ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
http://web.icf.ro/rrch/

Rev. Roum. Chim.,
2011, *56*(4), 299-316

Dedicated to Professor Alexandru T. Balaban on the occasion of his 80th anniversary

REVIEW

NEW INSIGHTS INTO THE MECHANISM OF ALKENE METATHESIS

Carmen I. MITAN,* Valerian DRAGUTAN and Ileana DRAGUTAN

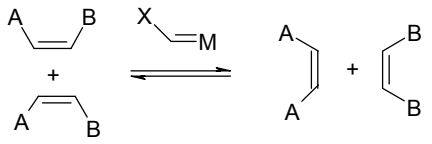
Institute of Organic Chemistry, Roumanian Academy, Spl. Independentei, 202 B, sect. 6, Bucharest, Roumania

Received September 8, 2010

The diversity of alkene metathesis reactions, presently applied to their full potential in synthesis of complex scaffolds and assemblies or as key steps in the total synthesis of natural products, demands a deep understanding of the intricate metathesis mechanism since not all of the catalysts are efficient for all of the substrates, nor do they trigger the identical mechanistic pathways, though they share the same main intermediates (the generally accepted metallacarbene and metallacyclobutane). Beyond that, metathesis processes are occasionally complicated by the occurrence of side reactions resulting in a number of by-products. Unveiling the influence of reaction conditions, and in particular of the catalytic system and the active species generated thereof during metathesis of a chosen substrate is paramount for obtaining high yields in the targeted product, at low costs. This paper focuses on relevant kinetic and mechanistic aspects reported to date for alkene metathesis induced by Ru-alkylidene complexes, concentrating on the interplay ligand dissociation – initiation step – overall catalytic activity, as determined by the catalyst structure.

INTRODUCTION

Alkene metathesis is basically a catalytic transalkylidenation reaction formally occurring by scission of two olefinic carbon-carbon double bonds with formation of two new C=C bonds (Scheme 1).[1] Continuously improved activity and selectivity of catalysts (especially those based on W, Mo and Ru), and the availability of a number of commercial initiators, have revolutionized the metathesis field during the past two decades promoting this reaction to its current status of a prime mover in organic synthesis, polymer chemistry, materials science etc., as largely illustrated in authoritative books,[2] book chapters[3] and excellent reviews.[4-6]



Scheme 1 – General Representation of Alkene Metathesis.

Metathesis encompasses a range of well-established synthetic methodologies such as ring-closing metathesis (RCM), ring-opening metathesis (ROM), cross-metathesis (CM), enyne metathesis (EM), acyclic diene metathesis (ADMET) and ring-opening metathesis polymerization (ROMP). Presently alkene metathesis is expanding beyond these traditional reactions towards less conventional, highly innovative and promising pathways such as asymmetric ring-closing metathesis (ARCM), asymmetric ring-opening metathesis (AROM), ring-opening cross metathesis (ROCM), ring-closing enyne metathesis (RCEYM), ring-rearrangement metathesis (RRM), ring-closing alkyne metathesis (RCAM), alternating ring-opening metathesis polymerization (AROMP).

In the context of the intense progress in organometallic chemistry and catalysis a great deal of transition metal complexes have been employed as metathesis catalysts.[7] Starting primarily with ill-defined systems (based on W, Mo),[8] this class moved quickly to the more efficient metal

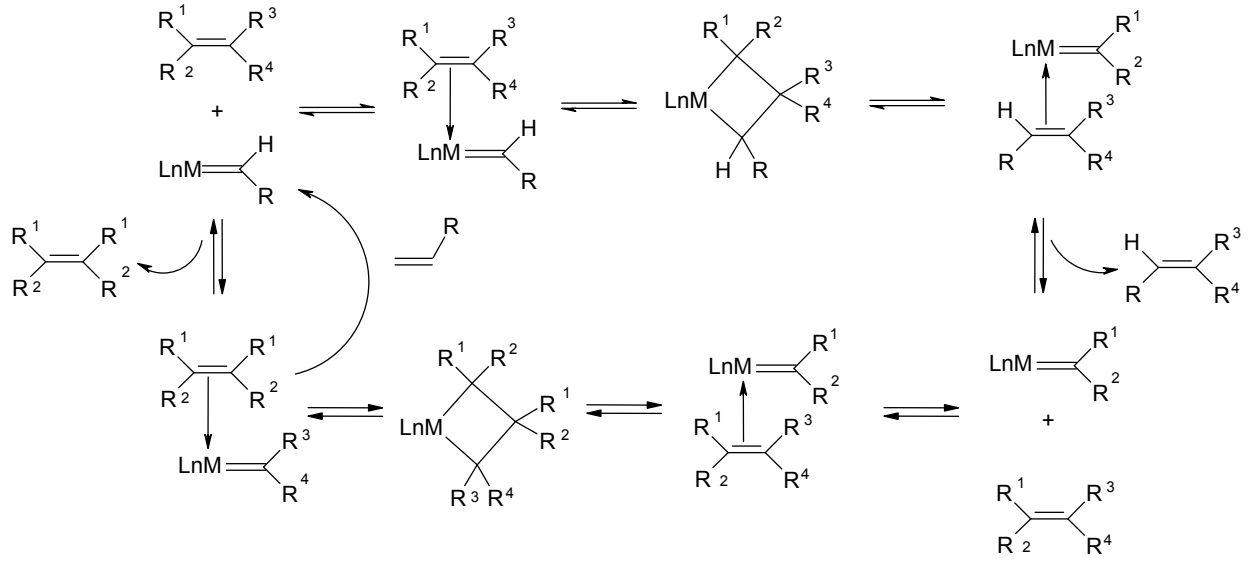
* Corresponding author: cmitan@yahoo.com

alkylidenes of which Schrock'[9] and Grubbs'[2a] catalysts have gained unanimous recognition. More specific tasks could be additionally achieved with a host of finely elaborated ruthenium-based precursors recognized either by the name of their promoters (Blechert,[10,11] Grela,[12,13] Nolan,[14] Verpoort[15] or by the particular ligands (actor or ancillary) they incorporate, *e.g.* NHC,[16-20] Schiff base,[21-25] arene,[26] indenylidene,[27,28] allenylidene[29,30] etc. Most developed representatives soon saw promotion through several generations (*e.g.* Grubbs 1st to 3rd generation), which parallel changes in ligands and correspond to an improvement in their catalytic performance in view of commercialization.

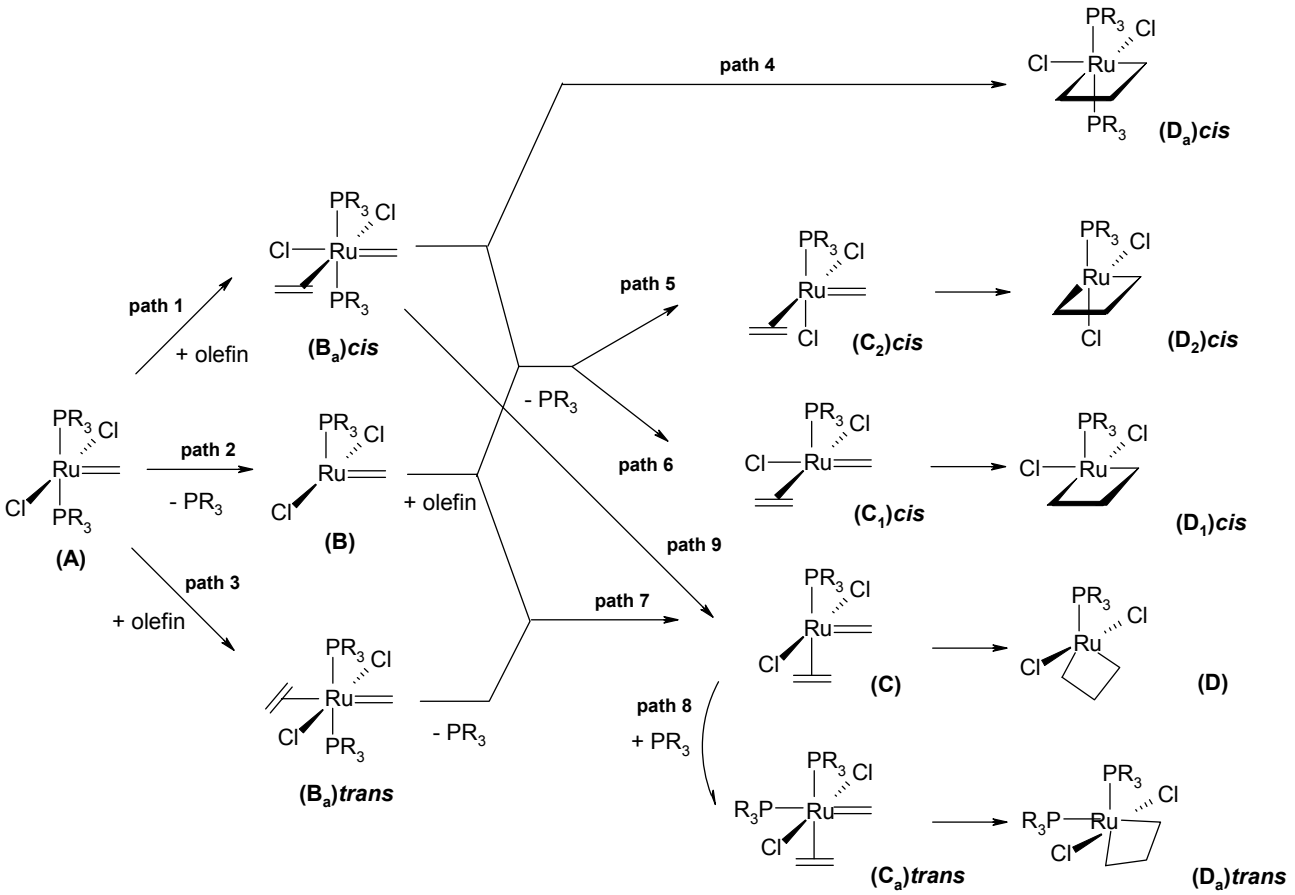
The metal-catalyzed formation of a new C=C bond between two olefins occurs under mild reaction conditions with high control over factors such as chemo-, region-, and stereoselectivity (Scheme 1).[31] While Schrock type catalysts,[32] Mo-imido alkylidenes, offer advantages of their high activity and enantioselectivity, Grubbs type catalysts,[33] Ru-alkylidene, offer high tolerance of functional groups, air stability and are easy to handle. Ruthenium-alkylidene complexes with general formula $[(PR_3)(L)Cl_2Ru{=}CHR']$ require one ligand loss, respectively the trialkyl phosphine PR_3, to generate the catalytic "active species" $[(L)Cl_2Ru{=}CHR']$ with a vacant coordination site able to interact with an olefin substrate. The active species, of the d^6-Ru(II)-based catalyst are d^4-Ru(IV) metal complexes with basic ligands which display a preference for soft Lewis bases and π-acids (olefins) over hard bases (oxygen containing compounds: alcohols, amides, aldehydes, carboxylic acids).[34] The efficiency of olefin metathesis catalysts is essentially influenced by the choice of the metal and ligands.[35]

THE MECHANISM OF ALKENE METATHESIS CATALYZED BY RUTHENIUM ALKYLIDENE CATALYSTS

The Hérisson-Chauvin olefin metathesis mechanism involves the formation of a metallacyclobutane intermediate by coordination of the olefinic substrate onto a transition metallacarbene complex (Scheme 2).[31b] The generally accepted catalytic cycle of transition metal catalyzed the formation of a new double bond consists in a reversible sequence of [2+2] cycloadditions – cycloreversion, *i.e.*:[36] alkene coordination to the metallacarbene complex, cycloaddition, and cycloreversion to the/a new alkene and metallacarbene by breaking of two different bonds. The newly formed metallacarbene complex, after coordination with a new olefin molecule, metallacyclobutane formation, and double bond reordering, gives the metathesis product and re-forms the ruthenium carbene initiator which restarts the cycle. As the product no longer participates in the catalytic cycle, the equilibrium is thus shifted towards formation of further product molecule (Scheme 2). According to the principle of detailed balance (PDB),[37] at equilibrium the reverse and forward rates of all chemical reactions or all elementary steps involved are identical, and the reverse reaction proceeds through the same series of elementary steps as the forward reaction.

