

SYNLETT Spotlight

Diethylzinc

Compiled by Pierre-Georges Echeverria



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

Diethylzinc (ZnEt_2 , bp = 118 °C at 760 mmHg) is an inexpensive and commonly used diorganozinc reagent.¹ Due to its high pyrophoric nature, diethylzinc is often commercialized as a solution in organic solvent (hexane, toluene, or heptane).

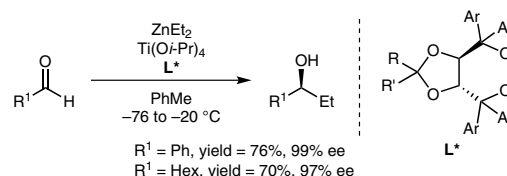
ZnEt_2 was first synthesized by Frankland in 1849 by heating ethyl iodide with zinc metal.² To facilitate purification,

other methods have been developed, such as the transmetalation of a zinc halide with an organometallic reagent.³ The use of this reagent has gained attention thanks to its application in asymmetric synthesis.

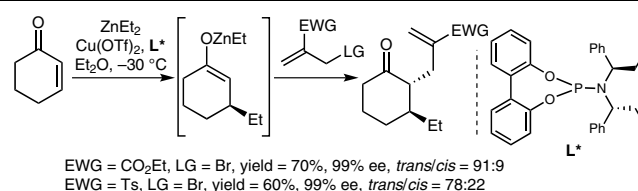
Diethylzinc is a versatile nucleophile that is suited for metal catalysis due to the highly covalent character of the carbon–zinc bond and the low Lewis acidity of zinc(II). Moreover, the empty low-lying *p*-orbitals allow facile transmetalation reactions.

Abstracts

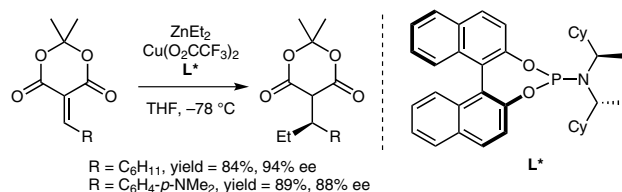
(A) *1,2-Addition*: Seebach and co-workers reported the 1,2-addition of diethylzinc to aliphatic and aromatic aldehydes in the presence of $\text{Ti}(\text{O}i\text{-Pr})_4$ and TADDOL derivatives as ligands, which led to enantiopure alcohols in good yields.⁴ Walsh and co-workers described also the synthesis of tertiary alcohols by the asymmetric addition of ZnEt_2 to ketones catalyzed by a titanium catalyst with a chiral diamine ligand.⁵



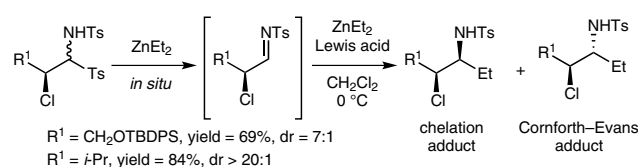
(B) *1,4-Addition to Cyclic Enones*: Alexakis and co-workers reported an asymmetric copper-catalyzed 1,4-addition of diethylzinc to cyclic enones using a phosphoramidite ligand, followed by C-enolate trapping resulting in the synthesis of α,β -disubstituted ketones with a high degree of stereoselectivity.⁶



(C) *1,4-Addition to Reactive Acceptors*: Carreira and co-workers developed the copper-catalyzed highly stereoselective conjugate addition of diethylzinc to Meldrum's acid derived acceptors with phosphoramidite ligands.⁷



(D) *Addition to α -Chloro Aldimines*: Walsh and co-workers described a highly diastereoselective synthesis of α -chloro amine *via* a nucleophilic addition to α -chiral imine derivatives that proceeds through an unusual chelation transition state instead of a Cornforth–Evans model.⁸



