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Self-Supported Oligomeric Grubbs/Hoveyda-Type Ru–Carbene Complexes for Ring-Closing Metathesis

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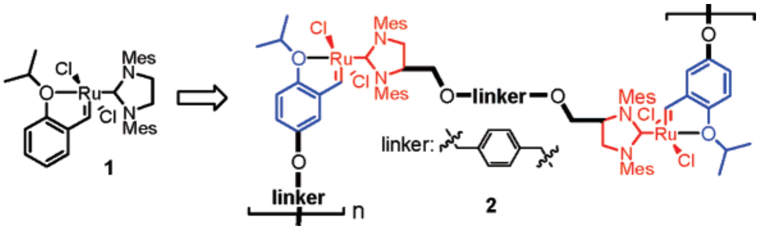
ABSTRACT



On the basis of the release–return metathesis mechanism, self-supported oligomeric Grubbs/Hoveyda-type Ru–carbene complexes have been designed and synthesized as a new type of recoverable catalyst for ring-closing metathesis. The catalytic activities of the self-supported oligomeric Ru–carbene complex in ring-closing metathesis are comparable to those of their homogeneous counterpart as they work homogeneously and are recovered heterogeneously.

To solve the problems of homogeneous catalysts associated with the difficulties in the recovery and reuse of the expensive metal catalysts, as well as the product contamination caused by metal leaching, a number of approaches for the immobilization or heterogenization of homogeneous catalysts have been employed. These include the common grafting of the catalyst to supports or conducting the catalytic reactions in biphasic systems.[1] Another promising and recent strategy involves heterogenization of the homogeneous catalysts or precursors through the formation of "self-supporting" metal−organic polymeric (or oligomeric) networks.[2] Recently, Sasai[2d] and Ding[2e−j] elegantly designed and demonstrated the feasibility of the self-supported chiral metal−organic coordination polymers for enantioselective catalysis. Quite recently, Son and Sweigart also reported a nanosized self-supported organometallic catalyst for polymerization of phenylacetylene.[2k] In comparison to other methods, the self-supporting strategy can produce heterogeneous catalysts without using any supports with high density

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of catalytically active units. Our hypothesis takes advantage of the self-supporting strategy, and it could also be conceptually possible to generate self-supported catalysts or catalyst precursors with which the catalysis can be conducted homogeneously; however, the catalysts could be recovered heterogeneously. In principle, the coupling of an active catalyst, bearing two active sites with a ligand having two ligating moieties, would provide the self-supported oligomeric (or polymeric) catalyst precursor.

The prerequisite of this strategy would be that the oligomeric catalyst precursors should be dissociated under the catalysis condition to generate a homogeneous active catalyst, and after catalysis, it should be reassociated to regenerate the oligomeric catalyst precursor again. In this respect, the structural feature and release and return metathesis mechanism of the Grubbs−Hoveyda Ru complex **1** may provide an excellent opportunity for the generation of this type of self-supported oligomeric catalyst precursor (Figure 1).[3] In the presence of olefinic substrates, the catalytically active Ru-methylidene species can be dissociated from the oligomeric matrix of **2**, which would be reassociated after catalysis to form the corresponding catalyst precursor.[4] Although numerous immobilization methods to recover metathesis Grubbs/Hoveyda-type Ru catalysts have been reported,[5] no work has been done to demonstrate the validity of this strategy to generate self-supported metathesis Ru complexes. Herein, we report the preliminary results of the generation of self-supported oligomeric Grubbs/Hoveyda-type Ru−carbene complexes for ring-closing metathesis.

