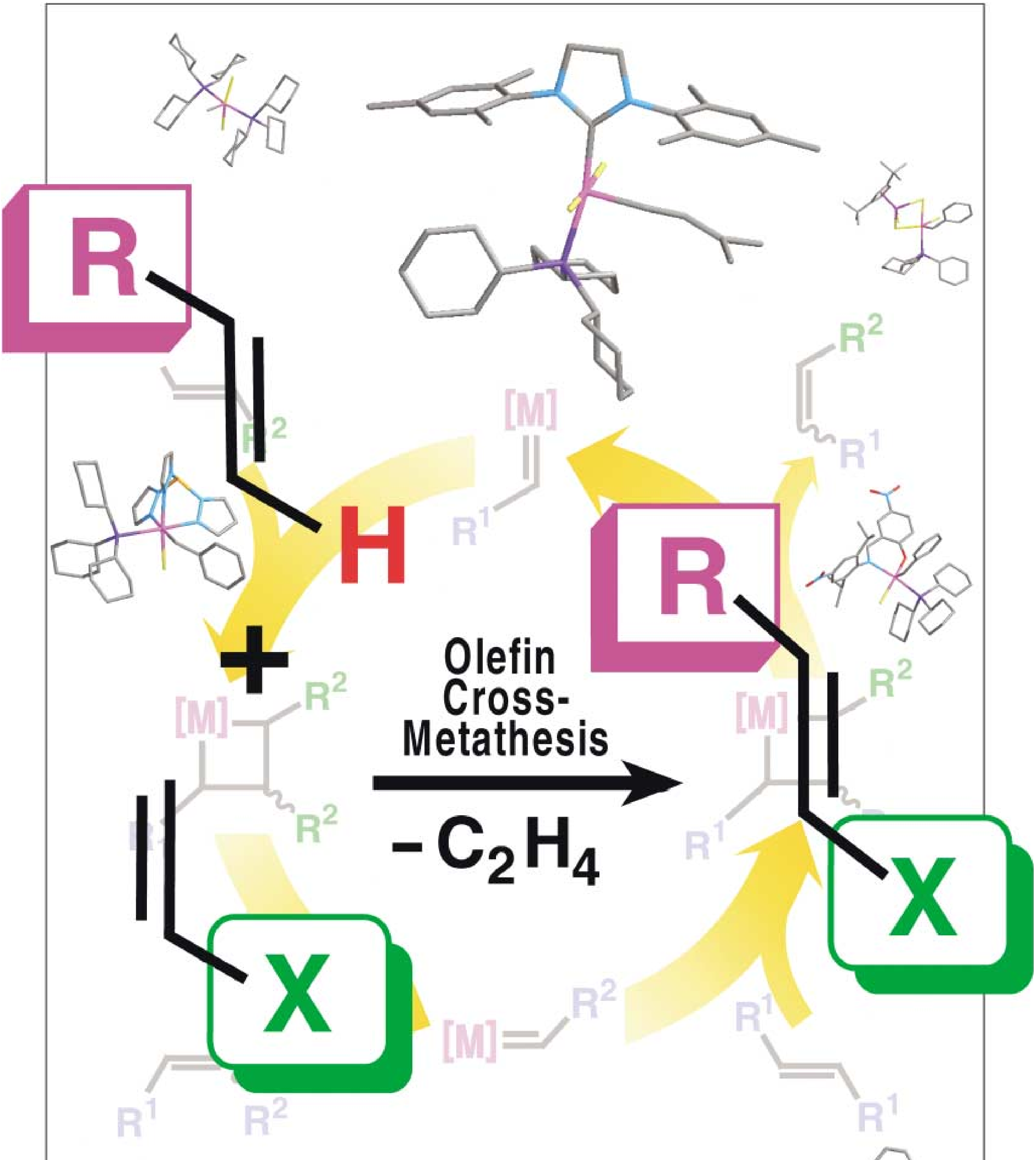
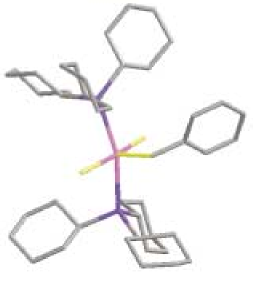


