Ruthenium Alkylidene Complexes

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Deactivation of Ruthenium Olefin Metathesis Catalysts through Intramolecular Carbene–Arene Bond Formation

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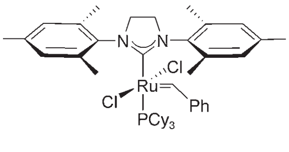
Dedicated to Professor Ekkehard Winterfeldt on the occasion of his 75th birthday

Since the development of Grubbs catalysts of the first ([$RuCl_2(PCy_3)_2(=CH-C_6H_5)$] (**1**; Cy = cyclohexyl) and second (**2**) generation, many modified ruthenium complexes for olefin metathesis have been reported,[1] for which strikingly different influences of the ligands on the efficiency of C−C bond formation have been observed. For example, notable effects have been found in the class of alkoxy benzylidene ligands first introduced by Hoveyda and co-workers. Phosphine-free complexes such as the second-generation Hoveyda–Grubbs catalyst (**4**; $IMesH_2$ = 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene)[2] are especially well-suited for cross metathesis with electron-deficient olefins such as α,β-unsaturated nitriles.[3] The stability and the initiation rate of the precatalyst could be tuned by steric and electronic effects of the substituents.[4]



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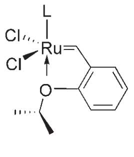
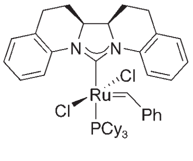


3, L = PCy_3
4, L = $IMesH_2$



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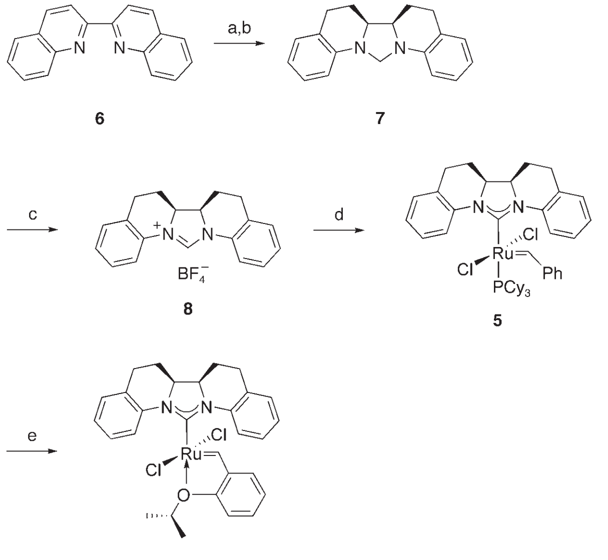
Additional intramolecular interactions of functional groups or atoms with the metal center have been reported for some ligands.[3c,5,6] Grubbs and co-workers recently found an accelerating effect in olefin metathesis through fluorine–ruthenium interaction. Besides knowledge of such ligand and substituent effects, an understanding of catalyst decomposition and transformation to catalytically inactive ruthenium species is of major importance for the rational design and improvement of metathesis catalysts. Fundamental studies have been presented by Grubbs and co-workers and by Dinger and Mol.[7] Herein, we report a novel deactivation reaction pathway transforming active ruthenium catalysts with alkoxy benzylidene ligands into catalytically inactive carbene complexes.

During our study of diastereoselective ring rearrangement metathesis reactions (dRRM), we found that the neutral ligand that remains on the metal center has a pronounced effect on conversion and diastereoselectivity.[8] While only moderate diastereoselectivities could be seen for the first-generation catalysts (**1**, **3**), the sterically more demanding and more active second-generation catalysts (**2**, **4**) led to significantly higher selectivities. Thus, we focused on the development of a bulky ruthenium carbene complex to increase the diastereoselective interaction between the olefine moiety and the catalytically active ruthenium species. To do this, we connected the *N*-aryl substituent with the N-heterocyclic carbene (NHC) through a C_2 unit. Unlike in **2** or **4**, the aromatic moiety in this new ruthenium complex (**5**, Scheme 1) should exert a much stronger steric influence on the ruthenium alkylidene moiety through torsion of approximately 45° and hindered rotation.

