## Magnetic nanoparticle-supported Hoveyda–Grubbs catalysts for ring-closing metathesis reactions<sup>†</sup>

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Magnetically recyclable Hoveyda–Grubbs catalyst can be readily assembled using magnetic nanoparticles as support, and this catalyst combines convenient recyclability and excellent activity on ring-closing metathesis (RCM) reactions.

The Grubbs-type<sup>1</sup> and Hoveyda–Grubbs-type<sup>2</sup> catalysts are the most widely used catalysts in ring-closure metathesis (RCM). They are extraordinarily versatile to tolerate a variety of functional groups in the alkenes and are compatible with a wide range of solvents. Despite these advantages, the separation of the soluble catalyst from the product and any reaction solvent remains difficult. Current effort<sup>3</sup> toward solving the problem is focused on anchoring catalysts to solid or soluble matrices *via* ligand exchange.<sup>4</sup> In this context, immobilized catalysts offer inherent operational and economic advantages over their homogeneous counterparts.

During recent years we have witnessed a significant progress on nanoparticle catalysis because the nanoparticle-based catalysts not only show superior catalytic activities to their corresponding bulk materials,<sup>5</sup> but also increase their loading capacity. However, one issue associated with the application of nanoparticle-based catalysis is the removal of the catalysts from the reaction system by conventional methods, such as filtration, which frequently leads to the blocking of filters and valves (Fig. 1).

Recently, magnetic nanoparticles (MNPs)<sup>6</sup> emerged as new catalyst supports because of their facile separation from the



Fig. 1 Illustration of the separation of magnetic nanoparticle catalysis from the reaction system in RCM reaction.

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**Fig. 2** (a) TEM image of magnetic nanoparticles; (b) magnetization curves of magnetic nanoparticles.

reaction mixture with the aid of an external magnet.<sup>7</sup> In this respect, the development of an MNP catalysts based on ruthenium carbene complexes would find a wide range of applications both in academia and industry. Herein, we report our recent effort in developing a magnetic nanoparticle-supported Hoveyda–Grubbs ruthenium carbene complex for promoting RCM reactions, which lead to a convenient synthesis of five-, six- and seven-membered carbocycles or heterocycles in high yields.

The method utilized for the preparation of magnetic nanoparticles (iron oxide) was reported by Hyeon,<sup>8</sup> and the procedure allowed us to prepare monodispersed iron oxide nanoparticles (about 10 nm) in a narrow range of particle-size distribution. The formed magnetic nanoparticles were characterized by transmission electron microscopy (TEM), and the TEM image of the nanoparticles (Fig. 2(a)) shows that they are relatively uniform with an average size of 10 nm. The magnetic behavior of the magnetic nanoparticles was investigated using a Magnetic Properties Measurement System-5 (MPMS, Quantum Design) magnetometer. The



Scheme 1 Synthesis of magnetic nanoparticle-supported catalyst 3.

field-dependent magnetization curve at 300 K reveals that the catalyst is superparamagnetic with a saturation magnetization of 36.5 emu g<sup>-1</sup> (Fig. 2(b)). Surface modification of magnetic nanoparticles with amino groups was then carried out using organic silane bifunctional groups (3-aminopropyltriethoxy-silane, APTS), which served as robust anchors to immobilize the functional ligands on the iron oxide shells of the magnetic nanoparticles. The resulting amino-functionalized particles had an amino group loading level of 0.28 mmol g<sup>-1</sup>.

Scheme 1 shows the synthesis of the magnetic nanoparticle supported Hoveyda–Grubbs catalyst. Ligand  $1^{4o}$  was coupled to the magnetic nanoparticles under standard conditions to form **2**, which was then treated with the first-generation Grubbs catalyst in the presence of CuCl to provide the desired magnetic Hoveyda–Grubbs catalyst **3** as a purple powder. The Ru loading level of the obtained magnetic catalyst as determined by ICP-AES is 0.025 mmol g<sup>-1</sup>.

