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Digest paper

Recent developments in asymmetric alkynylations

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ABSTRACT

Catalytic asymmetric syntheses of enantioenriched propargyl alcohols and amines have been a central topic in organic synthesis. Toward this, a great deal of research has been put forth to build synthetically useful chiral non-racemic organic molecules with propargyl functionality. In this digest article, we have summarized the recent advances in the catalytic enantioselective 1,2-alkynylation of carbonyls and imines, including poorly reactive α-ketoesters and α-ketimine esters.

Contents

Introduction

Enantioenriched propargyl alcohols and amines constitute an important class of compounds owing to their unique reactivity and applicability in complex molecule synthesis (Scheme 1).[1] The

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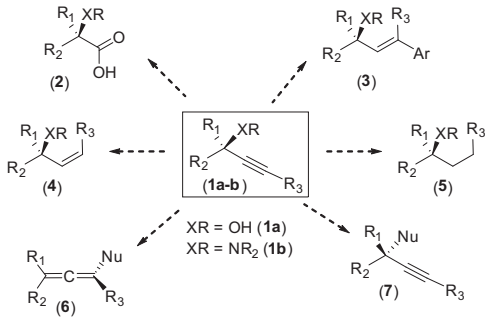
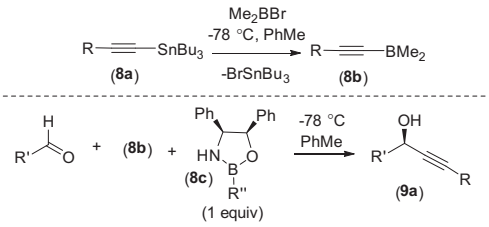
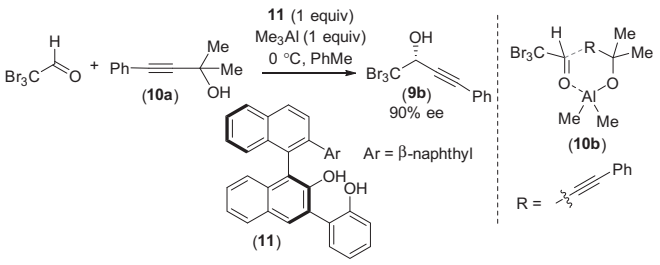


Scheme 1. Propargyl alcohols/amines as potential intermediates.



Scheme 2. Alkynyl borane addition onto aldehyde.



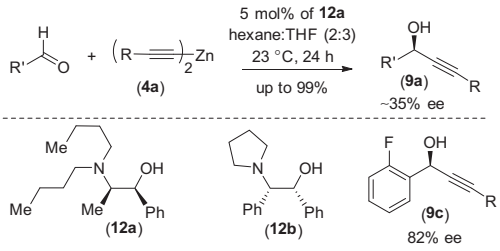
Scheme 3. Asymmetric alkynylation under MPV-condition.

alkynyl functionality derived from a direct addition of terminal alkyne onto carbonyls and imines provides a great synthetic platform for further derivation.[2] The addition of an acetylide gives an opportunity to adjoin two complex pieces while carrying out a convergent synthesis and generating a stereocenter. Accordingly, enantioselective preparation of chiral propargyl alcohols and amines has been a central topic in organic synthesis and this trend continues to facilitate the evolution of synthetic concepts and methodologies. In this digest, we focused on the recent advances on catalytic enantioselective 1,2-alkynylation of carbonyls and imines.

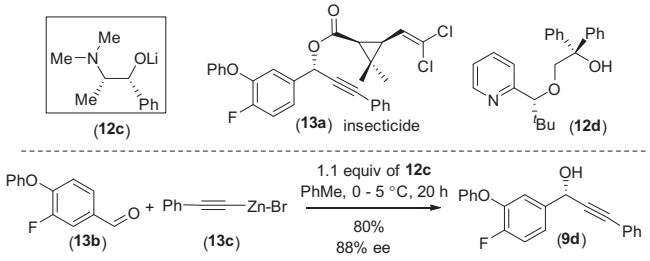
Catalytic enantioselective alkynylation of carbonyls

Catalytic asymmetric alkynylation of carbonyl compounds is one of the most efficient routes for the synthesis of optically active propargylic alcohols. Alkynylation of a ketone provides access to tertiary propargylic alcohols in enantioenriched form. These are useful and versatile building blocks for a variety of functionalized molecules, such as pharmaceutically important drug candidates as well as a number of biologically active natural products.[3] Initially stoichiometric amounts of metal reagents, such as organolithiums, have been used.[4]

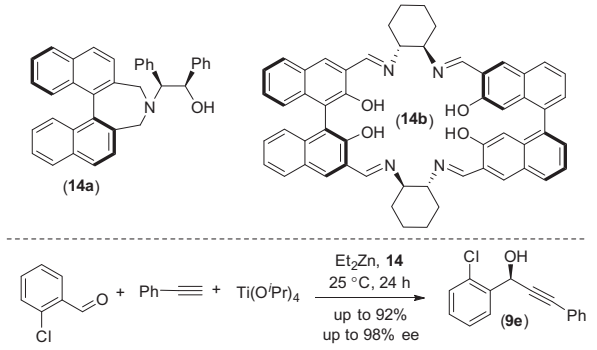
In 1994, Corey and Cimprich developed the asymmetric boron alkynylide addition to aldehydes in the presence of stoichiometric



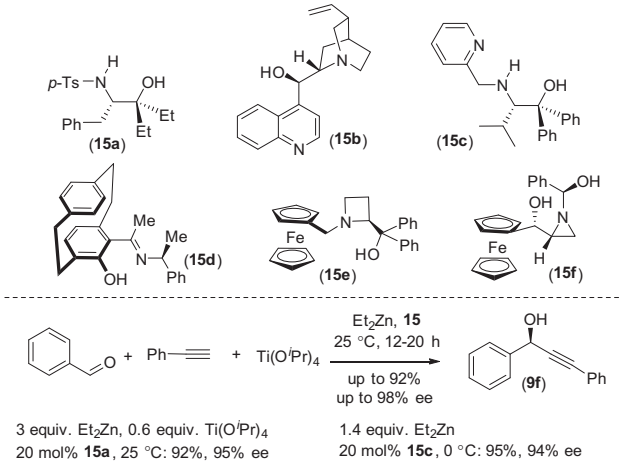
Scheme 4. Asymmetric alkynylation using aminoalcohol ligands.



Scheme 5. Asymmetric alkynylation with Zn-acetylide.



Scheme 6. BINOL-derived ligands in asymmetric alkynylation.



Scheme 7. Asymmetric alkynylation of benzaldehyde.

oxazaborolidine (Scheme 2).[5] In a one-pot procedure, bromodimethylborane was added to the alkynylstannane **8a** to generate the dimethyl-(alkynyl)borane **8b**. Oxazaborolidine **8c** was then added to the reaction mixture followed by an aldehyde. Excellent