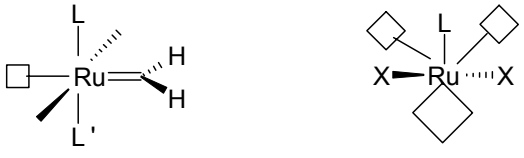


Scheme 2 – General Mechanism of Metathesis Catalyzed by Transition Metal Carbenes.



Scheme 3 – Postulated Mechanisms for Olefin Metathesis with Grubbs-type. Ruthenium Carbene Complexes (*J. Am. Chem. Soc.* **2004**, *126*, 3496).

As can be seen in Scheme 3, in the case of diphosphane ruthenium carbene complexes $[(PR_3)_2Cl_2Ru{=}CHR']$, two competing pathways were proposed for the first step of the mechanism: (i) a dominant one ("dissociative") proceeds by an initial loss of PR_3 to generate a 14-electron intermediate (**B**), followed by coordination of the olefinic substrate (path 2), or else first coordination of the olefinic substrate followed by loss of PR_3 ligand (path 1, and path 3), and (ii) a minor pathway ("associative") in which the olefin coordinates to the catalyst to form an 18-electron olefin π complex ($\mathbf{B_a}$), followed by [2+2] cycloaddition (path1/4).[38,39] In an early study on mechanism performed by Grubbs and Sanford, the first step of the second dissociative pathway (path 1, and path 3) was also named associative.[40] The rate determining step, metallacycle formation, is a 14-electron complex in the "dissociative" pathway and a 16-electron complex in the "associative" pathway.[38] The coordination of olefin may occur *cis* (path 5 and 6) or *trans* (path 7) relative to the phosphane ligand in the 16-electron olefin π complexes (**C**). The calculated activation energies $\Delta E^{\#}$ indicate as favorable two reaction pathways: (1) the dissociative pathway 2 proceeding through formation of the 14 electron complex (**B**) with subsequent coordination of the olefin *trans* to the phosphane ligand (**C**), and (2) olefin metathesis is initiated by a *trans* associative exchange of the phosphane ligand by the olefin (path 3). For both possibilities, metallacyclobutane formation (path 7) leads to the trigonal bipyramidal metallacyclobutane intermediate (**D**).[39] The barrier difference for the intramolecular cycloaddition reaction was connected to carbene ligand rotation. Diamagnetic complexes of transition metals with partially occupied d-orbitals (d^2 to d^8) generally maintain their geometry upon ligand removal. The Ru(II) intermediate in metathesis catalysis can be classified as pseudo-octahedral, with a free coordination site occupying the sixth vertex, and Ru(IV) as a pentagonal bipyramid with two free coordination sites in the pentagon close to the spectator ligand L (Fig. 1).[41]



Ru(II), d^6-ML_5

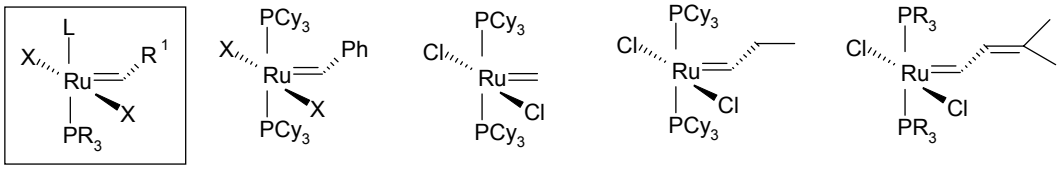
16-valence electrons
one formally coordination site
Structure derived from octahedron

Ru(IV), d^4-ML_5

14-valence electrons
two formally coordination sites
Structure derived from pentagonal bipyramid

Fig. 1 – Electronic Classification and Geometry of Ruthenium Complexes in Alkene Metathesis.

First generation Grubbs catalysts



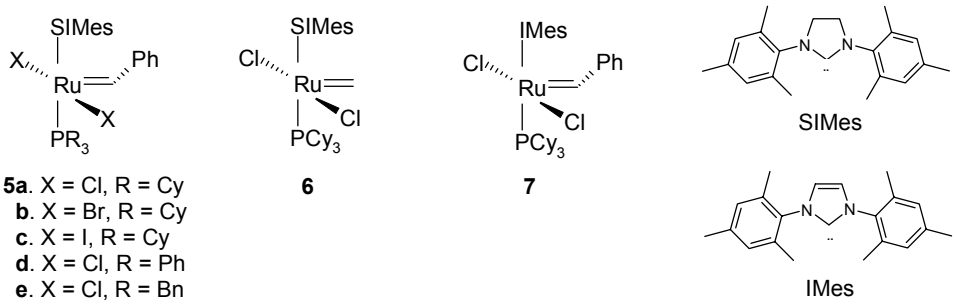
1a. X = Cl
b. X = Br
c. X = I

2

3

4a. R = Cy
b. R = Cp

Second generation Grubbs catalysts



5a. X = Cl, R = Cy
b. X = Br, R = Cy
c. X = I, R = Cy
d. X = Cl, R = Ph
e. X = Cl, R = Bn

6

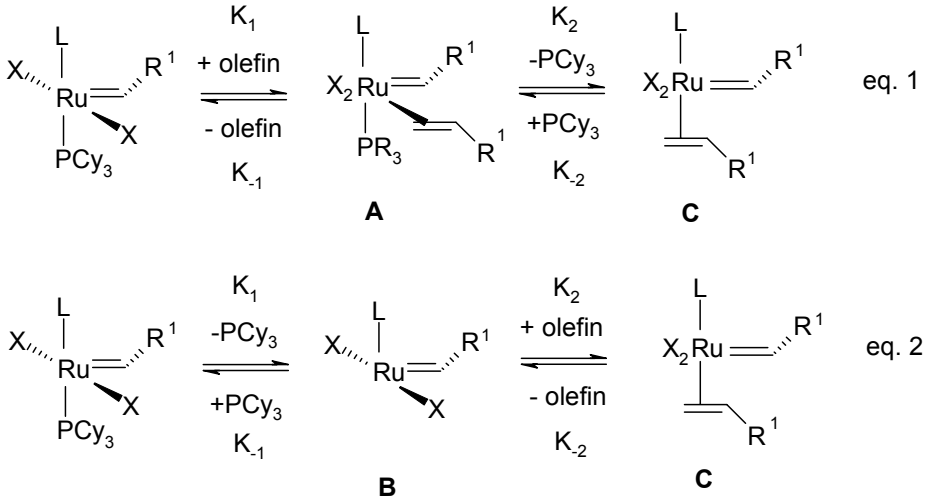
7

Fig. 2 – Ruthenium Complexes of the General Formula $L(PR_3)(X)_2Ru{=}CHR^1$.

Two limiting cases were used for studying the mechanism of the leaving ligand substitution (phosphane) with the olefinic substrate in order to determine the difference in reactivity between the first generation Grubbs catalysts, the bis-phosphane complexes **1-4**, and the second generation Grubbs catalysts, the NHC-coordinated complexes **5-7**, and also the influence of L, X, PR_3, R^1 ligands on the rates of phosphane dissociation and catalyst activity (Scheme 4, Fig. 2). The first limiting case, namely associative (Scheme 4, eq.1), involves coordination of the olefin to the Ru center to form the coordinatively saturated (18-electron) intermediate **A**, followed by the dissociation of the leaving ligand, while the second one, namely dissociative (Scheme 4, eq. 2), implies dissociation of the leaving ligand to form the 14-electron intermediate **B**, followed by coordination of the olefinic substrate. The associative pathway was taken into consideration due to the known preference for the 18-electron intermediate over the 14-electron counterpart.[40]

Because in both cases a 16-electron intermediate **C** (undetectable by spectroscopic methods) is formed, a degenerate exchange reaction model between free and bound PR_3 in Ru complexes of general formula $L(PR_3)(X)_2Ru{=}CHR^1$ was required as a model system for phosphane/olefin substitution (Scheme 5, eq. 1). The exchange rate constant (K_B) of the bound phosphane (P_B) with the free phosphine (P_F) at 80^0C, determined by ^{13}P-NMR magnetization transfer (MT), decreased over 2 orders of magnitude in case of **5a** comparative to **1a**. This is

an unexpected result since the sterically bulky and highly basic SIMes ligand was designed to accelerate the phosphane dissociation event, whereas an inverse relationship between the phosphane exchange rate and the olefin metathesis activity was observed. Changing the tricyclohexylphosphane ligand in **4a** with a tricyclopentylphosphane ligand (**4b**) results in a 4-fold increase of K_B, both ligands having similar steric and electronic parameters. The difference between the saturated imidazole ring (SIMes = 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene) (**5a**) and the unsaturated imidazole ring (IMes = 1,3-dimesitylimidazol-2-ylidene) (**7**) is close to an order of magnitude. The phosphine exchange rate increases about 2 orders of magnitude in the series Cl < Br < I and the catalytic activity of **1a-c** are inversely proportional to K_B. The trend is identical in the NHC series, the di-iodide catalyst **5c** exchanges phosphine almost 225 times faster than the dichloride complex **5a**. The large size of the iodide ligand increases the steric bulk and thus speeds up the initiation event promoting PR_3 dissociation. As a general rule, phosphines, larger and more electron donating, and halogens which are smaller and more electron withdrawing lead together to more active catalysts.[40] The steric bulk of the spectator ligand contributes to phosphane dissociation, but more basic or bulkier phosphines than PCy_3 result in unstable complexes.[38, 40b] The steric demand of PR_3 ligands is characterized by the Tolman cone angle, and in the case of NHC ligands, by the $\%V_{Bur}$ molecular descriptor. The bulkiness of the groups bound to the nitrogen atoms of the NHC ligand and the shortened length of the Ru-carbene bond (L) increase the steric congestion around the metal center when compared to the PCy_3 ligand.[42] The catalyst lifetime and turnover numbers are dependent on the thermal stability of the catalyst, greater thermal stability being achieved by replacement of the phosphane spectator ligand with the *N*-heterocyclic carbene (NHC) ligand. Due to the specific character of the NHC ligands, which are strong σ donors, relatively weak π acceptors and have a low tendency to dissociate, NHCs lower the initiation step but increase the propagation step due to an increased thermal stability of the 14-electron complex.[20b, c]



Scheme 4 – The Initiation Step *via* Associative (eq. 1) or Dissociative (eq. 2) Mechanism.

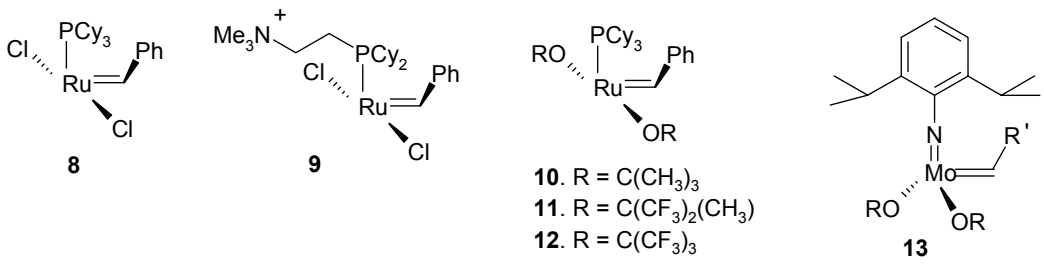
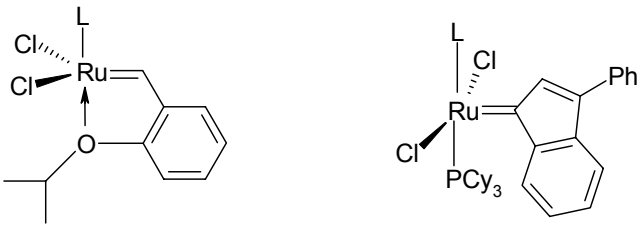


Fig. 3 – Monophosphane Ru-alkylidene Complexes (**8**-**12**) and Schrock's Mo Complexes (**13**).

