Ring-Opening Metathesis. A Ruthenium Catalyst Caught in the Act

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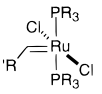
Selectivity and reactivity in olefin metatheses are dictated by the nature of the intermediates involved in the catalytic cycle. For example, the stability and molecular weight distribution of living polymers in ring-opening metathesis polymerization (ROMP, eq 1)[1] are thought to be affected not only by the ligands of the initial catalyst (*i.e.*, **1**−**4**)[2] but also by the local functionality attached to the growing alkylidene.[3] Similarly,



1 R = Cy, R' = Ph
2 R = Cy, R' = HC=CPh$_2$
3 R = Ph, R' = Ph
4 R = Ph, R' = HC=CPh$_2$

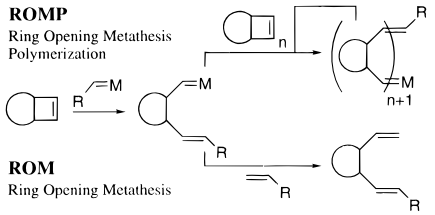
the alkylidenes transiently formed during olefin cross-metatheses strongly influence the product selectivity observed in ring-opening metathesis (ROM, eq 2).[4] The work reported herein offers insight into these mechanistic issues. Specifically, we detail our studies on a novel metathesis-active ruthenium alkylidene isolated in a stoichiometric ring-opening metathesis, a ruthenium complex that contains an intramolecularly-coordinated alkene in place of one of the phosphine ligands.

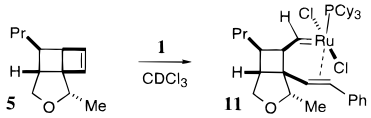
While exploring selectivity issues in the ROM of functionalized cyclobutenes (Table 1), we noted that substituents near the strained ring strongly influence the outcome of the reaction.[4b] While substrates with a methyl group in one configuration provide a moderately regio- and highly stereoselective ROM (entries 1 and 2), substrates with a methyl in the opposite stereochemistry fail to undergo a ROM (entries 3 and 4). Further studies establish that all the cyclobutenes in Table 1 react with **1** to yield new ruthenium alkylidenes; however, unlike the complexes derived from **5** and **6**, the new ruthenium complexes derived from **9** and **10** do not go on to the expected ROM products when excess monosubstituted olefin is introduced.[4c] Examination of the alkylidene (**11**) generated from the addition of **1** to cyclobutene **5** (eq 3) by NMR indicated that only one tricyclohexylphosphine ligand is bound to the ruthenium. Proton-phosphorus coupling suggested that the alkylidene hydrogen is co-planar with the ruthenium-phosphine bond (J_{HP} = 9 Hz).[2c]

Table 1. Ring-Opening Metatheses[a]

entry	substrate	major product	yield[b]
1	**5** R = Pr, R' = H	**7** R = Pr, R' = H	72% (8:1)
2	**6** R = H, R' = Pr	**8** R = H, R' = Pr	81% (7:1)
3	**9** R = Pr, R' = H	–	0%
4	**10** R = H, R' = Pr		0%

[a] Cross-metathesis of cyclobutene substrates with TBS-pent-4-en-1-ol catalyzed by 5 mol % of **1**. [b] Isolated yields after silica gel chromatography (regioisomeric ratios; *trans* for major isomer:*cis* and *trans* for minor regioisomer).





It is noteworthy that complex **11** has sufficient stability to be purified to homogeneity in 70% yield through silica gel chromatography. Crystallization of **11** allowed for determination of its structure (Figure 1). As suggested by solution NMR data, the alkylidene C−H is *syn*-periplanar to a single tricyclohexylphosphine ligand. It is noteworthy that, in comparison with related metathesis-active ruthenium complexes (**1**−**4**), one of the phosphine ligands has been replaced by a tethered olefin. The novel structural arrangement of this complex is of particular interest since it is consistent with the general structure proposed by Grubbs *et al.* for the active terminus in ruthenium-catalyzed ROMP processes.[5]

As illustrated in eqs 4−6, complex **11** purified away from the second phosphine ligand, as well as minor contaminants,[7] is an active olefin metathesis catalyst. Diene **12** is produced in 74% yield when cyclobutene **6** and styrene are treated with 5

(1) For representative ROMP references, see: (a) Lynn, D. M.; Kanaoka, S.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 784−790. (b) Nomura, K.; Schrock, R. R. *Macromolecules* **1996**, *29*, 540. (c) Pu, L.; Wagaman, M. W.; Grubbs, R. H. *Macromolecules* **1996**, *29*, 1138−1143. (d) Chauvin, Y.; Saussine, L. *Macromolecules* **1996**, *29*, 1163−1166. (e) Dorogovets, T. E.; Mudarisova, R. K.; Monakov, Y. B. *Bashk. Khim. Zh.* **1995**, *2*, 19−29. (f) Kanaoka, S.; Grubbs, R. H. *Macromolecules* **1995**, *28*, 4707−4713. (g) Wu, Z.; Grubbs, R. H. *Macromolecules* **1995**, *28*, 3502−3508. (h) Mortell, K. H.; Gingras, M.; Kiessling, L. L. *J. Am. Chem. Soc.* **1994**, *116*, 12053−12054.