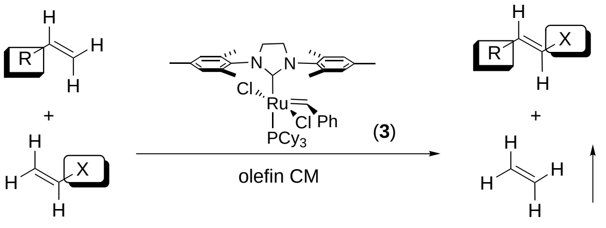
Olefin cross-metathesis (CM) represents an underdeveloped area of metathesis chemistry. Addressing issues of product selectivity and stereoselectivity are central to the utility of CM. Where selective reactions can be achieved, these reactions are formally equivalent to C–H activation of alkenes and selective allylic oxidation processes where only simple olefinic precursors are employed. For more information see the following pages.



# Formal Vinyl C–H Activation and Allylic Oxidation by Olefin Metathesis

Arnab K. Chatterjee and Robert H. Grubbs*

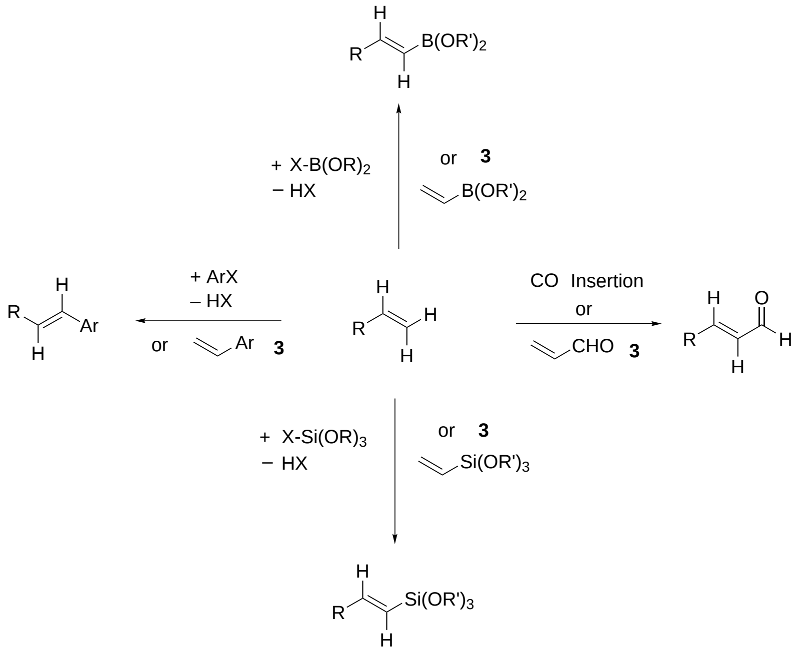
A general process for the substitution of C–H bonds of simple olefins and for the directed allylic oxidation of trisubstituted olefins would provide efficient new methods for the synthesis of complex molecules. Conceptually, many reactions in organic synthesis are analogous to C–H activation and directed oxidation processes. While a substantial amount of research has focused on these reactions, the recognition of (other) known reactions as formal processes towards the same products is also an important undertaking. Herein we describe olefin cross metathesis (CM) as a formal vinylic C–H activation or a formal allylic oxidation reaction.



Scheme 1. Direct cross-coupling of olefins.

With the advent of single-component functional-group-tolerant catalysts such as $[\mathrm{Mo(CHCMe_2Ph)(NAr)\{OCMe(CF_3)_2\}_2}]$ (**1**) and $[\mathrm{Ru(CHPh)(PCy_3)_2Cl_2}]$ (**2**), the olefin metathesis reaction has provided new methods for the construction of complex organic molecules by ring-closing metathesis (RCM) and ring-opening-metathesis polymerization (ROMP) and offers a unique solution for the substitution of alkene C–H bonds.[1] However, a transformation that is often overlooked is CM[2] of readily available α-olefins with simple functionalized olefins, and is presumably a consequence of the low catalytic activities of **1** and **2** towards intermolecular metathesis.[3] The advent of more active catalysts that still retain excellent functional-group compatibility (e.g. **3**),[4] has led to a reexamination of CM as a general synthetic reaction. With these more active catalysts, the range of functionalized products available by CM has been greatly expanded and a number of highly efficient CM transformations have been described.[5] For this reaction to reach its full potential, a general way of visualizing the reaction and the factors that control the yield and stereoselectivity of the desired cross products is required.

