Lipase-mediated flow synthesis of nature-inspired phenolic carbonate and carbamate derivatives as antiradical and antimicrobial agents

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Green chemistry allows the control of environmental hazards and pollution, reducing chemical waste and dangerous effects on workers' health. Recently, the use of continuous biocatalysis has taken widespread in APIs synthesis, stimulating the application of immobilized enzymes in packed bed reactors (PBRs), allowing the overcoming of some practical problems connected to batch procedures, such as product inhibition, biocatalyst stability and product and/or intermediate degradation [1]. In this work, two novel continuous synthetic protocols have been developed exploiting the combination of the two enabling technologies above mentioned, flow chemistry and biocatalysis. Starting from natural phenolic compounds such as tyrosol and hydroxytyrosol, a three-step procedure has been optimized (Figure 1), obtaining carbonate and carbamate derivatives, exploiting immobilized *Candida antarctica* lipase B (CaLB) as a biocatalyst in an unconventional organic medium as *tert*-amyl alcohol. Thanks to the use of an immobilized biocatalyst in a PBR, reaction time, work-up efficiency and productivity were highly increased compared to the traditional batch synthesis. Six compounds were synthesized with biocatalyzed phosgene-free procedures, and, according to the biological results, the antimicrobial and antiradical activities of the parent compounds were left unchanged, improving at the same time their lipophilicity.

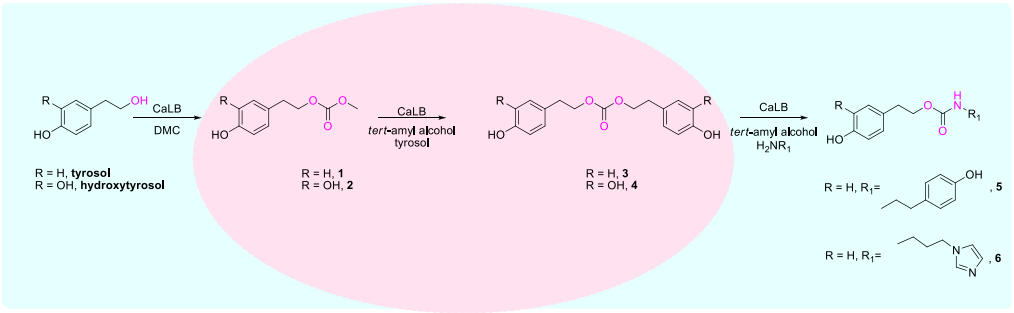

Figure 1: Three-step procedure for the synthesis of carbamate derivatives.

[1] L. Tamborini. P. Fernandes, F. Paradisi, F. Molinari, *Trends in Biotechnology*, **2018**, 36, 73-88.

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