

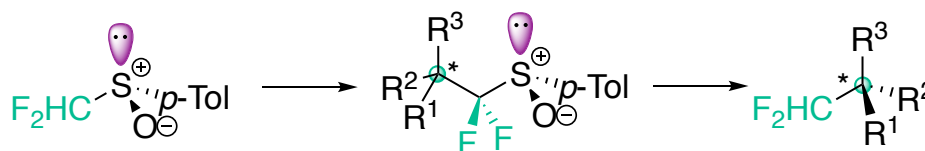
New insights into enantioselective difluoromethylation by means of sulfoxides as chiral and traceless auxiliaries

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The introduction of fluorine or a fluorinated group in a molecule often leads to compounds having many beneficial physico-chemical and biological properties.^{1–4} The emergence of molecules bearing new fluorinated substituents has been noticed during the last decades and an increasing importance has then been given to the synthesis of these molecules, which are important components of agrochemicals and pharmaceuticals.⁵ The difluoromethyl group has been described as a bioisostere of hydroxyl, thiol and amine groups.⁶ Structural, spectroscopic and computational studies have provided evidence of the high lipophilicity, stability and the hydrogen bond donor character of this functional group.⁷ These remarkable properties induced by the -CHF₂ group in agrophores and pharmacophores and the limited number of examples regarding enantioselective difluoromethylation that have been reported in literature^{8,9} led us to develop a new synthetic pathway to access difluoromethylated scaffolds of high added value.

Inspired by Hu's work¹⁰, we developed a straightforward stereoselective introduction of a -CHF₂ group in an array of compounds by means of an enantiopure aryl difluoromethyl sulfoxide used as a chiral and traceless auxiliary. We wish here to present this approach as a new way to access difluoromethylated building-blocks with high optical purity¹¹.



Scheme : Strategy to access highly enantioenriched difluoromethylated building blocks

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