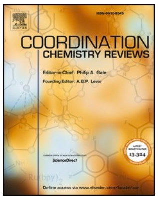
Coordination Chemistry Reviews 542 (2025) 216827

Contents lists available at ScienceDirect

Coordination Chemistry Reviews

journal homepage: www.elsevier.com/locate/ccr



Review

Challenges in olefin metathesis: past, present and future

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ARTICLE INFO

Keywords:
Olefin metathesis
Ruthenium
Selectivity
CAAC ligand
NHC ligand

ABSTRACT

Olefin metathesis has become a cornerstone in modern synthetic chemistry, enabling diverse applications across organic synthesis, polymer science, and industrial processes. Despite its transformative impact, significant challenges persist, including catalyst stability, functional group tolerance, selectivity, and scalability. Ruthenium-based catalysts dominate the field, yet their sensitivity to oxygen, moisture, and harsh conditions limits industrial applicability. Functional group incompatibility and the difficulty in achieving precise product selectivity further hinder its versatility, particularly in cross-metathesis (CM) and ring-closing metathesis (RCM). Advances in catalyst recycling, green chemistry practices, and alternative systems using earth-abundant metals like iron are promising but remain underdeveloped. Expanding substrate scope, improving mechanistic understanding, and integrating metathesis with other catalytic processes offer opportunities for innovation. Addressing these issues through predictive catalysis, novel ligand design, and artificial intelligence-driven insights will enhance the sustainability and efficiency of metathesis, cementing its role as a pivotal reaction in future chemical synthesis.

1. Introduction

Carbon's exceptional bonding versatility makes it a cornerstone of molecular design [1]. Once confined to pharma and petrochemicals, carbon-based research now spans many fields. A surge in carbon–carbon bond studies has been observed, with synthesis dominating, affirming synthetic chemistry's central role in expanding molecular innovation.

Synthesis from carbon containing molecules faces the challenge of working with a strong and unpolarized bond, arising from its covalent nature [1,2]. As a result, early synthetic methodologies primarily relied on the use of reactive molecular motifs or functional groups containing heteroatoms positioned near the target carbon atoms involved in cleavage or bonding (see Fig. 1 for an example of an aldol condensation). Other approaches often resorted to harsh reaction conditions to overcome the intrinsic strength of the C—C bond, frequently sacrificing molecular selectivity (e.g., vulcanization reactions). [3,4] Unfortunately, even in the former milder conditions, the inclusion of such reactive motifs compromised chemoselectivity. This often led to unselective cleavage or undesired functionalization, making functional tolerance a common problem.

In this context, organic chemistry focused for decades on exploring functional group configurations to enable novel synthetic pathways, while the development and use of protecting groups emerged as a pivotal strategy to address the reactivity and liability of functional groups. A significant milestone in organic synthesis was the introduction of transition metals. Beyond simply exploiting differences in electronegativity to polarize bonds, the incorporation of d-orbitals revolutionized the field through the formation of coordinative bonds and metal complexes. These coordination molecules are now recognized for facilitating well-defined reaction steps (e.g., oxidative addition, reductive elimination, migratory insertion), enabling alternative reaction pathways that overcome the intrinsic thermodynamic limitations of traditional organic chemistry [2]. Consequently, this advancement unlocked diverse and sophisticated strategies for carbon-carbon bond formation.

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https://doi.org/10.1016/j.ccr.2025.216827
Received 17 March 2025; Accepted 15 May 2025
Available online 11 June 2025

Furthermore, when the synthetic process is optimized to allow the recovery of the organometallic reagent, catalytic conditions can be achieved. Organometallic catalysis enables repeated reaction cycles under stable conditions, offering economic and ecological benefits like improved atom economy, milder conditions, reduced waste, fewer derivatives, and enhanced selectivity over stoichiometric methods [6].

After years of extensive research and development, the field of organometallic catalysis has expanded into a vast and diverse domain, encompassing numerous subfields. Given this breadth, it is impossible to explore every detail without narrowing the scope of the discussion. Therefore, the next section focuses on carbon-carbon double bond structures. In detail, alkenes, or olefins, are molecules with a carbon–carbon double bond, comprising sigma and π interactions. Their unique electronic structure leads to shorter and stronger bonds with distinct reactivity. Ethylene exemplifies this, showing higher chemical activity due to accessible π-electrons. Notably, ethylene dominates global production volumes of organic compounds, driven by its widespread demand as a versatile synthetic precursor [2].

A variety of methods exist for obtaining double bonds, with elimination reactions being among the most common approaches. It is important to emphasize, however, that in such cases, the double bond is formed from a pre-existing single bond. Similarly, widely utilized methodologies such as the Mizoroki-Heck coupling provides convenient routes for the functionalization of double bonds. [7,8] However, these approaches still rely on the presence of a pre-existing carbon-carbon double bond.

The discussion that follows will focus exclusively on reactions that generate alkene bonds through the coupling of two molecules, to end in olefin metathesis. The first examples of such reactions correspond to homologation procedures, which in their simplest forms are equivalent to methylene couplings (Fig. 2) [9]. While some of these methods may appear outdated, it is critical to recognize that the practices of applied synthetic chemistry often diverge from cutting-edge methodologies developed in academic research.

The objective of this section is not to present an exhaustive compendium of the most innovative approaches reported over the past decade, nor to provide a chronological review of all alkene synthesis methodologies. Instead, the focus is on highlighting methods of significant practical utility, offering a clearer understanding of the context in which olefin metathesis demonstrates its exceptional utility. Priority is given to methodologies that have proven to be broadly applicable for the efficient production of valuable products.

Traditionally, methodologies that lead to alkenes have relied on carbonyl bonds as an excellent starting point, given their widespread availability and high reactivity [10].

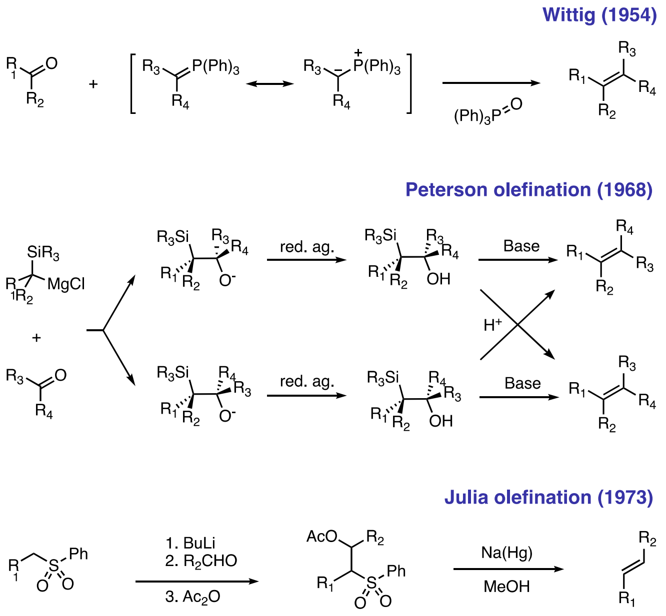


Fig. 2. Three carbonyl methodologies widely used to form alkene bonds [10–12].

In the 1970s, Julia and Paris reported a versatile two-step olefination method. The first step involves a relatively standard nucleophilic attack of a phenylsulfonyl carbanion on the carbonyl bond of an aldehyde or ketone, followed by in-situ esterification. In the second step, the alkoxide derivative is reduced with sodium amalgam, leading to the formation of an *E*-alkene via reductive elimination [10,13–15]. While the mechanism of the first attack is well understood, the latter step's mechanism is not fully defined. However, the stereoselectivity of the product suggests equilibrated intermediates involving vinylic radicals [9,16–18]. Numerous modifications of the reaction have broadened the scope of applications. One notable example is the Julia–Kocienski olefination, which replaces the phenyl substituent of the sulphone by a tetrazole ring. This increases the *E*-alkene selectivity and allows the reaction to proceed in a one-pot protocol. [19,20]

Alternatively, carbonyl olefination can be achieved using Grignard-like reagents derived from alkyl silanes [11]. Introduced in 1968 by Peterson, this method generates a beta-hydroxy silane as a mixture of enantiomers from substrates including an aldehyde group or a ketone's asymmetric carbonyl. Upon separation, each enantiomer can be conveniently converted to the desired olefin-stereoisomer by acidic or basic treatment [21]. In basic media, elimination is triggered by deprotonation of the alcohol, typically forming a four-membered 1,2-oxasiletanide. This cyclic intermediate then reorganizes to produce the alkene and the hydroxysilonalate anion. Alternatively, acid treatment leads to hydrolytic elimination, placing the substituents in an anti-configuration and yielding the complementary stereoisomer [9].

Wittig proposed an earlier carbonyl olefination reaction for ketones and aldehydes [12]. The reaction and its ylide reagent, which make it

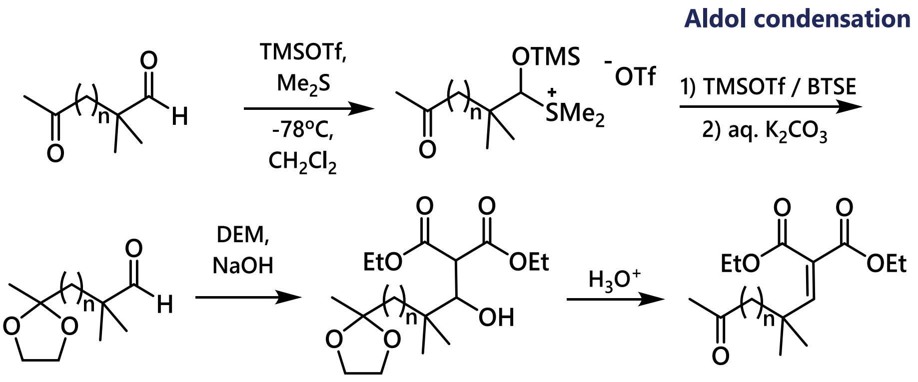


Fig. 1. Aldol condensation reaction with trimethylsilyl triflate protecting group on the acetone group to avoid undesired functionalization [5].

possible, are named after him (i.e. the Wittig reagent). This method, the oldest among those mentioned, is also the most well-known due to its extensive and valuable application in a wide range of synthetic protocols. Indeed, as a result of this contribution, Wittig was awarded the Nobel Prize in Chemistry in 1979. The reaction mechanism is believed to proceed via a betaine intermediate or a concerted oxaphosphetane, depending on the substituents of both the ylide and the carbonyl [22].

Regarding the olefination methods mentioned, the choice of technique depends on the overall synthesis. The Wittig reaction is typically preferred as the final step in total synthesis protocols due to its superior functional group tolerance and high stereocontrol. In contrast, the Julia olefination is an attractive option for achieving high yields of *E*-alkenes ($>$80 %). Meanwhile, the Peterson olefination offers the versatility of controlling the stereoisomer by adjusting the acid-base conditions during the elimination step [9].

To conclude this section, it is important to note that all the aforementioned methods involve a bond rearrangement process in their mechanisms that thus is not entropically unfavored. This feature is crucial to the efficiency of these reactions and will be further explored in the following discussion.

With the exception of the Julia olefination, both the Wittig and Peterson mechanisms involve a four-membered cyclic intermediate. These ring structures are formed during cycloaddition processes, either through multiple steps or in a concerted manner. This type of reaction has extensive applications in synthetic chemistry, with paradigmatic examples such as the Diels-Alder reaction and the Huisgen reaction (Fig. 3). [23,24] The latter is particularly relevant in the context of ‘click chemistry,’ where 1,3-cycloadditions are ground-breaking.

During cycloadditions, unsaturated bonds interact to form new single bonds in a ring, thereby reducing the overall bond multiplicity of the reagents. From a thermodynamic perspective, this approach prevents the formation of unstable intermediates and keeps the reaction’s energetic cost moderate, except in certain cases under harsh conditions or when activation by light is required. [25,26] Cycloadditions are often used in intermediate steps of synthesis to couple two fragments. Therefore, it is not surprising that highly efficient alkene homologation reactions, such as the Wittig and Peterson reactions, involve four-membered cycles resulting from these bond rearrangements.

The viability of cycloadditions is governed by rules related to the symmetry and phase of molecular orbitals (MOs). For a rearrangement to occur, the interaction between the MOs must be favourable. This allows the removal of density from a molecule’s bonding orbital and its placement into an antibonding orbital of the other reagent. In the case of the Wittig reaction, for example, the planar rotation of the carbonyl molecule’s orbitals is crucial (see Fig. 4), made possible by the readily accessible unsubstituted oxygen.

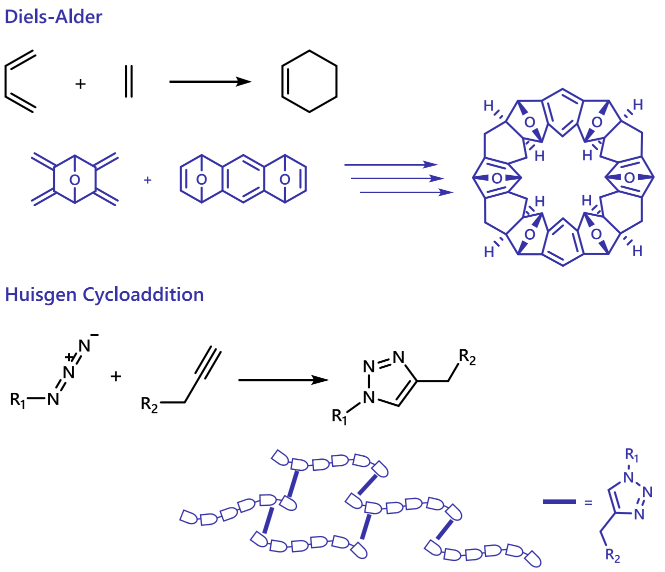


Fig. 3. Notable examples of supramolecular structures formed via rearrangement of unsaturated bonds.

Due to the abundance of carbon-carbon double bonds in plant-derived products and other accessible feedstocks, alkenes are convenient reagents for [2+2]-cycloaddition reactions. However, thermodynamically, this reaction is prohibited by the orbital phase of the MOs (see Fig. 4). While it is possible to modify the orbital phase of the lowest unoccupied molecular orbital (LUMO) through photochemistry, a more fruitful approach is the use of metal ylidenes, traditionally referred to as olefin metathesis.

2. Why olefin metathesis?

Olefin metathesis excels in targeting carbon-carbon double bonds. It is a straightforward and versatile chemical reaction with limitless applications, making it an invaluable tool in chemistry. Take for instance, it is capable to lead to a high degree of control over the synthesis, as the reaction conditions can be tailored to meet the specific needs of the process. Additionally, olefin metathesis distinguishes itself from other methodologies due to its high precision and functional group tolerance, enabling the transformation of simple molecules into more complex ones. [27,28]

Moreover, metathesis reactions are regarded as environmentally friendly, because they do not require large quantities of co-reagents, thus producing significantly less waste. Consequently, the metathesis reaction aligns with green chemistry principles on two fronts: firstly, it is catalytic, and secondly, it reduces the number of steps in the synthetic process compared to other non-stoichiometric reactions, eliminating the need to handle and generate inorganic waste. This makes olefin metathesis a more sustainable choice for chemical reactions. [29,30]

The extensive field of alkene metathesis and its widespread implementation are the results of many years of research and mechanistic investigation. Among the key contributors, Chauvin’s mechanistic insights were pivotal in establishing the foundations for a deeper understanding of the reaction [31]. Furthermore, seminal contributions to the mechanistic understanding of the reaction were made by Katz, McGinnis, and coworkers, particularly through a series of studies involving second- and third-row transition metals [32] such as molybdenum and tungsten. [33–35] Equally significant were the contributions of Schrock and Grubbs, who respectively developed the first practical catalysts and their more viable alternatives. Together with Chauvin the three scientists are regarded as the fathers of alkene metathesis, for which they were awarded the Nobel Prize in Chemistry in 2005. Their work paved the way for the development of a myriad of derivatives designed to fine-tune reaction performance for specific applications.

In fact, when it comes to double bond formation, metathesis reactions can be integrated into a wide variety of synthetic processes. Moreover, only minor adjustments to the catalyst are typically required, which adds to the process’s appeal. Some of the most common scenarios for alkene transposition are illustrated in Fig. 5.

The decomposition of olefin metathesis catalysts is a significant challenge in achieving efficient and selective metathesis reactions. The primary decomposition pathways including ligand dissociation, beta-hydride elimination [36], metal-carbene dimerization [37], oxidation, and acid-induced protonation, each contribute to the loss of catalytic activity. Specially Jensen, Fogg and coworkers have highlighted the main issue, and how to control them. [38–40] Actually, by understanding these processes and implementing stabilization strategies such as ligand modification, solvent control, and catalyst immobilization, researchers can enhance catalyst longevity and improve reaction efficiency. In detail, phosphine disproportionation and ligand dissociation for ruthenium catalysts, specially for first generation Grubbs series, can undergo decomposition due to phosphine dissociation and next formation of dinuclear ruthenium species or inert ruthenium clusters [41],

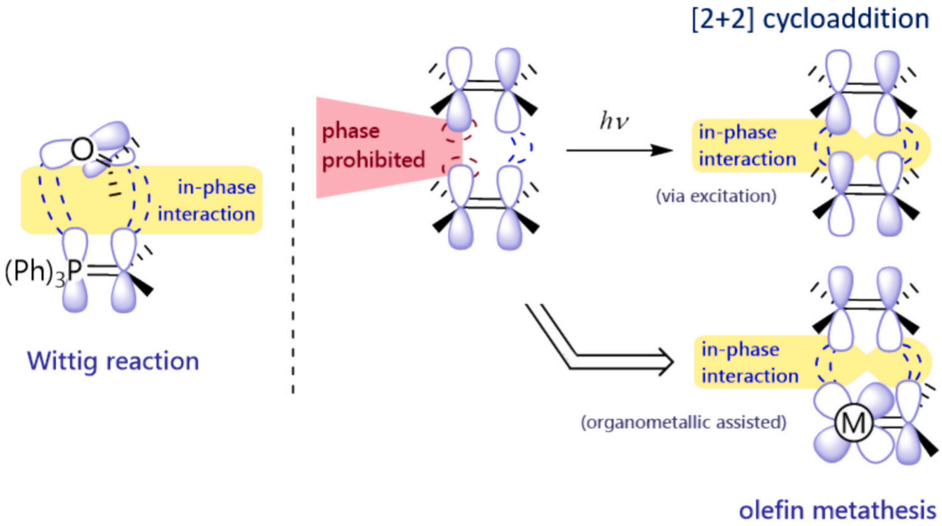


Fig. 4. The viability of bond formation processes justified by the appropriate phase of the involved orbitals.

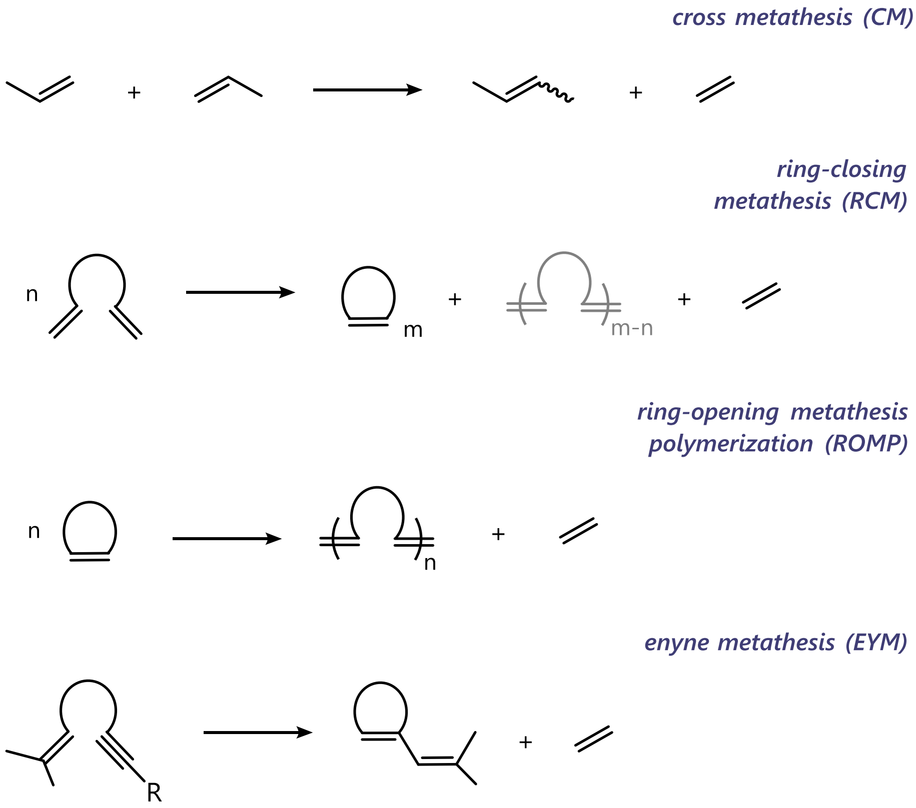


Fig. 5. Most relevant types of olefin metathesis reactions.

knowing that these species can be obtained by metal-carbene coupling, where two metal-carbene species react to form an inactive dinuclear complex. The replacement of phosphines by *N*-heterocyclic carbene (NHC) ligands is not trivial either, since the substituents on their imidazole rings must be protected. [42–44] To point out that NHC ligands are protected toward oxidation by air, while molybdenum and tungsten catalysts, unlike their ruthenium counterparts, are highly sensitive to oxygen and moisture. However, it should be noted that with π-acidic compounds, even ruthenium catalysts can degrade due to activation of the ylidene group, which can react with the alkyl substituents of the NHC ligands, as demonstrated by Diver [45], Cavallo [46] and co-workers. When exposed to air, these catalysts rapidly oxidize, leading to the formation of oxo-metal species that are catalytically inactive. Another problem is the beta-hydride elimination where the ylidene bond undergoes a rearrangement toward the formation of a metal hydride species, [47,48] specially in presence of alcohols [49]. Olefin metathesis catalysts can also degrade in the presence of acidic protons. While the NHC ligand can dissociate once protonated its carbene group [50], this process is particularly relevant for molybdenum and tungsten systems, where acidic impurities in the reaction medium can protonate the metal-carbene complex, leading to loss of catalytic activity. Ongoing research continues to explore novel ligand architectures and reaction conditions that further extend the operational lifetime of these valuable catalytic systems.

3. Chronology of olefin metathesis

Olefin metathesis first emerged in a series of new polymerization protocols reported by various chemical companies. In 1960, the biopharmaceutical company DuPont published a groundbreaking article on the polymerization of norbornene (Fig. 6, left). A lithium-aluminum complex combined with titanium tetrachloride catalyst facilitated the formation of a polymeric chain of cyclopentane rings, linked in a *cis*-1,3-fashion with *trans* C=C bonds. This reaction demonstrated remarkable stereospecificity and tacticity, allowing for the easy attainment of high molecular weight polymers [51].

Several years later, building on a prior publication by Ziegler et al. in which 1-butene was synthesized from ethylene [52], Natta's group reported a similar polymerization protocol for cyclopentene. In this case, molybdenum and tungsten halides were used as catalysts, yielding both *cis* and *trans*-cyclopentanamers (Fig. 6, right) [53].

In 1964, researchers from the petrochemical group Phillips Petroleum Co. presented a non-polymeric application of olefin metathesis. They described the coupling of short linear olefins, a process referred to as the disproportionation of olefins. This approach, similar to Natta's work, utilized various molybdenum and tungsten catalysts. Despite the high temperatures involved (ranging from 100 to 200 °C), the substrates and products remained in equilibrium, making the process unsuitable for more ambitious synthetic applications [54].

At the same time, Calderon and coworkers at Goodyear made significant advancements in the field of polymerization. Their work led to the development of a soluble catalyst system capable of initiating ring-opening polymerization, which effectively converted propylene into ethylene and 2-butene [55]. Calderon's investigations established a connection between the scrambling of acyclic olefins, as observed by Banks and Bailey, and the polymerization of cyclic olefins, as demonstrated by DuPont and Natta. He proposed that the reaction mechanism was driven by the cleavage of carbon-carbon double bonds, rather than the transfer of alkyl groups between olefins through single-bond cleavage. This crucial insight into the reaction mechanism paved the way for later breakthroughs in the field.

