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Targeting a Mirabegron Precursor by BH_3-Mediated Continuous Flow Reduction Process

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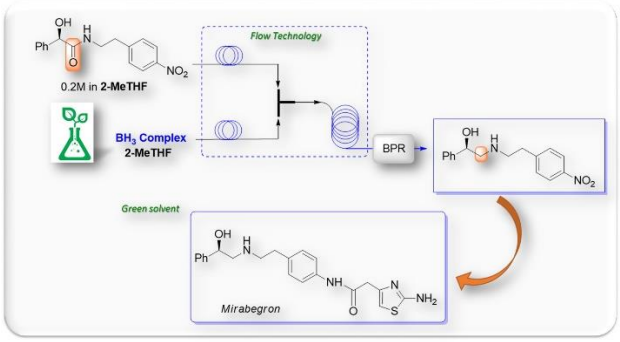
Graphical abstract



CATTOD Highlight

- Flow chemistry set up for pharmaceutical applications
- Continuous flow reduction using BH3 solutions
- Straightforward and green preparation of Mirabegron precursor

Abstract

A continuous-flow reduction of (*R*)-2-hydroxy-N-[2-(4-nitrophenyl)ethyl]-2-phenylacetamide, involved in the synthetic pathway of Mirabegron, has been developed. This study demonstrated the possibility to safely handling BH_3 complexes within microfluidic reactors using 2-MeTHF as greener alternative to traditional solvents, and without requiring any additive such as DMI. In addition, NMR and HPLC purity analysis revealed that the sole by-product of this process is the diamine **3**, which wouldn't affect the following synthetic steps towards Mirabegron.

1. Introduction

The phenylethanolamine core occurs in important molecules such as neurotransmitter noradrenaline and it is also contained in many naturally occurring molecules such as several alkaloids and compounds of pharmaceutical interest with different activities ranging from bronchodilation to antifungal activity (Fig. 1). [1,2]