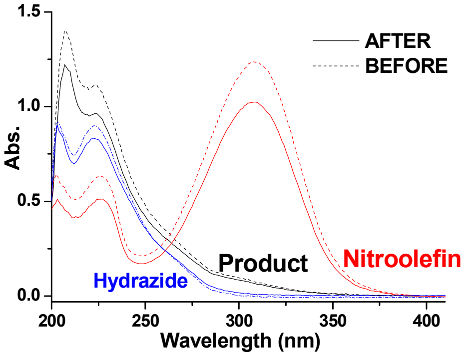


Figure 4. The variations of concentration after adding mesoporous materials

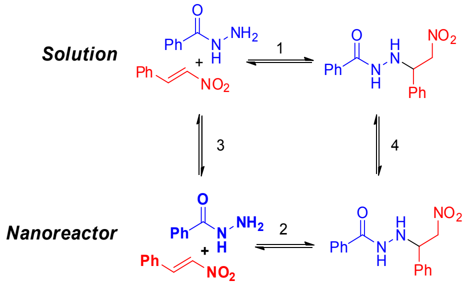
Competition between the nanoreactors and solvent can cause a subtle shift in the dynamic balance.

The results can be calculated based on the principles of physical chemistry after a kinetic model was built according to Scheme 1.[13] The results are shown as follows:

$$K' = {(k_1 + abk_2)}\Big/{(k_1' + ck_2')} > K$$

$$\text{OR} \qquad K'/K = \mathrm{Z} > 1$$

The equilibrium constant can be influenced by the adsorption and confinement effect of the nanoreactor. The variation in K' is determined by the system polarity (compounds, solvent, and surface of the nanoreactor), solvation effects, and the catalytic center.



Scheme 1. The competitive relationship between nanoreactor and nanoreactor-free

Hypothesis (i) is plausible and does not contradict Hypothesis (ii). Both theories may be valid. The former is kinetically based, while the latter is thermodynamically based.

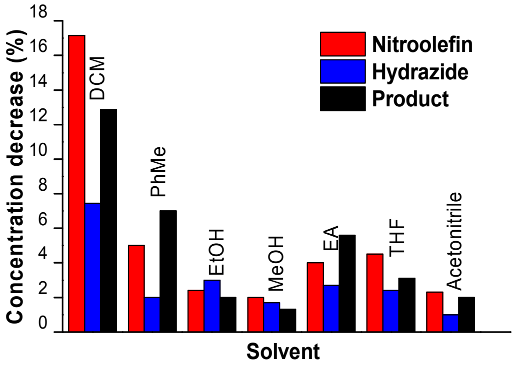


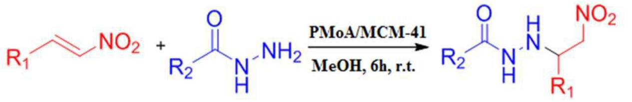
Figure 5. The percentage of concentration decrease in different solvents

Similar trials were performed in different solvents. Chemical disequilibrium was not observed in most of the solvents, except in DCM and PhMe. This phenomenon is well-illustrated in Figure 5, where the concentration in different solvents evidently decreases after addition of the nanoreactors, as determined through UV spectrophotometry. Thus, a competitive balance between the solvent and inner surface of the nanoreactor is maintained such that the entropy change, as well as the Gibbs free energy change, is remarkably unsatisfactory if the solvent is unsuitable.

After a series of experiments, the optimal reaction conditions were identified as follows: 0.1 mmol of nitro-olefins, 0.15 mmol of hydrazides, and 0.0030 g of PMoA/MCM-41 in 0.5 mL of methanol at room temperature for 6 h. The substrate scope of the aza-Michael reaction was then explored (Table 2). Phenyl groups bearing either electron-withdrawing or electron-donating groups were well tolerated under the reaction conditions, leading to satisfactory yields of the final products for almost every system except in Entry 7. We hypothesize that hydrogen ions react with *p*-$N(CH_3)_2$ to form a strong electron-withdrawing group that is non-reactive. The results of these experiments show that electron-withdrawing substituents can increase the reaction activity (Entry 4 - Entry 6, Table 2). The effectiveness of the nanoreactor in two typical solvents, namely, methanol (polar solvent) and dichloromethane (non-polar solvent), was closely studied.[13]

