# Immobilisation of the Grubbs III Olefin Metathesis Catalyst with Polyvinyl Pyridine (PVP)

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**Abstract:** A new concept for immobilising Grubbs III catalyst by direct coordination of ruthenium to polyvinyl pyridine (PVP) is presented. PVP was prepared by precipitation polymerisation, which led to small bead sizes (0.2–2 μm) and large surface areas. Compared to commercial resins, this phase showed superior properties when employed in model ring-closing metathesis (RCM) and in representative RCM, enyne and CM reactions with various substrates. The concept of immobilisation was also applied to Raschig rings made from a glass polymer composite material, which can be incorporated into devices for continuous flow processes.

**Key words:** catalysis, immobilisation, olefin metathesis, microwave assistance, Ru-catalyst, polymer support

During recent years, olefin metathesis using modern ruthenium catalysts such as Grubbs I–III (**1**, **2**, **5**) and Hoveyda–Grubbs carbenes (**3**, **4**, Figure 1) has become a key reaction in organic synthesis.[1]

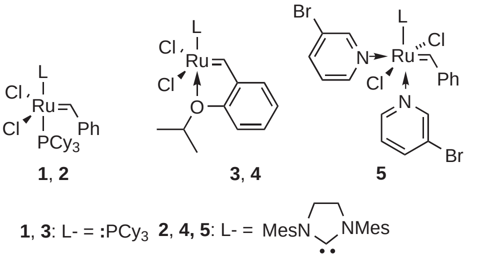

**Figure 1** Ruthenium-based catalysts **1**–**5** for olefin metathesis (Cy = cyclohexyl, Mes = 2,4,6-trimethylphenyl).

In order to remove various ruthenium by-products from the reaction mixture several protocols such as scavengers,[2a–c] biphasic extraction,[2d] and silica gel chromatography have been proposed. Another strategy to make Ru-based olefin metathesis more economical is immobilisation of these homogeneous catalyst on a solid phase.[3] Several attempts have been made to immobilise Grubbs-type carbenes **1** and **2** on solid or soluble supports either via ligand L (Figure 1) or via the alkylidene moiety.[4] Hoveyda established catalysts **3** and **4**[5] as remarkably robust complexes promoting olefin metathesis by a release–return mechanism.[6] Recently, various Hoveyda–Grubbs carbenes were attached to different resins or soluble supports preferentially via the 2-alkoxy-benzylidene fragment.[7]

However, for practicability reasons reversible attachment of catalysts to a solid phase is highly desirable.[8] The possibility of reloading the solid phase opens the door for utilising solid supports which have been specially designed for the individual catalytic process without considering their costs as much as would be relevant for covalently bound catalysts. Indeed, this concept should be of particular relevance in continuous flow processes[9] using reactors filled with heterogeneous or immobilised homogeneous catalysts.[10] The attachment ought to be strong enough in order to suppress leaching of the catalyst. However, after inactivation of the catalyst it is beneficial if it can be removed and the solid phase can be reactivated with fresh catalyst. In fact, this strategy would particularly gain interest in industrial applications.[11]

In this report we describe a straightforward procedure for immobilisation Grubbs III by means of coordinative binding. In contrast to the concept of grafting, we pursued a polymerisation strategy using the active species as part of the monomer in order to guarantee high loading.[12] Thus, as polymeric material, we chose polyvinyl pyridine (PVP) as part of a monolithic highly porous polymer/glass composite material which was obtained by precipitation polymerisation of vinyl pyridine and divinyl benzene (DVB) as cross linker.[13] The polymeric phase was prepared from a heated solution (70 °C) of the monomers and AIBN as radical initiator in a nonpolar solvent (*n*-alkane $C_{14}$–$C_{17}$ mixture). After 12 hours the precipitation of small interconnected polymer particles (5.3 mass% degree of crosslinking) occurred. The BET surface area is low (<5 $m^2/g$).[14,15] The polymeric material consists of very small particles (0.2–2 μm) compared to commercial resins (10–50 μm). Despite the small size of the individual bead-like particles the material can easily be filtered. Indeed, the optimised polymerisation process creates polymeric bridges between these particles, which resulted in an extended, monolithic polymeric phase (Figure 2, a and b).

