

Simple and Highly Z-Selective Ruthenium-Based Olefin Metathesis Catalyst

Giovanni Occhipinti, Fredrik R. Hansen, Karl W. Törnroos, and Vidar R. Jensen*

Department of Chemistry, University of Bergen, Allégaten 41, N-5007 Bergen, Norway

S Supporting Information

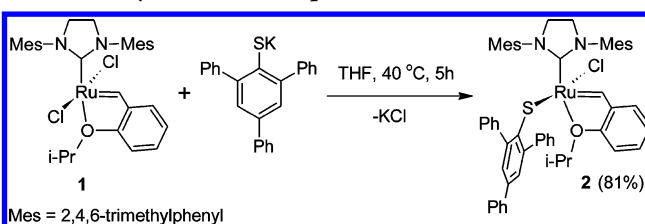
ABSTRACT: A one-step substitution of a single chloride anion of the Grubbs–Hoveyda second-generation catalyst with a 2,4,6-triphenylbenzenethiolate ligand resulted in an active olefin metathesis catalyst with remarkable *Z* selectivity, reaching 96% in metathesis homocoupling of terminal olefins. High turnover numbers (up to 2000 for homocoupling of 1-octene) were obtained along with sustained appreciable *Z* selectivity (>85%). Apart from the *Z* selectivity, many properties of the new catalyst, such as robustness toward oxygen and water as well as a tendency to isomerize substrates and react with internal olefin products, resemble those of the parent catalyst.

Olefin metathesis (OM) has evolved to become one of the most flexible ways to make C–C bonds.^{2,3} This change has to a large extent been spurred by the development of well-defined and tunable homogeneous catalysts.¹ In general, OM results in a mixture of *Z* and *E* isomers, usually with the thermodynamically preferred *E* isomer as the major component. Frequently, however, the target product is a single isomer. For example, syntheses of many natural products and pharmaceuticals require selective formation of the *Z* isomer.⁴ Thus, the development of *Z*-selective catalysts has been an important and challenging goal in OM during the last 10–15 years.

Highly *Z*-selective catalysts based on Mo and W were obtained^{5,6} by following a straightforward and intuitive strategy, namely, using two monoanionic, monodentate ligands with very different sizes to give monoalkoxide–pyrrolide (MAP) catalysts.⁶ These complexes are otherwise similar to the underlying class of “nonselective” catalysts. In contrast, the same design strategy has led to only modest selectivity for Ru.⁷ Highly *Z*-selective Ru catalysts were recently reported, but these are based on a different design involving a distinct bidentate N-heterocyclic carbene (NHC)–adamantyl ligand.^{8–10} Thus, it is not straightforward to draw upon the known structure–property relationships and the great design flexibility of the underlying class of nonselective Ru-based catalysts.^{3,11}

Herein we show that the highly *Z*-selective Ru-based OM catalyst **2** can be obtained in high yield (81%) in one step from the five-coordinate second-generation Grubbs–Hoveyda-type catalyst precursor **1** by substituting a single chloride anion with the sterically demanding 2,4,6-triphenylbenzenethiolate ligand (Scheme 1). This strategy gives the highly stereoselective catalyst **2**, in accordance with predictions from DFT calculations,¹² while largely conserving the properties of **1**.

Scheme 1. Synthesis of Complex 2



Single-crystal X-ray diffraction revealed that the molecular structure of **2** (Figure 1) is typical for Grubbs–Hoveyda

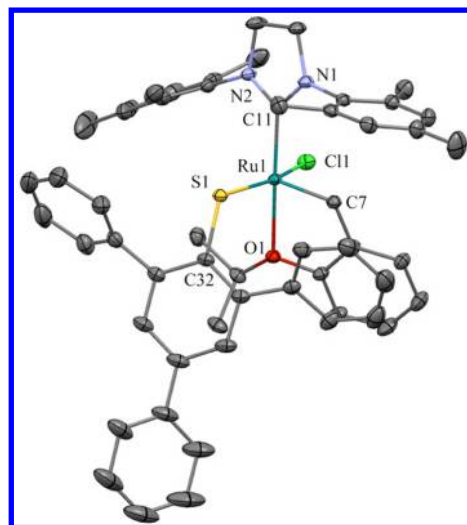


Figure 1. X-ray structure of **2** with displacement ellipsoids drawn at the 50% probability level. H atoms and solvent molecules (dichloromethane and pentane) have been omitted for clarity. Selected geometrical parameters: Ru1–C7 = 1.8343(15) Å, Ru1–C11 = 2.0026(13) Å, Ru1–Cl1 = 2.3948(4) Å, Ru1–O1 = 2.2369(11) Å, Ru1–S1 = 2.3125(4) Å, Ru1–S1–C32 = 113.30(5)°, C11–Ru1–S1 = 91.25(4)°, C11–Ru1–Cl1 = 91.65(4)°.

