

Isodesmic Functional Group Transfers of Olefins

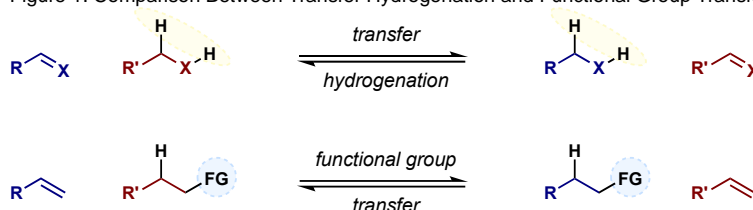
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April 17th, 2018

INTRODUCTION

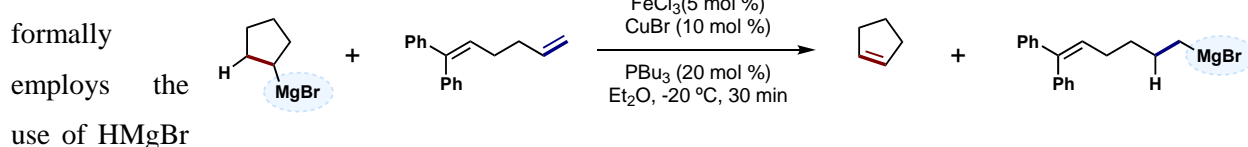
Isodesmic reactions are transformations in which the types of bonds broken in the reactants are the same as those formed in the products.¹ The last fifty years have seen tremendous advances in the uses and applications of isodesmic reactions, namely, olefin metathesis and transfer hydrogenation.² More recently, a new type of isodesmic reaction has emerged in which a functional group is transferred between olefins.² Analogous to transfer hydrogenation, isodesmic functional group transfer reactions consist of donor molecules which provide functional groups to be transferred, and acceptor molecules to which the functional group is added (Figure 1).² This mode of reactivity is not new, but has experienced a renaissance within the last five years, offering several potential advantages to traditional approaches which achieve the same transformation. Firstly, isodesmic functional group transfer can be used to avoid the use of potentially hazardous chemicals such as HCN, HCl, CO or SiH₄, which are instead incorporated into a donor molecule.² Secondly, these reactions can be used for functional groups which are either inaccessible or are only accessible under harsh conditions. Lastly, some isodesmic functional group transfers provide chemists with access to the reverse transformation, which can be strategically valuable in the context of synthesis.

Figure 1. Comparison Between Transfer Hydrogenation and Functional Group Transfer.



C-M BOND FORMATION:

First explored by Cooper and Finkbeiner in 1962,³ transfer hydromagnesiation of alkenes has been improved upon in recent years by Hayashi⁴ and Thomas.⁵ Catalyzed by titanium, iron, or copper, this reaction



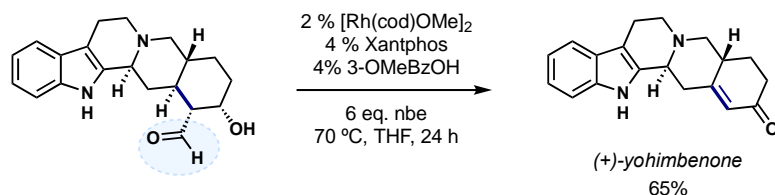
as a reagent. The products of the transfer hydromagnesiation are particularly useful for accessing products not obtainable via traditional Grignard reagent formation (Scheme 2).^{4,5} In 2002, Woerpel and coworkers established a protocol for a silver-catalyzed silacyclopropanation using cyclohexylsilylcyclopropane as a donor molecule.^{6,7} This method provides access to a wide variety of useful silylcyclopropanes without the use of dissolving metal reduction to form free silylene.^{6,7}

1,4-CYCLOHEXADIENES

Early work at the turn of the century by Walton⁸ and Studer⁹ demonstrated isodesmic functional group transfers using 1,4-cyclohexadienes as donor molecules. Owing to the low bond dissociation energy of bisallylic C-H bonds and the resonance stabilization of the resulting arene, these reactions proceed irreversibly to functionalize olefins with a number of a different functional groups.^{8,9} In 2013, Oestreich and coworkers reported an isodesmic hydrosilylation of alkenes using an aryl borane catalyst which significantly improved the known hydrosilylation.¹⁰ In 2014, this work was expanded to include SiH₄ surrogates, allowing mild access to trihydro-alkylsilanes.¹¹

C-C BOND FORMATION:

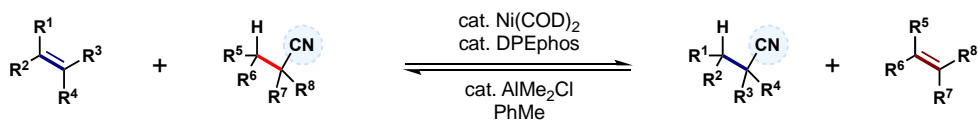
Following initial reports by Brookhart and Jun in 1999,^{12,13} Dong and coworkers disclosed an isodesmic transfer hydroformylation reaction in 2015.¹⁴ To demonstrate the mild conditions and an application of their method, Dong and coworkers used retrohydroformylation as their final step in the synthesis of yohimbenone (Figure 3).¹⁴



synthesis of yohimbenone (Figure 3).¹⁴ In 2016 Morandi and coworkers reported an analogous isodesmic transfer hydrocyanation reaction.¹⁵ Significantly, Morandi demonstrated

that both hydrocyanation and retrohydrocyanation were under thermodynamic control. This implies that the direction of the reaction relies simply on the choice of donor or acceptor molecule as a means of introducing a driving force to the forward or reverse reaction, respectively (Figure

Figure 4. General Transfer Hydrocyanation Reaction.



4).^{14,15} While these seminal reports are impressive and interesting, the concepts explored by functional group transfer continues to inspire the development of new methodologies in organic synthesis.

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