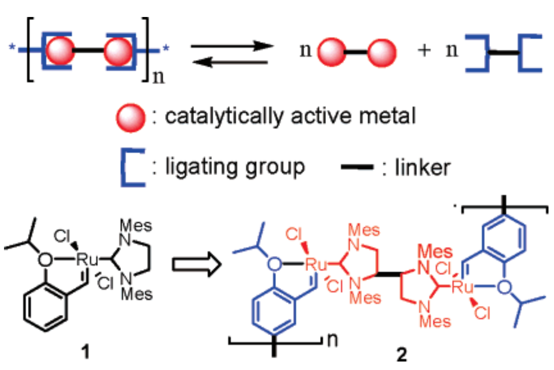
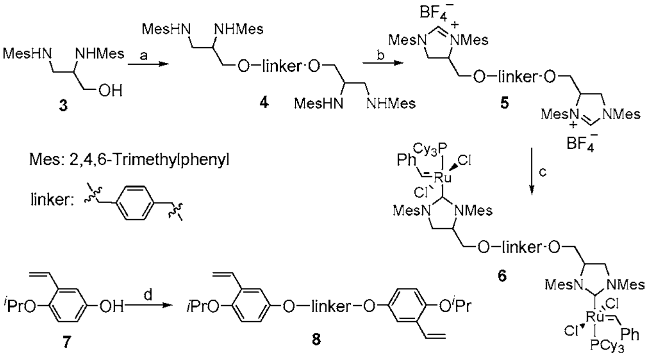


Figure 1. Schematic representation of the self-supported oligomeric Grubbs/Hoveyda-type Ru complexes.

To generate the self-supported oligomeric Grubbs/Hoveyda-type Ru−carbene complex, as shown in Scheme 1, dimeric dihydroimidazolium tetrafluoroborate **5** and isopropoxystyrene **8** having a 1,4-bismethylenephenyl linker were synthesized starting from **3**[6] and **7**,[7] respectively. Reaction of the hydroxy bismesityl **3** with α,α-dibromo-*p*-xylene followed by ring formation using triethylorthoformate[8] provided the desired dimeric dihydroimidazolium tetrafluoroborate **5** in two steps in 45% yield. Reaction of the dimeric N-heterocyclic carbene generated in situ from **5** with Grubbs first-generation Ru complex $(Cy_2P)_2Cl_2Ru({=}CHPh)$ in toluene afforded the novel dimeric Grubbs second-generation Ru−carbene complex[9] **6** in 48% yield.[10]

Scheme 1[a]



[a] Reagents and conditions: (a) NaH, THF, α,α-dibromo-*p*-xylene, rt, 19 h, 78%; (b) $HC(OEt)_3$, NH_4BF_4, toluene, 110 °C, 6 h, 57%; (c) KHMDS, toluene, rt, 15 min, then $(Cy_3P)_2Cl_2Ru({=}CHPh)$, 3 h, 48%; (d) NaH, α,α-dibromo-*p*-xylene, THF, rt, 17 h, 98%.

First, the coupling efficieny of the dimeric Ru−carbene complex **6** with isopropoxybenzylidene was examined in the presence of CuCl in methylene chloride at 40 °C affording

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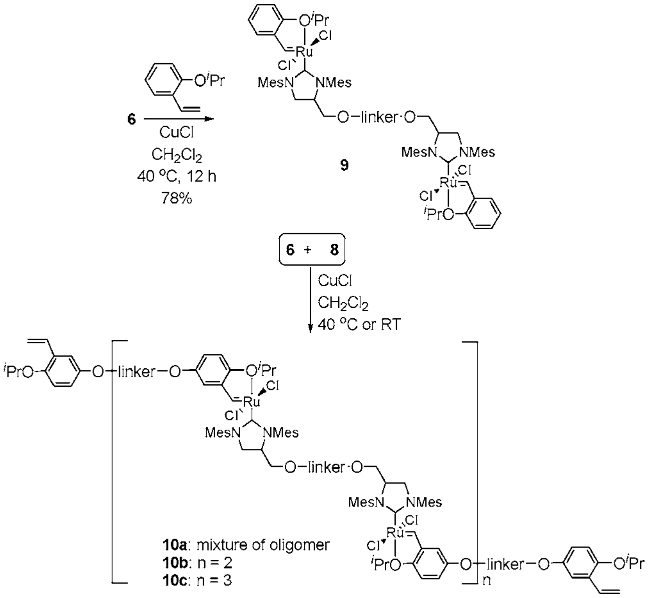
(10) In a nitrogen-filled drybox, a solution of imidazolium salt **5** (40.0 mg, 0.042 mmol) and potassium bis(trimethylsilyl)amide (KHMDS, 18.46 mg, 0.092 mmol) in toluene (2 mL) was stirred for 15 min, and then a solution of Grubbs catalyst first generation (76.16 mg, 0.092 mmol) in toluene (1 mL) was added. The reaction mixture was transferred to a Schlenk flask. The flask was capped and removed from the drybox and stirred at room temperature for 3 h. After evaporation of toluene under a vacuum, the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4:1) to give the product **6** (38 mg, 0.02 mmol, 48.4%) as a dark brownish solid. ^1H NMR ($CDCl_3$): δ 19.13 (s, 2H), 8.98 (br s, 2H), 7.35 (m, $J = 8.6$ Hz, 2H), 7.15−6.99 (m, 14H), 6.94−6.56 (m, 2H), 5.96 (br s, 2H), 4.40−4.32 (m, 6H), 4.13−3.83 (m, 4H), 3.78−3.21 (m, 4H), 2.76−2.39 (m, 9H), 2.19−2.15 (s, 9H), 2.04−1.89 (m, 12H), 1.51−1.27 (m, 36H), 1.00−0.91 (m, 36H). ^{31}P NMR ($CDCl_3$) δ 51.3 ppm. Anal. Calcd for $C_{102}H_{140}Cl_4N_4O_2P_2Ru_2$: C, 65.86; H, 7.59; N, 3.01. Found: C, 65.82; H, 7.64; N, 3.52.

