A Special Case of Divergent Synthesis

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Divergent synthesis has emerged as a powerful tool to promote rapid access to a plethora of natural and unnatural compounds with discrete structural features. As a common practice, starting material(s) are advanced to a *key common intermediate* from where several distinct products are produced in a short and efficient manner, typically in less than five steps. In this work, we present a special case of this tactic, in which natural products from the chiral pool serve as the common intermediate. The so called "natural product to divergency" logic has already been presented before with impressive results, leading to valuable for drug discovery purposes libraries of natural-product-like compounds.^[1] Here, we demonstrate the potential of (–)-caryophyllene oxide as a starting point for divergency and convert it to a number of natural and unnatural compounds, some of them being synthesized for the first time.^[2] All our targets are reached within 5 steps or less and were selected on the basis of their unique structural features within the family of compounds they belong.



Figure 1: Conversion of(-)-caryophyllene oxide to several natural products

References:

[1] K. Morrison, P. J. Hergenrother, Nat. Prod. Rep. 31 (2014) 6-14.

[2] A. Maliori, T. Athanasiadou, V. Pompidou, G. G. Bagkavou, C. I. Stathakis, Org. Lett. 24 (2022) 6242–6246; T. Athanasiadou, G. G. Bagkavou, P. Karagianni, C. I. Stathakis, Org. Lett. 26 (2024) 2897–2901.