The synthesis of the NHC ligand started from commercially available 2,2′-biquinoline (**6**). The first step was hydration to octahydrobiquinoline; the result of the hydration was strongly dependent on the catalyst system. PtO_2 and H_2 under ambient pressure led to the formation of a 3:1 mixture of the *meso* and racemic forms. Simple chromatography on silica gel



Scheme 1. Synthesis of ruthenium complexes **5** and **11**: a) PtO_2, H_2, CH_2Cl_2, RT, 4 h, 61%; b) $HC(OMe)_3$, HCOOH, toluene, 90°C, 8 h, 98%; c) Ph_3CBF_4, CH_2Cl_2, RT, 3 h, 85%; d) $KOC(CH_3)_2CH_2CH_3$, hexane, **1**, 50°C, 16 h, 65%; e) 2-Isopropoxystyrene, CH_2Cl_2, RT, 1.5 h, 95%.

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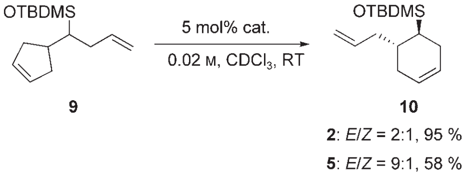
yielded 61% of the pure *meso* compound. Subsequent transformation into carbene precursor **8** turned out to be quite problematic. The usual reaction conditions for cyclization with trimethyl orthoformate and formic acid led to the formation of aminal **7** in near quantitative yield. The reduction of the highly strained intermediate iminium salt could not even be avoided by the use of acetic acid. The synthesis of the desired imidazolium salt (**8**) finally succeeded using tritylium tetrafluoroborate as a hydride abstractor.

From tetrafluoroborate salt **8**, we synthesized complex **5** using the procedure of Nolan and co-workers.[9] Catalyst **5** was obtained as a green microcrystalline solid in 65% yield. The green color of this complex is unusual, as ruthenium complexes of the second generation are usually purple or brown. The novel catalyst **5** was used in different metathesis reaction protocols (RCM, CM). Complex **5** was found to be of limited stability in solution even in the absence of olefin substrate. Thus, conversions were generally much lower than for **2**. Nevertheless, test reactions for diastereoselective ring rearrangements showed very promising results. RRM of **9** with **5**, for example, delivered the product with an *E*/*Z* selectivity of 9:1 and a conversion of 58% (Scheme 2).[8]



Scheme 2. Diastereoselective RRM of **9** using catalysts **2** and **5**. TBDMS = *tert*-butyldimethylsilyl.

We expected an increase in stability when introducing an isopropoxy benzylidene ligand. Following the method of Hoveyda and co-workers for the synthesis of the second-generation Grubbs–Hoveyda catalyst **4**,[2a] we obtained the air-stable catalyst **11** in an unsatisfactory yield of only 12% by stirring a mixture of **5**, 2-isopropoxy styrene, and CuCl in CH_2Cl_2. As byproducts, we observed the Hoveyda I complex **3** and the copper NHC complex in equal amounts (43% each). The transformation of **5** to **3** is remarkable, as usually the phosphine ligand is exchanged with the alkoxy benzylidene ligand and the N-heterocyclic carbene ligand remains untouched. Reaction without CuCl finally resulted in the formation of the desired ruthenium catalyst **11** as an air-stable, olive green solid in 95% yield (Scheme 1).

Investigations of the stability of **11** in solution showed very remarkable results. Storage of samples in the presence of air led to a decrease in the intensity of the benzylidene signal at $\delta = 17.33$ ppm in the ^{1}H NMR spectrum over the course of two weeks. After this period, the signal disappeared completely, and an entirely new set of signals appeared along with some minor signals from decomposition products. The new complex **12** was fully characterized by mass spectrometry, IR and NMR spectroscopy, and X-ray crystallographic analysis (Figure 1).[10]

