

## A New Concept for the Noncovalent Binding of a Ruthenium-Based Olefin Metathesis Catalyst to Polymeric Phases: Preparation of a Catalyst on Raschig Rings

Anna Michrowska,<sup>†,||</sup> Klaas Mennecke,<sup>‡</sup> Ulrich Kunz,<sup>§</sup> Andreas Kirschning,<sup>\*,‡</sup> and Karol Grela<sup>\*,†</sup>

Contribution from the Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224, Warsaw, Poland, Institut für Organische Chemie, Leibniz Universität Hannover, Schneiderberg 1B, D-30167 Hannover, Germany, and Institut für Chemische Verfahrenstechnik, Technische Universität Clausthal, Leibnizstrasse 17, D-38678 Clausthal-Zellerfeld, Germany

Received June 2, 2006; E-mail: grela@icho.edu.pl; andreas.kirschning@oci.uni-hannover.de.

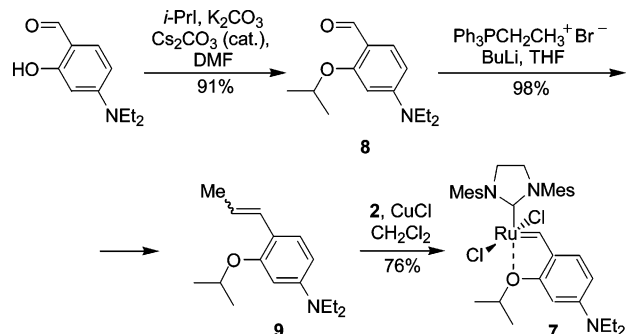
**Abstract:** A new concept for noncovalent immobilization of a ruthenium olefin metathesis catalyst is presented. The 2-isopropoxybenzylidene ligand of a Hoveyda–Grubbs carbene is further modified by an additional amino group (**7**) and immobilization is achieved by treatment with sulfonated polystyrene forming the corresponding ammonium salt. In this novel strategy for the immobilization of ruthenium-based metathesis catalysts, the amino group plays a two-fold role, being first an active anchor for immobilization and second, after protonation, activating the catalysts (electron donating to electron withdrawing activity switch). The polymeric support was prepared by precipitation polymerization which led to small bead sizes (0.2–2  $\mu\text{m}$ ) and large surface areas. Compared to commercial resins this tailor-made phase showed superior properties in immobilization of complex **7**. This concept of immobilization was applied to glass–polymer composite megaporous Raschig rings. Ru catalyst **7** on Raschig rings was used under batch conditions in various metathesis reactions, including ring-closing (RCM), cross- (CM) and enyne metathesis, to give products of high chemical purity with very low ruthenium contamination levels (21–102 ppm). The same ring can be used for up to 6 cycles of metathesis.

### 1. Introduction

During recent years, olefin metathesis has gained a position of increasing significance. The development of modern ruthenium metathesis catalysts, such as Grubbs I–III (**1**, **2**, **5**) and Hoveyda–Grubbs carbenes (**3**, **4**, Figure 1) combining high activity with an excellent tolerance to a variety of functional groups has been the key to widespread applications of olefin metathesis in organic synthesis and polymer chemistry.<sup>1</sup>

Despite general superiority offered by this family of catalysts, they share some disadvantages. Since olefin metathesis reactions are expected to be used in pharmaceutical processes, the most undesirable feature of these complexes is that during the reaction they form ruthenium byproducts, which are difficult to remove from the reaction products.<sup>2</sup> Several protocols to remove ruthenium impurities by addition of various scavengers,<sup>2a–c</sup>

**Scheme 1.** Synthesis of EDG-substituted Complex **7**



biphasic extraction,<sup>2d</sup> and silica gel chromatography<sup>2e</sup> have been proposed. From an economic point of view on the whole chemical process the catalyst's cost is another important attribute. In this respect, immobilization of homogeneous catalysts offers inherent operational and economic advantages over the parent soluble catalysts.<sup>3</sup> Several attempts have been

<sup>†</sup> Institute of Organic Chemistry, Polish Academy of Sciences.

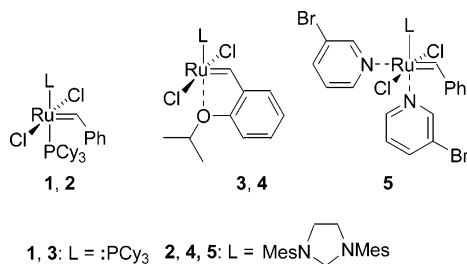
<sup>‡</sup> Institut für Organische Chemie, Leibniz Universität Hannover.

