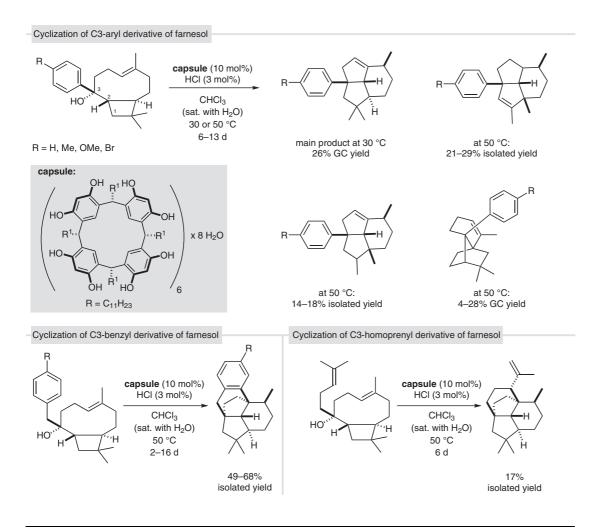
I. NÉMETHOVÁ, D. SCHMID, K. TIEFENBACHER* (UNIVERSITY OF BASEL AND ETH ZURICH, BASEL, SWITZERLAND)

Supramolecular Capsule Catalysis Enables the Exploration of Terpenoid Chemical Space Untapped by Nature *Angew. Chem. Int. Ed.* **2023**, 62, e202218625 DOI: 10.1002/anie.202218625.

Unprecedented Terpenoid Skeletons Accessed via Supramolecular Capsule Catalysis



Significance: Tiefenbacher and co-workers report a terpene cyclization/rearrangement cascade of C3-modified farnesol derivatives co-catalyzed by hydrochloric acid and a supramolecular capsule. The latter self-assembles as a spherical hexamer from six calix[4]resorcinarene units and eight water molecules through a hydrogen bond network and maintains its structure in apolar media. Several unprecedented terpenoid scaffolds and non-natural derivatives of presilphiperfolane- and neoclovene-based natural products could be accessed utilizing this method.

Comment: While sesquiterpene cyclases are able to catalyze the cyclization of farnesylphosphate itself and slightly modified derivatives, heavily C3-modified sesquiterpene derivatives are not accessible *via* this enzymatic pathway. The reported supramolecular capsule catalysis approach, enables access to several electronically diverse aryl-, benzyl-, and homoprenyl-substituted derivatives. In control experiments without a capsule or in the presence of a strongly binding guest, no formation of the desired products was observed.

Category

Organo- and Biocatalysis

Key words

terpene cyclization

supramolecular capsule

resorcin[4]arene

farnesol derivatives

Synfact of the Month