



Ruthenium-catalyzed Metathesis Reaction Using Fixed-bed Continuous Flow Reactor

INTRODUCTION

Olefin metathesis is an excellent method for the preparation of new rings and valuable intermediates in organic synthesis and polymer chemistry. The development of metathesis catalysts that combine high activity with a tolerance towards different functional groups has been important for the widespread utilization of this application. Out of all the various catalysts that have been reported, the ruthenium type catalysts¹⁻³, have the widest application due to their easy handling and substrate variability.

The most undesirable feature of these complexes is that they decompose to form ruthenium byproducts, which are difficult to remove. When metathesis was carried out using homogeneous catalysts, the recovery and reuse of the catalysts, and catalyst-product separations hampered their wide application. The ability to immobilize or heterogenize these catalysts would, therefore, possess major operational and economic advantages as well as increase the use of this application still further^{4,5}.

The catalysts immobilized on solid supports had limited success in metathesis reactions so far since the resulting anchored catalysts were found to be less reactive than their homogeneous analogues. It has been found that ruthenium complexes of general formula⁶ (Figure 1), containing two or more oxygen atoms demonstrate comparable activity in homogeneous and much higher activity in heterogenized catalytic systems in comparison to known heterogeneous or immobilized metathesis catalysts.



ThalesNano has successfully immobilized the novel catalysts on mesoporous silica MCM-417, on which they retained high levels of activity, thus, the obtained catalysts could potentially be applied in fixed-bed flow reactors (like the X-Cube™ or the H-Cube Pro™).

The supported catalyst was evaluated in metathesis reactions both in batch and in the X-Cube™. This flow system provides fast optimization of the reaction conditions (flow rate, temperature, pressure, solvent, substrate concentration) in a short period of time with only a few mg of substrate needed.

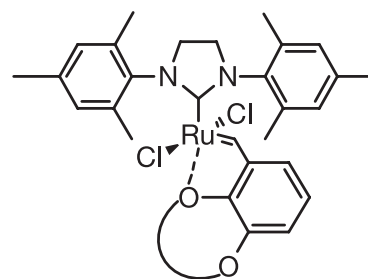


Figure 1. General structure of the catalyst

RESULTS OF FLOW METATHESIS

As test reaction, a ring closing metathesis (RCM) of diethyl diallyl malonate (Figure 2.) was performed in the X-Cube™ microfluidic reactor. 280 mg of the 10% complex containing immobilized catalyst on MCM-41 (Figure 3) was placed into a CatCart®. The solution was pumped through the cartridge at room temperature. The samples were taken in each hour and the conversion was determined by GC.



The concentration of the substrate was 0.05 M in cyclohexane, the flow rate was 0.1 mL/min at room temperature. The solvent should be apolar in order to avoid the leaching of the catalyst.

When using either *n*-hexane or cyclohexane, leaching was not observed. The performance of the heterogenized catalyst only slightly decreased during 6 hours (conversion: 92.4 to 89.3 %). After 6 hours the catalyst activity started to decline. The collected solution was tested in an RCM reaction in order to clarify that our system was really catalyzed heterogeneously.

To investigate, we added fresh diethyl malonate to the reaction mixture, but observed no conversion. It means that after 50% consumption of starting malonate, a part of supernatant (without heterogeneous catalyst) was transferred to another flask. Both reactions were continued under identical conditions, and sampled after 1 and 2 hours respectively. We found that supernatant did not give any activity. Based on previous in-house experiments, chemistry performed normally in the X-Cube™ can also be carried out in our novel multi-purpose instrument the H-Cube Pro™.

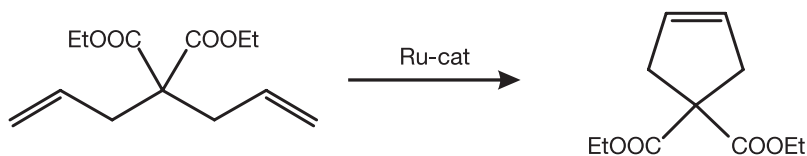


Figure 2. Ring-closing metathesis reaction of diethyl diallyl malonate

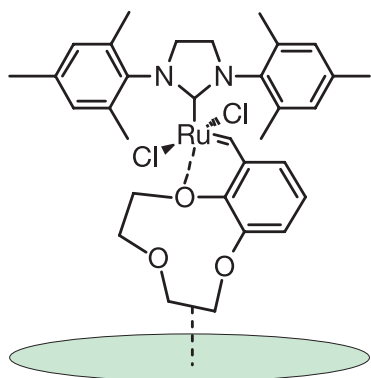


Figure 3. The ruthenium complex immobilized on MCM-41



H-Cube Pro™

References

- [1] Schwab, P.; Grubbs, R. H.; Ziller, J. W.; Synthesis and Applications of $\text{RuCl}_2(\text{CHR}')(\text{PR}_3)_2$: The Influence of the Alkylidene Moiety on Metathesis Activity; *J. Am. Chem. Soc.*; **1996**; 118 (1); 100–110
- [2] Scholl, M.; Ding, S.; Lee, C. W.; Grubs, R. H.; Synthesis and Activity of a New Generation of Ruthenium-Based Olefin Metathesis Catalysts Coordinated with 1,3-Dimesityl-4,5-dihydroimidazol-2-ylidene Ligands; *Org. Lett.*; **1999**; 1 (6); 953-956
- [3] Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. M.; Efficient and Recyclable Monomeric and Dendritic Ru-Based Metathesis Catalysts; *J. Am. Chem. Soc.*; **2000**; 122 (4); 8163-8179
- [4] Michrowska, A.; Mennecke, K.; Kunz, U.; Kirschning, A.; Grela, K.; A New Concept for the Noncovalent Binding of a Ruthenium-Based Olefin Metathesis Catalyst to Polymeric Phases: Preparation of a Catalyst on Raschig Rings; *J. Am. Chem. Soc.*; **2006**; 128 (40); 13261–13267
- [5] De Clercq, B.; Lefebvre, F.; Verpoort, F.; Immobilization of multifunctional Schiff base containing ruthenium complexes on MCM-41; *Applied Catalysis A: General*; **2003**; 247; 345–364
- [6] Hung. Pat. Appl. P1000664 (2010)
- [7] Trewyn, B. G.; Slowing, I. I.; Giri, S.; Chen, H.-T.; Lin, V.; S.-Y.; Synthesis and Functionalization of a Mesoporous Silica Nanoparticle Based on the Sol–Gel Process and Applications in Controlled Release; *Acc. Chem. Res.*; **2007**; 40 (9); 846-853

ThalesNano Nanotechnology Inc.

Zahony u. 7.
H-1031 Budapest
Hungary
Tel.: +36 1 880 8500
Fax: +36 1 880 8501
E-mail: sales@thalesnano.com

US Office ThalesNano

50 S. Penn St. Suite B-2
Hatboro
PA. 19040
USA
Phone: +1 732 274 3388
E-mail: USAsales@thalesnano.com

UK Office

Carl Jones
Head of European Sales
Tel.: +44 (0) 7868 843 819
E-mail: UKsales@thalesnano.com