

Olefin Metathesis Catalysts

A Dormant Ruthenium Catalyst Bearing a Chelating Carboxylate Ligand: In Situ Activation and Application in Metathesis Reactions**

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Dedicated to *Süd-Chemie* on the occasion of its 150th anniversary

The tremendous success of olefin metathesis is largely due to the evolutionary development of active, well-defined molybdenum- and ruthenium-based catalysts.^[1] In the case of Grubbs' first-generation precatalyst, [(Cy₃P)₂Cl₂Ru=CHPh], major progress has been attained by optimizing the ligand sphere around the ruthenium center. Key advances include the development of N-heterocyclic carbene (NHC) complexes (e.g. Grubbs' second-generation catalyst **1a**) and derivatives containing a chelating 2-alkoxybenzylidene (e.g. Hoveyda's catalyst **1h**).^[1] It has been recently demonstrated that also ruthenium alkylidene complexes bearing carboxylates, sulfonates, and aryloxides (**1b–1g**, **1i–1m**; Figure 1) can reach metathesis efficiencies comparable or superior to those achieved by catalysts **1a** and **1h**.^[2] The highly active aryloxide catalysts **1c–1e** developed by Fogg and co-workers have shown a high affinity for silica, enabling their efficient removal in a single chromatographic pass^[2c]—a significant bonus in view of the efforts that are usually necessary to obtain colorless and metal-free products as required for all compounds intended for later biological use when working with established catalyst systems.^[3]

Mol and co-workers exchanged one of the chloride ligands on Grubbs' first-generation precatalyst for a perfluoroglutaric acid group bound to a Merrifield-type resin.^[4] The groups of Buchmeiser, Blechert, and Nuyken have prepared a series of complexes (**1b**, **1i–1m**) bearing perfluorocarboxylic or triflic

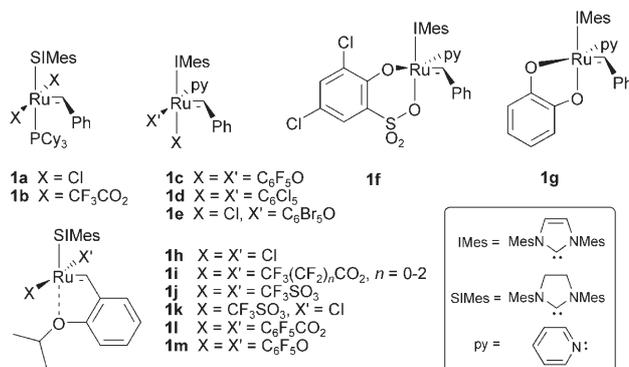


Figure 1. Grubbs and Hoveyda precatalysts (**1a**, **1h**) and selected pseudo-halide ruthenium alkylidenes (**1b–1g**, **1i–1m**) derivatives. Mes = mesityl = 2,4,6-trimethylphenyl.

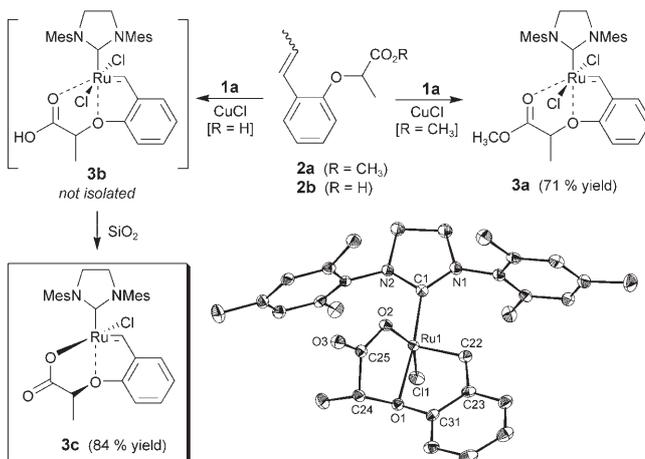
acid residues as well as their immobilized versions.^[5] The chloride-free versions of the nitro^[6a] and asarone^[6b] Hoveyda-type catalysts were reported by Buchmeiser and co-workers to be advantageous in the living polymerization of some 1,6-heptadiynes.^[7] Hoveyda and co-workers introduced various chiral phenol-tethered alkylidenes to give excellent catalysts for enantioselective metathesis.^[8] Boehringer–Ingelheim disclosed a nitro-Hoveyda catalyst^[6a] bearing ionically tagged carboxylic acid moieties for applications in an ionic liquid/supercritical CO₂ biphasic system.^[9]

Recently, we reported the highly active and stable “scorpio catalyst” **3a** in which an alkoxybenzylidene ligand

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[**] M.M. thanks the CNRS, the Ministère de la Recherche, and the Region Bretagne.

