

Ring closing metathesis in water with or without surfactants in the presence of $\text{RuCl}_2(\text{PPh}_3)_2(\text{CHPh})$

K. Joju Davis, Denis Sinou*

*Laboratoire de Synthèse Asymétrique, Associé au CNRS, CPE Lyon, Université Claude Bernard Lyon 1, 43,
Boulevard du 11 Novembre 1918, 69622 Villeurbanne Cedex, France*

Received 23 January 2001; accepted 23 May 2001

Abstract

The ring closing metathesis (RCM) of acyclic dienes has been successfully achieved in water through the use of the Grubbs' catalyst $\text{RuCl}_2(\text{PPh}_3)_2(\text{CHPh})$, with or without surfactants. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Ring closing metathesis; Grubbs' catalyst; Water; Surfactants

1. Introduction

Organometallic homogeneous catalysis is now a well-used methodology in organic synthesis and has resulted in an increasing number of applications for the production of chemicals [1,2]. Generally, these systems have the advantages of high activity as well as high selectivity, and also good reproducibility. Most chemical transformations, in the laboratory or in the industry, need organic solvents as reaction media. Due to environmental problems, there is a need to use water as a solvent: water is safe, benign and cheap. However, one of the problems is the insolubility of most organic substances in water, even if water-soluble organometallic catalysts are now well known [3]; a decrease of reaction rate is often observed and, therefore, increase of catalyst loading or reaction temperature is usually needed. One way to improve the solubility of organic substrates in water, as well as that of the homogeneous organometallic cat-

alyst, is the use of surfactants that can form micelles. Indeed, surfactants have been used in organometallic catalysis such as hydrogenation [4–15], even in an asymmetric way, hydroformylation [16], Suzuki coupling reaction [12,17–20], and more recently allylic alkylation [21,22].

The recent development of ruthenium and molybdenum catalysts, such as $(\text{PCy}_3)_2\text{Cl}_2\text{Ru}=\text{CHPh}$ [23,24] or $\text{Mo}(\text{CHCMe}_2\text{Ph})[\text{N}(2,6\text{-}(i\text{-Pr})_2\text{C}_6\text{H}_3)][\text{OCMe}(\text{CF}_3)_2]_2$ [25] for metal catalyzed olefin metathesis, has an important impact in synthetic organic chemistry.¹ Some water-soluble ruthenium complexes have been prepared and have been shown to initiate ring closing metathesis (RCM) in water [31–33]. Classical initiators are also active for ring opening metathesis polymerization (ROMP) in aqueous media [34–37].

As a continuous interest in the field of organometallic catalysis in water, we expected that the RCM reaction could be performed under these conditions using the commercially available Grubbs' catalyst. We have

* Corresponding author. Tel.: +33-4-72-446263;
fax: +33-4-72-448160.
E-mail address: sinou@univ-lyon1.fr (D. Sinou).

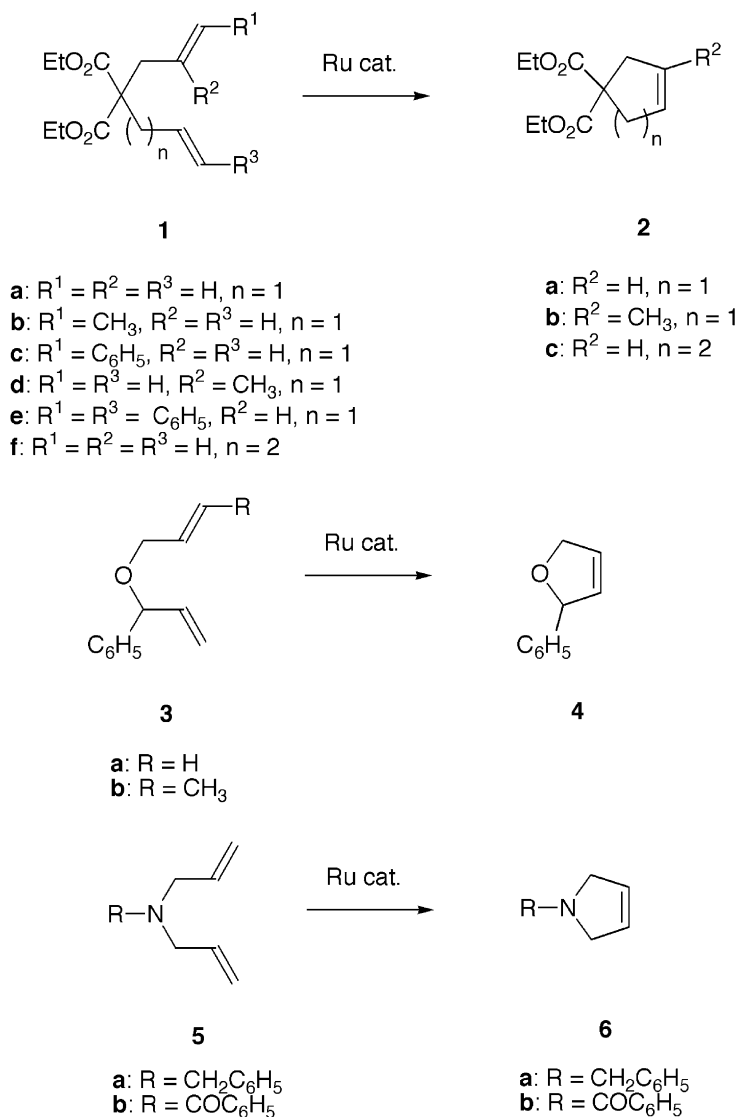
¹ For recent reviews on the use of olefin metathesis in organic chemistry, see [26–30].