Recently, Grubbs and coworkers showed that 3-bromo pyridine can form a 2:1 complex with the Grubbs II catalyst **2** to yield the active olefin metathesis catalyst **5**.[16] Ruthenium complex **5** is active in many types of metathesis reactions[17] including challenging CM with acrylonitrile.[16]

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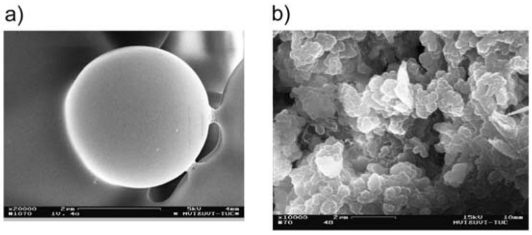
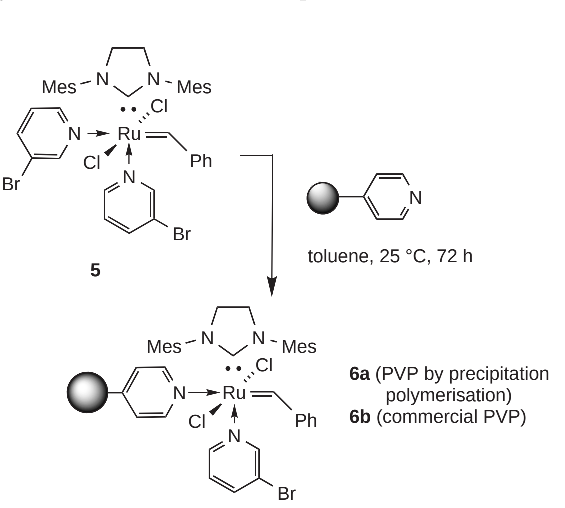


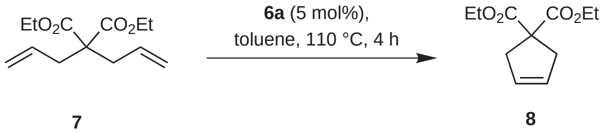
**Figure 2** a) Bridging to neighbouring polymer particles visualised by scattering electron microscopy (visualised by SEM). b) Morphology of polyvinyl pyridine (PVP; by SEM).

We found that the Grubbs III catalyst **5** can easily be immobilised through ligand exchange using polyvinyl pyridine (obtained by precipitation polymerisation, Scheme 1).[18,19] The immobilisation was achieved by employing PVP in ten-fold excess (with reference to pyridine moieties on the polymer) which resulted in complete (96%) immobilisation of catalyst **5** as was judged gravimetrically as well as by ICP-MS. The resulting immobilised catalyst **6a** is relatively stable towards air. Degradation was encountered after two weeks.[20] For comparison reasons, we also employed commercial polyvinyl pyridine (from Acros) and treated it with Ru-complex **5** to yield immobilised Ru-complex **6b**.



**Scheme 1** Preparation of polymer-bound Ru-complexes **6a** (powder) and **6b** (the exact stereochemistry in the coordination sphere of the Ru centre is unknown).[19]

Malonate **7** served as model diene. Transformation of **7** to cyclopentane **8** in the presence of catalyst **6a** (5 mol%, toluene, 110 °C, 4 h; 0.297 mmol Ru/g polymer) was quantitative, while polymer **6b** yielded the cyclisation product **8** in only 11% under identical conditions. In addition, we tested whether coordination can only be achieved with the Grubbs III catalyst **5**. Thus, PVP (10 equiv) generated by precipitation polymerisation was treated for 72 hours with the Grubbs II catalyst **2** (1 equiv) in toluene in the absence as well as in the presence of CuCl.[5] In both cases it was hoped that ligand exchange with $PCy_3$ occurs, in the latter case the addition of the copper salt should facilitate dissociation of the remaining phosphane ligand. The resulting samples were employed in ring-closing metathesis of malonate **7** (5 mol%, toluene, 110 °C, 4 h) and were repeatedly used. The results of these experiments are summarised in Scheme 2 and Figure 3.



