

Project 2.6 Development of sequential reactions involving Michael additions to enones with subsequent fluoroalenylation and fluoroalkylthiolation

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Background:

The incorporation of fluorine atoms or fluorinated groups into the structure of organic molecules severely alters their chemical, physical, and biological properties. Such compounds have found many applications in medicinal chemistry (>20% of drugs, including top sellers), agrochemistry (>30% of crop protection chemicals), materials science, and other fields. Therefore, there is a great need for the development of efficient and reliable methods for the synthesis of selectively fluorinated organic scaffolds. Highly attractive fluoroalkyl(thio)lated ketones are typically accessed by simple additions to corresponding enolates, often formed in-situ by deprotonation, featuring challenges with control of regioselectivity and making impossible consequent attachment of other functionalities. We envisioned that these challenges could be addressed by development of methodologies utilizing reactivity of α,β -unsaturated ketones.

Aim:

The main objective of this proposal is the discovery, development, and understanding of a series of new methodologies for fluoroalkylative and fluoroalkylthiolative functionalizations of enones. The projected strategy is based on Michael addition of organometallic species to α,β -unsaturated ketones followed by fluoroalkylation or fluoroalkylthiolation of the resulting enone in a one-pot cascade process. Such severely underdeveloped cascade processes enable concomitant installation of multiple functionalities in single synthetic step. The developed toolbox of synthetic methods would provide selective entry to a range of substituted ketones bearing fluoroalkyl or fluoroalkylthio group of potentially vital importance for many branches of chemistry, including medicinal chemistry and material sciences.

Requirements:

- Master's degree in chemistry (or related field);
- good knowledge of organic chemistry;
- ability of analysis and interpretation of experimental data using techniques such as NMR, MS and UV/Vis;
- experience in experimental work, will be an added advantage;
- good knowledge of English.