catalysts, featuring two anionic ligands oriented trans to each other. The regularity and lack of deviation from the structure of the underlying class of catalysts suggest that the thiolate ligand, although much larger than a chloride, does not impose much steric congestion in **2**. For example, the orientation of the NHC ligand (SIMes) is almost perfectly symmetric with respect to the

Received: November 23, 2012

Table 1. Metathesis Homocoupling of Terminal Olefins with Catalyst 2

entry	substrate	cat. loading (mol %)	P (bar)	DMAN ^a loading (mol %)	solvent	substrate conc. (M)	t (h)	T (°C)	conv. (%) ^b	yield (%) ^c	% Z ^b
1	1-octene	0.25	1	0.12	THF	4	0.5	40	17	14	86
							1.5		33	27	83
							3		45	37	81
							6		64	53 (42)	75
2 ^d	1-octene	0.25	1·10 ⁻⁵	0.12	THF	5.4	5.5	50	75	64 (55)	85
3	1-octene	5	1	2.5	THF	0.5	3	40	67	42	66
							10		>99	66	23
4	1-octene	0.01	1·10 ⁻⁵	0	neat	—	0.5	60	5	4	93
5	1-octene	0.01	1·10 ⁻⁵	0.05	neat	—	4	60	19	17 (12)	87
6	1-octene	0.01	1·10 ⁻⁵	0	neat	—	4	60	24	20 (15)	86
7	1-octene	0.01	1	0.05	neat	—	4	40	8	8 (7)	87
8	1-octene ^e	0.01	1	0.05	neat	—	0.5	40	0	0	—
9	1-hexene	0.25	1	0.12	THF	4	1.5	40	55	36 (6)	76
10	1-hexene	0.25	1·10 ⁻⁵	0.12	THF	4	1.5	40	15	12	85
							6.0		55	42 (10)	67
11	1-hexene	5	1	2.5	THF	0.5	3	40	76	49	64
							10		>99	54	26
12	1-hexene	0.04	1·10 ⁻⁵	0.2	neat	—	2	60	12	11 (3.5)	90
13	Me undecenoate ^f	0.25	1	0.12	THF	4	2	40	7	7	80
							8		46	41 (40)	60
14	allyl-TMS ^g	0.25	1	0.12	THF	4	35	40	6	3 (2.5)	96
15 ^d	allyl-TMS ^g	0.25	1	0.12	THF	4	18	60	22	12 (11)	95
16	4-phenyl-1-butene	0.25	1	0.12	THF	4	0.5	40	16	11	91
							2		73	30 (29)	89
17	allylbenzene	0.25	1	0.12	THF	4	0.5	40	44	9	82
							2		>99	13	45
18	allylbenzene	0.25	1	0	THF	4	0.5	40	38	12	80
							2		>99	14	39
19	allylbenzene	0.25	1·10 ⁻⁵	0.12	THF	4	0.5	40	26	7	83
20	allylbenzene ^h	0.25	1·10 ⁻⁵	0.12	THF	4	0.5	40	22	8	83
							2		96	27 (21)	52
21	allylbenzene	0.25	1·10 ⁻⁵	0.12	THF ⁱ	4	2	40	75	20 (15)	72
22	allyl acetate	0.25	1	0.12	THF	4	4	40	16	16	82
							8		19	19 (16)	74
23 ^d	allyl acetate	1	1	0	THF	3	1	60	13	13	93
24 ^d	allyl acetate	5	1	0	THF	0.5	22	60	100	100	81
25	N-allylaniline	0.25	1	0.12	THF	4	18	40	6	6 (5)	89
26 ^d	N-allylaniline	0.25	1	0.12	THF	4	2.5	60	28	28	87
27	2-(allyloxy)ethanol	0.25	1	0.12	THF	4	2	40	7	1	74
							8		63	1	45

^a1,8-Bis(dimethylamino)naphthalene (H⁺ sponge). ^bDetermined by ¹H NMR analysis. ^c¹H NMR yields (values in parentheses are isolated yields).