the dimeric Grubbs/Hoveyda-type complex **9** in 78% yield.[11] Under the same reaction conditions, the coupling reaction between dimeric Ru−carbene complex **6** and isopropoxybenzylidene **8** (1:1 molar ratio), in the presence of CuCl in methylene chloride at 40 °C for 12 h, provided an inseparable mixture of oligomeric Ru complexes **10a**, which can be isolated by precipitation from ethyl acetate as a brownish solid (Scheme 2).[12] Inductively coupled plasma analysis (ICP-AES) indicated that 12 wt % of Ru was incorporated in the oligomeric mixture. When the same reaction was carried out at room temperature for 4 h, two oligomeric Ru−carbene complexes **10b** ($n = 2$) and **10c** ($n = 3$) were formed as major products. The ^1H NMR analysis (comparison of the integration of the resonance signals of $Ru{=}C(H)Ph$ at 16.43 ppm with the free $=CH_2$ at 5.69 ppm, dd, $J = 17.8$, 1.3 Hz and 5.24 ppm, dd, $J = 11.1$, 1.3 Hz) indicated that the isolated complexes have two (**10a**: $n = 2$) and three (**10b**: $n = 3$) repeating units with an isopropoxybenzylidene moiety at the terminal, as shown in Scheme 2.

Scheme 2. Synthesis of Dimeric **9** and Oligomeric Grubbs/Hoveyda-Type Ru−Carbene Complexes **10**



The mixture of oligomeric Ru complex **10a** and both of the isolated oligomeric Ru−carbene complexes **10a** and **10b** was soluble in halogenated solvents such as methylene chloride and chloroform but not soluble in ethyl acetate and toluene. These observations suggest that the RCM using oligomeric Ru complexes **10** can be conducted homogeneously in methylene chloride, and the catalysts may be recovered by precipitation in ethyl acetate. Figure 2 shows the pictures of **10a** in methylene chloride (Figure 2a) and in ethyl acetate (Figure 2b). The ICP-AES analysis of the supernatant of **10a** in ethyl acetate indicates that less than 1 ppm of Ru is leached into the organic phase.

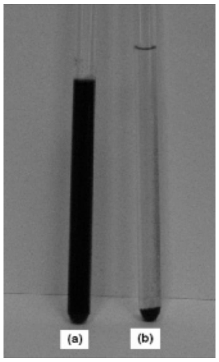


Figure 2. Pictures of **10a** in (a) methylene chloride and (b) ethyl acetate.

The catalytic activities of the original Grubbs/Hoveyda **1**, novel dimeric Ru complexes **6** and **9**, and the oligomeric Ru complexes **10a−c** were tested for the ring-closing metathesis of the benchmark substrate, *N*,*N*-bisallyl *p*-toluene sulfonamide, using 5 mol % of Ru, and the results are summarized in Table 1.