<sup>§</sup> Institut für Chemische Verfahrenstechnik, Technische Universität Clausthal.

<sup>||</sup> Current address: Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470, Mülheim/Ruhr, Germany.

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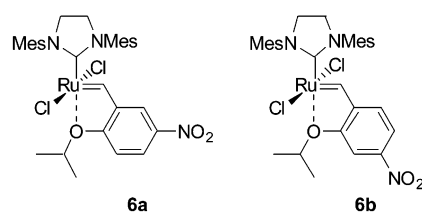
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**Figure 1.** Ruthenium-based catalysts 1–5 for olefin metathesis (Cy = cyclohexyl, Mes = 2,4,5-trimethylphenyl).

made to immobilize Grubbs-type carbenes **1–2** on solid or soluble supports either via ligand L (Figure 1) or via the carbene moiety.<sup>4</sup> Hoveyda established catalysts **3–4**<sup>5</sup> as remarkably robust complexes promoting olefin metathesis by a release/return mechanism.<sup>6</sup> Recently, various Hoveyda–Grubbs carbenes were attached to different resins or soluble supports preferentially via the 2-alkoxybenzylidene fragment.<sup>7</sup> Our group has recently presented a Hoveyda–Grubbs complex covalently bound to a PS-DES resin.<sup>7b</sup>

However, for practicability reasons *noncovalent attachment* of catalysts to a solid phase is highly desirable. The possibility of reloading the solid phase opens the door for utilizing 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<sup>8</sup> using reactors filled with heterogeneous or im-



**Figure 2.** Highly active EWG-substituted catalysts **6a** and **6b**.

mobilized homogeneous catalysts.<sup>9</sup> The attachment ought to be strong enough to suppress leaching of the catalyst. After inactivation of the catalyst it is beneficial if it can be removed from the solid phase and the reactor can be reactivated with fresh catalyst by simple washing protocols. Thus, this concept avoids physical removal of the fixed bed inside the reactor which can be costly. Therefore, this strategy is of major relevance for industrial applications, particularly when continuous-flow processes with immobilized homogeneous catalysts or enzymes are pursued for which the first examples are operating. Indeed, this concept has been successfully demonstrated in research laboratories and even in industrial processes for immobilized enzymes.<sup>10</sup>

Some concepts for the noncovalent attachment of chemical catalysts to solid supports have been developed.<sup>11</sup> Recently, Reiser and Werner disclosed electrostatic binding (Nafion sulfonic acid) of azabis(oxazoline)–copper complexes and their use in asymmetric cyclopropanations.<sup>12</sup> Additionally, task-specific ionic liquids can be loaded as liquid films on polar supports such as silica gel.<sup>13</sup> These polar layers have been used to immobilize ionic transition metal catalyst<sup>14a,b</sup> and polar organocatalysts.<sup>14c</sup>

Recently we have successfully tested the concept of noncovalent attachment in the preparation of Grubbs III generation catalyst **5** *coordinatively bound* to polyvinyl pyridine resin.<sup>15</sup> In this paper we describe a straightforward noncovalent procedure for immobilization of a new Hoveyda-type Ru complex *by means of electrostatic binding*.

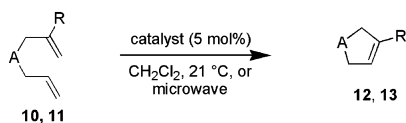
## 2. Results and Discussion

**Catalyst Design.** We demonstrated that the 5- and 4-nitro-substituted complexes **6a** and **6b** (Figure 2) initiate olefin metathesis dramatically faster than the parent Hoveyda–Grubbs catalyst **4**.<sup>16,17</sup> We proposed that the electron-withdrawing (EWG) nitro group in the benzylidene fragment of **6a** and **6b** would weaken O–Ru chelation and facilitate faster initiation of the catalytic cycle.<sup>16,17</sup>

In accordance with this assumption we observed that complex **7**<sup>18</sup> (Scheme 1), bearing the electron-donating (EDG) diethyl-

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**Scheme 2.** Model Reactions for Evaluating Catalysts **4** and **7** in Solution.