detailed in this paper a full account of our study in this field.

2. Experimental

All manipulations and reactions involving ruthenium alkylidenes were performed by the use of standard Schlenk techniques under an atmosphere of nitrogen. Distilled deionized water was used and

was rigorously degazed by purging with nitrogen. Substrates **1a** [38], **1b** [38], **1c** [39], **1d** [40], **1e** [41], **1f** [38], **3a** [42], **3b** [43], **5a** [44], **5b** [45], and products **2a** [46], **2b** [47], **2c** [48], **4** [49], **6a** [50] and **6b** [50], have been previously prepared. All detergents, sodium dodecyl sulfate (SDS), sodium dodecyl sulfonate (SDSO₃Na), cetyltrimethylammonium hydrogen sulfate (CTAHSO₄), decaoxyethylene dodecyl ether (Brij 35), polyoxyethylenesorbitane monopalmitate (Tween 40), *N*-hexadecyl-*N,N*-



Scheme 1.

dimethyl-3-ammonio-1-propanesulfonate (HDAPS), *N*-dodecyl-*N,N*-dimethyl-3-ammonio-1-propanesulfonate (DDAPS), and $(\text{PCy}_3)_2\text{Cl}_2\text{Ru} = \text{CHC}_6\text{H}_5$, are from commercial sources and used as obtained. The conversions were determined by GLC with a 30 m capillary OV1 column after calibration.

2.1. General RCM procedure

In a typical reaction, Grubbs' catalyst (10 mg, 5 mol%) and surfactant (0.05 M) were placed in a Schlenk tube under nitrogen, and water (1.5 ml) was added, followed by diene substrate (0.25 mM). The reaction mixture was vigorously stirred at room temperature for the indicated time. The reaction mixture was quenched by exposure to air for 6 h, and it was extracted with diethyl ether (2×5 ml). The ether solution was dried over sodium sulfate and concentrated under reduced pressure. The product was analyzed by gas chromatography and ^1H NMR spectra, and eventually purified by column chromatography.

3. Results and discussion

Initial attempt to study the activity of $(\text{PCy}_3)_2\text{Cl}_2\text{Ru} = \text{CHC}_6\text{H}_5$ toward RCM in water in the presence of surfactant is centered upon the cyclization of diethyl diallylmalonate **1a** (Scheme 1). Cyclopentene diester **2a** was obtained with 51% conversion after 1 h reaction at room temperature in the presence of 5 mol% catalyst when the cyclization was performed in water without any surfactant (Table 1, entry 1). Addition of SDS as the surfactant in a ratio $[\text{substrate}]/[\text{SDS}] = 5$ gave almost quantitatively the cyclized product **2a** after 1 h, and even after 30 min, although 58% conversion was observed after 15 min (Table 1, entries 2–4). This increase in reaction rate is probably due to the formation of micelles. Unfortunately, no insight about the mechanism of the educt and product transfer during the reaction was possible. It is to be noticed that decreasing the catalyst concentration to 1 mol% gave only 53% conversion in **2a** after 1 h (Table 1, entry 5). Surprisingly, increasing or decreasing the amount of surfactant gave also lower conversion (Table 1, entries 6 and 7). Fig. 1 shows the difference in the reaction rates using various amounts of surfactants.

