**SYNLETT**

**Spotlight 306**

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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**2-Methyl-2-propanesulfinamide (Ellman’s Sulfinamide): A Versatile Chiral Reagent**

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**Introduction**

Enantiopure 2-methyl-2-propanesulfinamide (tert-butanesulfinamide) was introduced by Ellman in 1997.1 As a chiral ammonia equivalent, it can easily condense with aldehydes and ketones to afford tert-butanesulfinyl imines in high yields (Scheme 1).2 The tert-butanesulfinyl group activates these imines for the addition of many different classes of nucleophiles and serves as a powerful chiral directing group to provide products with generally high diastereoselectivity. Subsequent removal of the tert-butanesulfinyl group under mild conditions cleanly provides the amine products. Many versatile building blocks3 including syn- and anti-1,2- or 1,3-amino alcohols,4,5 α-branched and α,α-dibranched amines,6 α- or β-amino acids and esters7,8 can be efficiently synthesized by using this methodology. In addition, this methodology can also be used in the synthesis of antibiotics, biologically active compounds, and other complex natural products.9 Furthermore, tert-butanesulfinamide has been used in the synthesis of asymmetric ligands10 or catalysts11, and in a few cases, appears as the chirality-bearing component.12

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**Scheme 1 Synthesis of sulfinyl aldimines or ketimines**

Each configuration of 2-methyl-2-propanesulfinamide is readily available in a two-step process of catalytic asymmetric oxidation of tert-butyl disulfide, followed by the reaction of the tert-butanesulfinyl product 4 with an amide anion (Scheme 2).13

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**Scheme 2 Preparation of (R)-tert-butanesulfinamide**

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**Abstracts**

(A) Ellman and co-workers have demonstrated the facile synthesis of chiral α,α-dibranched amines through 1,2-addition of organolithium reagents to N-tert-butanesulfinyl ketimines, which proceeds with high yields and diastereoselectivities.6b

(B) N-tert-Butylsulfinyl imines have been used in a highly diastereoselective multi-component reaction of phenyl diazocacetates, alcohols, and imines, which provides readily access to β-amino-α-hydroxyesters in high optical purity.4d

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Ellman and co-workers have reported the copper-catalyzed addition of bis(pinacolato) diboron to N-tert-butanesulfinyl aldimines with excellent diastereoselectivity for diverse chiral ω-amino boronic acids. Furthermore, the N-sulfinyl ω-amino boronic ester addition products can be used as intermediates in the asymmetric synthesis of bortezomib.

Morton and co-workers synthesized chiral aziridines using trimesylsulffonium iodide with good yields and diastereoselectivities. Chemla and Ferreira reacted a racemic allenylzinc substrate with various N-tert-butanesulfinyl imines to achieve trans-ethynylaziridines as diastereomerically and enantiomerically pure compounds in good yields. Ellman and co-workers have synthesized a novel bis(sulfinyl)imidoamidine using N-tert-butanesulfinamide as starting material, Ellman and co-workers have reported the copper-catalyzed addition of bis(pinacolato)diboron to various N-tert-butanesulfinyl imines to achieve trans-ethynylaziridines as diastereomerically and enantiomerically pure compounds in good yields.

Using N-tert-butanesulfinamide as staring material, Ellman and co-workers have synthesized a novel bis(sulfinyl)limidoamidine (siam) ligand in three straightforward steps. The complex of tert-butanesulfinyl imines to achieve trans-ethynylaziridines as diastereomerically and enantiomerically pure compounds in good yields.

Ellman and co-workers have developed a new class of organocatalysts that incorporate the N-sulfinyl urea substituent, which is acidifying and serves as a chiral controlling element. The condensation of tert-butanesulfinamide with the appropriate isocyanate in one step provides urea in good yields. Chemla and Ferreira reacted a racemic allenylzinc substrate with the appropriate isocyanate in one step to provide the aziridine as diastereomerically and enantiomerically pure compound in good yields.

## References