

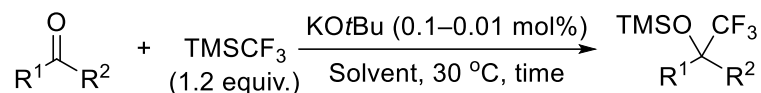
Alkoxide-Catalyzed Nucleophilic Trifluoromethylation of Aldehydes and Ketones

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It is well known that introduction of fluoroalkyl groups into bioactive molecules can extend the positive effects. Several elegant approaches for the trifluoromethylation of organic compounds are now available. Nucleophilic addition of a trifluoromethyl anion (CF_3^-) equivalent to a carbonyl group is one of the simplest approaches to access α -functionalized trifluoroethanol derivative. Trifluoromethyltrimethylsilane (TMSCF_3 , Ruppert–Prakash reagent)¹ is often employed for this purpose, which is activated by catalytic amount of fluoride species or Lewis bases forming the corresponding silicate intermediate.²

Here we report a highly efficient, general, and operationally simple strategy affording α -substituted trifluoroethanol derivatives. With potassium alkoxide as a catalyst, such as potassium *t*-butoxide, the reaction of TMSCF_3 and carbonyl compounds including aromatic, aliphatic aldehydes and ketones smoothly proceeds to give the desired products in nearly quantitative yield at room temperature. Lithium and sodium *t*-butoxide were not effective at all, and potassium alkoxide was the best suited catalyst for this reaction. This method achieved 99% yield of product with the use of 0.01 mol% catalyst, even though it took 24 h for the completion. Not only THF but also 1,4-dioxane, toluene, and dichloromethane were successfully applied as the solvent to this reaction affording the product in over 90% yield. Low-boiling dichloromethane is effective for the synthesis of volatile trifluoromethylated compounds, such as the product derived from benzaldehyde. We also attempt to realize an enantioselective trifluoromethylation of carbonyl compounds by using a chiral potassium alkoxide catalyst.



Scheme 1. KOtBu-Catalyzed Nucleophilic Trifluoromethylation of Carbonyl Compounds.

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