Novel Divergent Synthetic Pathway to Fluorinated Pseudodipeptides

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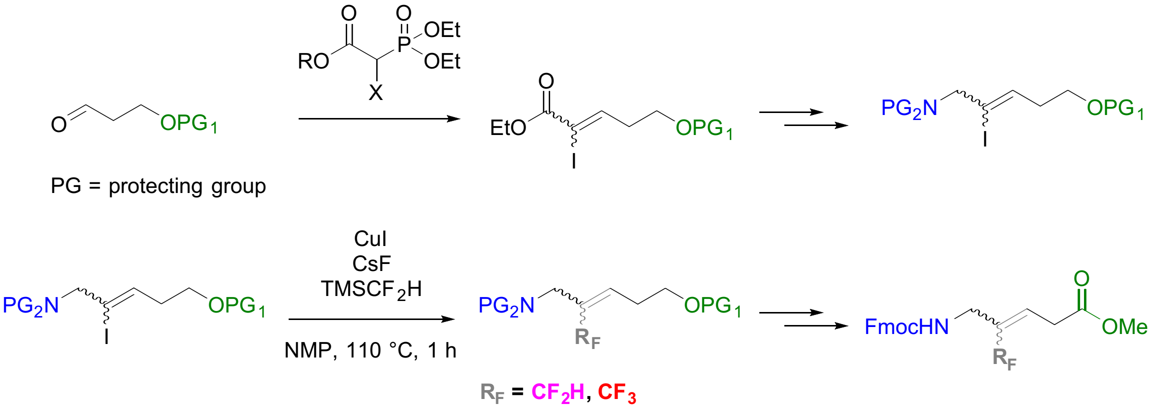
Fluorine chemistry has been extensively studied for decades, due to its wide set of applications (medicinal chemistry, medical imaging, materials, agrochemicals…). In this context, fluorinated alkene moieties have proven to be good mimics of the peptide bond, owing to their similar steric and electronic properties[1]. The strength of the C– F bond also imparts a better stability (i.e., towards peptide cleavage and isomerisation). Fluoropeptidomimetics containing a fluoroalkene or a trifluoromethylalkene moiety have been synthesised using various methods[2] and have a broad range of applications, such as bioactive substances (e.g., anti-cancer agents).[1b] However, there have been no reports of fluoropeptidomimetics containing a difluoromethylalkene moiety, to our knowledge. Furthermore, although the difluoromethylation of aromatic compounds has been developed using different approaches (metallocatalysis, photocatalysis, electrochemistry…)[3], this transformation has been scarcely reported using aliphatic substrates[4]. Therefore, herein, we report the advances in the search for a divergent synthetic pathway to fluorinated pseudodipeptides, with a late-stage introduction of the difluoromethyl- or trifluoromethylalkene moiety.



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