In this context, Calderon published a brief communication in the same year, which holds historical significance as it marks the first recorded use of the term "metathesis" to describe this type of reaction [56]. Furthermore, he proposed two distinct mechanisms for this bond rearrangement (Fig. 7).

Finally, Calderon further advanced the understanding of olefin metathesis by evaluating the reaction using deuterated alkenes to differentiate between the contributions of transalkylation and transalkylidenation mechanisms. The primary product of the metathesis of 2-butene with 2-butene-d^8 was identified as $C_4H_4D_4$, supporting a scheme based on alkylidene group exchange. Additionally, the reaction mixture from the metathesis of 2-pentene with 6-dodecene contained all six olefins predicted by the proposed transalkylidenation mechanism. The absence of other olefins suggested that side reactions involving double bond migration did not occur. Moreover, the *cis-trans* equilibria were achieved as a result of the transalkylidenation step itself, which was relatively non-selective in the formation of geometric isomers.

These contributions were pivotal in defining the novel reaction and clarifying the transformations taking place. However, a comprehensive understanding of the mechanism still required further investigation. The next section continues with the chronology of the mechanistic journey, which involved a combination of traditional experimental chemistry, enhanced by new technical developments, and the emerging field of computational studies.

3.1. *Mechanistic discussion*

Building on Banks and Bailey's work, Bradshaw provided further insight into the 'olefin dismutation' process, proposing a pairwise mechanism known as the quasi-cyclobutane-based model (Fig. 8, top) [57]. While this mechanism was widely accepted for some time, Chauvin and Harrison demonstrated its limitations by evaluating different types of metathesis reactions: the disproportionation of acyclic olefins, the polymerization of cyclic olefins, and telomerization. Their findings revealed several key factors that any proposed mechanism had to fulfil across all three scenarios. These included the formation of a stable growth center enabling the reversible formation of high molecular weight polymers, as well as a statistically redistributed alkylidene group. Furthermore, a kinetically driven statistical distribution of low molecular weight cross-reaction products, with the conservation of unsaturated hydrocarbon fragments on the catalytic center, indicated that cross-reaction products arose from non-consecutive reactions.

As a result, the original quasi-cyclobutane intermediate model was considered unsatisfactory. In its place, alternative intermediates such as a one-carbon metal carbene complex and metallacyclobutanes containing an odd number of carbons were proposed. This shift in understanding led to the now widely accepted mechanism for olefin metathesis, established by Chauvin [31]. His model involves the formation of a metallacyclobutane intermediate and a fourteen-electron (14e) metal-ylidene complex as key intermediates (Fig. 8, bottom), even though Chen and co-workers stated that the metallocyclobutanes could not be intermediates, but really be considered as transition states [58].

In addition to Chauvin's seminal work, other significant contributions have furthered the understanding of this mechanism. Of particular importance is Cardin's work on transition-metal carbenes as intermediates, with a special focus on rhodium [59–62]. In particular, in 1975 two parallel works were published giving importance to the formation of the metallacyle, by Katz and McGinnis [32], and also interestingly, although other mechanisms were proposed earlier, Grubbs' subsequent experimental work provided additional support for Chauvin's model. [63,64]

3.2. *First-practical catalysts*

In 1978, Tebbe reported an efficient catalyst for olefin homologation

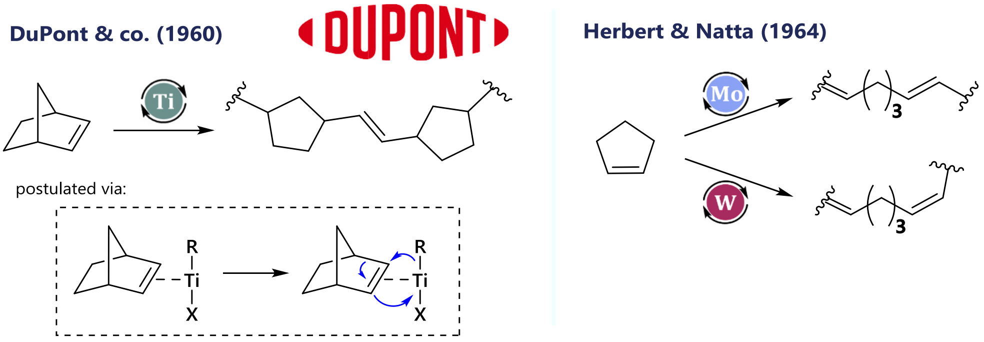


Fig. 6. First reports of olefin metathesis on polymerization reactions reported by the DuPont company and by Herbert and Natta.

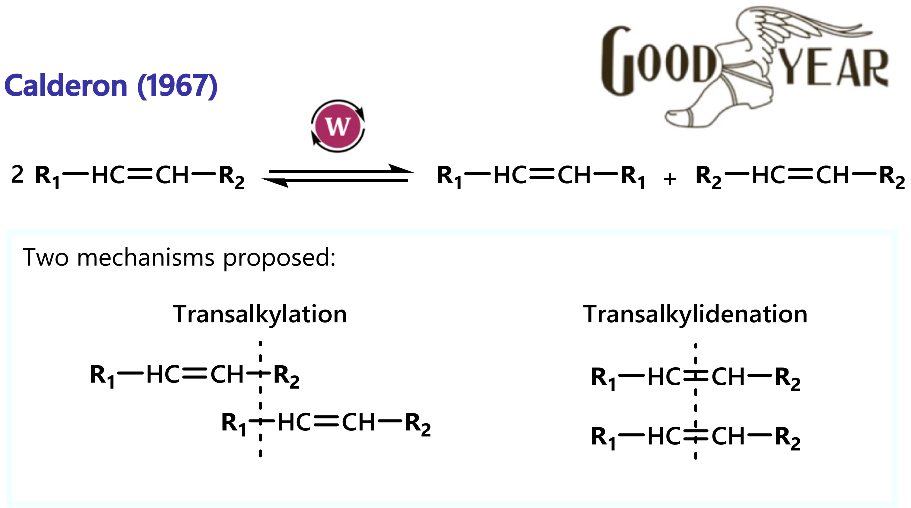


Fig. 7. Calderon's work on metathesis of internal olefins and the two mechanisms proposed [56].

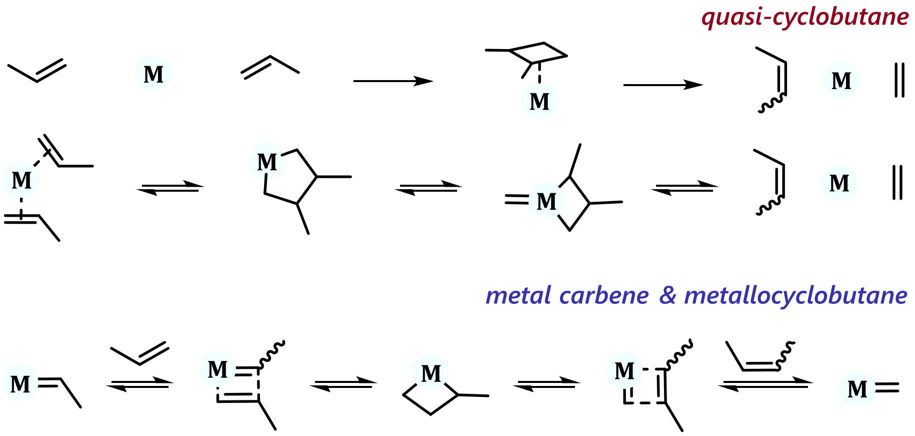


Fig. 8. Bond rearrangement configurations proposed in olefin metathesis. Supra: the diolefin quasi cyclobutane discarded mechanisms. Infra: the Chauvin's mechanism with the ylidene/metallacyclobutane characteristic intermediates.

[65]. While titanium-ylidenes were already known to facilitate olefin metathesis, they were prone to rapid decomposition into inactive species. Tebbe cleverly introduced the aluminum group to stabilize the methylene compound, which can be activated in situ (Fig. 9). However, a significant limitation of Tebbe's approach is that longer alkylidenes tend to undergo unwanted methanation reactions [66].

Despite this drawback and the availability of more efficient metathesis catalysts, the use of the Tebbe reagent remains particularly advantageous in total synthesis protocols that involve olefin-carbonyl steps. This is because the Tebbe reagent not only facilitates olefin metathesis but also enables the formation of carbon-carbon double bonds between olefins and carbonyl compounds. Its versatility has found widespread application in the synthesis of complex organic molecules, including natural products and pharmaceuticals. Today, Tebbe's reagent continues to be a popular choice due to its reliability, ease of use, and compatibility with a wide range of functional groups (see example in Fig. 9, below) [67].

Relevant contributions to olefin metathesis were made by Schrock, particularly through his work with tungsten and molybdenum alkylidenes [68], which led to the discovery of the first stable transition-metal-methylidene (Fig. 10, top-left) [69]. This important development followed earlier reports on high oxidation state tantalum (Ta) and niobium (Nb) alkylidene complexes, which unfortunately were not suitable for olefin metathesis [70]. However, Schrock's group later reported alkoxide-containing tantalum alkylidene complexes that proved effective as metathesis catalysts [71].

Molybdenum (Mo) and ruthenium (Ru)-based catalysts differ in several key ways, with the most notable being the reactivity of the M=C bond [72]. Direct comparisons of Mo and Ru catalysts are rare, but they show that catalyst conversions and selectivities can vary greatly, moderately, or minimally. Notably, some reactivities, such as alkyne metathesis, are only achievable with Mo and W catalysts. Moreover, Mo and W catalysts have had greater success when incorporated into solid supports for heterogenized homogeneous catalysis, which is crucial for industrial processes. Metal contamination of products, particularly a concern in the pharmaceutical industry (where contamination limits are set at 20 ppm), remains one of the key challenges. In the case of Ru, the high catalyst loading required (up to 20 %) due to its lower activity, exacerbates contamination issues. [73–76] However, more recently, the extraction of Ru following metathesis conversions is critical to prevent product contamination, degradation, or undesired isomerization caused by residual Ru traces. Indeed, Ru removal is a prerequisite for compliance with regulatory standards [73]. The use of scavengers emerges as a practical solution for Ru removal, as the inherent basicity of this species facilitates the precipitation of adducts through acid-base reactions [74].

Despite their sensitivity to water [77], oxygen [78], and protic functionalities, Mo-based catalysts are preferred in certain scenarios [75,76]. In general, they do not exhibit higher activity, but they have

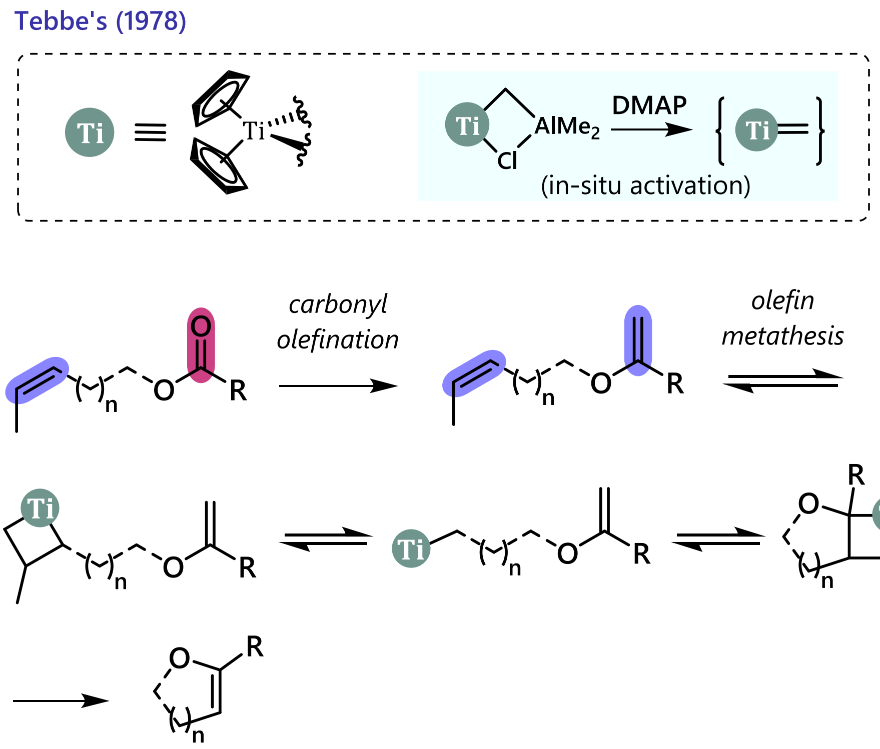


Fig. 9. Tebbe's titanium catalyst in a synthetic process first acts on a carbonyl bond, which is converted into an alkene to be further reacted in a ring closure metathesis reaction.

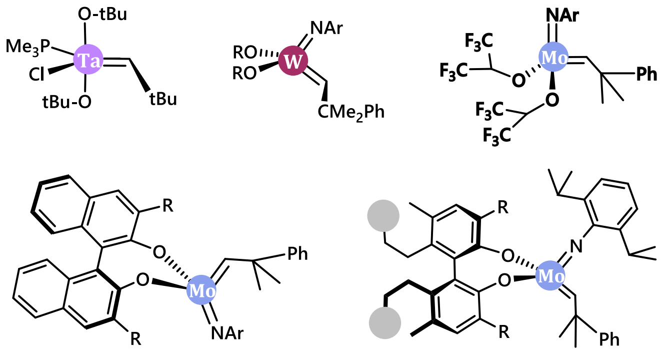


Fig. 10. Relevant examples of olefin metathesis catalysts of the Schrock type that are used in a wide range of different applications.

also led to the development of commercial catalysts and chiral versions for pioneering asymmetric metathesis catalysis (Fig. 10, bottom).[79–85] In detail, one of their key applications is in ring-closing metathesis (RCM), where they facilitate the formation of cyclic alkenes, critical in pharmaceuticals and complex natural products. Mo catalysts are particularly effective for ring-opening metathesis polymerization (ROMP), used in the synthesis of specialty polymers with tailored properties, such as high-performance elastomers. Additionally, they excel in cross-metathesis (CM), enabling functionalization of alkenes in organic synthesis. Compared to other Ru-based metathesis catalysts, Mo catalysts exhibit higher reactivity toward terminal olefins and alkynes and are less tolerant of functional groups [75]. However, their sensitivity to air and moisture and limited functional group compatibility remain challenges in industrial applications. Actually, this has hindered their widespread development and application in both industry and research, despite potential solutions [86].

3.2.1. The Grubbs catalyst

The most widely used metal in olefin metathesis made its debut in later years. Similar to the development of Schrock's catalysts, the first reported Ru carbenes in 1971 were not active in olefin metathesis (Fig. 11, left) [87]. Indeed, the first Ru catalysts exhibiting metathesis reactivity were introduced by Grubbs in the late 1980s. These catalysts, much like the systems developed by Ziegler and Natta, facilitated the polymerization of 7-oxanorbornene in water as the solvent [88]. However, no explicit carbene moiety was attributed to these catalysts at that time. It was not until 1992 that Grubbs introduced the first Ru-carbene complex with metathesis activity (Fig. 11, right) [89]. This pioneering complex efficiently catalyzed the RCM of functionalized dienes and the ROMP of low-strain olefins, all without the need for a co-catalyst. In this work, Grubbs demonstrated that these vinylidene complexes were highly efficient molecular catalysts, not only for various metathesis reactions, such as the ring-closing of terminal diolefins, but also for polymerization reactions.

In that same year, Noel's group contributed to the ROMP of cycloolefins using a Ru catalyst, with diazo esters as initiators (Fig. 12) [90]. Three years later, they demonstrated the in-situ formation of the active carbene catalyst upon the addition of the initiators, as confirmed by proton magnetic resonance [91]. That year, Grubbs attracted considerable attention by reporting the well-defined catalyst, later known as the 1st generation Grubbs catalyst (Fig. 13) [92]. Due to its ease of use (i.e. air stability and compatibility with a wide range of functional groups),

Ruthenium carbene (OM inactive)

1st ruthenium OM catalyst

Fig. 11. First example of a stable ruthenium ylidene complex, and the first ruthenium complex active in olefin metathesis.

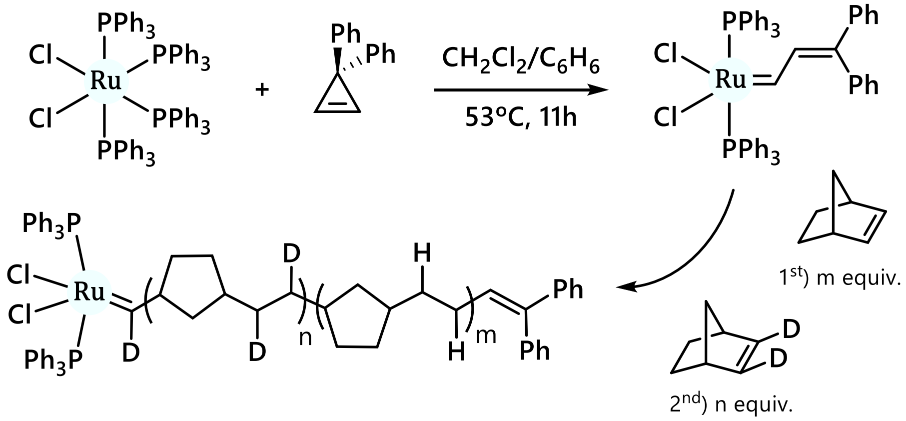
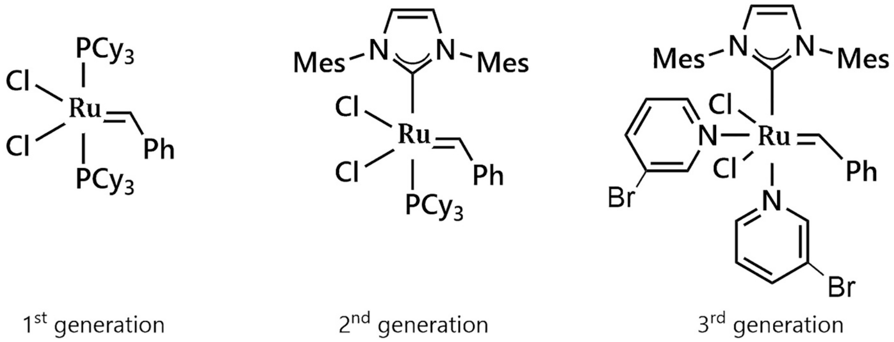


Fig. 12. Ring-opening olefin metathesis polymerization through in-situ formation of ylidene.



1^{st} generation

2^{nd} generation

3^{rd} generation

Fig. 13. Structures of Grubbs' ruthenium catalysts.

its use expanded rapidly, [92–94] and several variations soon followed. Indeed, until the last decade, it remained the most widely used olefin metathesis catalyst [29].

As knowledge of the metathesis reaction advanced, it became clear that the dissociation of one of the phosphines was necessary for the catalyst to enter the catalytic cycle. This led Grubbs to propose a new catalyst design, in which one of the phosphines was replaced by a NHC ligand [95]. Beyond its inherent stability, this modification was based on the fact that, like phosphines, NHCs exhibit strong sigma-donor properties. [96–98] However, unlike phosphines, the π-accepting character of the NHC is significantly reduced due to delocalization between the carbon and the two nitrogens [99]. This modification had two key effects: first, it increased the electron density on the Ru atom, [100–102] stabilizing the electron-deficient Ru-ylidene (14e); second, the *trans*-effect was greater, and the phosphine's lability increased, facilitating catalyst activation. [103–106]

Although the role of the *trans*-effect in activation has been a topic of discussion in recent years, the catalyst proved to be excellent and an improvement over the previous bis-phosphine variants. More details on these catalysts are provided below, but it is important to note that Grubbs' catalysts remain relevant even thirty years later. In fact, their reactivity is now being recognized even outside of metathesis applications (Fig. 14). [107,108] The versatility of these catalysts increases with the library of NHC ligands used [96], where activity—and particularly selectivity—is especially influenced by the steric hindrance [109,110] of ligands such as IMes, IPr, [111,112] and their saturated counterparts.

Finally, in 2002, the 3^{rd} generation of Grubbs catalysts, characterized by higher activation rates, was introduced by Grubbs (Fig. 15). [113,114] Moreover, their preparation was straightforward, involving a single reaction step on already commercially available older-generation Grubbs catalysts. Despite their potential advantages, their implementation in synthetic protocols has been limited due to several factors, most notably the lack of well-defined guidelines for their applications. This is even evident when compared to the extensive use and established protocols for 2^{nd} generation Grubbs catalysts, making chemists more inclined to rely on the older, well-understood catalysts for their proven effectiveness.

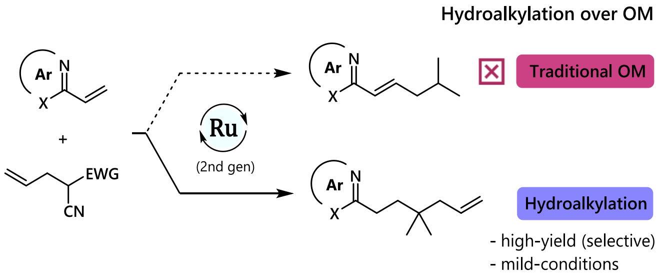


Fig. 14. Example of an alternative use of a 2^{nd} generation Grubbs catalyst.

Apart from the initial NHC ligands in Ru-based catalysts, new series of NHC ligands have emerged together with other ones to get the most versatile due to their functional group tolerance, air and moisture stability, and wide applicability in both industrial and academic research. One class of ligands that has garnered significant attention in recent years is cyclic(alkyl)(amino)carbene (CAAC) ligands. [115,116] These ligands provide unique electronic and steric properties that influence the performance of olefin metathesis catalysts in significant ways. In olefin metathesis, CAAC ligands were first introduced by Bertrand and coworkers in 2005. [117,118] They differ from traditional NHCs by

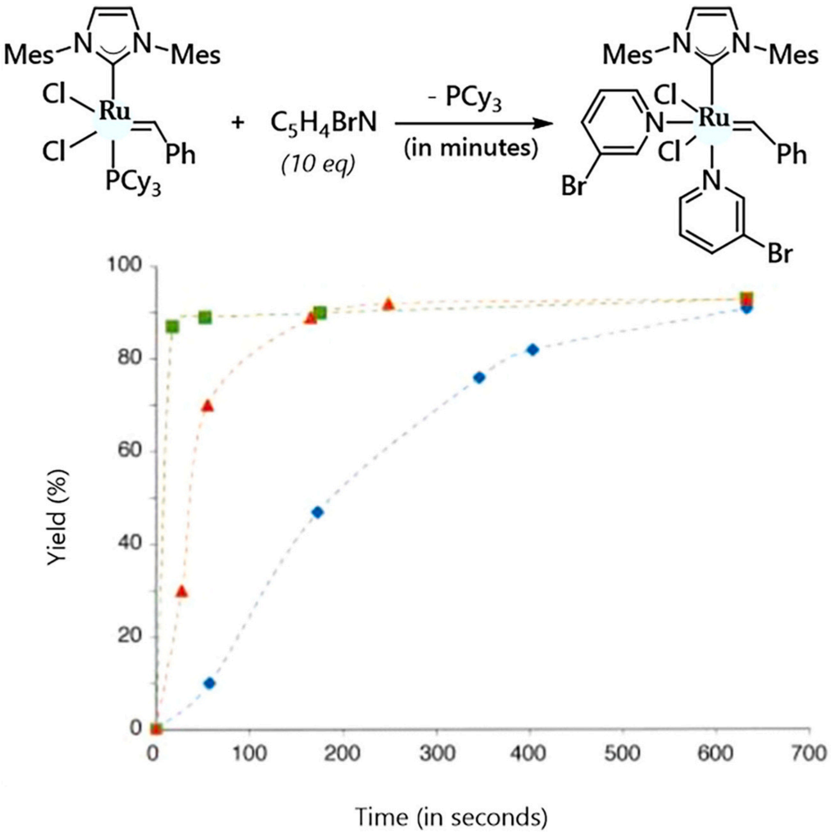


Fig. 15. Synthesis of 3rd generation Grubbs catalysts from 2nd generation Grubbs catalysts (supra). Adapted plot of comparison of initiation rates from Love's work [113].

having an electron-donating alkyl group adjacent to the carbene carbon instead of an electronegative nitrogen. [119,120] This structural difference imparts CAACs with several distinctive characteristics including greater σ-donating ability. CAAC ligands are stronger electron donors compared to NHCs, leading to more electron-rich metal centers. On the other hand, CAAC ligands exhibit better back-donation properties due to their vacant p orbital, making them electronically more flexible, and thus, enhancing their π-accepting ability. The cyclic framework provides a tunable steric environment that can influence catalyst stability and selectivity, and particularly, CAAC ligands are known to stabilize radical species, which can have implications in catalytic cycles where single-electron processes occur [121].

