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Magnetic nanoparticle supported polyoxometalates (POMs) *via* non-covalent interaction: reusable acid catalysts and catalyst supports for chiral amines[†]

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Magnetic polyoxometalates (POMs) are obtained by a simple sonication between functionalized magnetic nanoparticles and polyoxometalates. This material can be used not only as a highly active acid catalyst, but also as a catalyst support for chiral amines.

Magnetic nanoparticles (MNPs), which are available from cheap materials via simple synthesis and easily tunable by structural surface modifications, have drawn much attention in the past few decades due to their vast applications including drug delivery, biosensors, enzyme immobilization, environmental remediation and so on.¹ Recently, their application as catalyst supports has become a hot topic due to their unique properties such as high surface area, good dispersion, superparamagnetic behavior as well as low toxicity.² The most attractive feature of MNP-supported catalysts is that they can be recycled by simple magnetically driven separation, thereby eliminating the requirement of catalyst filtration and centrifugation. Furthermore, improved activity is usually achieved in the nanometre-sized supported catalyst due to the high surface area and good dispersion properties. In the past few years, several transition-metal catalysts,^{2a} enzyme catalysts^{2a} as well as organocatalysts³ have been successfully immobilized on MNPs with good catalytic activity and reusability. Up to now, most of these MNP-supported catalysts employed covalent immobilization strategies, requiring additional synthetic manipulation in most cases. Non-covalent immobilization, endowed with the merits such as easy modification and combinatorial flexibility, has been much less explored with MNPs.⁴

Due to their strong acidity and favorable redox properties, polyoxometalates (POMs) and their derivatives have been widely used in organic synthesis and catalytic reactions as acid and oxidation catalysts.⁵ Meanwhile, their applications as catalyst supports have also been explored and good reusability could be realized by taking advantage of their large framework.^{6,7} However, since bulk POMs have low specific surface

area $(1-5 \text{ m}^2 \text{ g}^{-1})$,⁸ their immobilization on large surface area materials are important to achieve better performance in many heterogeneous catalytic applications.⁵ Various solid supports such as silica, active carbon and mesoporous molecular sieve, have been used to immobilize POMs. However, to the best of our knowledge, MNPs have not been used as POM supports. Herein, we report the non-covalent immobilization of POMs on MNPs as efficient acid catalysts for the Friedel–Crafts reaction of indole and chalcones. Furthermore, the MNP-POMs can also serve as a support for chiral amine catalysts.

The MNP-supported POM catalysts were prepared via the well-applied "acid-base" strategy. Since MNPs are acid sensitive. they were first protected with a 1–2 nm thickness silica layer.⁹ The obtained SiO₂-MNP was then treated with the commercial (3-aminopropyl)triethoxysilane in refluxing toluene to afford MNP-1.^{3b-d} The loading of amino groups on MNP-1 was shown to be 1.46 mmol g^{-1} as determined by elemental analysis. Following the same procedure, MNP-2 was also prepared and the loading of imidazolium group was determined to be 0.60 mmol g^{-1} (Scheme 1).^{3b} The immobilization of POM on MNP-1 or MNP-2 was achieved by sonication of a mixture of MNPs (MNP-1 or MNP-2) and POM (H₃PW₁₂O₄₀, 1.1 equiv.) in dry THF for 1 h. The MNP supported POMs (MNP-1-PW and MNP-2-PW) were isolated by magnetic decantation and washed twice with THF. The molar ratio of functional group (amino or imidazolium group) and POM was determined to be nearly 1:1 in the immobilized catalysts. The magnetic core was analyzed by XRD and the observed diffraction pattern is consistent with the JCPDS database for magnetite (Fig. 1a). The roomtemperature magnetization curves (Fig. 1b) proved that the magnetic nanoparticles are superparamagnetic.

With the immobilized POM catalysts in hand, the Friedel-Crafts reaction of indole and chalcone was chosen as a model reaction to examine the acidic catalytic activity and reusability. To our



Scheme 1 Preparation of MNP-1-PW and MNP-2-PW.

