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Stereoselective synthesis of hernandulcin, peroxylippidulcine A, lippidulcines A, B and C taste evaluation

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Sucrose abuse is strongly associated to many undesirable health effects. Artificial sweeteners are a popular alternative but many raise questions regarding their safety. The Mexican plant *Lippia dulcis* contains trace amounts of (+)-hernandulcin, a compound so sweet – 1000 times more that sucrose–that few leaves are enough to sweeten a cup of tea. Recent studies revealed that the plant also produces several derivatives of this molecule: The peroxylippidulcines and the lippidulcines A, B and C. However, these sesquiterpenes have been isolated in such a small amount that it has not been possible to assess their taste. A multigram scale-up and optimization for the synthetic route of (+)-hernandulcin, allowed us to accomplish the first stereoselective synthesis of lippidulcines A, B and C. With modified version of the Kornblum–DeLaMare rearrangement, and a highly regioselective and stereoselective ketone reduction with the MeCBS reagent we synthesized the compounds and confirmed the previously assigned absolute configuration. The taste evaluations indicate that lippidulcine A is a cooling agent with a mint after taste, while none of these sesquiterpenes are sweet. Indeed, the insertion of a hydroxy group on the side chain of hernadulcin annuls its intense sweetness.

Biography

Marco Giulio Rigamonti studied chemical engineering at Polytechnique of Milan and graduated with top marks under the supervision of Prof. F Gatti in 2014. Currently he is pursuing a PhD in Polytechnique de Montreal with Prof. G Patience, working on spray drying, computational analysis and scale up for Li-ion battery manufacturing and catalyst for fluidized bed reactors.

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