As shown in Scheme 1, CM affords the same products that would result from an analogous C–H activation/substitution pathway, combining both a α-olefin substituent (R) with a functional group (X). There are several similarities between this interpretation of CM and some C–H activation processes (e.g. arene borylation).[6] Both reactions can be driven to completion by the loss of a volatile gas: ethylene, propylene, or isobutylene in CM and molecular hydrogen in some cases of arene borylation. Furthermore, both reactions use widely available chemicals to provide synthetically useful functionalized products. It is noteworthy that when very good stereoselectivities are observed in CM, the obtained product can be considered formally to as a result of chemoselective C–H activation of a terminal methylene proton. Scheme 2 illustrates a variety of these chemoselective C–H-activation products that can are also accessible by CM, including some that are not accessible by other metal-catalyzed processes such as vinyl siloxane coupling[7] and CO insertion. The analogy between CM and C–H-activation processes allows for a conceptually new way of viewing CM, beyond a simple statistically governed scrambling of α-olefins. Additionally, in most cases, the metathesis reaction is milder and produces higher yields of the desired substituted product than of the corresponding C–H-substitution product. Therefore, CM can be viewed as a conceptual equivalent of a selective and general vinyl C–H-activation process to yield highly functionalized products.



Scheme 2. Substitution and insertion reactions by CM.

By a judicious choice of olefin partners, the regioselectivity of CM can be superior to that of other metal-catalyzed processes. In addition to using readily available olefins as *both* coupling components in place of reactive functionalities such as alkyl halides and aldehydes, these reactions also provide different (and in certain instances improved) regioselectivities that would not be obtained from addition reactions to alkyne functionalities. For example, the resulting regiospecificity

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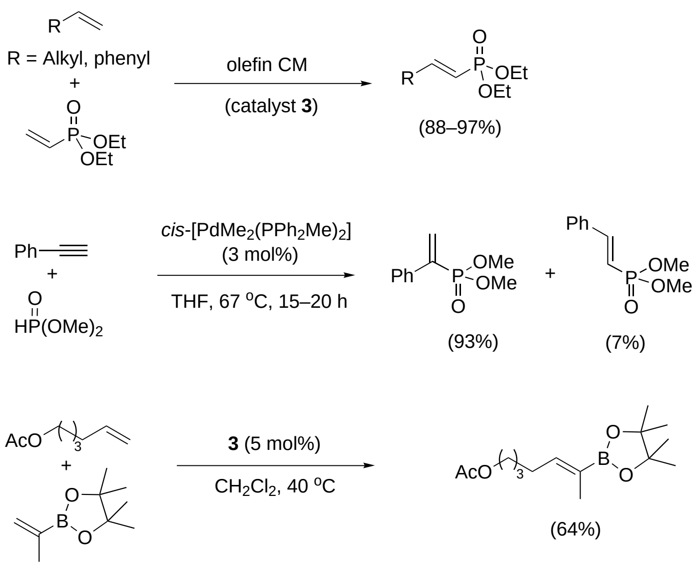
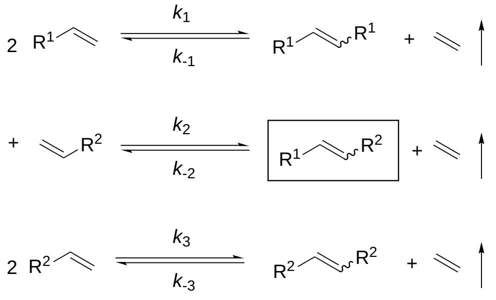


Scheme 3. Unique regioselectivity in olefin CM.

from CM routes is opposite to that from the hydrophosphorylation of alkynes (Scheme 3). The addition across terminal alkynes leads to mainly geminal 1,1-disubstituted product and only a small amount of the 1,2-disubstiuted product,[8] whereas the 1,2-disubstituted product can be directly accessed from CM of commercially available diethylvinylphosphonate with a variety of α-olefins in excellent yield. In addition, CM of 1,1-disubstituted vinyl borates is regiospecific, whereas the hydroboration reaction of the corresponding unsymmetrical internal alkyne provides a mixture of regioisomers.[9]