(2) For representative metathesis catalysts references, see: (a) Feldman, J.; Schrock, R. R. In *Progress in Inorganic Chemistry*; Lippard, S. J., Ed.; John Wiley & Sons, Inc.: New York, 1991; Vol. 39, pp 1−74. (b) Grubbs, R. H.; Pine, S. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 5, Chapter 9.3. (c) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100−110. (d) Weck, M.; Schwab, P.; Grubbs, R. H. *Macromolecules* **1996**, *29*, 1789−1793. (e) Nugent, W. A.; Feldman, J.; Calabrese, J. C. *J. Am. Chem. Soc.* **1995**, *117*, 8992−8998. (f) Nguyen, S. T. Ph.D. Thesis, California Institute of Technology, January 1995. (g) Wu, Z.; Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 5503−5511. (h) Wache, S.; Herrmann, W. A.; Artus, G.; Nuyken, O.; Wolf, D. *J. Organomet. Chem.* **1995**, *491*, 181−188. (i) Grubbs, R. H. *J. Macromol. Sci., Pure Appl. Chem.* **1994**, *A31*, 1829−1833. (j) Schrock, R. R. *Pure Appl. Chem.* **1994**, *66*, 1447−1454. (k) Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9858−9859. (l) Couturier, J.-L.; Tanaka, K.; Leconte, M.; Basset, J.-M.; Ollivier, J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 112−114.

(3) (a) Brzezinska, K.; Wolfe, P. S.; Watson, M. D.; Wagener, K. B. *Macromol. Chem. Phys.* **1996**, *197*, 2065−2074. (b) Patton, P. A.; McCarthy, T. J. *Macromolecules* **1987**, *20*, 778−782. (c) Hamilton, J. G.; Ivin, K. J.; McCann, M.; Rooney, J. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1379−1381.

(4) (a) Randall, M. L.; Tallarico, J. A.; Snapper, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 9610−9611. (b) Snapper, M. L.; Tallarico, J. A.; Randall, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 1478−1479. (c) Tallarico, J. T.; Randall, M. L.; Snapper, M. L. *Tetrahedron* **1997**, *53*, in press. (d) Bespalova, N. B.; Bovina, M. A.; Sergeeva, M. B.; Oppengeim, V. D.; Zaikin, V. G. *J. Mol. Catal.* **1994**, *90*, 21−27. (e) Schneider, M. F.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 411−412. (f) Schneider, M. F.; Lucas, N.; Velder, J.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 257−259.

(5) Wu, Z.; Benedicto, A. D.; Grubbs, R. H. *Macromolecules* **1993**, *26*, 4975−4977.

(6) Crystallographic data for **11**: $C_{37}H_{57}Cl_2OPRu$, fw = 411.87, monoclinic, space group = $P2_1/n$, color = yellow, unit cell parameters a = 12.399(2) Å, b = 13.067(3) Å, c = 22.177(3) Å, α = 90°, β = 100.837-(11)°, γ = 90°, V = 3529.0(11) Å^3, Z = 4, T = 163 K. Full-matrix least-squares on F^2 with 9632 reflections (5629 independent reflections, 379 parameters) converged to $R_1(I > 2\sigma(I))$ = 0.0567, wR2(all data) = 0.1031, GOF = 1.192.

(7) Minor contaminants include unreacted **1**, **5**, and the regioisomeric alkylidene complex.

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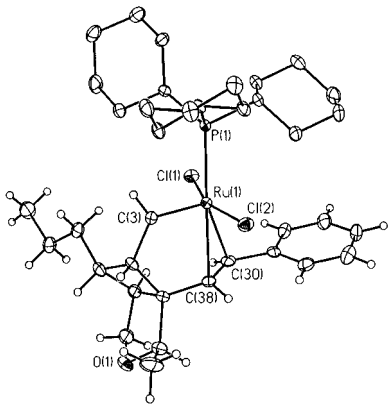
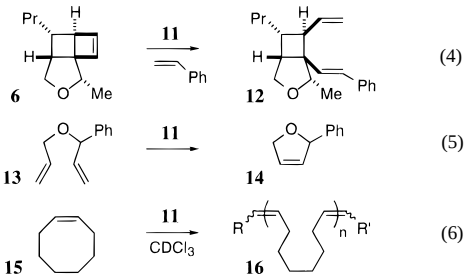


Figure 1. ORTEP drawing of **11** with 30% thermal ellipsoids.[6]

mol % of **11** (eq 4). Similarly, ring-closing metathesis (RCM)