Supporting information for this article, including full experimental details and ¹H and ¹³C NMR spectra, is available on the WWW under <http://www.angewandte.org> or from the author.



Scheme 1. Synthesis and solid-state structure of new precatalyst **3c** (all heteroatom and selected carbon atom labels shown).

is doubly chelated to the ruthenium center through coordination of both the ether and an attached ester group.^[10] In pursuit of this concept, we became interested in ruthenium complex **3b** bearing a free carboxylic acid function, which might lend itself to noncovalent-type immobilization.^[11] During this investigation, however, an unprecedented bias of such a system to reorganize its ligand sphere was observed. Namely, when we attempted to prepare **3b** by reacting a ligand precursor **2b** with Grubbs' alkylidene and CuCl as a phosphane scavenger in dichloromethane, instead of the expected product a new complex was isolated in 84% yield after purification by silica gel column chromatography (Scheme 1). The structure of this new green crystalline complex has been assigned to **3c** based on mass spectrometry, NMR spectroscopy, and X-ray analysis. The direct formation of a ruthenium carboxylate combined with silica gel mediated elimination of HCl is not prece-

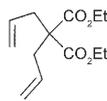
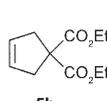
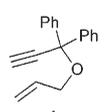
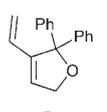
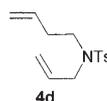
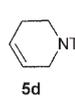
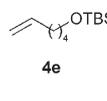
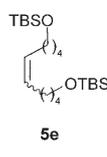
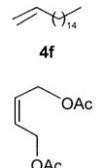
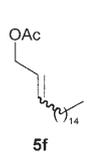
dentented.^[12]

The solid-state structure of **3c** reveals some interesting properties. Analogous to most Hoveyda-type catalysts, the ruthenium center in **3c** is pentacoordinate, and the geometry of the ligands is very close to square-pyramidal. In contrast to the structure of **3a** in which an oxygen atom (O2) forms the additional coordination site of the ruthenium on one of the tops of the square bipyramid,^[10] in **3c** the O2 oxygen atom replaces one of the chlorines in the coordination of the central metal ion in the *cis* position with respect to the O1 oxygen center. The O–Ru interactions are stronger in the case of **3c** from a geometrical point of view. The O2–Ru1 distance is quite short (2.055 Å, compared with 2.536 Å in **3a**) while the O2–C25 distance is significantly elongated (1.291 Å, compared with 1.194 Å in **3a**).^[10] The fact that the carboxylate moiety coordinates ruthenium by replacing one of the chlorine atoms influences the geometry around the ether oxygen. The O1 atom in **3c** presents a geometry which suggests sp³ hybridization, with valence angles values closer to 110°. The O1–C31 bond length is 1.409 Å, and it is significantly longer than the analogous O1–C26 bond in the Hoveyda catalyst or the O1–C36 bond in **3a**.^[10] The coordination of the ruthenium by the oxygen atom O1 in compound **3c** seems to take place by a single

lone electron pair, which suggests a different strength and character of the interaction to that in **3a** or other Hoveyda type complexes.^[13]

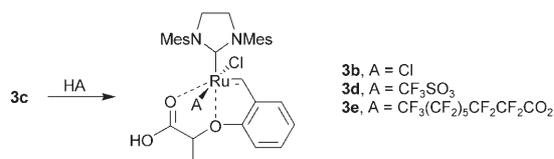
To inspect if these structural differences are reflected in the chemical activity of **3c**, we used a standard set of metathesis reactions. The model ring-closing metathesis (RCM) reaction of diallyltosylamide (**4a**) revealed that **3c** has extremely low potency, with only 14% conversion observed after 24 h at reflux (Table 1). Interestingly, when one equivalent of HCl (relative to **3c**) was added after that time to the reaction mixture, the conversion proceeded to near completion within the next 90 min. Intrigued by this result, we monitored the reaction between **3c** and HCl by ¹H NMR spectroscopy. The observed fast disappearance of the signal for the benzylidene proton at $\delta = 16.52$ ppm and

Table 1: Representative metathesis reactions.^[a]