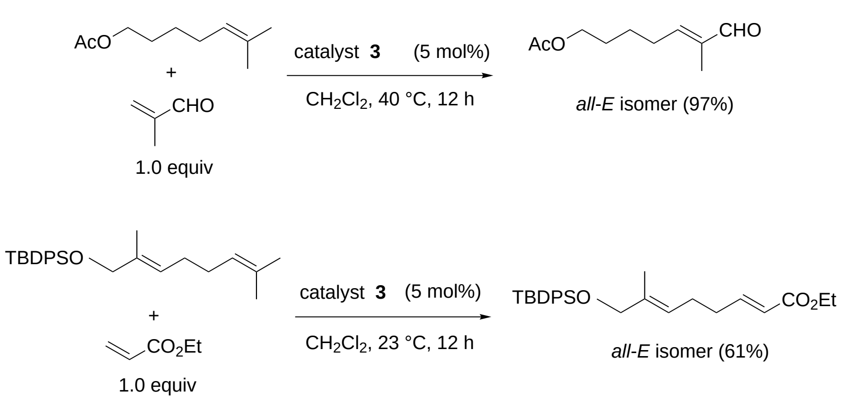
Earlier we demonstrated the CM of vinyl borates and vinyl siloxanes in the presence of catalyst **2**, but the range of substrates amenable to CM has been greatly expanded by using **3**. For example, trisubstituted[10] and α,β-unsaturated carbonyl-containing olefins are metathesis-active substrates in the presence of the more active catalyst **3**. This reaction provides a route to the apparent selective allylic oxidation of isoprenoid groups. For example, if a prenyl/isoprenoid olefin is treated with a functionalized olefin such as methacrolein, the overall transformation is the apparent oxidation of one of the *trans* terminal methyl groups (Scheme 4). Moreover, since the CM reaction can be conducted with acrylate esters, acids, and allylic alcohols, all oxidation states and desired protecting groups can be directly accessed without any protecting-group or oxidation-state adjustments of the products. Furthermore, by using bulky protecting groups within a single CM substrate, certain trisubstituted olefins can remain inert to the CM-reaction conditions.

For these CM-functionalization reactions to become generally useful, methods are required to increase the efficiency of these transformations. Traditionally, CM reactions are driven to the desired product by using an excess of the more readily available cross partner. Most other efficient cross-coupling strategies use differentiated functionalities such as vinyl stannanes and alkyl chlorides in Stille couplings to allow equal stoichiometry of reactants in the reaction. However, under certain circumstances CM reactions can be highly efficient with equal stoichiometries of reactants. In CM reactions there are three equilibria and six rate constants (Scheme 5). If the rates of all the reactions are similar or if the reaction is allowed to proceed for a long period of time, statistical ratios are obtained with nearly 50% yield of cross product. However, if one olefin forms the homodimer at a slower rate ($k_3$) than the other reactions (as a result of either steric or electronic factors) such that $k_1$, $k_{-1}$, $k_2$, $\gg k_3$, and all the possible ethylene is removed from the system such that all terminal olefins are consumed, then only the cross product is produced. These reaction conditions would allow much greater yields than the statistically predicted 50% CM product. Since the only pathway for loss of ethylene from the $R^2$-containing olefin is by CM with an $R^1$ olefin. The utility of this approach has been demonstrated in the cross-metathesis of α,β-unsaturated esters (Scheme 6) and quaternary allylic compounds (Scheme 6); steric or electronic factors result in the formation of the cross product in much higher yields than 50%, with excellent olefin stereoselectivity.

