One-pot Synthesis of Protected 2-(methylthio)ethyl Hydrazines

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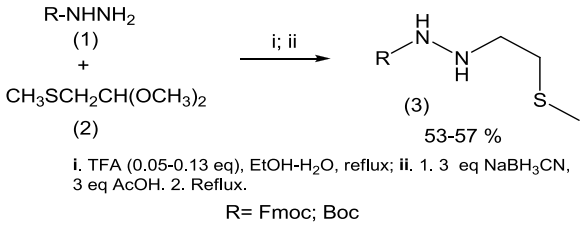
Replacement of amino acids by α-aza-amino acids in peptide structure increases biostability of these compounds that is a promising challenge for design of bioactive compounds [1]. However, due to instability hydrazinecarboxilic acid and its derivatives, this replacement cannot be done in straightforward way, and protected alkylhydrazines are used as aza-amino acid precursors. The most common method of synthesis of these precursors is reductive hydrazine alkylation by using aldehydes or ketones [1;2]. However, the presence of an electronegative atom in aldehyde or ketone molecule destabilizes this carbonyl compound and reduces the yield of the synthesis. To improve this situation we have developed a one-pot synthesis procedure for preparation of protected alkylhydrazines. Here we report preparation of protected (2-methylthio)ethyl hydrazines from (2-merhylthio)acetaldehyde dimethylacetal (**Scheme**) (3).



Equimolar mixture of (**1**) and (**2**) in 90% EtOH/H_2O was refluxed in the presence of TFA. After the condensation reaction was complete, $NaBH_3CN$ and AcOH were added for the reduction step. Boron adducts were easily decomposed by refluxing of the reaction mixture. Products (**3a-b**) were obtained with moderate yield, which could be improved by further optimization.

References

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