STUDIES TOWARDS THE TOTAL SYNTHESIS OF TUSCORON C

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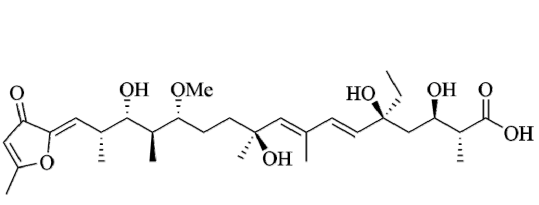
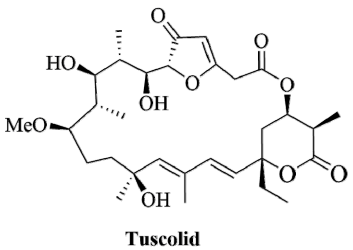
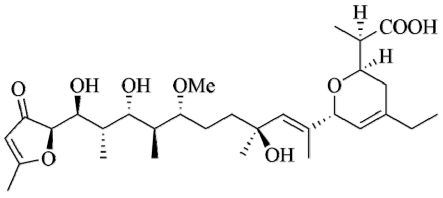
In the course of a screening program for new metabolites from myxobacterium *Sorangium cellulosum*, a new class of closely related polyketide compounds named tuscolid and tuscoron A & B have been isolated by the group of Höfle.[1] Tuscolid is based on a 22-membered macrolactone ring with an uncommon chiral furanone, an extended polypropionate segment in combination with an *E*,*E*-diene that is attached to a δ-lactone. The tuscorons in turn have been assigned as linear and biosynthetically derived tuscolid derivatives with a structurally related furanone and polypropionate backbone. We have discovered three further members, tuscorons C-E, which are presumably intermediates in the biosynthetic conversion of tuscolid to the tuscorons. Furthermore, we have developed a proposal for the full stereochemistry of these complex polyketides by NMR studies in combination with molecular modeling and chemical methods. In addition, we have designed concise synthetic strategies towards a first total synthesis of this class of structurally unique and biosynthetically intriguing class of natural products. Key steps include highly stereoselective substrate controlled aldol reactions and an efficient late stage Stille cross-coupling reaction on highly elaborate and sterically very demanding fragments. A modular synthetic approach was designed based on a late stage diversification strategy to enable access to all members of this class of complex polyketides.



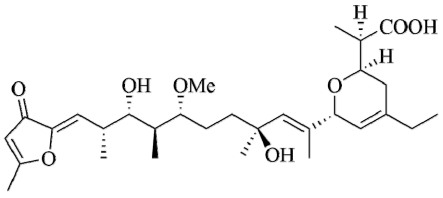
Tuscoron C



Tuscolid



Tuscoron B



Tuscoron A

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[1] J. Niggemann, M. Herrmann, K. Gerth, H. Irschik, H. Reichbach, G. Höfle, *Eur. J. Org. Chem.* **2004**, 487-492.