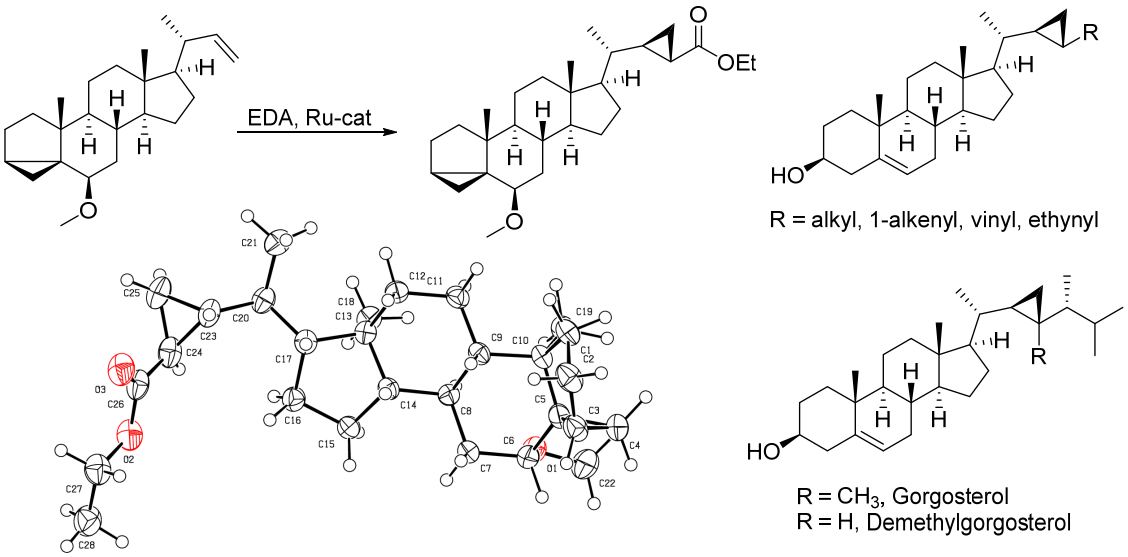
FORMAL SEMISYNTHESIS OF DEMETHYLGORGOSTEROL USING AN ENANTIOSELECTIVE CYCLOPROPANATION AS KEY STEP

Nicolai Rosenbaum[a], Lisa Schmidt[a], Susanne Moser[a] and Stefan Bräse[a,b]

[a]Institute of Organic Chemistry, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany
[b]Institute of Toxicology and Genetics, Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany

Gorgosterol and its derivative demethylgorgosterol are marine steroids found in soft corals with a unique cyclopropane-containing side chain. Recently, gorgosterol was identified as new chemotype of FXR antagonist, as well as exhibiting activity as growth inhibitor of human colon tumor cell lines.[1] We aim to develop a short and efficient semisynthesis of these steroids to further investigate their possible medicinal applications and their biological role in coral symbiosis.



As key step to install the cyclopropane unit we used a known protocol.[2] The resulting ester represents a versatile moiety for subsequent reactions and we used it to synthesize a small library of simple derivatives. However, cyclopropanation with diazopropionate and the creation of the last stereocenter remain challenging and are currently under investigation.

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[1] a) M. Y. Putra, G. Bavestrello, C. Cerrano, B. Renga, C. D'Amore, S. Fiorucci, E. Fattorusso, O. Taglialatela-Scafati, *Steroids*, **2012**, *77*, 433–440. b) A. I. Elshamy, A. F. Abdel-Razik, M. I. Nassar, T. K. Mohamed, M. A. Ibrahim and S. M. El-Kousy, *Nat. Prod. Res.*, **2013**, *27*, 1250–1254.

[2] S. Chanthamath, S. Iwasa, *Acc. Chem. Res.*, **2016**, *49*, 2080–2090.