Entry	Substrate	Catalyst	Conversion (%) <sup>a</sup>	Entry	Substrate	Catalyst	Conversion (%) <sup>a</sup>
1	<b>10</b>	<b>7</b>	<1 (59) <sup>b</sup>	6	<b>11</b>	<b>7</b>	0 <sup>f</sup>
2	<b>10</b>	<b>4</b>	65	7	<b>11</b>	7×(-)-CSA <sup>c</sup>	99
3	<b>10</b>	7×HCl	3				
4	<b>10</b>	7×C <sub>8</sub> F <sub>17</sub> CO <sub>2</sub> H	72				
5	<b>10</b>	7×(-)-CSA <sup>c</sup>	82 (88) <sup>d</sup>				

<sup>a</sup> Complex **7** (5 mol %), CH<sub>2</sub>Cl<sub>2</sub>, 21 °C, 1 h; GC conversion. <sup>b</sup> **7** (1 mol %), CH<sub>2</sub>Cl<sub>2</sub>, microwave heating (60 °C, 200 W), 4 min. <sup>c</sup> CSA = camphor-10-sulfonic acid. <sup>d</sup> 7×(-)-CSA (1 mol %), CH<sub>2</sub>Cl<sub>2</sub>, microwave heating (60 °C, 200 W), 2 min. <sup>e</sup> Complex **7** (5 mol %), CH<sub>2</sub>Cl<sub>2</sub>, 21 °C, 16 h; GC conversion. <sup>f</sup> Under refluxing conditions conversion with **7** was quantitative (45 °C, 16 h).

amino group<sup>19</sup> shows little or no activity in olefin metathesis with model substrates **10** and **11** (Scheme 2, entries 1, 6).

As it can be further seen from Scheme 2, complex **7** is only able to promote RCM with diene **10** under microwave irradiating conditions [entry 1;  $\mu$ w conditions: **7** (1 mol %), CH<sub>2</sub>Cl<sub>2</sub>, 60 °C, 200 W] to yield cyclopentene **12** in 25% (after 2 min) and 59% yield (after 4 min), respectively. However, in a striking contrast, the in situ formed salts of aniline **7** obtained by treatment with organic acids are of high activity (Scheme 2, entries 4, 5, 7), surpassing the parent Hoveyda–Grubbs complex **4** in terms of initiation speed.<sup>18b</sup> Again, ring-closure of **10** can be accelerated under microwave conditions leading to complete transformation within 2 min (entry 5).

We envisaged that after reaction with polymer-supported acids, like Dowex resin, the new Ru-complex **7** can be conveniently immobilized by ion exchange. In this novel strategy for the immobilization of ruthenium-based metathesis catalysts, the amino group plays a two-fold role, being first an active anchor for immobilization (vide supra) and second, after protonation, activating the catalysts (*electron donating to electron withdrawing activity switch*).

**Preparation of the Polymeric Phases. Catalytic Performance of Polymer-Bound 7A–7C.** For the present application a sulfonated polymeric phase was required which should be suited for the ion exchange based immobilization of catalyst **7**.

