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Towards Highly Active and Robust Alkyne Metathesis Catalysts: Recent Developments in Catalyst Design**

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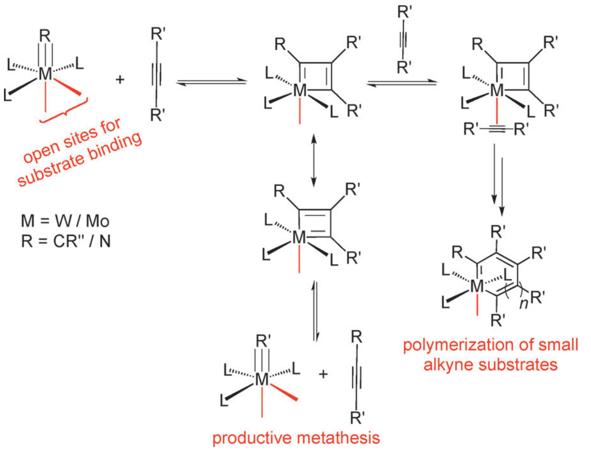
Though alkyne metathesis has crossed several barriers after the initial discovery of the heterogeneous catalyst system based on tungsten oxide and silica, it is still in its infancy as a synthetic method.[1] It is highly desired to develop a catalyst that can operate under ambient conditions and tolerate air and moisture without compromising the metathesis activity and functional-group compatibility.[1,2] This Highlight is intended to showcase some recent developments in the catalyst design and spotlight the immense potential of this unique multi-bond-exchange reaction.

Subsequent to the discovery of the Mortreux system consisting of $[Mo(CO)_6]$ and phenol additives,[1,3] Schrock and co-workers pioneered the development of metal alkylidyne complexes, such as the prototype neopentylidyne complex $[Me_3CC{\equiv}W(OCCMe_3)_3]$.[2,4] Since then, a significant number of reports have appeared in the literature regarding the synthesis and applications of several molybdenum- and tungsten-based alkylidyne complexes, including solid-supported catalysts.[2,4–9] The Mo^{III} trisamido species $[Mo(NArR)_3]$ (Ar = 3,5-dimethylphenyl, R = *tert*-butyl), initially developed by Cummins and co-workers,[5] has received particular attention, as it can serve as the precursor to metathesis-active catalysts, either by in situ activation using dichloromethane,[6] leading to the formation of mixed species such as $[MoCl(NArR)_3]$ and $[MoCH(NArR)_3]$, or by a reductive recycling approach[7] in the presence of excess of magnesium and $R'CHCl_2$ ($R' = H$, Me, Et) to generate the corresponding alkylidyne $[Mo(CR')(NArR)_3]$. The alkylidyne $[Mo(CR')(NArR)_3]$ reacts with substituted phenols and generates highly active catalysts in situ and has been successfully employed in the synthesis of conjugated polymers and shape-persistent macrocycles with high efficiency.[2d,7,8] The alkylidyne was also grafted onto silica and polyhedral oligomeric silsesquioxane (POSS), a homogeneous mimic of silica, where the silanols replace the aniline ligands and the resulting catalyst system is reported to have high stability, presumably owing to the greatly minimized bimolecular decomposition pathway of the catalyst.[9] In addition, the polymerization of small alkyne substrates (Scheme 1) such as 2-butyne, the common metathesis by-product of propynyl substrates, can also be inhibited, as the bulky POSS spatially blocks concurrent substrate binding at the two open binding sites of the hexavalent molybdenum and tungsten centers. However, lack of structural tunability represents a potential drawback of this silica-based heterogeneous catalyst system.



Scheme 1. Postulated mechanism of alkyne metathesis and the polymerization of small alkyne substrates.

Over the past two decades, even though the alkylidyne-based alkyne metathesis catalysts have shown great promise, many serious issues remained unsolved, such as their high sensitivity to air and moisture, incompatibility with terminal alkyne substrates, low or no reactivity towards heterocyclic substrates, and the undesired polymerization of small alkyne substrates by homogeneous catalyst systems, except the POSS-based catalyst. Below, we focus on some recent findings in catalyst ligand design, particularly those studies probing the electrophilicity as well as the substrate binding sites in the central transition metal (Mo or W), which can shed light on solving some of the issues listed above and would help in the design of highly active alkyne metathesis catalysts. Furthermore, recent use of alkyne metathesis catalysts to realize living ring-opening alkyne metathesis polymerization (ROAMP) for the first time is also covered, for which the judicious selection of suitable ligand is shown to have direct impact on controlling the polydispersity, thus further illustrating the importance of tuning the catalyst activity through rational ligand design.

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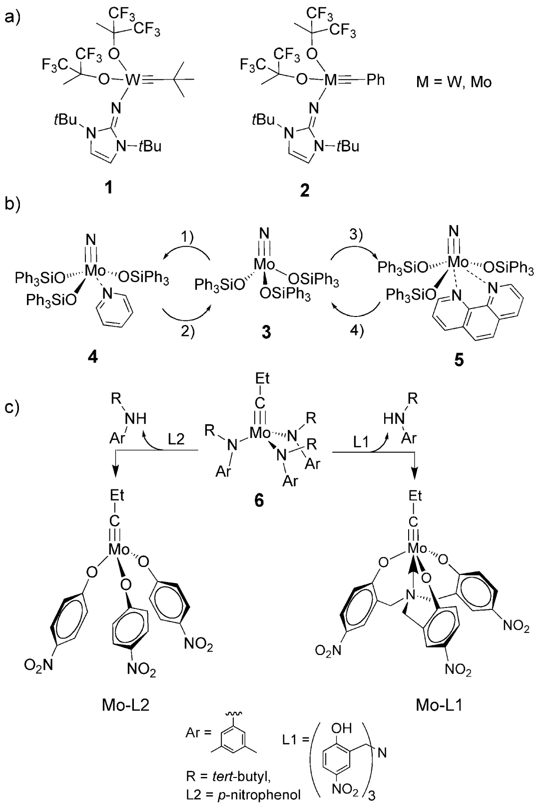
Among the variants of the Schrock-type alkylidyne complexes, the imidazolin-2-iminatotungstenneopentylidyne complexes such as **1** and **2** (Scheme 2a) recently reported by Tamm and co-workers display high catalytic activity in a variety of metathesis reactions at ambient temperature and with low catalyst loadings.[10] The approach of introducing imidazolin-2-imide ligands is based on the strong electron-donating capacity of the imidazolium ring towards the Mo or W center. Theoretical calculations showed that the combination of electron-withdrawing alkoxides, such as hexafluoro-*tert*-butoxide, with strongly electron-donating imidazolin-2-imide ligands provides a proper balance between the stability and the electrophilicity of the resulting tungsten alkylidyne complexes of type **1**. A comparison of the metathesis activity of the W and Mo benzylidyne complexes of type **2** showed superior performance for the tungsten system. Such an observation is in agreement with the DFT studies, which show a higher activation barrier for the Mo complex. This result can be rationalized when the higher Lewis acidity of W compared to Mo is taken into consideration. The higher activation barrier for the molybdenum-based catalyst system is presumably due to the electron-rich imidazoline ligand, which lowers the electrophilicity of the already less Lewis acidic Mo and thus the catalytic performance.



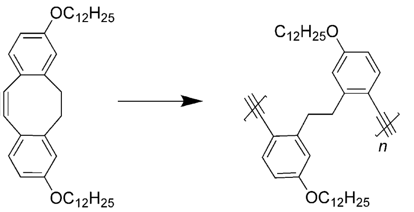
Scheme 2. Some recently developed alkyne metathesis catalysts: a) Tungsten/molybdenum carbynes containing imidazolin-2-imide ligands. b) Preparation of air-stable molybdenum nitride complexes and their in situ activation using chemical and thermal stimuli; 1) pyridine (5 equiv); 2) 80 °C; 3) 1,10-phenanthroline; 4) $MnCl_2$, toluene, 80–100 °C. c) In situ generation of the multidentate catalyst from the trisamido Mo^{VI} propylidyne precursor **6**.

Other than the alkylidynes, Fürstner and co-workers obtained some outstanding results from molybdenum nitride complexes containing triphenyl siloxide ligands (Scheme 2b).[11] Complexation of the active siloxide complexes with 1,10-phenanthroline can preserve the catalyst and make it indefinitely stable in air. These phenanthroline adducts are per se unreactive with alkynes, but the catalytic activity can be restored upon exposure to certain metal salts, such as $MnCl_2$, $FeCl_2$, $FeCl_3$, $MgCl_2$, and $CoCl_2$, which can form stable complexes with phenanthroline. The activation of the complex can be performed in situ, either before the addition of the substrate or in the presence of the substrate. Lower stability under atmospheric conditions was observed for some of the pyridine adducts of the triphenyl siloxide complexes (e.g. **4**) that are sufficiently stable to be weighed in air, and the catalytic activity can be restored by heating at 80 °C, leading to the decomplexation of pyridine. Although the phenanthroline adducts of the molybdenum nitride complexes exhibit very high stability under atmospheric conditions, their metathesis activity is not excellent. Furthermore, some of the molybdenum nitride complexes react stoichiometrically with aldehydes and acid chlorides to give the corresponding nitriles.[11] The phenanthroline adducts of the benzylidyne complexes containing siloxide ligands, however, showed significantly enhanced metathesis activity, although their stability under atmospheric conditions is less than that of the corresponding nitride complexes. A series of representative alkyne metathesis reactions showed the remarkable metathesis activity and the practical application of these new catalysts. These Mo^{VI} nitride–phenanthroline based complexes are the first known alkyne metathesis catalysts to date that combine both stability under atmospheric conditions and good catalytic activity upon in situ activation.