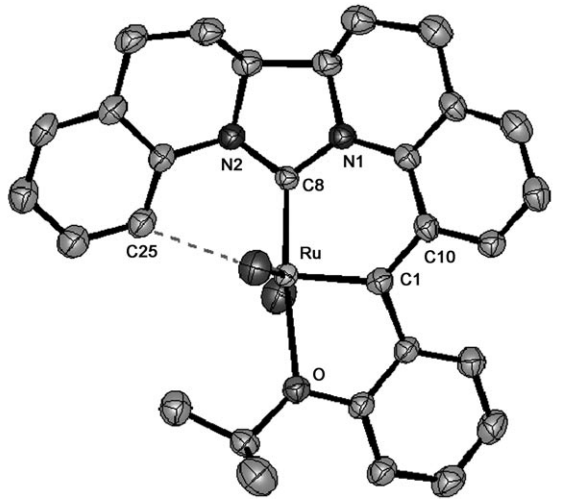


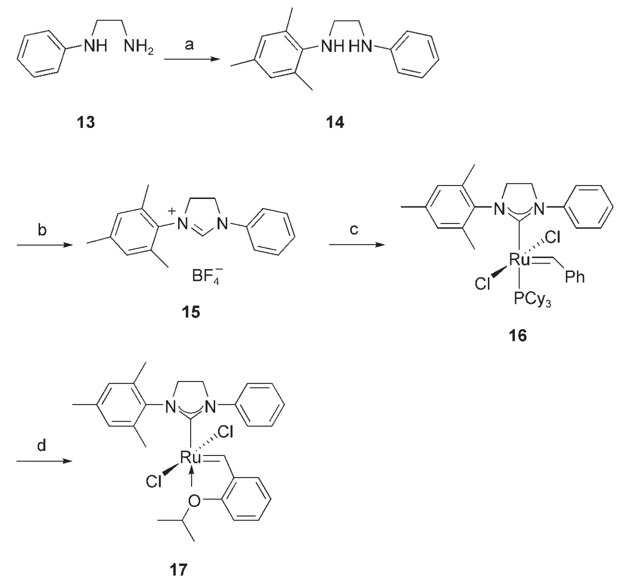
Figure 1. Crystal structure of **12** (ORTEP drawing, thermal ellipsoids are shown at 50% probability). Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru–C1 1.842(4), Ru–C8 1.907(4), Ru–O 2.255(3), C1–C10 1.461(6), C25···Ru 2.408(0); C1-Ru-C8 93.3(2), C1-Ru-O 80.7(2), C8-Ru-O 173.8(2), Ru-C1-C10 125.7(3).

The crystal structure shows the formation of an intramolecular carbene–arene bond between the benzylidene carbon atom (C1) and the *ortho* position of the *N*-aryl ligand (C10). The length of the C1–C10 bond (1.461(6) Å) is between that of a single and a double bond. The NHC ligand with its boomerang shape is very close to the ruthenium center, thus leading to a strong agostic interaction between the hydrogen atom on C25 and the ruthenium atom. The C25–Ru separation of 2.408(0) Å is clearly shorter than was found for Ru–F and Ru–Cl interactions in comparable ruthenium benzylidene complexes.[6]

This unexpected C–H insertion prompted us to synthesize a phosphine-free second-generation ruthenium complex with similar unsubstituted *ortho* positions on one of the *N*-aryl ligands. We presumed that a bond might be formed between the benzylidene carbon atom and the β-position of the *N*-aryl substituent if oxygen is present and if the approach of the reactive positions is not impeded by steric hindrance. Consequently, we synthesized ruthenium complex **17**. Carbene precursor **15** was synthesized following the procedure we reported for unsymmetrically substituted carbenes (Scheme 3).[11]

The air-stable NHC–phosphine complex **16** can be obtained in excellent yield from the addition of **1** to a solution of the carbene generated in situ from **15** in hexane. The reaction of **16** and 2-isopropoxy styrene afforded the phosphine-free complex **17**. Under inert conditions, the crude product contained only **17**, which is analogous to the Hoveyda–Grubbs catalyst. But to our surprise, we could isolate two different green compounds from the chromatographic purification. The olive green complex **17** was isolated (67% yield), but we also obtained the dark green, crystalline C–H insertion product **18** in 10% yield.

