

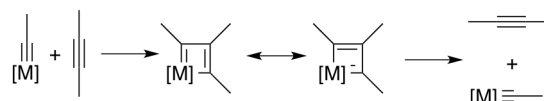
ALKYNE METATHESIS

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November 10th, 2014

INTRODUCTION

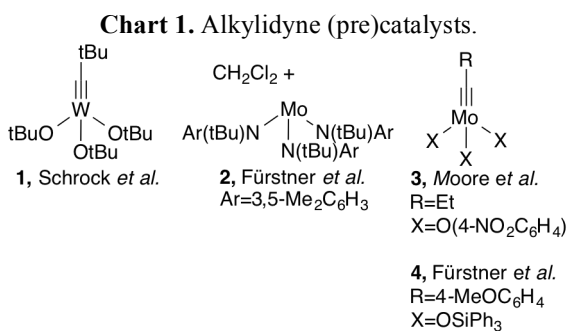
The metathesis of unsaturated carbon-carbon bonds has had a tremendous impact on organic and materials chemistry, making these bonds a unique point of retrosynthetic disconnection. Whereas olefin metathesis is a well-developed process, the analogous reaction of alkynes remains a lesser-studied transformation.¹ Shortly after the first reports of catalytic alkyne scrambling in the 1960s and 1970s, Katz and McGinnis proposed a mechanism in 1975 (Scheme 1).² This proposed mechanism gave way to an intense period of organometallic research in the 1980s, resulting in the development of highly active catalysts and strong mechanistic evidence.³ Despite these early advances, organic chemists have been reluctant to adopt this reaction into their research programs. However, with the recent development of highly active and functional group tolerant catalysts, alkyne metathesis has become a much more attractive transformation for use in synthesis.



Scheme 1. Mechanism of alkyne metathesis.

THE ADVENT OF WELL-DEFINED ALKYLIDYNE CATALYSTS

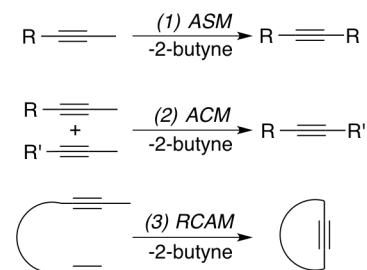
Early reports of alkyne metathesis employed “instant” catalysts formed *in situ* from Mo(CO)₆ and phenolic additives.⁴ Despite the attractiveness of this simple recipe, yields are modest, reactivity is



unpredictable, and the structure of the active catalyst is not fully understood, which limits the potential for rational catalyst development. Following Katz' proposal that a metal alkylidyne could be the active species, Schrock *et al.* reported catalyst **1** (Chart 1) and demonstrated its ability to scramble alkynes.³ Improved catalysts have since been developed by Moore *et al.* and Fürstner *et al.*^{5,6}

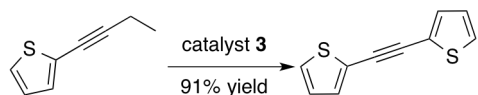
PREPARATIVE ALKYNE METATHESIS

Similar to olefin metathesis, alkyne metathesis falls into several categories, including (1) alkyne self metathesis (ASM), (2) alkyne cross metathesis (ACM) and (3) ring-closing alkyne metathesis (RCAM) (Scheme 2).¹ Several techniques have been developed to achieve useful yields for these processes. Moore *et al.* introduced a precipitation-driven



Scheme 2. Modes of metathesis.

strategy in which the alkyne byproduct precipitates from the reaction mixture.⁷ Fürstner *et al.* discovered that molecular sieves can absorb the small alkyne byproduct.⁶ The use of these techniques allows for preparative metatheses to become feasible on *nonterminal* alkynes. Catalysts **1** and **2** were shown by Fürstner *et al.* to be limited in scope due to their highly Lewis acidic metal centers. In 2004, Moore *et al.*

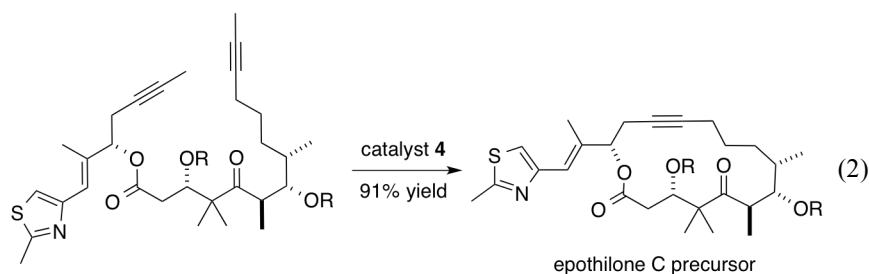


reported the highly active catalyst **3** (Chart 1).⁶ This catalyst is effective for ASM including challenging Lewis basic thiophenes (Eq. 1). This technology has been applied to the

synthesis of polythiophenes.⁸ Unfortunately, **3** can rapidly polymerize the small alkyne byproducts, thus necessitating modification of the substrates or catalyst.⁹

In 2010, Fürstner demonstrated RCAM on highly functionalized diynes using catalyst **4** (Chart 1).⁵ The catalyst is tolerant of a

number of reactive functional groups and affords cyclic alkyne products in excellent yields. In one example, a precursor to epothilone C is formed in a 91% yield (Eq. 2).



CONCLUSION AND FUTURE DIRECTIONS

With highly active and selective catalysts in hand, and an established mechanism, alkyne metathesis is poised to transform the fields of alkyne, macrocycle, and polymer synthesis. Future work should focus on the use of terminal alkyne substrates as these present unique challenges that only until very recently are being addressed.¹⁰ Additional research into the less defined catalyst systems (such as the “instant” Mo(CO)₆ derived catalysts) can provide insight into other mechanisms by which the metathesis can occur.

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