We also performed the RCM reaction in the presence of another anionic surfactant, SDSO_3Na (Table 1, entries 8–10). We obtained lower conversions in **2a** close to those obtained in water only, whatever be the surfactant concentration.

We then used the cationic surfactant CTAHSO_4 (Table 1, entries 11–17). We obtained only 44 and 66% conversion after 30 min and 1 h, respectively. Increasing the amount of surfactant increased slightly the conversion, although decreasing this amount had no influence on the conversion. So, it seems that there is no influence of a cationic surfactant on the activity of the catalyst.

The use of non-ionic surfactants such as Brij 35 (Table 1, entries 18 and 19) or Tween 40 (Table 1, entries 20 and 21) gave almost the same conversion, quite similar to those observed in water alone, whatever be the amount of surfactant used.

Finally, the zwitterionic surfactants HDAPS (Table 1, entries 22–25) or DDAPS (Table 1, entry 26) also gave quite similar results, with no influence of the amount of surfactant on the conversion: approximately 40–45% conversion was obtained after 30 min reaction.

We then extended the RCM reaction in water catalyzed by $(\text{PCy}_3)_2\text{Cl}_2\text{Ru} = \text{CHC}_6\text{H}_5$ to other dienes in the presence or not of the surfactant. Treatment of **1b** with 5 mol% catalyst in water in the presence of SDS as the surfactant gave 94% conversion to cyclic diester **2a** after 30 min (Table 2, entry 4). Surprisingly, we observed 95% conversion when the reaction was performed without surfactant (Table 2, entry 3), although the water system is completely heterogeneous. Even decreasing the catalyst concentration to 2.5 mol% gave the cyclized product **2a** in 96% conversion after 10 min, compared to 89% in the presence of SDS (Table 2, entries 5 and 6); in the latter case lower conversion was observed, although the surfactant homogenized the reaction system.

Phenyl-substituted diene **1c** gave also the cyclopentene diester **2a** almost quantitatively in the presence of 5 or 2.5 mol% of the catalyst when the reaction was performed in water only (Table 2, entries 7 and 9). We noticed again in this case that the presence of the surfactant decreased slightly the activity of the catalyst (Table 2, entries 8 and 10). Dibenzylidene derivative **1e** gave no reaction at all under the above conditions

Table 1

RCM of **1a** initiated by $(PCy_3)_2Cl_2Ru = CHC_6H_5$ in water with or without various surfactants^a

Entry	Surfactant	[1a]/[surfactant]	Catalyst (mol%)	Time (min)	Conversion in 2a ^b (%)
1	No	–	5	60	51
2	SDS	5	5	60	97
3	SDS	5	5	30	96
4	SDS	5	5	15	58
5	SDS	5	1	60	53
6	SDS	10	5	30	70
7	SDS	2.5	5	30	62
8	SDSO ₃ Na	5	5	30	46
9	SDSO ₃ Na	10	5	30	42
10	SDSO ₃ Na	2.5	5	30	34
11	CTAHSO ₄	5	5	60	66
12	CTAHSO ₄	5	5	30	44
13	CTAHSO ₄	5	1	60	55
14	CTAHSO ₄	10	5	30	61
15	CTAHSO ₄	7.5	5	30	62
16	CTAHSO ₄	2.5	5	30	43
17 ^c	CTAHSO ₄	5	5	30	46
18	Brij 35	5	5	30	43
19	Brij 35	10	5	30	47
20	Tween 40	5	5	30	59
21	Tween 40	10	5	30	50
22	HDAPS	5	5	60	66
23	HDAPS	5	5	30	42
24	HDAPS	7	5	30	42
25	HDAPS	10	5	30	45
26	DDAPS	5	5	30	44