A potential mechanism for the catalytic activity of nanoreactor PMoA/MCM-41 in the aza-Michael addition reaction between aromatic nitroenes and aromatic hydrazides is suggested based on our previously established theories and experimental results.[13] PMoA on the surface of MCM-41 markedly lowers the activation energy of the reactions is required after enrichment and adsorption by the mesoporous nanoreactor.

Table 2. Substrate scope of the the aza-Michael reaction[a]



Entry	R_1	R_2	Products	Yield (%)[b]
1	C_6H_5	C_6H_5	**3a**	96 (90)
2	*p*-MeC_6H_4	C_6H_5	**3b**	77 (76)
3	*p*-$OMeC_6H_4$	C_6H_{52}	**3c**	87(85)
4	*p*-BrC_6H_4	C_6H_5	**3d**	75(70)
5	*p*-ClC_6H_4	C_6H_5	**3e**	80(81)
6	*p*-FC_6H_4	C_6H_5	**3f**	90(84)
7	*p*-$NMe_2C_6H_4$	C_6H_5	**3g**	-
8	*o*-ClC_6H_4	C_6H_5	**3h**	99(92)
9	2,4-*di*-ClC_6H_3	C_6H_5	**3i**	92(89)
10		C_6H_5	**3j**	93(80)
11	C_6H_5	*p*-Cl C_6H_4	**3l**	90(83)
12	C_6H_5	*p*-BrC_6H_4	**3m**	87(84)
13	C_6H_5	*p*-OMe C_6H_4	**3n**	96(81)
14	C_6H_5	*o*-ClC_6H_4	**3o**	92(90)
15	C_6H_5	*o*-MeC_6H_4	**3p**	93(89)

[a] Reaction conditions: nitroolefins (0.1 mmol), hydrazide (0.15 mmol), PMoA/MCM-41 (0.0030 g) in methanol (0.5 mL) at r.t. for 6 h. [b] Isolated yield catalyzing by PMoA/MCM-41 (catalyzing by PMoA).

An important question remains: **Where does the energy to change the chemical equilibrium come from?** The extra energy can be expressed as RTlnZ. The extra energy not only affects the chemical equilibrium but speeds up the chemical reaction. This problem is more apparent and easier to understand by considering Hypothesis (ii) but cannot be explained by Hypothesis (i). The answer to the abovementioned question is: **The energy comes from the surface energy of the nanoreactor.** Under ideal conditions, the nanoreactor returns to its original position through regeneration. The reusability of the nanoreactor was studied (Figure 6), and catalytic activity was maintained even after the nanoreactor was used for several cycles.

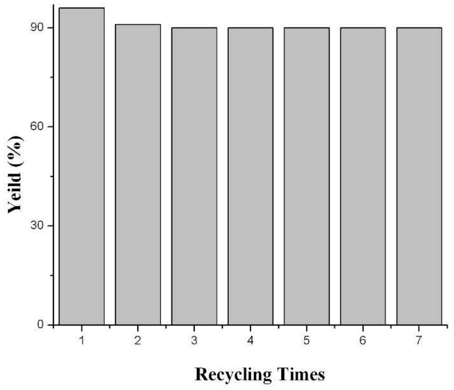


Figure 6. Recycling of the catalyst

In conclusion, the nanoreactor PMoA/MCM-41 could catalyze aza-Michael reactions efficiently and influence the resulting chemical equilibrium. Pores and suitable polarities were necessary but insufficient conditions for the reaction to proceed. PMoA/MCM-41 is not merely a heterogeneous catalyst but also a special microreaction environment. The effects of PMoA/MCM-41 in other similar reactions should be determined in future experiments.

