An Air-Stable, Reusable, Bimetallic Version of Grubbs' Catalyst for Alkene Metathesis

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Received 13 August 2002

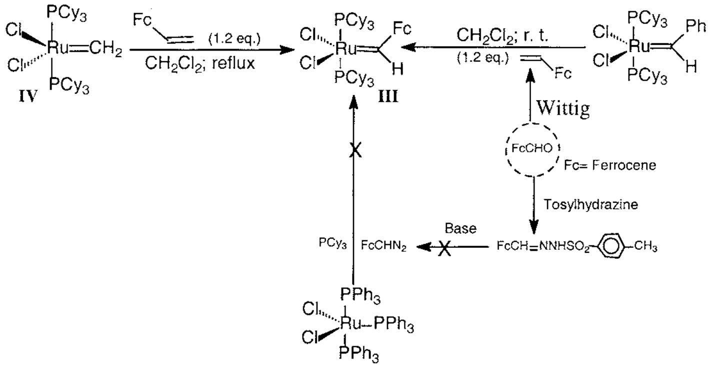
Abstract: RCM, cross-metathesis and ring-opening cross-metathesis are efficiently catalyzed by a new, air-stable, bimetallic analog of Grubbs' Ru-based metathesis catalyst, which can be recovered and recycled.

Key words: metathesis, ruthenium, carbene complexes, catalysis, organometallic reagents

Grubbs' ruthenium-based catalysts[2] (**I**, **II**) for alkene-metathesis received wide attention owing to their versatility in promoting different kinds of transformations like ring-closing metathesis (RCM), cross-metathesis (CM), ring-opening-cross-metathesis (ROCM) and ring-opening metathetic polymerization (ROMP). The first three have been extensively exploited in synthetic organic chemistry.

Based on kinetic studies, Grubbs and coworkers concluded[3] that the first step is dissociative: one of the phosphine ligands dissociates to provide a 14*e* complex. Rate of alkene coordination to this intermediate (initiation) is competitive with the rate of phosphine 're-association'; for an efficient catalyst, former must predominate. Steric and electronic attributes of the carbene ligand tacitly influence this initiation process. For instance, an electron-rich and bulky substituent on the carbene ligand is likely to promote dissociation of phosphine. At the same time, it would also favor coordination of an alkene over recombination of a free phosphine ligand on steric grounds. Combining this argument with our interest in ferrocene-based materials, we have described herein synthesis and metathesis reactions of a novel analog of catalyst **I** (Figure 1) that features a ferrocene substituent on the carbene carbon. Ferrocene is electron-rich and has a considerable steric bulk – thus it addresses both electronic and steric criteria to promote metathesis. Preliminary results indicate that the catalytic efficiency of the new complex, **III**, is comparable to Grubbs' catalyst **I**, and the robust, air-stable complex can be very conveniently stored, recovered and recycled.[4]

Attempted base-induced decomposition of the tosylhydrazone of ferrocenecarboxaldehyde failed to produce ferrocenyldiazomethane; thermolysis produced only 1,2-diferrocenylethene. The complex **III** was, therefore, prepared[5] by treatment of vinylferrocene with complex **I** at ambient temperature (Scheme 1), and isolated (87%) as an air-stable, dark purple solid.[6] It is soluble in common solvents for alkene metathesis like benzene, toluene and dichloromethane.



Scheme 1

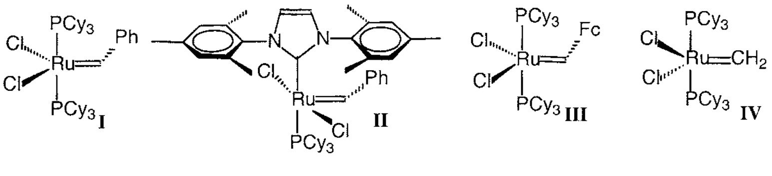


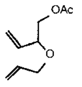
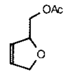
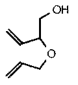
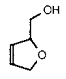
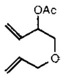
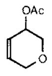
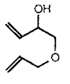
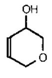
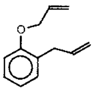
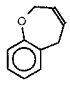
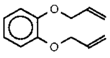
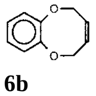
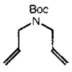
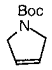
Figure 1

Synlett 2002, No. 11, Print: 29 10 2002.
Art Id.1437-2096,E;2002,0,11,1925,1927,ftx,en;G22802ST.pdf.

