

Asymmetric Synthesis of 1,3-Diamines

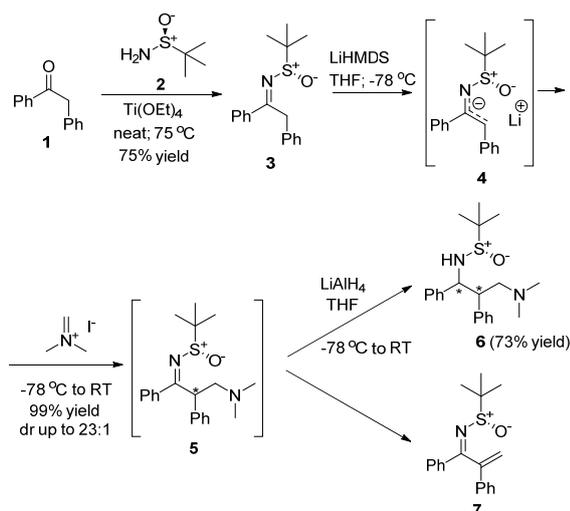
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Application of *tert*-butanesulfinyl (Ellman's) imine as a chiral auxiliary in asymmetric synthesis is well known and extensively studied [1, 2]. To our knowledge, asymmetric synthesis of 1,3-diamines by stereoselective introduction of Eschenmoser's salt in α -position of *N*-sulfinyl imine (**3**) was not reported.

N-Sulfinyl imine (**3**) can be successfully used in Mannich-type reaction with Eschenmoser's salt to produce *N*-sulfinyl-1-imino-3-amine (**5**) in good diastereomeric ratio (up to 23 : 1) and conversion (Scheme 1). Because of undesired elimination of dimethylamine to furnish *N*-sulfinyl alkene (**7**), isolation of *N*-sulfinyl-1-imino-3-amine (**5**) was not possible. Therefore, it was reduced *in situ* to corresponding 1,3-diamine **6** in good yield (up to 73%) and diastereomeric ratio.

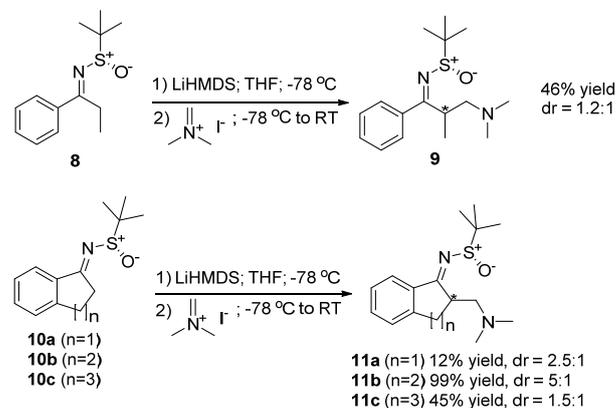


Scheme 1. Synthesis of 1,3-diamine **6**

The synthesis of the *N*-sulfinyl-1-imino-3-amine (**5**) was optimized by varying several reaction parameters. Effects of temperature, order and rate of base addition, rate of Eschenmoser's salt addition, molar ratio, reducing agents, nitrogen substituents and counter-ion of Eschenmoser's salt, as well as quenching methods were investigated. Conversion of substrates was examined using LC/MS method.

Substrate scope (Scheme 2) was examined under the optimal conditions. The desired Mannich-type products were formed in poor to high yields and diastereomeric ratios.

Several theoretical rationalizations of the origin of diastereoselectivity in analogous reactions of Ellman's imine can be found in literature; however, they can hardly be applied to our system due to the complexity and substrate-dependent nature of the reaction. Our studies towards better understanding of the mechanism of Mannich-type reaction are underway.



Scheme 2. Synthesis of 1,3-diamines **9** and **11(a-c)**

1,3-Diamines have found numerous applications as chiral ligands, catalysts and reagents. For instance, 1,3-diamine-based Takemoto-type organocatalysts have been successfully used in enantioselective Michael addition reaction [3].

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