Grubbs Catalysts Immobilized on Merrifield Resin for Metathesis of Leaf Alcohols by using a Convenient Recycling Approach

Liang Xia+,[a, b] Tao Peng+,[b] Gang Wang,[b] Xiaoxue Wen,[b] Shouguo Zhang,*[b] and Lin Wang*[a, b]

Three new types of heterogeneous catalysts were prepared using a facile approach by the immobilization of Grubbs catalysts on PEGylated Merrifield resin. One of the immobilized catalysts was more efficient than the free catalyst for the metathesis of leaf alcohols in conversion and selectivity and was reused repeatedly (up to 5 cycles) with only a slight loss of activity (10.5%). The long-chain PEGylated linker provided an appropriate distance between the resin and the catalytic center so that the ruthenium catalysts acted as the free catalyst.

Alkenes could be prepared by olefin metathesis reactions which were initiated by re-combination of two pairs of original olefin carbon-carbon double bonds to form two new pairs of carbon-carbon double bonds. Grubbs catalysts were widely used for olefin metathesis reactions. Various Grubbs catalysts were reported up to now. First generation of Grubbs catalyst (GI) was resistant against oxygen and water. However, it was prone to decompose at high temperature.[1,2] Second generation of Grubbs catalyst (GII) was prepared with improved thermal stability and catalytic activity.[3,4] Unfortunately, it was sensitive to water and oxygen.[5] Although Grubbs catalysts made great progress in catalytic efficiency and selectivity, the expensive price limited their applications.

As homogeneous catalysts, recycling Hoveyda Grubbs catalysts for reuse were very difficult.[6] In order to improve their recovery, Grubbs catalysts were connected to different supports to prepare supported catalysts, which would be divided into homogeneous and heterogeneous categories according to their status in the reaction solution. Many homogeneous carrier loaded Grubbs catalysts were reported. For example, Matthew Sheets and Marc Mauduit immobilized Hoveyda Grubbs catalysts on ionic liquids for olefin metathesis with high efficiency.[7–9] Gravert and Harwig immobilized Hoveyda Grubbs catalysts on Polyethylene glycol (PEG) for ring closing metathesis (RCM) reactions with high efficiency.[10] However, the recycling procedures of these homogeneous catalysts were tedious and time-consuming. Many heterogeneous carrier loaded Grubbs catalysts were also reported. For example, Robert H. Grubbs immobilized RuCl$_2$ ($=$CHCH$=$CPh$_2$) (PPh$_3$)$_2$ on polystyrene-divinylbenzene (PS-DVB) for Ring-Opening Metathesis Polymerization (ROMP) reactions of cyclic olefins.[11] Michal Bieniek immobilized Hoveyda Grubbs catalyst on butyldiethylsilyl polystyrene (PS-DES) for metathesis of substituted olefins.[12] Robert H. Grubbs immobilized Hoveyda Grubbs catalysts on silica gel for a number of metathesis reactions.[13] There are also some reports about using new kinds of supports, such as magnetic nanoparticle, mesoporous molecular silicas and aluminas, to immobilize Grubbs catalysts for metathesis.[14–16] These results showed that the heterogeneous catalysts were recycled conveniently over a number of reaction cycles. However, they were prepared with long reaction steps and some of them had longer reaction times, lower conversions and catalytic activities than free catalysts.

In sum, heterogeneous catalysts showed comparative advantages in recycling, which indicated that immobilization on proper solid support could help the Grubbs catalysts recycle efficiently. Inspired by linker strategy in solid phase synthesis, the immobilization strategy should be optimized by keeping a long distance between solid support and catalyst. Merrifield resin was a good heterogeneous support with good swelling and recycling activity. PEG linker was a polymer that was soluble in many solvents. Merrifield resin and PEG linker could act as the proper support and linker. Next, it was important to select a proper catalyst as a supported research object. 1,3-bis (2,4,6-trimethylphenyl)-2-imidazolidinylidene)(3,6-dichlorophenyl[d][2, 7]dithio)(o-isopropoxyphenylmethylene) ruthenium (Ru-3b, 7) was developed from Hoveyda Grubbs catalyst with high Z/E selectivity for many substrates.[17] We hoped to immobilize Ru-3b on Merrifield resin through PEG linker but there were no connection sites in the catalyst structure. In this paper, three similar catalysts (7a, 7b and 7c) of Ru-3b were designed and synthesized, phenolic hydroxyl or mercapto were used as immobilization sites. Therefore three supported catalysts (Ru-a,

[a] Dr. L. Xia,+ Prof. L. Wang
Beijing University of Technology
College of Life Science and Bio-engineering Department
Beijing, 100124 (P. R. China)
E-mail: xlxialiang12345@163.com
wanglin@bmi.ac.cn