^dThe reaction conditions were partially optimized. ^eThe substrate used was stored for a long time under air, and the atmosphere employed was air rather than Ar. ^fMethyl undecenoate. ^gAllyltrimethylsilane. ^hCy₃PO (1.25 mol %) was added to the reaction mixture. ⁱContaining 5 mol % degassed water.

two anionic ligands, as shown by the nearly identical bond angles the NHC carbene atom forms with sulfur and chlorine (C11–Ru1–S1 = 91.3°, C11–Ru1–S1 = 91.7°).

Despite the presence of two sterically demanding phenyl substituents at the ortho positions, the arylthiolate ligand forms a relatively acute bond angle with Ru [Ru1–S1–C32 = 113.30(5)°]. Divalent sulfur prefers narrower bond angles than, for example, divalent oxygen, as illustrated by the wider Ru–O–C angles of aryloxy-substituted Ru–alkylidene complexes with insignificant steric congestion (127–130°).¹³ At the same time, there is little doubt that the Ru–S–C bond angle would widen in response to significant steric pressure. In a similar vein, one might speculate that the presence of severe steric congestion in **2** would impose a weakening (lengthening) of the dative Ru–O bond compared with that in **1**. In fact, the opposite

is observed, as this bond is slightly shorter in **2** [2.2369(11) Å] than in **1** [2.256(1) Å].¹⁴

Because of the acute Ru–S–C bond angle, the triphenylbenzene moiety points toward the site opposite the NHC ligand. As a result of the steric pressure from the relatively large triphenylbenzene moiety, the substituents of the alkylidene ligand and of the incoming olefin both prefer to be oriented away from this “wall”, thus promoting the formation of Z olefins.¹²

In the absence of an acid (e.g., a carboxylic acid), the stability of complex **2** is comparable to that of other Ru-based catalysts. In contrast to the case for acids, the presence of a relatively strong base such as the proton sponge 1,8-bis(dimethylamino)-naphthalene (DMAN) is tolerated very well by **2** [see the Supporting Information (SI) for details].

Solutions of **2** (e.g., in CD_2Cl_2) can be stored under Ar for a few days without signs of decomposition. The temperature stability of the new complex is good [e.g., it exhibits negligible decomposition after 24 h in tetrahydrofuran (THF) at 60 °C] but lower than that of the parent catalyst **1**. Complex **2** also tolerates well the presence of water and to some extent also oxygen.¹⁵ The oxygen tolerance of **2** appears to be better than that of the carboxylate-coordinated version of the NHC–adamantyl chelate Ru catalysts and comparable to that of the improved nitrate version of the latter.¹⁰ The substrates tested in this work were generally used as received or at most degassed.

Complex **2** was tested as a catalyst for metathesis homocoupling of nine different terminal olefins (see Table 1). To facilitate comparison, all of the substrates were tested with reaction conditions identical to those of entry 1. Despite the fact that the substrates tested displayed considerable variation in reactivity, most of them were subjected to tests using rather standard reaction conditions. In only a few cases (where indicated) were the reaction conditions partially optimized for a particular substrate.

In general, **2** displayed both high catalytic activity and *Z* selectivity, the latter frequently in the range 80–95%, which is comparable to or slightly lower than those of the best NHC–adamantyl chelate Ru catalysts.^{9,10} In fact, the activity is remarkable for a catalyst as selective as **2**, even considering the fact that many of the catalytic experiments reported for other *Z*-selective catalysts were performed at lower temperatures than those in Table 1. Nonfunctionalized linear substrates such as 1-octene and 1-hexene (entries 1–12) were easily converted to the target products, reaching turnover numbers (TONs) of up to 2000 (1500 isolated) in only 4 h in combination with a *Z* selectivity higher than 85% (entries 5–7).

