SYNLETT
Spotlight 280

This feature focuses on a re-agent chosen by a postgradu-ate, highlighting the uses and preparation of the reagent in current research

## Simmons–Smith Reagent (Et$_2$Zn, CH$_2$I$_2$): An Efficient Reagent in Organic Synthesis

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Introduction

The diethylzinc/diiodomethane or zinc-diiodomethane (Et$_2$Zn, CH$_2$I$_2$ or Zn, CH$_2$I$_2$ = ICH$_2$ZnI) known as Sim-mons–Smith reagent is probably the best known car-benoid reagent in organic syntheses.[1] This ether soluble reagent has been used mainly for the conversion of al-kenes into cyclopropanes[1] via stereospecific and supra-facial CH$_2$ addition using chiral auxiliaries,[2] reagents[3] and catalysts.[4]

Due to the presence of cyclopropanes in many biological-ly and medicinally important molecules,[5] natural prod-ucts,[6] essential oils[7] and the marine cyanobacteriums,[8] some recent applications of Simmons–Smith reagent are reported herein.

Abstracts

(A) Asymmetric reaction of allylic alcohols with Al Lewis acid/N Lewis base bifunctional Al(salalen) cata-lyst in the presence of Simmons–Smith reagent has been reported by Katsuki and Shitama in quantitative yields with high enantiomeric excess. The hydroxyl group is a prerequisite serving as an anchor for zinc.[9]
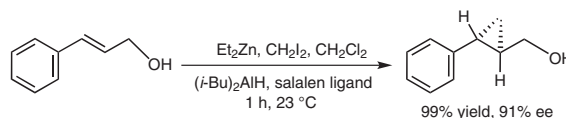
(B) A catalytic asymmetric Simmons–Smith cyclopropana-tion of silyl enol ethers **1** using dipeptide **2** as a ligand has been described. A variety of optically active cyclo-propyl silyl ethers **3** can be obtained in high yields and with an ee up to 96%. The dipeptide can be recovered af-ter the reaction in good yield and reused without the loss of reactivity or enantioselectivity.[10]
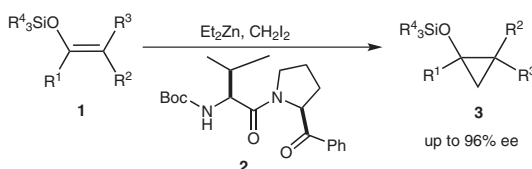
(C) White et al. have reported asymmetric total syntheses of solandelactones. The key step in these syntheses involved directed Simmons–Smith cyclopropanation which this reaction preceded in quantitative yield (97%).[11]
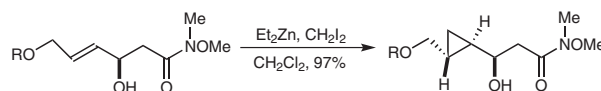
(D) A highly diastereoselective cyclopropanation proto-col for allylic amines **1** has been demonstrated by Davies et al. giving access to complete conversion into *syn*-**2** in 98% de with Simmons–Smith reagent, and *anti*-**3** in 98% de in the presence of TFA.[12]
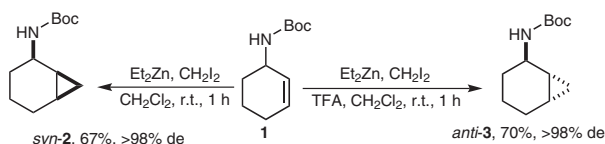
(E) Recently, an efficient asymmetric synthesis of conformationally constrained (2*S*,3*S*)-piperidinedicarboxylic acid derivatives has been reported by Zhuo et al. This was the first successful example of cyclopropanation of an allylic amine by masking the amine as a carbamate without the presence of a chelating group (OH or OR) using Simmons–Smith reagent.[13]
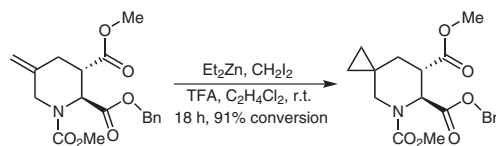
(F) A highly stereoselective synthesis of chiral aminocyclopropanes through cyclopropanation of chiral enamides using the Simmons–Smith reagent has been explored by Hsung et al. Various substrates are transformed with moderate to good diastereoselectivity to cyclopropane products. The method includes the synthesis of the cyclopropane fragment of the nucleoside.[14]
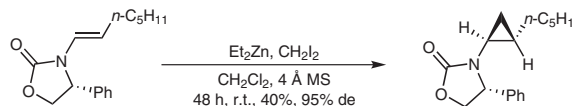
(G) A series of novel fluorocyclopropyl nucleosides with antiviral activity has been synthesized starting from acetol using the Simmons–Smith reagent. All the synthesized nucleosides were assayed against several viruses.[15]
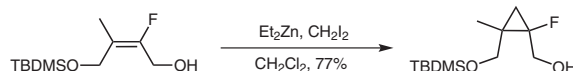
(H) The Simmons–Smith reagent has been applied to prepare a new class of haloalkylzinc compounds leading to transition metal carbenes. Halomethylzinc and halobenzylzinc compounds react with ruthenium and iridium complexes to form methylene and benzylidene complexes including the Grubbs catalyst.[16]
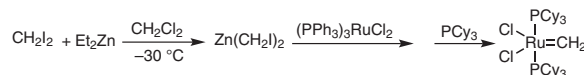
(I) The total synthesis of the natural metabolite (+/–)-cascarillic acid **3** has been achieved by a sequential cross-metathesis and Simmons–Smith cyclopropanation between 1-octene **1** with an appropriate unsaturated carboxylic acid **2**. Interestingly, the smooth conditions required for both the cross-metathesis and the cyclopropanation allow the combination of the two processes in one single pot. Compared to other racemic syntheses, this high yielding (up to 90%), selective (the *E/Z* ratio near 80:20) and shorter procedure is expected to be generalized to other naturally occurring *trans*-cyclopropane derivatives.[17]
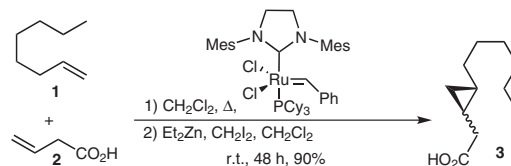
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