[b] Dr. L. Xia,+ Dr. T. Peng,+ Dr. G. Wang, X. Wen, Dr. S. Zhang, Prof. L. Wang
Beijing Institute of Radiation Medicine
Beijing, 100850 (P. R. China)
E-mail: pengtao@bmi.ac.cn
zhangshouguo1409@sina.com
wanglin@bmi.ac.cn

[+] These authors contributed equally to this work.
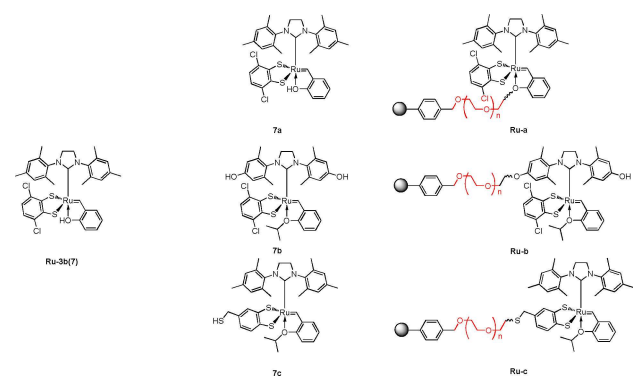
Scheme 1. Design of the three supported catalysts.

Ru-b, **Ru-c**) were prepared by immobilizing **7a**, **7b** and **7c** on PEGylated Merrifield resin (**6**; Scheme 1). These catalysts were expected to be recycled efficiently while maintaining the high *Z/E* stereoselectivity as the free catalyst.

(Z)-hex-3-ene-1, 6-diol was an important intermediate which was prepared by a long route including drastic oxidation reaction.[18,19] In our work *(Z)-hex-3-ene-1, 6-diol* was prepared efficiently by catalyzing *leaf alcohols* with Ru-3b and the new catalysts (**Ru-a**, **Ru-b** and **Ru-c**). As we expected, three new catalysts showed similar catalytic activities to **Ru-3b**. **Ru-b** was better than **Ru-a** and **Ru-c** in catalytic activities and conversions. Recycling experiments showed that **Ru-b** could be reused for more than 5 times in recycling.

The solid phase catalysts were designed as three parts. The first part and second part were Merrifield resin and PEG polymer. They acted as the support and linker. Pseudo-dilution effect of Merrifield resin and good solubility of PEG polymer in many solvents ensured the catalytic activities. The third part was the Grubbs catalyst. Similar structures of **Ru-3b** were prepared. The specific design was as follows: **7a** retained the main structure of **Ru-3b**, *1-isopropoxy-2-vinylbenzene* was replaced by *2-vinylphenol* as the oxonium group. The phenolic hydroxyl group of the oxonium group was regarded as the connection site. **Ru-a** was prepared by etherification of PEGylated resin (**6**) and the exposed phenolic hydroxyl group in **7a**. **7b** introduced a phenolic hydroxyl group on the carbene structure (**4** and **4′** positions) by replacing raw material *2, 4, 6-trimethylaniline* with *4-amino-3, 5-dimethylphenol*. *Phenolic hydroxyl group* served as the attachment site of **7b**. **Ru-b** was prepared by connection of **7b** and **6**. **7c** was designed based on **Ru-3b**. Mercapto group was introduced on the benzene ring complexed with dithiole. The original chlorine groups were not retained on the benzene. **Ru-c** was prepared by connection of **7c** and **6** (Scheme 1).

Ru-3b (**7**) was prepared according to literatures.[20–24] (details see supporting information). **7a**, **7b** and **7c** were prepared from similar raw materials by complexation reaction. **5** was prepared from Merrifield resin (The Cross-Linking degree (% DVB) = 1 %, Particle size = 100 mesh, Loading rate = 0.52 mmol/L) and PEG 200 by etherification under microwave. **6** was prepared from **5** by Appel reaction. **Ru-a** was prepared by

etherification of **7a** with **6**, total yield = 59.7 %, calculated loading rate = 3.05×10^{-3} mmol/g (Ru), which was calculated by formula L × (W′-W)/ (W″-W), **L**: loading rate of Merrifield resin, **W**: original weight of Merrifield resin, **W′**: actual weight of **Ru-a**, **W″**: theoretical weight of **Ru-a**. Elemental analysis showed 1 g **Ru-a** loaded 0.32 mg ruthenium. Loading rate of **Ru-a** (Ru/g) was 3.17×10^{-3} mmol/g after calculation. Comparing with the Infrared Spectroscopy (IR) of **6**, appearance of methyl and benzene signals showed that **7a** had been loaded on **6**. The detailed IR was shown as follows: 2846~2920 (CH_2), 3024~3058 (CH_3), 1739 (alkene), 1421, 1492, 1510, 1600 (benzene).

