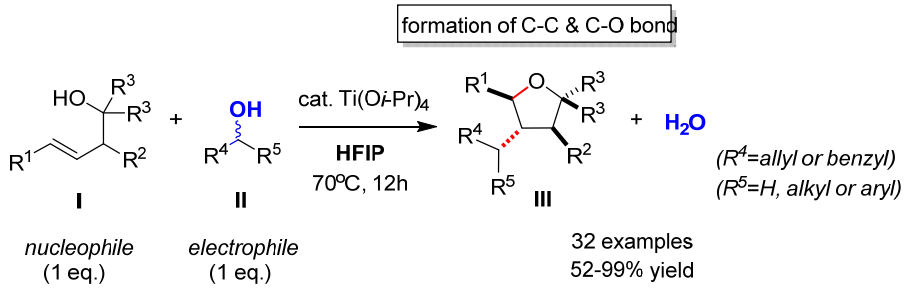
# HFIP SOLVENT ENABLES ALCOHOLS TO ACT AS ALKYLATING AGENTS IN STEREOSELECTIVE HETEROCYCLIZATION

Yuxiang Zhu, Ignacio Colomer and Timothy J. Donohoe

Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, United Kingdom
yuxiang.zhu@chem.ox.ac.uk

Oxygen-containing heterocycles are precursors of many valuable synthons in both synthetic and medicinal chemistry, which facilitate the synthesis of a broad array of natural products with biological activity. We have found that the polar and hydrogen bonding solvent hexafluoroisopropanol (HFIP) plays an important role in the stereocontolled synthesis of complex oxygen heterocycles from simple linear precursors.

Our novel method for the stereoselective functionaolisation of homoallyl alkenes uses readily available allyl or benzyl alcohols as alkylating agents (**Scheme 1**). Ti(O*i*Pr)$_4$ in HFIP plays a unique role in this reaction, as the *in-situ* formation of the complex Ti(Oi-Pr)$_2$(OHFIP)$_2$, was found to initiate the cyclisation, leading to a formal 5-*endo*-trig cyclisation that involves the stereoselective formation of a C-C and a C-O bond in a single synthetic step. This method has been proven to be efficient and atom economic as only catalytic amount of Ti(O*i*Pr)$_4$ is used and water is the only by product. Moreover, a wide range of the homoallyl alcohol (**I**) and alcohol initiator (**II**) show excellent compatibility with the system, and further functionalisation of the products enables access to the synthetically useful heterocyclic molecules.




Scheme 1. Stereoselective homoallyl alcohol (I) functionalization in HFIP

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[1] Y. Zhu.; I. Colomer.; A. L. Thompson and T. J. Donohoe. *J. Am. Chem. Soc. In press*