SYNLETT Spotlight 342

N-Sulfinyl Imines

Compiled by Ping Song

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

N-Sulfinyl imines (sulfinimines) play an important role in asymmetric reactions. They display unique reactivity and stereoselectivity in the synthesis of amino group containing natural products and bioactive compounds. Furthermore, a wide variety of sulfinimines is efficiently prepared for many types of asymmetric reactions, and the chiral sulfinyl in the resultant product is easily removed under comparatively mild conditions.¹

Preparation

Three synthetic routes were developed, for example, asymmetric oxidation,² iminolysis of sulfinate esters,³ and condensation of a sulfinamide with aldehydes or ketones.⁴ The most common and versatile method is the direct condensation of aldehydes or ketones with sulfinamide.

Scheme 1

Abstracts

(A) Sulfinimines were used to prepare functionalized amines with high stereoselectivity. Organometallic reagents, such as Grignard reagents^{5a} and organolithium,⁵ are added to sulfinimines to get the desired products in high diastereoselectivity. Both aliphatic and aromatic sulfinimines proceeded in very high diastereoselective ratios when arylboronic acid was employed.⁶

(B) The sulfinimines-mediated asymmetric Strecker reaction provided efficiently chiral α -amino acids.⁷ Polyhydroxy α -amino acids were derived from polyhydroxy sulfinimines through smooth deprotection of the sulfinyl.⁸ Quaternary α -stereogenic centers of α -amino acids were controlled by tuning the solvents.⁹ The (*S,R*)-product was afforded predominantly in hexane while the contrary (*R,R*)-isomer was the major product in DMF.

(C) β -Amino esters or acids were prepared efficiently via addition of the sodium enolate of methyl acetate to sulfinimines in high diastereoselectivity.^{10a} Lithium enolate effected the better yield.^{10b} The stereoselective Michael–nucleophilic addition domino reaction from sulfinimines was another route towards β -amino esters.¹¹

(D) β -Amino ketones were prepared by addition of prochiral lithium enolates of Weinreb amides to sulfinimines.^{5,12} Reduction of *N*-sulfinyl β -amino ketones led to *syn*- and *anti*-1,3-amino alcohols.¹²

(E) The aza-Diels–Alder reactions of sulfinimines as dienophile with Rawal dienes resulted in dihydropyridones with ee values up to 90%.^{13a} When a Lewis acid catalyst was added, both activated and non-activated dienes could be used in this reaction.^{13b}

(F) The pure sulfinimines have been applied in the aza-Baylis–Hillman reaction. The resulting allylic amines reacted with electrophiles led to highly functionalized 3-sulfinyl and 3-sulfonyl 2,5-*cis*-dihydropyrroles.¹⁴

(G) Addition of suitably protected α -amino acid to pure sulfinimines led to *syn*- and *anti*- α,β -diamino esters with high dr and good yields.¹⁵ The water content in THF was an important factor determining the selectivity.^{15b}

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