ISSN 0936-5214

Ring-closing metathesis catalyzed by complex **III** was studied with several substrates and the results are summarized[7] in Table 1. The yields are generally excellent while the reaction time is short. About 2–2.5 mol% of catalyst was sufficient for quantitative conversion in most instances. Efficiency of the catalyst compares well with Grubbs' first-generation catalyst **I** – the propagation steps are identical for both the catalysts. Substrates with free hydroxyl groups seem to require longer period for complete conversion than corresponding acetates. For substrate **6a**, oligomeric side-products (via competitive *ADMET*) accounted for diminished yield.

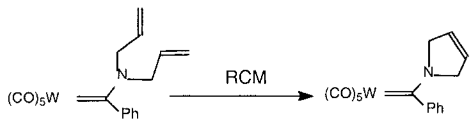
Table 1 RCM using Catalyst **III**[a]

Entry	Substrates (Concn)	Product	Catalyst (mol%)	Time/ Temp	Yield (%)
1	 **1a** (0.1 M)	 **1b**	2.5	15 min/r.t.	98
2	 **2a** (0.1 M)	 **2b**	2.5	2 h/r.t.	90
3	 **3a** (0.1 M)	 **3b**	2.5	15 min/r.t.	97
4	 **4a** (0.1 M)	 **4b**	2.5	1.5 h/ r.t.	92
5	 **5a** (0.05 M)	 **5b**	2.5	30 min/r.t.	98
6	 **6a** (0.05 M)	 **6b**	2.5	1.5 h/r.t.	67
7	 **7a** (0.1 M)	 **7b**	2	30 min/r.t.	97

[a] All the reactions were carried out in CH_2Cl_2 at room temperature under Ar.

The carbene complex **8a**, which closely resembles the organic substrate **7a**, requires more quantity of catalyst (10 mol% of **I** or **III**) than **7a**, and longer time for completion[8] (Scheme 2). Thermal activation does not compensate for use of less amount of catalyst. When 7.5 mol% of vinylferrocene was added after 30 min and the solution was heated under reflux, yield improved to 99%. This indicated that it was indeed possible to regenerate the active catalyst **III** under this reaction condition.[9]

Another organometallic substrate, **9a**, required 10 mol% of catalyst **III** to provide a high yield of corresponding RCM product, **9b**. Interestingly in this case, the complex that is released after the ring-closing step is similar to original catalyst **I**, yet the catalyst requirement is relatively high. Again, use of 5 mol% of catalyst augmented with 7.5 mol% of vinylferrocene added after 20 min, afforded the RCM product in 91% yield after 4 hours at ambient temperature (Scheme 3), indicating in situ regeneration of catalyst **III**.

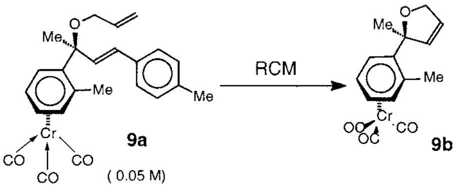


8a (0.05 M) **8b**

Entry	Cat. III (mol%)	Time/Temp	Yield (%)
1	10	3 h/r.t.	98
2	5	4 h/reflux	68
3	5	i) 30 min /r.t. ii) 1.5 h/reflux[a]	99

[a] After addition of 7.5 mol% of vinylferrocene

Scheme 2



Entry	Cat. III (mol%)	Time/Temp.	Yield (%)
1	10	1.5 h/r.t.	93
2	5[a]	4 h/r.t.	91

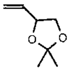
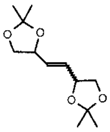
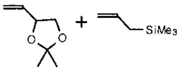
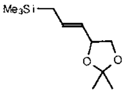
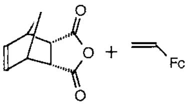
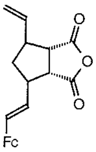
[a] 7.5 mol% Vinylferrocene was added after 20 min.

Scheme 3

Unlike RCM, cross-metathesis worked best when heated under reflux in dichloromethane (Table 2). Cross-metathesis of the substrate **10a** with catalyst **I** was recently reported.[10] Yields obtained with the catalysts **I** and **III** are comparable. Ring-opening cross-metathesis of bicyclic substrate **12a** also worked well with catalyst **III**.

Attempts were made to recover the catalyst **III** from the reaction mixture at the end of the reaction. In a preliminary attempt, after the substrate **7a** was completely converted by 2.5 mol% catalyst to RCM product **7b**, vinylferrocene (4 mol%) was added to the solution and it was heated under reflux for 40 min. Precipitation by methanol afforded 45% of the catalyst **III** in sufficiently pure form (NMR) and without any loss of activity as tested by subsequent runs. Improvement of catalyst recovery protocol, anchoring the catalyst on insoluble support and ROMP activity are currently being studied in this laboratory.

Table 2 Cross-Metathesis using Catalyst **III**[a]

Entry	Substrate (Concn)	Product	Cat. III (mol%)	Time/ Temp.	Yield (%)
1.	 **10a** (0.5 M)	 **10b**	5	6 h/ reflux	83
2.	 **11a** (0.5 M)[b]	 **11b**	5	6 h/ reflux	81
3.	 **12a** (0.5 M)[c]	 **12b**	5	1.5 h/ reflux[d]	72

[a] All reactions were carried out in dichloromethane and in each case *E*/*Z* >9:1.

[b] 3 equiv allyltrimethylsilane was used.

[c] 20% molar excess of vinylferrocene was used.

[d] No ROMP product was detected.

Acknowledgement

Financial support from Reliance Industries Ltd. and grant of a research fellowship (TKM) from CSIR, India, are gratefully acknowledged.

References

(1) Current address: Department of Organic Chemistry, Indian Association for the Cultivation of Science, Kolkata – 700 032, India. E-mail: ocas@mahendra.iacs.res.in.

(2) (a) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (b) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012. (c) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (d) Schuster, M.; Blechert, S. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2036. (e) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371. (f) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446.

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(4) Recycling catalyst: (a) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J. Jr.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791. (b) Dowden, J.; Savovic, J. *Chem. Commun.* **2001**, 37. (c) Fürstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem.–Eur. J.* **2001**, *7*, 3236. (d) Ahmed, M.; Barrett, A. G. M.; Braddock, D. C.; Cramp, S. M.; Procopiou, P. A. *Tetrahedron Lett.* **1999**, *40*, 8657. (e) For a survey of Ru-based initiators with other alkylidene groups, see: Frenzel, U.; Nuyken, O. *J. Polym. Sci. A* **2002**, *40*, 2895.

(5) We have followed the procedures described in (a) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100. (b) Trnka, T. M.; Day, M. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2001**, *40*, 3441.

(6) Vinylferrocene (61 mg, 0.29 mmol) in 1 mL dichloromethane was added to a solution of Ru-benzylidene complex, **I**, (200 mg, 0.243 mmol) in dichloromethane (5 mL). The reaction mixture was stirred at room temperature for 40 min when color of the solution turned from purple to red-violet. Volume of the solvent was reduced followed by addition of dry methanol at 0 °C, which afforded $(Pcy_3)_2Cl_2Ru{=}C(H)Fc$, **III**, as dark brown solid powder in 87% yield (198 mg). ^1H NMR (CD_2Cl_2): δ 19.00 (s, 1 H, Ru=CH), 4.70 (s, 2 H, Cp), 4.43 (s, 2 H, Cp), 4.14 (s, 5 H, Cp), 2.54 (broad s, 6 H, Pcy_3), 1.21–1.74 (m, 60 H, Pcy_3). ^{13}C NMR (CD_2Cl_2): δ 292.14, 104.23, 71.55, 71.21, 69.77, 32.66, 32.04, 30.11, 28.40, 26.98. ^{31}P NMR (CD_2Cl_2): δ 34.4 (s, Pcy_3). Details of preparation and complete characterization including crystal structure will be reported separately.

(7) Reactions were performed in 1–2 mmol scale in dichloromethane. Yields represent isolated yields of products after purification by chromatography. All compounds were characterized by their IR, ^1H and ^{13}C NMR spectra, and satisfactory elemental analyses were obtained for all new compounds.

(8) For examples of RCM on organometallic substrates, see: (a) Sültemeyer, J.; Dötz, K. H.; Hupfer, H.; Nieger, M. *J. Orgmet. Chem.* **2000**, *606*, 26. (b) Zhang, L.; Herndon, J. W. *Tetrahedron Lett.* **2002**, *43*, 4471. (c) Licandro, E.; Maiorana, S.; Vandoni, B.; Perdicchia, D.; Paravidino, P.; Baldoli, C. *Synlett* **2001**, 757. (d) Maity, B. C.; Swamy, V. M.; Sarkar, A. *Tetrahedron Lett.* **2001**, *42*, 4373.

(9) The Ru=CH_2 complex, **IV**, does not readily react with vinylferrocene at room temperature. However, on heating under reflux in dichloromethane with 1.2–1.5 equivalent of vinylferrocene, complex **IV** affords >80% yield of complex **III**.

(10) Maishal, T. K.; Sinha-Mahapatra, D. K.; Paranjape, K.; Sarkar, A. *Tetrahedron Lett.* **2002**, *43*, 2263.