Abstract

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New Strategies Towards the Total Synthesis of the Natural Product Mumbaistatin

The structurally complex polyketide mumbaistatin was proofed to be the strongest naturally occuring inhibitor of glucose-6-phosphat translocase-1 known today. Since this enzyme plays a key role in the hepatic glucose production, it exhibits a promising target for pharmacological intervention in the treatment of type-2 diabetes mellitus. Due to this, mumbaistatin and derivatives are potential drugs in the therapy of this disease. As a result of its pharmacologic relevance many efforts have been devoted towards its total synthesis, which havn't been successful yet.

This work discloses the first synthetic access towards the spirolactone scaffold of the cyclised form of mumbaistatin, which turned out to be the major challenge during previous studies. Key steps of the elaborated strategy are a *Diels-Alder* cycloaddition for the construction of the anthraquinone skeleton and an anionic homo-*Fries* rearrangement which results in the formation of the spirolactone moiety. Besides the preparation of various dealkyl-analogs of mumbaistatin the developed strategy facilitated the synthesis of a more complex dideoxymumbaistatin derivative which strongly resembles the natural product in its closed form.