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CHEMO-ENZYMATIC FLOW SYNTHESIS OF TYROSOL AND HYDROXYTYROSOL CARBONATES AND CARBAMATES AS NOVEL ANTIRADICAL AND ANTIMICROBIAL AGENTS

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Nowdays, most chemical and pharmaceutical industries aim at developing new synthetic strategies towards the eco-sustainability concepts reported by the twelve principles of green chemistry, reducing pollution, waste and dangerous effects on workers' health.[1] In this context, food-derived phenolic compounds have been recently described as object of interest of nutraceutical, cosmetic and drugs companies, due to their antioxidant, metal chelator, free radical scavenger, antimicrobial and antiinflammatory properties.[2,3] However, their relevance as active ingredients is still limited according to their solubility, metabolic/chemical stability and bioavailability issues. In addition, carbonate and carbamate chemical moieties play an important role in modern drug discovery and medicinal chemistry; thus, the development of environmentally friendly methods, exploiting no toxic and biodegradable chemicals, is necessary.[4,5] In this work a chemo-enzymatic continuous flow synthesis of new carbonate and carbamate derivatives has been developed. Starting from tyrosol and hydroxytyrosol as natural phenolic compounds, novel more lipophilic derivatives were synthetized, increasing or leaving unaltered the antiradical and antimicrobial properties of the parent compounds. *Candida antarctica* lipase B (CaLB) was adopted as commercially available immobilized biocatalyst, suitably packed in a packed bed reactor, and used in an unconventional organic medium as *tert*-amyl alcohol. A reproducible, efficient, safe, phosgene-free procedure to obtain carbonates has been set-up, followed by the nucleophilic attack using different amines to obtain the desired carbamates (**Figure 1**, compounds **15-18**). Sixteen compounds were synthetized in moderate to good yields demostrating the versatility of the procedure (**Figure 1**).

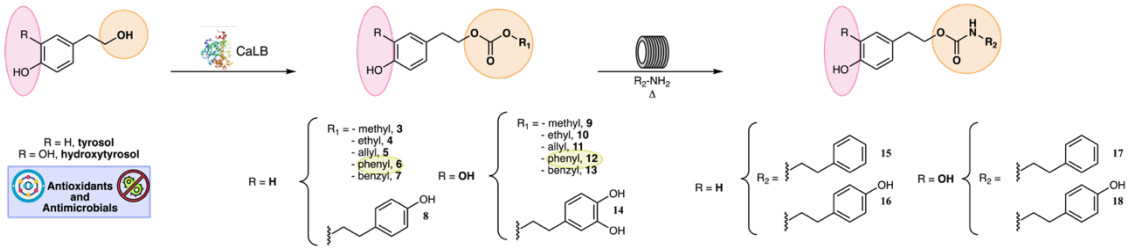

Figure 1: Chemo-enzymatic flow synthesis of phenolic nature-inspired carbonate and carbamate derivatives.

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