**Scheme 2**

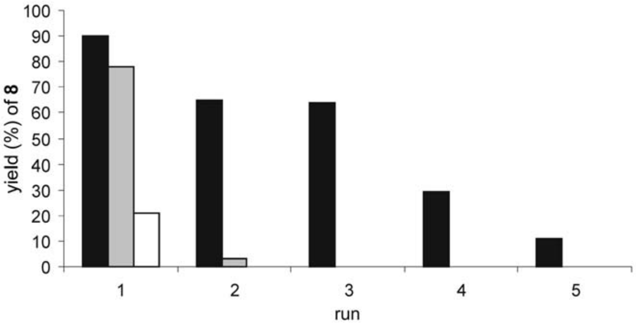


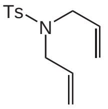
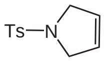
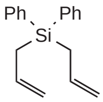
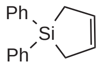
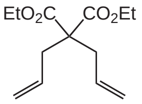
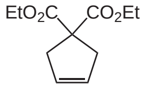
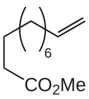
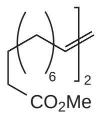
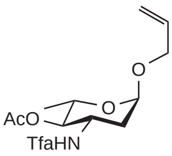
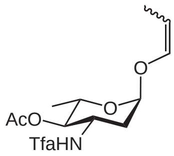
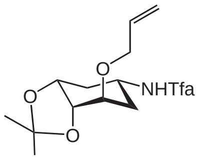
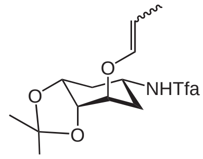
**Figure 3** Reusability of Ru-doped PVP polymer (prepared by precipitation polymerisation) treated with a) Grubbs III **5** (black), b) Grubbs II **2** (grey) and c) Grubbs II **2** + CuCl (white) in RCM [preparation of cases b) and c) see text].[21]

Obviously, the Grubbs III catalyst is the best choice for conducting ligand exchange reaction with polymer-bound pyridine. In terms of reusability polymer **6a** behaves similar to many covalently attached examples described in the literature[4] although in selected cases longer living systems have been described.[4b] After the fifth run, activity is lost which can either be ascribed to lack of thermal stability[22] or to the inherent problem of leaching during the catalytic cycle. Importantly, the solid phase can be reactivated by a washing protocol (1 N HCl, 1 N NaOH, $H_2O$, MeOH, toluene, then addition of **5**), which is an advantage over the solid phase concepts described so far.

Having evaluated the coordinative immobilisation of olefin metathesis catalysts to PVP we studied the applicability of catalyst **6a** in a more general sense (Table 1).[21]

In the case of allylethers **12** and **13** only double bond migration to the *E*/*Z*-mixture of enol ethers occurred, a phenomenon that has frequently encountered in olefin metathesis chemistry.[23,24] Snapper and coworkers showed that the Grubbs II catalyst **2** in the presence of small amounts of $H_2$ is able to isomerise a cyclic allyl ether into the corresponding enol ether via postulated Ru–hydride complexes.[25a] However, in the present case, the isomerisation proceeds without the presence of any external hydrogen source.[24a] It is known that in the presence of an additional base isomerisation of olefinic double bonds may also proceed.[25b] Here, the additional base may come from the vacant sites on the PVP phase.

**Table 1** RCM and CM with Solid-Phase-Bound Catalyst **6a** (Powder)[a]

| Substrate | | Product | | Temp, time | Yield (%) |
|---|---|---|---|---|---|
|  | **9** |  | **14** | 100 °C, 5 h | 96 |
|  | **10** |  | **15** | 100 °C, 5 h | 99 |
|  | **7** |  | **8** | 100 °C, 5 h | 99 |
|  | **11** |  | **16** | 100 °C, 4 h | 80 |
|  | **12** | <br>*E*/*Z* = 1:2 | **17** | 100 °C, 7 h | 98[b] |
|  | **13** | <br>*E*/*Z* = 1:3 | **18** | 100 °C, 5 h | 77[c] |

[a] Conditions: reactions were carried out under argon in toluene with 5 mol% of catalyst **6a**.

[b] A 50% yield in toluene at 40 °C and no conversion in $CH_2Cl_2$ at 40 °C.

[c] A 25% yield (*E*/*Z* = 1:3) with catalyst **2**.

Exploiting Barrett's concept of boomerang catalysts using 1-octene or triphenyl phosphane was tested here to improve reusability of **6a** but it rather gave reduced yields (35% for **14** compared to 96%; conditions: 5 mol% **6a**, toluene, 100 °C).[26]

In summary, we have described a new metod for the coordinative immobilisation of Grubbs III olefin metathesis catalyst to polyvinyl pyridine (PVP) with coordinative properties. The solid-phase-bound catalyst shows very good chemical reactivity and good recyclability and importantly can easily be reactivated with fresh catalyst, which opens the possibility of using catalysts of type **6a** under continuous flow conditions in flowthrough reactors.

Current work focuses on altered, non-covalently attached catalysts which show a longer life time when repeatedly used and which can be employed in multistep applications under continuous flow conditions.

## Acknowledgment

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(15) **Preparation of Polyvinyl Pyridine Phase by Precipitation Polymerisation.**
First, a mixture of 4-vinylpyridine (43.20 g, 410.8 mmol) and divinylbenzene (3.86 g; purity 65% besides ethyl benzene) was prepared. This mixture was filled up with an *n*-alkane (C14–C17 fraction) to a total volume of 300 mL, AIBN (327 mg, 2 mmol) was added and the temperature was raised to 70 °C. The reaction mixture is kept at this temperature for 24 h. Then the solid material formed was filtered, rinsed with $CHCl_3$ and further purified by extraction in a Soxhlet extractor with $CHCl_3$ and finally dried under reduced pressure to yield PVP (4.85 mmol/g capacity).

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(18) Indeed, this idea has been shown to be powerful for the immobilisation of enzymes using nickel NTA-linkers on sepharose for coordinatively trapping enzymes tagged with a His-tag.

(19) **Preparation of Functionalised Polyvinyl Pyridines 6a and 6b.**
A suspension of ruthenium catalyst **5** (140 mg, 0.16 mmol; prepared according to ref. 16) and PVP (**6a**: 400 mg, 1.84 mmol; **6b**: 373 mg, purchased from Acros) in toluene (3 mL) was shaken under argon at r.t. for 72 h. The polymer was filtered and washed with five portions of toluene (2 mL) to yield functionalised polymer **6** (polymer obtained by precipitation polymerisation: 510 mg, 0.15 mmol ruthenium; 96% and polymer from Acros: 477 mg, 0.09 mmol ruthenium; 80%).

(20) In comparison, treatment of catalyst **5** with pyridine yielded a new material which from mass spectrometric analysis does not contain bromine but which turned out to be highly unstable and quickly degraded under nitrogen even at –20 °C.

(21) **General Procedure for Metathesis Reactions with Polymer 6a.**
To a suspension of polymer **6a** (5 mol%) in dry toluene (0.02 M, 10 mL) under nitrogen was added the substrate (0.25 mmol). The resulting mixture was shaken for 4–7 h at 100 °C. At the end of the reaction (GC monitoring) the polymer was filtered off and washed with several portions of $CH_2Cl_2$. The solution was concentrated under reduced pressure and in most cases the crude material was

sufficiently pure. In order to obtain analytically pure samples the crude material was purified by flash column chromatography (mixture of PE–EtOAc as eluent).
**Studies on the Stability of Polymer-Bound Catalysts 6a.** Repeated reactions were carried out according to the general procedure given above by dissolving diallyl malonate **7** (55 μL, 0.228 mmol) in toluene (3 mL). After each reaction the polymer was filtered, washed with five portions of toluene (2 mL), dried under vacuum and reused for the next run. The crude products were isolated quantitatively; the yield of the RCM product **8** was determined after purification by flash column chromatography: 1st run (2 h; 43.5 mg, 0.2 mmol; 89%); 2nd run (2 h; 31.7 mg, 0.14 mmol; 65%); 3rd run (2 h; 30.5 mg, 0.14 mmol; 64%); 4th run (2 h; 13.8 mg, 60 μmol; 29%); 5th run (6 h; 4.8 mg, 22 μmol; 10%).

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