A Novel Asymmetric Synthesis of (*S*)- Ketamine using (*S*)-*tert*-Butanesulfinamide and 1,2-Cyclohexandione

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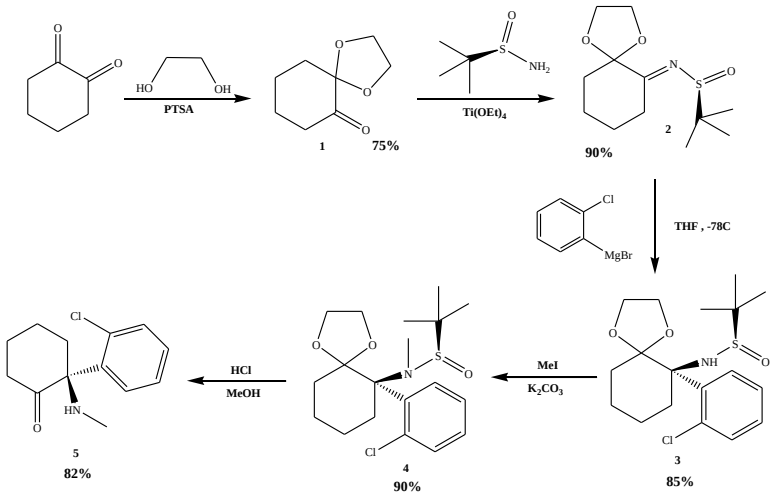
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Abstract

The asymmetric synthesis of (*S*)-Ketamine with good selectivity was accomplished by a new strategy. In this work, our approach is described in Scheme 1. Intermediate monoketal intermediate 1 can be easily obtained after partial conversion of one ketone function in 1, 2-cylohexadione into a ketal using ethyleneglycol. Then, we obtained the sulfinylimine by the condensation of (*S*)-*tert*-Butanesulfinamide (TBSA) with 1,4-dioxaspiro[4.5]decan-6-one 2 in 90% yield. We have found, Ti(OEt)4 to be ideal water scavenger and Lewis acid for the preparation of (*S*)-N-*tert*-butanesulfinyl ketimine. Further reaction with appropriate Grignard reagent (ArMgBr) generate chiral center in 85% yield and with 85% diastereoselectivity. Methylation of the amine 3 by methylamine afforded the 4. Finally, the sulfinyl and ketale protecting groups were removed from the compound 4 by brief treatment with stoichiometric quantities of HCl in a protic solvent gave the ketamine in near quantitative yield.

Keyword: (*S*)-Ketamine, asymmetric synthesis, (*S*)- *tert*-Butanesulfinamide, 1,2-cyclohexadione, monoketal



Scheme 1. Asymmetric synthesis of S-Ketamine