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# N,N- Diisopropylcarbamate of $\alpha$ -hydroxystyrenes: A New Entry to $\alpha$ - hydroxy- $\beta$ - phenylethylamines and ephedrines



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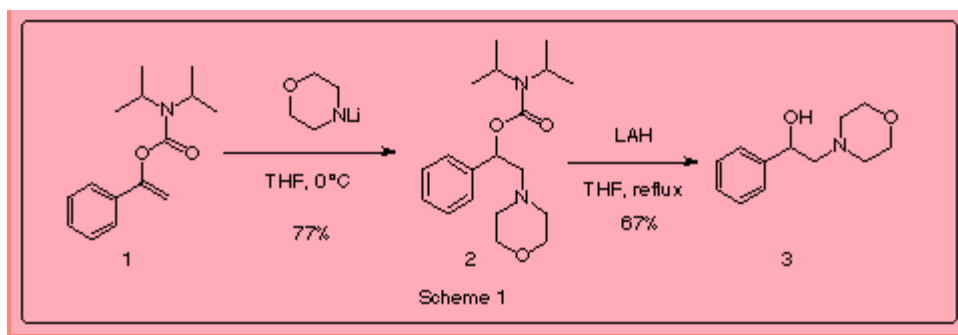
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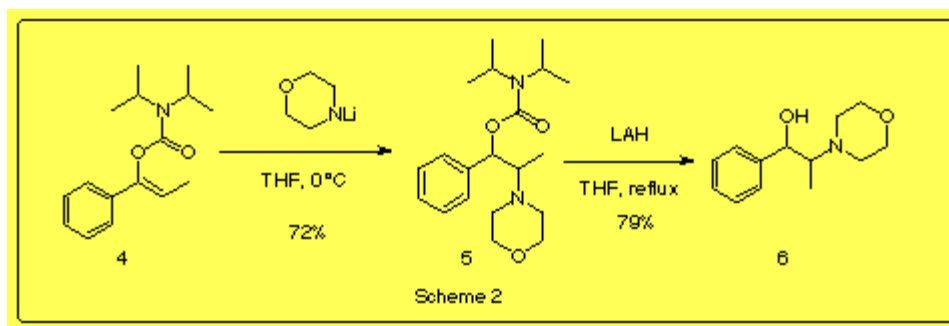
Our group has been investigating on the transformation of styrene derivatives into  $\beta$ -phenylethylamines [1]. We had previously worked on the carbolithiation of styrenic compounds and we achieved successfully the hydroxylation of the  $\alpha$ -position of styrene [2]. However this method proved to be unsuccessful when applied to addition of lithium amides [3].

$\beta$ -hydroxy- $\beta$ -phenylethylamines are very interesting due to their wide variety of pharmacological properties [4]. To achieve their synthesis we had to change our strategy. Instead of leaving the introduction of the oxygen atom at C- $\alpha$  for the end of the synthesis, we decided to start from  $\alpha$ -hydroxystyrene derivatives, where the oxygen atom was present previously to the nucleophilic addition stage. Previously it had been reported that enolcarbamates could support the addition of organolithium without reaction of the carbonyl group [5]. Thus we prepared the N,N-diisopropylcarbamate of the enol of acetophenone **1**. We treated it with the lithium amide of morpholine obtaining the addition compound **2** in a 77% yield, the cleavage of isopropylcarbamates is performed by reduction with lithium aluminum hydride [6], thus we obtained  $\beta$ -hydroxyl- $\beta$ -phenylethylamine **3** in 67% yield.





Another interesting analogs of  $\beta$ -phenylethylamines are ephedrine like compounds. To carry out the synthesis of this skeleton, we prepared the N,N-diisopropylcarbamate of the enol of propiophenone **4**, this was reacted with the lithium amide of morpholine affording addition product **5** in 72% yield, the cleavage of carbamate group presenting **5** with lithium aluminum hydride gave amino alcohol **6** in 79% yield.



We think our method for the synthesis of  $\beta$ -phenylethylamine derivatives, constitutes a interesting approach with good yields. Actually we are checking the scope of this methodology for a wide variety of primary and secondary amines.

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