Catalysis at the Interface of Ruthenium Carbene and Ruthenium Hydride Chemistry: Organometallic Aspects and Applications to Organic Synthesis

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Keywords: Catalysis / Hydride complexes / Isomerization / Metathesis / Ruthenium

Soon after the introduction of stable and defined ruthenium precatalysts for olefin metathesis it was discovered that double bond migrations may interfere with the metathesis reaction. This undesired side reaction has been attributed to the formation of ruthenium hydride species from metathesis-active ruthenium carbene species in situ. Over the past few years, several studies have indeed revealed the existence of pathways leading from ruthenium carbene to ruthenium hydride complexes. Furthermore, a number of examples have been published recently where typical precatalysts for olefin metathesis were found to promote non-metathesis transformations efficiently in preparatively useful yields and selectivities, presumably via the in situ formation of ruthenium hydride species. These results open up a pathway to the development of novel catalyzed reaction sequences that combine ruthenium carbene- and ruthenium-hydride-mediated steps. This paper provides an overview of the field and covers organometallic aspects as well as synthetic applications.

1. Olefin Metathesis and Non-Metathesis Side Reactions

The discovery of stable and defined carbene complexes of molybdenum[1] and ruthenium[2] as efficient precatalysts for olefin metathesis has made this transformation one of the most important C−C bond forming reactions.[3−8] Molybdenum-based complexes such as **1** are generally considered to be more reactive towards highly substituted and electron-rich double bonds than are ruthenium-based complexes, e.g., **2**. The latter are, however, more stable towards air and moisture and are more tolerant towards polar functional groups. A significant improvement of the metathesis activity of ruthenium carbene complexes was achieved by the introduction of one N-heterocyclic carbene ligand.[9,10] Ruthenium complexes **3**,[11] **4**,[12] and **5**[13,14] are examples of these second-generation catalysts and they are often used when **2** is not sufficiently reactive (Figure 1).

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Bernd Schmidt was born in 1967. After studying chemistry at the RWTH Aachen, he received his diploma in 1991. From 1991 to 1994 he worked towards his Dr. rer. nat. on the field of organoboron chemistry under the guidance of Gerhard E. Herberich in the Department of Inorganic Chemistry of the RWTH. After receiving his Dr. rer. nat., he moved to the University of Southampton, UK, to join the group of Philip Kocienski as a postdoctoral fellow, funded by the Deutsche Forschungsgemeinschaft. During this time he worked on the field of chromium and tungsten carbene complexes and their application to the synthesis of complex target molecules. After returning to Germany, he started his independent research directed toward the "habilitation" at the University of Dortmund, associated with the group of Peter Eilbracht. The research was supported by a Liebig Fellowship of the Fonds der Chemischen Industrie and a DFG-Habilitations Fellowship. After completion of the habilitation in early 2001, he was appointed Privatdozent for organic chemistry at the University of Dortmund. His research interests are in the field of organic synthesis (target molecule synthesis and development of novel synthetic methods) and homogeneous catalysis, especially olefin metathesis.

MICROREVIEWS: This feature introduces the readers to the author's research through a concise overview of the selected topic. Reference to important work from others in the field is included.

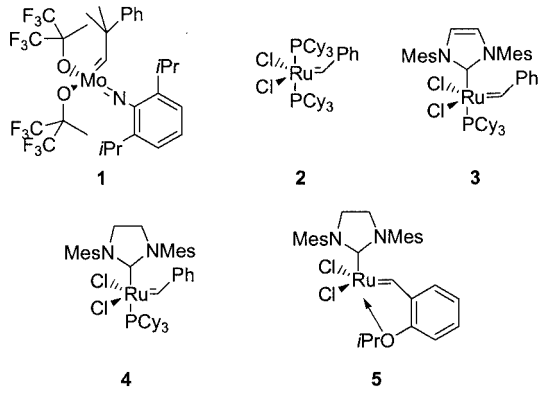
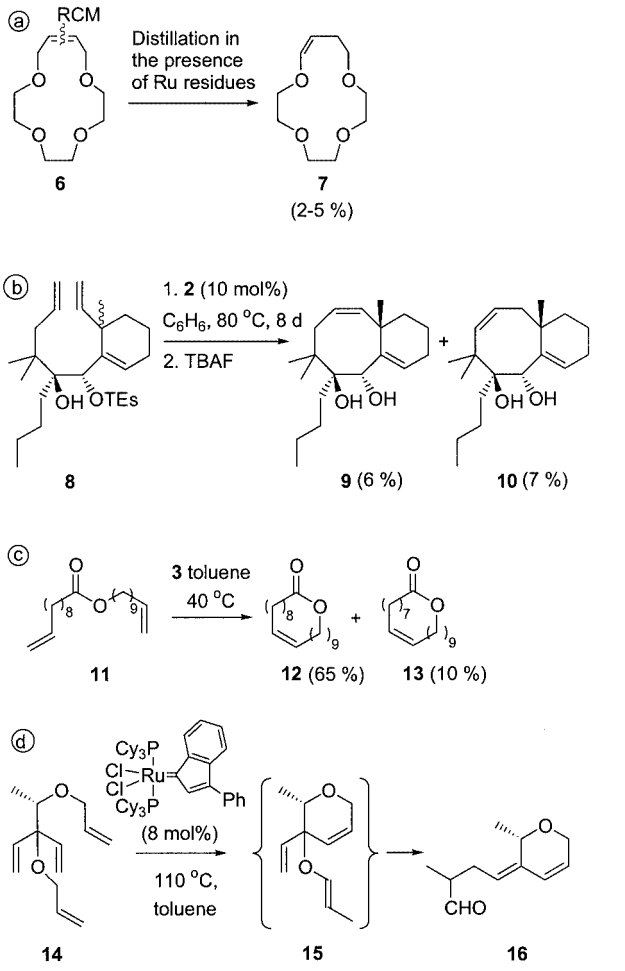


Figure 1. Stable and defined precatalysts for olefin metathesis

It was recognized early that in cases where **2** catalyses the metathesis reaction only slowly, rather high catalyst loadings are required to obtain preparatively useful rates of conversion. This observation was attributed to a monomolecular decomposition pathway of the catalytically active ruthenium methylidene species. The structure of the decomposition products could, however, not be determined.[15] Several reports published over the past few years indicate that decomposition products of ruthenium metathesis catalysts might be responsible for undesired side reactions, especially alkene isomerization. For instance, Maynard and Grubbs reported that distillation of **6**, obtained via ring closing metathesis, often results in the formation of small amounts of isomerization product **7** if ruthenium residues are not removed prior to distillation (Scheme 1, a).[16] Prunet et al. investigated the ring closing metathesis of diene **8** with a view towards preparing the carbocyclic moiety of taxol. Only minor amounts of two cyclized products were obtained: the expected cyclooctene **9** and an unexpected isomer **10**, which obviously results from an isomerization *subsequent* to the metathesis step (Scheme 1, b).[17] A similar observation had previously been reported by Taylor et al., who attributed the isomerization of the primary metathesis product to trace amounts of acid present in the solvent.[18] An example where double bond isomerization occurred *prior* to ring closing metathesis was reported by Fürstner et al.: ring closure of **11** yields the expected 21-membered macrocycle **12** along with minor amounts of a 20-membered macrocycle, **13**. Formation of **13** is obviously the result of a double bond isomerization and subsequent ring closing metathesis with liberation of propene (Scheme 1, c).[19] An unexpected outcome of the attempted double ring closing metathesis of tetraene **14** was reported by our group: instead of a spirocyclic product, aldehyde **16** was obtained in very low yield, but as a single diastereoisomer, along with unidentified nonvolatile byproducts. We assume that ring closing metathesis to the six-membered ring occurs in the first step, followed by ruthenium-catalyzed isomerization of the remaining allyloxy moiety to enol ether **15**, which then undergoes a Claisen rearrangement (Scheme 1, d).[20] An approach to the same structural motif on a preparatively useful scale was recently

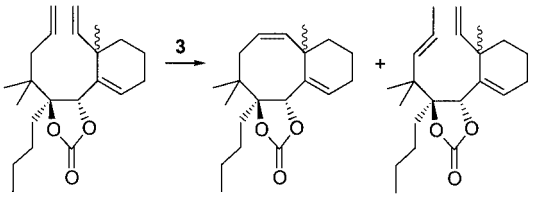


Scheme 1. Examples for isomerization reactions interfering with olefin metatheses

developed by Dixneuf et al. using a ruthenium-catalyzed isomerization/Claisen rearrangement sequence.[21,22]

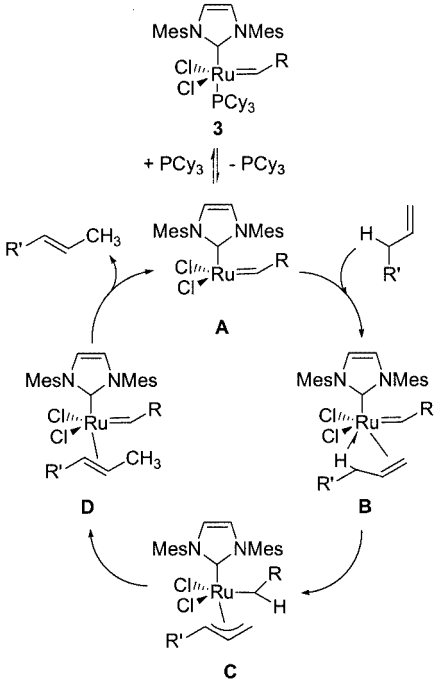
Different proposals have been made to explain the formation of products resulting from double bond isomerization. Nolan, Prunet, et al. have investigated the competition of ring closing metathesis and double bond isomerization in some detail for the model system **17**.[23] Cyclooctene **18** and isomerization product **19** were obtained in varying amounts, and the composition of the reaction mixture depends strongly on the solvent, as illustrated in Scheme 2. Addition of small amounts of tricyclohexylphosphane oxide ($POCy_3$) completely suppresses the isomerization and leads to quantitative conversion into **18**.