The synthesis of heteroleptic 2nd generation Grubbs complexes typically follows a ligand exchange approach, where a free NHC reacts with readily available 1st generation Grubbs complexes containing a replaceable phosphine ligand, such as PCy_3. This process often relies on the in situ generation of free carbenes by treating imidazolinium salts with a strong base [122]. Similarly, the formation of 2nd generation Grubbs complexes incorporating CAAC ligands instead of NHCs can be achieved from the 1st generation Grubbs catalyst via a comparable ligand exchange protocol. [120,123–125] A variety of CAAC-based catalysts has been developed by modifying the benzylidene moiety. For instance, Grela et al. demonstrated that introducing an amino group at position 4 of the benzylidene fragment led to a more active complex, attributed to the increased lability of the benzylidene unit [126]. Structural modifications of CAAC ligands in Ru complexes also involve altering substituents at the quaternary carbon or on the *N*-aryl group adjacent to the carbene. Further modifications, such as amino and ammonium groups attached to the *N*-aryl moiety [127], expand the structural diversity of CAAC Ru-based catalysts. These alterations not only enhance solubility in green protic media but also preserve catalytic activity and chemical stability.

One of the major advantages of CAAC ligands in olefin metathesis is their ability to enhance the stability and longevity of catalysts. Traditional Grubbs-type catalysts with phosphine or NHC ligands tend to undergo decomposition via ligand dissociation or decomposition pathways such as β-hydride elimination. [128,129] The strong σ-donating nature of CAAC ligands results in more robust metal-ligand bonding, thereby preventing unwanted decomposition pathways [36]. Additionally, CAAC ligands can protect the active species from undesired bimolecular deactivation processes. Their steric bulk ensures that metal centers remain well-protected, leading to longer catalyst lifetimes even in challenging reaction conditions.

The increased electron donation from CAAC ligands leads to more reactive metal centers, which can promote faster catalyst initiation and higher TOFs. This is particularly beneficial in RCM and CM, where fast catalyst activation is crucial for high product yields. Moreover, the improved π-accepting ability of CAAC ligands facilitates rapid ligand exchange and substrate coordination, ensuring that the catalytic cycle proceeds efficiently. Studies have demonstrated that CAAC-modified Ru catalysts exhibit significantly higher metathesis activity than their NHC- or phosphine-based counterparts [36,130,131]. And actually, CAAC-based catalysts have been shown to exhibit improved selectivity in certain cases due to their steric influence on the metathesis transition state. Finally, sustainability in catalysis is a growing concern, and the development of metathesis catalysts that can operate under green conditions is highly desirable. CAAC-based catalysts have shown promise in aqueous or solvent-free conditions, thanks to their enhanced stability and resistance to hydrolysis. This makes them particularly attractive for industrial applications where reducing the environmental impact of synthetic processes is a priority.

4. Limitations and main challenges

Due to the wide range of applications in which olefin metathesis catalysts are used, the nature of their limitations varies depending on the desired outcome. A particularly illustrative example is the selectivity of a catalyst for dimerization (i.e. CM) or cyclization (i.e. RCM), which may or may not be suitable depending on the target product. This trade-off is part of the price paid for a highly versatile and multi-directional catalytic system.

Thus, while this section focuses on two of the most common limitations of Grubbs catalysts, many others may arise in more specific contexts, depending on the overall process in which the catalyst is employed.

4.1. Mechanistic understanding: Grubbs 1st vs 2nd generations case

Organometallic chemistry is fundamentally governed by a set of simple reaction steps involving interactions between a metal center and its coordinated ligands, such as oxidative addition, reductive elimination, and ligand substitution (or exchange). While two catalysts may broadly follow the same reaction mechanism, subtle differences in ligand interactions can result in significant changes in reactivity. These variations arise because such differences profoundly influence the thermodynamics and kinetics of the process [132]. However, elucidating these effects is far from straightforward and often requires both detailed experimental and computational investigations. It is not uncommon for initial hypotheses regarding the origins of these effects to prove incorrect. The following example illustrates a case where the initially proposed explanation for a catalyst's superior activity turned out to be more nuanced than anticipated.

The difference in activity between the 1st and 2nd generation Grubbs catalytic systems was initially attributed to faster dissociation of the leaving phosphine in the 2nd generation catalyst. This behaviour was thought to result from the stronger *trans*-effect exerted by the NHC ligand. While this explanation regarding the coordination effect is accurate, a deeper understanding of the differences in initiation efficiency emerged from a landmark study by Grubbs in 2001 [133]. In the initial sections of their work, the authors investigated the mechanism of catalyst activation, with a specific focus on phosphine ligand displacement. However, since the activated complex and the coordinative intermediate (CI) of the reacting olefin were incompatible with the spectroscopic techniques available at the time, the authors introduced an exchange rate parameter (k_B) to evaluate the phosphine exchange process (see Fig. 16, supra). The data obtained provided compelling evidence for a dissociative mechanism rather than an associative pathway for both the 1st and 2nd generation systems. [134,135]

Specifically, the exchange rate was observed to be independent of phosphine concentration over a defined range (0.04–0.77 M), and the initiation entropies ($\Delta S^{\ddagger}$) were found to have positive values exceeding 10 au in most cases—both indicative of dissociative processes. Furthermore, an examination of the catalytic reactions of both generations of catalysts with ethyl vinyl ether (EVE) (Fig. 16, infra) revealed that the 1st generation catalyst exhibited a dependence on the concentration of the alkene, while the 2nd generation catalyst showed no such dependence. Notably, phosphine dissociation in the 1st generation catalyst was actually faster once saturation of the olefin was achieved.

These findings led to the proposal of a revised paradigm: the superior efficiency of the 2nd generation catalyst is attributed not to faster phosphine dissociation but to a higher chemoselectivity of the 14-electron species toward alkene binding and metathesis progression, as compared to phosphine re-coordination [136]. For the 2nd generation catalyst, the rate constant for alkene binding was demonstrated to exceed that of phosphine re-coordination (i.e. for L = SIMes, $k_2 > k_{-1}$, see Fig. 16, infra).

Regarding the computational perspective, studies suggest that the dissociative mechanism is kinetically favoured for phosphine-containing Grubbs catalysts, with the rate-determining step identified as phosphine dissociation. [137–143] These computational findings are consistent with the experimental observations discussed earlier. Furthermore, calculations indicate that the Gibbs energy barrier for phosphine dissociation from the Grubbs complex is significantly influenced by both solvent effects and entropy contributions [144].

On the other hand, most 2nd generation Grubbs catalysts currently in use are in the form of the Hoveyda chelated precatalyst (HG), which exhibits distinct initiation behaviour. Spectroscopic investigations conducted by Plenio and co-workers on HG and its derivatives revealed that initiation occurs through a combination of dissociative and interchange pathways, depending on the size of the olefin [145]. The interchange pathway refers to an associative mechanism in which the entering olefin facilitates, in a concerted manner, the opening of the chelate. In both cases, the cleavage of the Ru—O bond is driven by the rotation of the benzylidene dihedral angle. The dominant reaction pathway is determined by the steric and electronic properties of the Ru complex and the olefin involved in the metathesis reaction. [146,147]

With respect to the olefin side, since the interchange pathway is initiated by the binding of the alkene, it is favoured by less bulky and more electron-rich olefins, such as 1-hexene or butyl vinyl ether (BVE). In contrast, for olefins that are less electron-rich or more sterically demanding, such as diethyl-diallyl malonate (DEDAM) and styrene, the dissociative pathway becomes dominant. On the other hand, modifications to the catalyst structure, such as the addition of electron-withdrawing groups to the benzylidene ether, result in an electron-

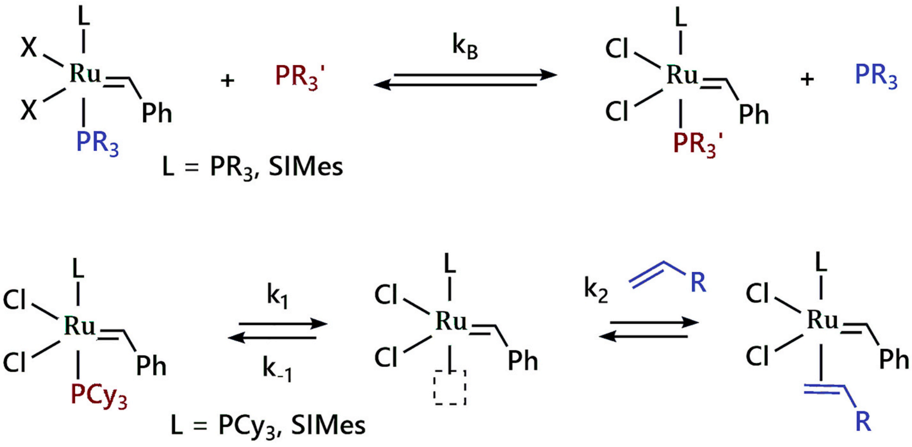


Fig. 16. The diagram shows the phosphine exchange reaction (and associated constant of the process) on the top, and the competition between the phosphine and the alkene in a dissociation mechanism (with the respective constants) on the bottom.

deficient Ru center, which accelerates both activation mechanisms. Additionally, substituting the 2-isopropoxy group with a smaller 2-methoxy group significantly enhances the olefin-dependent interchange mechanism.

Except some discussion of the associative mechanism [145], the optimal scenario is to promote both dissociative and interchange activation pathways, which occurs with olefins possessing high electron density and low steric hindrance. In general, a substantial increase in the rate of pre-catalyst activation is observed when olefin concentrations are elevated [148]. This enhancement is believed to result from an improvement in the interchange pathway.

4.2. Activity of the catalyst

Another challenge associated with Ru-based olefin metathesis catalysts is their relatively low activity, which can limit their range of applications. This reduced activity stems directly from their enhanced stability. However, deactivation side-reactions can exacerbate this issue, often requiring high catalyst loadings to achieve effective catalytic processes. Such requirements can be problematic, particularly in fine chemical applications, where Ru contamination is strictly regulated [29]. The underlying cause of this reduced activity includes the increased strength of the metal-ylidene bond and the lower electrophilicity of the metal center in Grubbs catalysts, compared to the more reactive counterparts in Schrock catalysts.

Moreover, as described in the previous subsection, the catalyst is typically found in its precatalyst form. This inactive state helps prevent undesired degradation during handling but necessitates an activation step, in which the 14-electron active complex must be formed for the catalytic cycle to begin. In olefin metathesis, this pre-catalyst-to-active-catalyst transition usually involves the removal of one of the ligands from the metal center, and it is often the slowest step in the process. As a result, this step ultimately determines the overall activity of the system. Significant efforts have been dedicated to understanding and optimizing this process. [133,137,149–153] One example that highlights the impact of the dissociation step on activity is Piers' ruthenium catalyst (Fig. 17) [154]. This complex is a 14-electron catalyst that does not require ligand loss to initiate catalysis, leading to higher activity, though at the cost of some loss of robustness.

The initiation rate can be influenced by several factors, including the solvent, the concentration of olefin, the temperature, and the presence of additives [155]. With these factors in mind, the focus now shifts to the effects of the organometallic complex structure on activation processes, which can vary significantly even among Ru-based analogues. While this variability necessitates additional efforts to understand each specific case, it also provides an opportunity to tailor the catalyst to achieve desired behaviours. For example, introducing a sulfur donor into an HG-type pre-catalyst enables the development of a family of photo-switchable olefin metathesis systems, offering a high degree of control over olefin metathesis polymerization [156].

To gain a comprehensive understanding of the catalyst initiation process, both experimental and computational tools are typically required, as not all kinetic studies are feasible. On the experimental side, spectroscopic methods, such as hydrogen nuclear magnetic resonance (H-NMR) and UV–vis spectroscopy, have traditionally been employed, often using EVE or BVE as olefins. These alkenes form Fischer carbenes upon initiating the pre-catalyst [157], which, due to their electronic structure, cannot continue the olefin metathesis [133].

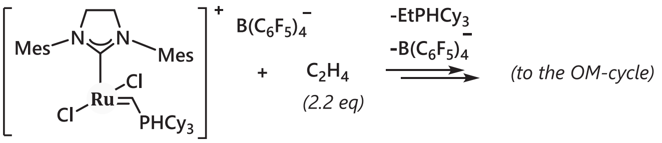


Fig. 17. Initiation step of the Piers catalyst for an olefin metathesis reaction with ethylene.

4.3. Diastereocontrol for Z-alkenes

In the formation of carbon-carbon double bonds during olefin metathesis, mixtures of *E* and *Z* isomers are produced. However, the reversible nature of the reaction typically favours the thermodynamically stable E product. As a result, the *trans*-isomer (*E*) often dominates due to secondary metathesis events. One remarkable exception occurs in the RCM of small cycles, where the ring strain typically favours the formation of only the *Z*-isomer. For internal olefins, the *E*-isomer generally constitutes about 90 % of the product [158].

Since this thermodynamic control arises from the equilibrium between reagents and product, the design of *Z*-selective catalysts must account for the following considerations:

a) *Initial High Z-Selectivity:*

In olefin metathesis catalysts, the product stereoisomerism is typically determined by the orientation of the reacting olefins in the key metallocyclobutane intermediate [159]. Therefore, *Z*-selective catalysts are often designed to ensure that all substituents in the metallocyclobutane adopt a *cis* configuration. This is typically achieved by manipulating the steric constraints around the metal center [160].

b) *Avoiding secondary metathesis:*

Due to the previously mentioned reversibility of the reaction, a kinetic preference toward the *Z*-olefin alone is insufficient. It is crucial that the olefin does not re-enter the catalytic cycle, a process known as secondary metathesis events. If this occurs, the olefin may react with the metal alkylidene, leading to isomerization and the formation of thermodynamic *E*-products. Consequently, the catalyst must be engineered not only to promote the initial formation of *Z*-olefins but also to prevent their re-conversion into *E*-olefins, thereby preserving the stereochemical purity of the product. Factors that tend to induce secondary reactivity, even though they appear positive, such as long reaction times, must be avoided. Thus, achieving a delicate balance between the catalyst's structure and activity is crucial. [161,162]

In the context of Mo and W catalysts, *Z*-selectivity has been successfully achieved through the use of directing groups and large ligands (Fig. 18). These modifications alter the geometry of the coordination sphere, ideally restricting the catalyst to conformations that lead exclusively to the *Z*-product. [163–167] Ru catalysts have also been subjected to similar strategies. However, the use of very large ligands on Ru has presented several drawbacks. This is mainly due to the inherently lower reactivity of Ru catalysts compared to their early-transition metal counterparts, which results in reduced activity in alkene metathesis when large ligands are employed. [154,168–172] Below, we present some of the most significant reported cases of Ru-based *Z*-stereoselective catalysts.

Some of the earlier approaches involved introducing asymmetries into the system. The use of unsymmetrical carbenes, including CAACs, resulted in a lower *Z* content compared to Grubbs and HG catalysts (see Fig. 19). While 2^{nd} generation HG catalysts produced an *E*:*Z* ratio of

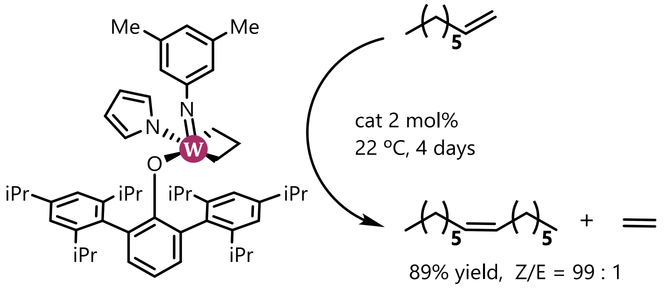


Fig. 18. Example of a highly selective Schrock olefin metathesis for the coupling of terminal olefins.

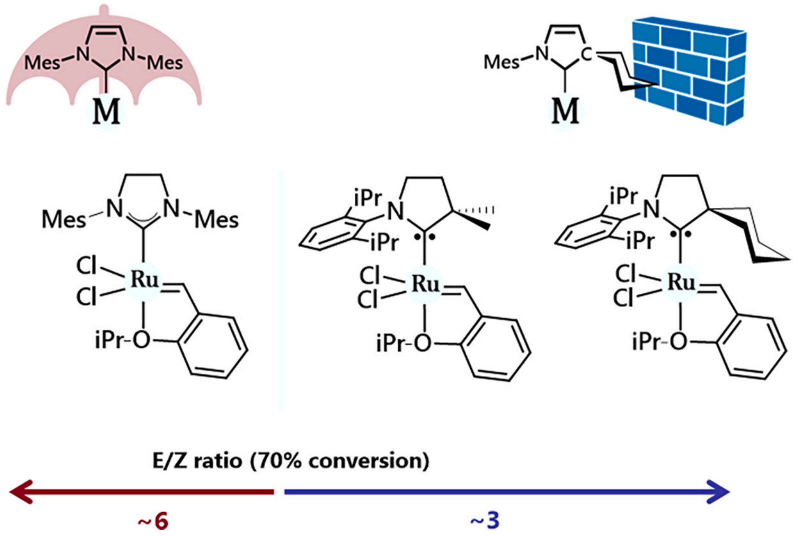


Fig. 19. Comparison of *cis*:*trans* alkene ratio between traditional HG second-generation catalyst and improved catalysis with asymmetric systems.

approximately 6:1, CAACs reduced the *E*:*Z* ratio to below 2.5:1, both at a conversion rate of 70 %. [124,173] Another promising development has been the use of acyclic diaminocarbene ligands as catalysts. These have been shown to enhance the formation of the *Z*-isomer in CM, resulting in an *E*:*Z* ratio of 1:1 at up to 75–80 % conversion (Fig. 20) [174].

Looking at another aspect of Ru catalyst structure, Grubbs made significant modifications by replacing a chloride ligand with a larger mesityl sulfonate anion and substituting an IMes ligand with a bulkier IPr ligand (i.e. 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene). This modification resulted in a catalyst that achieved a significantly lower *E*:*Z* ratio of 2.7 in CM, compared to the homologous bis-chloride complex which exhibited an *E*:*Z* ratio of 6.3. Furthermore, this newer catalyst displayed reduced susceptibility to secondary metathesis reactions, indicating enhanced control over the reaction [175]. Jensen further explored variations of thiolate-based ligands by replacing the isopropyl substituents with mesityl groups (Fig. 21). Similar to Grubbs' catalyst, the performance of Jensen's catalyst was highly dependent on several factors, including the properties of the substrate and the reaction conditions. Notably, catalyst loading and solvent choice were identified as critical parameters influencing the overall reaction efficiency, underlining the importance of optimizing these conditions for maximal catalyst performance. [176,177]

The most notable Ru-based catalysts for *Z*-selectivity were reported by Grubbs. In these catalysts, accidental chelation of the ancillary NHC-ligand facilitated RCM and CM, yielding approximately 90 % of the product as the *Z*-isomer (Fig. 22). The performance of these catalysts was further enhanced by eliminating ethylene gas under tetrahydrofuran (THF) reflux conditions. Further research with chelated ligands focused on replacing the chloride ligands with bulky bidentate ligands (Fig. 23). Catalyst activity was assessed by determining initiation rates through their reaction with butyl vinyl ether (BVE), which undergoes only one catalytic cycle. The most significant difference in computed constants was observed between monodentate and bidentate ligands. While increasing the bulkiness of the ligands resulted in a decrease in the *E*:*Z* ratio, this came at the expense of the catalyst's activity. Additionally, the electronics of the bidentate moiety were found to significantly affect catalyst performance. [133,178,179] Interestingly, non-C–H-activated catalysts did not exhibit such a pronounced effect under identical conditions and ligands. [180–182]

Further experimental observations have shown that, while the chelating bridge plays a key role in achieving *Z*-selectivity, increasing the size of the bridge does not further improve selectivity (Fig. 24, left). Surprisingly, increasing the size of the mesityl group on the non-chelated side of the catalyst resulted in enhanced activity and selectivity (Fig. 24, right). [183,184] Modifications to the backbone of the NHC ligand showed negligible effects on the performance of this

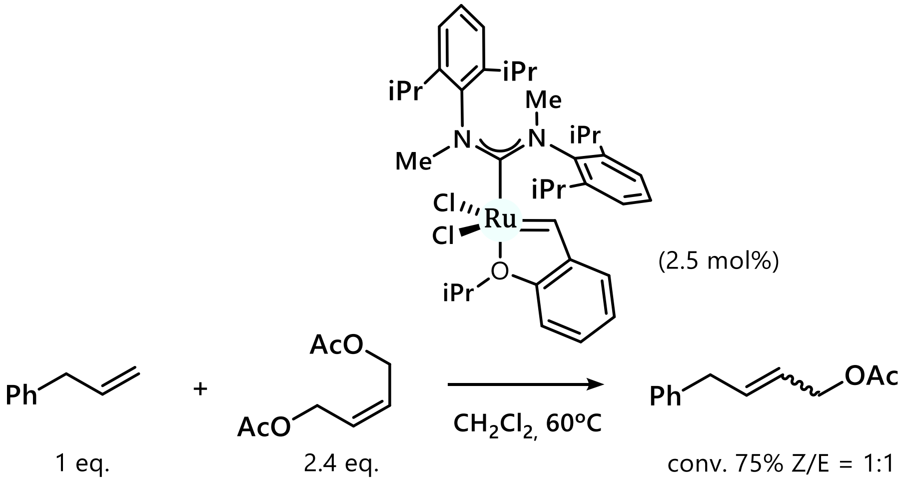


Fig. 20. Ruthenium-acyclic diaminocarbene catalyst in a cross-metathesis example.

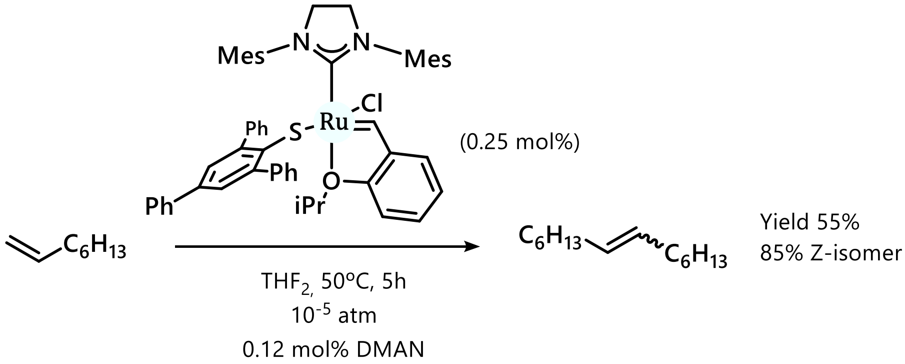


Fig. 21. Selective self-metathesis for 1-octene carried with a ruthenium-thiolate catalyst. In this context, DMAN stands for 1,8-bis(dimethylamino)naphthalene.