Entry	Substrate 4	Product 5	Cat. (mol %), time, temperature	Yield of 5 [%] ^[b]	3c [%] ^[c]
1			3a (1), 1 h, 0°C ^[d]	55	–
2			3c (5), 24 h, 40°C	14	–
3			3b (5), 1 h, 40°C	96 (90)	95
4			3b (1), 3 h, 40°C	96 (93)	–
5			3b (0.6), 5.5 h, 40°C	92 (87)	–
6			3b (0.3), 5.5 h, 40°C	93 (90)	–
7			3a (5) 15 min, 40°C	99	–
8			3a (1), 6 h, 0°C ^[d]	70	–
9			3c (5), 2 h, 20°C	0	–
10			3c (5), 2 h, 40°C	10	–
11			3c (5), 2 h, 100°C ^[e]	88 (84)	17
12			3b (5), 24 h, 40°C	95 (86)	–
13	3d (5), 24 h, 40°C	65	–		
14	3e (5), 24 h, 40°C	87	–		
15			3a (5), 15 min, 40°C	99	–
16			3c (5), 24 h, 40°C	49	–
17			3b (5), 1 h, 40°C	99 (88)	96
18			3b (1), 3 h, 40°C	96 (90)	–
19			3b (0.6), 5.5 h, 40°C	96 (89)	–
20			3b (0.3), 5.5 h, 40°C	99 (92)	–
21			3b (1), 24 h, 40°C ^[f]	98 (68)	–
22			3b (0.3), 24 h, 40°C	98 (75)	–
23			3c (5), 24 h, 40°C	0	97
24			3b (5), 24 h, 40°C	96 (89)	–
25			3b (5), 3 h, 40°C	98 (93)	–

[a] Conditions: **4a–4f** (0.02 M) in CH₂Cl₂. Conversions calculated from GC. Ts = *para*-toluenesulfonyl, TBS = *tert*-butyldimethylsilyl. [b] Yields of isolated products are given in parentheses. See Supporting Information for details. [c] Yield of catalyst **3c** recovered after the reaction. [d] Ref. [10]. [e] Reaction in toluene. [f] 89% conversion after 3 h.

quantitative formation of the new benzylidene signal at $\delta = 16.73$ ppm and a broad singlet at $\delta = 10.55$ ppm suggest that this reaction leads to the dichloro complex **3b** (Scheme 2).



Scheme 2. In situ formation of **3b**, **3d**, and **3e**.

By evaporation of the solvent and crystallization of the residue from dichloromethane/*n*-pentane, it was possible to isolate pure **3b** in 90% yield. Mass spectrometry and IR spectroscopy analyses were in agreement with the proposed structure. Unlike **3c**, this complex (both prepared in situ and isolated in pure form) shows high activity in metathesis reactions (Table 1). This renders alkylidene **3c** a potentially interesting chemically switchable catalyst.^[14] Consequently, we became interested to see if the activity of **3c** could be controlled by application of different acids. Using NMR spectroscopy, we monitored the reactions between **3c** and two representative organic acids: triflic acid and perfluorononanoic acid (Scheme 2). In both cases, fast disappearance of the signal for the benzylidene in **3c** ($\delta = 16.52$ ppm) and formation of new signals ($\delta = 17.16$ and 16.61 ppm, respectively) was observed. Dormant catalyst **3c** and in situ generated **3b**, **3d**, and **3e** were used as initiators in the RCM reaction of diallylmalonic acid diethyl ester (**4b**; Table 1 and Figure 2).

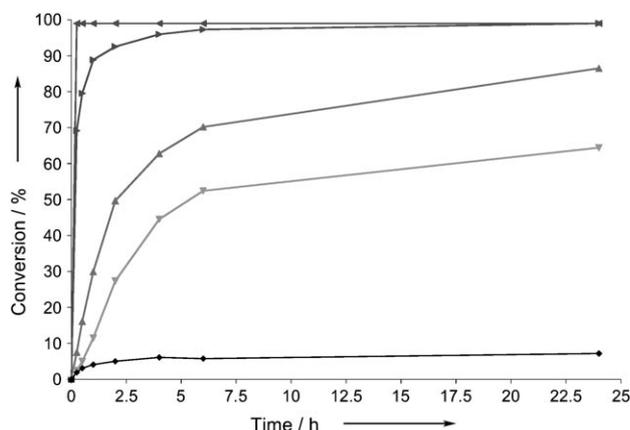


Figure 2. Benchmark RCM activity of **3a** (\circ) **3c** (\diamond), and in situ prepared **3b** (\triangleright , **3c** + HCl), **3d** (∇ , **3c** + TfOH), and **3e** (\triangle , **3c** + $C_8F_{17}CO_2H$). Conditions: 0.02 M **4b** in CH_2Cl_2 , 40 °C, 24 h.