Reactivities of the dimeric Ru complexes **6** (entry 2) and **9** (entry 3) were quite comparable or even higher compared with the original Grubbs/Hoveyda Ru complex **1** (compare entry 1). Under the same reaction conditions, the catalytic activities of the mixture of oligomeric Ru complexes **10a** (entry 4) were slightly decreased when compared with the dimeric Grubbs/Hoveyda Ru complex **9**. This is probably due to the slow dissociation of the catalytically active Ru-methylidene species from the oligomeric matrix. The isolated oligomeric Ru complexes **10b** (entry 5) and **10c** (entry 6) showed catalytic activities similar to the mixture of the oligomeric Ru complex **10a**. After catalysis, however, both **10b** and **10c** were converted to the inseparable mixture of oligomeric Ru complexes similar with **10a**, in which both **10b** and **10c** were also detected. These results suggest that the self-supported oligomeric Ru−carbene complex **10b** or **10c** dissociated under the RCM conditions to generate the

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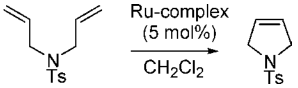
(11) Ruthenium carbene complex **6** (44.4 mg, 0.023 mmol), CuCl (5.18 mg, 0.052 mmol), and CH_2Cl_2 (3 mL) were placed in a Schlenk flask equipped with a condenser. Then the 2-isopropoxyvinylbenzene (8.49 mg, 0.052 mmol) was added, and the resulting solution was stirred under nitrogen at 40 °C for 3 h. The reaction mixture was concentrated in a vacuum, and the resulting residue was purified by column chromatography on silica (*n*-hexane/EtOAc = 2:1) to give **9** as a green solid, which was washed with the minimal amount of CH_2Cl_2 and a hexane mixture and dried under a vacuum affording a green microcrystalline solid **9** (25.6 mg, 76%). ^1H NMR ($CDCl_3$): δ 16.49 (s, 2H), 7.51−7.44 (m, 2H), 7.21 (s, 4H), 7.06 (s, 8H), 6.92−6.84 (m, 4H), 6.79 (d, $J = 8.4$ Hz, 2H), 4.94 (sept, $J = 6.2$ Hz, 2H), 4.59−4.53 (m, 2H), 4.48 (d, $J = 4.9$ Hz, 2H), 4.33 (t, $J = 10.5$ Hz, 2H), 4.09 (t, $J = 8.3$ Hz, 2H), 3.69−3.63 (m, 4H), 2.42 (s, 24H), 2.29 (s, 12H), 1.26 (d, $J = 6.1$ Hz, 12H). ^{13}C NMR ($CDCl_3$): δ 297.9, 211.2, 152.2, 145.3, 139.5, 138.8, 137.1, 129.9, 129.6, 129.5, 129.3, 127.8, 122.8, 122.3, 112.9, 74.9, 73.2, 67.8, 30.9, 21.1, 18.7. Anal. Calcd for $C_{72}H_{86}Cl_4N_4O_4Ru_2$: C, 61.10; H, 6.12; N, 3.96. Found: C, 61.06; H, 6.54; N, 3.88.

(12) A solution of Ru complex **6** (38.0 mg, 0.02 mmol), CuCl (2.02 mg, 0.02 mmol), and the dimeric **8** (9.4 mg, 0.02 mmol) in methylene chloride (3 mL) was refluxed for 12 h under N_2. After evaporation of the methylene chloride, ethyl acetate (5 mL) was added to provide an inseparable mixture of oligomeric Ru complexes **10a** as a brownish solid (38.0 mg). The same reaction was conducted at room temperature for 4 h and concentrated in vacuo. The resulting material was purified by column chromatography on silica (CH_2Cl_2/MeOH = 4:1) to afford **10b** (13.2 mg) and **10c** (15.4 mg) as greenish solids.