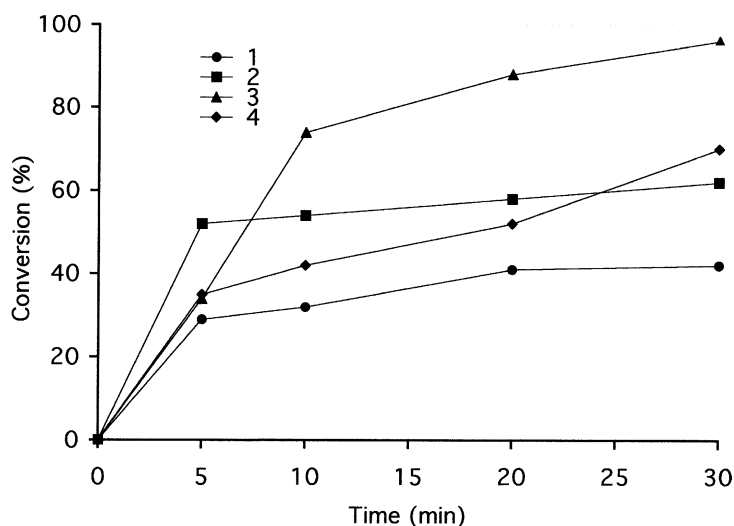
^a Reactions conditions: [substrate] = 0.17 mol l⁻¹, 1.5 ml H₂O, 25 °C, all the experiments were done at least twice.^b Determined by GC with a 30 m capillary column OV1.^c Reaction performed in 4 ml H₂O.Fig. 1. Reaction rate of the RCM of **1a** in water in the presence of various amounts of SDS: (1) without SDS; (2) [1a]/[SDS] = 2.5; (3) [1a]/[SDS] = 5; (4) [1a]/[SDS] = 10.

Table 2
RCM of **1a–f**, **3a** and **3b**, and **5a** and **5b** initiated by $(\text{PCy}_3)_2\text{Cl}_2\text{Ru} = \text{CHC}_6\text{H}_5$ in water with or without SDS^a

Entry	Substrate	Product	Surfactant	Catalyst (mol%)	Time (min)	Conversion (%) ^b (Yield %) ^c
1	1a	2a	No	5	30	42
2	1a	2a	Yes	5	30	96 (90)
3	1b	2a	No	5	30	95
4	1b	2a	Yes	5	30	94 (91)
5	1b	2a	No	2.5	10	96
6	1b	2a	Yes	2.5	10	89
7	1c	2a	No	5	30	94
8	1c	2a	Yes	5	30	82 (80)
9	1c	2a	No	2.5	10	100
10	1c	2a	Yes	2.5	10	79
11	1d	2b	No	5	30	24
12	1d	2b	Yes	5	30	23
13	1f	2c	No	5	30	95
14	1f	2c	Yes	5	30	95 (89)
15	3a	4	No	5	30	100
16	3a	4	Yes	5	30	100 (88)
17	3b	4	No	5	30	99
18	3b	4	Yes	5	30	97 (90)
19	5b	6b	No	5	30	100 (90)
20	5b	6b	Yes	5	30	26
21	5b	6b	No	5	10	87
22	5b	6b	Yes	5	10	84
23	5b	6b	Yes	5	60	9
24 ^d	5b	6b	Yes	5	30	67
25 ^e	5b	6b	Yes	5	15	73
26 ^e	5b	6b	Yes	5	30	72

^a Reactions conditions: [substrate] = 0.17 mol l^{-1} , [substrate] : [surfactant] = 5, 1.5 ml H₂O, 25 °C, all the experiments were done at least twice.

^b Determined by GC with a 30 m capillary column OV1.

^c Isolated yield after column chromatography.

^d Reaction performed under a flow of nitrogen.

^e Reaction performed under reduced pressure.

(5 mol%, 30 min, room temperature) with or without SDS.

When the gem-disubstituted olefin **1d** was exposed to 5 mol% catalyst for 30 min, cyclopentene **2b** was obtained in only 24 or 23% conversion in the absence or presence of the surfactant, respectively (Table 2, entries 11 and 12).

Cyclization of diene **1f** with 5 mol% catalyst in water without or with surfactant gave the cyclohexene diester **2c** in 95% conversion after 30 min (Table 2, entries 13 and 14).

In order to demonstrate that this methodology could be extended to a variety of dienes, ethers **3a** and **3b**, amine **5a**, and amide **5b** were examined. Ethers **3a** and **3b** were readily and quantitatively cyclized to the

dihydrofuran derivative **4** in 30 min in water in the presence of 5 mol% catalyst (Table 2, entries 15–18). There is again no effect of added surfactant on the conversion.

