

# Factors governing selectivity in hydrogen atom transfer based aliphatic C–H bond functionalization

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Site-selective aliphatic C–H bond functionalization represents an important goal of modern synthetic organic chemistry. By avoiding the prefunctionalization of substrates associated to traditional functional group manipulation and interconversion, the direct functionalization of these bonds provides access to transformations of high synthetic potential that can offer advantages both in terms of decreased waste generation and reaction step economy.

Among the available methodologies, those based on hydrogen atom transfer (HAT) to radical and radical-like species have attracted considerable interest and accordingly, the factors that govern reactivity and site-selectivity in these processes have been discussed in detail.<sup>1</sup> These include bond strengths, electronic, steric and stereoelectronic effects, conjugation and hyperconjugation, and, with cyclohexane derivatives, torsional effects. Medium effects have also emerged as a powerful tool that has been successfully employed to dramatically alter both reactivity and site-selectivity in HAT based C–H functionalization procedures.<sup>2</sup>

Within this framework, we have been interested in the study of HAT reactions from aliphatic C–H bonds, with the main objective of obtaining quantitative kinetic information on the role of structural and medium effects on the reactivity and selectivity patterns. This goal has been achieved through time-resolved kinetic studies on the reactions of a prototypical alkoxy radical such as cumyloxy ( $\text{PhC}(\text{CH}_3)_2\text{O}$ ,  $\text{CumO}^\bullet$ ) with a wide variety of substrates, accompanied by product studies on C–H bond oxidation of selected substrates with hydrogen peroxide catalyzed by iron and manganese complexes.<sup>3</sup> The results of these studies will be discussed, accompanied by recent examples on the application of these concepts to synthetically useful C–H functionalization procedures.

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