The catalyst formed with HCl was the most active, while TfOH and perfluorononanoic acid gave initiators of lower yet different activities. The results show that the nature of the acid has a major impact on the initiation behavior of the formed complex, suggesting a high degree of tunability.

The most undesirable feature of modern homogeneous metathesis catalysts is that they often form deeply colored

ruthenium by-products, which are difficult to remove from the desired products.^[3] To our delight, catalyst **3b** displays a high affinity to silica, enabling its efficient removal. For example, in the RCM of **4b** (5 mol% Ru, 1 h in refluxing CH_2Cl_2 , 0.2 mmol scale) filtration of the crude reaction mixture through a Pasteur pipette filled with 650 mg of silica gel yielded colorless product **5b** (Ru contamination of crude **5b** is 48 ppm, as determined by inductively coupled plasma mass spectrometry (ICP-MS)), while in the case of **1a** and **1h** the removal of the catalyst was obviously incomplete under identical conditions (Figure 3). By washing of the Pasteur

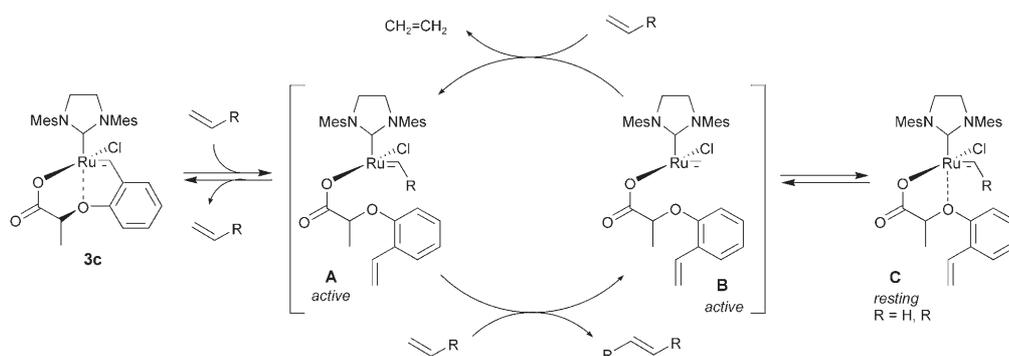


Figure 3. Efficiency of catalyst removal using silica gel for **3b** (left), **1h** (center), and **1a** (right) after RCM of **4b** (5 mol% Ru, 2 h, 40 °C, CH_2Cl_2).

pipette containing “**3b**” further with ethyl acetate it was possible to regenerate up to 95% of the catalyst (Table 1). Irrespective of the use of **3b** or **3c** in the metathesis reaction, the “sleeping form” of the catalyst, **3c**, was always obtained after the above recycling protocol. Therefore, we suppose that **3b** is readily transformed into **3c** as soon as it has been deposited onto silica gel. The regenerated complex shows identical analytical data to that of freshly prepared **3c** and can be used, with similar results, in further metathesis reactions.

Previous studies have shown that Grubbs-type precatalysts $[L/LX_2Ru=CHR]$ initiate by dissociating a PR_3 ligand L , while in case of the Hoveyda-type complex (**1h**), where L is a tethered ether ligand, initiation requires breaking of the Ru–O bond.^[15] Importantly, both Grubbs- and Hoveyda-type precatalysts provide the same propagating species $[(SImes)X_2Ru=CH_2]$ and $(SImes)X_2Ru=CHR]$ after a single turnover.^[15] The extremely low activity of carboxylate **3c** can be explained in view of the same mechanistic picture. In this case, propagating species **A** and **B** contain the chelating styrene fragment during the whole metathesis event, favoring constant background formation of catalytically inactive species **C** (Scheme 3). Interestingly, **3c** shows *latent* behavior,^[16] being inert at room temperature but highly active at elevated temperatures (Table 1, entries 9–11).

In summary, our results highlight the not yet fully explored fluxionality of the ligand sphere of carboxylate-type ruthenium complexes. The recyclable dormant alkylidene **3c** can be used as a chemo- and thermally switchable catalyst^[14,16] in some applications. It is expected that the new structural motif represented by **3c** will offer a unique



Scheme 3. Plausible mechanism of olefin $RCH=CH_2$ metathesis with **3c**.

platform for generating new greener metathesis catalysts,^[3] for example, through reaction with supported,^[11] polyethylene-glycolated, ionically tagged,^[9] or perfluorinated carboxylic and sulfonic acids. Such studies are underway and will be reported in due course.

Received: March 24, 2007

Published online: July 27, 2007

Keywords: carbenes · carboxylate ligands · homogeneous catalysis · olefin metathesis · ruthenium

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