Table 1. Ring-Closing Metathesis of *N*,*N*,-Bisallyl *p*-Toluene Sulfonamide Using **1** and Dimeric **6** and **9** and Oligomeric Ru Complexes **10a**∼**10c**[a]



entry	Ru complex	time[b]	conv. (%)[c]
1	**1**	1.5 h	>98
2	**6**	30 min	>98
3	**9**	2 h	>98
4	**10a**	3.5 h	>98
5	**10b**	3.0 h	>98
6	**10c**	3.5 h	>98
7[d]	**10a**	3.5 h	>98
8	–	5 h	>98
9	–	8 h	>98
10	–	12 h	>98
11[e]	**10b**	3.0 h	>98
12[f]	**10c**	3.5 h	>98

[a] Reactions were carried out using 5 mol % of Ru at 40 °C in methylene chloride (0.5 M). [b] Time for completion. [c] Determined by ^{1}H NMR analysis. [d] Mixture of oligomeric catalysts recovered from entry 4. [e] Catalysts recovered from entry 5. [f] Catalysts recovered from entry 6.

catalytically active Ru-methylidene species and the dimeric isopropoxybenzylidene **8**, and after catalysis, they reassociated with different ratios to form a mixture of oligomeric Ru−carbene complexes.

The insolubility of the oligomeric Ru−carbene complexes **10a**∼**c** in ethyl acetate could prove to be beneficial for the catalyst recovery and reuse.[13] Hence, the mixture of oligomeric complexes **10a** can be recovered heterogeneously by precipitation using ethyl acetate and reused (entries 7−10). Similarly, the oligomeric mixture of Ru complexes formed after RCM with either **10b** (entry 11) or **10c** (entry 12) could also be recovered and reused. However, the catalytic activities were slowly decreased upon reuse, which may partly be due to the decomposition of active Ru−carbene species providing ethyl acetate-soluble ones. In ICP-AES analysis of the ethyl acetate layer after the first run with **10a** (entry 4), 16 ppm (about 1.13%) of Ru was leached out into the ethyl acetate layer. Nevertheless, it should be noted here that the feasibility of this new type of self-supported complex for catalyst recovery and reuse has been successfully demonstrated.

In conclusion, we have designed and synthesized a new type of self-supported catalyst for the homogeneous catalysis and heterogeneous recovery. As proof of this concept, self-supported oligomeric Grubbs/Hoveyda-type Ru−carbene complexes were generated for ring-closing metathesis. The catalytic activities of the self-supported oligomeric Ru−carbene complexes are comparable to those of their homogeneous counterpart as they work homogeneously and are recovered heterogeneously. However, the dissociation rate from the oligomeric matrix and association efficiency may need to be increased to improve the cataytic activity and reusability of the self-supported Ru complexes. Nevertheless, this approach might provide a new direction for the development of a recoverable catalyst. Further studies on the impact of a linker in ligands and/or a catalyst on both the structure of assemblies and their catalytic performance are underway in this laboratory.

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Supporting Information Available: Detailed synthetic procedures, spectral data of **4**−**9** and **10a**∼**10c**, and ^{1}H NMR spectra of **5**, **6**, **9**, **10b**, and **10c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) Representative procedure for RCM: A 10 mL oven-dried round-bottom flask equipped with a reflux condenser was charged with oligomeric Ru catalyst **10a** (12.0 mg, 0.014 mmol of Ru). The flask was evacuated and filled with N_2. *N*,*N*-Diallyl-*p*-toluenesulfonamide (120.0 mg, 0.279 mmol) was then added in anhydrous CH_2Cl_2 (5.0 mL); the flask was then heated to gentle reflux for 3 h; and the solvent was evaporated. Ethyl acetate (5 mL) was added to the residue, and the precipitated mixture of oligomeric Ru complexes **10a** was recovered by filtration and washed with ethyl acetate (5 mL × 2). After evaporation of the ethyl acetate, ^{1}H NMR analysis of the crude residue revealed complete conversion, and the product was isolated by flash chromatography (*n*-hexane/EA = 3:1) to afford pure product as a white crystal (61 mg, 99%). A second run of the metathesis using the recovered mixture of oligomeric Ru complexes **10a** (or from **10b** or **10c**) was conducted in the same way as described for the first run, but the reaction time was prolonged until completion of the reaction by TLC. This reaction was repeated, each time using the catalyst recovered from a previous cycle. The results are listed in Table 1.