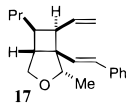
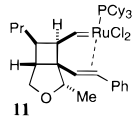
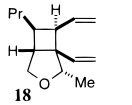
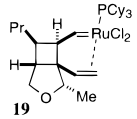


of **13** with 1 mol % of **11** provides **14** in 84% yield (eq 5).[8] Moreover, ^{1}H NMR studies monitoring the ROMP of cyclooctene (**15**) indicate that the initiation rate of catalyst **11** is four times slower while the propagation rate is approximately eight times faster than the corresponding initiation and propagation rates for catalyst **1** (eq 6).[2k] The higher propagation activity of **11** is consistent with the known inhibitory effects of excess phosphine on the rate of metathesis for other ruthenium systems.[9] Furthermore, the slower initiation rate can be explained by the increased steric congestion about the alkylidene compared to complex **1**.[10]

Structural variants of ruthenium catalyst **11** that display faster initiation rates could prove useful for various ROM, ROMP, and RCM applications. While it appears difficult to generate a variety of these complexes from other strained ring systems, related alkylidenes are indeed accessible by mixing 1,5-diene-containing precursors with catalyst **1**. Two examples of this stoichiometric transformation are shown in Table 2.

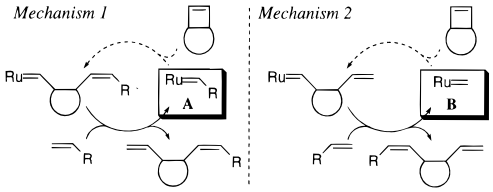
The insight that complex **11** provides into the nature of the ROM catalytic cycle is also of importance.[11] As summarized in Scheme 1, early work predicted that the reactivity of alkylidene **A** is, in part, responsible for the high cross-metathesis selectivity observed in ROM (*Mechanism 1*);[12] however, a more recent contribution suggested that **B** may have a role in the catalytic cycle (*Mechanism 2*).[4f] Identification of the products formed when **11** or **19** is treated with a monosubstituted olefin should differentiate between the two possible catalytic cycles. A mechanism that involves intermediate **A** would predict dienes **17** or **18** as products (eq 7). On the other hand, if **B** is involved,

Table 2. New ruthenium alkylidenes[a]

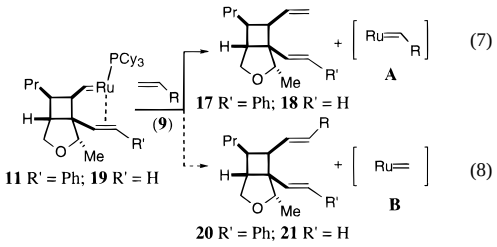
entry	diene	new alkylidene
1	 **17**	 **11**
2	 **18**	 **19**

[a] New alkylidenes are formed by reacting 1 equiv of diene with **1**.

Scheme 1. Active Alkylidenes in ROM Catalytic Cycle



products **20** or **21** should be obtained (eq 8). Treatment of **11** or **19** with monosubstituted olefins such as styrene provides exclusively dienes **17** or **18**. Furthermore, if cyclobutene **9**, which traps the newly formed alkylidene (**A** or **B**), is included in the experiment, similar results are obtained. These results support the involvement of alkylidene **A** in the ROM catalytic cycle (*Mechanism 1*).



In summary, the isolation and characterization of ROM intermediate **11** has allowed for several advances in the understanding of ruthenium-catalyzed olefin metatheses. Since metathesis active complex **11** contains only one tricyclohexylphosphine ligand, the auxiliary nature of one of the two phosphine ligands found in catalysts **1**−**4** is demonstrated. In addition, alkylidene **11** provides insight into the structural nature of metathesis-active termini of relevant living polymers. Furthermore, stoichiometric reactions between complex **11** and monosubstituted olefins serve to identify the ruthenium alkylidenes involved in the ROM catalytic cycle. Finally, the preparation and isolation of novel ruthenium complexes based on complex **11** should provide a new platform for metathesis catalysts with differing but useful reactivity profiles. It is our hope that understanding the structural and electronic features at work in ROMP and ROM processes will prove helpful in applying metathesis toward new synthetic challenges, as well as for developing the next generation of catalytic systems.

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Supporting Information Available: Experimental procedures and data on new compounds, as well as crystallographic details are provided (14 pages). See any current masthead page for ordering and Internet access instructions.

JA971285R

(8) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856−9857.

(9) Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897.

(10) As pointed out by the referees, displacement of the intramolecularly coordinated olefin could also account for the slower initiation rate of complex **11**. Further studies are required to distinguish between these possibilities. Also see ref 3b.

(11) Care must be exercised in relating complex **11** to the catalytic cycle (Halpern postulate: "compounds that are readily isolable are probably not true intermediates." Spessardm, G. O.; Miessler, G. L. *Organometallic Chemistry*; Prentice-Hall, Inc.: Upper Saddle River, NJ 1996; p 278).

(12) Bencze, L.; Ivin, K. J.; Rooney, J. J. *J. Chem. Soc., Chem. Commu.* **1980**, 834−835. Also see ref 4a.