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Fig. 1 (a) XRD of the magnetic core (Fe₃O₄); (b) magnetic curve of MNP-1 (solid line) and MNP-1-PW (dashed line).

delight, the reaction proceeds very well in many solvents and the best results were obtained when using THF as solvent (Table S2, ESI†). With the optimized conditions, the substrate scopes were next explored. As shown in Table 1, the reactions between different chalcones and indoles proceeded smoothly to give the desired products with good yields.

The recyclabilities of **MNP-1-PW** and **MNP-2-PW** were then evaluated. After each run, CH_2Cl_2 was added to dilute the reaction mixture and the organic layer was simply decanted with the assistance of a small magnet. The catalyst was quickly concentrated to the side wall of the reaction vial once a magnet is placed nearby. After a simple wash by CH_2Cl_2 and subsequent vacuum removal of residual solvent, the catalyst was reused for the next run. Both magnetic POMs showed excellent activity and reusability for 12 recycles (Fig. 2).¹⁰

In our previous studies, it was found that the POMs were efficient catalyst supports for chiral amine catalysts *via* non-covalent interaction.⁷ However, the POM-supported chiral amines generally showed limited reusability due to the loss of catalyst upon biphasic recycle and reuse. Bearing in mind the excellent reusability of MNP supported catalysts, we have tested magnetic POMs as non-covalent supports for chiral amines. As shown in Scheme 2, chiral amine hybrids with magnetic POMs can be easily prepared by mixing **MNP-PW** and chiral amine *via* sonication in dry THF. The resulting hybrid solid was washed with THF and dried under vacuum at room temperature. The presence of chiral amine (compound **A** as

 Table 1
 Substrate scope of Friedel–Crafts reactions^a

R^{1} H R^{2} H R^{2} H R^{2} R^{2} R^{2} H R^{2} R^{2} H R^{2} H R^{2} H H R^{2} H H R^{2} H H H R^{2} H							
			MNP-1-PW		MNP-2-PW		
Entry	\mathbb{R}^1	\mathbb{R}^2	t/h	$\operatorname{Yield}^{b}(\%)$	t/h	Yield ^{b} (%)	
1	Н	5-MeO	20	93	20	94	
2	Н	5-Me	20	96	20	96	
3	Н	5-Br	7	98	6	97	
4	Н	5-C1	7	97	6	97	
5	Н	5-I	7	99	6	98	
6	Н	6-C1	7	98	6	98	
7	4-Cl	Н	12	90	12	92	
8	4-Me	Н	12	88	12	90	

^a Reaction conditions: Catalyst (5 mol%), indole derivative (0.25 mmol), chalcone derivative (0.20 mmol), THF (0.2 mL). ^b Isolated yield.



Fig. 2 Reusability of **MNP-1-PW** (black columns) and **MNP-2-PW** (gray columns). *Reaction conditions*: indole (0.25 mmol), chalcone (0.20 mmol), THF (0.2 mL), catalyst (5 mol%), 12 h.



Scheme 2 Preparation of magnetic POM supported chiral amine catalyst MNP-1-PW-A.

shown in Scheme 2) in the hybrids was confirmed by IR (see Fig. S3, ESI[†]). In spite of the multidentate nature of chiral amines and POM, the hybrid magnetic solid remains as nanometer sized particles (Fig. S4, ESI[†]) and is well dispersible in organic solvents such as DCM (Fig. 3c). The loading of the catalyst was 0.55 mmol g^{-1} as determined by elemental analysis.

The **MNP-PW**-supported chiral amine catalysts were next evaluated in typical enamine-based asymmetric direct aldol reactions. With the identified optimal catalyst **MNP-1-PW-A** (see ESI† for the screening results),¹¹ the reaction scope was then examined with a series of aldehyde acceptors and aldol donors using the optimized catalyst. In the presence of 5 mol% of **MNP-1-PW-A**, acetone reacted with various aromatic aldehydes to afford the desired products with high yields and enantioselectivities (Table 2). Other aldol donors such as



Fig. 3 Catalyst recycling: (a) *Reaction conditions*: 4-nitrophenylaldehyde (0.25 mmol), acetone (0.20 mL), MNP-1-PW-A (5 mol%), 13 h. (b) TEM image of catalyst MNP-1-PW-A after 10 cycles; (c) MNP-1-PW-A dispersed in CH_2Cl_2 ; (d) catalyst separation by a small magnet.

