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SYNTHESIS OF SUBSTITUTED COUMARINS FROM 2-HYDROXYALDEHYDES, MALEIMIDES AND TRIBUTYLPHOSPHINE VIA MICROWAVE AND CONTINUOUS FLOW

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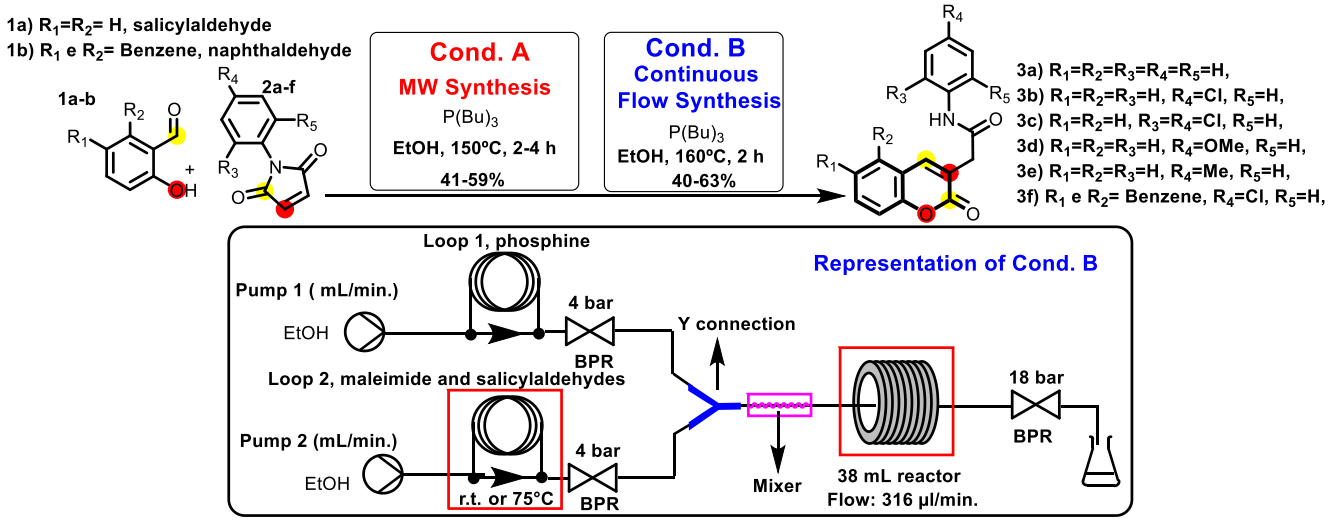
ABSTRACT

Coumarins have an aromatic ring condensed to a pyran-2-one with uses in several research areas such as cosmetics, food additives, and medicinal chemistry due to its pharmacological properties.[1] They can be obtained through classical synthetic routes such as Knoevenagel and Pechmann condensation[2], Perkin, Wittig and Reformatsky reactions.[3] Continuous flow chemistry is characterized as an enabling technology with advantages over batch synthesis, such as high precision on heat and mass transfer, reproducibility, sustainability and easy scale-up[4] In this study, coumarins were synthesized using salicylaldehydes **(1a-b)**, arylmaleimides **(2a-f)** and tributylphosphine through the synthetic transposition from microwave to continuous flow, as a new methodology. Initially, coumarins **(3a-f)** were obtained using **condition A** in the microwave heating. Then, under continuous flow conditions (**condition B**), two solutions of the reagents were introduced into the flow reactor using two loops and two independent pumps. The loop containing the solution of maleimide and salicylaldehyde was heated to 75°C in some cases. A total flow of 316 µL/min., BPR, Y connection, static mixer and EtOH were used. The coumarins **(3a-f)** were isolated in 40-63% yields via simple vacuum filtration and washing with cold EtOH.



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