Experimental

Typical synthetic procedure (with 3a as an example): A solution of benzohydrazide (0.0204g, 1.5 mmol), (E)-(2-nitrovinyl) benzene (0.0149 g, 1 mmol), PMoA/MCM-41 (0.0030 g) were stirred at r.t. in metha-nol (0.5 mL) for 6 h. After completion of the reaction, as indicated by TLC, the reaction mixture was concentrated under reduced pressure. The residue was directly purified by chromatography to afford the product 3a as a white solid.

Acknowledgements

We thank the National Natural Science Foundation of China (Nos. 21162026, 21262034 and 21362036) and Doctoral Fund of Xinjiang University (No. BS110111). We also thank Xinjiang University Analytical & Testing Center for instrumental analyses and Adamas-beta Chemical Co. for all chemical reagents.

Notes and references

[a] Key Laboratory of Oil & Gas Fine Chemicals, Ministry of Education & Xinjiang Uyghur Autonomous Region, College of Chemistry and Chemical Engineering, Xinjiang University, Urumqi 830046, China. E-mail: hyhai97@126.com

[b] College of Chemistry and Chemical Engineering, Southwest Petroleum University, 8 Xindu Road, Xindu, Chengdu, 610500, China. E-mail: xiezhf72@gmail.com

† Electronic Supplementary Information (ESI) available: experimental details and characterization. See DOI: 10.1039/c000000x/

1 Z. Chen, Z. Guan, M. Li, Q. Yang, C. Li, *Angew. Chem. Int. Ed.,* 2011, **50**, 4913.

2 Y. Yang, X. Liu, X. Li, J. Zhao, S. Bai, J. Liu, Q. Yang, *Angew. Chem. Int. Ed.*, 2012, **124**, 9298.

3 (a) X. Dong, Y. Hui, S. Xie, P. Zhang, G. Zhou, Z. Xie, *RSC Adv.*, 2013, **3**, 3222. (b) S. Xie, Y. Hui, X. Long, C. Wang, Z. Xie, *Chin. Chem. Lett.,* 2013, **15**, 5798.

4 (a) H. S. Chen, P. H. Chen, S. H. Huang, and T. S. Perng, *Chem. Commun.,* 2014, **50**, 4379; (b) A. Ostafin, K. Landfester, *Nanoreactor engineering for life sciences and medicine.* Artech House: Boston, 2009; 1-45.

5 (a) M. S. Kim, M. Jeon., W. K. Kim, J. Park, S. I. Lee, *J. Am. Chem. Soc*., 2013, **135**, 15714; (b) K. Renggli, G. M. Nussbaumer, R. Urbani, T. Pfohl, N. Bruns, *Angew. Chem. Int. Ed.,* 2014, **53**, 1443; (c) T. K. Kim, J. J. L. M. Cornelissen, R. J. M. Nolte, J. C. M. van Hest, *Adv. Mater.,* 2009, **21**, 2787; (d) X. Zheng, Y. Lv, Q. Kuang, Z. Zhu, X. Long, S. Yang, *Chem. Mater.*, 2014, **26**, 5700; (e) A. M. Lebedeva, W. T. Chamberlain, M. Schröder, A. N. Khlobystov, *Chem. Mater.,* 2014, **26**, 6461; (f) A. Zalineeva, A. Serov, M. Padilla, U. Martinez, K. Artyushkova, S. Baranton, C. Coutanceau, P. B. Atanassov, *J. Am. Chem. Soc.*, 2014, **136**, 3937; (g) C. Liu, J. Li, J. Qi, J. Wang, R. Luo, J. Shen, X. Sun, W. Han, L. Wang, *ACS Appl. Mater. Interfaces,* 2014, **6**, 13167.