The observed catalyst performance was strongly dependent on both the substrate and the reaction conditions. Low catalyst loadings, moderately high temperatures, and the presence of small amounts of coordinating solvents such as THF typically enhanced the overall performance. Before we turn to the reactions of the individual substrates, it may be instructive to consider what may be termed the “inherent selectivity” of **2**, that is, the selectivity theoretically achieved in the absence of isomerization of the product as well as competing unselective catalysts (including those potentially generated from decomposition of **2**). The inherent selectivity of **2** is clearly very high, as demonstrated by the fact that experiments run to only low conversions (to limit the influence of *Z*–*E* isomerization of the product; see below) normally reached *Z* selectivities above 85% and in some cases above 90%. Of course, a more accurate assessment of the inherent selectivity can be obtained if the internal olefin product does not react with the catalyst. This is the case for metathesis of allyltrimethylsilane (allyl-TMS), for which the two TMS groups in the product effectively shield the double bond from reaction with the catalyst, resulting in a *Z* selectivity of up to 96% (entries 14 and 15). Certainly, the inherent selectivity varies from substrate to substrate, but it is still clear that in metathesis experiments run to higher conversions, such as in entries 3 (1-octene) and 11 (1-hexene), isomerization of the product explains much more of the deviation from 100% *Z* selectivity than does “imperfect” inherent selectivity.

Z–*E* isomerization of internal olefin products, presumably proceeding via reversible OM, was quantified for the two products of 1-hexene metathesis (Table S5 in the SI). It is evident that the catalyst progressively reduced the *Z* content, while under identical reaction conditions, the corresponding isomerization of

(*E*)-5-decene was not observed. This problem stems from the ability of **2** to react with internal olefins and is a side effect of the high catalytic activity mentioned above.

A similar but weaker tendency was also observed for the NHC–adamantyl chelate Ru catalysts,^{9,10} and as was suggested for the latter catalysts, hydride-induced isomerization and secondary metathesis events mediated by nonselective metathesis-active decomposition products may be additional causes of this phenomenon.¹⁰ The presence of DMAN appeared to reduce the *Z*–*E* isomerization (e.g., see entries 5 vs 6 and 17 vs 18). Presumably, the proton sponge inhibits a catalyst decomposition pathway, thus prolonging the lifetime of **2**. The rate of *Z*–*E* isomerization depended on both the nature of the substrate and the reaction conditions and increased with substrate conversion. Unfortunately, the optimal reaction conditions also depended on the substrate. For example, high catalyst loading and high dilution were favorable for allyl acetate, allowing complete conversion with a relatively high *Z* selectivity of 81% (entry 24). In contrast, for 1-octene and 1-hexene (entries 3 and 11), very similar conditions led to almost complete loss of *Z* selectivity at close to 100% substrate conversion (after 10 h).

Similarly to **1** and other Ru-based OM catalysts, **2** also isomerizes many substrates, and this tendency appears to increase with the progress of the reaction.¹⁶ This side reaction, which may be useful for some applications,¹⁷ is believed to be caused by new Ru species generated during the catalytic metathesis transformations.¹⁸ Attempts to suppress it using acids or quinones led to partial decomposition of **2** and the formation of small amounts of **1** (as detected by ¹H NMR spectroscopy), while the addition of a small amount of either tricyclohexylphosphine oxide (Cy_3PO) or water reduced the amount of substrate isomerization, albeit at the expense of lower catalytic activity (entries 20 and 21). A similar beneficial effect was obtained using static vacuum, which also appeared to slow both isomerization and OM but increased the selectivity for the latter. The rate of substrate isomerization was also influenced by the presence of the proton sponge. However, this effect was rather small and appeared to depend on both the nature of the substrate and the reaction progress (e.g., compare entries 5 vs 6 and 17 vs 18).

Despite the above-described isomerization issues, it was possible to obtain 7-tetradecene from 1-octene in an isolated yield of 55% with a *Z* selectivity of 85% under partially optimized reaction conditions (entry 2). This result suggests that it should also be possible to obtain better yields for other substrates. However, the optimization of each individual process may be time-consuming and was beyond the scope of this work.

Methyl undecenoate (entry 13) appeared to be less reactive than 1-octene or 1-hexene and also underwent little isomerization compared with the unfunctionalized substrates above. Both the lower reactivity and the reduced tendency to isomerize for this substrate may be caused by its donor function (ester). The *Z* selectivity achieved with this substrate was somewhat lower than those obtained for 1-octene and 1-hexene.