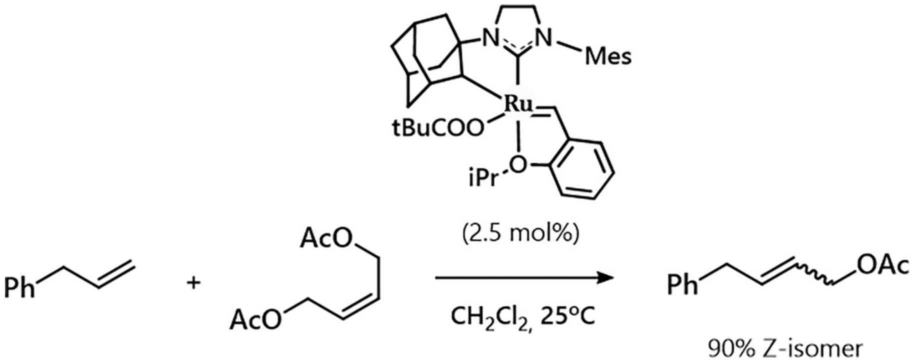


Fig. 22. Cross-metathesis exhibiting high *Z*-selectivity facilitated by a ruthenium adamantyl-based chelate catalyst.

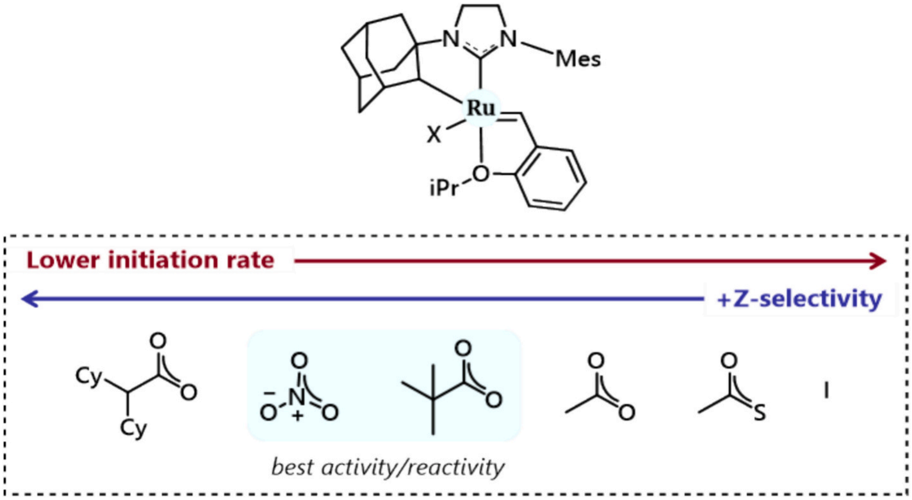


Fig. 23. The initiation rate constants, catalyst effectiveness, and *Z* selectivity are all impacted by the anionic X-ligand. Highlighted the systems with optimal *Z*-selectivity and activity rates.

adamantyl-chelated system [185]. However, it is crucial that the activated carbon within the adamantyl group makes this family of catalysts particularly susceptible to decomposition, which presents a significant challenge to their long-term efficiency (Fig. 25). Although modifications to the chelating moiety had minimal impact on the selectivity and activity of the adamantyl-based chelate catalyst, the introduction of the highlighted aryl substituent significantly enhanced the reaction, achieving near-complete *Z*-selectivity with a Turn-Over Number (TON) of approximately 8000.

4.4. Size selective reaction

Building on previous discussions, CM reactions may offer significant environmental advantages. Actually, metathesis reactions theoretically require fewer co-reagents and generate considerably less waste, aligning well with the principles of green chemistry and enhancing synthetic efficiency. [186–188]

Knowing that CM represents a highly effective strategy for synthesizing complex molecules, achieving selectivity in CM protocols remains a notable challenge, particularly when dealing with specific

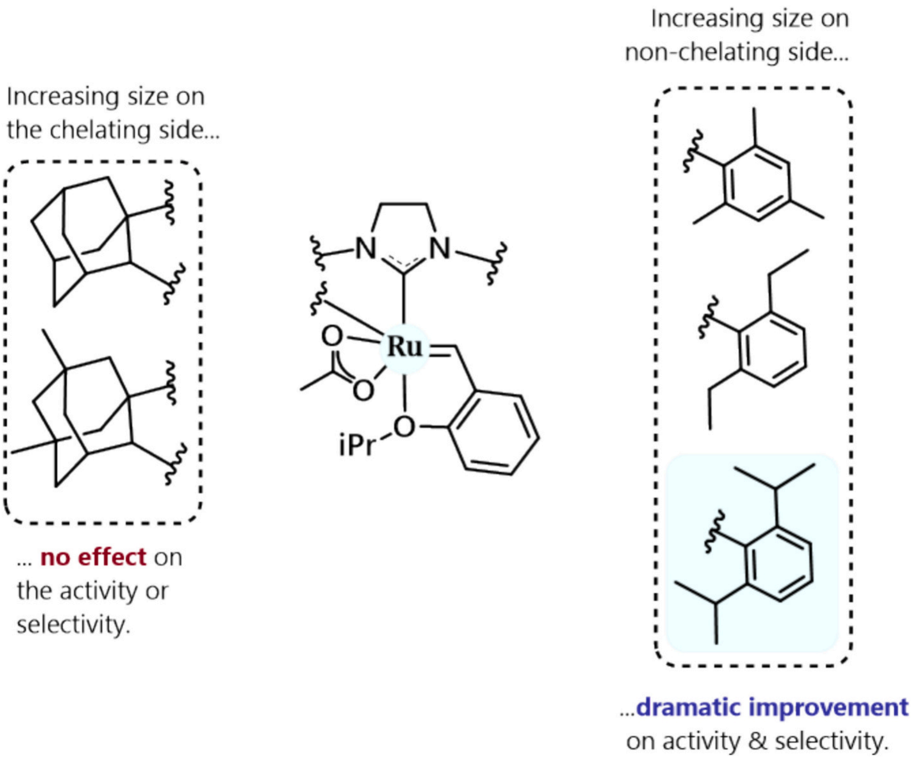


Fig. 24. Effect on selectivity and activity of the substituents on the imidazole ring of the NHC in Hoveyda catalysts, with chelating capacity.

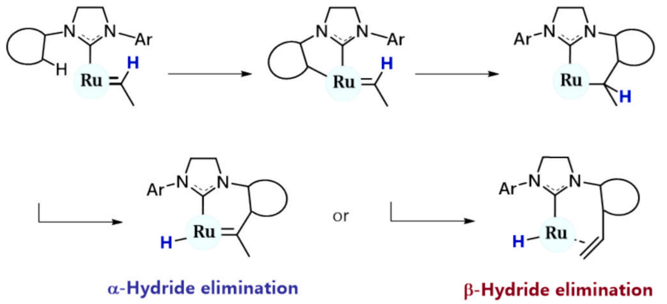


Fig. 25. Main deactivation mechanisms of adamantyl-chelate olefin metathesis catalyst and C—H activated complexes.

combinations of functional groups. This challenge primarily stems from the catalyst's intrinsic preference for one olefin over another, which is often dictated by the electronic richness of the alkene bond. As a result, CM reactions frequently yield predominantly homocoupling products, where terminal olefins couple with themselves. This behaviour was systematically explored in a landmark study by Grubbs and coworkers, who developed a predictive model categorizing alkenes into distinct reactivity groups. This model has provided critical insights into the outcomes of CM reactions [189]. The Grubbs group's work culminated in a comprehensive empirical model for olefin reactivity in CM reactions, designed to predict product preferences, regioselectivity, and chemoselectivity. By classifying olefins based on their tendency to undergo homodimerization and the subsequent reactivity of those homodimers in secondary metathesis reactions, they established a broad ranking of olefin reactivity in CM. This framework allowed researchers to fine-tune product selectivity by choosing olefins with contrasting reactivities, determined by their steric and electronic properties—factors influenced by substituents, functional groups, or protective groups. In essence, the success of a CM reaction hinges on selecting cross-partners with low homodimerization rates and reactive homodimers that can readily participate in secondary metathesis cycles (Table 1). Additionally, the Grubbs group highlighted the critical importance of selecting an appropriate olefin metathesis catalyst to achieve the desired selectivity. This empirical framework has since served as a cornerstone for designing and optimizing selective CM reactions, including more complex multicomponent CM processes.

However, the previously established model does not inherently provide solutions to overcome the limitations it describes. One significant challenge is the lack of chemoselectivity, which often prevents the efficient integration of metathesis into synthetic protocols for many target species.

Historically, various strategies have been employed to address selectivity issues in CM reactions. These include optimizing reaction conditions and employing kinetic control to favour the desired cross-coupling products over homocoupling. Adjusting parameters such as solvent polarity and temperature has also proven effective in influencing reaction kinetics and improving selectivity. In some cases, substrate selection or reversible modification has been used to facilitate the desired CM reactions, aligning more effectively with the Grubbs Model. Nonetheless, while post-reaction treatments can resolve selectivity challenges, they often require additional purification steps, which increase time and resource demands. In practice, a combination of these approaches is often necessary to optimize both selectivity and efficiency in CM reactions. [190–192] Despite these concerns on Grubbs catalysts, they are ideal for certain applications. [188,193] In detail, in organic synthesis, Grubbs catalysts enable the formation of complex molecules through selective alkene functionalization. They are widely used to synthesize fine chemicals, pharmaceuticals, and natural product derivatives, often simplifying multi-step synthetic routes. The compatibility of Grubbs catalysts with polar functional groups, such as esters, amides, and alcohols, enhances their versatility in CM reactions. On the other hand, in materials science, they facilitate the preparation of functionalized polymers and specialty materials by incorporating targeted olefinic units into macromolecular backbones.

An additional and highly effective strategy to enhance selectivity involves modifying the catalyst itself [194]. This typically focuses on

Table 1
Types of olefins within Grubbs empirical model classification.

		1^{st} gen Grubbs	2^{nd} gen Grubbs
↑ REACTIVITY	**Type I** /fast homodimerization/ Homo dimers still reacting	terminal olefins, allyl silanes, allylic alcohols, ethers, esters, allyl boronated esters, allyl halides	terminal olefins, allylic alcohols, esters, allyl boronated esters, allyl halides, styrenes (no large ortho substituent) allyl phosphonates, allyl silanes, allyl phosphine oxides, allyl sulphides, protected allyl amines
	Type II /slow homodimerization/ Homodimers hardly reacting	styrene, 2° allylic alcohols, vinyl dioxolanes, vinyl boronates	styrenes (large ortho substituent), acrylates, acrylamides, acrylic acid, acrolein, vinyl ketones, unprotected 3° allylic alcohols, vinyl epoxides, 2° allylic alcohols, perfluorinated alkane olefins
	Type III /no homodimerization/	vinyl siloxanes	1,1-disubstituted olefins, vinyl phosphonates, non-bulky trisubstituted olefins, phenyl vinyl sulfone, 4° allylic carbons (every alkyl substituents), 3° allylic alcohols (protected)
Reaction between 2 Type I olefins			→ Statistical CM
Reaction between 2 olefins of the same type (non-Type I)			→ Non-selective CM
Reaction between olefins of different types			→ Selective CM

tailoring the ligand structure to improve selectivity for the desired products. Interestingly, these modifications do not always target the metal center directly but often involve adjustments to the second coordination sphere of the complex [195].

A novel approach to catalyst modification proposed by Diver leveraged size recognition of alkenes to direct CM selectivity [196]. Diver's insight was inspired by the observation that alkenes within the same type can exhibit notable size differences. This led to the development of a size-selective catalyst capable of distinguishing between alkenes based on their bulk. By confining the space around the active site, the catalyst restricted its activity toward bulkier olefins (Scheme 1). This configuration allowed selective homodimerization of smaller alkenes, operating reversibly alongside productive coupling. Notably, the persistent reactivity of Type 1 homodimers was anticipated to enable their continuous consumption, thereby generating active metal carbenes that facilitate CM product formation. This innovative approach exemplifies how catalyst design can overcome key limitations in CM selectivity, paving the way for broader applications.

In 2019, Diver and co-workers published a related study involving a macrocyclic azolium salt capable of forming carbene-based catalysts upon coordination with Ru, to improve the selectivity of metathesis. This system demonstrated utility in reactions such as enyne metathesis and palladium-catalyzed processes, including cross-coupling and Buchwald-Hartwig amination (Fig. 26) [197].

Later, in 2020, the same research team achieved a significant milestone with the synthesis of a macrocyclic ruthenium carbene catalyst [196], specifically engineered for precise cross-alkene metathesis (Fig. 27). This catalyst demonstrated varying reactivity with different type 1 alkenes during homodimerization, a behaviour linked to the aggregate size of the allylic substituents. This distinct reactivity profile allowed for selective product formation in competitive cross-alkene metathesis reactions involving two distinct type 1 alkenes and tert-butyl acrylate.

The observed selectivity was attributed to the macrocyclic catalyst's ability to discriminate between alkenes based on their size, showcasing its potential for controlled and targeted transformations. Despite the success in introducing selective reactivity, the study also reported low TONs, highlighting a limitation that may need to be addressed for broader practical applications.

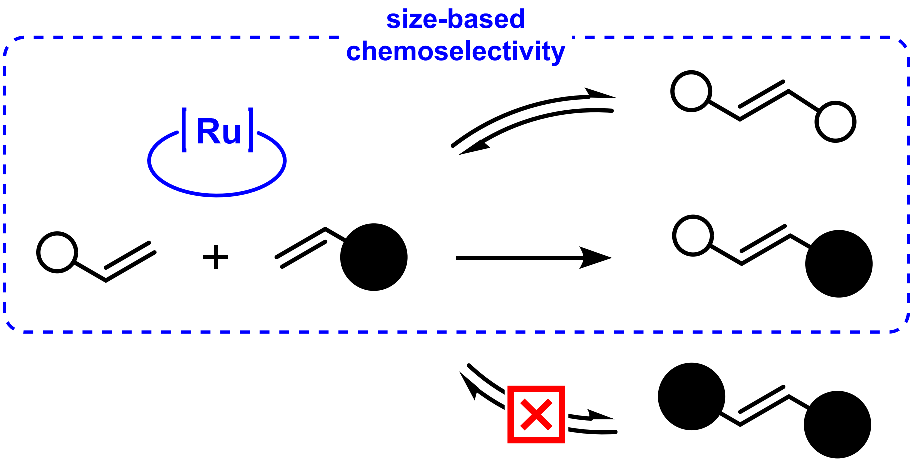
The introduction of bridges between the two ends of a heterocyclic carbene, while relatively uncommon, is not unprecedented. Several studies have explored the synthesis and application of macrocyclic ligands containing heterocyclic motifs such as imidazolium, azolium, and NHC groups. These ligands have been investigated for their potential in diverse fields, including coordination chemistry, anion recognition, and catalysis. Research on their synthesis, characterization, and coordination chemistry has often focused on the unique structural features of these ligands and their influence on the properties of transition metal complexes. [198–205]

4.5. *Stereo-retention in metathesis reactions*

As previously noted, the thermodynamic equilibrium of olefin metathesis reactions typically exerts a strong influence on *trans*-olefin formation. In RCM, however, the strain inherent in small cyclic products often prevents the formation of *E*-isomers, leading to high selectivity for less twisted macrocyclic moieties. *E*-selectivity generally re-emerges for larger rings, such as those with 12 or more members (Fig. 28). [206–208]

This trend holds true for classical Grubbs catalysts (1^{st} and 2^{nd} generation), although the reaction outcome can vary significantly based on factors such as the [catalyst:substrate] ratio, solvent, cofactors, and, most critically, the catalyst system employed [193].

A significant proportion of medium- and large-sized macrocycles have the potential to exhibit biological activity. In biological applications, stereoselectivity becomes an unavoidable factor due to the inherent complexity of biochemical structures and the intrinsic asymmetry of molecular receptors and targets. Historical examples in drug development underscore the risks of disregarding isomerism, from the infamous thalidomide tragedy to the more recent controversies surrounding resveratrol [209]. Furthermore, even in less critical applications, such as the development of pheromones or fragrances, the selectivity of unsaturated carbon bonds is essential to achieving the desired outcomes (see Fig. 29). In industrial processes, many of these products are synthesized using reactive distillation—a powerful technique that combines chemical reaction and distillation in a single step, improving efficiency and reducing costs. This approach is particularly significant in high-temperature processes, such as those used for the



Scheme 1. Schematic representation of cross-metathesis with chemoselectivity based on the size of the alkene substituents.

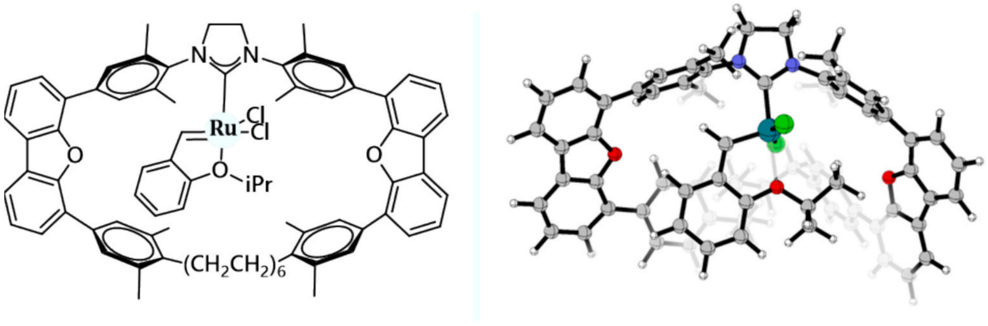


Fig. 26. Macrocyclic N-Heterocyclic Carbene presented by Davalos, Sylvester, and Diver [197].

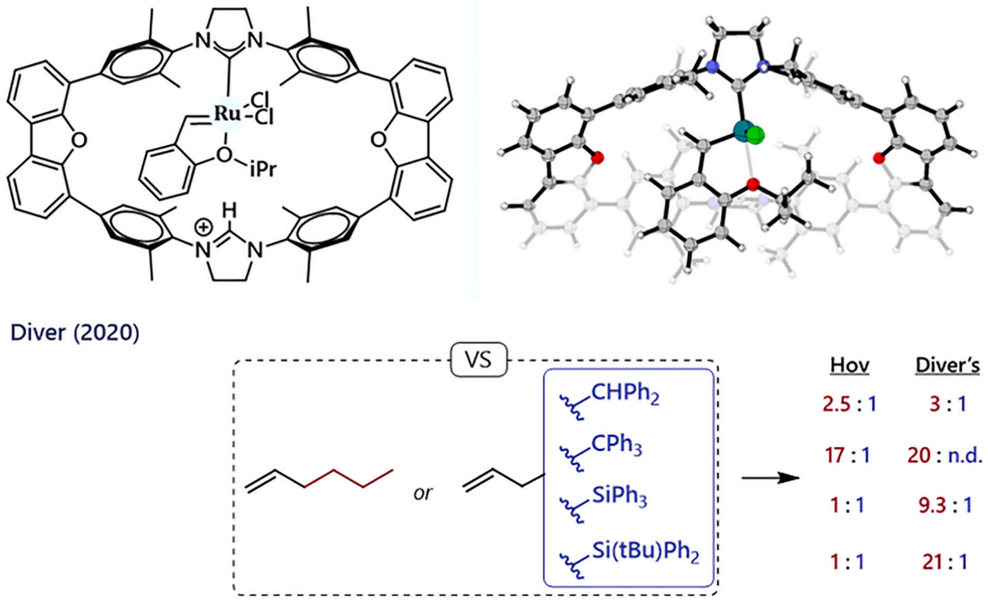
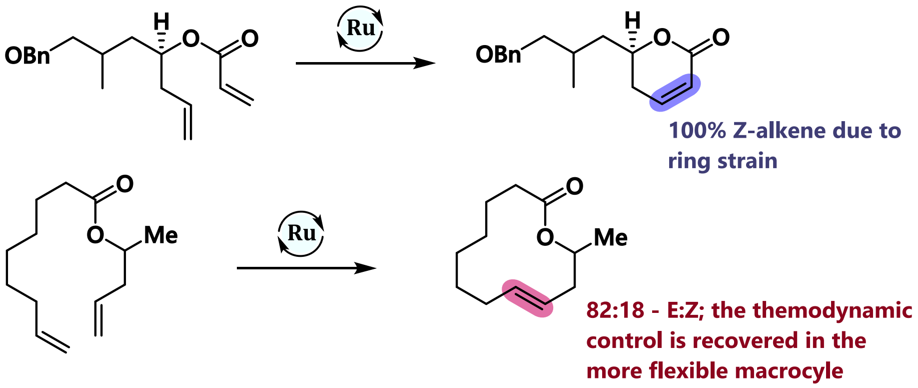


Fig. 27. Macrocyclic ruthenium carbene for size-selective alkene metathesis presented by Zhang and Diver in 2020. Below, reported selectivity on competitive coupling reactions with tert-butyl acrylate.

production of macrocyclic musks. Unfortunately, at elevated operational temperatures, Mo, W, and Ru *Z*-selective catalysts tend to lose their selectivity or undergo decomposition. It is reasonable to assume that these deactivation pathways are exacerbated under high-temperature conditions, thereby limiting the synthetic utility of these catalysts. [210,211]

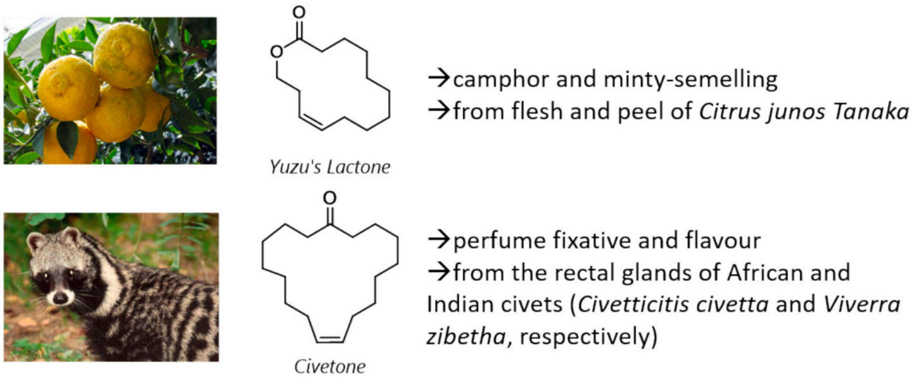
To address these challenges, the research team led by Kajetanowicz and Grela developed a novel catalyst capable of producing *Z*-alkenes with high selectivity, even under the extreme conditions described above [212]. Their investigations led to the design of an innovative



100% Z-alkene due to ring strain

82:18 - E:Z; the themodynamic control is recovered in the more flexible macrocyle

Fig. 28. Differences on stereoselectivity outcome depending on cycle size.



→camphor and minty-semelling
→from flesh and peel of *Citrus junos Tanaka*

→perfume fixative and flavour
→from the rectal glands of African and Indian civets (*Civetticitis civetta* and *Viverra zibetha*, respectively)

Fig. 29. Examples of bio-based macrocycles whose properties and applications depend on the *Z*-isomerism of their structures.

dithiolane-based ligand, thioquinoxaline. This ligand is stabilized by resonance, enabling the catalyst to maintain high *Z*-selectivity at temperatures as high as 150 °C in dense mixtures. Remarkably, this thioquinoxaline-based complex not only performs well under harsh conditions but also retains activity comparable to that of existing stereoretentive catalysts under standard reaction conditions.

The experimental work of Kajetanowicz and Grela focused on improving a catalyst for the synthesis of *Z*-configured macrocyclic musks, which are highly prized in the fragrance and food industries (see Fig. 29). The employed catalyst is a *Z*-stereoretentive type, meaning it preserves the *Z*-configuration of at least one of the starting alkenes throughout the reaction. Conceptually, it is important to note that the stereoretentive approach requires one of the coupling partners to be an internal olefin with *Z*-isomerism (see Fig. 30). This condition is attributed to the fact that the system enforces the retention of the starting alkene's configuration, rather than directly inducing *Z*-olefin formation [213].