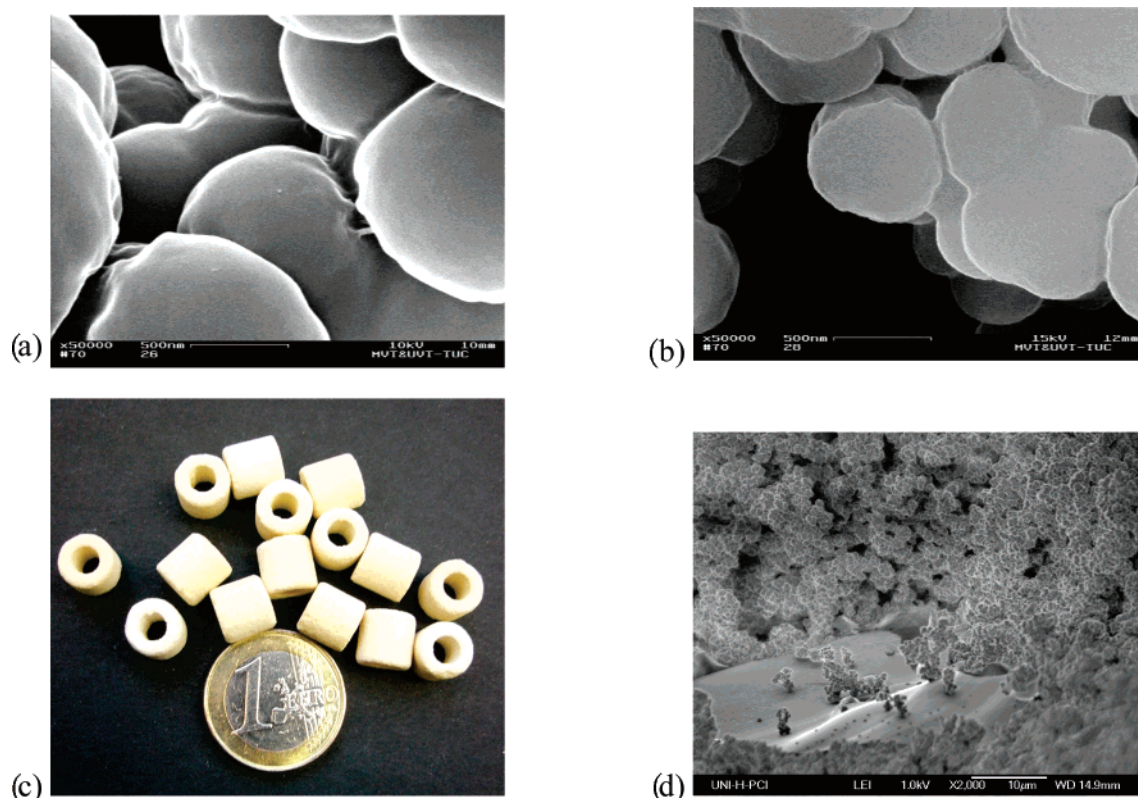
One key issue that one shall address in this context is the nature of the solid phase and the setting in which it is employed, aspects which are often overlooked by synthetic organic chemists in solid phase assisted synthesis.<sup>20</sup> We have therefore decided to investigate the nature of the solid phase in more detail, by comparing the commercially available ion-exchange resin Dowex 50Wx2 (loading 5 mmol/g dry resin; average particle size 560  $\mu$ m) with a tailor-made sulfonated polystyrene. We have found that the latter can be prepared from a heated solution (70 °C) of the monomers: styrene, divinylbenzene, and AIBN as radical initiator in a nonpolar solvent (*n*-alkane C14–C17 mixture). After 12 h the precipitation of small interconnected polymer particles occurred. In the following, sulfonation was achieved by treatment of the filtered and washed polymeric particles with a solution of chlorosulfonic acid to yield an acidic ion-exchange resin **A** [3.25 mmol/g capacity; 5.3 mass% degree of cross-linking; BET surface area is low (<5 m<sup>2</sup>/g) yielding gel like polymer particles].<sup>21</sup> This polymeric material consists of very small particles (0.2–2  $\mu$ m) compared to commercial ion-exchange resins (10–50  $\mu$ m). Despite the small size of the individual beadlike particles the material can easily be filtered. Indeed, the optimized polymerization process creates polymeric bridges between these particles which results in an extended, monolithic polymeric phase (Figure 3a and b).

Treatment of this sulfonated polystyrene polymer (**A**) and Dowex 50Wx2 resin (**B**) with a solution of catalyst **7** in CH<sub>2</sub>Cl<sub>2</sub> at ambient temperature for 3 h yielded functionalized polymers **7A** and **7B** (Figure 4).<sup>22</sup> Performance of these new catalysts was compared by converting diene **11** into **13** (5 mol % catalyst, in CH<sub>2</sub>Cl<sub>2</sub> at 45 °C) with the following observation: catalyst **7A** 1st run >99%, 2nd run 88%, 3rd run 56%, 4th run 68%, 5th run 38%, and 6th run 10%; catalyst **7B** 1st run 98%, 2nd run 33%). From these primary experiments it is evident that the sulfonated polystyrene **A** obtained through precipitation polymerization shows properties for ion exchange of larger species such as complex **7** superior to those of the commercially available ion-exchange resin Dowex 50Wx2 (**B**).

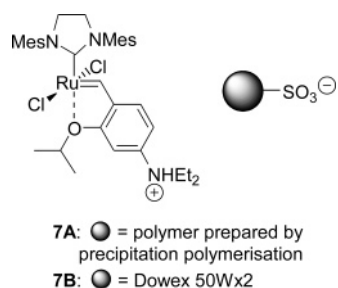
Another advantage of the tailor-made support **A** is that the polymerization process can be carried out in the presence of megaporous Raschig glass rings to yield a highly porous polymer–glass composite material (**C**) (Figure 3c and d). In this case the polymeric phase is protected toward mechanical stress inside the glass pores which is an advantage in industrial applications. Furthermore, when batch-type reactions are conducted, the solid phase can be easily removed as a single piece when required. Recently, we reported that such monolithic polymer–glass composite materials, obtained by precipitation polymerization, can be used in solid phase assisted solution phase synthesis or applied in continuous-flow reactors (PASS-flow microreactors).<sup>15,23,24</sup>

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**Figure 3.** Polymeric phases **A** and **C** used for immobilization of **7**. (a) Sulfonated polymer **A** particles (0.2–2  $\mu\text{m}$  diameter). (b) Bridging to neighboring polymer particles visualized by scattering electron microscopy (SEM). (c) Megaporous glass Raschig rings. (d) View (visualized by SEM) on the sulfonated glass polymer composite material (**C**) of Raschig rings.