The active species **8**, a 14-electron monophosphane alkylidene type **B** (Scheme 4), is an intermediate in the metathesis reaction but also in the catalyst decomposition process.[43] The coordinatively unsaturated structure of **8** has some similarity with the four-coordinate Mo and W olefin metathesis catalysts but, due to its short life time, was not isolated or observed by spectroscopic methods; only his analogue **9** was detected by ESI mass spectra.[44] The first isolated 14-electron Ru alkylidene complexes **10-12** contain two tertiary alkoxide ligands, instead of halide ligands, and are inactive or "dormant" at room temperature in RCM of diethyl diallylmalonate but all of them become highly active in presence of HCl. The alkoxide X-type ligands, which are larger and more electron donating than iodide ligands, shield the metal from the incoming substrate and diminish olefin binding by decreasing the electrophilicity of the Ru(II) centre. These complexes have an unusual trigonal pyramidal geometry, instead of a tetrahedral geometry as observed in the Schrock's Mo (**13**) and W systems.[45]

The nature of the substituent R^1 on the carbene α–carbon has a large influence on the initiation rate of the catalyst, an alkylidene and a metylidene is generated after one turnover of a typical ring opening metathesis or ring closing metathesis and becomes the propagating species. The methylidene complexes **2** and **6** are extremely poor initiators for olefin metathesis at ambient temperature, but **6** is an active catalyst which can achieve multiple catalytic turnover numbers (Fig. 2). More sterically bulky and electron donating R^1 groups gave a higher initiation rate, while small and not donating groups are ineffective in promoting PR_3 ligand dissociation.[40] The Hoveyda-Grubbs complexes (**14a-c**)[35d] and the Ru-3-phenylindenylidene complexes (**15a-c**)[28] are more resistant to harsh reaction conditions and temperature and functional groups tolerant than their benzylidene analogues (Fig. 4). As a result of steric (large isopropoxy group) and electronic factors (iPrO→Ru electron donation), the catalyst **14b** proved to initiate slower than **5a**.[35a,e]

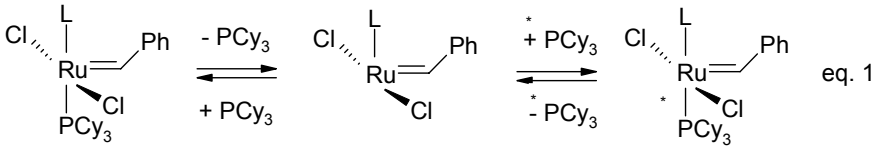
For all of the catalysts K_B is independent of the phosphine concentration [PR_3], over a wide range (0.04-0.77 M), and the values of the activation entropies ($\Delta S^{\ddagger}$) and activation enthalpies ($\Delta H^{\ddagger}$) are in excellent agreement with ligand dissociation energies (ΔE) calculated by Herrmann (25.8 Kcal/mol for $(NHC)(PMe_3)(Cl)_2Ru{=}CH_2$ with NHC = 1,3-dihydroimidazol-2-ylidene, and 24.9 Kcal/mol for $(PMe_3)_2(Cl)_2Ru{=}CH_2$). These results confirm a dissociative pathway (Scheme 4; eq. 2).[40]

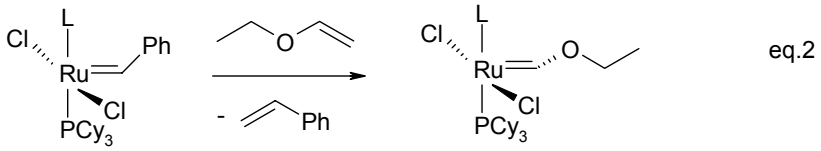


14a-c **15a-c**

a. L = PCy_3, b. L = SIMes, c. L = IMes

Fig. 4 – The Hoveyda-Grubbs Complexes (**14a-c**) and Ru-3-phenylindenylidene Complexes (**15a-c**).



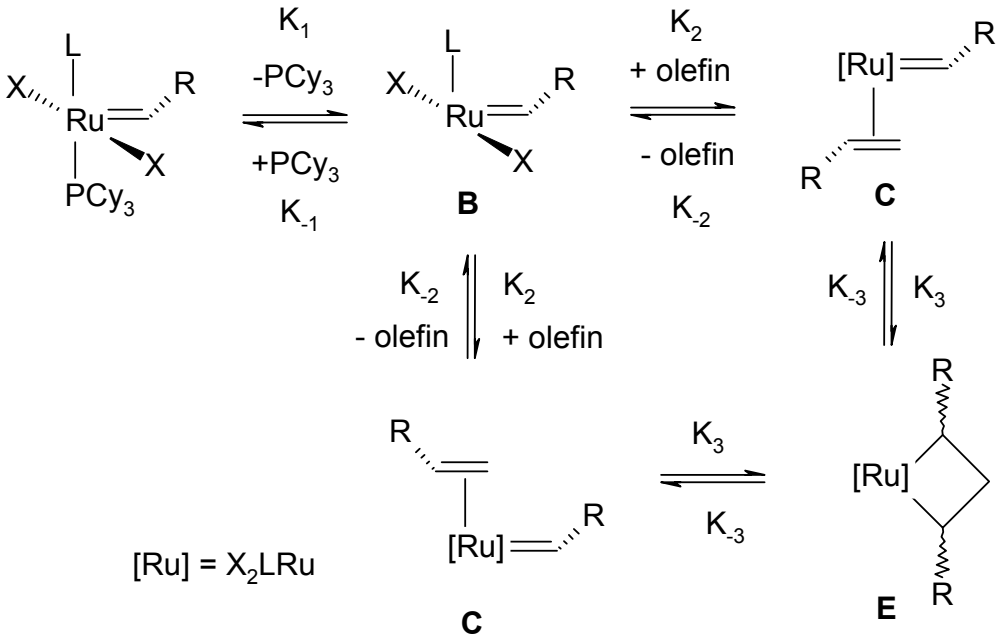


Scheme 5 – The Phosphine Exchange *via* a Dissociative Pathway.

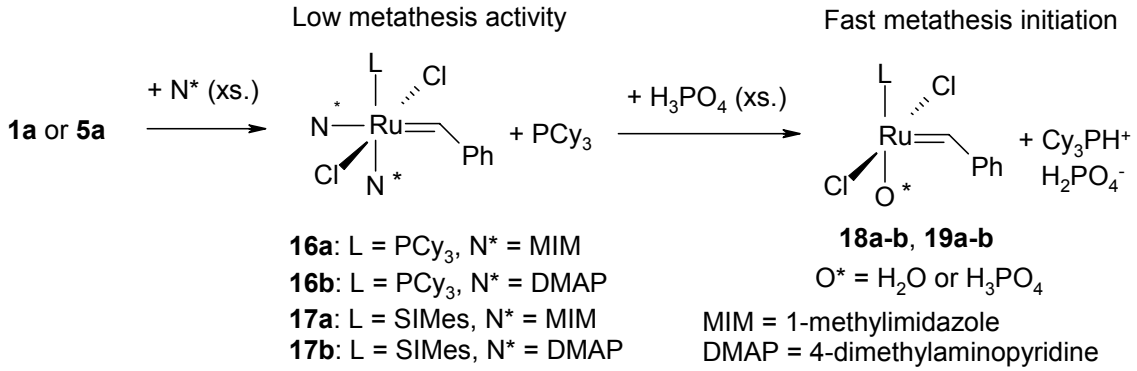
The reaction of Ru-alkylidene (Scheme 5, eq. 2) with ethyl vinyl ether to give Fischer carbenes $[L(PCy_3)(Cl)_2Ru=CH\text{-}OEt]$ is quantitative and irreversible and was chosen as a model for studying the initiation rate. The ^1H NMR spectroscopy at 35^0C for the reaction of **5a** with ethyl vinyl ether indicated an initiation rate constant $K_{obs} = (4.6\pm0.3)x10^{-4}$ s^{-1}, independent of olefin concentration and almost equal with the predicted phosphane dissociation rate constant $K_B = (4.6\pm0.3)x10^{-4}$ s^{-1} suggesting that the rate determining step of the reaction is the phosphane dissociation. In the case of the **1a** catalyst, K_{obs} is dependent on olefin concentration over a concentration range of 30 to 120 equiv. of olefin. The saturation conditions recorded with UV-spectroscopy indicated fist-order kinetics over 5-half-lives, the initiation reaction being followed by the formation of the Ru-vinyl ether product (484 nm). The rate constant of 0.018 ± 0.001 s^{-1} obtained at 20^0C is in agreement with the rate constant $K_B = 0.016\pm0.002s^{-1}$ of the phosphane exchange determined by ^{13}P-NMR magnetization transfer (MT). In both cases the first step involves dissociation of bound PCy_3 ($K_1 = K_b = K_{obs}$) to form 14-electron active species which is able to regenerate the substrate by coordination with free PCy_3 or to participate in the metathetic cycle by coordination with the olefin (Scheme 6).[40]

The ratio of K_{-1} to K_2 determines whether the catalyst binds the olefin or returns to its resting state. A difference of over 4 orders of magnitude for the ratio K_{-1}/K_2 between **1a** (15300) and **5a** (1.25) explains the dramatically increased olefin metathesis activity of **5a** as compared to **1a**; **1a** initiates relatively rapidly but the rebinding of phosphine ($K_{-1}[PCy_3]$) is competitive with olefin coordination (K_2[olefin]), while **5a** initiates relatively slowly but the 14-electron species can turnover multiple cycles before rebinding with PCy_3. The high activity of the NHC catalysts **5a**, which was initially attributed to its ability to promote phosphine dissociation (increasing K_1) now is assigned to its improved selectivity for binding
π-acidic olefinic substrates in the presence of σ-donating free phosphine (decreasing K_{-1}/K_2).[40]

Evidence for an associative initiation step came from the ROMP of cyclooctene (COE) with hexacoordinated catalysts **16b** and **17b**, their initiation rates exhibiting a linear dependency on the substrate concentration in contrast to catalysts **1a** and **5a.** A favorable ratio between the rates of initiation and propagation steps leads to a high control of the polymer molecular weight and PDI (polydispersity index) in ROMP reactions. Due to the slow initiation, relative to propagation, performed by the **5a** catalyst in ROMP, polymerizations proceed without molecular weight control (Scheme 7).[46]

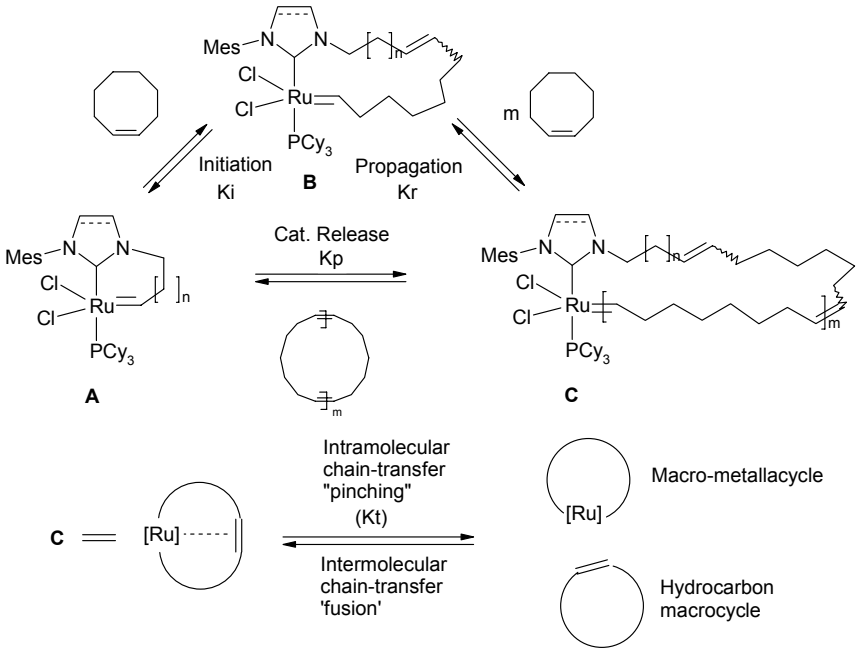


Scheme 6 – A General Mechanism for Olefin Metathesis Catalyzed by **1-7**.



Scheme 7 – Formation of Fast Initiating Complexs **18a,b**, **19a,b** *via* Protonation of the *N*-donor Ligands in an Inhibited Mixture of Catalysts **1a** and **5a**.