+ R-CHO MNP-1-PW-A 5 mol%						
Entry	R	t/h	$\operatorname{Yield}^{b}(\%)$	ee (%) ^c		
1	$2-NO_2C_6H_4$	12	83	89		
2	$3-NO_2C_6H_4$	12	87	89		
3	4-CF ₃ C ₆ H ₄	30	81	90		
4	4-CNC ₆ H ₄	30	80	87		
5	$4-ClC_6H_4$	48	72	87		
6	$2-BrC_6H_4$	48	77	88		
^a Reactio (0.25 mm	<i>n conditions</i> : Cataly nol). ^b Isolated yield	st (5 mol% . ^c Determi), acetone (0.20 mI ined by chiral HPI	L), aldehyde LC.		

cyclohexanone and cyclopentanone also worked very well in this catalytic system (Table 3). For comparison, the results obtained from the same reactions using POM-chiral amine hybrid **PW-A** are also listed in Table 3 (entries 1 *vs.* 2). The magnetic POM supported catalyst **MNP-1-PW-A** showed slightly higher stereoselectivity and enantioselectivity albeit with a little loss of activity.

The recyclability of **MNP-1-PW-A** was examined using the model reaction between acetone and 4-nitrobenzylaldehyde. The process of the catalyst recycling is the same as the **MNP-1-PW** in the Friedel–Crafts reaction. To our delight, the non-covalently assembled magnetic chiral amine catalyst showed excellent reusabilities. The yield and enantioselectivity was maintained at similar level even after 11 cycles (Fig. 3a), which is significantly improved comparing with POM supported chiral amines. The TEM image of the catalyst after 10 recycles indicated that the catalyst is quite robust and no significant aggregation was found (Fig. 3b).

In summary, we have successfully developed, for the first time, a novel type of non-covalently immobilized POM catalysts using magnetic nanoparticles as supports. These immobilized acid catalysts showed excellent catalytic capabilities in Friedel–Crafts reactions of indoles and could be reused for at least 11 times. In addition, the immobilization of chiral amines on MNPs was

Table 3 MNP-1-PW-A catalyzed aldol reaction of various aldoldonors a

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	+ R-CHO neat r.t.				R		
Entry	n	R	t/h	$\mathrm{Yield}^{b}\left(\%\right)$	syn/anti ^c	ee^{d} (%)	
1	1	4-NO ₂ C ₆ H ₄	5	97	6:94	97	
2^e	1	$4 - NO_2C_6H_4$	6	86	23:77	95	
3	1	$2 - NO_2C_6H_4$	5	97	24:76	98	
4	1	$3-NO_2C_6H_4$	5	96	16:84	98	
5	1	$4-CF_3C_6H_4$	12	88	17:83	97	
6	1	$4-ClC_6H_4$	48	86	20:80	96	
7	2	$2 - NO_2C_6H_4$	8	98	13:87	99	
8	2	$3-NO_2C_6H_4$	8	97	14:86	98	
9	2	$4 - NO_2C_6H_4$	6	97	14:86	97	
10	2	$4-CF_3C_6H_4$	11	93	13:87	98	
11	2	$4-ClC_6H_4$	48	92	17:83	98	

^{*a*} Reaction conditions: Catalyst (5 mol%), ketone (0.20 mL), aldehyde (0.25 mmol). ^{*b*} Isolated yield. ^{*c*} Determined by chiral HPLC. ^{*d*} Determined by chiral HPLC. ^{*e*} **PW-A** (1 mol%) was employed.

realized *via* non-covalent assembly with POMs as a noncovalent anchor. The resulted non-covalently assembled catalyst could be reused up to 11 times with essentially no loss of activity and enantioselectivity.

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- 11 MNP-2-PW-A demonstrated similar performance in the aldol reaction and the results are listed in Tables S4 and S5 (ESI[†]).