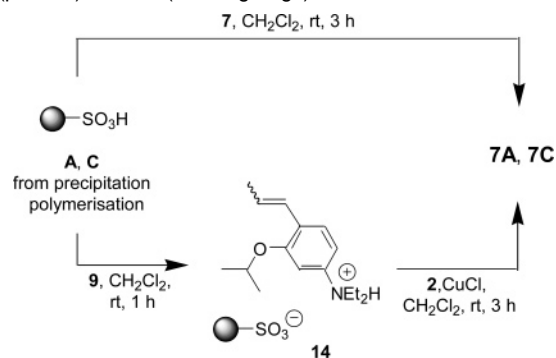


**Figure 4.** Structure of immobilized **7A** and **7B**.

Therefore, we employed the polymer **A** and the megaporous Raschig rings **C** as supports in the following studies by first searching for the best immobilization procedure.<sup>25</sup> As described above, catalyst **7A** can be obtained by direct immobilization of diethylamine containing complex **7** in the presence of polymeric sulfonic acid obtained from precipitation polymerization. Alternatively, the same catalyst can be prepared indirectly by ion exchange of easily accessible aniline derivative **9** (*E/Z* ratio 2:1; Scheme 1) to yield functionalized polymer **14** which then was subjected to cross olefin metathesis conditions in the presence of Grubbs II catalyst **2** (Scheme 3). At this point it has to be noted that the direct immobilization of **7** leads to a cationic exchange resin with partial loading (some sulfonic acid moieties remain unaltered) while the “indirect” immobilization strategy allows saturation of all  $\text{SO}_3^-$ -groups with both aniline **9** and the carbene complex **7**. Unlike the latter approach the direct immobilization affords a resin which is still partially acidic.

(25) This aspect is of particular importance when continuous flow processes are envisaged.

**Scheme 3.** Alternative Approaches for the Preparation of Catalyst **7A** (powder) and **7C** (Raschig rings)



Therefore, the “indirect” procedure was chosen for all further experiments. Copper(I) chloride is well suited to force the exchange of **14** with **2** to completion by trapping the phosphane ligand.<sup>5</sup> Indeed, with the resulting catalyst **7A** the model RCM of diene **11** yielded **13** in 100% conversion (5 mol % **7A**, DCM, 45  $^\circ\text{C}$ , 3 h) while preparation of **7A** from **2** in the absence of CuCl furnished a catalyst which afforded the cyclization product **13** with only 50% conversion under identical reaction conditions.

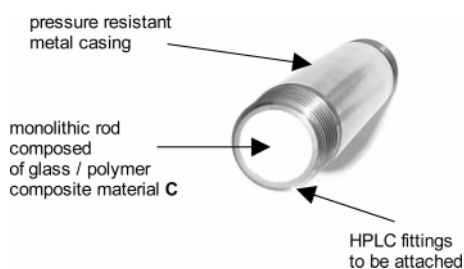
Using the same “indirect” immobilization procedure we also prepared catalyst **7C** immobilized on glass–polymer composite Raschig rings (Figure 3c) which can be used for combinatorial chemistry and high-throughput screening.<sup>7a,26</sup> For the final recyclability studies catalyst **7C** (loading 3  $\mu\text{mol}$  Ru/ring) and the model substrate **11** were used. After each run (5 mol % of

(26) Mayr, M.; Wang, D.; Kröll, R.; Schuler, N.; Prühs, S.; Fürstner, A.; Buchmeiser, M. R. *Adv. Synth. Catal.* **2005**, *347*, 484–492.

**Table 1.** RCM and CM with Catalyst **7C** (bound to Raschig rings)<sup>a</sup>

Entry <sup>b</sup>	Substrate	Product	Temp.[°C], (time [h])	Conversion (%)
1		<b>15</b> →	<b>22</b> 45 (18)	99
2		<b>16</b> →	23 45 (2)	99
			60 (4 min) <sup>c</sup>	71 <sup>c</sup>
3		<b>10</b> →	<b>12</b> 45 (18)	97
4		<b>17</b> →	<b>24</b> 45 (2)	99
5		<b>18</b> →	<b>25</b> 45 (4)	99
6		<b>19</b> →	26 22 (18)	95
				<i>E/Z</i> = 1.2:1
7		<b>20</b> →	27 45 (24)	68 <sup>d</sup>
				<i>E/Z</i> = 11:1
8		<b>21</b> →	<b>28</b> 45 (16)	99