Both solids are air-stable. In CH_2Cl_2, **17** converts completely into **18** within a few hours.[12] The insertion could be



Scheme 3. Synthesis of ruthenium complexes **16** and **17**: a) [Pd$_2$(dba)$_3$], (±)-binap, 2-bromomesitylene, NaO*t*Bu, toluene, 80 °C, 72 h, 91 %; b) NH_4BF_4, $CH(OEt)_3$, HCOOH, 120 °C, 18 h; 85 %; c) **1**, $KO(CH_3)_2CH_2CH_3$, hexane, 50 °C, 12 h, 97 %; d) 2-isopropoxystyrene, CH_2Cl_2, 40 °C, 0.5 h, 67 %. dba = *trans,trans*-dibenzylideneacetone, binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

monitored by NMR spectroscopy, which showed the decrease of the benzylidene signal at $\delta = 16.65$ ppm. The isolated complexes **12** and **18** were found to be completely inactive in various metathesis reaction protocols. The crystal structure confirms the formation of the insertion product (Figure 2).[10] Complex **18** crystallizes in the monoclinic space group *C*2/*c*.

The insertion reaction could only be observed in solution in the presence of atmospheric oxygen. No insertion was found for solutions stored under inert atmosphere. These findings are in accordance with the proposed reaction sequence of a pericyclic reaction followed by oxidation and re-aromatization steps (Scheme 4). In these complexes, several mesomeric forms can be considered. Favored by the geometry of the alkoxy benzylidene ligand, valence structure **A** can undergo a pericyclic cyclization reaction to form **B**. This step is reversible, but the subsequent oxidation with oxygen renders the reaction irreversible (**C**). Elimination and re-aromatization finally yields the insertion product **D**.

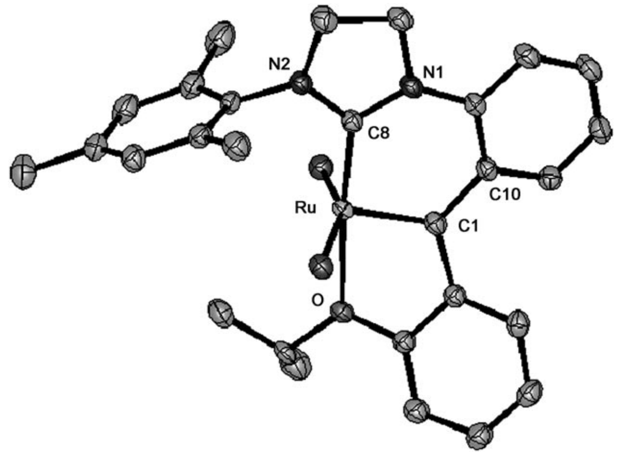
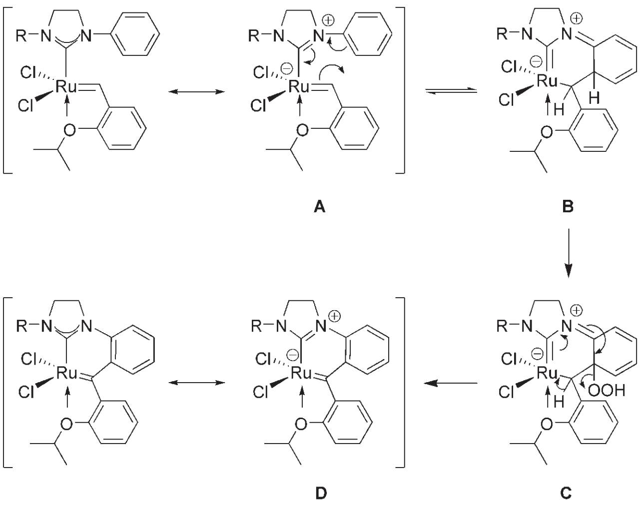


Figure 2. Crystal structure of **18** (ORTEP drawing, thermal ellipsoids are shown at 50% probability). Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru–C1 1.841(2), Ru–C8 1.928(2), Ru–O 2.217(2), C1–C10 1.470(3); C1-Ru-C8 94.0(1), C1-Ru-O 81.1(1), C8-Ru-O 175.1(1), Ru-C1-C10 124.6(2).



Scheme 4. Proposed mechanism for the insertion reaction.

These results are of importance for further development of olefin metathesis catalysts. Complexes with *N*-aryl substituted NHC ligands, especially those of the Grubbs–Hoveyda type lacking steric hindrance in the *ortho* position of the arene ligand, can give rise to intramolecular C–H insertion. This insertion leads to metathesis-inactive ruthenium complexes. The transformation only occurs in the presence of atmospheric oxygen. Olefin metathesis precatalysts of this kind should therefore be handled under inert atmosphere. Their purification via column chromatography and their recycling is thus more difficult.

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