Based on the experimental observations, the authors proposed a mechanism for the isomerization process (Scheme 3) that involves coordination of the alkene to the 14-electron fragment **A**. In the resulting π complex, **B**, an agostic interaction (indicated by a "half" arrow) might facilitate deprotonation at the allylic position leading to a σ-alkyl/π-allyl complex **C**, which reacts to give the carbene complex **D**. Dissociation of the isomerized alkene regenerates the catalytically active species **A**.[23]



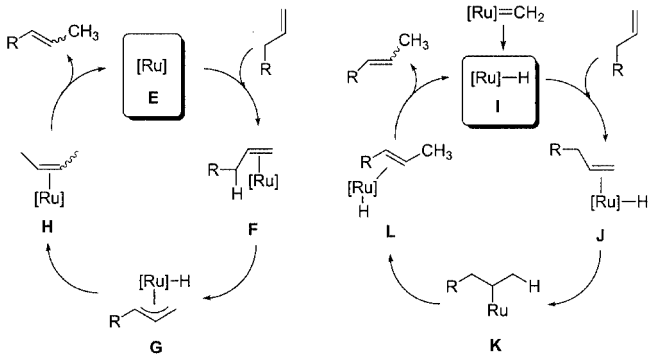
17 Solvent	18	19
$ClCH_2CH_2Cl$, 83 °C	90 %	10 %
$MeOCH_2CH_2OMe$, 85 °C	0 %	100 %
$ClCH_2CH_2Cl$, 83 °C + 0.5 % $POCy_3$	100 %	0 %

Scheme 2. Competing RCM and isomerization processes



Scheme 3. Proposed mechanism for alkene isomerization via π-allyl complexes

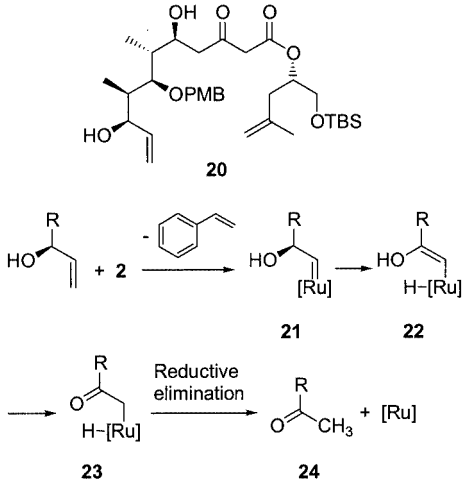
This mechanism is a modification of the π-allyl hydride mechanism (Scheme 4, left cycle), which is one of the two commonly proposed mechanisms for olefin isomerization.[24] In the π-allyl hydride mechanism, an intermediate **G** is assumed to form that results from migration of the hydride from the allylic position of the alkene substrate to the metal center. Reductive elimination gives the η^2 complex **H**, from which the substrate dissociates to regenerate the catalytically active species **E**. The second mechanism (Scheme 4, right cycle) is believed to occur via a hydrometalation/β-hydride elimination sequence, which requires the presence of a coordinatively unsaturated ruthenium hydride species **I**. Coordination of the alkene gives the π complex **J**, which undergoes a migratory insertion (hydrometalation) to give the σ-alkyl complex **K**. β-Hydride elimination leads to the π complex **L**, from which the catalytically active species **I** is regenerated by dissociation of the isomerized alkene.



Scheme 4. Mechanistic proposals for double bond isomerization in alkenes. π-Allyl hydride mechanism (left) and hydrometalation/β-hydride elimination mechanism (right)

It was stated, by Fürstner et al., that ruthenium hydride complexes are formed as byproducts in some cases during the preparation of second-generation metathesis catalysts.[25] If these are present as an impurity in the metathesis catalyst, they might be responsible for the observed isomerization reactions. Alternatively, ruthenium hydride species might be formed by decomposition of the ruthenium carbene species under the reaction conditions.

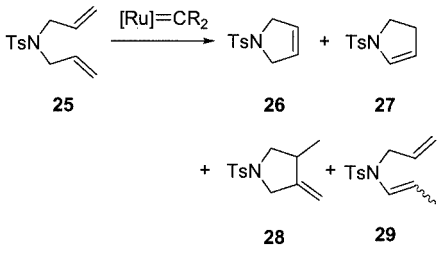
Apart from alkene isomerization, few other non-metathesis side reactions have been reported. A degradation of allylic alcohols that requires *stoichiometric* amounts of ruthenium catalysts has been observed by Hoye and Zhao in the course of studies directed toward the synthesis of Calipteloside A (Scheme 5).[26]



Scheme 5. Stoichiometric degradation of allyl alcohols to ketones

The authors observed that RCM of precursor **20** did not take place in the presence of the first-generation catalyst **2**; instead, the carbene complex was consumed and the allylic alcohol moiety was degraded to a methyl ketone. A mechanism was postulated that involves formation of the carbene complex **21** by reaction of **2** with the less-hindered double bond of **20**, followed by rearrangement to a ruthenium hy-

dride species **22**, keto−enol tautomerization to ketone **23**, and finally reductive elimination to a methyl ketone **24** (Scheme 5).[27] *N*-Tosyldiallylamine (**25**) and some other diallyl systems have been reported to undergo a cycloisomerization to **28** in competition to the expected ring closing metathesis reaction, leading to **26**.[28,29] With cationic ruthenium allenylidene complexes as precatalysts, isomerization products **27** and **29** were also obtained (Scheme 6).[30]



Scheme 6. RCM and competing cycloisomerization

A close investigation into the kinetics revealed that the RCM product **26** is formed immediately after addition of the catalyst, while formation of **27**, **28**, and **29** begins after an induction period.[30] From this observation, Bassetti et al. concluded that the formation of these products is mediated by a decomposition product of the initial metathesis catalyst, rather than by the catalyst itself or an impurity. Competing formation of **28** in the metathesis of **25** has also been observed by Connon and Blechert using precatalyst **5** or a polymer-bound analogue.[29] Based on NMR-tube experiments, these authors also attribute the formation of **28** to a decomposition product of the metathesis catalyst. This decomposition product has been characterized by a signal in the ^{1}H NMR spectrum at $\delta = -5.05$ ppm. Although the decomposition products that cause the cycloisomerization side reaction were not identified explicitly as ruthenium hydrides, it is not unlikely that such species are involved in cycloisomerization reactions.[31,32]

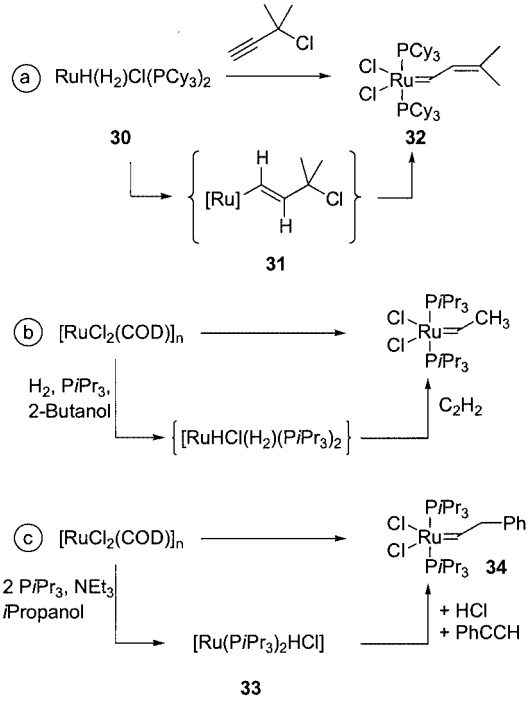
As for any catalytic method, undesired side reactions, such as those described above, are a serious limitation for ruthenium-catalyzed olefin metathesis. Over the past few years, however, some examples for *selective* non-metathesis transformations mediated by ruthenium carbene complexes have been described and a first summary of this field has been published recently by Alcaide and Almendros.[33] Apart from olefin metathesis, ruthenium carbene complexes apparently catalyze two groups of reactions under certain circumstances: radical reactions, e.g., atom radical transfer additions, such as the Kharash reaction,[34,35] and reactions that are normally catalyzed by ruthenium hydrides or involve the formation of ruthenium hydrides during the catalytic cycle.

In this paper, we focus on the interface of ruthenium carbene- and ruthenium hydride-catalyzed transformations. The following aspects are covered: a) organometallic relationship between Ru=CR_2 and Ru−H complexes; b) selective syntheses catalyzed by or involving ruthenium hydride species generated in situ from ruthenium carbene complexes; c) combinations of metathesis steps and ruthenium hydride-mediated steps in catalyzed sequences.

2. Interconversion of Ru Carbene and Ru Hydride Species

As outlined in the previous section, it is likely that Ru−H species resulting from decomposition of metathesis-active Ru carbene catalysts are responsible for several non-metathesis side reactions. This section provides an overview of the relationship between ruthenium hydride and ruthenium carbene species from an organometallic point of view.

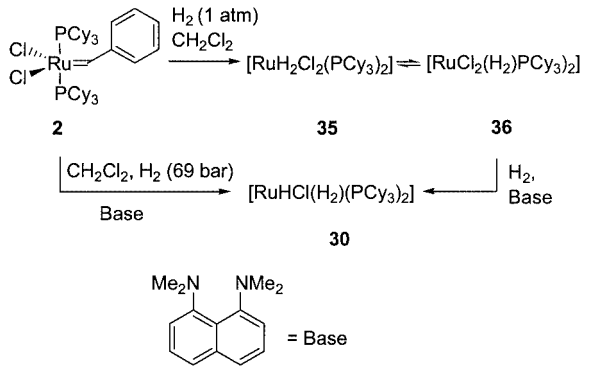
Apart from the standard route normally used for the preparation of ruthenium metathesis catalysts,[36] alternative routes have been devised since the mid-1990s that avoid the use of hazardous or less conveniently accessible reagents. Some of these processes start from ruthenium hydride complexes, either isolated or generated in situ from other precursors. Propargyl chlorides, for instance, insert into the Ru−H bond of ruthenium hydride complex **30** to give the σ-vinyl complex **31**, which rearranges rapidly to the metathesis-active carbene complex **32** (Scheme 7, a).[37] The well-known ruthenium hydride [$RuHCl(PPh_3)_2$] also reacts with propargyl chlorides to give ruthenium carbene complexes.[38] Instant routes, starting from easily prepared or commercially available precursors that are converted into ruthenium hydrides in situ have also been developed. Treatment of $RuCl_3$ [39] or $[RuCl_2(COD)]_n$ [40] with hydrogen, phosphane ligands, and a reducing agent gives ruthenium hydride complexes that react with alkynes in an insertion/



Scheme 7. Ru carbene complexes prepared from Ru hydrides and propargyl chlorides

rearrangement sequence that finally leads to ruthenium carbene complexes (Scheme 7b). Conversion of $[RuCl_2(COD)]_n$ into a 14-electron ruthenium hydride complex **33** has been achieved by using 2-propanol as a hydride-donating reagent. Protonation of **33** and treatment with phenylacetylene gives ruthenium carbene complex **34** (Scheme 7, c).[41] A Fischer-type ruthenium carbene complex has been obtained from the same hydride **33** by treatment with ethyl vinyl ether. The primary insertion product undergoes a rearrangement to give a carbene complex that contains a hydride ligand at the ruthenium center.[42]

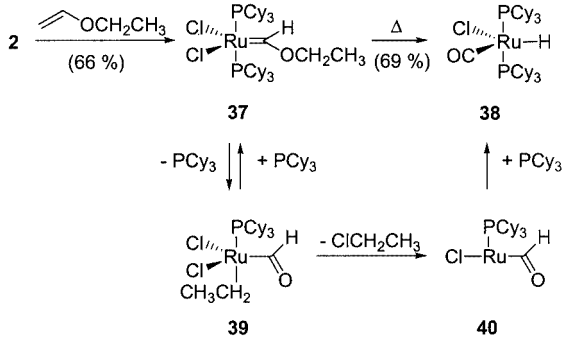
More recently, some pathways leading from ruthenium carbene to ruthenium hydride complexes have been discovered and investigated mechanistically. Hydrogenolysis of the first-generation Grubbs catalyst **2** yields, depending on the conditions, hydride, dihydride, and dihydrogen complexes (Scheme 8).[43] Under hydrogen, the dihydride complex **35** is obtained, which is in equilibrium with a dihydrogen complex **36**. HCl abstraction from **36** gives the hydride/dihydrogen complex **30**, which is also accessible directly from carbene complex **2** if a base such as 1,8-(dimethylamino)naphthalene is present. Complex **30** had previously been prepared from a halide-free dihydride complex and dichloromethane.[44]



Scheme 8. Hydrogenation of first-generation Grubbs catalyst

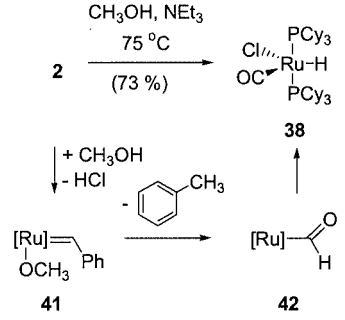
Ruthenium hydrides containing an additional CO ligand result from the thermal decomposition of Fischer-type ruthenium carbene complexes: treatment of **2** with ethyl vinyl ether gives carbene complex **37**, which upon heating loses chloroethane to give $[RuHCl(CO)(PCy_3)_2]$ (**38**).[45] The proposed mechanism for this transformation[46] involves formation of a formyl complex **39** that eliminates chloroethane to give **40**. Re-coordination of the phosphane ligand induces CO extrusion and formation of **38**, which has been characterized by X-ray crystallography (Scheme 9).[45]

The same hydride **38** results when **2** is treated with methanol in the presence of base.[47] Here, however, a mechanism is postulated that proceeds via substitution of one chloride ion by methanol and transfer of two hydrogen atoms to the benzylidene ligand (which is cleaved from the complex as toluene). Extrusion of CO occurs from the resulting formyl complex **42**, leading to hydride **38**. It should be noted that



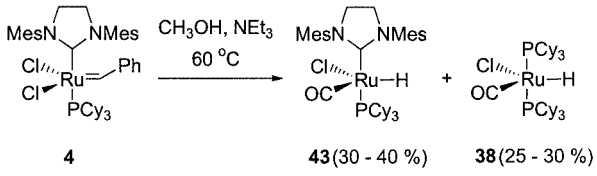
Scheme 9. Thermal decomposition of a Fischer-type Ru carbene complex

the same product results if other primary alcohols are used (Scheme 10).