We observed no cyclization of the amine **5a**, as previously noticed by Grubbs and coworkers [51], whatever be the conditions used. However, amide **5b** was readily cyclized in water only in the presence of the catalyst $(\text{PCy}_3)_2\text{Cl}_2\text{Ru} = \text{CHC}_6\text{H}_5$ to give the heterocycle **6b** in 100 and 87% conversion after 30 or 10 min, respectively (Table 2, entries 19 and 21). When this cyclization was performed in the presence of SDS, formation of heterocycle **6b** was observed in 84, 26, and 9%, after 10, 30, and 60 min, respectively. This surprising behavior prompts us to perform the same

reaction under a flow of nitrogen or under reduced pressure in order to eliminate the ethylene formed in the reaction. Under these conditions, we obtained effectively the cyclized amide in 67 and 72%, respectively, even after 30 min.

4. Conclusion

In conclusion, we have demonstrated that RCM occurred in water without water-soluble catalyst using the well-known Grubbs' catalyst $\text{RuCl}_2(\text{PPh}_3)_2(\text{CHPh})$, and that surfactant is not needed. Water is an excellent medium for this reaction, although both catalyst and substrate are insoluble in water, and in spite of the heterogeneity of the system.

References

- [1] B. Cornils, W.A. Herrmann, *Applied Homogeneous Catalysis with Organometallic Compounds*, VCH, Weinheim, 1996.
- [2] M. Beller, C. Bolm, *Transition Metals for Organic Synthesis*, VCH, Weinheim, 1998.
- [3] B. Cornils, W.A. Herrmann, *Aqueous-phase Organometallic Catalysis: Concepts and Applications*, VCH, Weinheim, 1998.
- [4] G. Oehme, E. Paetzold, R. Selke, *J. Mol. Catal.* 71 (1992) L1.
- [5] I. Grassert, E. Paetzold, G. Oehme, *Tetrahedron* 49 (1993) 6605.
- [6] I. Grassert, V. Vill, G. Oehme, *J. Mol. Catal. A* 116 (1997) 231.
- [7] I. Grassert, U. Schmidt, S. Ziegler, C. Fischer, G. Oehme, *Tetrahedron* 9 (1998) 4193.
- [8] G. Oehme, I. Grassert, S. Ziegler, R. Meisel, H. Fuhrmann, *Catal. Today* 42 (1998) 459.
- [9] T. Dwars, U. Schmidt, C. Fischer, I. Grassert, R. Kempe, R. Fröhlich, K. Drauz, G. Oehme, *Angew. Chem., Int. Edit. Engl.* 37 (1998) 2851.
- [10] R. Selke, J. Holz, A. Riepe, A. Börner, *Chem. Eur. J.* 4 (1998) 769.
- [11] S. Trinkhaus, R. Kadyrov, R. Selke, J. Holz, L. Götze, A. Börner, *J. Mol. Catal.* 144 (1999) 15.
- [12] G. Oehme, I. Grassert, E. Paetzold, R. Meisel, K. Drexler, H. Fuhrmann, *Coordin. Chem. Rev.* 185–186 (1999) 585.
- [13] F. Robert, G. Oehme, I. Grassert, D. Sinou, *J. Mol. Catal.* 156 (2000) 127.
- [14] B.E. Hanson, H. Ding, C.W. Kohlpaintner, *Catal. Today* 42 (1998) 459.
- [15] H. Ding, B.E. Hanson, J. Bakos, *Angew. Chem., Int. Edit. Engl.* 34 (1995) 1645.
- [16] M.S. Goedheijt, B.E. Hanson, J.N.H. Reek, P.C.J. Kamer, P.W.N.M. van Leeuwen, *J. Am. Chem. Soc.* 122 (2000) 1650.