Ru-b and **Ru-c** were prepared and characterized according to **Ru-a**. **Ru-b**: yield = 63.4 %. Elemental analysis showed 1 g **Ru-b** loaded 1.0 mg ruthenium. Characterized loading rate = 9.96×10^{-3} mmol/g. Calculated loading rate = 9.90×10^{-3} mmol/g). Appearance of methyl, hydroxyl and benzene signals showed that **7b** had been loaded on **6**. IR: 3448.41 (s, OH), 2850~2918 (d, CH_2), 3058~3081 (d, CH_3), 1664 (s, alkene), 1450, 1510, 1544, 1600 (q, benzene).

Ru-c: yield = 53.7 %, elemental analysis showed 1 g **Ru-c** loaded 0.47 mg ruthenium, characterized loading rate = 4.63×10^{-3} mmol/g. Calculated loading rate = 4.50×10^{-3} mmol/g. Appearance of methyl, methylene and benzene signals showed that **7c** had been loaded on **6**. IR: 2856~2920 (d, CH_2), 3058~3081 (d, CH_3), 1739 (s, alkene), 1421, 1492, 1510, 1600 (q, benzene) (Scheme 2).

Leaf alcohols were catalyzed with **Ru-3b**, **Ru-a**, **Ru-b** and **Ru-c**. A solution of *Z* or *E* leaf alcohol and **Ru-3b** in tetrahydrofuran (THF) was shaken for 10 h at 25 °C. Mixtures of products were gained via silica gel chromatography [Petroleum ether (PE): Ethyl Acetate (EA) = 20:1]. *Z/E* ratios of the mixtures [*(Z)-hex-3- ene-1, 6-diol* and *(E)-hex-3-ene-1, 6-diol*] were calculated according to ^{1}H NMR results. The reaction conditions of **Ru-a**, **Ru-b** or **Ru-c** catalyzing leaf alcohols were the same as **Ru-3b**, yields and *Z/E* ratios of products were shown in Table 1.

Table 1. Catalysis of (*Z*) leaf alcohol or (*E*) leaf alcohol with **Ru-3b**, **Ru-a**, **Ru-b** or **Ru-c**.

Entry[a]	Substrate	Catalyst	Yield	Ratio (*Z/E*)
1	*Z* leaf	**Ru-3b**	46.0 %	90:10
2	*E* leaf	**Ru-3b**	62.3 %	14:86
3	*Z* leaf	**Ru-a**	35.1 %	88:12
4	*E* leaf	**Ru-a**	73.2 %	23:77
5	*Z* leaf	**Ru-b**	50.0 %	92:8
6	*E* leaf	**Ru-b**	75.0 %	3:97
7	*Z* leaf	**Ru-c**	45.6 %	88:12
8	*E* leaf	**Ru-c**	63.8 %	11:89

[a] Group.

The control experiment was carried out with **6** instead of three catalysts. The reaction solution was analyzed by HPLC, showing that **6** had no catalytic efficiencies.

Results showed that a high ratio of *Z/E* product was gained with *Z* leaf alcohol as the raw material. On the contrast, a high ratio of *E/Z* product was gained with *E* leaf alcohol as the raw material. When *Z* leaf alcohol was substrate, the product of **Ru-**
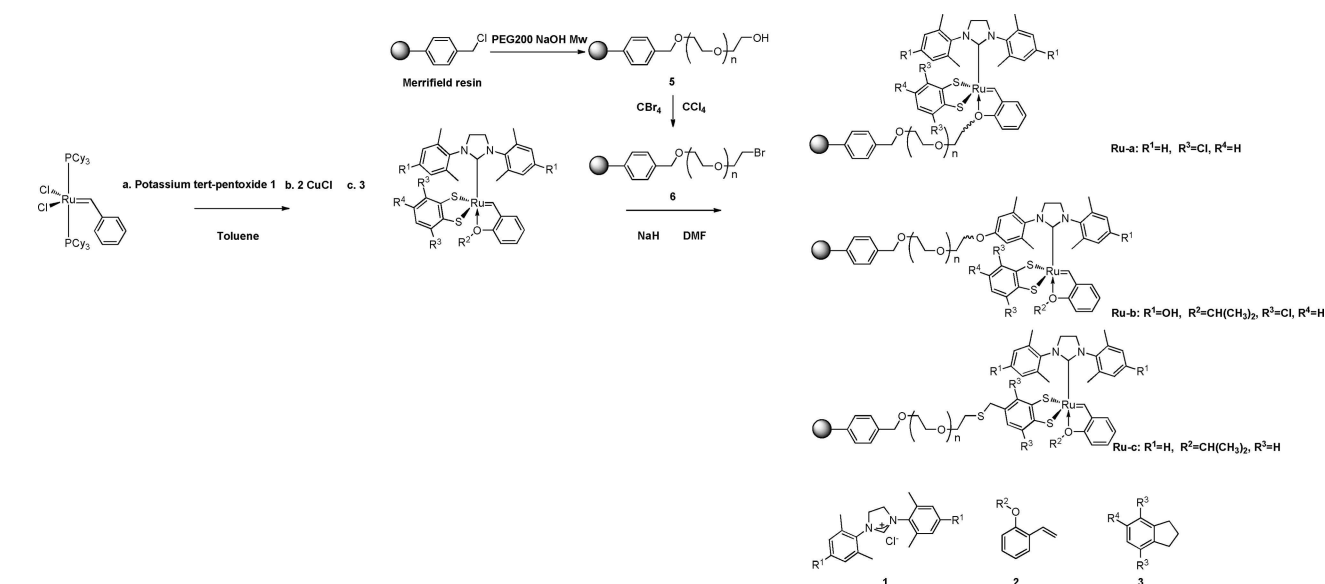
Scheme 2. Synthetic route for the preparation of the three supported catalysts.