<sup>a</sup> Conditions: one Raschig ring **7C** (loading 3  $\mu\text{mol Ru}/\text{ring}$ , 5 mol %) per reaction was used. For a description of the equipment used, see ref 28. <sup>b</sup> Crude products from entries 1–8 were obtained after removal of the Raschig ring, washing with dichloromethane, and evaporation of solvent under reduced pressure. Conversions were calculated by <sup>1</sup>H NMR spectroscopy and/or GC analysis. <sup>c</sup> **7C** (1 mol %), CH<sub>2</sub>Cl<sub>2</sub>, microwave heating (60 °C, 200 W), 4 min. <sup>d</sup> Two Raschig rings **7C** were used.

**Figure 5.** PASSflow reactor (without HPLC connectors) employed in preliminary RCM experiments with **7C**.

catalyst, 21 °C, 24 h) the reaction mixture was removed with a Pasteur pipet, and the ring was rinsed with minimal amounts of dichloromethane and reused. As we found, the same ring can be used for up to 6 runs of metathesis, however with gradual loss of activity: 1st run 85%, 2nd run 68%, 3rd run 54%, 4th run 53%, 5th run 52%, 6th run 56%, 7th run 13%, and 8th run 11%. At this point the solid phase can easily be reactivated by a washing protocol (1 N HCl, H<sub>2</sub>O, 1 N NaOH, H<sub>2</sub>O, 1 N HCl, H<sub>2</sub>O, methanol, and dichloromethane).<sup>27</sup> The contamination level

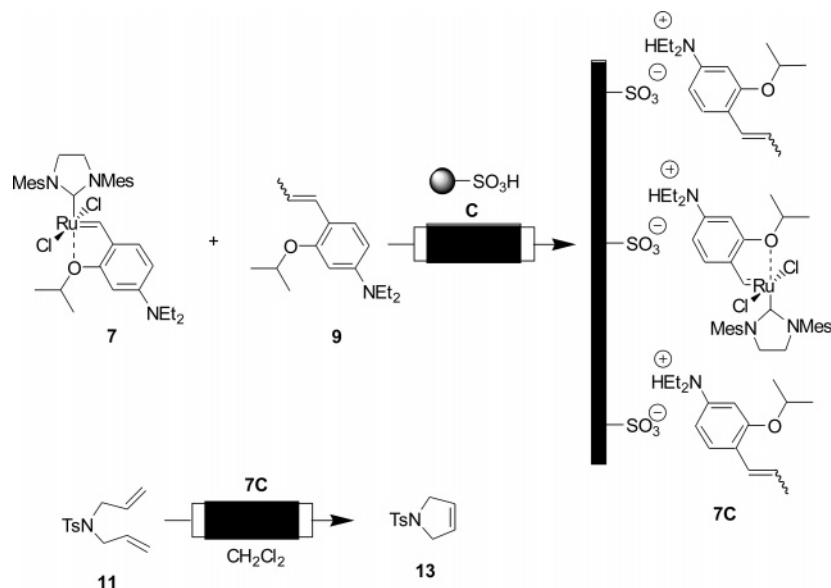
(27) The reactivation of Raschig rings was tested using RCM of diethyl diallylmalonate **16** (5 mol % of **7C**, CH<sub>2</sub>Cl<sub>2</sub>, 45 °C, 2 h). After each reaction cycle the old catalyst was removed from the ring by washing with 1 N HCl, H<sub>2</sub>O, 1 N NaOH, 1 N HCl, H<sub>2</sub>O, and methanol. Then fresh catalyst **7** was loaded as described above and the “recharged” ring was used in the next cycle of metathesis. This experiment gave the following results: Initial catalyst, loading 3.0  $\mu\text{mol}/\text{ring}$ , conversion 99%; 1st recharging, loading 3.0  $\mu\text{mol}/\text{ring}$ , conversion 87%; 2nd recharging, loading 3.0  $\mu\text{mol}/\text{ring}$ , conversion >99%; 3rd recharging, loading 2.8  $\mu\text{mol}/\text{ring}$ , conversion 99%. See the Supporting Information for details.

of product **13** with ruthenium was determined to be around 100 ppm (by ICP-MS). This is significantly lower than the ruthenium contamination reported for Hoveyda’s catalyst on sol–gel pellets (up to 1 wt %).<sup>7a</sup> It should be noted, however, that despite the diminution in Ru loading, the catalytic activities of the recycled Hoveyda’s pellets are still high and a single sol–gel pellet can be used for up to 20 reaction cycles.<sup>6</sup> Recently, another interesting report on a disk-shaped monolithic Ru catalyst for combinatorial chemistry has been published.<sup>26</sup> In the case of this system the reported leaching was >3% while the average contamination of products with ruthenium was around 70 ppm. The catalyst was, however, designed as “one-way” disks, therefore no recycling or multiple use was attempted.