Allyl-TMS (entries 14 and 15) turned out to be the least reactive of the present substrates, and, as mentioned above, also provided the highest *Z* selectivity because isomerization of the product was negligible. Whereas a conversion of only 6% was obtained after 35 h at 40 °C, increasing the temperature to 60 °C resulted in much improved conversion (22% after 18 h) while retaining a high *Z* selectivity (95%).

The reactivities of 4-phenyl-1-butene and allylbenzene were very high, comparable to those observed for 1-octene and 1-

hexene. As also seen for the latter olefins, the tendency of the substrate to isomerize was significant. Addition of a small amount of either C_3PO or water was found to suppress this usually undesirable side reaction to some extent (entries 20 and 21). Higher *Z* selectivity was obtained for 4-phenyl-1-butene than for allylbenzene (91 vs 82% at low conversion).

In contrast, for allyl acetate and *N*-allylaniline, no isomerization of the starting material was observed. The reactivities of these substrates were lower than that of 1-octene but higher than that of allyl-TMS. Under identical reaction conditions, the reactivity was higher for allyl acetate and the *Z* content of the product was higher for *N*-allylaniline.

Finally, we also tested 2-(allyloxy)ethanol (entry 27), which is known to be a challenging substrate because of the presence of the alcohol function. The formation of a small amount of the homocoupling product (ca. 1%) with a *Z* selectivity of 73% was observed after 2 h, along with a considerable fraction of isomerized substrate (ca. 6%).¹⁹ Longer reaction times resulted only in further isomerization of the starting material and *Z*–*E* isomerization of the product. Although it appears that **2** decomposed after only about four turnovers, the observed product formation and selectivity demonstrated at least some degree of tolerance toward this functional group. To date, the NHC–adamantyl chelate Ru catalysts are the only *Z*-selective OM catalysts for which clear robustness toward alcohol functionalities has been demonstrated.⁹

In summary, we have developed a new, very active, and highly *Z*-selective Ru-based OM catalyst (**2**) that offers *Z* selectivity for metathesis homocouplings comparable to those of the best *Z*-selective Ru-based catalysts reported to date. The new catalyst was readily prepared from **1** in a one-step ligand-exchange reaction, demonstrating for the first time that a strategy similar to that used for Mo/W is also viable for Ru. Higher TONs (up to 2000 in the homocoupling of 1-octene) than reported to date for other *Z*-selective catalysts can be achieved along with reasonably high *Z* selectivity (>85%). The new catalyst is structurally closely related to the parent catalyst **1** and derives from **1** many of its attractive properties, such as its catalytic activity and general robustness. However, the same is true for some of its less desirable properties, such as its tendency to isomerize terminal olefins and its reactivity toward internal olefins. Fortunately, **2** has a number of handles for structural modifications that could potentially reduce such problems.

■ ASSOCIATED CONTENT

● Supporting Information

Experimental details and additional data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

Vidar.Jensen@kj.uib.no

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors gratefully acknowledge financial support from The Norwegian Research Council via the KOSK II (Grant 177322/V30) and FORNY (Grant 203379) Programs and thank Dr. Bjarte Holmelid for assistance with the HRMS-DART and GC-HRMS analyses. F.R.H. gratefully acknowledges a Ph.D. scholarship from the University of Bergen.