Scheme 10. Hydrido-carbonyl complexes formed from ruthenium carbene complexes and primary alcohols

The analogous reaction of second-generation catalyst **4** also gives hydrido-carbonyl complexes, but with lower selectivity. Dinger and Mol,[48] as well as Grubbs et al.,[49] published that **4**, upon reaction with methanol, yields hydrides **43** and **38** as a mixture, along with minor amounts of other hydride complexes (Scheme 11). Grubbs et al. have also been able to detect **43** as a byproduct formed during the preparation of second-generation catalyst **4**, and they attribute its formation to the use of methanol as a washing solvent.[49] A hydride complex analogous to **43**, which bears an unsaturated N-heterocyclic carbene ligand, has been prepared from **38** by exchange of one phosphane ligand.[50]



Scheme 11. Reaction of second-generation catalysts with methanol

No hydride complex results from the reaction of Grubbs catalyst **2** with allyl alcohol. Instead, the dichloro complex $[RuCl_2(CO)(PCy_3)_2]$ is formed in solution. It appears to be likely that ruthenium hydride species are intermediates in this process.[51]

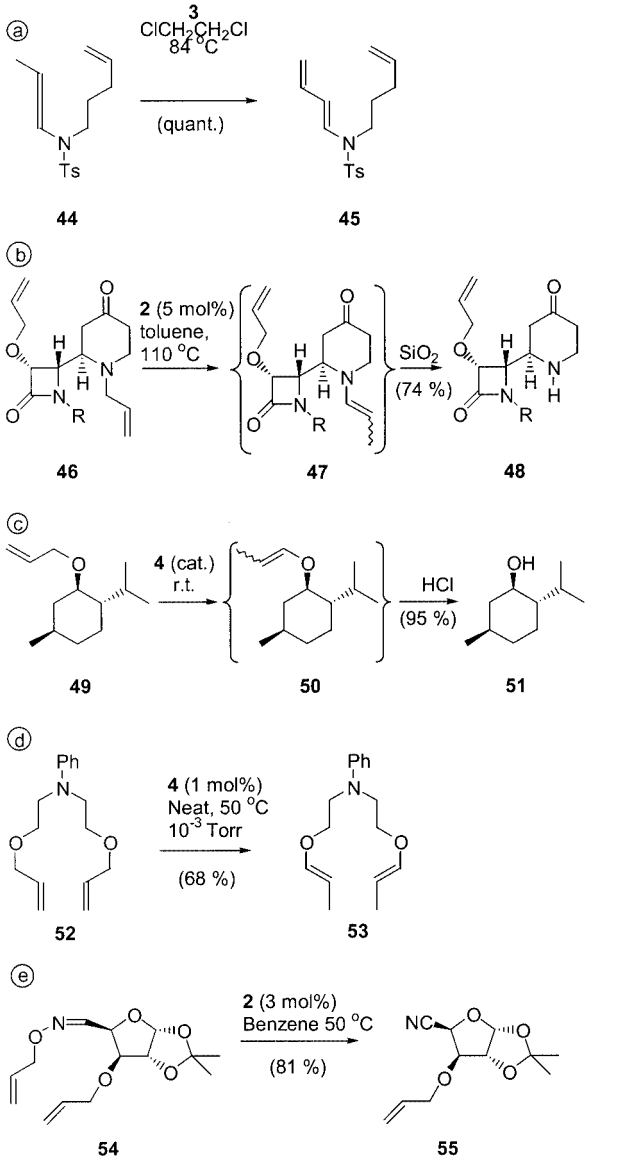
The catalytic activity of ruthenium hydride complexes in a variety of transformations has been documented in reviews.[52,53] The hydride **38**, for instance, which had previously been prepared[54] from $RuCl_3$, PCy_3, and methanol,[55] is an efficient catalyst for hydrogenation,[48,50,56,57] isomerization,[47,48] and hydrovinylation.[58] Similar catalytic activity has been described for hydride complexes bearing a saturated[48] or an unsaturated[50] N-heterocyclic carbene ligand.

3. Transformations Catalyzed by or Involving Ru Hydrides Generated in situ from Ru Carbene Complexes

In this section, we present an overview of non-metathesis transformations mediated by ruthenium carbene complexes that occur with high selectivity and that are likely to proceed via ruthenium hydride species.

3.1 Isomerization

Some examples for the isomerization of C−C double bonds catalyzed by ruthenium carbene complexes have been reported over the past few years, where the isomerization is no longer a side reaction but is the strongly preferred or even exclusively observed pathway. For instance, Rutjes et al. observed a quantitative isomerization of the allenamide **44** to the conjugated diene **45** (Scheme 12, a).[59] The group of Alcaide has developed a protocol for the deprotection of allylamines[60a,61] and allyllactams[60b,61] that relies on the selective isomerization to enamines and enamides, respectively, catalyzed by first-generation catalyst **2**. Hydrolysis or oxidative cleavage liberates the deprotected amines or lactams. The sequence is illustrated for the particularly remarkable conversion **46** → **48**, where the allylamine is selectively isomerized to intermediate **47** in the presence of an allyl ether moiety (Scheme 12, b). This finding is surprising, as the deprotection of allyl ethers using a ruthenium metathesis catalyst has been reported shortly afterwards by Cossy et al.[62] The conditions applied in this study are, however, different from those used by Alcaide et al. For example, second-generation catalyst **4** catalyzes the isomerization of allyl ether **49** to a vinyl ether **50** in chlorinated solvents at ambient temperature. Cleavage of **50** with aqueous HCl yields deprotected alcohol **51** (Scheme 12, c). Highly selective isomerization of allyl ethers in the presence of catalytic amounts of **4** has also been observed by Wagener et al. for compounds of type **52** under conditions that are normally used to achieve acyclic diene metathesis polymerization (Scheme 12, d).[63] No double bond isomerization appears to be involved in a recently published conversion of sugar-derived oximes to nitriles that are catalyzed by first-generation Grubbs catalyst **2**. For example, **54** does not cyclize to the expected RCM product under metathesis conditions; instead, formal elimination of allyl alcohol occurs to yield the nitrile **55**. Remarkably, no isomerization of the second allyl ether function is observed in this case



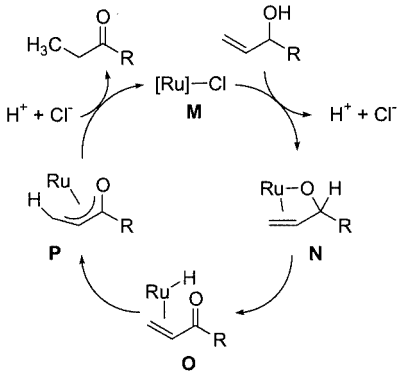
Scheme 12. Selective isomerization of allyl ethers and allyl amines to vinyl ethers and vinyl amines

(Scheme 12, e). It cannot be said, however, whether or not a ruthenium hydride species plays a role in this transformation.[64]

Mechanistic proposals for double bond isomerization reactions have already been discussed above. While Cossy et al. proposed the presence of ruthenium hydride species and, thus, a hydrometalation/β-hydride elimination pathway, as outlined in Scheme 4,[62] Wagener et al. favor the π-allyl hydride mechanism, as they could not observe any metal hydride species by spectroscopic means; the metal hydride-catalyzed pathway, however, could also not be definitely excluded.[63]

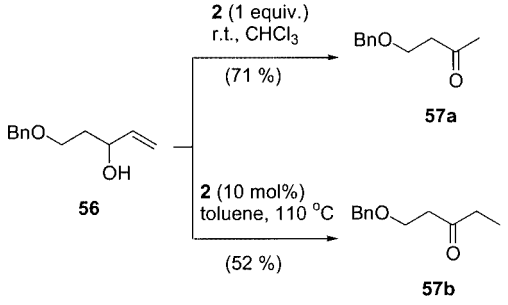
The isomerization of allylic alcohols to ketones, often referred to as redox isomerization, can be catalyzed by ruthenium complexes, and examples for the use of Grubbs catalyst in this transformation have been published recently. It is believed that the mechanism of this transformation in-

volves replacement of a ruthenium-bound chloride ion in **M** by the allylic alcohol, giving intermediate **N**. β-Hydride elimination gives enone **O**, which is coordinated to a Ru−H species and undergoes subsequent migratory insertion into the Ru−H bond, leading to η^3 complex **P**. The complex **P** is cleaved from the metal by protonation to yield **M** and the ketone (Scheme 13).[65]



Scheme 13. Proposed mechanism for redox isomerization of allylic alcohols to ketones

The stoichiometric fragmentation of allylic alcohols to methyl ketones in the presence of Grubbs catalyst has been discussed above (Scheme 5).[26] More recently, Gurjar and Yakambram described a catalytic isomerization of allylic alcohols to ketones in the presence of the same catalyst.[66] If, for instance, **56** is treated with one equivalent of **2** at ambient temperature, the methyl ketone **57a** is obtained, analogously to the observations reported by Hoye and Zhao. In contrast, treatment of **56** with a catalytic amount of **2** in toluene under reflux induces isomerization to ethyl ketone **57b** (Scheme 14).

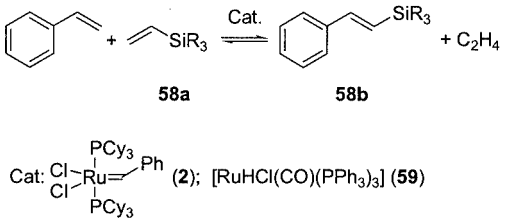


Scheme 14. Redox isomerization of allylic alcohols vs. fragmentation

Successful isomerization of allylic alcohols is also possible with significantly lower amounts of catalyst (4 mol %) in dichloromethane under reflux.[67] A 2:1 mixture of redox isomerization and fragmentation product had previously been obtained in an unsuccessful ring closing metathesis reaction conducted using an extremely high catalyst loading.[68]

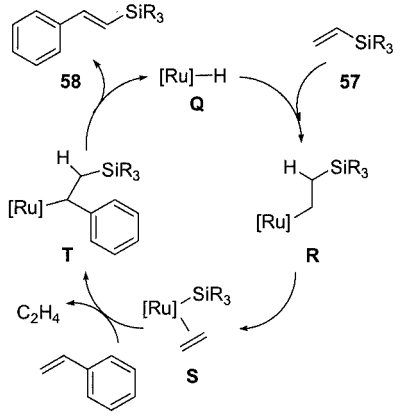
3.2 Activation of Silanes

Studies in the groups of Marcieniec and Fischer have revealed that styrene reacts with vinylsilanes **58a** in the presence of ruthenium carbene complex **2**[69] or the ruthenium hydride complex [RuHCl(CO)$(PPh_3)_3$] (**59**)[70] to give the same cross-metathesis product **58b** and ethylene (Scheme 15).