b group showed higher *Z/E* ratio than products of other three groups. When *E* leaf alcohol was catalytic substrate, the product of **Ru-b** group showed higher *E/Z* ratio than products of other three groups (Table 1). Showing that **Ru-b** was more efficient than **Ru-3b**, **Ru-a** and **Ru-c**. There were three explanations for this. (1) Compared with **Ru-a**, the immobilization center of **Ru-b** was farther from its catalytic center. (2) Low efficiency of **Ru-c** might due to lack of chlorine group in the benzene compared with **Ru-3b**. (3) Compared with **Ru-3b**, hydroxyl on the carbene of **Ru-b** was an electronic donating group which might improve its catalytic activity.

With *Z* leaf alcohol as substrate, single recycling experiments of **Ru-a**, **Ru-b** and **Ru-c** were performed respectively. Recovery efficiencies were calculated by formula: **W'/W**, **W'**: recycling weight of the catalysts. **W**: original weight of the catalysts. Recovery efficiency and yield of **Ru-b** was higher than that of **Ru-a** and **Ru-c** (Table 2). Therefore **Ru-b** was selected for

the multiple recycling experiments. *Z* leaf alcohol was catalyzed by **Ru-b** for 5 cycles. The catalytic results were analyzed by HPLC. Results showed that Entry 1–4 had high recovery efficiencies (>80%), Entry **5** had low recovery efficiency which might due to large filter loss. Conversions (>35%) and Z product ratio (>85%) decreased gradually as we expected (Table 3).

Grubbs catalysts were immobilized on various carriers for multiple catalysis. Inspired by the role of linker in solid phase synthesis, three new Grubbs catalysts immobilized on PEGylated Merrifield resin were prepared for metathesis of leaf alcohols. Multiple recycling experiments were performed by catalyzing *Z* leaf alcohol with **Ru-b** for 5 cycles. Recovery efficiencies, yields and *Z/E* ratios were calculated and the results showed the conclusions as follows: (1) Results of leaf alcohols catalyzed by four catalysts showed that *cis*-products were obtained mainly when the *cis*-based materials were used for catalysis. *Trans*-products were obtained mainly when the *trans*-type raw materials were used for catalysis. (2) PEG linker strategy was successful, three catalysts showed similar activities to Ru-3b with convenient recycling approach, Ru-b was the best catalyst for metathesis of leaf alcohols which could be reused for more than 5 times. (3). *(Z)-hex-3-ene-1, 6-diol* was prepared from leaf alcohol by olefin metathesis reaction, which promoted the application of Grubbs catalysts. The catalysts will be used for more substrates, and our work might provide a new idea for immobilization of other catalysts.

Experimental Section

For experimental details please see the Supporting Information.

Table 2. Recovery of **Ru-a**, **Ru-b** and **Ru-c**.

Entry[a]	Substrate	Catalyst	Yield	Ratio (*Z/E*)
1	*Z* leaf	**Ru-a**	37.3%	69:31
2	*Z* leaf	**Ru-b**	57.6%	92:8
3	*Z* leaf	**Ru-c**	50.3%	88:12
[a] Group.				

Table 3. Recovery efficiencies of **Ru-b** (repeated five times).

Entry[a]	Substrate	Catalyst	Yield	Ratio (*Z/E*)
1	*Z* leaf	**Ru-b**	57.6%	95:5
2	*Z* leaf	**Ru-b**	50.5%	92:8
3	*Z* leaf	**Ru-b**	48.3%	90:10
4	*Z* leaf	**Ru-b**	40.0%	88:12
5	*Z* leaf	**Ru-b**	36.9%	85:15
[a] Group.				

Conflict of Interest

The authors declare no conflict of interest.

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