- [17] E. Paetzold, G. Oehme, *J. Mol. Catal.* 152 (2000) 69.
- [18] N.A. Bumagin, V.V. Bykov, L.I. Sukhomlinova, T.P. Tolstaya, I.P. Beletskaya, *J. Organomet. Chem.* 486 (1995) 259.
- [19] A.V. Cheprakov, N.V. Ponomareva, I.P. Beletskaya, *J. Organomet. Chem.* 486 (1995) 297.
- [20] D. Badone, M. Baroni, R. Cardamone, A. Ielmini, U. Guzzi, *J. Org. Chem.* 62 (1997) 7170.
- [21] S. Kobayashi, W.W.-L. Lam, K. Manabe, *Tetrahedron Lett.* 41 (2000) 6115.
- [22] C. Rabeyrin, C. Nguefack, D. Sinou, *Tetrahedron Lett.* 41 (2000) 7461.
- [23] P. Schwab, M.B. France, J.W. Ziller, R.H. Grubbs, *Angew. Chem., Int. Edit. Engl.* 34 (1995) 2039.
- [24] P. Schwab, R.H. Grubbs, J.W. Ziller, *J. Am. Chem. Soc.* 118 (1996) 100.
- [25] R.R. Schrock, J.S. Murdzek, G.C. Bazan, J. Robbins, M. DiMare, M.O. Regan, *J. Am. Chem. Soc.* 112 (1990) 3875.
- [26] M. Schuster, S. Blechert, *Angew. Chem., Int. Edit. Engl.* 109 (1997) 2036.
- [27] A. Furstner, *Top. Catal.* 4 (1997) 285.
- [28] K.J. Ivin, *J. Mol. Catal.* 133 (1998) 1.
- [29] R.H. Grubbs, S. Chang, *Tetrahedron* 54 (1998) 4413.
- [30] S.K. Armstrong, *J. Chem. Soc., Perkin Trans. I* (1998) 371.
- [31] B. Mohr, D.M. Lynn, R.H. Grubbs, *Organometallics* 15 (1996) 4317.
- [32] T.A. Kirkland, D.M. Lynn, R.H. Grubbs, *J. Org. Chem.* 63 (1998) 9904.
- [33] D.M. Lynn, B. Mohr, R.H. Grubbs, L.M. Henling, M.W. Day, *J. Am. Chem. Soc.* 122 (2000) 6601.
- [34] M.A. Hillmyer, C. Lepetit, D.V. McGrath, B.M. Novak, R.H. Grubbs, *Macromolecules* 25 (1992) 3345.
- [35] W.J. Feast, D.B. Harrison, *J. Mol. Catal.* 65 (1991) 63.
- [36] B.M. Novak, R.H. Grubbs, *J. Am. Chem. Soc.* 110 (1988) 960.
- [37] B.M. Novak, R.H. Grubbs, *J. Am. Chem. Soc.* 110 (1988) 7542.
- [38] R. Grigg, J.F. Malone, T.R.B. Mitchell, A. Ramasubbu, R.M. Scott, *J. Chem. Soc., Perkin Trans. I* (1984) 1745.
- [39] S. Hanessian, R. Leger, *J. Am. Chem. Soc.* 114 (1992) 3115.
- [40] W.J. Doran, H.A. Shoule, *J. Am. Chem. Soc.* 59 (1937) 1625.
- [41] R.S. Atkinson, J.R. Malpass, K.L. Skimer, K.L. Woodthorpe, *J. Chem. Soc., Perkin Trans. I* (1984) 1905.
- [42] M. Carda, E. Castillo, S. Rodriguez, S. Uriel, J.A. Marco, *Synlett* (1999) 1639.
- [43] M. Kunishima, K. Hioki, D. Nakata, S. Nagowa, *Chem. Lett.* (1999) 683.
- [44] G.B. Butler, R.L. Bunch, *J. Am. Chem. Soc.* 71 (1949) 3120.
- [45] N.O. Brace, *J. Org. Chem.* 36 (1971) 3187.
- [46] W.A. Nugent, J. Feldman, J.C. Calabrese, *J. Am. Chem. Soc.* 117 (1995) 8992.
- [47] E.E. Schweizer, G.J. O'Neill, *J. Org. Chem.* 30 (1965) 2082.
- [48] G.B. Bachman, H.A. Tanner, *J. Org. Chem.* 4 (1939) 493.
- [49] G.C. Fu, R.H. Grubbs, *J. Am. Chem. Soc.* 114 (1992) 5426.
- [50] F. Anderlini, *Chem. Ber.* 22 (1889) 2514.
- [51] G.C. Fu, S.T. Nguyen, R.H. Grubbs, *J. Am. Chem. Soc.* 115 (1993) 9856.