6 For selected examples under neat conditions, see: (a) B. Karimi, M. Vafaeezadeh, *Chem. Commun.*, 2012, **48,** 3327; (b) S. Palaniappan, S. M. Ram, *Green Chem.*, 2002, **4**, 53; (c) Y. Leng, J. Wang, D. Zhu, X. Ren, H. Ge, L. Shen, *Angew. Chem., Int. Ed.,* 2009, **48,** 168; (d) K. A. Chakraborti, B. Singh, V. S. Chankeshwara, R. A. Patel, *J. Org. Chem.,* 2009, **74**, 5967; (e) J. R. Kalbasi, J. A. Massah, *Bull. Korean Chem. Soc.,* 2010, **31**, 2361; (f) F. Su, L. Ma, D. Song, X. Zhang, Y. Guo, *Green Chem.*, 2013, **15**, 885.

7 (a) A. Purgotti, *Gazz. Chim. Ital.* 1918, **48**, 58; (b) K. Manabe, S. Iimura, X. Sun, S. Kobayashi, *J. Am. Chem. Soc.*, 2002, **124**, 11971; (c) K. Manabe, S. Kobayashi, *Adv. Synth. Catal.* 2002, **344**, 270; (d) K. Manabe, X. Sun, S. Kobayashi, *J. Am. Chem. Soc.*, 2001, **123**, 10101.

8 M. Minakawa, H. Baek, Y. M. A. Yamada, J. W. Han, Y. Uozumi, *Org. Lett.*, 2013, **15**, 5798.

9 (a) D. D. Díaz, D. Kühbecka, J. R. Koopmansc, *Chem. Soc. Rev.,* 2011, **40**, 427; (b) A. Jesor-ka, O. Orwar, *Nat. Nanotech.,* 2012, **7,** 6; (c) L. Gaitzsch, D. Appelhans, L. Wang, G. Battaglia, B. Voit, *Angew. Chem. Int. Ed.,* 2012, **51**, 4448. (d) Q. T. Nguyen, J. Wu, V. Doan, J. B. Schwartz, H. S. Tolbert, *Science,* 2000, **288**, 652; (e) C. Dai, A. Zhang, J. Li, K. Hou, M. Liu, C. Song, X. Guo, *Chem. Commun., 2014,* **50**, 4846; (f) M. Shakeri, L. Roiban, V. Yazerski, G. Prieto, R. J. M. K. Gebbink, *ACS Catal.,* 2014, **4**, 3791; (g) A. Stein, BJ. Melde, RC. Schroden, *Adv. Mater.,* 2000, **12**, 1403.

10 (a) T. C. Kresge, E. M. Leonowicz, J. W. Roth, C. J. Vartuli, S. J. Beck, *Nature*, 1992, **359**, 710; (b) N. Shadjou, M. Hasanzadeh, *RSC Adv.,* 2014, **4**, 18117.

11 (a) S. Wu, P. Liu, Y. Leng, J. Wang, *Catal. Lett.,* 2009, **132**, 500; (b) FJ. Mendez, A. Llanos, M. Echeverria, R. Jauregui, Y. Villasana, Y. Diaz, G. Liendo-Polanco, MA. Ramos-Garcia, T. Zoltan, JL. Brito, *Fuel,* 2012, **110**, 249; (c) X. Dong, DJ. Wang, K. Li, Y. Zhen, H. Hu, G. Xue, *Mater. Res. Bull.,* 2014, **57**, 210; (d) B. Wang, J. Zhang, X. Zou, H. Dong, P. Yao, *Chem. Eng. J.,* 2015, **260**, 172.

12 (a) W. Zhang, L. Xu, W. Shi, C. Wang, Y. Hui, Z. Xie, *Russ. J. Gen. Chem.,* 2014, **84**, 782; (b) Z. An, Y. Guo, L. Zhao, Z. Li, J. He, *ACS Catal.*, 2014, **4**, 2566; (c) I. Podolean, C. Hardacre, P. Goodrich, N. Brun, R. Backov, SM. Coman *Catal. Today,* 2013, **200**, 63; (e) U. Balakrishnan, N. Ananthi, S. Velmathi, MR. Benzigar, SN. Talapaneni, SS. Aldeyab, K. Ariga, A. Vinu, *Microporous Mesoporous Mater.,* 2012, **155**, 40.

13 For detailed information, see the Supporting Information.