Previous studies achieved notable success in replacing the traditional chloride ligands in olefin metathesis catalysts with dithiolate-chelate ligands (Fig. 31). This substitution caused a shift in the bonding mode of the reacting alkenes, moving from the typical bottom-bound configuration to a side-bound arrangement [214]. According to the prevailing model, this configuration reduces the mobility of alkene substituents during the catalytic cycle, effectively constraining them to remain on the same side, opposite the NHC moiety. While steric effects are believed to play a dominant role, some reports suggest that electronic factors may also contribute to this behaviour. [176,215]

Although the side-bound orientation might seem unconventional, it

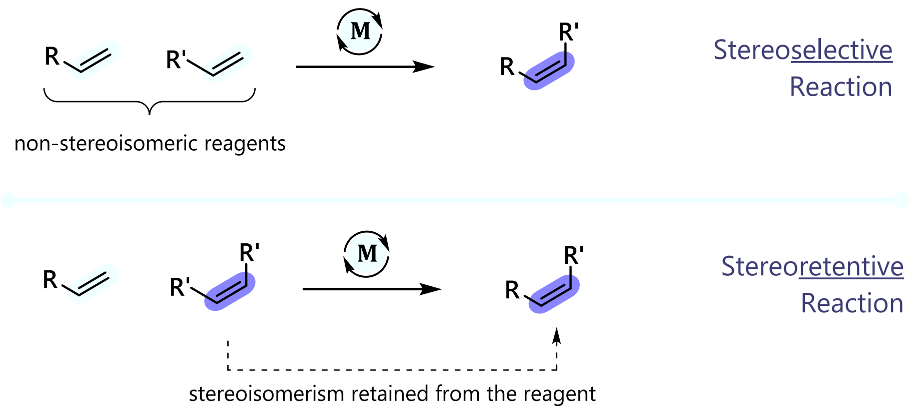


Fig. 30. Conceptual comparison on the differences between stereoselective and stereoretentive on cross-metathesis.

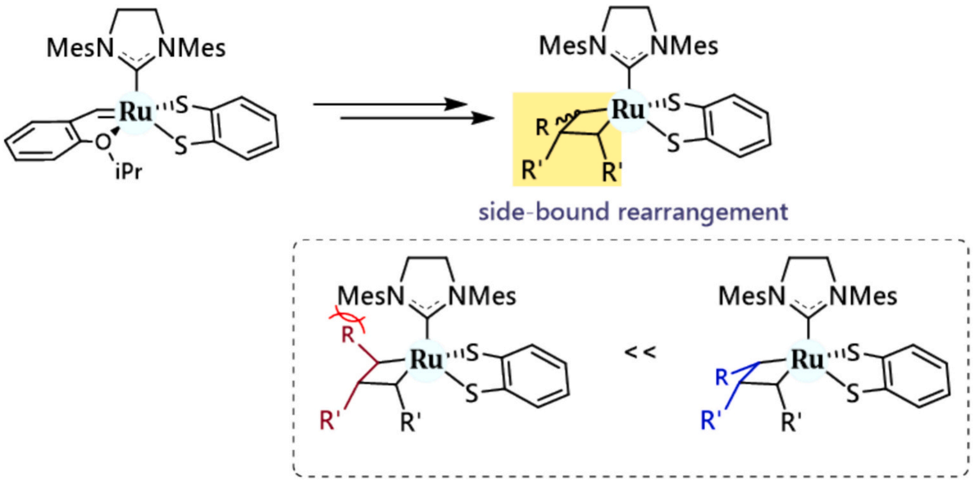


Fig. 31. Dithiolate-chelate catalyst for stereoretentive olefin metathesis.

is not uncommon, even in traditional dichloride olefin metathesis catalysts. Several studies have demonstrated that solvent and electronic factors significantly influence the configuration of chlorides in 2nd generation catalysts. For instance, Cavallo's calculations revealed that, while the bottom-bound olefin complex is more stable by 3 kcal/mol in the gas phase, the side-bound complex becomes more stable by the same energy margin in CH_2Cl_2 due to differences in dipole interactions. In terms of reactivity, however, the bottom-bound complex was favoured for metallacyclobutane formation, with energy differences of 11 and 4 kcal/mol in the gas and solution phases, respectively. Thus, despite the higher stability of the side-bound configuration in solution, olefin metathesis reactivity predominantly occurs via the bottom-bound *trans*-dichloride conformation, especially when steric effects are amplified by alkene substituents [216].

A notable limitation of the bis(sulfur)-based catalysts is their susceptibility to deactivation via an additional pathway (Fig. 32). This arises from the proximity of the sulfur anion, a potent nucleophile, to the unsaturated ylidene carbon [215]. Although this deactivation mechanism does not completely inactivate the catalyst, it reduces its activity and compromises *Z*-selectivity.

The issue of catalyst deactivation remains a persistent challenge in catalysis, often stemming from catalyst aggregation or poisoning of the active sites. In thiocatechol-based systems for olefin metathesis catalysts, a common strategy to mitigate this involves reducing the nucleophilicity of the sulfur atoms. By diminishing the sulfur atom's electron-donating ability—effectively making it a "softer" nucleophile—the likelihood of undesired reactions is minimized (Fig. 32). This strategy has been validated through experimental and computational studies, showing improvements in both conversion and *Z*-selectivity.

A pioneering approach by Hoveyda introduced a 3,6-dichloro substitution on the benzene-1,2-dithiolate ligand (Fig. 33, thio-2) [215]. This modification enhanced catalyst stability, increased functional group tolerance, and improved robustness—marking a significant advance over traditional Mo- and W-based *Z*-selective systems. Furthermore, these modified catalysts demonstrated superior performance in CM reactions, particularly with readily available disubstituted alkene feedstocks such as oleic acid, minimizing undesired substrate self-metathesis. The authors attributed these improvements to the electron-withdrawing effects of the 3,6-dichloro substitutions, which enabled enhanced catalytic protocols beyond *Z*-selective synthesis. [217,218]

Building on these findings, researchers in Tianjin and Beijing

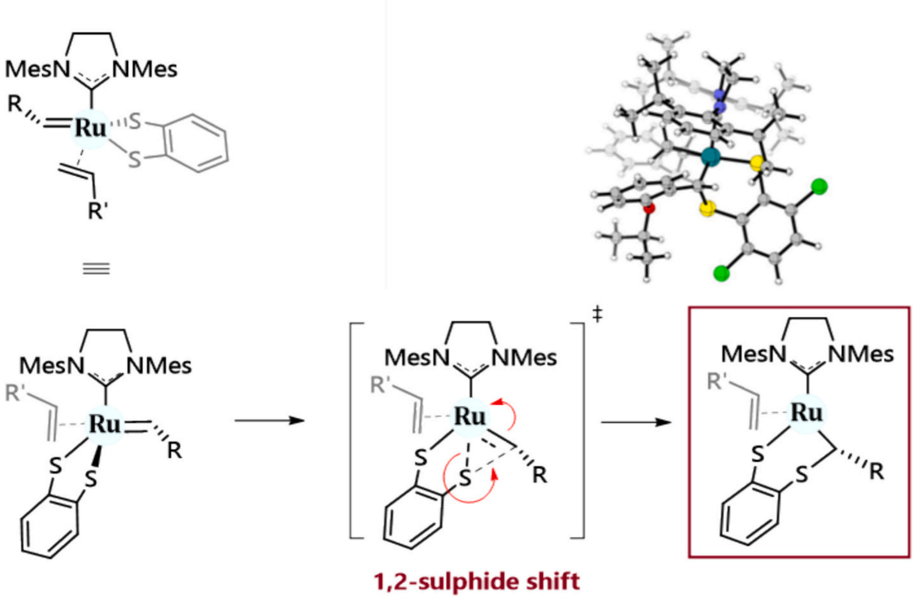


Fig. 32. Mechanism of sulfur nucleophilic attack on the ylidene carbon as a proposed deactivation pathway.

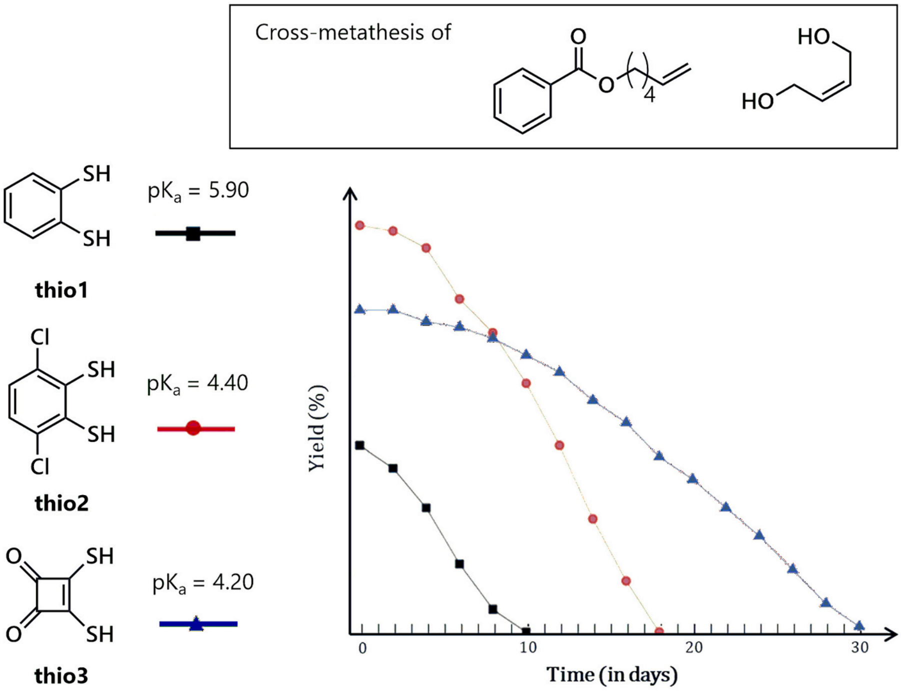


Fig. 33. Enhanced stability of the thio-3 system (adapted from Reference 215).

proposed an alternative system using a 3,4-dimercapto-3-cyclobutene-1,2-dione-chelated ligand (thio-3) [219]. This novel chelate was hypothesized to outperform previous systems due to the increased Brønsted acidity of the sulfur atoms in the ligands (Fig. 33). The relative stability of these complexes was evaluated by tracking their decomposition rates over time. Stored at room temperature without nitrogen protection, the catalysts were tested in the CM reaction of hex-5-en-1-yl benzoate with (*Z*)-but-2-ene-1,4-diol. While the other catalysts (thio-1 and thio-2) lost completely the activity after 10 and 18 days, respectively, the thio-3-based catalyst retained 31 % product yield and remained active for up to 30 days. Importantly, no changes in stereoselectivity were observed, with *Z*-stereoretention consistently maintained throughout the study. These findings strongly support the approach proposed by Hoveyda. Interestingly, despite discrepancies in decomposition-activity experiments, DFT calculations revealed no significant differences in the associated energy profiles.

Another notable advancement involved the introduction of naphthalene-based ligands, designed to reduce the spatial distance between sulfur atoms. These modifications altered the coordination angles at the metal center, yielding results comparable to those achieved with the thio-2 system [220]. Subsequently, higher catalytic activity was reported when four chloride atoms were incorporated at positions 2, 4, 5, and 7 of 1,8-dimercaptonaphthalene [221]. This further validated the hypothesis that increasing the electron-withdrawing character of the ligands enhances catalytic performance.

5. Perspective: challenges and unsolved issues in olefin metathesis

As it has been reviewed in this manuscript, olefin metathesis is as a highly versatile and transformative reaction in synthetic chemistry, with broad applications in organic synthesis and polymer science. Despite its immense success and widespread utility, olefin metathesis continues to face numerous challenges and unresolved issues. These limitations stem from the complexity of the reaction mechanism, the diversity of substrates, and the inherent constraints of the catalysts themselves. This discussion till now outlined the major challenges and concerns in olefin metathesis, focusing on catalytic efficiency, selectivity, environmental impact, and industrial scalability. We must do a step forward toward predictive catalysis, [222,223] from the past insights. [224,225] Probably the efforts on iron based catalysts will not be the solution, [226–228] despite the last seminal insights, [229,230] and maybe the use of catalysts soluble and active in water could be the solution, and/or in air [231]. In detail, iron and manganese olefin metathesis catalysts have gained attention as earth-abundant and environmentally friendly alternatives to traditional Ru-, Mo-, and W-based catalysts [227]. However, their practical applications remain limited due to several inherent weaknesses [232], primarily related to stability, reactivity, and selectivity [226]. One of the major challenges with iron and manganese catalysts is their susceptibility to rapid decomposition. Unlike Ru-based systems, which benefit from robust ligand frameworks and oxidation-resistant properties, iron and manganese catalysts readily undergo oxidation, leading to the formation of catalytically inactive species. This instability is particularly problematic under air or moisture exposure, necessitating strict handling conditions. Additionally, these catalysts often exhibit limited functional group tolerance. Iron and manganese-based systems are more prone to undesired side reactions such as hydrogenation, homocoupling, and radical-induced decomposition. These side reactions not only reduce catalytic efficiency but also complicate the control of reaction selectivity. Another significant drawback is their relatively low efficiency in key metathesis reactions. While some advancements have been made in ligand design to enhance their performance, iron and manganese catalysts still struggle to match the high turnover frequencies (TOFs) and turnover numbers (TONs) of their Ru and Mo counterparts. Their limited substrate scope further restricts their utility in industrial and synthetic applications. Efforts to improve these catalysts focus on ligand tuning, stabilization strategies, and exploring synergistic effects with co-catalysts. Despite these efforts, overcoming their inherent weaknesses remains a major challenge. Until these issues are addressed, iron and manganese catalysts will likely remain niche alternatives rather than mainstream replacements for more established metathesis systems.

The ongoing challenges of olefin metathesis are the following:

1. Catalyst stability

Catalyst stability remains a critical issue in olefin metathesis, particularly for processes requiring prolonged reaction times or elevated temperatures. Many commonly used catalysts, such as those based on Ru (e.g., Grubbs catalysts), Mo, or W, suffer from thermal degradation or decomposition under harsh conditions. For example, the 2nd generation Grubbs catalyst, while more stable than its predecessors, can still degrade in the presence of oxygen, moisture, or acidic byproducts formed during the reaction.

This instability limits the broader applicability of metathesis in industrial processes, where reaction conditions are often challenging and need to be cost-effective. Furthermore, the reactivation of degraded catalysts is not yet feasible, leading to inefficiencies and increased costs. Research efforts are ongoing to design catalysts with improved robustness, such as those incorporating ligand frameworks that stabilize the active species. However, achieving a balance between stability and catalytic activity remains a significant challenge.

2. Functional group tolerance

Although modern metathesis catalysts exhibit high functional group tolerance, certain functional groups still pose challenges, particularly in the presence of protic or highly electron-withdrawing species. For instance, alcohols, amines, nitriles, and carboxylic acids can deactivate metathesis catalysts through ligand exchange or coordination to the metal center. This sensitivity restricts the scope of substrates that can be efficiently employed in metathesis reactions, particularly in complex molecule synthesis where multiple functional groups are present.

Efforts to address this limitation have focused on developing catalysts with enhanced functional group tolerance, such as those incorporating NHC ligands. While these catalysts have broadened the range of compatible substrates, challenges persist, especially when dealing with unprotected functionalities or highly functionalized molecules. Future advancements in this area will require a deeper understanding of catalyst-substrate interactions and the development of novel ligand architectures.

3. Catalyst recycling and environmental impact

The recycling of olefin metathesis catalysts is a critical issue from both economic and environmental perspectives. Most current metathesis catalysts, particularly those based on precious metals like Ru, are expensive and generate waste upon disposal. The pharmaceutical and fine chemical industries are especially sensitive to this issue due to stringent regulatory limits on metal contamination in final products.

Although strategies for catalyst recycling have been explored, such as immobilizing catalysts on solid supports or designing recoverable catalyst systems, these approaches often lead to reduced activity or selectivity. Additionally, the development of heterogeneous metathesis catalysts, while promising, has yet to achieve the same level of efficiency and versatility as their homogeneous counterparts. Addressing these challenges will require innovative approaches to catalyst design and recovery [233], as well as the development of greener alternatives to current metathesis systems. Recovering at least the Ru metal should be a must in industrial applications [188].

On the other hand, the environmental impact of olefin metathesis is a growing concern, particularly in the context of green chemistry principles. While metathesis reactions are often considered environmentally friendly due to their atom economy, the reliance on precious metal catalysts and the generation of toxic by-products remain significant issues. Using low level catalyst loading and metal recovery could minimize this risk. Moreover, the energy-intensive nature of some metathesis processes, such as those requiring high temperatures or pressures, can offset their environmental benefits. Ideally, most organometallic reactions involved in olefin metathesis occur under relatively mild conditions, typically at temperatures below 100 °C, and often even lower, around 50 °C. Additionally, when applicable, such as in ethenolysis [234], these reactions generally proceed under pressures of 10 bar or less. However, defining the precise threshold for what constitutes "mild conditions" remains an open and somewhat subjective question in catalysis. The challenge lies in establishing a universal benchmark, as different reactions and catalyst systems may have varying tolerances and requirements. In addition, in the specific case of olefin metathesis, the lower temperature range, around 50 °C [235], could be considered a reasonable boundary for mild conditions, and specially Ru catalysts with CAAC ligands can achieve better than with NHCs, [236–238] and apart from working in open air [237,239], they have the capacity to bond to Mo, as well [240]. Moreover, another crucial aspect to consider is the solvent choice. While many metathesis reactions are typically conducted in organic solvents, performing them in water presents an unusual but noteworthy exception. The ability to conduct metathesis in aqueous media not only expands the scope of the reaction but also aligns with the principles of green chemistry, promoting sustainability and reducing the environmental impact of the process [231].

To address these concerns, researchers are exploring the use of more sustainable catalysts, such as those based on earth-abundant metals like iron or cobalt. While progress has been made in developing these catalysts, their performance still lags behind that of traditional Ru-based systems. Additionally, the development of solvent-free or aqueous-phase metathesis reactions represents an important area of research for improving the environmental profile of metathesis processes.

4. Selectivity and control

Achieving precise control over product selectivity is a persistent challenge in olefin metathesis, [241–243] particularly for reactions involving multiple possible products, such as CM. Factors such as steric and electronic effects, catalyst molecular geometry, and reaction conditions can significantly influence the outcome of metathesis reactions, often leading to undesired byproducts or low yields of the target compound.

For example, in CM reactions, controlling selectivity between homodimerization and cross-product formation is notoriously difficult. Similarly, in RCM, the formation of different isomers (e.g., *cis/trans*) can complicate product isolation and purification. Advances in ligand design and catalyst engineering have improved selectivity to some extent, but achieving complete control over product distribution remains a formidable task, particularly in complex or highly functionalized systems.

5. Industrial scalability and cost

While olefin metathesis has found widespread application in laboratory-scale synthesis, its adoption in industrial processes is hindered by several factors, including the high cost of catalysts, limited substrate availability, and challenges associated with reaction scalability. For instance, the use of Ru-based catalysts, which dominate the field, is economically prohibitive for large-scale applications due to the high cost of Ru and the low natural abundance of the metal.

Furthermore, the scalability of metathesis reactions often requires significant modifications to reaction conditions, such as solvent choice, temperature, and pressure. These changes can adversely affect catalyst performance and product yield, making the transition from laboratory to industrial scale challenging. Efforts to develop cost-effective and scalable metathesis processes will require a combination of catalyst innovation, process optimization, and advances in reactor design.

6. Substrate scope and reactivity

The reactivity of olefin metathesis catalysts is highly dependent on the electronic and steric properties of the substrates, which can limit the scope of compatible starting materials. For example, substrates with highly strained or sterically hindered double bonds often exhibit low reactivity or require specialized catalysts. Additionally, substrates with electron-rich or electron-deficient olefins can pose challenges due to unfavorable interactions with the catalyst.

Expanding the substrate scope of olefin metathesis will require the development of catalysts that can accommodate a broader range of olefin conformations and electronic properties. This may involve the design of catalysts with tuneable ligand environments or the incorporation of cooperative effects, such as bimetallic or metal-ligand cooperativity.

7. Mechanistic understanding

Despite significant advances in the understanding of olefin metathesis mechanisms, many aspects of the reaction remain poorly understood. For instance, the factors governing catalyst activation, deactivation, and product distribution are not yet fully elucidated. Additionally, the role of secondary interactions, such as non-covalent interactions in the catalyst, [244,245] and between the catalyst and substrate, in influencing reaction outcomes is an area of active investigation [246]. These non-covalent interactions as well as entropy adjustments could lead to enhance the performance in latent olefin metathesis catalysis.

Improving mechanistic understanding will be crucial for addressing the challenges outlined above and for the rational design of next-generation catalysts. Advances in computational chemistry and in-situ spectroscopic techniques have provided valuable insights into metathesis mechanisms, [172,247,248] but further work is needed to bridge the gap between theoretical predictions and experimental observations that will lead to assist artificial intelligence [224,225], feeding with big data, as well.

8. Integration with other reactions

The integration of olefin metathesis with other catalytic transformations, such as hydrogenation, oxidation, or C—H activation, presents an exciting opportunity for streamlining synthetic processes. However, achieving seamless integration is challenging due to the incompatibility of metathesis catalysts with the conditions required for many other reactions. For example, the sensitivity of metathesis catalysts to oxygen and moisture often precludes their use in tandem with oxidative transformations.

Developing metathesis catalysts that can operate under a broader range of conditions or designing dual-function catalysts capable of performing multiple transformations will be critical for realizing the full potential of metathesis in integrated synthetic strategies.

In conclusion, Ru catalysts are generally more stable in air and tolerate a broader range of functional groups, whereas Mo and W catalysts are more reactive but highly sensitive to air and moisture. However, while olefin metathesis has revolutionized modern synthetic chemistry, numerous challenges and concerns remain unresolved. Addressing these issues will require a multidisciplinary approach, combining advances in catalyst design, mechanistic understanding, and process optimization. By overcoming these limitations, olefin metathesis has the potential to become an even more powerful and sustainable tool for chemical synthesis, paving the way for new applications in pharmaceuticals, materials science, and beyond.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

A.P. is a Serra Húnter Fellow and received ICREA Academia Prize 2019. A.P. thanks the Spanish Ministerio de Ciencia e Innovación for project PID2021-127423NB-I00 and the Generalitat de Catalunya for project 2021SGR623. The FWO is gratefully acknowledged for support of this work. J.P.M. acknowledges financial support from the Polish National Science CenterPolish National Science Center through the SONATA-19 grant UMO-2023/51/D/ST4/01561.

Data availability

No data was used for the research described in the article.