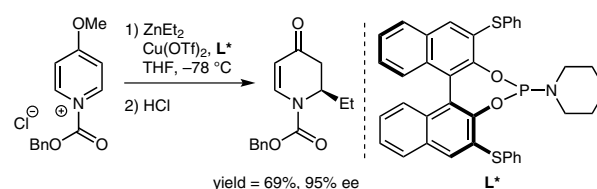
SYNLETT 2014, 25, 1937–1938

Advanced online publication: 07.07.2014

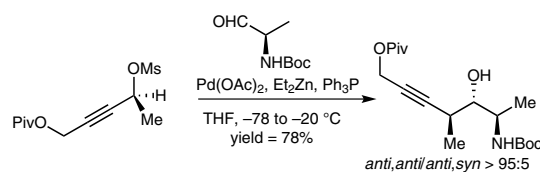
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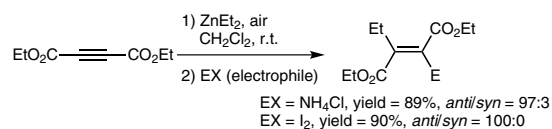
(E) *Addition to N-Acylpyridinium Salts*: Feringa and Minnaard developed a catalytic enantioselective addition of diethylzinc to *N*-acylpyridinium salts with good yields and excellent enantioselectivities. This method was applied to the synthesis of natural alkaloids.⁹



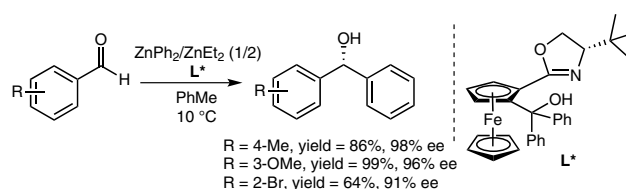
(F) *Marshall Homopropargylation*: Taking advantage of zinc(II)'s ability to perform transmetalation, allenyl zinc compounds were synthesized from diethylzinc. Then, addition to an aldehyde gave the desired *anti* homopropargylic alcohol adducts with high de. Marshall and co-workers synthesized various enantioenriched homopropargylic alcohols and applied this method to the synthesis of superstolide A.¹⁰



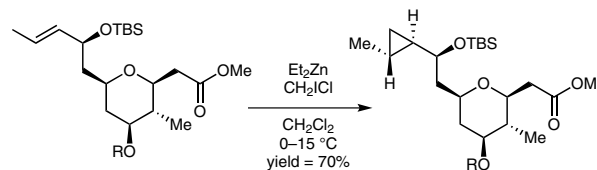
(G) *Alkyl Radical Addition*: Stereoselective synthesis of diethyl fumarate derivatives was accomplished under mild conditions *via* a direct *anti* carbozincation of diethyl acetylenedicarboxylate through diethylzinc-mediated alkyl radical addition.¹¹



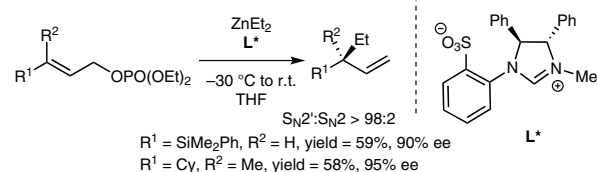
(H) *Phenyl Transfer to Aldehydes*: Bolm and co-workers have shown that in the synthesis of diarylmethanol compounds the use of diethylzinc can improve the enantioselectivity of the reaction.¹²



(I) *Simmons–Smith Reaction*: ZnEt₂ was also used in asymmetric Simmons–Smith reactions.¹³ This reaction was employed in many syntheses of natural products: for instance in 2008, Willis and co-workers described the synthesis of (–)-clavosolide D:¹⁴ treatment of the allylic alcohol with Et₂Zn and CH₂ICl led to the formation of a cyclopropane with excellent yield and diastereoselectivity.



(J) *Enantioselective Allylic Substitution*: In 2009, the group of Hoveyda reported that chiral *N*-heterocyclic carbene complexes are efficient catalysts in the copper-free enantioselective allylic alkylation using diethylzinc and allylic phosphates. This reaction led to enantioenriched allylic moieties with quaternary centers.¹⁵



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