While macrocyclization is generally limited to low molecular weight polymers, and requires high-dilution conditions to suppress intermolecular reaction of the end-group, the advantages of ring-expansion metathesis polymerization (REMP) of cycloolefins to yield cyclic polymers, with cyclic Ru-alkylidene having a long alkyl chain between the R^1 and NHC ligands, consist in: (1) potential to produce cyclic polymers from cyclic monomers, (2) tolerance for high concentration, including bulk polymerization, (3) the ability to produce homopolymers without linkage groups, including pure hydrocarbon macrocycles, (4) access to a broad range of molecular weights extending up to 10^6Da. The steps involved in REMP are catalyst initiation, propagation, catalyst release and intermolecular chain transfer (Scheme 8). A facile access to different kinetically controlled polymer product distributions could be performed controlling the relative values of K_i, K_p, K_r, K_t by manipulation of the catalyst structure and reaction conditions. Saturated NHC ligands (**22**, **23**) increased catalyst activity toward polymerization in comparison with unsaturated analogues (**20**, **21**). It is noteworthy that REMP in presence of catalysts bearing five-carbon tethers (**20**, **22**) resembled a step-like growth mechanism, with a steep increase occurring only after a 95% monomer conversion, as a result of fast catalyst release that competed with propagation; in presence of six-carbon tethers (**21**, **23**) the mechanism was similar to a chain-growth polymerization mechanism giving high molecular weight polymer before full monomer conversion due to a faster propagation relative to catalyst release or chain transfer (Fig. 5).[47]

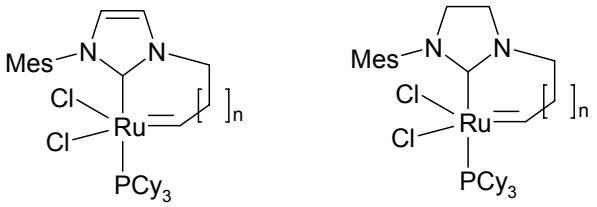


Scheme 8 – The Steps Involved in Ring Expansion Metathesis Polymerization (REMP).

It should be outlined that the regioselective conversion of the alkylidene complexes **5a**, **20-23** with butyl vinyl ether (BVE) to the corresponding Fischer carbenes showed first order kinetics over the time investigated. The catalyst **20** and **22** perform faster initiation in comparison with catalysts **21** and **23**. Significantly, shortening the tether length by one carbon atom increased the initiation rate by 25 and 48 times for the catalysts with saturated and unsaturated NHC ligands. As opposed to the observed rates of polymerization (**23** > **22** > **21** > **20**), the catalyst **22** was found to initiate slightly faster than the complex **5a,** under identical conditions. The decreased polymerization rate of **20** and **22** in contrast to their fast initiation rate supports the previous hypothesis that the catalyst release is strongly favored over polymer propagation for this systems.[47]

The molecular weight *versus* the conversion profile of polycyclooctene (PCOE) during the REMP of cyclooctene using cyclic catalysts **20-23** was strongly affected by the tether's length, and in all cases the polydispersity indices (PDI's) ranged from 1.3 to 1.8. A large increase in molecular weight at the beginning of the polymerization was achieved with catalysts **21** and **23**. The catalyst structure seems to kinetically control the molecular weight of polymer products, but after full monomer conversion the molecular weight of PCOE was found to have an equilibrium value that was independent of the catalyst structure and the initial monomer/catalyst ratio.[47]

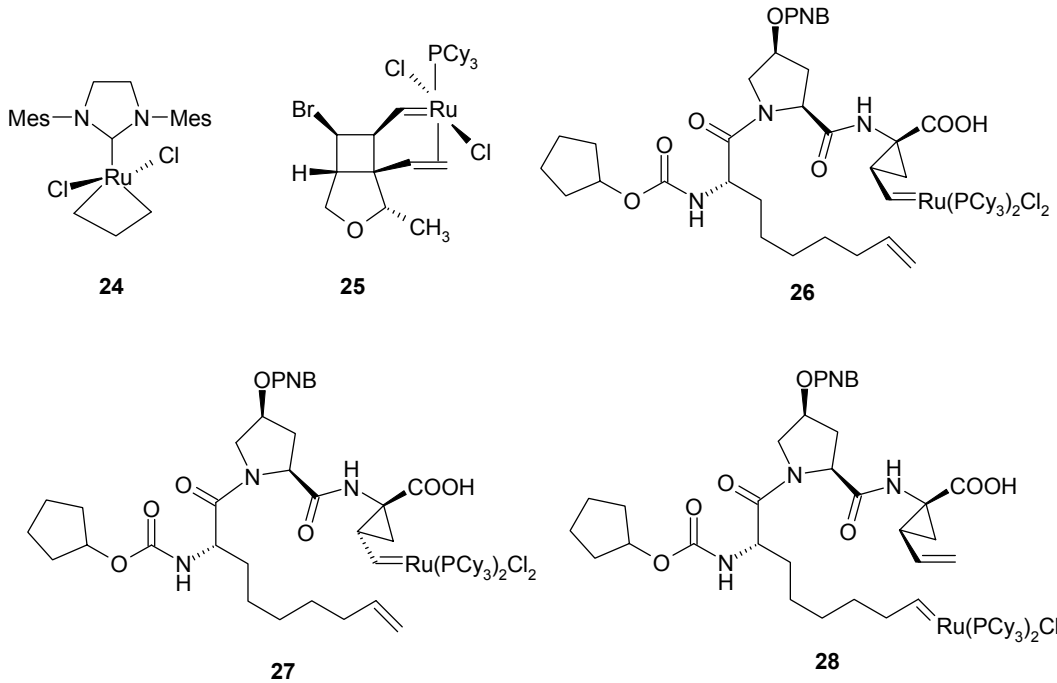
Two analytical data confirm the initiation by a dissociative mechanism (Fig. 6), respectively the NMR[48a] spectra of ruthenacyclobutane **24** and X-ray[48b] of **25**. The detection of the 18-electron Ru complexes **26-28** by NMR has been rationalized assuming initiation as occurring through an associative mechanism (Scheme 3, path 1 or path 3) or a late recombination with free phosphine (Scheme 3, path 8).[49]



20. n = 3
21. n = 4

22. n = 3
23. n = 4

Fig. 5 – Cyclic Ru-alkylidene Complexes.



24 **25** **26**

27 **28**

Fig. 6 – Ru-complexes **(**Rutenacyclobutane (**24**), Complex π (**25**), and Ru-alkylidene (**26-28**)) Detected with Spectroscopic Methods.

Turning back to the catalysts **1a**, **5a** and **6** it should be pointed out that experimental[38,40] and computational evidence,[39] is consistent with a dissociative process *via* a tetracoordinated intermediate. For catalysts **1a**, **5a** and **6,** the dissociative mechanism with *trans* olefin coordination is favored over the other alternatives, that is a facile dissociation of PR_3 followed by a barrierless coordination of alkene *trans* to L and rearrangement of the resulting π complex gives the ruthenacycle by migratory insertion, or reverse reaction. Increasing σ-donor ability of L facilitates the initial dissociation of PR_3 and destabilizes the intermediate π complex, which makes the insertion more favorable.[50a] Strong σ donors have to be located *trans* to the alkene and poor σ donor ligands have to be in a *cis* relationship to the alkene ligands.[50b,41] Catalysts containing sterically bulky and electron donating phosphane ligands display the highest catalytic activity due to an increased *trans*-effect which accelerates dissociation of PR_3 ligands and stabilizes the Ru(IV) metallacyclobutane intermediate.[51]

As depicted in Fig. 7, the Grubbs catalysts differ in their intramolecular rate to transform Ru-carbene intermediates into ruthena(IV)cyclobutanes, the rate limiting step for the 1-st generation Grubbs catalysts being the cycloaddition step, whereas the rate limiting step for the 2nd generation Grubbs catalysts is phosphine dissociation. The electronic stability of the active carbene conformation in the 2nd generation catalysts could explain their high activity as compared to the 1-st generation Grubbs catalysts (Fig. 7).[50a]

Based on extended Hückel calculations only a "collinear" conformation of the metal-carbene-olefin complex will be productive in metathesis, *i.e.* which maximizes the π bonding around the d^6 metal center. For many electron counts, neither the π complex **33** nor a metallacyclobutane **35** may be the stable geometry but instead an intermediate non-classical structure **34**, partway between these two (Fig. 8).[52]

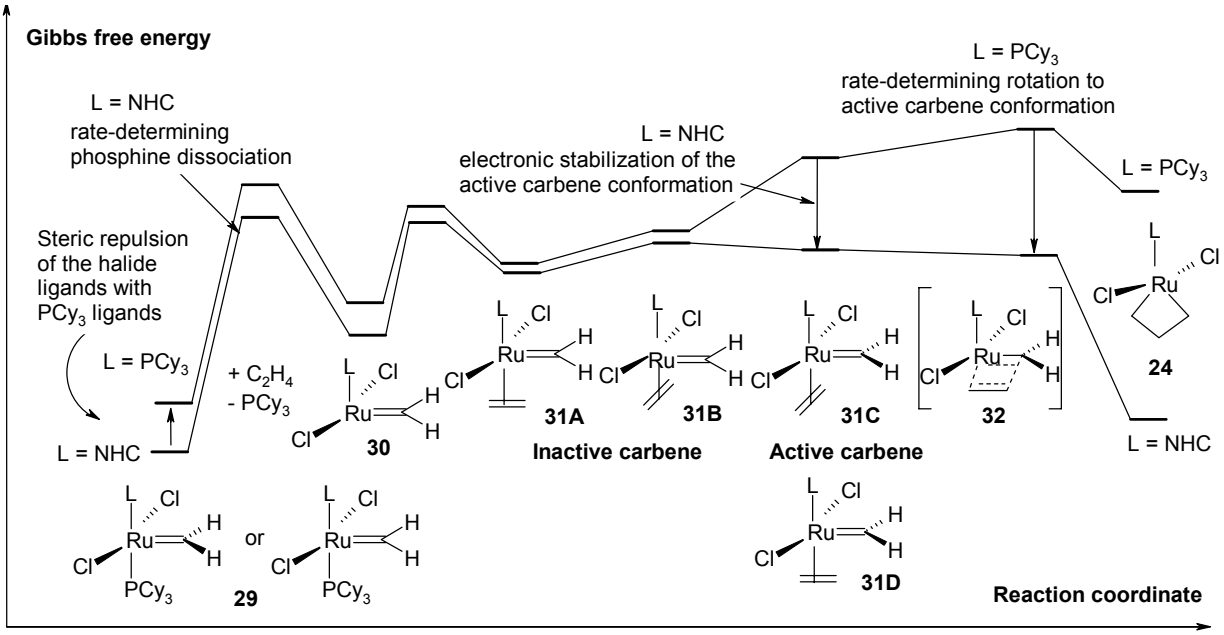


Fig. 7 – Semiquantitative Gibbs Free Energy Diagram of Mechanistic Pathways of the First and Second Generation Grubbs Catalyst. Intrisic carbene rotation barriers are in order of magnitude of 10 KJ mol^{-1}, but will be strongly influenced by sterically demanding substituents (*Adv. Synth. Catal.* **2007**, *349*, 204).

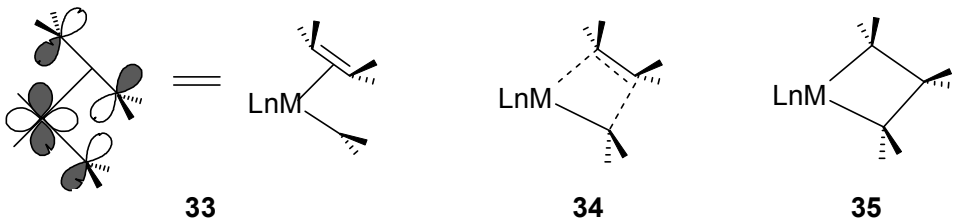


Fig. 8 – The Conformation of the Metal-Carbene-Olefin Complex.

