

# 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

Pierre-Georges Echeverria was born in 1987 in France. He graduated from the engineering school ENSIACET (Toulouse, France) in 2011 and received his M.Sc. in organic chemistry from Paul Sabatier University (Toulouse). He is currently finishing his PhD under the supervision of Dr. Phannarath Phansavath and Dr. Virginie Vidal at Chimie ParisTech. His research focuses on the total synthesis of mirabalin, a complex marine macrocycle.

PSL Research University, Chimie ParisTech – CNRS, Institut de Recherche de Chimie Paris, 11 rue Pierre et Marie Curie, 75005 Paris, France

E-mail: pg.echeverria@chimie-paristech.fr

### Introduction

Diethylzinc ( $\text{ZnEt}_2$ , bp = 118 °C at 760 mmHg) is an inexpensive and commonly used diorganozinc reagent.<sup>1</sup> Due to its high pyrophoric nature, diethylzinc is often commercialized as a solution in organic solvent (hexane, toluene, or heptane).

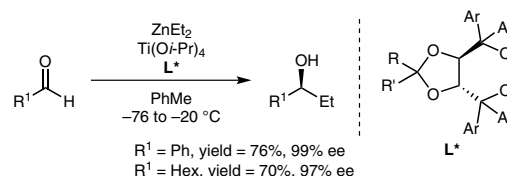
$\text{ZnEt}_2$  was first synthesized by Frankland in 1849 by heating ethyl iodide with zinc metal.<sup>2</sup> To facilitate purification,

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

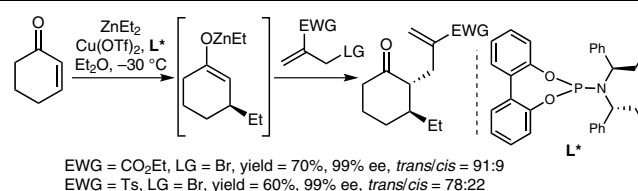
Diethylzinc is a versatile nucleophile that is suited for metal catalysis due to the highly covalent character of the carbon–zinc bond and the low Lewis acidity of zinc(II). Moreover, the empty low-lying *p*-orbitals allow facile transmetalation reactions.

### Abstracts

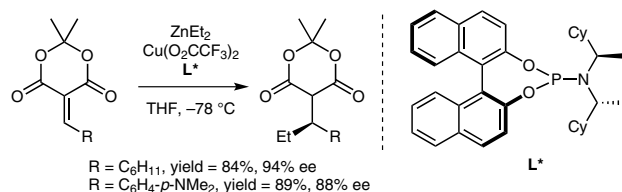
(A) *1,2-Addition*: Seebach and co-workers reported the 1,2-addition of diethylzinc to aliphatic and aromatic aldehydes in the presence of  $\text{Ti}(\text{O}i\text{-Pr})_4$  and TADDOL derivatives as ligands, which led to enantiopure alcohols in good yields.<sup>4</sup> Walsh and co-workers described also the synthesis of tertiary alcohols by the asymmetric addition of  $\text{ZnEt}_2$  to ketones catalyzed by a titanium catalyst with a chiral diamine ligand.<sup>5</sup>



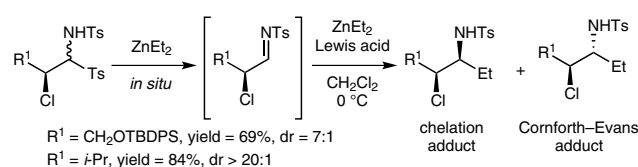
(B) *1,4-Addition to Cyclic Enones*: Alexakis and co-workers reported an asymmetric copper-catalyzed 1,4-addition of diethylzinc to cyclic enones using a phosphoramidite ligand, followed by C-enolate trapping resulting in the synthesis of  $\alpha,\beta$ -disubstituted ketones with a high degree of stereoselectivity.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