Although current alkyne metathesis catalyst design is predominated by the use of monodentate ligands, in an attempt to study the effect of a multidentate ligand on the catalytic performance of molybdenum alkylidynes, we synthesized a Mo^{VI} propylidyne catalyst containing a substituted triphenolamine ligand (Scheme 2c).[12] Intriguingly, the new multidentate catalyst (Mo-L1) showed significantly enhanced catalytic activity, longer lifetime, and broader substrate scope than the corresponding catalyst containing the analogous monodentate ligands (Mo-L2), thus substantiating the advantages of the multidentate ligand design strategy. The most attractive feature of Mo-L1 is the high metathesis activity towards many challenging substrates, such as those containing nitro and aldehyde functional groups. Furthermore, with one substrate binding site blocked by the multidentate ligand, the undesired polymerization of small alkynes is completely inhibited. The new design strategy relies on the fact that the polymerization side reaction requires two substrate binding sites available at the metal center of the catalyst to allow the "ring expansion" mechanism to occur (Scheme 1).[7b] Therefore, we hypothesized that the trigonal-pyramidal geometry of the central amine would facilitate the effective coordination of the three phenol moieties to the Mo center, with the three methylene units blocking one substrate binding site of the Mo center. The single-crystal X-ray structure analysis as well as the characterization by ^{15}N NMR spectroscopy confirmed the coordination of the central nitrogen atom to the Mo center both in the solid state and in solution. The high catalytic activity of the multidentate catalyst system is attributed to two major factors: 1) stronger complexation offered by the multidentate ligand (entropy-favored) in comparison to a monodentate ligand, thus making the catalyst more robust and elongating its life time; and 2) spatial blocking of one substrate binding site of the molybdenum alkylidyne complex completely inhibits the undesired alkyne polymerization and also greatly minimizes the nonproductive substrate binding, thus enabling the metathesis of heterocycles containing donor moieties.

The great importance of ligand design and selection is also shown in polymer chemistry. The first living ring-opening alkyne metathesis polymerization (ROAMP, dibenzo[8]annulene substrates), which is catalyzed by a system consisting of the trisamido Mo^{VI} propylidyne **6** and electron-deficient phenol ligands, was recently reported by Nuckolls and coworkers (Scheme 3).[13] The commercially available Schrock tungsten catalyst $[(t\text{BuO})_3\text{W}{\equiv}\text{C}t\text{Bu}]$ showed cross-metathesis reactions between internal triple bonds in the polymer backbone ("back-biting"), thus leading to broadening of the molecular-weight distribution. The key requirement to prevent chain transfer and the resulting increase in the polydispersity is to find a catalyst system that can selectively react with strained alkynes over internal alkynes. In this context, a series of alcohols and phenols (e.g., 2-nitrophenol, 2-naphthol, phenol, *tert*-butyl alcohol, etc.) were screened in combination with the trisamido Mo^{VI} propylidyne precursor for the ROAMP reaction of dibenzo[8]annulene **7**. A polydispersity index (PDI) close to 1.0 was achieved by using 2- and 3-nitrophenol and 3,5-bis(trifluoromethyl)phenol, while other alcohols and phenols showed higher PDIs. Although no direct correlation between the $\mathrm{p}K_\mathrm{a}$ values of the various alcohols and phenols and the catalyst performance in polymerization reactions is observed, this catalyst system, to a certain extent, addresses the long-standing question about the possibility of achieving alkylidyne-catalyzed living ROAMP reactions.

In summary, the recent findings highlighted herein show that proper balance of the electrophilicity and the number of available substrate binding sites at the transition-metal (Mo/W) center as well as catalyst complexation with heterocyclic donor ligands can play key roles in improving the catalyst metathesis activity, substrate scope, and tolerance to atmospheric conditions. Alkylidyne-catalyzed living ROAMP reactions can also be realized by suitable design and selection of catalyst systems. Thus, judicious rational design of ligands can give access to highly active alkyne metathesis catalysts and tackle many of the current problems associated with alkylidyne-catalyzed metathesis reactions. Furthermore, these findings can open up many new possibilities for utilizing this powerful metathesis approach for the synthesis of a broad spectrum of ethynylene-containing novel polymers, macrocycles, and natural products, and, most importantly, the user-friendliness of the alkyne metathesis catalysts.



7 **8**

Scheme 3. ROAMP reaction of dibenzo[8]annulene **7**. Reaction conditions: $[(t\text{BuO})_3\text{W}{\equiv}\text{C}t\text{Bu}]$, toluene, 24 °C or $[(\text{N}(t\text{Bu})\text{Ar})_3\text{MoCCH}_2\text{CH}_3]$ (Ar = 3,5-dimethylphenyl), alcohol/phenol, toluene, 24 °C.

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