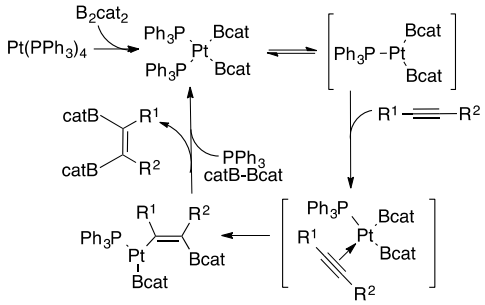
CATALYTIC, ENANTIOSELECTIVE DIBORATION OF ALKENES

Reported by Silvia C. Bobeica December 1st, 2014

INTRODUCTION

Methodology development for carbon-boron bond formation has been driven by the versatility of these bonds in many transformations, including amination, oxygenation and carbon-carbon bond formation.[1] Efficient catalytic, enantioselective processes using easily obtainable starting materials such as alkenes, to deliver diborated products that could be differentially functionalized are most sought after. Since the first report of a platinum-catalyzed *syn*-selective addition of a diboron compound to alkynes by Suzuki and Miyaura,[2] efforts have been directed at understanding the nature of the reactive catalyst and how to harness its reactivity toward alkenes. The catalytic cycle proposed by Suzuki and Miyaura was analyzed in stoichiometric experiments by Iverson and Smith and is presented in Scheme 1.[3] This mechanism offered two potential strategies to control enantioselectivity: the use of a chiral diboron compound and the use of a chiral catalyst. The first example of a modestly enantioselective platinum-catalyzed diboration of a terminal alkene was achieved using a platinum-dibenzylidene acetone complex and chiral diborane compounds.[4]

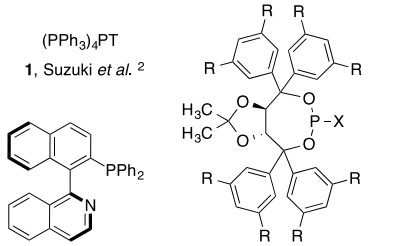


Scheme 1. Representative catalytic cycle for alkyne diboration.

RECENT DEVELOPMENTS

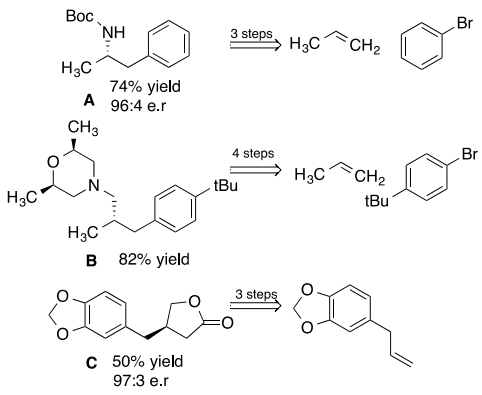
Morken and coworkers report the first practical catalytic enantioselective diboration of an alkene using Rh(I) complexes and chiral metal ligands. Although enantioselectivities range from modest to very good, not all tested substrates react consistently and some undergo unproductive β-hydride elimination leading to monoborated products in significant amounts.[5] Platinum complexes bearing TADDOL-derived ligands that have considerably better and predictable enantioselectivities have also been described and detailed mechanistic investigations have been performed with **4**.[6,7] Hydroxyl-directing groups can also control control alkene diboration stereoselectivity.[8] These stereocontrol elements allowed for diverse uses of vicinal boronates in synthesis.

Chart 1. Diboration catalysts



APPLICATIONS

Vicinal bis(boronate) compounds have been used the synthesis of complex targets[9] and novel tranformations of carbon-boron bonds are still being developed. Alkene diboration followed by oxidation to the 1,2 diol performed preferentially at the less sterically crowded alkene, provides a synthetic complement osmium-catalyzed dihydroxylation which occurs preferentially with electron rich, and therefore more substituted double bonds. Morken and coworkers illustrate the use of 1,2-bis(pinacolboronates) in cross-coupling reactions with organic electrophiles.[9] Using monochloroalkenes as coupling partners leads to homologation of the primary boronate to homoallylic alcohols, also important synthetic building blocks. Other representative examples of efficiently obtained synthetic targets include: chiral phenethylamines **A**, compounds with important pharmaceutical properties, fenpropimorph **B**, a potent fungicide or lignan lactone precursors **C**, building blocks for a class of compounds with diverse biological activities (Scheme 2).[9]



Scheme 2. Examples of complex synthetic targets achieved through cascades of diboration and cross-coupling.

CONCLUSION AND FUTURE DIRECTIONS

With the advent of practical enantioselective alkene diboration, vicinal bis(boronate) compounds have become retrosynthetic targets with important advantages such as availability of diverse, stereospecific transformations that can offer rapid access to complex structures, and complement already established methods such as dihydroxylation. More importantly, primary boronates can be converted selectively leaving the secondary boronate available for subsequent functionalization. An interesting, yet unreported transformation would be the conversion of 1,2-boronates to 1,2 diamines, a motif found in many medicinal agents and chiral ligands or auxiliaries.[10]

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