

Metal-free α -trifluoromethylthiolation and α -trifluoromethylselenolation of carbonyl derivatives

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The incorporation of a SCF_3 or a SeCF_3 group into organic molecules is a topic of great interest, especially for the pharmaceutical and agrochemical industries [1,2]. Due to their high lipophilicity and high electron-withdrawing character (Hansch lipophilicity parameter $\pi_R = 1.44$ (SCF_3) vs $\pi_R = 1.29$ (SeCF_3)), these moieties represent a powerful opportunity to influence the pharmacokinetics properties of a drug molecule.

In the last years, new structural units, rising from the association between chalcogens and fluorinated moieties, have been introduced into carbonyl compounds, as emerging class with potential applications on several fields. New reagents have been developed as sources of electrophilic SCF_3 and SeCF_3 groups; however, a widespread use of such fluorinated compounds is hampered by the very limited number of strategies available for their preparation. In this contest, we have developed two methodologies for the preparation of α - SCF_3 [3] and α - SeCF_3 substituted carbonyl derivatives starting from non activated ketones or their derivatives (Fig. 1).

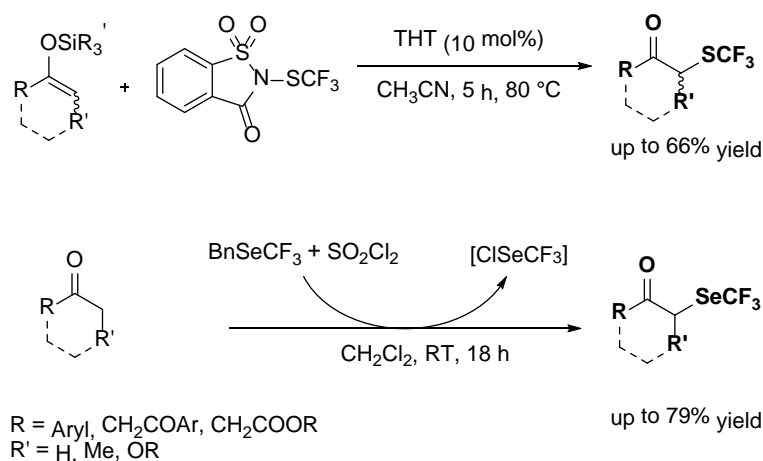


Figure 1: α -trifluoromethylthiolation and α -trifluoromethylselenolation of carbonyl derivatives

[1] W.K. Hagmann, *J. Med. Chem.*, **2008**, 51, 4359-4369

[2] M. Carland, T. Fenner, "The Use of Selenium-Based Drugs in Medicine" published in "Metallotherapeutic Drugs and Metal-Based Diagnostic Agents: The Use of Metals in Medicine", Marcel Gielen and Edward R.T. Tiekink editors. **2005**, 313-332.

[3] S. S. Abubakar, M. Benaglia, S. Rossi, R. Annunziata, *Catalysis Today* **2017**, doi: 10.1016/j.cattod.2017.09.013