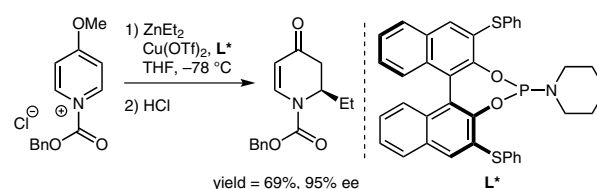
(C) *1,4-Addition to Reactive Acceptors*: Carreira and co-workers developed the copper-catalyzed highly stereoselective conjugate addition of diethylzinc to Meldrum's acid derived acceptors with phosphoramidite ligands.<sup>7</sup>



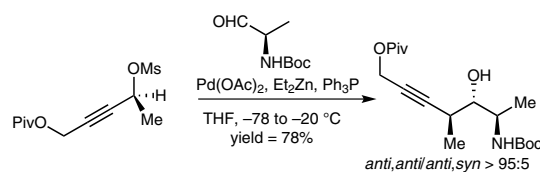
(D) *Addition to  $\alpha$ -Chloro Aldimines*: Walsh and co-workers described a highly diastereoselective synthesis of  $\alpha$ -chloro amine *via* a nucleophilic addition to  $\alpha$ -chiral imine derivatives that proceeds through an unusual chelation transition state instead of a Cornforth–Evans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



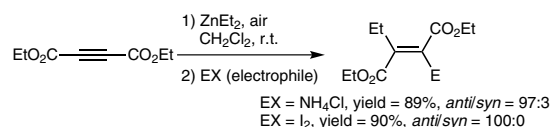
(E) *Addition to N-Acylpyridinium Salts*: Feringa and Minnaard developed a catalytic enantioselective addition of diethylzinc to *N*-acylpyridinium salts with good yields and excellent enantioselectivities. This method was applied to the synthesis of natural alkaloids.<sup>9</sup>



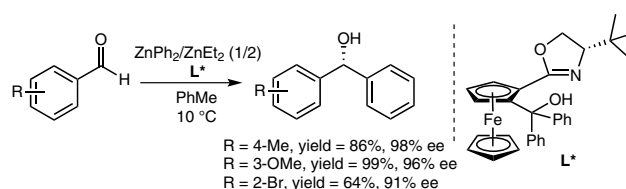
(F) *Marshall Homopropargylation*: Taking advantage of zinc(II)'s ability to perform transmetalation, allenyl zinc compounds were synthesized from diethylzinc. Then, addition to an aldehyde gave the desired *anti* homopropargylic alcohol adducts with high de. Marshall and co-workers synthesized various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



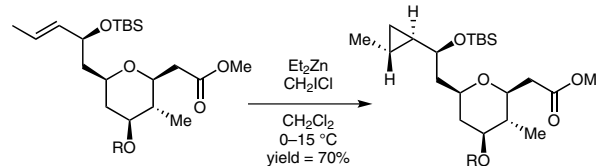
(G) *Alkyl Radical Addition*: Stereoselective synthesis of diethyl fumarate derivatives was accomplished under mild conditions *via* a direct *anti* carbozincation of diethyl acetylenedicarboxylate through diethylzinc-mediated alkyl radical addition.<sup>11</sup>



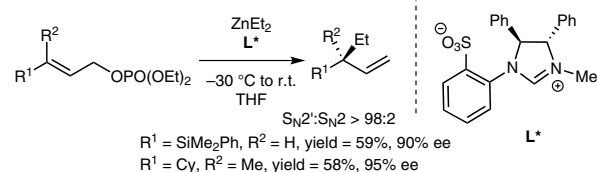
(H) *Phenyl Transfer to Aldehydes*: Bolm and co-workers have shown that in the synthesis of diarylmethanol compounds the use of diethylzinc can improve the enantioselectivity of the reaction.<sup>12</sup>



(I) *Simmons–Smith Reaction*: ZnEt<sub>2</sub> was also used in asymmetric Simmons–Smith reactions.<sup>13</sup> This reaction was employed in many syntheses of natural products: for instance in 2008, Willis and co-workers described the synthesis of (–)-clavosolide D:<sup>14</sup> treatment of the allylic alcohol with Et<sub>2</sub>Zn and CH<sub>2</sub>ICl 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.<sup>15</sup>



## References

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