Due to nonclassical nature of ruthenacyclobutane **36** the CCC fragment interacts strongly with the Ru atom *via* one of the vacant d orbitals of Ru, and two C-C σ-bonds are donating electron density to the metal centre which confers stability. (Fig. 9).[53]

The potential energy surface corresponding to the **31→TS1(32)→36→TS1(32)→31** region became flat due to π-orbital interactions between the $Ru=CH_2$ and the olefin fragments in **TS1(32)**, and due to the presence of the two σ-CC agostic orbital interaction in **36**, which made easy metallacyclobutane formation and double bond reordering. Therefore, the metathesis reaction becomes a facile process,[53] and the [2+2] cycloaddition at a metal centre fits in a π-CAM principle.[54]

Along different lines, in a release/return mechanism the alkylidene (the benzylidene (**1, 5, 7**) or indenylidene (**15a-c**) - Grubbs' type catalysts) or bidentate Hoveyda-Grubbs catalysts (**14a-c**) are initiated in different modes: the former category initiates by the dissociation of a PCy_3 ligand to form the catalytic active 14-electron complex **8,** whereas the second initiates by breaking of the Ru-O chelation to form the catalytically active 14-electron complex **38**. Then, after a cross metathesis process, both types generate identical 14-electron Ru-alkylidene complexes **40** and Ru-methylidene complex **30** (Scheme 9).[55] After entering into the catalytic cycle, the 14-electron active species can turnover many times before phosphine reassociation to recover the initial 16-electron complex, a very useful feature in synthesis of immobilized catalysts. The presence of the Ru-methylidene is responsible for more than 90% of the catalytic cycle.[56, 57] Changes in the fluorescence intensity provide mechanistic information about the course of reactions in case of catalysts bearing fluorophore-tagged ligands on the leaving ligand (NHC_{EWG} ligand); an increased intensity of fluorescence confirms the release of the fluorophore from the metal center.[58]

The initial carbene product observed by ^1H NMR in the reaction of terminal olefins with ruthenium benzylidene is the alkylidene in the case of the sterically unhindered terminal olefins, and the methylidene for bulkier terminal olefins.

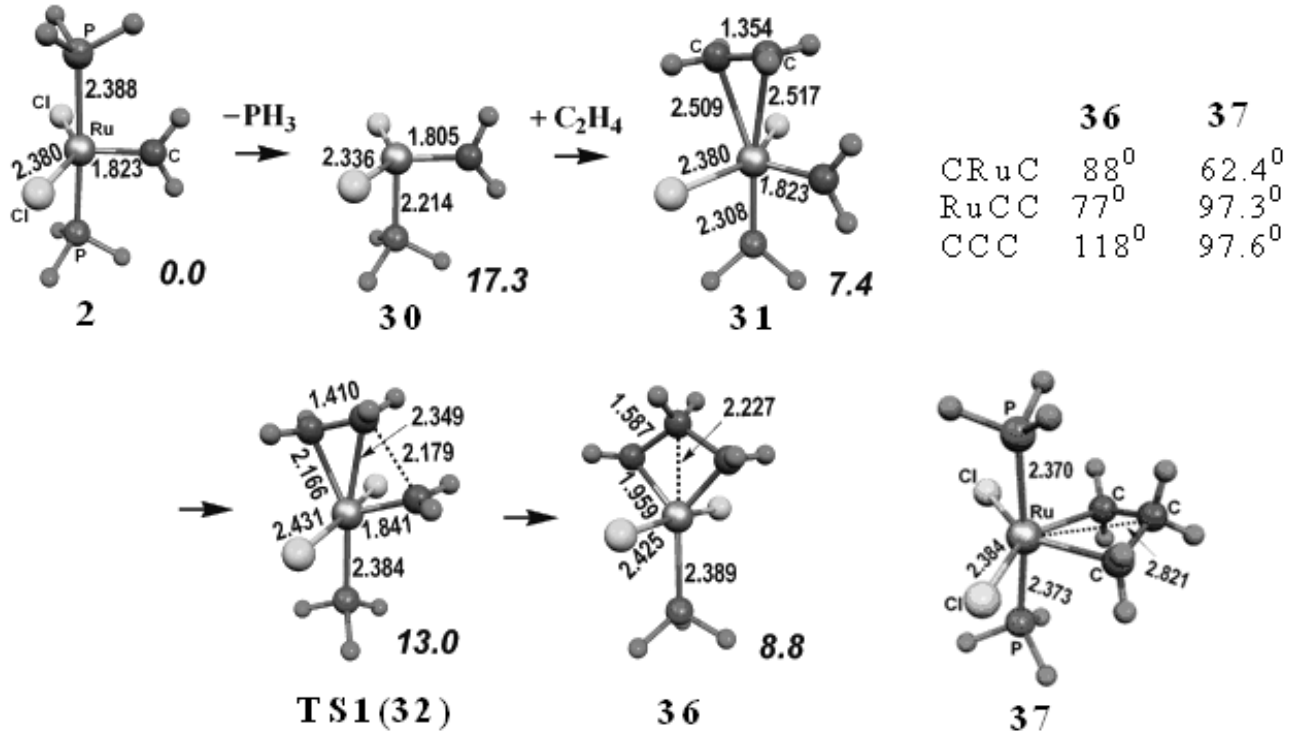
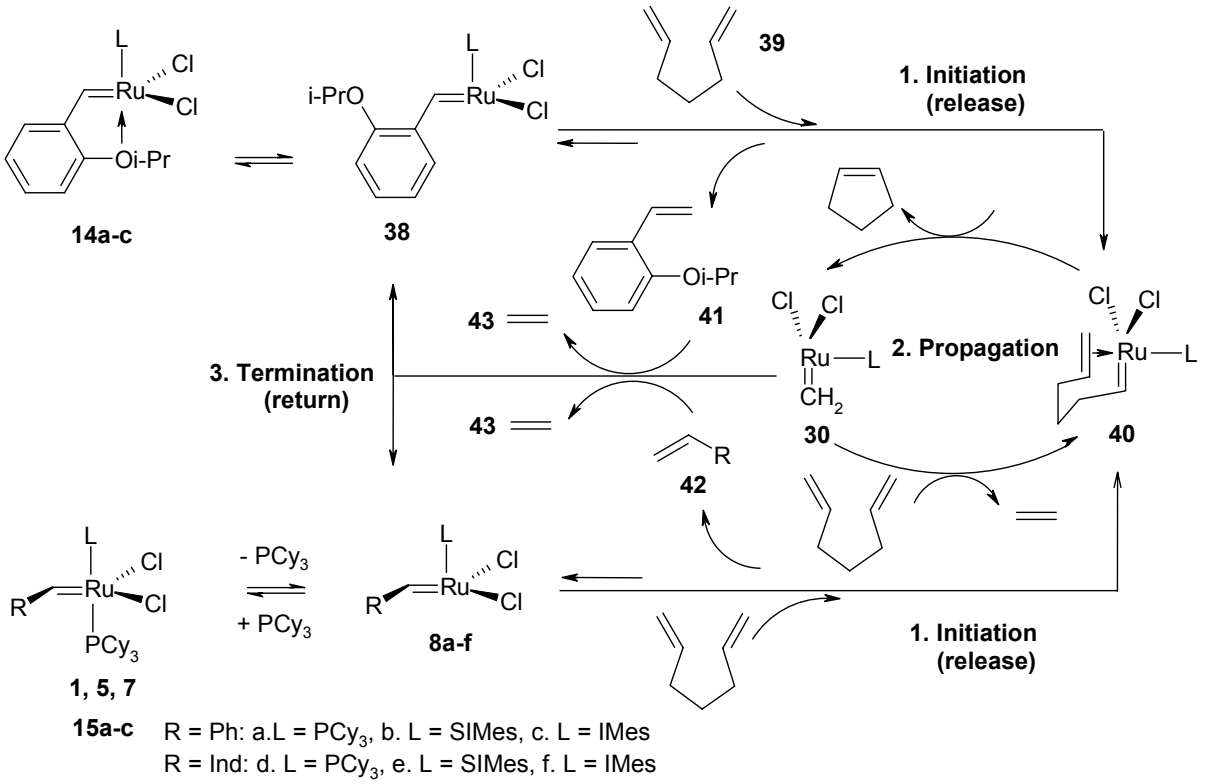


Fig. 9 – Generally Accepted Mechanism for Ruthenium Catalyzed Olefin Metathesis. The values in italics correspond to relative values of enthalpy in Kcal/mol. Bond lengths are in Angstroms (*Organometallics* **2004**, *23*, 76).

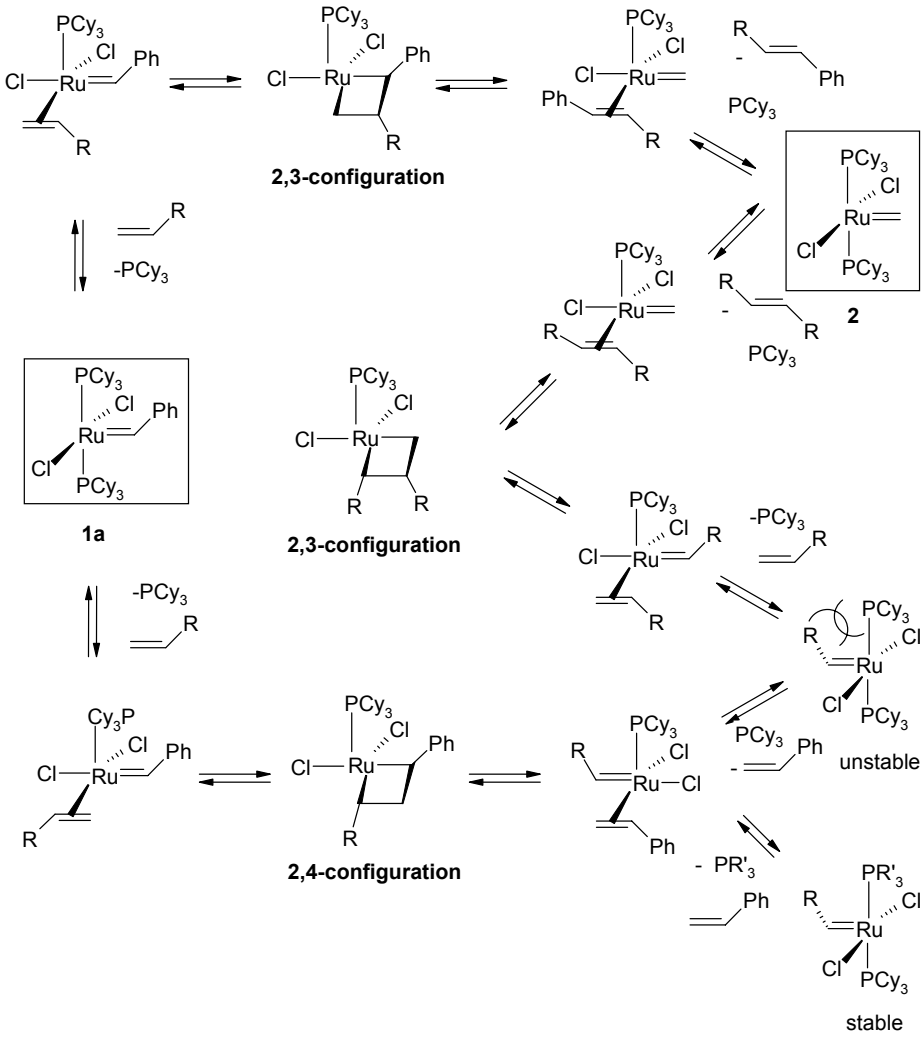


Scheme 9 – Proposed Route for the Release/Return Mechanism of Ru Carbene Complexes.

