RUTHENIUM-CATALYZED *TRANS*-HYDROFUNCTIONALIZATION OF INTERNAL ALKYNES

Reported by Mikiko Okumura April 19, 2016

INTRODUCTION

The hydrofunctionalization of alkynes has been widely been used in organic synthesis as an efficient means to construct highly substituted alkenes.[1] In particular, regio- and stereoselective formation of vinyl-metal compounds such as vinylboranes, vinylsilanes, and vinlystannanes through hydrometalation is of high importance since these products have broad applications in variety of reactions, such as cross-coupling reactions. Semihydrogenation is also a well-known hydrofunctionalization process that leads to disubstituted alkenes. A number of catalytic methods to achieve *cis*-selective hydrofunctionalization through suprafacial delivery of the hydro-functional group across the alkyne triple bonds have been well studied and developed with high selectivity and functional group tolerance.[1] However, the significance of *trans*-selective hydrofunctionalizations has long been underestimated, and the developments of such processes are in most cases still limited to stoichiometric processes with harsh conditions, which diminishes its synthetic utility.[2]

TRANS-HYDROFUNCTIONALIZATIONS USING RUTHENIUM CATALYSTS

Pioneering work in catalytic *trans*-hydrofunctionalization of the internal alkynes was reported by the Trost group in 2002, with the development of *trans*-selective hydrosilylation of internal alkynes using $[Cp^*Ru(MeCN)_3]PF_6$ as a catalyst (Figure 1).[3] In this reaction, *trans*-hydrosilyated products were obtained exclusively, with no *cis*-addition product observed in any cases. This seminal discovery sparked the advancements made in catalytic *trans*-selective hydrofunctionalizations using ruthenium complexes. In 2013, the Fürstner group reported the catalytic *trans*-hydrogenation of internal alkynes using a [Cp*Ru(COD)Cl]/AgOTf system (Figure 1).[4] Excellent stereoselectivity, as well as functional group

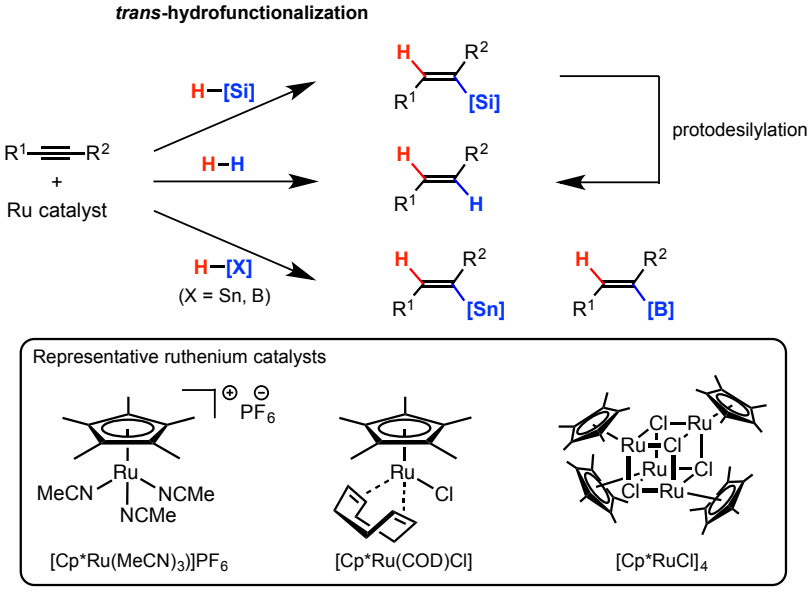
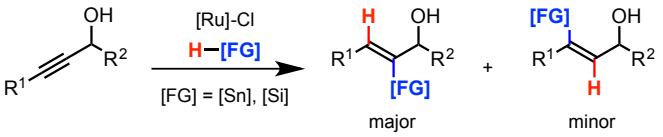


Figure 1. *trans*-Hydrofunctionalizations and representative ruthenium catalysts.

compatibility, were observed for many substrates, and the *cis*-hydrogenated products were not detected in all cases. This reaction system was further elaborated to *trans*-hydroborations[5] and *trans*-hydrostannations[6] (Figure 1). Furthermore, the resulting vinyl-metal compounds are highly valuable, and have already found applications to a number of natural product synthesis.[2] Although the regioselectivity of these reactions with unsymmetrical alkynes is typically governed by the steric nature of the substituents, it was later found that there is a profound directing effects by protic functional groups on the alkyne substrates that can control the regioselective outcome of *trans*-hydrostannations and *trans*-hydrosilylations with ruthenium catalyst bearing chloride ligands (Scheme 1).[7] These findings suggests a new opportunities for regio-controlled *trans*-hydrofunctionalizations.



Scheme 1. Directed *trans*-hydrofunctionalizations.

CONCLUSION AND FUTURE DIRECTIONS

The emergence of ruthenium-catalyzed *trans*-selective hydrofunctionalizations of internal alkynes has clearly provided new synthetic tools for chemists to access valuable substituted alkenes with high selectivity and functional group compatibility. The wide applicability of the resulting vinyl-metal compounds for further transformations also ensured their status as important transformations. However, since these methodologies are still in the early stages of development, there is room for further improvements. Broader substrate scopes for both alkynes and hydrofunctional groups are highly desirable, as these processes usually do not work for heteroatom-substituted or conjugated alkynes, and the scope of the hydrofunctional group is currently limited to the ones shown in Figure 1. Finally, further applications to natural product synthesis, especially in the context of late-stage diversity-orientated syntheses, would certainly provide additional momentum to this field.

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