References

[1] L.G. Wade, Organic Chemistry, Books a La Carte Edition, Pearson, 2016.
[2] *Shriver & Atkins' Inorganic Chemistry*, 5th ed.; P. W. Atkins, Ed.; Oxford University Press: Oxford; New York, 2010.
[3] M. Akiba, Vulcanization and crosslinking in elastomers, Prog. Polym. Sci. 22 (1997) 475–521, https://doi.org/10.1016/S0079-6700(96)00015-9.
[4] A. Kumar, R.J. Dhanorkar, S. Mohanty, V.K. Gupta, Advances in recycling of waste vulcanized rubber products *via* different sustainable approaches, Mater. Adv. 5 (2024) 7584–7600, https://doi.org/10.1039/D4MA00379A.
[5] S. Murata, M. Suzuki, R. Noyori, Trimethylsilyl Trifltate catalyzed aldol-type reaction of enol silyl ethers and Acetals or related compounds, Tetrahedron 44 (1988) 4259–4275, https://doi.org/10.1016/S0040-4020(01)86671-0.
[6] *Green Chemistry and Chemical Engineering*; B. Han, T. Wu, Eds.; Springer New York: New York, NY, 2019. doi:https://doi.org/10.1007/978-1-4939-9060-3.
[7] T. Mizoroki, K. Mori, A. Ozaki, Arylation of olefin with aryl iodide catalyzed by palladium, Bull. Chem. Soc. Jpn. 44 (1971) 581, https://doi.org/10.1246/bcsj.44.581.
[8] R.F. Heck, J.P. Nolley, Direct proton and fluorine-19 nuclear magnetic resonance study of boron trifluoride complexes with acetylacetone, methoxyacetonitrile, methoxypropionitrile, methylacetoacetate, methylmethoxyacetate, methoxymethylacetate, 2-methoxyethylacetate, and methylpyruvate, J. Org. Chem. 37 (1972) 2320–2322, https://doi.org/10.1021/jo00979a006.
[9] Carbon-Chain Homologations. In *Name Reactions for Homologations, Part I*; J. J. Li, Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2009; pp 335–612. doi:https://doi.org/10.1002/9780470487020.ch2.
[10] M. Julia, J.-M. Paris, Syntheses a l'aide de Sulfones v(+)- Methode de Synthese Generale de Doubles Liaisons, Tetrahedron Lett. 14 (1973) 4833–4836, https://doi.org/10.1016/S0040-4039(01)87348-2.
[11] D.J. Peterson, Carbonyl olefination reaction using silyl-substituted organometallic compounds, J. Org. Chem. 33 (1968) 780–784, https://doi.org/10.1021/jo01266a061.
[12] G. Wittig, U. Schöllkopf, Über Triphenyl-phosphin-methylene Als Olefinbildende Reagenzien (I), Mitteil. Chem. Ber. 87 (1954) 1318–1330, https://doi.org/10.1002/cber.19540870919.
[13] G. Sakaine, Z. Leitis, R. Ločmele, G. Smits, Julia-Kocienski olefination: a tutorial review, Eur. J. Org. Chem. 26 (2023) e202201217, https://doi.org/10.1002/ejoc.202201217.
[14] J. Pospíšil, T. Pospíšil, I.E. Markó, Sulfoxides in Julia−Lythgoe olefination: efficient and stereoselective preparation of Di-, tri-, and tetrasubstituted olefins, Org. Lett. 7 (2005) 2373–2376, https://doi.org/10.1021/ol050649e.
[15] P.X.T. Rinu, S. Radhika, G. Anilkumar, Recent applications and trends in the Julia-Kocienski olefination, ChemistrySelect 7 (2022) e202200760, https://doi.org/10.1002/slct.202200760.
[16] R.G. Linde, M. Egbertson, R.S. Coleman, A.B. Jones, S.J. Danishefsky, Efficient preparation of intermediates corresponding to C22-C27 and C28-C34 of FK-506, J. Org. Chem. 55 (1990) 2771–2776, https://doi.org/10.1021/jo00296a040.
[17] M. Ihara, S. Suzuki, T. Taniguchi, Y. Tokunaga, K. Fukumoto, Modification of the Julia alkenation using SmI_2-HMPA, Synlett 1994 (1994) 859–860, https://doi.org/10.1055/s-1994-23033.
[18] G. Lee, An efficient Julia olefination mediated by magnesium in ethanol, Tetrahedron Lett. 36 (1995) 5607–5608, https://doi.org/10.1016/00404-0399(50)1073Q.
[19] P.R. Blakemore, W.J. Cole, P.J. Kocieński, A. Morley, A stereoselective synthesis of *trans*-1,2-disubstituted alkenes based on the condensation of aldehydes with metallated 1-phenyl-1*H*-tetrazol-5-yl sulfones, Synlett 1998 (1998) 26–28, https://doi.org/10.1055/s-1998-1570.
[20] A.B. Smith, B.M. Brandt, Total synthesis of (−)-callystatin A, Org. Lett. 3 (2001) 1685–1688, https://doi.org/10.1021/ol0158922.
[21] P.F. Hudrlik, D. Peterson, Stereospecific olefin-forming elimination reactions of beta-hydroxyalkylsilanes, J. Am. Chem. Soc. 97 (1975) 1464–1468, https://doi.org/10.1021/ja00839a031.
[22] M.M. Heravi, V. Zadsirjan, M. Daraie, M. Ghanbarian, Applications of Wittig reaction in the total synthesis of natural macrolides, ChemistrySelect 5 (2020) 9654–9690, https://doi.org/10.1002/slct.202002192.
[23] J.B. Bauer, F. Diab, C. Maichle-Mössmer, H. Schubert, H.F. Bettinger, Synthesis of the [11]cyclacene framework by repetitive Diels–Alder cycloadditions, Molecules 26 (2021) 3047, https://doi.org/10.3390/molecules26103047.
[24] P. Avti, D. Maysinger, A. Kakkar, Alkyne-azide "click" chemistry in designing nanocarriers for applications in biology, Molecules 18 (2013) 9531–9549, https://doi.org/10.3390/molecules18089531.

[25] L.D. Elliott, K.I. Booker-Milburn, A.J.J. Lennox, Daisy-chaining photo- and thermal chemistry: multistep continuous flow synthesis of visible-light-mediated photochemistry with a high-temperature Cascade reaction, Org. Process Res. Dev. 25 (2021) 1943–1949, https://doi.org/10.1021/acs.oprd.1c00187.

[26] P. Sharma, M. Hakkarainen, Light responsive chemistry – a design strategy for remodelling benzoxazine architectures towards room temperature processing, Mater. Today Chem. 38 (2024) 102073, https://doi.org/10.1016/j.mtchem.2024.102073.

[27] B.W. Grau, A. Neuhauser, S. Aghazada, K. Meyer, S.B. Tsogoeva, Iron-catalyzed olefin metathesis: recent theoretical and experimental advances, Chem. A Eur. J. 28 (2022) e202201414, https://doi.org/10.1002/chem.202201414.

[28] M. Schuster, S. Blechert, Olefin metathesis in organic chemistry, Angew. Chem. Int. Ed. Engl. 36 (1997) 2036–2056, https://doi.org/10.1002/anie.199720361.

[29] *Olefin Metathesis: Theory and Practice*; K. Grela, Ed.; Wiley: Hoboken, New Jersey, 2014.

[30] A. Abera Tsedalu, A review on olefin metathesis reactions as a green method for the synthesis of organic compounds, J. Chem. 2021 (2021) 1–14, https://doi.org/10.1155/2021/3590613.

[31] P.J.-L. Hérisson, Y. Chauvin, Catalyse de Transformation Des Oléfines Par Les Complexes Du Tungstène. II. Télomérisation Des Oléfines Cycliques En Présence d'oléfines Acycliques, Makromol. Chem. 141 (1971) 161–176, https://doi.org/10.1002/macp.1971.021410112.

[32] T.J. Katz, J. McGinnis, Mechanism of the olefin metathesis reaction, J. Am. Chem. Soc. 97 (1975) 1592–1594, https://doi.org/10.1021/ja00839a063.

[33] T.J. Katz, J. McGinnis, S. Hurwitz, Selectivity in the olefin metathesis of unsymmetrically substituted ethylenes, J. Am. Chem. Soc. 98 (1976) 605–606, https://doi.org/10.1021/ja00418a047.

[34] T.J. Katz, J. McGinnis, Metathesis of cyclic and acyclic olefins, J. Am. Chem. Soc. 99 (1977) 1903–1912, https://doi.org/10.1021/ja00448a036.

[35] T.J. Katz, J. McGinnis, J. Am. Chem. Soc. 98 (1976) 606–608, https://doi.org/10.1021/ja00418a048.

[36] D.L. Nascimento, D.E. Fogg, Origin of the breakthrough productivity of ruthenium-cyclic alkyl amino carbene catalysts in olefin metathesis, J. Am. Chem. Soc. 141 (2019) 19236–19240, https://doi.org/10.1021/jacs.9b10750.

[37] G. Pareras, D. Detiana, A. Poater, MOF encapsulation of Ru olefin metathesis catalysts to block catalyst decomposition, Catalysts 10 (2020) 687, https://doi.org/10.1038/s41557-019-0319-5.

[38] J.C. Conrad, D.E. Fogg, Ruthenium-catalyzed ring-closing metathesis: recent advances, limitations and opportunities, Curr. Org. Chem. 10 (2006) 185–202, https://doi.org/10.2174/138527206775192942.

[39] G.A. Bailey, M. Foscato, C.S. Higman, C.S. Day, V.R. Jensen, D.E. Fogg, Bimolecular coupling as a vector for decomposition of fast-initiating olefin metathesis catalysts, J. Am. Chem. Soc. 140 (2018) 6931–6944, https://doi.org/10.1021/jacs.8b02709.

[40] D.L. Nascimento, M. Foscato, G. Occhipinti, V.R. Jensen, D.E. Fogg, Bimolecular coupling in olefin metathesis: correlating structure and decomposition for leading and emerging ruthenium-carbene catalysts, J. Am. Chem. Soc. 143 (2021) 11072–11079, https://doi.org/10.1021/jacs.1c04424.

[41] S.H. Hong, M.W. Day, R.H. Grubbs, Decomposition of a key intermediate in ruthenium-catalyzed olefin metathesis reactions, J. Am. Chem. Soc. 126 (2004) 7414–7415, https://doi.org/10.1021/ja0488380.

[42] S.H. Hong, A. Chlenov, M.W. Day, R.H. Grubbs, Double C-H activation of an N-heterocyclic carbene ligand in a ruthenium olefin metathesis catalyst, Angew. Chem. Int. Ed. 46 (2007) 5148–5151, https://doi.org/10.1002/anie.200701234.

[43] A. Poater, L. Cavallo, Mechanistic insights into the double C-H (De)activation route of a Ru-based olefin metathesis catalyst, J. Mol. Catal. A Chem. 324 (2010) 75–79, https://doi.org/10.1016/j.molcata.2010.02.023.

[44] A. Poater, N. Bahri-Lalehah, L. Cavallo, Rationalizing current strategies to protect N-heterocyclic carbene-based ruthenium catalysts active in olefin metathesis from C-H (de)activation, Chem. Commun. 47 (2011) 6674–6676, https://doi.org/10.1039/c1cc11594d.

[45] B.R. Galan, M. Gembicky, P.M. Dominiak, J.B. Keister, S.T. Diver, J. Am. Chem. Soc. 127 (2005) 15702–15703, https://doi.org/10.1021/ja0545618.

[46] A. Poater, F. Ragone, A. Correa, L. Cavallo, Exploring the reactivity of Ru-based metathesis catalysts with a π-acid ligand trans to the Ru-ylidene bond, J. Am. Chem. Soc. 131 (2009) 9000–9006, https://doi.org/10.1021/ja902552m.

[47] S. Manzini, A. Poater, D.J. Nelson, L. Cavallo, A.M.Z. Slawin, S.P. Nolan, Insights into the decomposition of olefin metathesis pre-catalysts, Angew. Chem. Int. Ed. 53 (2014) 8995–8999, https://doi.org/10.1002/anie.201403770.

[48] S. Manzini, C.A. Urbina-Blanco, A. Poater, A.M.Z. Slawin, L. Cavallo, S.P. Nolan, From olefin metathesis catalyst to alcohol racemization catalyst in one step, Angew. Chem. Int. Ed. 51 (2012) 1042–1045, https://doi.org/10.1002/anie.201106915.

[49] S. Manzini, D.J. Nelson, T. Lebl, A. Poater, L. Cavallo, A.M.Z. Slawin, S.P. Nolan, From ruthenium olefin metathesis catalyst to (eta(5)-3-phenylindenyl)hydrido complex via alcoholysis, Chem. Commun. 50 (2014) 2205–2207, https://doi.org/10.1039/c3cc49481k.

[50] M. Rouen, P. Queval, E. Borré, L. Falivene, A. Poater, M. Berthod, F. Hugues, L. Cavallo, O. Baslé, H. Olivier-Bourbigou, M. Mauduit, Selective metathesis of α-olefins from bio-sourced Fischer–Tropsch feeds, ACS Catal. 6 (2016) 7970–7976, https://doi.org/10.1021/acscatal.6b01428.

[51] W.L. Truett, D.R. Johnson, I.M. Robinson, B.A. Montague, Polynorbornene by coordination polymerization, J. Am. Chem. Soc. 82 (1960) 2337–2340, https://doi.org/10.1021/ja01494a057.

[52] K. Ziegler, E. Holzkamp, H. Breil, H. Martin, Polymerisation von Äthylen Und Anderen Olefinen, Angew. Chem. 67 (1955) 426, https://doi.org/10.1002/ange.19550671610.

[53] G. Natta, G. Dall'Asta, G. Mazzanti, Stereospecific homopolymerization of cyclopentene, Angew. Chem. Int. Ed. Engl. 3 (1964) 723–729, https://doi.org/10.1002/anie.196407231.

[54] R.L. Banks, G.C. Bailey, Olefin disproportionation. A new catalytic process, IEC Prod. Res. Dev. 3 (1964) 170–173, https://doi.org/10.1021/i360011a002.

[55] N. Calderon, E.A. Ofstead, W.A. Judy, Ring-opening polymerization of unsaturated alicyclic compounds, J. Polym. Sci. A1 (5) (1967) 2209–2217, https://doi.org/10.1002/pol.1967.150050901.

[56] N. Calderon, H.Y. Chen, K.W. Scott, Olefin metathesis - a novel reaction for skeletal transformations of unsaturated hydrocarbons, Tetrahedron Lett. 8 (1967) 3327–3329, https://doi.org/10.1016/S0040-4039(01)89881-6.

[57] C. Bradshaw, Olefin dismutation: reactions of olefins on cobalt oxide-molybdenum oxide-alumina, J. Catal. 7 (1967) 269–276, https://doi.org/10.1016/0021-9517(67)90105-4.

[58] C. Adlhart, C. Hinderling, H. Baumann, P. Chen, Mechanistic studies of olefin Metathesis by ruthenium carbene complexes using electrospray ionization tandem mass spectrometry, J. Am. Chem. Soc. 122 (2000) 8204–8214, https://doi.org/10.1021/ja9938231.

[59] D.J. Cardin, M.J. Doyle, M.F. Lappert, Rhodium(I)-catalysed dismutation of electron-rich olefins: rhodium(I) carbene complexes as intermediates, J. Chem. Soc. Chem. Commun. (1972) 927–928, https://doi.org/10.1039/c39720000927.

[60] D.J. Cardin, B. Çetinkaya, M.J. Doyle, M.F. Lappert, The chemistry of transition-metal carbene complexes and their role as reaction intermediates, Chem. Soc. Rev. 2 (1973) 99–144, https://doi.org/10.1039/CS9730200099.

[61] C.P. Casey, T.J. Burkhardt, Reactions of (diphenylcarbene)pentacarbonyltungsten (0) with alkenes. Role of metal-carbene complexes in cyclopropanation and olefin metathesis reactions, J. Am. Chem. Soc. 96 (1974) 7808–7809, https://doi.org/10.1021/ja00832a032.

[62] B.A. Dolgoplosk, K.L. Makovetsky, T.G. Golenko, Yu.T. Korshak, E.I. Tinyakova, On the mechanism of ring-opening polymerization of cyclo-olefins, Eur. Polym. J. 10 (1974) 901–904, https://doi.org/10.1016/0014-3057(74)90025-1.

[63] R.H. Grubbs, P.L. Burk, D.D. Carr, Mechanism of the olefin metathesis reaction, J. Am. Chem. Soc. 97 (1975) 3265–3267, https://doi.org/10.1021/ja00844a082.

[64] R.H. Grubbs, D.D. Carr, C. Hoppin, P.L. Burk, Consideration of the mechanism of the metal catalyzed olefin metathesis reaction, J. Am. Chem. Soc. 98 (1976) 3478–3483, https://doi.org/10.1021/ja00428a015.

[65] F.N. Tebbe, G.W. Parshall, G.S. Reddy, Olefin homologation with titanium methylene compounds, J. Am. Chem. Soc. 100 (1978) 3611–3613, https://doi.org/10.1021/ja00479a061.

[66] T.R. Howard, J.B. Lee, R.H. Grubbs, Titanium metallacarbene-metallacyclobutane reactions: stepwise metathesis, J. Am. Chem. Soc. 102 (1980) 6876–6878, https://doi.org/10.1021/ja00542a050.

[67] M.R. Becker, R.B. Watson, C.S. Schindler, Beyond olefins: new metathesis directions for synthesis, Chem. Soc. Rev. 47 (2018) 7867–7881, https://doi.org/10.1039/C8CS00391B.

[68] R.R. Schrock, J.S. Murdzek, G.C. Bazan, J. Robbins, M. DiMare, M. O'Regan, Synthesis of molybdenum imido alkylidene complexes and some reactions involving acyclic olefins, J. Am. Chem. Soc. 112 (1990) 3875–3886, https://doi.org/10.1021/ja00166a023.

[69] R.R. Schrock, Alkylcarbene complex of tantalum by intramolecular *alpha*-hydrogen abstraction, J. Am. Chem. Soc. 96 (1974) 6796–6797, https://doi.org/10.1021/ja00828a061.

[70] R.R. Schrock, Catalysis by transition metals: metal-carbon double and triple bonds, Science 219 (1983) 13–18, https://doi.org/10.1126/science.219.4580.13.

[71] R. Schrock, S. Rocklage, J. Wengrovius, G. Rupprecht, J. Fellmann, Preparation and characterization of active niobium, tantalum and tungsten metathesis catalysts, J. Mol. Catal. 8 (1980) 73–83, https://doi.org/10.1016/0304-5102(80)87006-4.

[72] A. Poater, X. Solans-Monfort, E. Clot, C. Copéret, O. Eisenstein, DFT calculations of d0 M(NR)(CHtBu)(X)(Y) (M =Mo, W; R = CPh_3, 2,6-iPr–C_6H_3; X and Y = CH_2tBu, OtBu, OSi(OtBu)$_3$) olefin metathesis catalysts: structural, spectroscopic and electronic properties, Dalton Trans. 2006 (2006) 3077–3087, https://doi.org/10.1039/b604481f.

[73] T.K. Olszewski, M. Bieniek, K. Skowerski, Ruthenium-based complexes bearing quaternary ammonium tags as versatile catalysts for olefin metathesis: from the discovery to practical applications, Org. Process Res. Dev. 24 (2020) 125–145, https://doi.org/10.1021/acs.oprd.9b00483.

[74] G. Szczepaniak, A. Ruszczyńska, K. Kosiński, E. Bulska, K. Grela, Highly efficient and time economical purification of olefin metathesis products from metal residues using an isocyanide scavenger, Green Chem. 20 (2018) 1280–1289, https://doi.org/10.1039/C7GC03324A.

[75] R.R. Schrock, Recent advances in high oxidation state Mo and W imido alkylidene chemistry, Chem. Rev. 109 (2009) 3211–3226, https://doi.org/10.1021/cr800502p.

[76] R.R. Schrock, High oxidation state multiple metal-carbon bonds, Chem. Rev. 102 (2002) 145–179, https://doi.org/10.1021/cr0103726.

[77] C.O. Blanco, J. Sims, D.L. Nascimento, A.Y. Goudreault, S.N. Steinmann, C. Michel, D.E. Fogg, The impact of water on Ru-catalyzed olefin metathesis: potent deactivating effects even at low water concentrations, ACS Catal. 11 (2021) 893–899, https://doi.org/10.1021/acscatal.0c04279.

[78] S.J. Ton, D.E. Fogg, The Impact of Oxygen on Leading and Emerging Ru-Carbene Catalysts for Olefin Metathesis: An Unanticipated Correlation between

Robustness and Metathesis Activity. doi:https://doi.org/10.1021/acscatal.9b03285.

[79] J.B. Alexander, D.S. La, D.R. Cefalo, A.H. Hoveyda, R.R. Schrock, Catalytic enantioselective ring-closing metathesis by a chiral Biphen−Mo complex, J. Am. Chem. Soc. 120 (1998) 4041–4042, https://doi.org/10.1021/ja974353i.

[80] S.S. Zhu, D.R. Cefalo, D.S. La, J.Y. Jamieson, W.M. Davis, A.H. Hoveyda, R. R. Schrock, Chiral Mo−Binol complexes: activity, synthesis, and structure. Efficient enantioselective six-membered ring synthesis through catalytic metathesis, J. Am. Chem. Soc. 121 (1999) 8251–8259, https://doi.org/10.1021/ja991432g.

[81] S.L. Aeilts, D.R. Cefalo, P.J. Bonitatebus Jr., J.J. Houser, A.H. Hoveyda, R. R. Schrock, A readily available and user-friendly chiral catalyst for efficient enantioselective olefin metathesis, Angew. Chem. 113 (2001) 1500–1504, https://doi.org/10.1002/1521-3757(20010417)113:8<1500::AID-ANGE1500>3.0.CO;2-I.

[82] X. Teng, D.R. Cefalo, R.R. Schrock, A.H. Hoveyda, Enhancement of enantioselectivity by THF in asymmetric Mo-catalyzed olefin metathesis. Catalytic enantioselective synthesis of cyclic tertiary ethers and spirocycles, J. Am. Chem. Soc. 124 (2002) 10779–10784, https://doi.org/10.1021/ja020671s.

[83] K.C. Hultzsch, J.A. Jernelius, A.H. Hoveyda, R.R. Schrock, The first polymer-supported and recyclable chiral catalyst for enantioselective olefin metathesis, Angew. Chem. Int. Ed. 41 (2002) 589–593, https://doi.org/10.1002/1521-3773(20020215)41:4<589::AID-ANIE589>3.0.CO;2-V.

[84] W.C.P. Tsang, J.A. Jernelius, G.A. Cortez, G.S. Weatherhead, R.R. Schrock, A. H. Hoveyda, An enantiomerically pure adamantylimido molybdenum alkylidene complex. An effective new catalyst for enantioselective olefin metathesis, J. Am. Chem. Soc. 125 (2003) 2591–2596, https://doi.org/10.1021/ja021204d.

[85] W.C.P. Tsang, K.C. Hultzsch, J.B. Alexander, P.J. Bonitatebus, R.R. Schrock, A. H. Hoveyda, Alkylidene and metalacyclic complexes of tungsten that contain a chiral biphenoxide ligand. Synthesis, asymmetric ring-closing Metathesis, and mechanistic investigations, J. Am. Chem. Soc. 125 (2003) 2652–2666, https://doi.org/10.1021/ja0210603.

[86] J. Heppekausen, A. Fürstner, Rendering Schrock-type molybdenum alkylidene complexes air stable: user-friendly precatalysts for alkene metathesis, Angew. Chem. Int. Ed. 50 (2011) 7829–7832, https://doi.org/10.1002/anie.201102012.

[87] M.L.H. Green, L.C. Mitchard, M.G. Swanwick, Carbene complexes of iron, molybdenum, and ruthenium: a new route to metal–carbene derivatives, J. Chem. Soc. A 0 (1971) 794–797, https://doi.org/10.1039/J19710000794.

[88] R.H. Grubbs, W. Tumas, Polymer synthesis and organotransition metal chemistry, Science 243 (1989) 907–915, https://doi.org/10.1126/science.2645643.

[89] S.T. Nguyen, L.K. Johnson, R.H. Grubbs, J.W. Ziller, Ring-opening metathesis polymerization (ROMP) of norbornene by a group VIII carbene complex in Protic media, J. Am. Chem. Soc. 114 (1992) 3974–3975, https://doi.org/10.1021/ja00036a053.

[90] A. Demonceau, A.F. Noels, E. Saive, A.J. Hubert, Ruthenium-catalysed ring-opening metathesis polymerization of Cycloolefins initiated by diazoesters, J. Mol. Catal. 76 (1992) 123–132, https://doi.org/10.1016/0304-5102(92)80151-6.

[91] A.W. Stumpf, E. Saive, A. Demonceau, A.F. Noels, Ruthenium-based catalysts for the ring opening metathesis polymerisation of low-strain cyclic olefins and of functionalised derivatives of norbornene and cyclooctene, J. Chem. Soc. Chem. Commun. (1995) 1127–1128, https://doi.org/10.1039/c39950001127.

[92] J. Wolf, W. Stüer, C. Grünwald, H. Werner, P. Schwab, M. Schulz, Ruthenium trichloride, tricyclohexyl- phosphane, 1-alkynes, magnesium, hydrogen, and water—ingredients of an efficient one-pot synthesis of ruthenium catalysts for olefin metathesis, Angew. Chem. Int. Ed. 37 (1998) 1124–1126, https://doi.org/10.1002/(SICI)1521-3773(19980504)37:8<1124::AID-ANIE1124>3.0.CO;2-C.

