TOWARDS THE SYNTHESIS OF ENANTIOENRICHED DIFLUOROMETHYL AND DIFLUOROMETHYLENE SCAFFOLDS

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ABSTRACT:

Within fluorinated moieties, the –CHF₂ group has aroused a growing interest in pharmaceutical and agrochemical fields in the last few years. Several chemists have already reported the synthesis of difluoromethylated compounds but the enantioselective introduction of the difluoromethyl motif has been scarcely described yet. Additionally, the synthetic access to difluoromethylene scaffolds remains underdeveloped. In this context, we desired to develop new pathways to access enantiopure difluoromethyl or difluoromethylene scaffolds. We were also focused on the deprotonation of the –CHF₂ group, which remains very challenging due to the poor stability of the generated carbanion.

Therefore, we recently developed a new strategy to synthesize enantiopure difluoromethyl sulfoxides, that were further used as chiral auxiliaries to obtain enantioenriched difluoromethyl alcohols through deprotonation of the sulfoxide.¹ At the same time, the acidity of diverse difluoromethyl sulfoxides was investigated by UV-visible spectrophotometry.² In relation with the deprotonation of the corresponding sulfoxides, we also managed to perform the deprotonation of difluoromethyl ketones with a catalytic organosuperbase followed by trapping with various electrophiles to access highly valuable difluoromethylene compounds.

Figure 1 : Deprotonative functionalization of difluoromethyl ketones

References