**Catalytic Performance of **7C** Bound to Raschig Rings. Use in High-Throughput Experiments.** The practicability of Raschig rings loaded with the Ru-complex **7** (3  $\mu\text{mol Ru}/\text{ring}$ ) in high-throughput synthesis<sup>7a,17</sup> was demonstrated by the examples shown in Table 1.<sup>28</sup> Ring-closing and enyne metathesis of representative substrates proceeds cleanly, with typically high conversion, as determined by GC/MS and <sup>1</sup>H NMR analysis, leading to various carbo- and heterocycles (entries 1–5) including the rather labile octahydro-1*H*-cyclopenta[*a*]cycloocten-1-one derivative **28** (entry 8), a potential building block in the synthesis of terpenoid natural products.<sup>29</sup> We have also demonstrated the ability of **7C** to perform homo cross-metathesis

(28) For high-throughput experiments described in Table 1 the Radleys 12 Place Heated Carousel Reaction Station ([www.radleys.com](http://www.radleys.com)) was used.

(29) (a) Michalak, K.; Wicha, J. *Tetrahedron Lett.* **2005**, *46*, 1149–1153. (b) Michalak, M.; Wicha, J. *Synlett* **2005**, 2277–2280.

**Scheme 4.** Immobilization of Ru-complex **7** Inside a PASSflow Reactor and RCM under Continuous Flow Conditions

(CM) of functionalized alkenes (entries 6–7). Interestingly, the homometathesis of **20** proceeds without double bond isomerization,<sup>30,31</sup> although complete conversion cannot be reached after 24 h of reflux (entry 7). Surprisingly, homodimer **27** is formed with remarkably high *E/Z*-selectivity (11:1) compared to the Grubbs-I catalyst **1** which commonly yields dimeric spacer-linked hexoses in the *E/Z* ratio of 3:1 to 5:1.<sup>32</sup> This excellent selectivity may be ascribed to the “bulky” of the solid phase. At the end of the reaction the catalyst **7C** can be simply removed with a pair of tweezers and rinsed with minimal amounts of dichloromethane, producing minimal solvent waste. The resulting crude products were pure according to GC/MS and <sup>1</sup>H NMR analyses. Additionally, we checked the ruthenium content in selected crude products and found low levels<sup>7a,26</sup> of ruthenium contamination as follows: **22**, 102 ppm; **26**, 21 ppm; **27**, 77 ppm; **28**, 30 ppm (ICP-MS analysis of Ru). These results show the potential applicability of glass–polymer composite Raschig rings in a high-throughput screening.<sup>33</sup> The reaction rates can be strongly accelerated by operating under microwave irradiation conditions (vide supra), but the pure products were isolated with slightly reduced yields (exemplified in entry 2).

**Attempts to Olefin Metathesis under Continuous Flow Conditions.** Catalyst **7C** was also preliminarily tested under continuous-flow conditions<sup>8b</sup> by introducing the functionalized composite material shaped as a monolithic glass rod (see analogous material shaped as Raschig rings, Figure 3d) inside

a metal jacketed reactor equipped with HPLC-fittings at both ends of the reactor for allowing connection to an HPLC-pump (Figure 5).<sup>9</sup>

Different immobilization-modes for catalyst **7** were tested. We found that the best strategy for immobilization is to pump a solution of the Ru-complex **7** and an excess of aniline **9** (1:19 mol ratio) in CH<sub>2</sub>Cl<sub>2</sub> through the reactor in a circular mode (Scheme 4). This protocol allows simultaneous immobilization of both the catalyst and its ligand inside the reactor. At the same time complete saturation of all SO<sub>3</sub>H groups is guaranteed.

