Cascade reactions provide rapid and efficient access to complex organic molecules in a straightforward manner. In case the cascade is initiated by an enzyme, its stereochemical course can be directed in an asymmetric fashion to furnish nonracemic products. This protocol is widely used in Nature for the biosynthesis of complex natural products but is largely underexploited as a synthetic tool. We have recently shown that the biohydrolysis of haloalkyl-oxiranes catalyzed by epoxide hydrolases triggers a hydrolysis-cyclisation cascade to furnish hydroxy-epoxides \((n = 1)\) or \(-tetrahydrofurans \((n = 2)\) with the simultaneous 'creation' of two asymmetric centers. The latter compounds were used as chiral building blocks for the asymmetric total synthesis of various natural products, such as the giberrelling synergist Pestalotin, a Jamaican rum constituent and the antitumor agent Panaxytriol.

Based on these encouraging results, we investigated a stereochemically more challenging transformation, i.e. the biocatalytic hydrolysis-rearrangement of a methylene-interrupted \(meso\)-bisepoxide. From a total of eight (theoretically possible) stereoisomers, only a single THF-product possessing four stereocenters was formed as the sole product in high d.e. and e.e. The latter reaction sequence strongly resembles a biomimetic strategy for the transformation of doubly unsaturated fatty acids into the THF-core of \(Annonaceous acetogenins\), a large and important group of bioactive secondary metabolites from tropical plants showing a diverse spectrum of bioactivity.

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