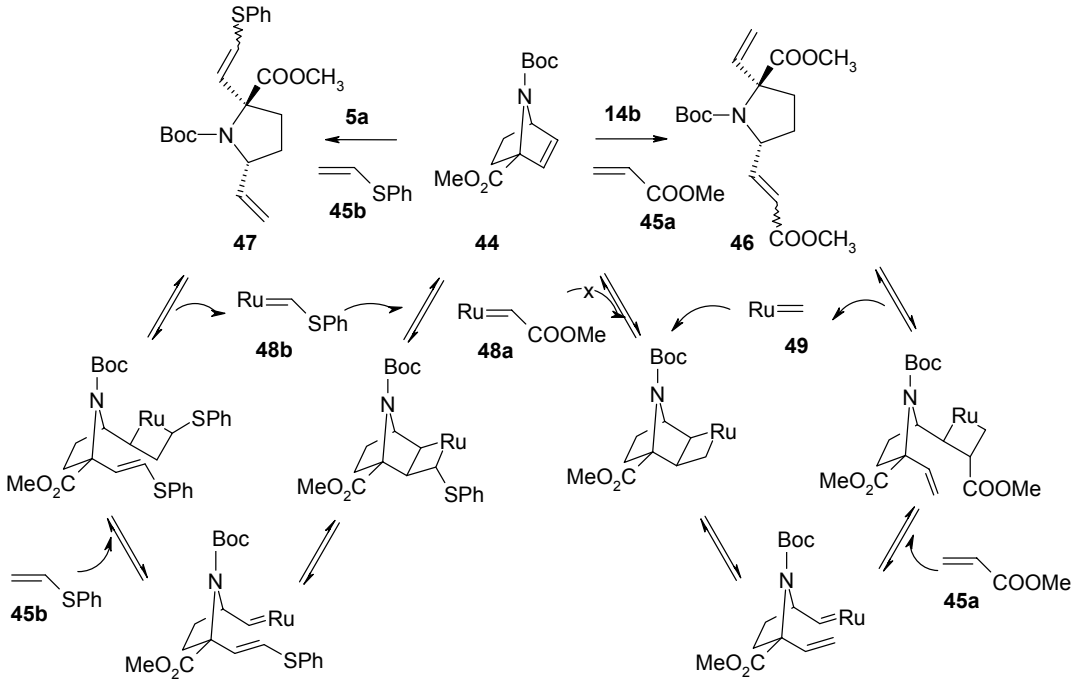
Monitoring by ^{1}H NMR the cross metathesis reaction of *trans*-Ru-benzylidene with sterically unhindered olefins indicated the formation of Ru-alkylidene in 10 minutes at RT, and the formation of Ru-methylidene, along with complete disappearance of Ru-alkylidene (in 2 hr). When the steric bulk of the olefin was increased the methylidene **2** was directly formed, while with 2,2-substituted olefins no activity was recorded under identical conditions. Due to the steric interaction with phosphine, the rate of the initial olefin binding is slow: bulkier olefins were found to react slower, whereas *trans* internal olefins proved slower than *cis* internal olefins.[59]

As Scheme 10 illustrates, the pathway involving the formation of the Ru-metallacycle with 2,4-configuration would predict the formation of the Ru-alkylidene, while the formation of the Ru-metallacycle having 2,3-configuration leads directly to Ru-methylidene.[59, 48b] The catalytic activity, as well as selectivity and reactivity of the metathetic process, is directly dependent on the relative stability of the initiating and propagating species involved in the catalytic cycle. Substituted alkylidene complexes decompose by a bimolecular mechanism implying loss of phosphine and, as a consequence, any attempts to increase the rate of phosphine loss augment in fact the rate of catalyst decomposition. Ru-methylidene complexes are less efficient than Ru-alkylidenes because the electron donating properties and relative size of Ru-alkylidenes increase dissociation of the phosphine and speed up metathesis. An intermediate case is benzylidene where phenyl group is somewhat electron withdrawing but its size assists phosphine dissociation.[38, 40]

In the synthesis of polysubstituted proline from 7-azanorbornene **44** using the tandem ring opening-cross metathesis (RO-CM), the propagating species are responsible for the formation of different regioisomers due to the opposing behaviour of electron poor and electron rich olefins. As presented in Scheme 11, in presence of **14b** olefins with electron withdrawing groups (EWG), *e.g.* acrylate **45a**, lead to **46**, while olefins with electron releasing group (ERG), such as phenylvinylthioether **45b**, give **47** in presence of **5a**.[50] The formation of the ruthenium alkylidene **48b** and the ruthenium methylidene **49,** instead of the ruthenium alkylidene **48a,** is in accord with the Grubbs' kinetics studies,[38, 40] the ester substituted alkylidene are much better initiators but are less stable than alkyl derivatives (Scheme 12).

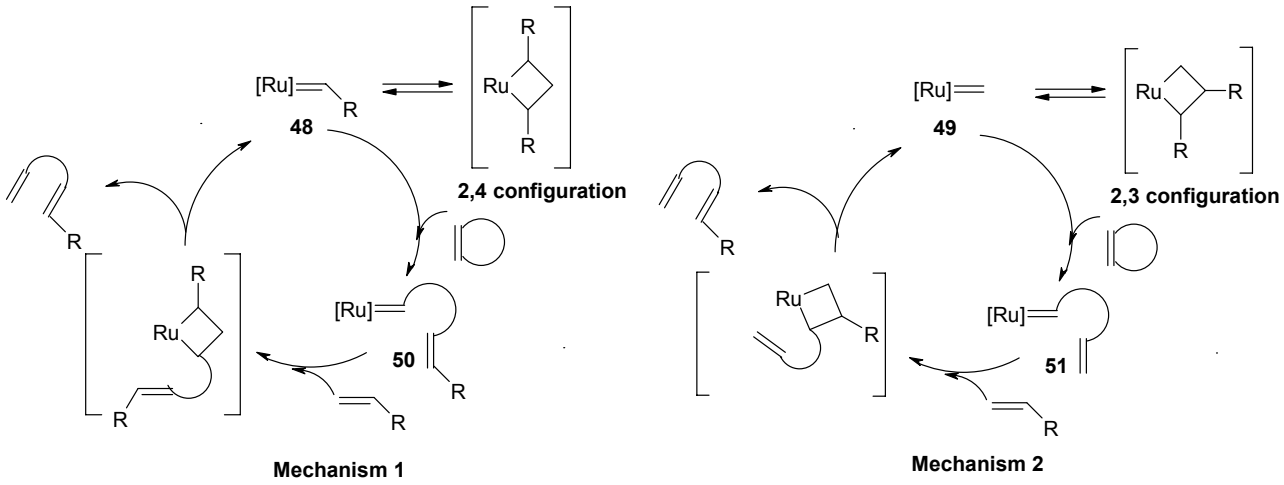


Scheme 10 – Mechanism of "Direct" Formation of Methylidene with Bulky Olefins.

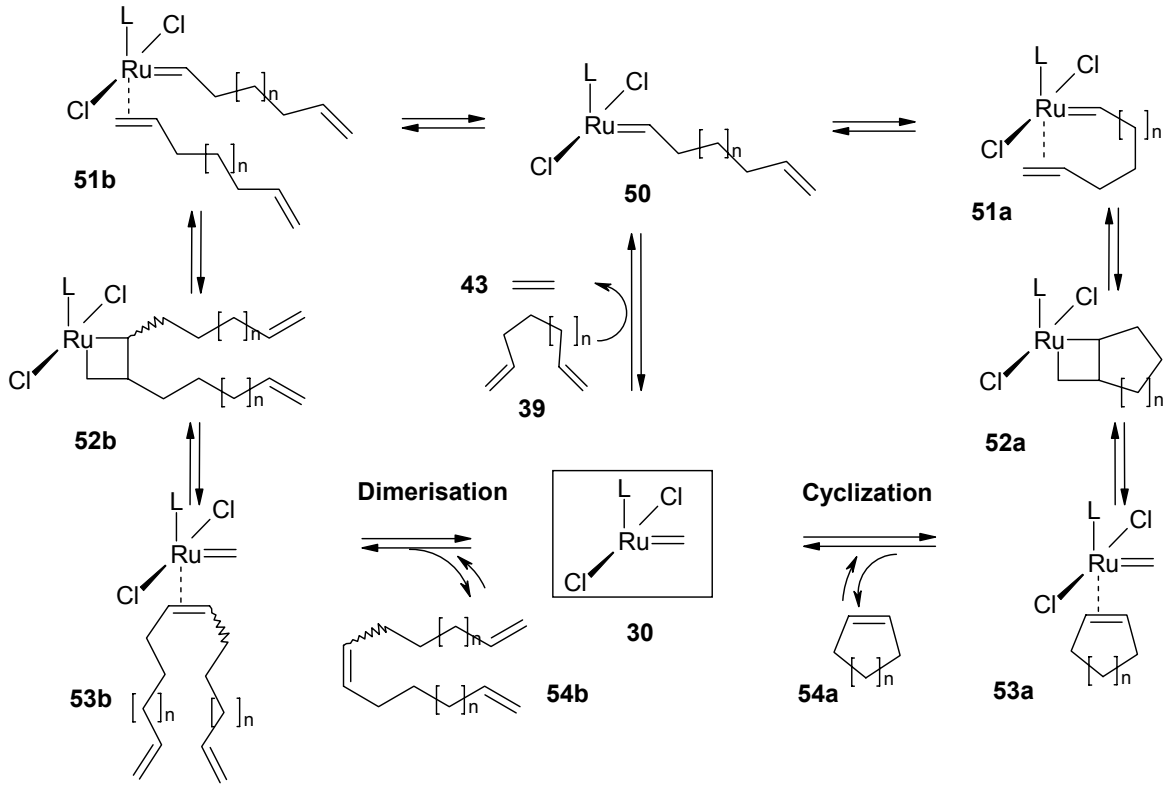


Scheme 11 – The Mechanism of 7-Azanorbornene **44** with Acrylate **45a** and Phenylvinylthioether **45b**.

Considering now Ru-metalacycles, it was documented that the selectivity of their formation is dependent on the temperature. At elevated temperatures the formation of **48,** instead of **49,** is to be expected (Scheme 12). The kinetic product is thus the Ru-alkylidene rather than the Ru-methylidene as has been determined in a cross metathesis experiment.[59, 48b, 60]



Scheme 12 – Selective Ring-Opening Cross Metathesis with Active Alkylidenes.

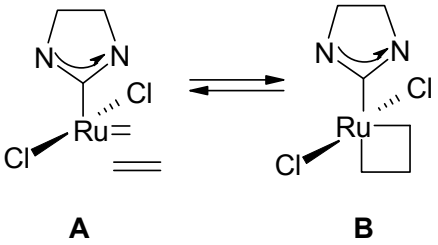


Scheme 13 – Mechanism of Intra- and Intermolecular Metathesis Reactions.

Competing intra- and intermolecular mechanistic pathways for metathesis of 1,7-octadiene **39** are showcased in Scheme 13. The reversible sequences of [2+2] cycloaddition – cycloreversion equilibria start with a transalkylidenation process between the Ru-methylidene **8** and the 1,7-octadiene **39** affording Ru-alkylidene **50** which is a key step in the formation of the metallacyclobutanes **52a, 52b** through the cyclic π-complex (**51a**) and the acyclic π-complex (**51b**). After breaking two bonds in **52a, 52b** the π-complexes (**53a, 53b**) are formed, from

which the 14-electron Ru-methylidene **8** is released together with the RCM product, the cycloalkene **54a,** and with the CM product, the dimer **54b**. Using density functional theory (DFT) at the MO6/B2//B3LYP/B1 level, energetics of the reaction path of ring formation via RCM was predicted, as well as the effective molarity (EM) for the formation of cyclohexene (**54a**). The concept of effective molarity gives the relative amounts of the cyclic and dimer product. The truncated models (**A**, **B**) were used for the calculation of electronic energies (CCSD(T)) (Fig. 10). Prediction of ring formation using the MO6 density functional proved to be significantly superior to B32YP. The calculation of free energy surface for the intramolecular cyclization of 1,7-octadiene and for the dimerization of 1,6-heptadiene indicated that for both reactions, the conversion of **50** to **51a**, **51b** is relatively fast, and the rate limiting step is the conversion of the metallacyclobutanes **52a**, **52b** to π–complexes **53a**, **53b**. For evaluating the relative rate for the competing reactions the calculated barrier heights were used, and the free energy difference between (**51a**, **51b**) and (**52a**, **52b**) was compared with the EM value of 82, measured in this case. Experimental determinations are in agreement with these results, the ^{1}H-NMR spectra for a solution of 1,7-octadiene (c= 4M) indicating a ratio of cyclohexene/oligomer of 20:1, therefore an EM value of 80.[61]

Taking into account the ensemble of experimental and theoretical findings regarding alkene metathesis it should be emphasized that, due to its reversible nature, concurrent side reactions such as ring-opening,[41b] cross metathesis, epimerization[49] and isomerization[62] etc. might occur, even during reaction workup, so that the reaction protocols must be rigorously controlled to minimize undesirable products. For instance, the yields of ring-closing metathesis reactions can be maximized by manipulating the competition between intramolecular ring-closing and intermolecular oligomerization reaction.[36a]



Electronic energies of **B** (Kcalmol^{-1})

B3LYP	-13.6
MO6-L	-22.1
MO6	-25.3
CCSD(T)	-23.7

Fig. 10 – Model Used for CCSD(T) Calculations.