Scheme 15. Cross-metathesis of styrene and vinylsilanes

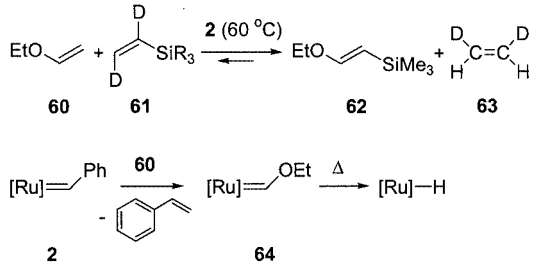
A mechanism for the ruthenium hydride-catalyzed reaction has been proposed (Scheme 16)[70] that involves insertion of the vinylsilane into the Ru−H bond of **Q** to give the σ-alkyl intermediate **R**, which undergoes β-silyl elimination to give the Ru−Si intermediate **S**. Ethylene is displaced by styrene, which inserts into the Ru−Si bond to give a new σ-alkyl intermediate **T**. β-Hydride elimination regenerates the catalytically active species **Q** and liberates the vinylsilane **58**. Alternatively, catalysts containing Ru−Si bonds can be employed in this reaction; these catalysts give comparable results.[70]



Scheme 16. Mechanism of the silylation of styrene with vinylsilanes catalyzed by Ru hydride

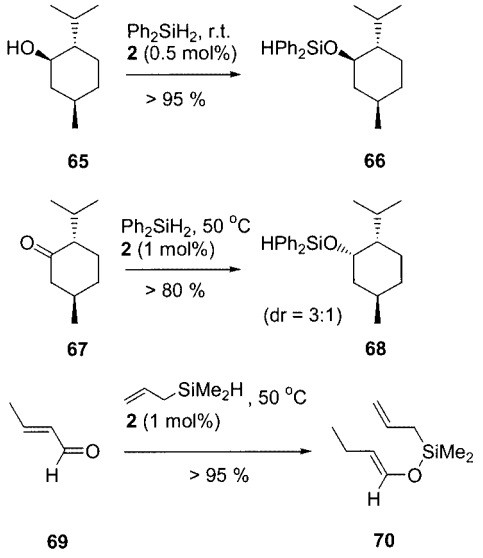
Naturally, the question arises if the reaction of styrene and vinylsilanes **58a** catalyzed by Grubbs catalyst **2** is a true cross-metathesis[8] (proceeding via the classical Chauvin mechanism) or if it proceeds via a ruthenium hydride-catalyzed silyl transfer mechanism. In this case, labeling studies using [D_8]styrene revealed that, in the presence of ruthenium carbene **2**, a metathesis mechanism operates that indeed proceeds via ruthenacyclobutanes.[69][71] Interestingly, this mechanism does not seem to be true for the reaction of vinylsilanes with vinyl ethers. A deuterium labeling study revealed that, from ethyl vinyl ether **60** and [D_2]vinylsilane **61**, deuterium-free **62** results exclusively if a catalytic amount of ruthenium carbene **2** is present. This result strongly suggests that the mechanism outlined in Scheme 16

works in this case. The ruthenium hydride species required to initiate the catalytic cycle is formed by reaction of precatalyst **2** with ethyl vinyl ether to give a Fischer-type ruthenium carbene complex **64**, which then decomposes to a ruthenium hydride species (Scheme 17). The latter process has already been discussed above (refer to Scheme 9 for details).[72]



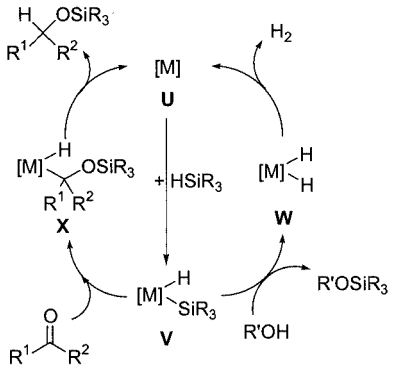
Scheme 17. Silylative coupling of vinyl ethers catalyzed by ruthenium carbene complex **2**

It has recently been demonstrated, that ruthenium carbene complex **2** can efficiently catalyze the dehydrogenative silylation of alcohols (e.g., **65** → **66**) and the hydrosilylation of carbonyl compounds (e.g., **67** → **68**) to silyl ethers. If an α,β-unsaturated aldehyde **69** is employed in the reaction, the corresponding silyl enol ether **70** is trapped (Scheme 18).[73]



Scheme 18. Dehydrogenative silylation and hydrosilylation mediated by ruthenium carbene **2**

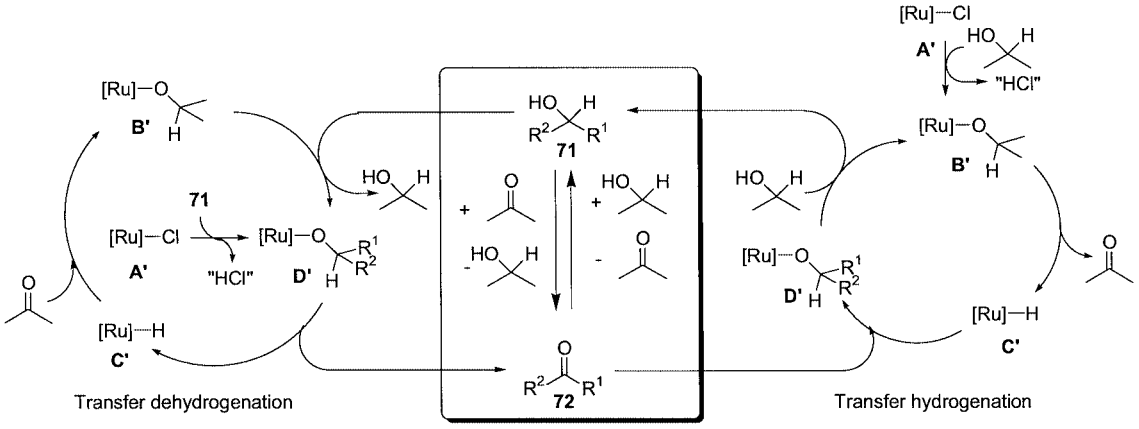
It is not clear what is the catalytically active species in these transformations, but it is likely that the ruthenium assists in the cleavage of the Si−H bond, presumably by oxidative addition of the silane to a metal fragment. Dehydrogenative silylation of alcohols and hydrosilylation of ketones are well-known processes and mechanistic proposals have been reviewed.[74,75] One mechanistic proposal is outlined in Scheme 19 in simplified form: the silane undergoes oxidative addition to the metal fragment **U**, resulting in the M−Si species **V**. Dehydrogenative silylation is described in the right cycle: nucleophilic attack of the alcohol at the silicon center leads to formation of a metal dihydride **W** and the silyl ether. Reductive elimination of hydrogen regenerates the catalytically active species **U**. Hydrosilylation of ketones might be rationalized by assuming the same M−Si species **V**, which reacts with the substrate in an insertion into the M−Si−bond (intermediate **X**), followed by reductive elimination of the product and regeneration of the catalytically active species **U**.



Scheme 19. Simplified catalytic cycle for transition metal-catalyzed dehydrogenative silylation of alcohols (right) and the hydrosilylation of ketones (left)

3.3 Transfer Hydrogenation/Dehydrogenation

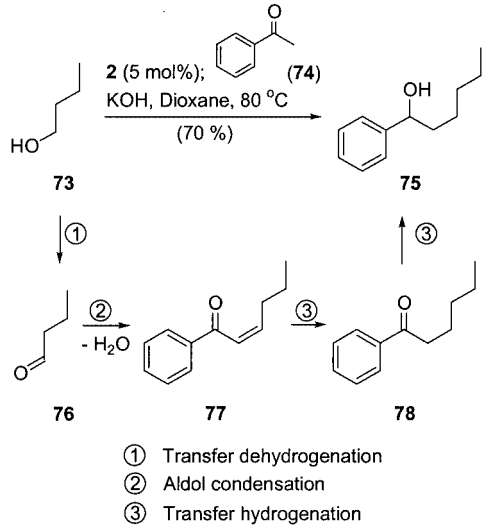
It was described in the 1970s that the ruthenium complex $[RuCl_2(PPh_3)_3]$ catalyzes the transfer hydrogenation of saturated and unsaturated ketones to secondary alcohols or saturated ketones, respectively, using secondary alcohols as a source of hydrogen.[76] More recently, cyclopentadienyl complexes of ruthenium have attracted considerable interest as precatalysts.[77,78] Catalyzed transfer hydrogenation and dehydrogenation have been reviewed,[79] and especially enantioselective variants have attracted considerable attention.[80] The simplified mechanistic picture outlined in Scheme 20 is sufficient to highlight the basic principles of these catalytic transformations. In a transfer hydrogenation, ketone **72** is reduced by an excess of a hydrogen-donating agent (e.g., 2-propanol or other primary or secondary alcohols) to give alcohol **71**. If the hydrogenating agent is 2-propanol, one equivalent of acetone is formed. The reverse reaction is a transfer dehydrogenation, where hydrogen is transferred from alcohol **71** to acetone (or another hydrogen acceptor). The reaction of ruthenium chloro complexes **A′** with the alcohols provides an entry into the catalytic cycle: in the transfer hydrogenation, **A′** reacts with 2-propanol to give an alkoxo complex **B′**, which undergoes reductive elimination of acetone with simultaneous formation of a ruthenium hydride species **C′**. Insertion of ketone **72** into the Ru−H bond gives alkoxo complex **D′**, which reacts with 2-propanol (present in a large excess, e.g., as a solvent or co-solvent). The hydrogenated product **71** results and **B′** is regenerated (Scheme 20, right cycle). In a transfer de-



Scheme 20. Simplified mechanisms of transfer hydrogenation and transfer dehydrogenation

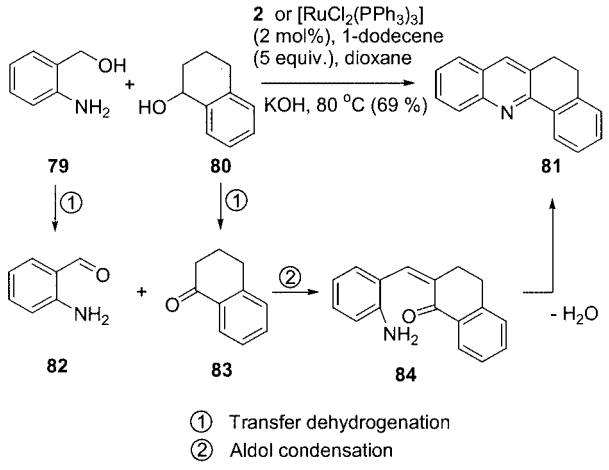
hydrogenation (Scheme 20, left cycle) entry into the catalytic cycle is possible by substitution of a chloride by the substrate **71**. Alkoxo complex **D′** results, which undergoes reductive elimination of **72**, giving the ruthenium hydride species **C′**, which inserts the hydrogen acceptor (e.g., acetone, which has to be present in large excess) giving alkoxo complex **B′**. Isopropanol is cleaved from **B′** by reaction with the substrate. When alcohols are used as hydrogen-donating agents, addition of a base is necessary to facilitate formation of the alkoxo complex. This fact has been omitted for simplicity in Scheme 20.

Grubbs catalyst **2** and other ruthenium complexes have recently been employed successfully in a transfer dehydrogenation/aldol condensation/double transfer hydrogenation sequence discovered by Cho, Shim, et al.[81] As outlined in Scheme 21, primary alcohols, e.g., 1-butanol (**73**), react with acetophenone (**74**) in the presence of a catalytic amount of **2** and KOH to give alcohol **75**. This result can be understood by assuming a transfer dehydrogenation of **73** to give butanal (**76**), which then undergoes an aldol condensation with **74**, yielding enone **77**. Enone **77** undergoes two subsequent transfer hydrogenations to give the final product **75** (Scheme 21).



Scheme 21. A transfer dehydrogenation/aldol condensation/double transfer hydrogenation sequence

Later, the same authors demonstrated that the sequence does not necessarily require a ketone such as **74**. If 1-phenylethanol is used instead of acetophenone in the presence of 1-dodecene as a hydrogen acceptor and $[RuCl_2(PPh_3)_3]$ as a catalyst, the same coupling product **75** is obtained.[82] This reaction has been applied to a synthesis of quinolines, which is outlined in Scheme 22: amino alcohol **79** and alcohol **80** are coupled in the presence of a catalytic amount of either $[RuCl_2(PPh_3)_3]$ or Grubbs catalyst **2** and excess 1-dodecene to give the quinoline **81**.[83] The reaction proceeds via transfer dehydrogenation of **79** and **80** with 1-dodecene as the hydrogen acceptor, giving **82** and **83**, followed by aldol condensation to give **84**. From **84**, water is eliminated to give the quinoline **81** (Scheme 22).

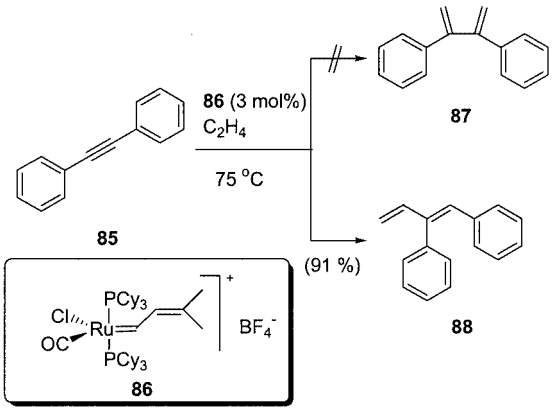


Scheme 22. Quinoline synthesis based on Ru-catalyzed transfer dehydrogenation

3.4 Hydrovinylation

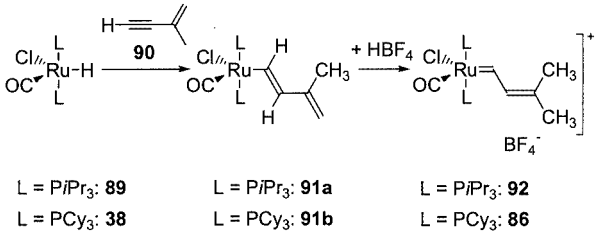
When Yi et al. investigated the utility of cationic carbene complex **86** in an intermolecular enyne metathesis reaction,[84] they observed the selective formation of hydrovinylation, rather than enyne metathesis products.[54] Alkyne **85**,

for instance, is converted selectively into conjugated diene **88**, rather than **87** (Scheme 23).



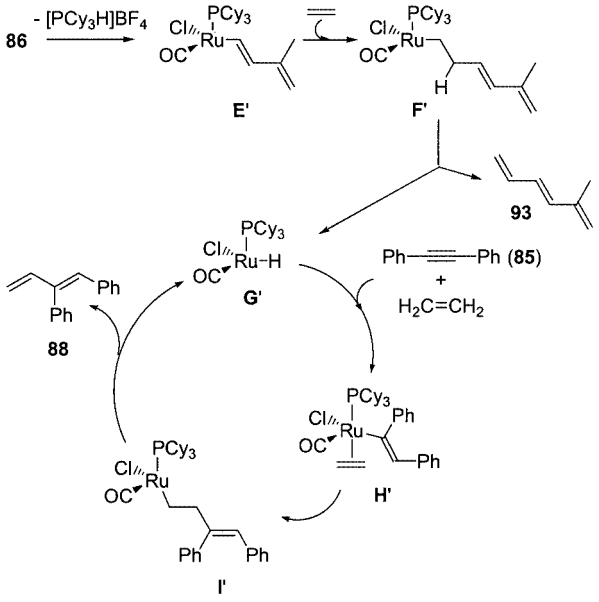
Scheme 23. Hydrovinylation mediated by carbene complex **86**

While enyne metathesis reactivity relies on metal carbene species, a hydrovinylation pathway can be rationalized by assuming a ruthenium hydride as the catalytically active species. There is indeed a close relationship between cationic ruthenium carbene complexes of type **86** and ruthenium hydride complexes [RuHCl(CO)L_2] (L = phosphane ligand). For instance, it has been demonstrated by Esteruelas et al. that hydride **89** reacts with enyne **90** in an insertion reaction to give vinyl complex **91a**, which can be protonated to give a cationic carbene complex **92**, which is the P*i*Pr_3 analogue of **86** (Scheme 24).[85] The PCy_3 complex **86** was prepared analogously from [RuHCl(CO)$(PCy_3)_2$] (**38**), which is, interestingly, the final product resulting from reaction of Grubbs catalysts with vinyl ethers or primary alcohols (refer to Schemes 9−11 for details).[54]



Scheme 24. Synthesis of cationic ruthenium carbene complex **92**

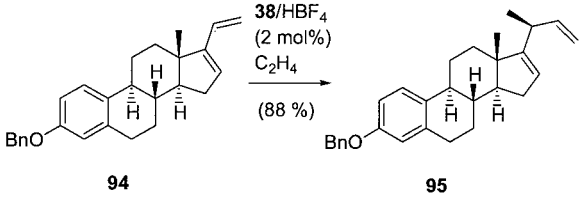
Yi et al. proposed a mechanism for the ruthenium carbene-catalyzed hydrovinylation reaction that assumes the presence of **38** as the actual catalytically active complex (Scheme 25). According to this proposal, **86** eliminates [$PHCy_3$]BF_4 by deprotonation of one terminal methyl group of the carbene ligand to give coordinatively unsaturated **E′**, which would then insert ethene (giving **F′**). From **F′**, triene **93** is eliminated in a β-hydrogen elimination to give coordinatively unsaturated hydride **G′**. The alkyne **85** inserts into the Ru−H bond and ethene is coordinated. The resulting vinyl complex **H′** undergoes a migratory insertion to give alkyl complex **I′**, from which the hydrovinylation product **88** is cleaved by β-H elimination (Scheme 25). This



Scheme 25. Proposed catalytic cycle for ruthenium hydride-mediated hydrovinylation

mechanism is supported by the following observations: a) [$PHCy_3$]BF_4 was observed by spectroscopic means; b) the δ-methyl group in **86** is acidic and deprotonation affords **91b** (Scheme 24); c) **86**, **91b**, and **38** are all catalytically active, which suggests that **G′** is indeed the entry point into the catalytic cycle.[54]

Very recently, the hydrovinylation catalyzed by either **86** or **38** has been extended to conjugated dienes.[86] It has been noted previously that the efficiency of **38** can be enhanced significantly by the addition of HBF_4.[58] The catalytic system **38**/HBF_4 has, for instance, been used to promote the transformation **94** → **95** outlined in Scheme 26.



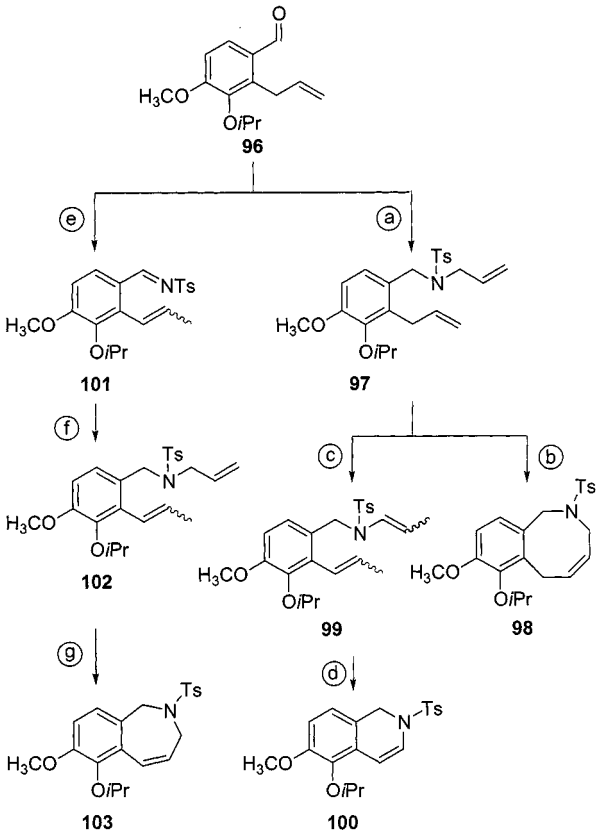
Scheme 26. Hydrovinylation of conjugated dienes catalyzed by **86** or **38**

4. Ru Carbene and Ru Hydride-Mediated Steps in Reaction Sequences

4.1 Isomerization, Followed by Metathesis

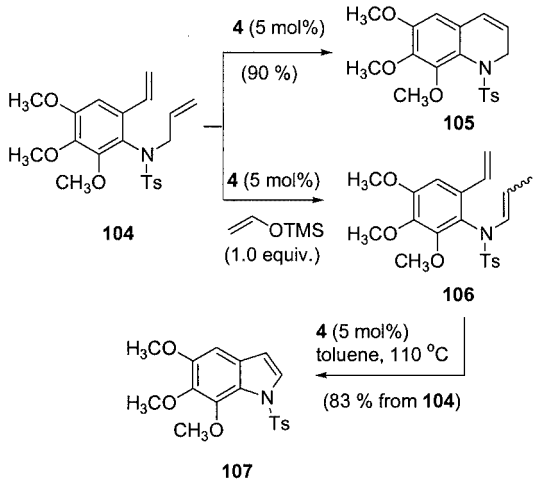
The selective isomerization of one or both double bonds in a certain metathesis substrate can sometimes facilitate the synthesis of the precursor and significantly enhance the flexibility of a synthetic strategy by making various ring sizes accessible from the same set of starting materials. This principle has recently been exploited in the synthesis of benzo-fused heterocycles.[87,88] From substituted benzaldehyde **96**, for instance, metathesis precursor **97** is available

by reductive amination in two steps. Compound **97** can be cyclized to the eight-membered azacycle **98** in the presence of ruthenium carbene complex **4**, or isomerized to **99** in the presence of the aforementioned ruthenium hydride complex [RuHCl(CO)(PPh_3)$_3$] (**59**). RCM of **99** catalyzed by **4** yields the six-membered azacycle **100**. Isomerization of one double bond gives access to the seven-membered azacycles: **96** is converted into its corresponding tosylamine, followed by ruthenium hydride-catalyzed isomerization of the double bond. The resulting compound **101** is converted in two steps into the metathesis precursor **102**, which is then cyclized using ruthenium carbene complex **4** to give the seven-membered azacycle **103** (Scheme 27). The efficiency of **59** in the catalysis of double bond isomerizations has also been demonstrated for allylamides[89] and α,β-unsaturated esters.[90]



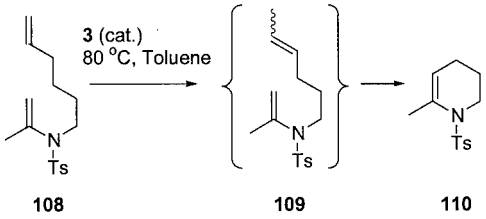
Scheme 27. Combination of Ru−H-mediated isomerization and Ru carbene-mediated RCM. Key: a) Allylamine, TsOH (cat.), 110 °C; $NaBH_4$, MeOH, 0 °C; TsCl, Et_3N, DCM, room temp. (93% overall). b) **4** (5 mol %), toluene, 60 °C (quant.) c) **59** (0.5 mol %), toluene, 110 °C. d) **4** (5 mol %), toluene, 110 °C (76% from **97**). e) Tosylamine, toluene, 110 °C; **59** (1 mol %), toluene, 80 °C. f) $NaBH_4$, MeOH, 0 °C (98%); NaH, THF, room temp., allyl bromide (64%). g) **4** (5 mol %), toluene, 60 °C, (quant.)

A similar sequence has been exploited for the synthesis of indoles. In this case, however, the isomerization catalyst is generated in situ from the metathesis catalyst **4** by addition of vinyloxytrimethylsilane as an additive.[91] It is not fully clear what happens to the ruthenium carbene complex **4** upon addition of vinyloxytrimethylsilane, but the authors report that the carbene functionality disappears and styrene is formed. An example for the application of this protocol is outlined in Scheme 28: allyl amide **104** can be cyclized to the expected RCM product **105** using ruthenium carbene complex **4**. In the presence of vinyloxytrimethylsilane, however, isomerization to enamide **106** occurs under otherwise identical conditions. Enamide **106** can be cyclized under normal RCM conditions to give indole **107**.



Scheme 28. Indole synthesis based on an isomerization/RCM sequence

An example of isomerization and RCM occurring in a single step has been reported previously. Enamide **108**, in the presence of ruthenium carbene complex **3**, is cyclized to **110** and not to the expected seven-membered ring.[59] Probably, under the reaction conditions, **3** is incompletely converted into an isomerization catalyst, which mediates the isomerization to **109** faster than it mediates ring closing metathesis. Compound **109** is then cyclized by **3** to give the cyclic enamide **110** (Scheme 29).

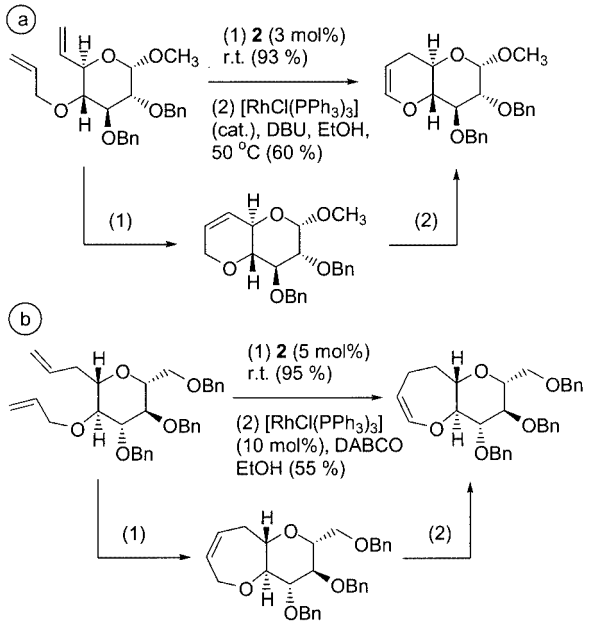


Scheme 29. Isomerization/RCM mediated by a single site catalyst

4.2 Metathesis, Followed by Isomerization

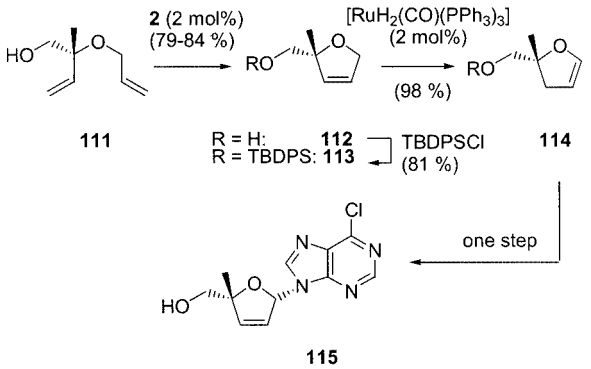
Ring closing metathesis of enol ethers or enamines is sometimes disadvantageous, because more-active (and less conveniently accessible) catalysts are required and high dilution has to be applied in most cases to suppress intermolecular metathesis. These problems normally do not arise in the cyclization of allyl ethers or allyl amines. Therefore, strategies have been developed that combine ring closing

metathesis followed by isomerization of the primary metathesis product. For instance, ruthenium-catalyzed RCM followed by a rhodium-catalyzed isomerization has been applied to the synthesis of *trans*-fused polyethers by van Boom et al. (Scheme 30, a)[92] and by Hirama et al. (Scheme 30, b).[93]



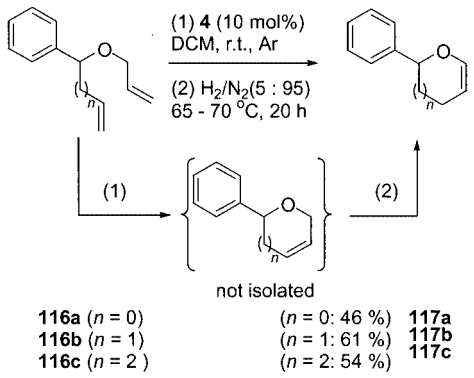
Scheme 30. Ru-catalyzed RCM and Rh-catalyzed isomerization (two-step procedure)

Ruthenium hydride complexes, e.g., $[RuH_2(PPh_3)_4]$, can also be used to mediate the isomerization of cyclic allyl ethers to cyclic enol ethers.[94] In combination with olefin metathesis, this process has been exploited by Trost et al. for the synthesis of nucleosides.[95] Thus, diallyl ether **111** is cyclized to **112**, which − after protection − isomerizes to enol ether **114** in the presence of dihydride complex $[RuH_2(CO)(PPh_3)_3]$. From **114** and related compounds, non-natural nucleosides, such as **115**, were synthesized in one step (Scheme 31).



Scheme 31. Ru carbene-catalyzed RCM and Ru hydride-catalyzed isomerization (two-step procedure)

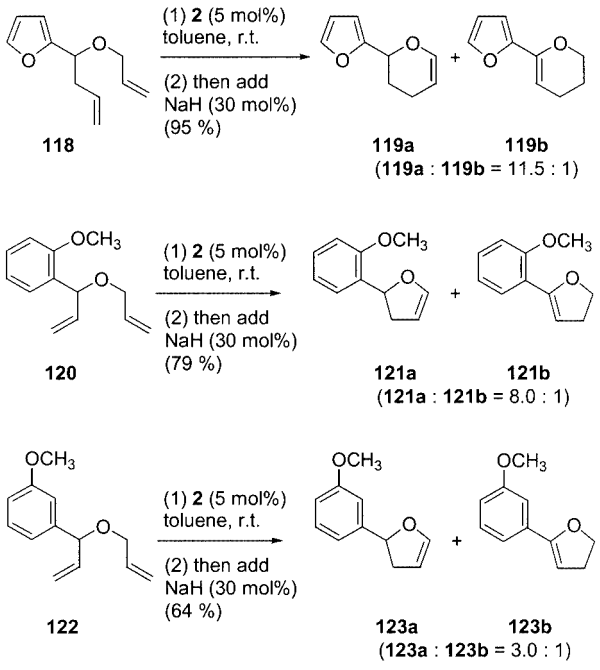
An olefin metathesis/isomerization sequence proceeding via a single-site ruthenium catalyst has been developed independently by Snapper et al.[96] and by our group.[97] Both protocols require modification of the ruthenium carbene catalyst after the metathesis step is complete (presumably to a ruthenium hydride species) and have been applied to the synthesis of cyclic enol ethers. In Snapper's protocol, an isomerization catalyst is obtained from the metathesis catalyst **4** by changing the reaction atmosphere from argon to a 95:5 nitrogen/hydrogen mixture. Under these conditions, less than 10% of hydrogenation products are formed. Scheme 32 illustrates the sequence for the synthesis of five-, six-, and seven-membered cyclic enol ethers **117a**−**c** from acyclic allyl ethers **116a**−**c**.[96]



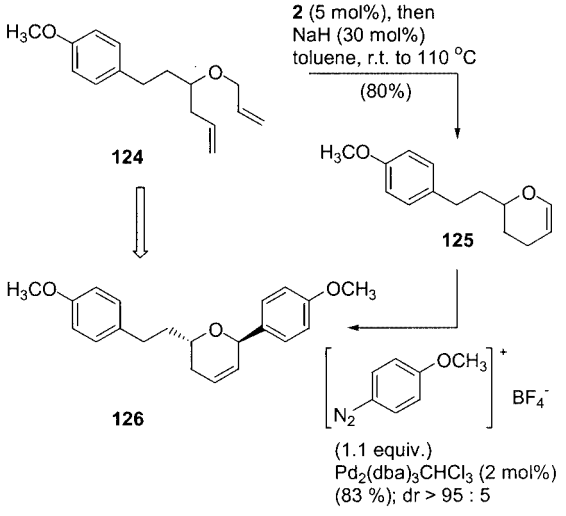
Scheme 32. Snapper's protocol for a Ru-catalyzed RCM/isomerization sequence (one-step procedure)

Our protocol differs mainly in the generation of the ruthenium hydride species. We found, that addition of substoichiometric amounts of inorganic hydrides, such as NaH or $NaBH_4$, to a completed metathesis reaction induces the formation of a species that catalyzes olefin isomerization at elevated temperatures. High regioselectivity was observed for dihydropyrans: for instance, application of the protocol to **118** gives **119** along with less than 10% of the thermodynamically preferred regioisomer where the double bond is in conjugation with the furyl moiety. For other examples of six-membered cyclic enol ethers, this regioisomer is not detectable. For dihydrofurans, significantly lower regioselectivities were observed: while *ortho*-methoxy-substituted **120** gives regioisomers **121a**,**b** as an 8:1 mixture, only a 3:1 ratio of **123a**,**b** was obtained from *meta*-substituted **122** (Scheme 33). The difference might be attributed to steric factors.[97]

We have recently demonstrated the usefulness of the metathesis/isomerization sequence for organic synthesis. In an approach to the carbon skeleton of cyclic diarylheptanoid natural products (**126**),[98] dihydropyran **125** was required. Compound **125** was conveniently obtained from allyl homoallyl ether **124** using the RCM-isomerization sequence. Heck reaction of **125** using an electron-rich aryldiazonium salt gives **126** as a single regio- and diastereoisomer in good yield (Scheme 34).[99]



Scheme 33. Schmidt's protocol for a Ru-catalyzed RCM/isomerization sequence (one-step procedure)

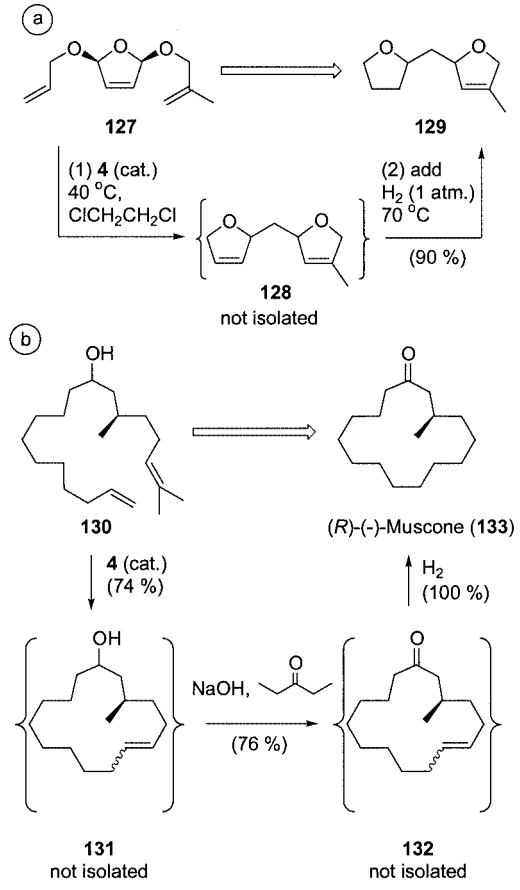


Scheme 34. Application of the RCM/isomerization sequence

4.3 Olefin Metathesis, Followed by Hydrogenation

Quite often in the synthesis of a target molecule, the C−C double bond constructed by olefin metathesis has to be hydrogenated in a subsequent step. Routinely, this is achieved by hydrogenation in the presence of palladium on charcoal in a two-step procedure. More recently, Cossy et al. published a single-step procedure using two compatible catalysts (metathesis catalyst **5** and hydrogenation catalyst PtO_2) to selectively hydrogenate cross-metathesis products.[100,101]

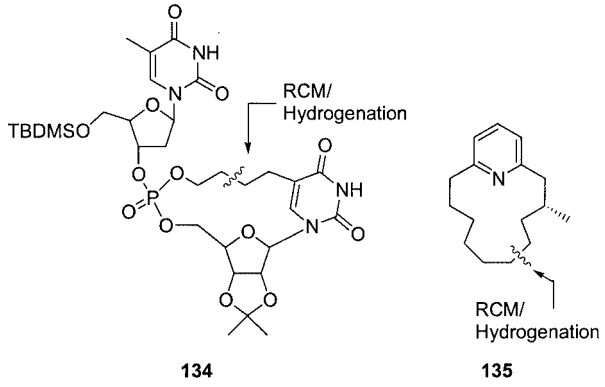
Sequential olefin metathesis/hydrogenation mediated by a single-site ruthenium catalyst was first applied to metathesis polymerization products. Watson and Wagener reported the ruthenium carbene-catalyzed homogeneous acyclic diene metathesis of α,ω-dienes. Absorbing the catalyst on silica after completion of the polymerization reaction gives an active hydrogenation catalyst, presumably a ruthenium hydride species.[102] Ruthenium carbene-catalyzed ring opening metathesis polymerization (ROMP) has been combined with an atom radical transfer polymerization and a hydrogenation reaction by Grubbs et al.[103] It was proposed by the authors that, under hydrogen at elevated temperatures, residual ruthenium species are converted into $[Ru(H_2)HCl(PCy_3)_2]$ (**30**), which is the actual hydrogenation catalyst (refer to Scheme 8 for details). Similarly, Fogg et al. described a ROMP/hydrogenation sequence using ruthenium carbene complex **2**. These authors demonstrated that, after completion of the hydrogenation reaction, a metathesis-active carbene complex can be regenerated by addition of a propargyl chloride (refer to Scheme 7 for the synthesis of ruthenium carbene complexes from hydrides). Thus, a cycling between hydrogenation and metathesis activity is possible in principle.[104,105] Application of an olefin metathesis/hydrogenation sequence to low-molecular weight products has been reported by Grubbs et al. and is outlined for two examples in Scheme 35. Ring opening/ring closing metathesis of cyclopentene **127** yields the primary metathesis product **128**, which, under hydrogen at 70 °C, is selectively converted into the tetrahydrofuran **129**. The ruthenium hydride **30** was detected in the reaction mixture (Scheme 30, a). A short synthesis of (*R*)-(−)-muscone con-



Scheme 35. Olefin metathesis/hydrogenation sequences

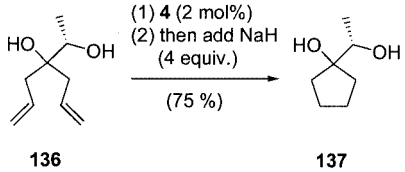
tains an additional transfer dehydrogenation step (Scheme 30, b): diene **130** is cyclized by a catalytic amount of **4** to give **131**. Subsequently, the ruthenium catalyst is used to mediate a transfer dehydrogenation with pentane-3-one as the hydrogen acceptor to the macrocyclic ketone **132**. The remaining C−C double bond is finally hydrogenated in quantitative yield, giving (*R*)-(−)-muscone (**133**) in 56% overall yield.[106]

Scheme 36 highlights two further examples for the application of the sequential metathesis/hydrogenation protocol: cyclic dinucleotide **134**[107] and the natural product (*R*)-(+)-muscopyridine **135**.[108] The C−C bonds constructed by RCM and hydrogenation are indicated by wavy lines.



Scheme 36. Application of sequential RCM/hydrogenation

In the examples described so far, activation of the metathesis catalyst for hydrogenation has been achieved by hydrogenolysis at elevated temperatures. We explored the alternative method of activation by using inorganic hydrides as additives (outlined above for the RCM/isomerization sequence; refer to Scheme 33 for details) for the RCM/hydrogenation sequence. When a substoichiometric amount of NaH is added to a metathesis reaction, hydrogenation occurs even at ambient temperature under hydrogen. In contrast, no hydrogenation is observed under hydrogen at ambient temperature in the absence of hydride additives. In the presence of protic functional groups, it is even possible to generate the hydrogen in situ by using excess NaH. This point is illustrated by the synthesis of cyclopentanes (e.g., **137**) from diallylcarbinols (e.g., **136**) (Scheme 37).[109]



Scheme 37. Activation of Ru metathesis catalysts for hydrogenation reactions at ambient temperature by addition of hydrides

5. Conclusions and Perspective

The examples discussed in this review illustrate that a close relationship exists between ruthenium hydride- and ruthenium carbene-catalyzed transformations. Ruthenium hydrides can serve as precursors for ruthenium carbene complexes, but ruthenium carbene complexes can also be converted into ruthenium hydride complexes by reaction with hydrogen or by decomposition. This organometallic relationship is probably responsible for several undesired side reactions, especially olefin isomerization. It also opens up, however, completely new and unforeseen applications of ruthenium-based metathesis catalysts. Combinations of ruthenium carbene-mediated (metathesis) steps and ruthenium hydride-mediated (e.g., isomerization, hydrogenation, and transfer hydrogenation) steps to sequences will most likely broaden the scope of ruthenium-catalyzed olefin metathesis beyond the high level that has already been reached today.

Acknowledgments

Our own contributions to the field were generously supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Department of Chemistry of the University of Dortmund. I thank Andrea Bokelmann for assistance in the preparation of the manuscript and Jolanda Hermanns and Bernd Plietker for proofreading the manuscript.

[1] R. R. Schrock, J. S. Murdzek, G. C. Bazan, J. Robbins, M. DiMare, M. O'Regan, *J. Am. Chem. Soc.* **1990**, *112*, 3875−3886.
[2] G. C. Fu, S. T. Nguyen, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1993**, *115*, 9856−9857.
[3] M. Schuster, S. Blechert, *Angew. Chem.* **1997**, *109*, 2124−2145; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2036−2055.
[4] S. K. Armstrong, *J. Chem. Soc., Perkin Trans. 1* **1998**, 371−388.
[5] R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413−4450.
[6] A. Fürstner, *Angew. Chem.* **2000**, *112*, 3140−3172; *Angew. Chem. Int. Ed.* **2000**, *39*, 3013−3043.
[7] R. R. Schrock, *Top. Organomet. Chem.* **1998**, *1*, 1−36.
[8] S. J. Connon, S. Blechert, *Angew. Chem.* **2003**, *115*, 1944−1968; *Angew. Chem. Int. Ed.* **2003**, *42*, 1900−1923.
[9] W. A. Herrmann, C. Köcher, *Angew. Chem.* **1997**, *109*, 2257−2282; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2162−2187.
[10] T. Weskamp, F. J. Kohl, W. Hieringer, D. Gleich, W. A. Herrmann, *Angew. Chem.* **1999**, *111*, 2573−2576; *Angew. Chem. Int. Ed.* **1999**, *38*, 2416−2419.
[11] J. Huang, E. D. Stevens, S. P. Nolan, J. L. Petersen, *J. Am. Chem. Soc.* **1999**, *121*, 2674−2678.
[12] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953−956.
[13] S. Gessler, S. Randl, S. Blechert, *Tetrahedron Lett.* **2000**, *41*, 9973−9976.
[14] S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179.
[15] M. Ulman, R. H. Grubbs, *J. Org. Chem.* **1999**, *64*, 7202−7207.
[16] H. D. Maynard, R. H. Grubbs, *Tetrahedron Lett.* **1999**, *40*, 4137−4140.
[17] D. Bourgeois, A. Pancrazi, L. Ricard, J. Prunet, *Angew. Chem.* **2000**, *112*, 742−744; *Angew. Chem. Int. Ed.* **2000**, *39*, 725−728.
[18] S. D. Edwards, T. Lewis, R. J. K. Taylor, *Tetrahedron Lett.* **1999**, *40*, 4267−4270.
[19] A. Fürstner, O. R. Thiel, L. Ackermann, H.-J. Schanz, S. P. Nolan, *J. Org. Chem.* **2000**, *65*, 2204−2207.

[20] B. Schmidt, H. Wildemann, *J. Org. Chem.* **2000**, *65*, 5817−5822.
[21] J. Le Nôtre, L. Brissieux, D. Sémeril, C. Bruneau, P. H. Dixneuf, *Chem. Commun.* **2002**, 1772−1773.
[22] H. B. Ammar, J. Le Notre, M. Salem, M. T. Kaddachi, P. H. Dixneuf, *J. Organomet. Chem.* **2002**, *662*, 63−69.
[23] D. Bourgeois, A. Pancrazi, S. P. Nolan, J. Prunet, *J. Organomet. Chem.* **2002**, *643−644*, 247−252.
[24] D. V. McGrath, R. H. Grubbs, *Organometallics* **1994**, *13*, 224−235.
[25] A. Fürstner, L. Ackermann, B. Gabor, R. Goddard, C. W. Lehmann, R. Mynott, F. Stelzer, O. R. Thiel, *Chem. Eur. J.* **2001**, *7*, 3236−3253.
[26] T. R. Hoye, H. Zhao, *Org. Lett.* **1999**, *1*, 169−171.
[27] T. R. Hoye, H. Zhao, *Org. Lett.* **1999**, *1*, 1123−1125.
[28] B. Cetinkaya, S. Demir, I. Özdemir, L. Toupet, D. Sémeril, C. Bruneau, P. H. Dixneuf, *Chem. Eur. J.* **2003**, *9*, 2323−2330.
[29] S. J. Connon, S. Blechert, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1873−1876.
[30] M. Bassetti, F. Centola, D. Sémeril, C. Bruneau, P. H. Dixneuf, *Organometallics* **2003**, *22*, 4459−4466.
[31] Y. Yamamoto, Y. Nakagai, N. Ohkoshi, K. Itoh, *J. Am. Chem. Soc.* **2001**, *123*, 6372−6380.
[32] B. Schmidt, *Angew. Chem.* **2003**, *115*, 5146−5149; *Angew. Chem. Int. Ed.* **2003**, *42*, 4996−4999.
[33] B. Alcaide, P. Almendros, *Chem. Eur. J.* **2003**, *9*, 1259−1262.
[34] J. A. Tallarico, L. M. Malnick, M. L. Snapper, *J. Org. Chem.* **1999**, *64*, 344−345.
[35] P. Quayle, D. Fengas, S. Richards, *Synlett* **2003**, 1797−1800.
[36] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100−110.
[37] T. E. Wilhelm, T. R. Belderrain, S. N. Brown, R. H. Grubbs, *Organometallics* **1997**, *16*, 3867−3869.
[38] M. A. O. Volland, F. Rominger, F. Eisenträger, P. Hofmann, *J. Organomet. Chem.* **2002**, *641*, 220−226.
[39] J. Wolf, W. Stüer, C. Grünwald, H. Werner, P. Schwab, M. Schulz, *Angew. Chem.* **1998**, *110*, 1165−1167; *Angew. Chem. Int. Ed.* **1998**, *37*, 1125−1126.
[40] J. Wolf, W. Stüer, C. Grünwald, O. Gevert, M. Laubender, H. Werner, *Eur. J. Inorg. Chem.* **1998**, 1827−1834.
[41] P. A. van der Schaaf, R. Kolly, A. Hafner, *Chem. Commun.* **2000**, 1045−1046.
[42] J. N. Coalter III, G. J. Spivak, H. Gérard, E. Clot, E. R. Davidson, O. Eisenstein, K. G. Caulton, *J. Am. Chem. Soc.* **1998**, *120*, 9388−9389.
[43] S. D. Drouin, G. P. A. Yap, D. E. Fogg, *Inorg. Chem.* **2000**, *39*, 5412−5414.
[44] M. L. Christ, S. Sabo-Etienne, B. Chaudret, *Organometallics* **1994**, *13*, 3800−3804.
[45] J. Louie, R. H. Grubbs, *Organometallics* **2002**, *21*, 2153−2164.
[46] Z. Wu, S. T. Nguyen, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1995**, *117*, 5503−5511.
[47] M. B. Dinger, J. C. Mol, *Organometallics* **2003**, *22*, 1089−1095.
[48] M. B. Dinger, J. C. Mol, *Eur. J. Inorg. Chem.* **2003**, 2827−2833.
[49] T. M. Trnka, J. P. Morgan, M. S. Sanford, T. E. Wilhelm, M. Scholl, T. L. Choi, S. Ding, M. W. Day, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 2546−2558.
[50] H. M. Lee, D. C. Smith, Z. J. He, E. D. Stevens, C. S. Yi, S. P. Nolan, *Organometallics* **2001**, *20*, 794−797.
[51] H. Werner, C. Grunwald, W. Stuer, J. Wolf, *Organometallics* **2003**, *22*, 1558−1560.
[52] T. Naota, H. Takaya, S. Murahashi, *Chem. Rev.* **1998**, *98*, 2599−2660.
[53] B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067−2096.
[54] C. S. Yi, D. W. Lee, Y. Z. Chen, *Organometallics* **1999**, *18*, 2043−2045.
[55] M. A. Esteruelas, H. Werner, *J. Organomet. Chem.* **1986**, *303*, 221−231.
[56] C. S. Yi, D. W. Lee, *Organometallics* **1999**, *18*, 5152−5156.
[57] C. S. Yi, D. W. Lee, Z. He, A. L. Rheingold, K.-C. Lam, T. E. Concolino, *Organometallics* **2000**, *19*, 2909−2915.
[58] C. S. Yi, Z. J. He, D. W. Lee, *Organometallics* **2001**, *20*, 802−804.
[59] S. S. Kinderman, J. H. van Maarseveen, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *Org. Lett.* **2001**, *3*, 2045−2048.
[60] [60a] B. Alcaide, P. Almendros, J. M. Alonso, M. F. Aly, *Org. Lett.* **2001**, *3*, 3781−3784. [60b] B. Alcaide, P. Almendros, J. M. Alonso, *Tetrahedron Lett.* **2003**, *44*, 8693−8695.
[61] B. Alcaide, P. Almendros, J. M. Alonso, *Chem. Eur. J.* **2003**, *9*, 5793−5799.
[62] C. Cadot, P. I. Dalko, J. Cossy, *Tetrahedron Lett.* **2002**, *43*, 1839−1841.
[63] J. C. Sworen, J. H. Pawlow, W. Case, J. Lever, K. B. Wagener, *J. Mol. Catal. A* **2003**, *194*, 69−78.
[64] A. Talukdar, *Synth. Commun.* **2002**, *32*, 3503−3508.
[65] B. M. Trost, R. J. Kulawiec, *J. Am. Chem. Soc.* **1993**, *115*, 2027−2036.
[66] M. K. Gurjar, P. Yakambram, *Tetrahedron Lett.* **2001**, *42*, 3633−3636.
[67] E. S. Greenwood, P. J. Parsons, M. J. Young, *Synth. Commun.* **2003**, *33*, 223−228.
[68] K. Nakashima, R. Ito, M. Sono, M. Tori, *Heterocycles* **2000**, *53*, 301−314.
[69] C. Pietraszuk, B. Marciniec, H. Fischer, *Organometallics* **2000**, *19*, 913−917.
[70] B. Marciniec, C. Pietraszuk, *Organometallics* **1997**, *16*, 4320−4326.
[71] C. Pietraszuk, B. Marciniec, H. Fischer, *Tetrahedron Lett.* **2003**, *44*, 7121−7124.
[72] B. Marciniec, M. Kujawa, C. Pietraszuk, *New J. Chem.* **2000**, *24*, 671−675.
[73] S. V. Maifeld, R. L. Miller, D. Lee, *Tetrahedron Lett.* **2002**, *43*, 6363−6366.
[74] E. Lukevics, M. Dzintara, *J. Organomet. Chem.* **1985**, *295*, 265−315.
[75] B. Marciniec, in *Applied Homogeneous Catalysis with Organometallic Compounds, Vol. 1* (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, Weinheim, **1996**, pp. 487−506.
[76] Y. Sasson, J. Blum, *J. Org. Chem.* **1975**, *40*, 1887−1896.
[77] J. B. Johnson, J.-E. Bäckvall, *J. Org. Chem.* **2003**, *68*, 7681−7684.
[78] M. Ito, A. Osaku, S. Kitahara, M. Hirakawa, T. Ikariya, *Tetrahedron Lett.* **2003**, *44*, 7521−7523.
[79] S. Gladiali, G. Mestroni, in *Transition Metals for Organic Synthesis, Vol. 2* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, pp. 97−119.
[80] V. Rautenstrauch, X. Hoang-Cong, R. Churland, K. Abdur-Rashid, R. H. Morris, *Chem. Eur. J.* **2003**, *9*, 4954−4967.
[81] C. S. Cho, B. T. Kim, T.-J. Kim, S. C. Shim, *J. Org. Chem.* **2001**, *66*, 9020−9022.
[82] C. S. Cho, B. T. Kim, H.-S. Kim, T.-J. Kim, S. C. Shim, *Organometallics* **2003**, *22*, 3608−3610.
[83] C. S. Cho, B. T. Kim, H.-J. Choi, T.-J. Kim, S. C. Shim, *Tetrahedron* **2003**, *59*, 7997−8002.
[84] C. S. Poulsen, R. Madsen, *Synthesis* **2003**, 1−18.
[85] M. A. Esteruelas, F. Liu, E. Onate, E. Sola, B. Zeier, *Organometallics* **1997**, *16*, 2919−2928.
[86] Z. He, C. S. Yi, W. A. Donaldson, *Org. Lett.* **2003**, 1567−1569.
[87] W. A. L. van Otterlo, E. L. Ngidi, C. B. de Koning, *Tetrahedron Lett.* **2003**, *44*, 6483−6486.
[88] W. A. L. van Otterlo, R. Pathak, C. B. de Koning, *Synlett* **2003**, 1859−1861.
[89] S. Krompiec, M. Pigulla, T. Bieg, W. Szczepankiewicz, N. Kuznik, M. Krompiec, M. Kubicki, *J. Mol. Catal. A* **2002**, *189*, 169−185.
[90] H. Wakamatsu, M. Nishida, N. Adachi, M. Mori, *J. Org. Chem.* **2000**, *65*, 3966−3970.
[91] M. Arisawa, Y. Terada, M. Nakagawa, A. Nishida, *Angew. Chem.* **2002**, *114*, 4926−4928; *Angew. Chem. Int. Ed.* **2002**, *41*, 4732−4734.

[92] M. A. Leeuwenburgh, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Synlett* **1997**, 1263−1264.
[93] H. Oguri, S. Tanaka, T. Oishi, M. Hirama, *Tetrahedron Lett.* **2000**, *41*, 975−978.
[94] D. P. Curran, P. B. Jacobs, R. L. Elliott, B. H. Kim, *J. Am. Chem. Soc.* **1987**, *109*, 5280−5282.
[95] B. M. Trost, B. S. Brown, E. J. McEachern, O. Kuhn, *Chem. Eur. J.* **2003**, *9*, 4442−4451.
[96] A. E. Sutton, B. A. Seigal, D. F. Finnegan, M. L. Snapper, *J. Am. Chem. Soc.* **2002**, *124*, 13390−13391.
[97] B. Schmidt, *Eur. J. Org. Chem.* **2003**, 816−819.
[98] M. S. Ali, Y. Tezuka, A. H. Banskota, S. Kadota, *J. Nat. Prod.* **2001**, *64*, 491−496.
[99] B. Schmidt, *Chem. Commun.* **2003**, 1656−1657.
[100] J. Cossy, F. C. Bargiggia, S. BouzBouz, *Tetrahedron Lett.* **2002**, *43*, 6715−6717.
[101] J. Cossy, F. C. Bargiggia, S. BouzBouz, *Org. Lett.* **2003**, *5*, 459−462.
[102] M. D. Watson, K. B. Wagener, *Macromolecules* **2000**, *33*, 3196−3201.
[103] C. W. Bielawski, J. Louie, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 12872−12873.
[104] S. D. Drouin, F. Zamanian, D. E. Fogg, *Organometallics* **2001**, *20*, 5495−5497.
[105] D. E. Fogg, D. Amoroso, S. D. Drouin, J. L. Snelgrove, J. C. Conrad, F. Zamanian, *J. Mol. Catal. A* **2002**, *190*, 177−184.
[106] J. Louie, C. W. Bielawski, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 11312−11313.
[107] P. Børsting, P. Nielsen, *Chem. Commun.* **2002**, 2140−2141.
[108] A. Fürstner, A. Leitner, *Angew. Chem.* **2003**, *115*, 320−323; *Angew. Chem. Int. Ed.* **2003**, *42*, 308−311.
[109] B. Schmidt, M. Pohler, *Org. Biomol. Chem.* **2003**, *1*, 2512−2517.

Received November 10, 2003
Early View Article
Published Online February 5, 2004