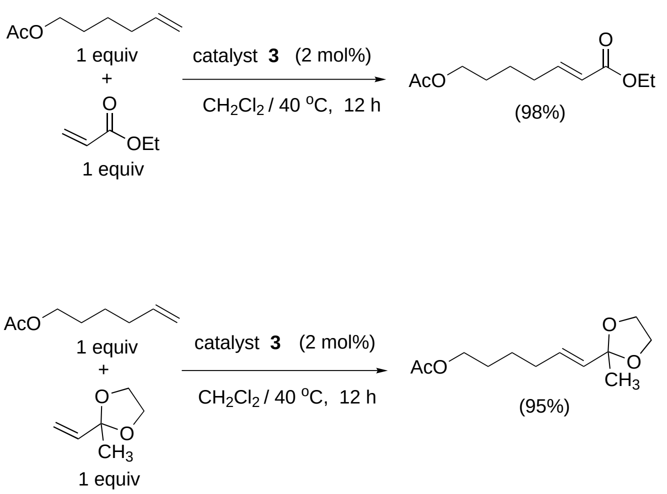


Scheme 5. Equilibria involved in olefin CM.

Stereoselective and chemoselective olefin CM provide new avenues for olefin metathesis to become useful in organic synthesis. In particular, CM can be viewed as a highly selective and efficient set of reactions that provide the same products as would selective C–H activation and allylic oxidation. As more active catalyst systems are discovered in the future, and thus a wider range of olefins can participate in CM, these reactions will provide an efficient process to functionalized products from readily available olefins.



Scheme 4. Selective allylic oxidation by olefin CM.



Scheme 6. Olefin CM with equal stoichiometry of substrates.

## *Experimental Section*

General procedure (Scheme 6): 5-Hexenyl-1-acetate (200 µL, 1.20 mmol, 1.0 equiv) and ethyl acrylate (130 µL, 1.20 mmol, 1.0 equiv) were added simultaneously by using a syringe to a stirred solution of **3** (20 mg, 0.024 mmol, 2.0 mol %) in $CH_2Cl_2$ (2.5 mL, 0.5 N in acrylate) under a nitrogen atmosphere. The flask was fitted with a condenser and heated at reflux under nitrogen for 12 hours. The reaction mixture was then concentrated in vacuo, and the residue was purified directly on a silica-gel column (2 × 10 cm), eluting with hexane/ethyl acetate (9:1) to provide the CM product as a clear colorless oil (253 mg, 1.18 mmol, 98 %).

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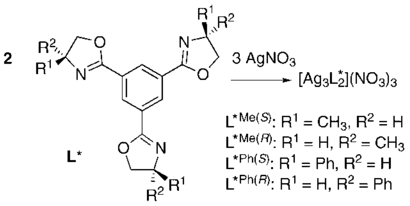
# An Enantiomerically Pure Propeller-Shaped Supramolecular Capsule Based on the Stereospecific Self-Assembly of Two Chiral Tris(oxazoline) Ligands around Three $Ag^I$ Ions**

Hae-Jo Kim, Dohyun Moon, Myoung Soo Lah, and Jong-In Hong*

The self-assembly of supramolecular structures by simply mixing ligands and labile metal ions has attracted considerable attention.[1] Among the self-assembled supramolecular capsules,[2] a few propeller-shaped structures have been described.[3] In most cases racemates were obtained; however, recently chiral ligands have been reported to induce enantiomerically pure supramolecular capsules and helical superstructures.[4] Herein we describe the completely stereospecific self-assembly of a propeller-shaped supramolecular capsule induced by a rigid chiral tris(oxazoline) unit acting as a tris-monodentate ligand and $Ag^I$ metal ions having tetrahedral coordination geometry. The stereochemistry arises from the self-recognition of the ligand chirality[5] during the self-assembly of the supramolecular capsule.

Chiral tris(oxazoline) ligands (L*) were used to induce a predetermined chiral helicity because it is easy to introduce chirality and rigidity within the self-assembled superstructure from simple chiral amino alcohols.[6] Simple mixing of $Ag^I$ ions and L* in a 3:2 ratio generated a single set of $^1$H NMR resonances, which implies the formation of only one self-assembled structure (Scheme 1). The stoichiometry of the complex was identified by electrospray ionization (ESI) mass spectrometry. In particular, examination of the isotope distribution of the peak at *m/z* 1101.0, attributable to either $\{[Ag_3L_2^{*Me}](NO_3)_2\}^+$ or $\{[Ag_6L_4^{*Me}](NO_3)_4\}^{2+}$, showed a peak spacing of one mass unit typical of a +1 charged species; this



Scheme 1. Self-assembly of L* and $Ag^I$ ions into a trinuclear complex.

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