CONCLUSIONS

Understanding the underpinnings of the overall mechanism of each type of metathesis reaction is of crucial importance for controlling the process course not only by choosing the right reaction conditions but also in selecting that unique catalyst able to afford maximum productivity and selectivity in metathesis of a specific substrate. At the same time, it can play a key role in addressing the challenge of creating long-lived and better performing initiators complying with current demands for green and atom economical synthesis. Development of new catalysts with increased thermal stability provides a higher control over the persistence of active species and over rates of product formation. Presently, olefin metathesis reactions have found wide applicability at laboratory scale for producing intricate compounds with precise stereostructure, or at industrial scale, in manufacturing of drugs, natural products, and mostly of valuable polymers not accessible by more conventional technologies.

Acknowledgements: This article is part of the research program on olefin metathesis active at the Centre of Organic Chemistry of the Roumanian Academy.

REFERENCES

1. a) K. J. Ivin and J. C. Mol, "Olefin Metathesis and Metathesis Polymerization", Academic Press, London, 1997; b) V. Dragutan, M. Dimonie and A.T. Balaban, "Olefin Metahesis and Ring-Opening Metathesis Polymerization of Cycloolefins", John Wiley, Chichester, U.K., 1985.
2. a) R.H. Grubbs, Ed., "Handbook of Metathesis", Vol. I-III, Wiley-VCH, Weinheim, **2003**; b) Y. Imamoglu and V. Dragutan, Eds., "Metathesis Chemistry: From Nanostructure Design to Synthesis of Advanced Materials", Springer, Dordrecht, The Netherlands, 2007; c) V. Dragutan, A. Demonceau, I. Dragutan and E. Sh. Finkelshtein, Eds., "Green Metathesis Chemistry: Great

Challenges in Synthesis, Catalysis and Nanotechnology", Springer, Dordrecht, The Netherlands, 2010; d) J. Cossy, S. Arseniyadis and C. Meyer, Eds., "Metathesis in Natural Product Synthesis", Wiley-VCH: Weinheim, Germany, 2010.

3. a) L. Delaude, A. Demonceau, I. Dragutan, and V. Dragutan, "Recent Advances in Ruthenium Catalysts for Alkene Metathesis", in: *Green Metathesis Chemistry: Great Challenges in Synthesis, Catalysis and Nanotechnology*, V. Dragutan, A. Demonceau, I. Dragutan and E. Sh. Finkelshtein, Eds., *NATO Science for Peace and Security Series A: Chemistry and Biology Series*, Springer-Verlag, New York, 2010, p. 3-16; b) D. Bicchielli, Y. Borguet, L. Delaude, A. Demonceau, I. Dragutan, V. Dragutan, C. Jossifov, R. Kalinova, F. Nicks and X. Sauvage, "Recent Applications of Alkene Metathesis in Fine Chemical Synthesis", in: *Green Metathesis Chemistry: Great Challenges in Synthesis, Catalysis and Nanotechnology,* V. Dragutan, A. Demonceau, I. Dragutan and E.Sh. Finkelshtein, Eds., *NATO Science for Peace and Security Series A: Chemistry and Biology Series*, Springer-Verlag, New York, 2010, p. 207-274; c) I. Dragutan, V. Dragutan, P. Filip and A. Demonceau, "Activation of Cycloolefin Metathesis by Ultrasonic Irradiation", in: *Green Metathesis Chemistry: Great Challenges in Synthesis, Catalysis and Nanotechnology)*, V. Dragutan, A. Demonceau, I. Dragutan and E. Sh. Finkelshtein Eds., *NATO Science for Peace and Security Series A: Chemistry and Biology Series*, Springer-Verlag, New York, 2010, p. 315-325; d) V. Dragutan, I. Dragutan and M. Dimonie, "A Selective Route for Synthesis of Linear Polydicyclopentadiene", in: *Green Metathesis Chemistry: Great Challenges in Synthesis, Catalysis and Nanotechnology*, V. Dragutan, A. Demonceau, I. Dragutan and E. Sh. Finkelshtein, Eds., *NATO Science for Peace and Security Series A: Chemistry and Biology Series*, Springer-Verlag, New York, 2010, p. 369-381; e) V. Dragutan, I. Dragutan and M. Dimonie, „Tuning Product Selectivity in ROMP of Cycloolefins with W-Based Catalytic Systems", in: *Green Metathesis Chemistry: Great Challenges in Synthesis, Catalysis and Nanotechnology*, V. Dragutan, A. Demonceau, I. Dragutan and E. Sh. Finkelshtein, Eds., *NATO Science for Peace and Security Series A: Chemistry and Biology Series*, Springer-Verlag, New York, 2010, p. 383-390; f) B. Allaert, N. Dieltiens, C. Stevens, R. Drozdzak, V. Dragutan, I. Dragutan and F. Verpoort, "Towards new generations of metathesis metal-carbene pre-catalysts" in: *Metathesis Chemistry: From Nanostructure Design to Synthesis of Advanced Materials*, Y. Imamoglu and V. Dragutan, (Eds)., *NATO Science for Peace and Security Series A: Chemistry and Biology Series*, Springer-Verlag, New York, 2007, p. 39-78.
4. a) D. Astruc, *New J. Chem*., **2005**, *29*, 42-56; b) A. H. Hoveyda and A. R. Zhugralin, *Nature,* **2007**, *450*, 243-251; c) R. R. Schrock, *Chem. Rev.,* **2009**, *109*, 3211-3226; d) G. C. Vougioukalakis, R. H. Grubbs *Chem. Rev*., **2010**, *110*, 1746-1787; e) A. M. Lozano-Vila, S. Monsaert, A. Bajek and F. Verpoort, *Chem. Rev.*, **2010**, *110*, 4865-4909; f) H. Clavier, K. Grela, A. Kirschning, M. Mauduit and S.P. Nolan *Angew. Chem. Int. Ed*., **2007**, *46*, 6786-6801; g) C. Samojłowicz, M. Bieniek and K. Grela, *Chem. Rev.*, **2009**, *109*, 3708-3742.
5. a) R.H. Grubbs, *Tetrahedron,* **2004**, *60*, 7117-7140; b) R. R. Schrock, *Adv. Syn. Catal.,* **2007***, 349*, 41-53; c) S. J. Connon and S. Blechert, *Angew. Chem. Int. Ed*., **2003**, *42*, 1900-1923; d) I. Dragutan, V. Dragutan, L. Delaude, A. Demonceau and A. F. Noels, *Rev. Roum. Chim.,* **2007**, *52*, 1013-1025; d) V. Dragutan, I. Dragutan, L. Delaude and A. Demonceau, *Chimica Oggi-Chem. Today* (Supplement Focus on Metathesis) **2009**, *27*, S9-12; e) I. Dragutan, V. Dragutan, L. Delaude and A. Demonceau, *Chimica Oggi-Chem. Today* (Supplement Focus on Metathesis), **2009**, *27*, S13-16; f) V. Dragutan, I. Dragutan and H. Fischer, *J. Inorg. Organomet. Polym. Mater*., **2008**, *18*,18-31; g) I. Dragutan, V. Dragutan and H. Fischer, *J. Inorg. Organomet. Polym. Mater*., **2008**, *18*, 311-324.
6. a) V. Dragutan, I. Dragutan, L. Delaude and A. Demonceau, *Coord. Chem. Rev.,* **2007**, *251*, 765-794.; b) I. Dragutan and V. Dragutan, *Platinum Metals Rev*. **2006**, *50*, 81-94; c) V. Dragutan, I. Dragutan and A.T. Balaban, *Platinum Metals Rev.,* **2000**, *44*, 168-172; d) V. Dragutan, I. Dragutan and A. T. Balaban, *Platinum Metals Rev.,* **2000**, *44*, 112-118; e) F. Ding, Y. Sun, S. Monsaert, R. Drozdzak, I. Dragutan, V. Dragutan and F. Verpoort, *Curr. Org. Synth*., **2008**, *5*, 291-304.
7. K. Öfele, E. Tosh, C. Taubmann and W. A. Herrmann *Chem. Rev.,* **2009,** 109*,* 3408-3444.
8. a) M. Dimonie, S. Coca, M. Teodorescu, L. Popescu, M. Chipara and V. Dragutan, *J. Mol. Catal.,* **1994**, *90*, 117-124; b) S. Coca, M. Dimonie, V. Dragutan, R. Ion, L. Popescu, M. Teodorescu, F. Moise and A. Vasilescu, *J. Mol. Catal.,* **1994**, *90*, 101-110; c. M. J. Abadie, M. Dimonie, C. Couve and V. Dragutan, *Eur. Polym. J.*, **2009**, *36*, 1213-1219.
9. R. R. Schrock, A. H. Hoveyda, *Angew. Chem. Int. Ed.*, **2003,** *42*, 4592-4633.
10. S. Blechert, H. Wakamatsu, *Angew. Chem. Int. Ed*., **2002**, *41*, 794-796.
11. S. Blechert, H.Wakamatsu, *Angew. Chem. Int. Ed*., **2002**, *41*, 2403-2405.
12. K. Grela, S. Harutyunyan and A. Michrowska, *Angew. Chem., Int. Ed.,* **2002,** *41*, 4038-4040.
13. R. Bujok, M. Bieniek, M. Masnyk, A. Michrowska, A. Sarosiek, H. Steüpowska, D. Arlt and K. Grela, *J. Org. Chem.,* **2004**, *69*, 6894-6896.
14. L. Jafarpour, H.-J. Schanz, E. D.Stevens and S. P. Nolan, *Organometallics,* **1999,** *18*, 5416-5419.
15. T. Opstal and F. Verpoort, *Angew. Chem. Int. Ed*., **2003**, *42***,** 2876-2879.
16. W. A. Herrmann, *Angew. Chem., Int. Ed.,* **2002**, *41*, 1290-1309.
17. W. A. Herrmann, T. Weskamp and V. P. W. Bohm, *Adv. Organomet. Chem*., **2001**, *48*, 1-69.
18. S. P. Nolan, Ed., "*N*-Heterocyclic Carbenes in Synthesis", Wiley-VCH, Weinheim, 2006.
19. F. Glorius, Ed., "*N*-Heterocyclic Carbenes in Transition Metal Catalysis", *Top. Organomet. Chem*. Vol. 21, **2007**.
20. a) V. Dragutan, I. Dragutan, L. Delaude and A. Demonceau, *Coord. Chem. Rev*., **2007,** *251*, 765-794; b) O. Schuster, L. Yang, H. G. Raubenheimer and M. Albrecht, *Chem. Rev.,* **2009**, *109*, 3445; c) D. Tapu, D. A. Dixon and C. Roe, *Chem. Rev.,* **2009**, *109*, 3385.
21. B. De Clercq and F. Verpoort, *Tetrahedron Lett*., **2002,** *43*, 9101-9104.
22. R. Drozdzak, B. Allaert, N. Ledoux, I. Dragutan, V. Dragutan and F. Verpoort, *Coord. Chem. Rev*., **2005**, *249*, 3055-3074.
23. R. Drozdzak, B. Allaert, N. Ledoux, I. Dragutan, V. Dragutan and F. Verpoort, *Adv. Synth. Catal.,* **2005**, *347*, 1721-1743.

