Enantiopure 2-methyl-2-propanesulfinamide (tert-butan sulfinamide) was introduced by Ellman in 1997. As a chiral ammonia equivalent, it can easily condense with aldehydes and ketones to afford tert-butanesulfinyl imines in high yields (Scheme 1). 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 blocks including syn- and anti-1,2- or 1,3-amino alcohols, α-branched and α,α-dibranched amines, α- or β-amino acids and esters 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. Furthermore, tert-butanesulfinamide has been used in the synthesis of asymmetric ligands or catalysts, and in a few cases, appears as the chirality-bearing component.

Each configuration of 2-methyl-2-propanesulfinamid is readily available in a two-step process of catalytic asymmetric oxidation of tert-butyl disulfide, followed by the reaction of the tert-butanethiosulfinate product with an amide anion (Scheme 2).
C. 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 α-amino boronic acids. Furthermore, the N-sulfinyl α-amino boronate ester addition products can be used as intermediates in the asymmetric synthesis of bortezomib.

(D) Morton and co-workers synthesized chiral aziridines using trimethylsulonium iodide with good yields and diastereoselectivities. Chemla and Ferreira reacted a racemic allenylzinc substrate with various N-tert-butanesulfinyl imines to achieve trans-ethylaziridines as diastereomerically and enantiomerically pure compounds in good yields.

(E) Using N-tert-butanesulfinamide as staring material, Ellman and co-workers have synthesized a novel bis(sulfinyl)imidoamidine (siam) ligand in three straightforward steps. The complex of bis(sulfinyl)imidoamide with copper(II) catalyzes the Diels–Alder reaction with exceptional levels of enantio- and diastereoselectivity.

(F) 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, which is proven to be an efficient organocatalyst in the enantioselective aza-Henry reaction.

References