■ REFERENCES

- (1) Schrock, R. R.; DePue, R. T.; Feldman, J.; Yap, K. B.; Yang, D. C.; Davis, W. M.; Park, L.; DiMare, M.; Schofield, M.; Anhaus, J.; Walborsky, E.; Evitt, E.; Krüger, C.; Betz, P. *Organometallics* **1990**, *9*, 2262. Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 9858. Schrock, R. R. *Tetrahedron* **1999**, *55*, 8141. Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. Schrodi, Y.; Pederson, R. L. *Aldrichimica Acta* **2007**, *40*, 45.
- (2) Buchmeiser, M. R. *Chem. Rev.* **2000**, *100*, 1565. Pederson, R. L.; Fellows, I. M.; Ung, T. A.; Ishihara, H.; Hajela, S. P. *Adv. Synth. Catal.* **2002**, *344*, 728. Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592. Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900. Fogg, D. E.; dos Santos, E. N. *Coord. Chem. Rev.* **2004**, *248*, 2365. Hoveyda, A. H.; Zhugralin, A. R. *Nature* **2007**, *450*, 243. Grubbs, R. H. *Adv. Synth. Catal.* **2007**, *349*, 34. Thayer, A. M. *Chem. Eng. News* **2007**, *85* (7), 37. Nolan, S. P.; Clavier, H. *Chem. Soc. Rev.* **2010**, *39*, 3305.
- (3) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746.
- (4) Fürstner, A.; Guth, O.; Rumbo, A.; Seidel, G. *J. Am. Chem. Soc.* **1999**, *121*, 11108. Fürstner, A.; Rumbo, A. *J. Org. Chem.* **2000**, *65*, 2608. Fürstner, A.; Seidel, G. *J. Organomet. Chem.* **2000**, *606*, 75. Gradillas, A.; Perez-Castells, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6086.
- (5) Malcolmson, S. J.; Meek, S. J.; Sattely, E. S.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2008**, *456*, 933. Ibrahim, L.; Yu, M.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3844. Jiang, A. J.; Zhao, Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 16630. Peryshkov, D. V.; Schrock, R. R.; Takase, M. K.; Müller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 20754.
- (6) Flook, M. M.; Jiang, A. J.; Schrock, R. R.; Müller, P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7962.
- (7) Teo, P.; Grubbs, R. H. *Organometallics* **2010**, *29*, 6045.
- (8) Endo, K.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 8525.
- (9) Keitz, B. K.; Endo, K.; Herbert, M. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 9686.
- (10) Keitz, B. K.; Endo, K.; Patel, P. R.; Herbert, M. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **2012**, *134*, 693.
- (11) Occhipinti, G.; Bjørsvik, H.-R.; Jensen, V. R. *J. Am. Chem. Soc.* **2006**, *128*, 6952. Samojłowicz, C.; Bieniek, M.; Grela, K. *Chem. Rev.* **2009**, *109*, 3708.
- (12) Jensen, V. R.; Occhipinti, G.; Hansen, F. *Novel Olefin Metathesis Catalysts. Int. Patent Appl. WO 2012032131*, 2012.
- (13) Chang, S.; Jones, L. II; Wang, C.; Henling, L. M.; Grubbs, R. H. *Organometallics* **1998**, *17*, 3460. Allaert, B.; Dieltiens, N.; Ledoux, N.; Vercaemst, C.; Van Der Voort, P.; Stevens, C. V.; Linden, A.; Verpoort, F. *J. Mol. Catal. A: Chem.* **2006**, *260*, 221. Binder, J. B.; Guzei, I. A.; Raines, R. T. *Adv. Synth. Catal.* **2007**, *349*, 395.
- (14) Barbasiewicz, M.; Bieniek, M.; Michrowska, A.; Szadkowska, A.; Makal, A.; Woźniak, K.; Grela, K. *Adv. Synth. Catal.* **2007**, *349*, 193.
- (15) The presence of water reduces the catalyst reactivity but improves the selectivity against OM. Only negligible decomposition of **2** was observed when a solution of the crystallized complex was dissolved in common (i.e., nondried, nondegassed) THF and exposed to air for ca. 1 h, but **2** decomposed rapidly when THF was replaced by a noncoordinating olefinic substrate such as 1-octene (entry 8).
- (16) Migration of the C=C double bond of the target product and/or the cross-metathesis reaction between the substrate and the 2-alkene isomer was also detected (see p S25 in the SI).
- (17) Alcaide, B.; Almendros, P.; Luna, A. *Chem. Rev.* **2009**, *109*, 3817.
- (18) Forman, G. S.; McConnell, A. E.; Tooze, R. P.; van Rensburg, W. J.; Meyer, W. H.; Kirk, M. M.; Dwyer, C. L.; Serfontein, D. W. *Organometallics* **2005**, *24*, 4528. Courchay, F. C.; Sworen, J. C.; Ghiviriga, I.; Abboud, K. A.; Wagoner, K. B. *Organometallics* **2006**, *25*, 6074.
- (19) The substrate was used as received.