[93] M. Gandelman, B. Rybtchinski, N. Ashkenazi, R.M. Gauvin, D. Milstein, A new general method for the preparation of metal carbene complexes, J. Am. Chem. Soc. 123 (2001) 5372–5373, https://doi.org/10.1021/ja0157393.

[94] M. Oliván, K.G. Caulton, The first double oxidative addition of CH_2Cl_2 to a metal complex: facile synthesis of $[Ru(CH_2)Cl_2\{P(C_6H_{11})_3\}_2]$, Chem. Commun. (1997) 1733–1734, https://doi.org/10.1039/a703097e.

[95] M. Scholl, S. Ding, C.W. Lee, R.H. Grubbs, Synthesis and activity of a new generation of ruthenium-based olefin metathesis catalysts coordinated with 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ligands, Org. Lett. 1 (1999) 953–956, https://doi.org/10.1021/ol990909q.

[96] H. Jacobsen, A. Correa, A. Poater, C. Costabile, L. Cavallo, Understanding the M (NHC) (NHC = N-heterocyclic carbene) bond, Coord. Chem. Rev. 253 (2009) 687–703, https://doi.org/10.3390/catal10060687.

[97] L.M. Azofra, S.V.C. Vummaleti, Z. Zhang, A. Poater, L. Cavallo, σ/π plasticity of NHCs on the ruthenium–phosphine and Ruthenium═Ylidene bonds in olefin metathesis catalysts, Organometallics 39 (2020) 3972–3982, https://doi.org/10.1021/acs.organomet.0c00536.

[98] P. De Fremont, N. Marion, S.P. Nolan, Carbenes: synthesis, properties, and organometallic chemistry, Coord. Chem. Rev. 253 (2009) 862–892, https://doi.org/10.1016/j.ccr.2008.05.018.

[99] A.J. Arduengo, Looking for stable carbenes: the difficulty in starting anew, Acc. Chem. Res. 32 (1999) 913–921, https://doi.org/10.1021/ar980126p.

[100] S. Diez-Gonzalez, N. Marion, S.P. Nolan, N-heterocyclic carbenes in late transition metal catalysis, Chem. Rev. 109 (2009) 3612–3676, https://doi.org/10.1021/cr900074m.

[101] D.J. Nelson, S.P. Nolan, Quantifying and understanding the electronic properties of N-heterocyclic carbenes, Chem. Soc. Rev. 42 (2013) 6723–6753, https://doi.org/10.1039/C3CS60146C.

[102] S. Díez-González, S.P. Nolan, Stereoelectronic parameters associated with N-heterocyclic carbene (NHC) ligands: a quest for understanding, Coord. Chem. Rev. 251 (2007) 874–883, https://doi.org/10.1016/j.ccr.2006.10.004.

[103] T. Weskamp, W.C. Schattenmann, M. Spiegler, W.A. Herrmann, A novel class of ruthenium catalysts for olefin Metathesis, Angew. Chem. Int. Ed. 37 (1998) 2490–2493, https://doi.org/10.1002/(SICI)1521-3773(19981002)37:18<2490::AID-ANIE2490>3.0.CO;2-X.

[104] J. Huang, E.D. Stevens, S.P. Nolan, J.L. Peterson, Olefin metathesis-active ruthenium complexes bearing a nucleophilic carbene ligand, J. Am. Chem. Soc. 121 (1999) 2674–2678, https://doi.org/10.1021/ja9831352.

[105] M. Scholl, T.M. Trnka, J.P. Morgan, R.H. Grubbs, Increased ring closing metathesis activity of ruthenium-based olefin metathesis catalysts coordinated with imidazolin-2-Ylidene ligands, Tetrahedron Lett. 40 (1999) 2247–2250, https://doi.org/10.1016/S0040-4039(99)00217-8.

[106] V. Dragutan, I. Dragutan, L. Delaude, A. Demonceau, NHC–Ru complexes—friendly catalytic tools for manifold chemical transformations, Coord. Chem. Rev. 251 (2007) 765–794, https://doi.org/10.1016/j.ccr.2006.09.002.

[107] A.S. Adhikari, N. Majumdar, Unconventional reactivity of a Grubbs catalyst: hydroalkylation overriding metathesis, Org. Lett. 25 (2023) 8611–8616, https://doi.org/10.1021/acs.orglett.3c03456.

[108] B. Alcaide, P. Almendros, A. Luna, Grubbs' ruthenium-carbenes beyond the metathesis reaction: less conventional non-metathetic utility, Chem. Rev. 109 (2009) 3817–3858, https://doi.org/10.1021/cr9001512.

[109] A. Poater, L. Falivene, C.A. Urbina-Blanco, S. Manzini, S.P. Nolan, L. Cavallo, How does the addition of steric hindrance to a typical N-heterocyclic carbene ligand affect catalytic activity in olefin metathesis? Dalton Trans. 42 (2013) 7433–7439, https://doi.org/10.1039/c3dt32980a.

[110] A. Leitgeb, M. Abbas, R.C. Fischer, A. Poater, L. Cavallo, C. Slugovc, A latent ruthenium based olefin metathesis catalyst with a sterically demanding NHC ligand (pre)catalysts, Cat. Sci. Technol. 2 (2012) 1640–1643, https://doi.org/10.1039/c2cy20311a.

[111] A. Poater, F. Ragone, A. Correa, L. Cavallo, Comparison of different ruthenium–alkylidene bonds in the activation step with N-heterocyclic carbene Ru-catalysts for olefins metathesis, Dalton Trans. 40 (2011) 11066–11069, https://doi.org/10.1039/c1dt10959f.

[112] V.A. Voloshkin, L.P. Zorba, S.P. Nolan, The influential IPr: 25 years after its discovery, Chem. Sci. 16 (2025) 2062–2082, https://doi.org/10.1039/D4SC07009G.

[113] J.A. Love, J.P. Morgan, T.M. Trnka, R.H. Grubbs, A practical and highly active ruthenium-based catalyst that effects the cross metathesis of acrylonitrile, Angew. Chem. 114 (2002) 4207–4209, https://doi.org/10.1002/1521-3757(20021104)114:21<4207::AID-ANGE4207>3.0.CO;2-G.

[114] V. Forcina, A. García-Domínguez, G.C. Lloyd-Jones, Kinetics of initiation of the third generation Grubbs metathesis catalyst: convergent associative and dissociative pathways, Faraday Discuss. 220 (2019) 179–195, https://doi.org/10.1039/C9FD00043G.

[115] Y. Cai, C. Kai, Y. Huang, F. Verpoort, Cyclic(alkyl)(amino)carbenes and the research prospect in olefin metathesis reaction, Chin. J. Org. Chem. 34 (2014) 1978–1985, https://doi.org/10.6023/cjoc201404032.

[116] D. Butilkov, A. Frenklah, I. Rozenberg, S. Kozuch, N.G. Lemcoff, Highly selective olefin metathesis with CAAC-containing ruthenium benzylidenes, ACS Catal. 7 (2017) 7634–7637, https://doi.org/10.1021/acscatal.7b02409.

[117] V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu, G. Bertrand, A rigid cyclic (alkyl)(amino)carbene ligand leads to isolation of low-coordinate transition-metal complexes, Angew. Chem. Int. Ed. 44 (2005) 5705–5709, https://doi.org/10.1002/anie.200502566.

[118] V. Lavallo, Y. Canac, A. DeHope, B. Donnadieu, G. Bertrand, A rigid cyclic (alkyl)(amino)carbene ligand leads to isolation of low-coordinate transition-metal complexes, Angew. Chem. Int. Ed. 44 (2005) 7236–7239, https://doi.org/10.1002/anie.200502566.

[119] R. Jazzar, J.-B. Bourg, R.D. Dewhurst, B. Donnadieu, G. Bertrand, Intramolecular hydroiminiumation and -amidiniumation of alkenes: a convenient, flexible, and scalable route to cyclic iminium and imidazolinium salts, J. Org. Chem. 72 (2007) 3492–3499, https://doi.org/10.1021/jo0703909.

[120] D.R. Anderson, V. Lavallo, D.J. O'Leary, G. Bertrand, R.H. Grubbs, Synthesis and reactivity of olefin metathesis catalysts bearing cyclic (alkyl)(amino)carbenes, Angew. Chem. Int. Ed. 46 (2007) 7262–7265, https://doi.org/10.1002/anie.200702085.

[121] X. Ou, G. Occhipinti, E.-J.Y. Boisvert, V.R. Jensen, D.E. Fogg, Mesomeric acceleration counters slow initiation of ruthenium-CAAC catalysts for olefin metathesis (CAAC = cyclic (alkyl)(amino) carbene), ACS Catal. 13 (2023) 5315–5325, https://doi.org/10.1021/acscatal.2c03828.

[122] X. Bantreil, S.P. Nolan, Synthesis of N-heterocyclic carbene ligands and derived ruthenium olefin metathesis catalysts, Nat. Protoc. 6 (2011) 69–77, https://doi.org/10.1038/nprot.2010.177.

[123] J.S. Kingsbury, J.P.A. Harrity, P.J. Bonitatebus, A.H. Hoveyda, A recyclable Ru-based metathesis catalyst, J. Am. Chem. Soc. 121 (1999) 791–799, https://doi.org/10.1021/ja983222u.

[124] D.R. Anderson, T. Ung, G. Mkrtumyan, G. Bertrand, R.H. Grubbs, Y. Schrodi, Kinetic selectivity of olefin metathesis catalysts bearing cyclic (alkyl)(amino) carbenes, Organometallics 27 (2008) 563–566, https://doi.org/10.1021/om7008028.

[125] V.M. Marx, A.H. Sullivan, M. Melaimi, S.C. Virgil, B.K. Keitz, D.S. Weinberger, G. Bertrand, R.H. Grubbs, Cyclic alkyl amino carbene (CAAC) ruthenium

complexes as remarkably active catalysts for ethenolysis, Angew. Chem. Int. Ed. 54 (2015) 1919–1923, https://doi.org/10.1002/anie.201410797.

[126] A. Michrowska, K. Mennecke, U. Kunz, A. Kirschning, K. Grela, A new concept for the noncovalent binding of a ruthenium-based olefin Metathesis catalyst to polymeric phases: preparation of a catalyst on Raschig rings, J. Am. Chem. Soc. 128 (2006) 13261–13267, https://doi.org/10.1021/ja063561k.

[127] M. Nagyházi, G. Turczel, Á. Balla, G. Szálas, I. Tóth, G.T. Gál, B. Petra, P. T. Anastas, R. Tuba, Towards sustainable catalysis – highly efficient olefin metathesis in protic media using phase labelled CyclicAlkyl amino Carbene (CAAC) ruthenium catalysts, ChemCatChem 12 (2020) 1953–1957, https://doi.org/10.1002/cctc.201902258.

[128] R. Gawin, A. Tracz, P. Krajczy, A. Kozakiewicz-Piekarz, J.P. Martínez, B. Trzaskowski, Inhibition of the decomposition pathways of ruthenium olefin Metathesis catalysts: development of highly efficient catalysts for ethenolysis, J. Am. Chem. Soc. 145 (2023) 25010–25021, https://doi.org/10.1021/jacs.3c10635.

[129] G. Occhipinti, D.L. Nascimento, M. Foscato, D.E. Fogg, V.R. Jensen, The Janus face of high trans-effect carbenes in olefin metathesis: gateway to both productivity and decomposition, Chem. Sci. 13 (2022) 5107–7117, https://doi.org/10.1039/d2sc00855f.

[130] S.A. Gonsales, Z.C. Mueller, F. Zhao, P.H.S. Paioti, L. Karmazin, J. Wan, F. Liu, K. N. Houk, A.H. Hoveyda, Cross-metathesis of Allenes. Mechanistic analysis and identification of a Ru-CAAC as the Most effective catalyst, J. Am. Chem. Soc. 143 (2021) 20640–20644, https://doi.org/10.1021/jacs.1c11453.

[131] D.L. Nascimento, I. Reim, M. Foscato, V.R. Jensen, D.E. Fogg, Challenging Metathesis catalysts with nucleophiles and Brønsted base: examining the stability of state-of-the-art ruthenium carbene catalysts to attack by amines, ACS Catal. 10 (2020) 11623–11633, https://doi.org/10.1021/acscatal.0c02760.

[132] A. Poater, L. Cavallo, A comprehensive study of olefin metathesis catalyzed by Ru-based catalysts, Beilstein J. Org. Chem. 11 (2015) 1767–1780, https://doi.org/10.3762/bjoc.

[133] M.S. Sanford, J.A. Love, R.H. Grubbs, Mechanism and activity of ruthenium olefin metathesis catalysts, J. Am. Chem. Soc. 123 (2001) 6543–6554, https://doi.org/10.1021/ja010624k.

[134] K.J. Laidler, J.H. Meiser, Physical Chemistry, Menlo Park/Calif, Benjamin/Cummings, 1982.

[135] J.D. Atwood, Inorganic and Organometallic Reaction Mechanisms, 2. ed., VCH, New York Weinheim, 1997.

[136] E. Pump, A. Poater, N. Bahri-Laleh, R. Credendino, L. Serra, V. Scarano, L. Cavallo, Regio, stereo and chemoselectivity of 2nd generation Grubbs ruthenium-catalyzed olefin metathesis, Catal. Today 388-389 (2022) 394–402, https://doi.org/10.1016/j.cattod.2020.04.071.

[137] F. Nuñez-Zarur, X. Solans-Monfort, L. Rodríguez-Santiago, M. Sodupe, Differences in the activation processes of phosphine-containing and Grubbs–Hoveyda-type alkene metathesis catalysts, Organometallics 31 (2012) 4203–4215, https://doi.org/10.1021/om300150d.

[138] G.C. Vougioukalakis, R.H. Grubbs, Ruthenium-based olefin metathesis catalysts coordinated with unsymmetrical N-heterocyclic carbene ligands: synthesis, structure, and catalytic activity, Chem. A Eur. J. 14 (2008) 7545–7556, https://doi.org/10.1002/chem.200800470.

[139] F. Nuñez-Zarur, X. Solans-Monfort, L. Rodríguez-Santiago, R. Pleixats, M. Sodupe, Mechanistic insights into ring-closing enyne metathesis with the second-generation Grubbs–Hoveyda catalyst: A DFT study, Chem. A Eur. J. 17 (2011) 7506–7520, https://doi.org/10.1002/chem.201003410.

[140] X. Solans-Monfort, R. Pleixats, M. Sodupe, DFT mechanistic study on diene metathesis catalyzed by Ru-based Grubbs–Hoveyda-type carbenes: the key role of π-electron density delocalization in the Hoveyda ligand, Chem. A Eur. J. 16 (2010) 7331–7343, https://doi.org/10.1002/chem.200903525.

[141] I.W. Ashworth, I.H. Hillier, D.J. Nelson, J.M. Percy, M.A. Vincent, What is the initiation step of the Grubbs-Hoveyda olefin metathesis catalyst? Chem. Commun. 47 (2011) 5428–5430, https://doi.org/10.1039/C1CC11230A.

[142] L. Cavallo, Mechanism of ruthenium-catalyzed olefin Metathesis reactions from a theoretical perspective, J. Am. Chem. Soc. 124 (2002) 8965–8973, https://doi.org/10.1021/ja016772s.

[143] S.F. Vyboishchikov, M. Bühl, W. Thiel, Mechanism of olefin metathesis with catalysis by ruthenium carbene complexes: density functional studies on model systems, Chem. A Eur. J. 8 (2002) 3962–3975, https://doi.org/10.1002/1521-3765(20020902)8:17<3962::AID-CHEM3962>3.0.CO;2-X.

[144] Y. Minenkov, G. Occhipinti, W. Heyndrickx, J.R. Jensen, The nature of the barrier to phosphane dissociation from Grubbs olefin metathesis catalysts, Eur. J. Inorg. Chem. 2012 (2012) 1507–1516, https://doi.org/10.1002/ejic.201100932.

[145] V. Thiel, M. Hendann, K.-J. Wannowius, H. Plenio, On the mechanism of the initiation reaction in Grubbs–Hoveyda complexes, J. Am. Chem. Soc. 134 (2012) 1104–1114, https://doi.org/10.1021/ja208967h.

[146] A. Michrowska, R. Bujok, S. Harutyunyan, V. Sashuk, G. Dolgonos, K. Grela, Nitro-substituted Hoveyda−Grubbs ruthenium carbenes: enhancement of catalyst activity through electronic activation, J. Am. Chem. Soc. 126 (2004) 9318–9325, https://doi.org/10.1021/ja048794v.

[147] S.J. Czarnocki, I. Czeluśniak, T.K. Olszewski, M. Malinska, K. Woźniak, K. Grela, Rational and then serendipitous formation of aza analogues of Hoveyda-type catalysts containing a chelating ester group leading to a polymerization catalyst family, ACS Catal. 7 (2017) 4115–4121, https://doi.org/10.1021/acscatal.7b00843.

[148] J.P. Martínez, B. Trzaskowski, Electrophilicity of Hoveyda-Grubbs olefin metathesis catalysts as the driving force that controls initiation rates, ChemPhysChem 23 (2022) e202200580, https://doi.org/10.1002/cphc.202200580.

[149] M.S. Sanford, M. Ulman, R.H. Grubbs, New insights into the mechanism of ruthenium-catalyzed olefin metathesis reactions, J. Am. Chem. Soc. 123 (2001) 749–750, https://doi.org/10.1021/ja003582t.

[150] I.W. Ashworth, I.H. Hillier, D.J. Nelson, J.M. Percy, M.A. Vincent, Olefin metathesis by Grubbs–Hoveyda complexes: computational and experimental studies of the mechanism and substrate-dependent kinetics, ACS Catal. 3 (2013) 1929–1939, https://doi.org/10.1021/cs400164w.

[151] K.M. Engle, G. Lu, S.-X.L. Luo, L.M. Henling, M.K. Takase, P. Liu, K.N. Houk, R. H. Grubbs, Origins of initiation rate differences in ruthenium olefin metathesis catalysts containing chelating benzylidenes, J. Am. Chem. Soc. 137 (2015) 5782–5792, https://doi.org/10.1021/jacs.5b01144.

[152] Y. Minenkov, G. Occhipinti, V.R. Jensen, Complete reaction pathway of ruthenium-catalyzed olefin metathesis of ethyl vinyl ether: kinetics and mechanistic insight from DFT, Organometallics 32 (2013) 2099–2111, https://doi.org/10.1021/om301192a.

[153] C.A. Urbina-Blanco, A. Poater, T. Lebl, S. Manzini, A.M.Z. Slawin, L. Cavallo, S. P. Nolan, The activation mechanism of Ru–indenylidene complexes in olefin metathesis, J. Am. Chem. Soc. 135 (2013) 7073–7079, https://doi.org/10.1021/ja402700p.

[154] P.E. Romero, W.E. Piers, R. McDonald, Rapidly initiating ruthenium olefin-metathesis catalysts, Angew. Chem. 116 (2004) 6287–6291, https://doi.org/10.1002/ange.200461374.

[155] Handbook of Metathesis. 1: Catalyst Development and Mechanism, 2. ed., Wiley-VCH, Weinheim, 2015.

[156] O. Eivgi, R.S. Phatake, N.B. Nechmad, N.G. Lemcoff, Light-activated olefin metathesis: catalyst development, synthesis, and applications, Acc. Chem. Res. 53 (2020) 2456–2471, https://doi.org/10.1021/acs.accounts.0c00495.

[157] M. Gimferrer, P. Salvador, A. Poater, Computational monitoring of oxidation states in olefin metathesis, Organometallics 38 (2019) 4585–4592, https://doi.org/10.1021/acs.organomet.9b00591.

[158] V. Amir-Ebrahimi, D.A. Corry, J.G. Hamilton, J.M. Thompson, J.J. Rooney, Characteristics of RuCl$_2$(CHPh)(PCy$_3$)$_2$ as a catalyst for ring-opening metathesis polymerization, Macromolecules 33 (2000) 717–724, https://doi.org/10.1021/ma991395d.

[159] K. Iudanov, N. Nechmad, A. Poater, G. Lemcoff, Selective cross-metathesis versus ring-closing metathesis of terpenes, taking the path less travelled, Angew. Chem. Int. Ed. 63 (2024) e202412430, https://doi.org/10.1002/anie.202412430.

[160] A.H. Hoveyda, C. Qin, X.Z. Sui, Q. Liu, X. Li, A. Nikbakht, Taking olefin metathesis to the limit: stereocontrolled synthesis of trisubstituted alkenes, Acc. Chem. Res. 56 (2023) 2426–2446, https://doi.org/10.1021/acs.accounts.3c00341.

[161] S. Shahane, C. Bruneau, C. Fischmeister, Z. Selectivity, Recent advances in one of the current major challenges of olefin metathesis, ChemCatChem 5 (2013) 3436–3459, https://doi.org/10.1002/cctc.201300688.

[162] M. Leconte, J.M. Basset, Stereoselectivity of metathesis of various acyclic olefins with chromium-, molybdenum-, and tungsten-based catalysts, J. Am. Chem. Soc. 101 (1979) 7296–7302, https://doi.org/10.1021/ja00518a027.

[163] S.J. Malcolmson, S.J. Meek, E.S. Sattely, R.R. Schrock, A.H. Hoveyda, Highly efficient molybdenum-based catalysts for enantioselective alkene metathesis, Nature 456 (2008) 933–937, https://doi.org/10.1038/nature07594.

[164] I. Ibrahem, M. Yu, R.R. Schrock, A.H. Hoveyda, Highly Z- and enantioselective ring-opening/cross-metathesis reactions catalyzed by stereogenic-at-Mo adamantylimido complexes, J. Am. Chem. Soc. 131 (2009) 3844–3845, https://doi.org/10.1021/ja900097n.

[165] A.J. Jiang, Y. Zhao, R.R. Schrock, A.H. Hoveyda, Highly Z -selective metathesis homocoupling of terminal olefins, J. Am. Chem. Soc. 131 (2009) 16630–16631, https://doi.org/10.1021/ja908098t.

[166] S.C. Marinescu, R.R. Schrock, P. Müller, M.K. Takase, A.H. Hoveyda, Room-temperature Z-selective homocoupling of α-olefins by tungsten catalysts, Organometallics 30 (2011) 1780–1782, https://doi.org/10.1021/om200150c.

[167] M.R. Reithofer, G.E. Dobereiner, R.R. Schrock, P. Müller, Monoaryloxide pyrrolide (MAP) imido alkylidene complexes of molybdenum and tungsten that contain 2,6-Bis(2,5-R$_2$-pyrrolyl)phenoxide ($R = $ i-Pr, Ph) ligands and an unsubstituted metallacyclobutane on its way to losing ethylene, Organometallics 32 (2013) 2489–2492, https://doi.org/10.1021/om400114h.

[168] A.G. Wenzel, R.H. Grubbs, Ruthenium metallacycles derived from 14-Electron complexes. New insights into olefin metathesis intermediates, J. Am. Chem. Soc. 128 (2006) 16048–16049, https://doi.org/10.1021/ja0666598.

[169] C.N. Rowley, E.F. Van Der Eide, W.E. Piers, T.K. Woo, DFT study of the isomerization and spectroscopic/structural properties of ruthenacyclobutane intermediates relevant to olefin metathesis, Organometallics 27 (2008) 6043–6045, https://doi.org/10.1021/om8008519.

[170] E.F. Van Der Eide, P.E. Romero, W.E. Piers, Generation and spectroscopic characterization of ruthenacyclobutane and ruthenium olefin carbene intermediates relevant to ring closing metathesis catalysis, J. Am. Chem. Soc. 130 (2008) 4485–4491, https://doi.org/10.1021/ja710364e.

[171] E.M. Leitao, E.F. Van Der Eide, P.E. Romero, W.E. Piers, R. McDonald, Kinetic and thermodynamic analysis of processes relevant to initiation of olefin metathesis by ruthenium phosphonium alkylidene catalysts, J. Am. Chem. Soc. 132 (2010) 2784–2794, https://doi.org/10.1021/ja910112m.

