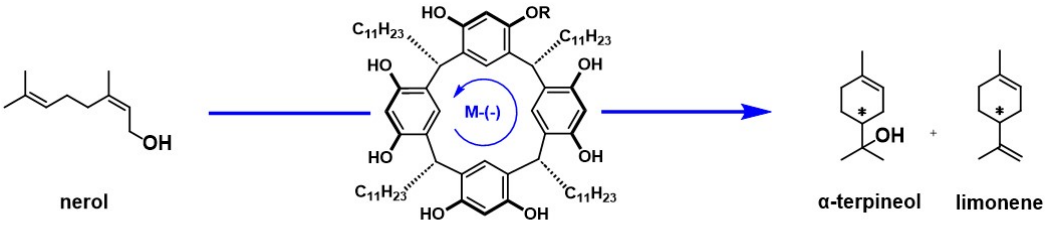
Exploration of Novel Optically Active Resorcin[4]arene Capsule Derivatives for Enantioselective THT Cyclizations

G. Persiani[1], D. Sokolova[2], K. Tiefenbacher[1,3]*

[1]Department of Chemistry, University of Basel, Mattenstrasse 24a, BPR 1096, CH-4058 Basel, Switzerland, [2]Department of Chemistry, University of Oxford, 12 Mansfield Rd, Oxford OX1 3TA, United Kingdom, [3]Department of Biosystems Science and Engeeniring, ETH Zürich, Mattenstrasse 26, CH-4058 Basel, Switzerland

Mimicking the capabilities of terpene cyclases in the tail-to-head terpene cyclizations (THT) represents a great challenge in asymmetric catalysis. Molecular containers, by entrapping guests in a closed cavity, are able to mimic to some extend the enzymatic pockets of natural enzymes. The hydrogen-bond-based resorcin[4]arene capsule, first reported by Atwood in 1997,[1] is able to catalyze the THT cyclization of terpens by stabilizing the cationic intermediates formed during the reaction cascade.[2] In this context, our group recently reported the first examples of optically active mono-alkylated resorcin[4]arene capsules and their application as supramolecular catalysts in the asymmetric THT cyclization of nerol.[3] Therefore, demonstrating that the chirality transfer from a rather large molecular container (approximately 1400 Å) onto the encapsulated substrate is possible. In this work we enlarged the scope of this supramolecular catalyst reporting 14 novel optically active resorcin[4]arene capsule derivatives, exploring the tolerance of the self-assembling of such systems towards structural modifications. Furthermore, the effects that these modifications have on the enantioselectivity of the THT cyclization studied are presented.



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[2] Q. Zhang, K. Tiefenbacher, *J. Am. Chem. Soc* . **2013**, 135, 16213-16219.
[3] D. Sokolova, G. Piccini, K.Tiefenbacher, *Angew. Chem. Int. Ed.* **2022**, 61, e20220338