To test the efficiency and reactivity of the new magnetic catalyst **3** in the RCM reaction, substrates **4–12** were treated with one single batch of catalyst **3** (2.5 mol%) in consecutive manner in  $CH_2Cl_2$  at 40 °C, and the corresponding products **4p–12p** were obtained in excellent yields (Table 1).

 Table 1
 Activity of magnetic catalyst 3 in RCM reactions<sup>a</sup>

Cycle	e Substrate		Product		Conversion(%) <sup>b</sup>
1	Ts-N	4	Ts-N	4p	>98
2	EtO2C	5	EtO <sub>2</sub> C	5p	>98
3	0 C <sub>10</sub> H <sub>21</sub>	6	0 C <sub>10</sub> H <sub>21</sub>	6р	98
4	C10H21	7	0 C <sub>10</sub> H <sub>21</sub>	7р	95
5	Ts <sup>-N</sup>	8	TS <sup>N</sup>	8p	95
6	EtO <sub>2</sub> C	9	EtO <sub>2</sub> C EtO <sub>2</sub> C	9p	95
7		10		10p	98
8	EtO <sub>2</sub> C CO <sub>2</sub> Et	11	EtO <sub>2</sub> C CO <sub>2</sub> Et	11p	95
9	C <sub>10</sub> H <sub>21</sub>	12	C <sub>10</sub> H <sub>21</sub> -	12p	96

<sup>*a*</sup> Conditions: substrate (0.5 mmol) and catalyst **3** (2.5 mol%) in  $CH_2Cl_2$  (5 ml) at 40 °C for 2 h (cycles 1–3) and 12 h (cycles 4–9). <sup>*b*</sup> Determined by <sup>1</sup>H NMR.

<b>Table 2</b> Experiments for recycle of magnetic cataly	Table 2	Experiments	for recycle	of magnetic	catalyst 3
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Te		м	Magnetic Catalyst 3 (2.5 mol %)							
15 1	4	×	CH₂CI₂, 40 ℃				4p			
cycle	1-13	14	15	16	17	18	19	20	21	22
conversion	>98%	96%	97%	97%	96%	97%	96%	96%	97%	95%

Condition s: 4 (0.5 mmol) and catlyst 3 (2.5 mol %) in CH\_2Cl\_2 (5 mL) at 40  $^{o}$ C for 2h (cycle 1-13), 4h (cycle 14-18) and 10h (cycle 19-22).

Ts-N	$\sum$	Ma	Magnetic Catalyst <b>3</b> (2.5 mol %)					TS-N		
10	7		CH <sub>2</sub> Cl <sub>2</sub> , 40 ℃				10p			
cycle	1-10	11	12	13	14	15	16	17	18	
conversion	>98%	98%	98%	96%	98%	96%	96%	96%	96%	

Conditions: 10 (0.5 mmol) and cattyst 3 (2.5 mol %) in  $CH_2CI_2$  (5 mL) at 40  $^oC$  for 2 h (cycle1-10), 4 h (cycle11-13) and 6 h (cycle 14-18).

For evaluation of recyclability, substrates 4 and 10 were selected, and the RCM reactions were run with recycled catalyst 3 up to 22 times. The results as illustrated in Table 2 show almost no loss of the catalytic efficiency.

It is worthwhile to mention that after the reaction, the catalyst was simply collected using a magnetic bar, and the reaction mixture was then transferred out of the flask. The isolated catalyst was washed twice with  $CH_2Cl_2$  and then employed in the next reaction under nitrogen.

In summary, we have developed a novel type of Hoveyda– Grubbs catalyst by assembling magnetic nanoparticles with Grubbs I catalyst. This type of catalyst was found to be effective in the synthesis of a series of cyclic olefins, and found to be active with no loss of catalytic efficiency after repeated use. We expect this type of magnetic nanoparticle-based catalyst to find broad applications in organic synthesis.

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