

# 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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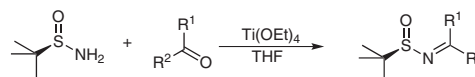


### Introduction

N-Sulfinyl imines (sulfonimines) 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 sulfonimines is efficiently prepared for many types of asymmetric reactions, and the chiral sulfinyl in the resultant product is easily removed under comparatively mild conditions.<sup>1</sup>

### Preparation

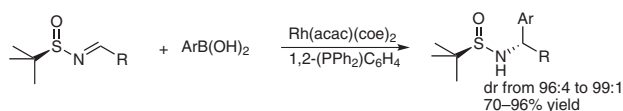
Three synthetic routes were developed, for example, asymmetric oxidation,<sup>2</sup> iminolysis of sulfinate esters,<sup>3</sup> and condensation of a sulfonamide with aldehydes or ketones.<sup>4</sup> The most common and versatile method is the direct condensation of aldehydes or ketones with sulfonamide.



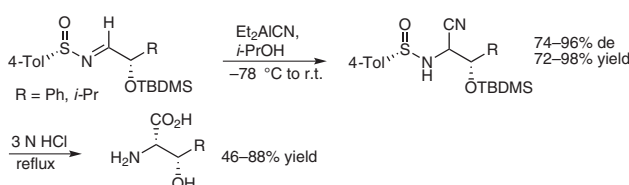
Scheme 1

### Abstracts

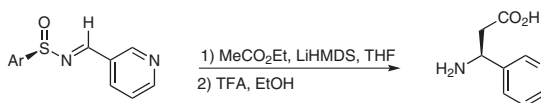
(A) Sulfonimines were used to prepare functionalized amines with high stereoselectivity. Organometallic reagents, such as Grignard reagents<sup>5a</sup> and organolithium,<sup>5</sup> are added to sulfonimines to get the desired products in high diastereoselectivity. Both aliphatic and aromatic sulfonimines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



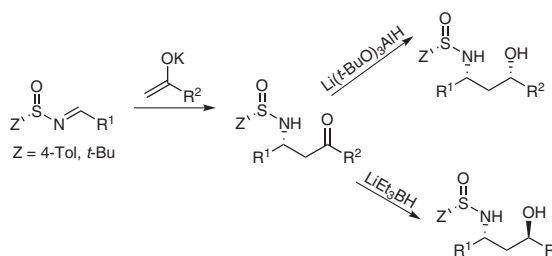
(B) The sulfonimines-mediated asymmetric Strecker reaction provided efficiently chiral  $\alpha$ -amino acids.<sup>7</sup> Polyhydroxy  $\alpha$ -amino acids were derived from polyhydroxy sulfonimines through smooth deprotection of the sulfinyl.<sup>8</sup> Quaternary  $\alpha$ -stereogenic centers of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



(C)  $\beta$ -Amino esters or acids were prepared efficiently via addition of the sodium enolate of methyl acetate to sulfonimines in high diastereoselectivity.<sup>10a</sup> Lithium enolate effected the better yield.<sup>10b</sup> The stereoselective Michael–nucleophilic addition domino reaction from sulfonimines was another route towards  $\beta$ -amino esters.<sup>11</sup>



(D)  $\beta$ -Amino ketones were prepared by addition of prochiral lithium enolates of Weinreb amides to sulfonimines.<sup>5,12</sup> Reduction of *N*-sulfinyl  $\beta$ -amino ketones led to *syn*- and *anti*-1,3-amino alcohols.<sup>12</sup>



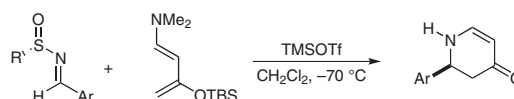
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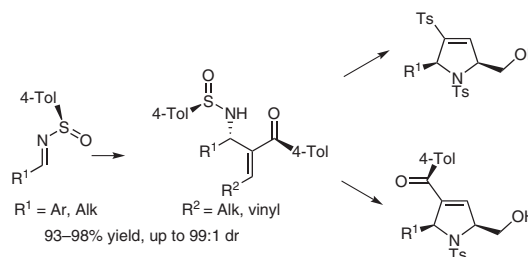
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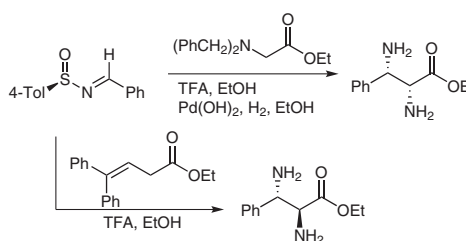
(E) The aza-Diels–Alder reactions of sulfinimines as dienophile with Rawal dienes resulted in dihydropyridones with ee values up to 90%.<sup>13a</sup> When a Lewis acid catalyst was added, both activated and non-activated dienes could be used in this reaction.<sup>13b</sup>



(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.<sup>14</sup>



(G) Addition of suitably protected  $\alpha$ -amino acid to pure sulfinimines led to *syn*- and *anti*- $\alpha,\beta$ -diamino esters with high dr and good yields.<sup>15</sup> The water content in THF was an important factor determining the selectivity.<sup>15b</sup>



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