Synthesis of quinoidic natural products. A new way towards 2'-Desalkyl-Mumbaistatin

Mumbaistatin is the strongest known inhibitor of glucose-6-phosphate translocase (G6P-T1), an enzyme, that controls glucose production in the liver. Therefore, Mumbaistatin displays a promising lead structure for the development of drugs for treatment of type 2 diabetes.

From the synthetic point of view, the structure of Mumbaistatin is very challenging due to its lability towards acids.

Although many attempts have been made, the total synthesis has not yet been reported. One of the major difficulties is the introduction of an acid moiety. We were able to realize this functionality via a biomimetic approach. In contrast to other attempts the sterically hindered part of the molecule has been built up intramolecularly. In one of the key steps, the aldol condensation has to be controlled. In a further innovative step, the bromo-radical induced oxidation of the benzylic position to a carbonyl group has been achieved. The main advantage of our strategy is, that the acid-labile groups are built up in the very last steps. The building blocks for the side chain to be introduced are known in the literature.

Additionally, we investigated synthetic pathways towards antibiotic angucyclins. The oxidative dearomatization by the Mimoun complex was studied in detail. With this reaction, rearranged products were obtained in different ratios. We have shown that this ratio can be controlled by the electronic nature of the protecting group.

We have also synthesized a highly functionalized side chain bearing the complete oxygenation pattern of the natural product.