[172] E.F. Van Der Eide, W.E. Piers, Mechanistic insights into the ruthenium-catalysed diene ring-closing metathesis reaction, Nat. Chem. 2 (2010) 571–576, https://doi.org/10.1038/nchem.653.

[173] J. Morvan, M. Mauduit, G. Bertrand, R. Jazzar, Cyclic (alkyl)(amino)carbenes (CAACs) in ruthenium olefin metathesis, ACS Catal. 11 (2021) 1714–1748, https://doi.org/10.1021/acscatal.0c05508.

[174] E.L. Rosen, D.H. Sung, Z. Chen, V.M. Lynch, C.W. Bielawski, Olefin metathesis catalysts containing acyclic diaminocarbenes, Organometallics 29 (2010) 250–256, https://doi.org/10.1021/om9008718.

[175] P. Teo, R.H. Grubbs, Facile synthesis of efficient and selective ruthenium olefin metathesis catalysts with sulfonate and phosphate ligands, Organometallics 29 (2010) 6045–6050, https://doi.org/10.1021/om1007924.

[176] R.K.M. Khan, S. Torker, A.H. Hoveyda, Readily accessible and easily modifiable Ru-based catalysts for efficient and *Z*-selective ring-opening metathesis polymerization and ring-opening/cross-metathesis, J. Am. Chem. Soc. 135 (2013) 10258–10261, https://doi.org/10.1021/ja404208a.

[177] G. Occhipinti, F.R. Hansen, K.W. Törnroos, V.R. Jensen, Simple and highly Z-selective ruthenium-based olefin metathesis catalyst, J. Am. Chem. Soc. 135 (2013) 3331–3334, https://doi.org/10.1021/ja311505v.

[178] K. Endo, R.H. Grubbs, Chelated ruthenium catalysts for Z -selective olefin metathesis, J. Am. Chem. Soc. 133 (2011) 8525–8527, https://doi.org/10.1021/ja202818v.

[179] B.K. Keitz, K. Endo, P.R. Patel, M.B. Herbert, R.H. Grubbs, Improved ruthenium catalysts for *Z*-selective olefin metathesis, J. Am. Chem. Soc. 134 (2012) 693–699, https://doi.org/10.1021/ja210225e.

[180] W. Buchowicz, J.C. Mol, M. Lutz, A.L. Spek, A novel ruthenium carbene dimer that is active in the metathesis of internal alkenes; the crystal structure of $Ru_2(=CHPh)_2(CF_3CO_2)_2(\mu\text{-}CF_3CO_2)_2(PCy_3)_2(\mu\text{-}H_2O)$, J. Organomet. Chem. 588 (1999) 205–210, https://doi.org/10.1016/S0022-328X(99)00376-9.

[181] W. Buchowicz, F. Ingold, J.C. Mol, M. Lutz, A.L. Spek, Novel ruthenium(II)$_2$ carboxylates as catalysts for alkene metathesis, Chem. A Eur. J. 7 (2001) 2842–2847, https://doi.org/10.1002/1521-3765(20010702)7:13<2842::AID-CHEM2842>3.0.CO;2-O.

[182] J.O. Krause, O. Nuyken, K. Wurst, M.R. Buchmeiser, Synthesis and reactivity of homogeneous and heterogeneous ruthenium-based metathesis catalysts containing electron-withdrawing ligands, Chem. A Eur. J. 10 (2004) 777–784, https://doi.org/10.1002/chem.200305031.

[183] P. Liu, X. Xu, X. Dong, B.K. Keitz, M.B. Herbert, R.H. Grubbs, K.N. Houk, Z-selectivity in olefin metathesis with chelated Ru catalysts: computational studies of mechanism and selectivity, J. Am. Chem. Soc. 134 (2012) 1464–1467, https://doi.org/10.1021/ja2108728.

[184] L.E. Rosebrugh, M.B. Herbert, V.M. Marx, B.K. Keitz, R.H. Grubbs, Highly active ruthenium Metathesis catalysts exhibiting unprecedented activity and Z -Selectivity, J. Am. Chem. Soc. 135 (2013) 1276–1279, https://doi.org/10.1021/ja311916m.

[185] K.M. Kuhn, J.-B. Bourg, C.K. Chung, S.C. Virgil, R.H. Grubbs, Effects of NHC-backbone substitution on efficiency in ruthenium-based olefin metathesis, J. Am. Chem. Soc. 131 (2009) 5313–5320, https://doi.org/10.1021/ja900067c.

[186] D.J. O'Leary, G.W. O'Neil, Cross-Metathesis. Handbook of Metathesis, 2nd ed, Wiley-VCH, 2015.

[187] I. Cheng-Sánchez, F. Sarabia, Recent advances in total synthesis via metathesis reactions, Synthesis 50 (2018) 3749–3786, https://doi.org/10.1055/s-0037-1610206.

[188] O.M. Ogba, N.C. Warner, D.J. O'Leary, R.H. Grubbs, Recent advances in ruthenium-based olefin metathesis, Chem. Soc. Rev. 47 (2018) 4510–4544, https://doi.org/10.1039/C8CS00027A.

[189] A.K. Chatterjee, T.-L. Choi, D.P. Sanders, R.H. Grubbs, A general model for selectivity in olefin cross metathesis, J. Am. Chem. Soc. 125 (2003) 11360–11370, https://doi.org/10.1021/ja0214882.

[190] M.B. Herbert, R.H. Grubbs, Z-selective cross metathesis with ruthenium catalysts: synthetic applications and mechanistic implications, Angew. Chem. Int. Ed. 54 (2015) 5018–5024, https://doi.org/10.1002/anie.201411588.

[191] S.J. Connon, S. Blechert, Recent developments in olefin cross-metathesis, Angew. Chem. Int. Ed. 42 (2003) 1900–1923, https://doi.org/10.1002/anie.200200556.

[192] S. Fustero, A. Simón-Fuentes, G. Haufe Barrio, Olefin Metathesis reactions with fluorinated substrates, catalysts, and solvents, Chem. Rev. 115 (2015) 871–930, https://doi.org/10.1021/cr500182a.

[193] G.C. Vougioukalakis, R.H. Grubbs, Ruthenium-based heterocyclic carbene-coordinated olefin metathesis catalysts, Chem. Rev. 110 (2010) 1746–1787, https://doi.org/10.1021/cr9002424.

[194] N.B. Nechmad, R. Phatake, E. Ivry, A. Poater, N.G. Lemcoff, Unprecedented Selectivity of sulfur chelated ruthenium iodide benzylidenes in olefin metathesis reactions, Angew. Chem. Int. Ed. 59 (2020) 3539–3543, https://doi.org/10.1002/anie.201914667.

[195] T.T. Nguyen, M.J. Koh, X. Shen, F. Romiti, R.R. Schrock, A.H. Hoveyda, Kinetically controlled E -selective catalytic olefin metathesis, Science 352 (2016) 569–575, https://doi.org/10.1126/science.aaf4622.

[196] Y. Zhang, S.T. Diver, A macrocyclic ruthenium carbene for size-selective alkene metathesis, J. Am. Chem. Soc. 142 (2020) 3371–3374, https://doi.org/10.1021/jacs.0c00081.

[197] A.R. Davalos, E. Sylvester, S.T. Diver, Macrocyclic N-heterocyclic carbenes: synthesis and catalytic applications, Organometallics 38 (2019) 2338–2346, https://doi.org/10.1021/acs.organomet.9b00152.

[198] Z. Shi, R.P. Thummel, Bridged dibenzimidazolinylidenes as new derivatives of tetraaminoethylene, Tetrahedron Lett. 36 (1995) 2741–2744, https://doi.org/10.1016/0040-4039(95)00386-Q.

[199] M.V. Baker, M.J. Bosnich, C.C. Williams, B.W. Skelton, A.H. White, Rapid communication. Imidazolium-linked cyclophanes, Aust. J. Chem. 52 (1999) 823–826, https://doi.org/10.1071/CH99104.

[200] E. Alcalde, N. Mesquida, L. Pérez-García, Imidazolium-based [14]heterophanes as models for anion recognition, Eur. J. Org. Chem. 2006 (2006) 3988–3996, https://doi.org/10.1002/ejoc.200600269.

[201] A. Fürstner, M. Alcarazo, H. Krause, C.W. Lehmann, Effective modulation of the donor properties of N-heterocyclic carbene ligands by "through-space" communication within a planar chiral scaffold, J. Am. Chem. Soc. 129 (2007) 12676–12677, https://doi.org/10.1021/ja076028t.

[202] O. Winkelmann, C. Näther, U. Lüning, Bimacrocyclic NHC transition metal complexes, J. Organomet. Chem. 693 (2008) 923–932, https://doi.org/10.1016/j.jorganchem.2007.11.064.

[203] M.S. Jeletic, I. Ghiviriga, K.A. Abboud, A.S. Veige, A new chiral Di-N-heterocyclic carbene (NHC) cyclophane ligand and its application in palladium enantioselective catalysis, Dalton Trans. 39 (2010) 6392–6394, https://doi.org/10.1039/c0dt00268b.

[204] P.G. Edwards, F.E. Hahn, Synthesis and coordination chemistry of macrocyclic ligands featuring NHC donor groups, Dalton Trans. 40 (2011) 10278–10288, https://doi.org/10.1039/c1dt10864f.

[205] N. Mesquida, I. Dinarès, A. Ibáñez, E. Alcalde, [1$_4$]Heterophane prototypes containing azolium and/or azole anion-binding motifs, Org. Biomol. Chem. 11 (2013) 6385–6396, https://doi.org/10.1039/c3ob41214h.

[206] A. Deiters, S.F. Martin, Synthesis of oxygen- and nitrogen-containing heterocycles by ring-closing metathesis. Chem. Rev. 104 (174) 2199-2238. doi:https://doi.org/10.1021/cr0200872.

[207] X. Shen, T.T. Nguyen, M.J. Koh, D. Xu, A.W.H. Speed, R.R. Schrock, A. H. Hoveyda, Kinetically E-selective macrocyclic ring-closing metathesis, Nature 541 (2017) 380–385, https://doi.org/10.1038/nature20800.

[208] M. Yu, C. Wang, A.F. Kyle, P. Jakubec, D.J. Dixon, R.R. Schrock, A.H. Hoveyda, Synthesis of macrocyclic natural products by catalyst-controlled stereoselective ring-closing metathesis, Nature 479 (2011) 88–93, https://doi.org/10.1038/nature10563.

[209] B. Salehi, A. Mishra, M. Nigam, B. Sener, M. Kilic, M. Sharifi-Rad, P. Fokou, N. Martins, J. Sharifi-Rad, Resveratrol: a double-edged sword in health benefits, Biomedicines 6 (2018) 91, https://doi.org/10.3390/biomedicines6030091.

[210] Q. Lin, G. Liu, K. Huang, S. Wang, H. Chen, Balancing design and control of an olefin metathesis reactive distillation column through reactive section distribution, Chem. Eng. Sci. 66 (2011) 3049–3055, https://doi.org/10.1016/j.ces.2011.04.005.

[211] M.A. Al-Arfaj, W.L. Luyben, Design and control of an olefin metathesis reactive distillation column, Chem. Eng. Sci. 57 (2002) 715–733, https://doi.org/10.1016/S0009-2509(01)00442-0.

[212] Ł. Grzesiński, M. Nadirova, J. Guschlbauer, A. Brotons-Rufes, A. Poater, A. Kajetanowicz, K. Grela, Late-stage functionalization of pharmaceuticals by C–O cross-coupling enabled by wingtip flexible N-heterocyclic carbenes, Nat. Commun. 15 (2024) 8981, https://doi.org/10.5281/zenodo.13384825.

[213] D.S. Müller, O. Baslé, M. Mauduit, A tutorial review of stereoretentive olefin metathesis based on ruthenium dithiolate catalysts, Beilstein J. Org. Chem. 14 (2018) 2999–3010, https://doi.org/10.3762/bjoc.14.279.

[214] A. Poater, F. Ragone, A. Correa, A. Szadkowska, M. Barbasiewicz, K. Grela, L. Cavallo, Mechanistic insights into the *cis–trans* isomerization of ruthenium complexes relevant to catalysis of olefin metathesis, Chem. A Eur. J. 16 (2010) 14354–14364, https://doi.org/10.1002/chem.201001849.

[215] M.J. Koh, R.K.M. Khan, S. Torker, M. Yu, M.S. Mikus, A.H. Hoveyda, High-value alcohols and higher-oxidation-state compounds by catalytic Z-selective cross-metathesis, Nature 517 (2015) 181–186, https://doi.org/10.1038/nature14061.

[216] A. Correa, L. Cavallo, The elusive mechanism of olefin metathesis promoted by (NHC)Ru-based catalysts: a trade between steric, electronic, and solvent effects, J. Am. Chem. Soc. 128 (2006) 13352–13353, https://doi.org/10.1021/ja064924j.

[217] T.S. Ahmed, R.H. Grubbs, A highly efficient synthesis of *Z*-macrocycles using stereoretentive, ruthenium-based metathesis catalysts, Angew. Chem. Int. Ed. 56 (2017) 11213–11216, https://doi.org/10.1002/anie.201704670.

[218] A.M. Johns, T.S. Ahmed, B.W. Jackson, R.H. Grubbs, R.L. Pederson, High trans kinetic selectivity in ruthenium-based olefin cross-metathesis through stereoretention, Org. Lett. 18 (2016) 772–775, https://doi.org/10.1021/acs.orglett.6b00031.

[219] T. Wang, Q. Xie, W. Guo, S. Wu, H. Zhang, J. Wang, B. Wu, A 3,4-dimercapto-3-cyclobutene-1,2-dione-chelated ruthenium carbene catalyst for Z -stereoretentive/stereoselective olefin metathesis, Dalton Trans. 48 (2019) 6473–6483, https://doi.org/10.1039/C9DT01016E.

[220] T. Wang, Q. Xie, W. Guo, S. Wu, H. Zhang, J. Wang, Synthesis and evaluation of naphthalene-1, 8-dithiolate chelating ruthenium carbene catalyst for Z-stereoretentive olefin metathesis, J. Organomet. Chem. 880 (2019) 62–67, https://doi.org/10.1016/j.jorganchem.2018.10.035.

[221] H. Zhang, J. Zhang, P. Ma, T. Wang, J. Wang, Synthesis and catalysis of a Z-stereoretentive ruthenium carbene catalyst chelated by 2,4,5,7-tetrachloro-1,8-dimercaptonaphthalene for olefin metathesis, New J. Chem. 46 (2022) 7669–7674, https://doi.org/10.1039/D2NJ00025C.

[222] J.P. Martínez, M. Solà, A. Poater, Predictive catalysis in olefin metathesis with Ru-based catalysts with annulated C60 fullerenes in the N-heterocyclic carbenes, Chem. A Eur. J. 27 (2021) 18074–18083, https://doi.org/10.1002/chem.202100840.

[223] J.P. Martínez, S.V.C. Vummaleti, L. Falivene, S.P. Nolan, L. Cavallo, M. Solà, A. Poater, In silico olefin metathesis with Ru-based catalysts containing N-heterocyclic carbenes bearing C_{60} fullerenes, Chem. A Eur. J. 22 (2016) 6617–6623, https://doi.org/10.1002/chem.201600383.

[224] R. Monreal-Corona, A. Pla-Quintana, A. Poater, Predictive catalysis: a valuable step towards machine learning, Trends Chem. 5 (2023) 935–946, https://doi.org/10.1016/j.trechm.2023.10.005.

[225] S. Escayola, N. Bahri-Laleh, A. Poater, $\%V_{Bur}$ index and steric maps: from predictive catalysis to machine learning, Chem. Soc. Rev. 53 (2024) 853–882, https://doi.org/10.1021/acsomega.9b00916.

[226] A. Poater, S.V.C. Vummaleti, E. Pump, L. Cavallo, Comparing Ru and Fe-catalyzed olefin metathesis, Dalton Trans. 43 (2014) 11216–11220, https://doi.org/10.1021/acs.inorgchem.6b01755.

[227] J. Pecak, R.A. Talmazan, D. Svatunek, K. Kirchner, M. Podewitz, Is Mn(I) more promising than Fe(II)—a comparison of Mn vs Fe complexes for olefin metathesis, Organometallics 43 (2024) 457–466, https://doi.org/10.1021/acs.organomet.3c00398.

[228] É. De Brito Sá, L. Rodríguez-Santiago, M. Sodupe, X. Solans-Monfort, Toward olefin metathesis with iron carbene complexes: benefits of tridentate σ-donating ligands, Organometallics 35 (2016) 3914–3923, https://doi.org/10.1021/acs.organomet.6b00641.

[229] D.S. Belov, L. Mathivathanan, M.J. Beazley, W.B. Martin, K.V. Bukhryakov, Stereospecific ring-opening metathesis polymerization of norbornene catalyzed by iron complexes, Angew. Chem. 133 (2021) 2970–2974, https://doi.org/10.1002/ange.202011150.

[230] S. Takebayashi, M.A. Iron, M. Feller, O. Rivada-Wheelaghan, G. Leitus, Y. Diskin-Posner, L.J.W. Shimon, L. Avram, R. Carmieli, S.G. Wolf, I. Cohen-Ofri, R. A. Sanguramath, R. Shenhar, M. Eisen, D. Milstein, Iron-catalysed ring-opening metathesis polymerization of olefins and mechanistic studies, Nat. Catal. 5 (2022) 494–502, https://doi.org/10.1038/s41929-022-00793-4.

[231] S. Guidone, O. Songis, F. Nahra, C.S.J. Cazin, Conducting olefin metathesis reactions in air: breaking the paradigm, ACS Catal. 5 (2015) 2697–2701, https://doi.org/10.1021/acscatal.5b00197.

[232] A. Brotons Rufes, J.P. Martínez, N. Joly, S. Gaillard, J.-L. Renaud, S. Posada Pérez, A. Poater, First row transition metals in olefin metathesis: the role of iron and manganese, ChemCatChem (2025) e00570, https://doi.org/10.1002/cctc.202500570.

[233] E.L. Rosen, C.D. Varnado Jr., K. Arumugam, C.W. Bielawski, Metal-centered oxidations facilitate the removal of ruthenium-based olefin metathesis catalysts, J. Organomet. Chem. 745-746 (2013) 201–205, https://doi.org/10.1016/j.jorganchem.2013.07.063.

[234] A. Sytniczuk, A. Kajetanowicz, K. Grela, "Inverted" cyclic(alkyl)(amino)carbene ligands allow olefin metathesis with ethylene at parts-per-billion catalyst loading. Chem Catal. 3 (2023) 100713. doi:https://doi.org/10.1016/j.checat.2023.100713.

[235] P.I. Jolly, A. Marczyk, P. Małecki, D. Trzybiński, K. Woźniak, A. Kajetanowicz, K. Grela, Specialized olefin metathesis catalysts featuring unsymmetrical N-heterocyclic carbene ligands bearing N-(fluoren-9-yl) arm, Catalysts 10 (2020) 599, https://doi.org/10.3390/catal10060599.

[236] M. Nagyházi, Á. Lukács, G. Turczel, J. Hancsók, J. Valyon, A. Bényei, S. Kéki, R. Tuba, Catalytic decomposition of long-chain olefins to propylene via isomerization-metathesis using latent bicyclic (alkyl)(amino)carbene-ruthenium olefin metathesis catalysts, Angew. Chem. Int. Ed. 61 (2022) e202204413, https://doi.org/10.1002/anie.202204413.

[237] A. Kajetanowicz, M. Chwalba, A. Gawin, A. Tracz, K. Grela, Non-glovebox ethenolysis of ethyl oleate and fame at larger scale utilizing a cyclic (alkyl)(amino)carbene ruthenium catalyst, Eur. J. Lipid Sci. Technol. 122 (2020) 1900263, https://doi.org/10.1002/anie.201612373.

[238] R. Gawin, A. Kozakiewicz, P.A. Guńka, P. Dąbrowski, K. Skowerski, Bis(cyclic alkyl amino carbene) ruthenium complexes: a versatile, highly efficient tool for olefin metathesis, Angew. Chem. Int. Ed. 56 (2017) 981–986, https://doi.org/10.1002/ejlt.201900263.

[239] O. Eivgi, A. Vaisman, N.G. Lemcoff, Latent, yet highly active photoswitchable olefin metathesis precatalysts bearing cyclic alkyl amino carbene (CAAC)/phosphite ligands, ACS Catal. 11 (2021) 703–709, https://doi.org/10.1021/acscatal.0c04909.

[240] K. Kundu, J.V. Musso, M.J. Benedikter, W. Frey, K. Gugeler, J. Kästner, M. R. Buchmeiser, Neutral and cationic molybdenum imido alkylidene cyclic alkyl amino carbene (CAAC) complexes for olefin metathesis, Chem. A Eur. J. 29 (2023) e202301818, https://doi.org/10.1002/chem.202301818.

[241] K.-Y. Yoon, J. Noh, Q. Gan, J.P. Edwards, R. Tuba, T.-L. Choi, R.H. Grubbs, Scalable and continuous access to pure cyclic polymers enabled by 'quarantined' heterogeneous catalysts, Nat. Chem. 14 (2022) 1242–1248, https://doi.org/10.1038/s41557-022-01034-8.

[242] E.-H. Kang, I.S. Lee, T.-L. Choi, Ultrafast Cyclopolymerization for polyene synthesis: living polymerization to dendronized polymers, J. Am. Chem. Soc. 133 (2011) 11904–11907, https://doi.org/10.1021/ja204309d.

[243] G.I. Peterson, S. Yang, T.-L. Choi, Synthesis of functional polyacetylenes via cyclopolymerization of diyne monomers with Grubbs-type catalysts, Acc. Chem. Res. 52 (2019) 994–1005, https://doi.org/10.1021/acs.accounts.8b00594.

[244] D. Sivanesan, B. Seo, C.-S. Lim, H. Kim, H.-G. Kim, Intramolecular hydrogen-bond-based latent initiator for olefin metathesis polymerization, Organometallics 40 (2021) 314–323, https://doi.org/10.1021/acs.organomet.0c00527.

[245] A. Brotons-Rufes, N. Bahri-Laleh, A. Poater, H-bonding leading to latent initiators for olefin metathesis polymerization, Faraday Discuss. 244 (2023) 252–268, https://doi.org/10.1039/D2FD00163B.

[246] A. Vaisman, Y. Vidavsky, M. Baranov, A. Lehrer, J.H. Baraban, N.G. Lemcoff, Latency for all: enabling latency of Hoveyda−Grubbs second-generation catalysts by adding phosphite ligands, J. Am. Chem. Soc. 146 (2024) 73–78, https://doi.org/10.1021/jacs.3c10826.

[247] A. Poater, E. Pump, S.V.C. Vummaleti, L. Cavallo, The right computational recipe for olefin metathesis with Ru-based catalysts: the whole mechanism of ring-closing olefin metathesis, J. Chem. Theory Comput. 10 (2014) 4442–4448, https://doi.org/10.1021/ct5003863.

[248] P.E. Romero, W.E. Piers, Mechanistic studies on 14-electron ruthenacyclobutanes: degenerate exchange with free ethylene, J. Am. Chem. Soc. 129 (2007) 1698–1704, https://doi.org/10.1021/ja0675245.

Glossary

BVE: Butyl Vinyl Ether
CAAC: Cyclic (Alkyl)(Amino)Carbenes
CM: Cross-Metathesis
DEDAM: Diethyl-Diallyl Malonate
DFT: Density Functional Theory
DMAN: 1,8-Bis(Dimethylamino)Naphthalene
EVE: Ethyl Vinyl Ether
HG: Hoveyda-Grubbs
IMes: 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene
IPr: 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
LUMO: Lowest Unoccupied Molecular Orbital
NHC: Nitrogen-Heterocyclic Carbene
NMR: Nuclear Magnetic Resonance
RCM: Ring-Closing Metathesis
ROMP: Ring-Opening Metathesis Polymerization
SIMes: 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene