Chelated Ruthenium Catalysts for Z-Selective Olefin Metathesis

Koji Endo and Robert H. Grubbs*

Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States

S *Supporting Information*

ABSTRACT: We report the development of ruthenium-based metathesis catalysts with chelating *N*-heterocyclic carbene (NHC) ligands that catalyze highly *Z*-selective olefin metathesis. A very simple and convenient procedure for the synthesis of such catalysts has been developed. Intramolecular C−H bond activation of the NHC ligand, promoted by anion ligand substitution, forms the appropriate chelate for stereocontrolled olefin metathesis.

Based on the continued development of well-defined catalysts, olefin metathesis has emerged as a valuable synthetic method for the formation of carbon−carbon double bonds.[1] Among the frontiers of catalyst development has been the quest for Z-selective olefin metathesis catalysts which would enable access to complex natural products[2] and stereoregular unique polymers.[3] Specifically, the use of Z-selective catalysts in olefin cross-metathesis (CM) represents a promising and useful methodology in organic chemistry. However, due to the thermodynamic nature of metathesis,[4] most catalysts give a higher proportion of the thermodynamically favored *E* olefin isomer. This fundamental aspect of olefin metathesis has limited its applications in some areas of chemistry.

Recently, some ruthenium-based catalysts which showed enhanced Z-selectivity have been reported; however, their selectivity is still not satisfactory for precisely stereocontrolled syntheses.[5] On the other hand, recently developed molybdenum- and tungsten-based catalysts have shown outstanding Z-selectivity in CM[2] and metathesis homocoupling[6] of terminal olefins. In particular, a bulky aryloxide-substituted Mo catalyst afforded the cross-coupled product of enol ether and allylbenzene with 98% of the Z isomer. As has been demonstrated in the past, Ru- and Mo-based systems show significant differences in selectivities and utility.[7]

For general use, metathesis catalysts should be not only tolerant toward various functional groups and impurities in reaction media but also readily synthesized from common reagents by simple reaction steps. Here, we report chelated Ru catalysts that catalyze highly Z-selective olefin metathesis, and their facile synthetic preparation.

We chose $[H_2IMes_2]RuCl_2[=CH\text{-}o\text{-}(O^iPr)C_6H_4]$ (**1a**, H_2I = imidazolidinylidene, Mes = mesityl) and the bulkier $[H_2IMesAdm]RuCl_2[=CH\text{-}o\text{-}(O^iPr)C_6H_4]$ (**1b**, Adm = 1-adamantyl) as precursors. **1b** was readily synthesized from commercially available **2** in excellent yield (Scheme 1).[8]

Reaction of **1a** with excess silver pivalate resulted in the formation of **3a**, which was observed only at early reaction

Scheme 1. Synthesis of 1b
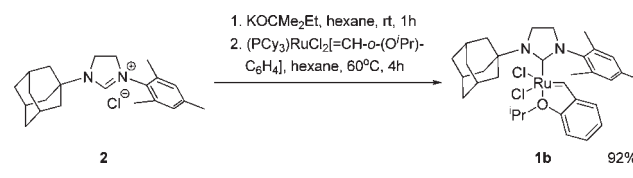
Scheme 2. Synthesis of 4a
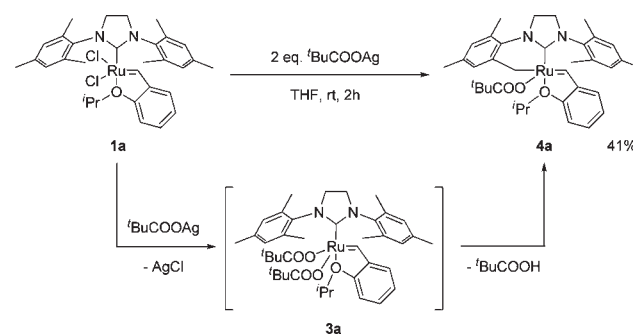
times.[9] Subsequent intramolecular C−H bond activation at the methyl position of the mesityl group resulted in the formation of **4a** with concomitant release of pivalic acid (Scheme 2). Such intramolecular C−H bond activations assisted by carboxylate ligands have been reported in other organometallic complexes.[10] Based on these previous reports, a plausible mechanism for the C−H bond activation in **3a** contains a six- (**A**) or four-membered (**B**) transition state (Figure 1). It should be noted that no other anionic ligands, including sulfonate,[5b] phosphonate,[5b] and trifluoroacetate,[11] promote such intramolecular C−H bond activation in **1a**. An X-ray crystal structure of **4a** clearly indicates C−H bond activation at the NHC ligand and subsequent formation of the six-membered chelated complex (Figure 2).

When **1b** was reacted with excess silver pivalate, C−H bond activation occurred at the adamantyl group, which resulted in the formation of the five-membered chelate complex $[(C_{10}H_{14})\text{-}H_2IMes]RuCl_2[=CH\text{-}o\text{-}(O^iPr)C_6H_4]$ (**4b**, Scheme 3). No dicarboxylate complex was detected as the C−H bond activation of **1b** was too fast, but observation of pivalic acid suggests the same reaction mechanism of intramolecular C−H bond activation. The C−H bond activation at the adamantyl group and the fast reaction may be attributed to the ligand geometry in **1b**. An X-ray
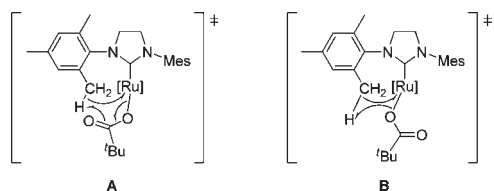
Figure 1. Plausible transition states of the intramolecular C—H bond activation in **3a**.

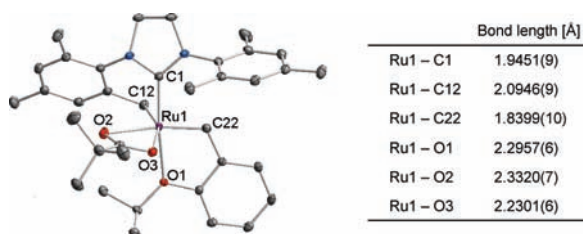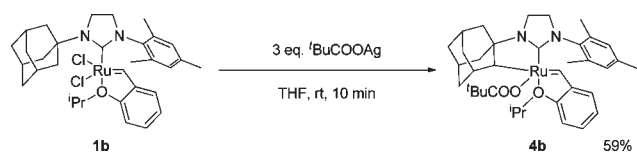|	Bond length [Å]
Ru1 – C1	1.9451(9)
Ru1 – C12	2.0946(9)
Ru1 – C22	1.8399(10)
Ru1 – O1	2.2957(6)
Ru1 – O2	2.3320(7)
Ru1 – O3	2.2301(6)

Figure 2. X-ray crystal structure and selected bond lengths of **4a**. Displacement ellipsoids are drawn at 50% probability. For clarity, hydrogen atoms have been omitted.

Scheme 3. Synthesis of 4b

crystal structure of **1b** showed that the adamantyl group is proximal to a vacant coordination site where the C—H bond activation occurs, and the distance between Ru and C12, where a new bond forms after C—H bond activation, is relatively short (2.80 Å).[12] The molecular structure of **4b** determined by X-ray crystallography revealed an adamantyl-contained chelate, which confirmed intramolecular C—H bond activation at the adamantyl group (Figure 3).

Complexes having a chelating NHC ligand derived from intramolecular C—H bond activation have been reported.[13] Most of them were formed during catalyst decomposition, and none have been reported to have catalytic activity. We investigated at first whether **4a,b** were still "active" as olefin metathesis catalysts, testing them in standard ring-closing metathesis (RCM) of diethyldiallyl malonate (**5**)[14] and ring-opening metathesis polymerization (ROMP) of norbornene (**7**). As shown in Figure 4, **4a,b** were metathesis active in the RCM reaction although activities were lower than with **1a**. Because of catalyst decomposition, conversion by **4a** was limited to ∼14%. On the other hand, **4b** was able to achieve almost full conversion at higher temperature (70 °C). In the ROMP of **7** affording polynorbornene (**8**), **4a,b** both showed high activities at the presented conditions.[16]

Encouraged by the results of the standard metathesis assays, we then tested the CM of allylbenzene (**9**) and *cis*-1,4-diacetoxy-2-butene (**10**).[14] Selected data of the CM are summarized in Table 1. Surprisingly, **4a,b** gave a much lower E/Z ratio of the cross-coupled product **11** (entries 1 and 2) compared to their parent nonchelated catalysts (entries 6 and 7). The E/Z ratio of

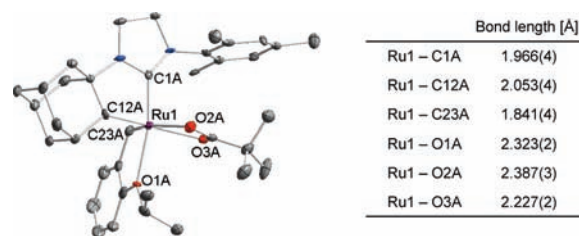|	Bond length [Å]
Ru1 – C1A	1.966(4)
Ru1 – C12A	2.053(4)
Ru1 – C23A	1.841(4)
Ru1 – O1A	2.323(2)
Ru1 – O2A	2.387(3)
Ru1 – O3A	2.227(2)

Figure 3. X-ray crystal structure and selected bond lengths of **4b**. Displacement ellipsoids are drawn at 50% probability. For clarity, hydrogen atoms have been omitted.
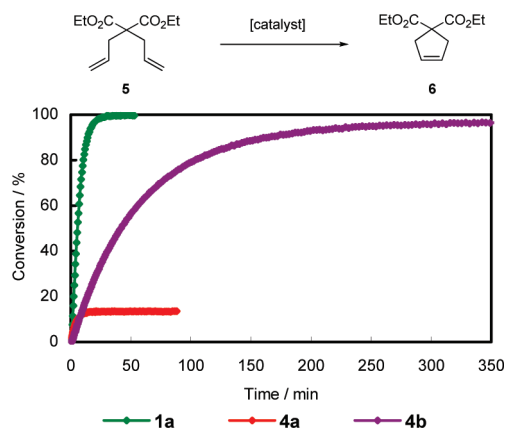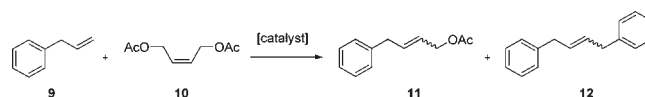

Figure 4. Plot of conversion versus time for the RCM of **5**. Reaction conditions were as follows. **1a**:[15] 1.0 mol % catalyst, 0.1 M substrate, 30 °C, CD_2Cl_2. **4a**: 1.0 mol % catalyst, 0.1 M substrate, 30 °C, C_6D_6. **4b**: 5.0 mol % catalyst, 0.1 M substrate, 70 °C, C_6D_6.

0.12 (90% Z isomer) with **4b** is among the lowest reported for Ru-based olefin metathesis catalysts. In addition, the homo-coupled product **12** afforded by **4b** also showed significantly low E/Z ratio (E/Z = 0.06, 95% Z isomer). The conversion to **11** was improved under THF reflux conditions, maintaining excellent Z-selectivity (entry 3). This was probably a result of more efficient removal of ethylene which was generated during the course of reaction. Unexpectedly, addition of water led to higher conversions and selectivity for the Z olefin products (entry 4). This result implies not only that water can be used to optimize reaction conditions but also that **4b** is tolerant toward water in organic solvent. Thus, dry solvent is not necessary for **4b** in olefin metathesis reactions. This feature enables easy use of the catalyst in common organic and polymer syntheses without strict reaction conditions. However, **4b** decomposed immediately when exposed to oxygen in solution, meaning that degassing of solvent is required to achieve high conversion. Notably, the reaction was reproducible on a synthetic scale (mmol scale, entry 5).

In summary, we have demonstrated the utility of chelated ruthenium catalysts for Z-selective olefin cross-metathesis reactions. The Z-selectivity achieved by **4b** is the best among reported Ru-based catalysts and comparable to those achieved with Mo- and W-based catalysts. Notably, this is the first time that Z-selectivity in the cross-metathesis of two different olefins has been demonstrated using a Ru-based catalyst. The Ru catalyst is readily synthesized from common reagents via simple reaction steps and is stable in the presence of water, which should

8526

dx.doi.org/10.1021/ja202818v |*J. Am. Chem. Soc.* 2011, 133, 8525–8527

Table 1. CM of 9 and 10[a]

						11		12	
entry	cat.	cat. load., mol %[b]	solvent	temp, °C	time, min	conv,[c] %	E/Z[d]	conv,[c] %	E/Z[d]
1	4a	2.5	C_6H_6	23	10	57.5	1.44	3.3	1.21
					60	57.4	1.44	3.0	0.69
2	4b	5.0	C_6H_6	70	30	32.5	0.13	24.8	0.07
					120	36.4	0.12	26.0	0.06
3	4b	5.0	THF	reflux	240	59.5	0.19	31.6	0.04
4	4b	5.0	THF/H_2O[e]	reflux	240	64.4	0.14	28.6	0.03
5[f]	4b	5.0	THF/H_2O[e]	reflux	240	61.6[g]	0.14	NA[h]	0.03
6	1a	2.5	C_6H_6	23	1	69.7	10.5	5.9	5.22
					30	66.3	10.7	10.2	6.86
7	1b	2.5	C_6H_6	23	1	0.15	3.10	NA[i]	NA[i]
					30	0.23	2.90	NA[i]	NA[i]

[a] Unless otherwise stated, all reactions were carried out using 0.20 mmol of **9**, 0.40 mmol of **10**, and 0.10 mmol of tridecane (internal standard for GC analysis) in 1.0 mL of solvent. [b] Catalyst loading based on **9**. [c] Conversion of **9** to the product determined by GC analysis. [d] Molar ratio of E and Z isomers of the product determined by GC analysis. [e] THF/H_2O = 1:1 (by volume). [f] Reaction was carried out using 1.0 mmol of **9**, 2.0 mmol of **10**, and 0.050 mmol of catalyst in 5.0 mL of solvent. [g] Isolated yield. [h] **12** was obtained with impurities. [i] GC signal of **12** was too small to quantify.

promote its application in precisely stereocontrolled organic and polymer syntheses.

■ ASSOCIATED CONTENT

ⓢ **Supporting Information.** Experimental procedures and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
rhg@caltech.edu

■ ACKNOWLEDGMENT

■ REFERENCES

(1) (a) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012–3043. (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29. (c) Schrock, R. R. *Chem. Rev.* **2002**, *102*, 145–179. (d) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 4592–4633. (e) Samojłowicz, C.; Bieniek, M.; Grela, K. *Chem. Rev.* **2009**, *109*, 3708–3742. (f) Vougioukalakis, G.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746–1787.

(2) Meek, S. J.; O'brien, R. V.; Llaveria, J.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2011**, *471*, 461–466.

(3) (a) Flook, M. M.; Jiang, A. J.; Schrock, R. R.; Muller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7962–7963. (b) Flook, M. M.; Gerber, L. C. H.; Debelouchina, G. T.; Schrock, R. R. *Macromolecules* **2010**, *43*, 7515–7522. (c) Torker, S.; Müller, A.; Chen, P. *Angew. Chem. Int. Ed.* **2010**, *49*, 3762–3766. (d) Flook, M. M.; Ng, V. W. L.; Schrock, R. R. *J. Am. Chem. Soc.* **2011**, *132*, 1784–1786.

(4) Grubbs, R. H., Ed. *Handbook of Metathesis*; Wiley-VCH: Weinheim, 2003; Vols. 1—3.

(5) (a) Rosen, E. L.; Sung, D. H.; Chen, Z.; Lynch, V. M.; Bielawski, C. W. *Organometallics* **2010**, *29*, 250–256. (b) Teo, P.; Grubbs, R. H. *Organometallics* **2010**, *29*, 6045–6050.

(6) (a) Jiang, A. J.; Zhao, Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 16630–16631. (b) Marinescu, S. C.; Schrock, R. R.; Müller, P.; Takase, M. K.; Hoveyda, A. H. *Organometallics* **2011**, *30*, 1780–1782.

(7) Cortez, G. A.; Baxter, C. A.; Schrock, R. R.; Hoveyda, A. H. *Org. Lett.* **2007**, *9*, 2871–2874.

(8) Jafarpour, L.; Hillier, A. C.; Nolan, S. P. *Organometallics* **2002**, *21*, 442–444.

(9) **3a** was detected by ${}^1H$ NMR and FAB-MS. See details in the Supporting Information.

(10) (a) Davies, D. L.; Donald, S. M. A.; Al-Duaij, O.; Macgregor, S. A.; Pölleth, M. *J. Am. Chem. Soc.* **2006**, *128*, 4210–4211. (b) Li, L.; Brennessel, W. W.; Jones, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 12414–12419. (c) Li, L.; Brennessel, W. W.; Jones, W. D. *Organometallics* **2009**, *28*, 3492–3500. (d) Tsurugi, H.; Fujita, S.; Choi, G.; Yamagata, T.; Ito, S.; Miyasaka, H.; Mashima, K. *Organometallics* **2010**, *29*, 4120–4129.

(11) Krause, J. O.; Nuyken, O.; Wurst, K.; Buchmeiser, M. R. *Chem. Eur. J.* **2004**, *10*, 777–784.

(12) For X-ray crystal structure and selected bond lengths of **1b**, see the Supporting Information.

(13) (a) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546–2558. (b) Leitao, E. M.; Dubberley, S. R.; Piers, W. E.; Wu, Q.; McDonald, R. *Chem. Eur. J.* **2008**, *14*, 11565–11572.

(14) Ritter, T.; Hejl, A.; Wenzel, A. G.; Funk, T. W.; Grubbs, R. H. *Organometallics* **2006**, *25*, 5740–5745.

(15) The RCM data were referred to ref 14.

(16) For reaction conditions and results, see the Supporting Information.

8527

dx.doi.org/10.1021/ja202818v |*J. Am. Chem. Soc.* 2011, 133, 8525–8527