24. R. Drozdzak, N. Ledoux, B. Allaert, I. Dragutan, V. Dragutan and F. Verpoort, *Cent. Eur. J. Chem*., **2005**, *3*, 404-416.
25. F. Ding, Y. Sun, S. Monsaert, R. Drozdzak, I. Dragutan, V. Dragutan and F. Verpoort, *Curr. Org. Synth.,* **2008,** *5*, 291-304.
26. A. Demonceau, A. W. Stumpf, E. Saive and A. F. Noels, *Macromolecules,* **1997**, *30*, 3127-3136.
27. a) A. Fürstner, J. Grabowski and C. W. Lehmann**,** *J. Org. Chem.,* **1999**, *64*, 8275-8280; b) A. Fürstner, O. Guth, A. Düffels, G. Seidel, M. Liebl, B. Gabor and R. Mynott, *Chem. Eur. J.,* **2001**, *7*, 4811-4820
28. a) S. Monsaert, R. Drozdzak, V. Dragutan, I. Dragutan and F. Verpoort, *Eur. J. Inorg. Chem.,* **2008**, 432–440; b) H. Clavier and S. P. Nolan, *Chem. Eur. J.,* **2007**, *13*, 8029. 151; c) F. Boeda, H. Clavier and S. P. Nolan, *Chem. Commun.,* **2008**, 2726-2740; d) H. Clavier, C. A. Urbina-Blanco, and S. P. Nolan, *Organometallics,* **2009**, *28*, 2848.
29. R. Castarlenas, C. Fischmeister, C. Bruneau and P. H. Dixneuf, "Allenylidene–Ruthenium Complexes As Versatile Precatalysts for Alkene Metathesis Reactions" in Bruneau C., Dixneuf P.H., Eds., "Metal Vinylidene and Allenylidene Complexes in Catalysis: From Reactivity to Applications in Catalysis", Wiley VCH, Weinheim, 2008.
30. V. Cadierno, J. Gimeno, *Chem. Rev.*, **2009**, *109,* 3512-3560.
31. a) R. H. Grubbs, *Angew. Chem. Int. Ed.,* **2006**, *45*, 3760; b) Y. Chauvin, *Angew. Chem. Int. Ed.* **2006**, *45*, 374; c) R. R. Schrock, *Angew. Chem. Int. Ed.,* **2006**, *45*, 3748.
32. a) R. R. Schrock and A. H. Hoveyda, *Angew. Chem. Int. Ed.,* **2003**, *42*, 4592; b) R. R. Schrock, *Chem. Rev.,* **2009**, *109*, 3211; c) H. F. T. Klare and M. Oestreich, *Angew. Chem. Int. Ed.,* **2009**, *48*, 2085.
33. a) A. Fürstner, *Topics in Catalysis,* **1997**, *4*, 285; b) R. H. Grubbs, S. Chany, *Tetrahedron*, **1998**, *54*, 4413; c) A. J. Phillips and A. D. Abell, *Aldrichimica Acta,* **1999**, *32*, 75; d) A. Fürstner, *Angew. Chem. Int. Ed.*, **2000**, *39*, 3012; e) L. Yet, *Chem. Rev.*, **2000**, *100*, 2963; f) S. N. Osipov and P. Dixneuf, *Russian J. Org. Chem*., **2003**, *39*, 1211; g) A. Deiters and S. F. Martin, *Chem. Rev.*, **2004**, *104*, 2199; h) D. Astruc, *New. J. Chem.*, **2005**, *29*, 42; i) P. Compain, *Adv. Synth. Catal.*, **2007**, *349*, 1829; j) S. K. Chattopadhyay, S. Karmakar, T. Biswas, K. C. Majumdar, H. Rahaman and B. Roy, *Tetrahedron*, **2007**, *63*, 3919.
34. T. M. Trnka and R. H. Grubbs, *Acc. Chem. Res.*, **2001**, *34*, 18.
35. a) I. Dragutan, V. Dragutan and P. Filip, *Arkivoc*, **2005**, (x), 105; b) V. Dragutan and I. Dragutan, *Platinum Metals Rev.*, **2005**, *49*, 123; c) H. Clavier, K. Grela, A. Kirsching, M. Mauduit and S. P. Nolan, *Angew. Chem. Int. Ed.*, **2007**, *46*, 6786; d) P. Deshmukh and S. Blechert, *Dalton Trans.,* **2007**, 2479; e) C. E. Diesendruck, E. Tzur and N. G. Lemcoff, *Eur. J. Inorg. Chem.*, **2009**, 4185; f) C. Samojłowicz, M. Bieniek and K. Grela, *Chem. Rev.,* **2009**, *109*, 3708; g) S. Díez-González, N. Marion, S. P. Nolan, *Chem. Rev.,* **2009**, *109*, 3612; h) G. C. Vougioukakakis, and R. H. Grubbs, *Chem. Rev.,* **2010**, *110*, 1746.
36. a) S. Monfette and D. E. Fogg, *Chem. Rev.,* **2009**, *109*, 3783; b) A. Poater, X. Solans-Monfert, E. Clot, C. Copret and O. Eisenstein, *J. Am. Chem. Soc.* **2007**, *129*, 8201.
37. a) R. L. Burwell and R. G. Pearson, *J. Phys. Chem.,* **1966**, *70*, 300; b) W. L. Holstein and M. Boudart, *J. Phys. Chem. B.,* **1997**, *101*, 9991.
38. E. L. Dias, S. T. Nguyen and R. H. Grubbs, *J. Am. Chem. Soc.,* **1997**, *119*, 3887.
39. a) F. Bernardi, A. Bottoni and G. P. Miscione, *Organometallics,* **2003**, *22*, 940; b) C. Adlhart and P. Chen, *J. Am. Chem. Soc.,* **2004**, *126*, 3496.
40. a) M. S. Sanford, M. Ulman and R. H. Grubbs, *J. Am. Chem. Soc.,* **2001**, *123*, 749; b) M. S. Sanford, J. A. Love and R. H. Grubbs, *J. Am. Chem. Soc.,* **2001**, *123*, 6543; c) S. Booyens, A. Roots, O. F. Wendt, *J. Organomet. Chem.*, **2007**, *692*, 5508-5512.
41. a) B. F. Straub *Adv. Synth. Catal.,* **2007**, *349*, 204; b) E. F. van der Eide and W. E. Piers, *Nature Chem.,* **2010**, *2*, 571; c) J. W. van Rensburg, P. J. Steynberg, M. M. Kirk, W. H. Meyer, G. S. Forman, *J. Organomet. Chem.*, **2006**, *691*, 5313-5516.
42. A. C. Hillier, W. J. Sommer, B. S. Yong, J. L. Petersen, L. Cavallo, S. P. Nolan, *Organometallics,* **2003**, *22*, 4322.
43. a) S. H. Hong, A. G. Wenzel, T. T. Salgurero, M. W. Day, and R. H. Grubbs, *J. Am. Chem. Soc.,* **2007**, *129*, 7961; b) S. H. Hong, M. W. Day, and R. H. Grubbs, *J. Am. Chem. Soc.,* **2004**, *126*, 7414.
44. H. Wang and J. O. Metzger, *Organometallics,* **2008**, *27*, 2761.
45. M. S. Sanford, L. M. Henling, M. W. Day, and R. H. Grubss, *Angew. Chem. Int. Ed.,* **2000**, *39*, 3451.
46. M. A. Dunbar, S. L. Balof, L. J. LaBeaud, B. Yu, A. B. Lowe, E. J. Valente and H.-J Schanz, *Chem. Eur. J.,* **2009**, *15*, 12435-12446.
47. a) A. J. Boydston, Y. Xia, J. A. Kornfield, I. A. Gorodetskaya and R. H. Grubbs, *J. Am. Chem. Soc.,* **2008**, *130*, 12775; b) Y. Xia, A. J. Boydston, Y. Yao, J. A. Kornfield, I. A. Gorodestskaya, H. W. Spiess, R. H. Grubbs, *J. Am. Chem. Soc.,* **2009**, *131*, 2670; c) A. J. Boydston, T. W. Holcombe, D. A. Unruh, J. M. Fréchet and R. H. Grubbs, *J. Am. Chem. Soc.,* **2009**, *131*, 5388.
48. a) P. E. Romero and W. E. Piers, *J. Am. Chem. Soc*., **2005**, 127, 5032; b) J. A. Tallarico, P. J. Bonitatebus, M. L. Snapper, *J. Am. Chem. Soc*., **1997**, *119*, 7157.
49. V. Farina, X. Zeng, X. Wei, Y. Xu, L. Zhang, N. Haddad, N. K. Yee, C. H. Senana Yake, *Catalysis Today*, **2009**, *140*, 74.
50. a) S. F. Vyboishchikov, M. Bühl and W. Thiel, *Chem. Eur. J.,* **2002**, *8*, 3962; b) B. F. Straub, *Angew. Chem. Int. Ed.,* **2005**, *44*, 5974.
51. A. C. Hillier, W. J. Sommer, B. S. Yong, J. L. Petersen, L. Cavallo and S. P. Nolan, *Organometallics,* **2003**, *22*, 4322.
52. O. Eisenstein, R. Hoffmann, *J. Am. Chem. Soc.,* **1981**, *103*, 5582.
53. C. H. Suresh and N. Koga, *Organometallics,* **2004**, *23*, 76.
54. R. N. Perutz and S. Sabo-Etienne, *Angew. Chem. Int. Ed.,* **2007**, *46*, 2578.
55. E. Colacino, J. Martinez and F. Lamaty, *Coord. Chem. Rev.,* **2007**, *251*, 726.
56. a) S. B. Garber, J. S. Kingsbury, B. L. Gray and A. H. Hoveyda, *J. Am. Chem. Soc.,* **2000**, *122*, 8168; b) J. S. Kingsbury and A. H. Hoveyda, *J. Am. Chem. Soc.,* **2005**, *127*, 4510; c) M. Bieniek, A. Michrowska, D. L. Usanov and K. Grela, *Chem. Eur. J.,* **2008**, *14*, 806.
57. a) M. R. Buchmeiser, *Chem. Rev*., **2009**, *109*, 303; b) I. Dragutan and V. Dragutan, *Platinum Metals Rev.,* **2008**, *52*, 71; c)I. Dragutan and V. Dragutan, *Platinum Metals. Rev.*, **2008**, *52*, 157; d) C. Copéret, J.-M. Basset, *Adv. Synth. Catal.,* **2007**, *349*, 78; e) S. Liu, J. Xiao, *J. Mol. Catal. A: Chem*., **2007**, *270*, 1; f) I. Dragutan, V. Dragutan, L. Delaude, A. Demonceau, *ARKIVOC*, **2005**, *(x)*, 206.

58. V. Sashuk, L. H. Peeck, H. Plenio, *Chem. Eur. J.,* **2010**, *16*, 3983.
59. M. Ulman and R. H. Grubbs, *Organometallics,* **1998**, *17*, 2484.
60. J. Carreras, A. Avenoza, J. H. Busto and J. M. Peregrina, *J. Org. Chem.,* **2009**, *74*, 1736.
61. a) S. Pandian, I. H. Hillier, M. A. Vincent, N. A. Burton, I. W. Ashworth, D. J. Nelson, J. M. Percy and G. Rinaudo, *Chem. Phys. Lett.,* **2009**, *476*, 37; b) P. Sliwa and J. Handzlik, *Chem. Phys. Lett.,* **2010**, *493*, 273.
62. a) B. Schmidt, *Eur. J. Org. Chem.,* **2004**, 1865; b) M. Arisawa, Y. Terada, C. Theeraladanon, K. Takahashi, M. Nakagawa and A. Nishida, *J. Organomet. Chem.,* **2005**, *690*, 5398; c) I. Dragutan and V. Dragutan, *Platinum Metals Rev.,* **2006**, *50*, 81; d) D. Bourgeois, A. Pancrazi, S. P. Nolan and J. Prunet, *J. Organomet. Chem.,* **2002**, *643*, 247; e) M. Arisawa, Y. Terada, K. Takahashi, M. Nakagawa and A. Nishida, *The Chemical Record,* **2007**, *7*, 238; f) Y. Kasaya, K. Hoshi, Y. Terada, A. Nishida, S. Shuto and M. Arisawa, *Eur. J. Org. Chem.,* **2009**, 4606; g) G. L. Morgans, E. L. Ngidi, L. G. Madeley, S. D. Khanye, J. P. Michael, C. B. de Koning and W. A. L. van Otterlo, *Tetrahedron,* **2009**, *65*, 10650.