As for any other boomerang system,<sup>4</sup> leaching could be a great problem under nonstatic conditions. However, we expected that the Ru species released into solution during olefin metathesis can be re-trapped by excess of ionically bound ligand **9** when circulating through the PASSflow column.<sup>34</sup> To test this, diene **11** was dissolved in CH<sub>2</sub>Cl<sub>2</sub> and circulated (2 mL/min, no measurable pressure drop) at 40 °C for 5 h through this catalytically active reactor (5 mol % of Ru) which quantitatively afforded cyclopentene **13** (Scheme 4). The same reactor was washed with CH<sub>2</sub>Cl<sub>2</sub> and reused for a second run under identical conditions. This time product **13** was obtained in 79% yield, while the third run did not yield the desired product. Toluene can be used as a solvent giving similar results. The reactor can be reactivated by first washing with 1 N HCl, H<sub>2</sub>O (to pH 7), 1 N NaOH, H<sub>2</sub>O (to pH 7), 1 N HCl, H<sub>2</sub>O (to pH 7), dry methanol, and CH<sub>2</sub>Cl<sub>2</sub> followed by reloading with Ru-complex **7** and ligand **9** as described above.

In principle, we demonstrated for the first time that RCM can be conducted under PASSflow continuous flow conditions using a noncovalently immobilized Ru-catalyst. However, catalyst leaching is more pronounced compared to the corresponding batch experiments with Raschig rings **7C** (instead of two, up to six runs were possible as described above) which can be ascribed to the additional forces exerted by the convective flow. Importantly reloading of the reactor is easily possible.

(30) (a) Review: Uma, R.; Crevisy, C.; Gree, R. *Chem. Rev.* **2003**, *103*, 27–52. (b) Alcaide, B.; Almendros, P. *Chem. Eur. J.* **2003**, *9*, 1258–1262. (c) Schmidt, B. *J. Org. Chem.* **2004**, *69*, 7672–7687 (d) Arisawa, M.; Terada, Y.; Nakagawa, M.; Nishida, A. *Angew. Chem.* **2002**, *114*, 4926–4928. (e) Gurjar, M. K.; Yakambam, P. *Tetrahedron Lett.* **2001**, *42*, 3633–3636. (f) Braddock, D. C.; Wildsmith, A. *J. Tetrahedron Lett.* **2001**, *42*, 3239–3242. (g) Hoye, T. R.; Zhao, H. *Org. Lett.* **1999**, *1*, 1123–1125.

(31) Interestingly, in the case of **5** immobilized on polyvinyl pyridine, exclusive C–C double bond isomerization instead of CM was observed for this substrate: ref 15.

(32) (a) Chen, G.-w.; Kirschning, A. *Chem. Eur. J.* **2002**, *8*, 2717–2729. (b) Kirschning, A.; Chen, G.-w.; Jaunzems, J.; Jesberger, M.; Kalesse, M.; Lindner, M. *Tetrahedron* **2004**, *60*, 3505–3521.

(33) The high activity of catalyst **7C** has also been confirmed at Solvay GmbH by its application in CM of allylated steroids with  $\alpha,\beta$ -unsaturated partners: Messinger, J.; Schön, U.; Mennecke, K.; Harmrohlf, K.; Kirschning, A. unpublished results.

(34) It has been recently demonstrated that free Ru carbene intermediates in solution can be scavenged by monolithic sol–gel glass-bound styrene ether ligands prior to the onset of competing transition metal decomposition. See Kingsbury, J. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 4510–4517.

Still, the Ru-complex **7** attached to the monolithic polymer **C** obtained from precipitation shows a better performance under continuous-flow conditions compared to batch reactions with commercial anionic exchange resin **B**.

### Conclusions

In summary, we have described a new strategy for the noncovalent immobilization of Ru-based olefin metathesis catalyst **7** that relies on electrostatic binding. This concept allows more efforts to be spent on the optimization of the solid phase, as its reuse is easily possible through reloading of the active catalyst by simple washing steps. We showed that for the present applications solid phases generated by precipitation polymerization are superior to commercial Dowex 50 × 2. The solid-phase bound catalyst **7** shows very good chemical reactivity and good recyclability. Catalyst **7C** on glass–polymer composite Raschig rings can be applied in combinatorial chemistry and high-throughput screening to give products of high purity and of low ruthenium contamination (21–102 ppm). It therefore may be found useful for preparing small quantities of compounds for biological screening.<sup>33</sup> This process can be automated and has been successfully applied to a parallel reactor. After deactivation the solid phase can be easily reactivated with fresh catalyst.

Even despite more pronounced catalyst deactivation, we demonstrated for the first time that olefin metathesis is possible

under PASSflow continuous flow conditions. Future work will be focused on a next generation of noncovalently attached catalysts which show a longer lifetime when repeatedly used and which can be employed in multistep applications under PASSflow continuous flow conditions. We believe that this concept has a great potential for immobilizing many different catalytic species.

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**Supporting Information Available:** Full experimental procedures and spectral, analytical data for reaction products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org/>.

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