Emmanuel Roulland, Med Chem (Los Angeles) 2017, 7:8(Suppl)
DOI: 10.4172/2161-0444-C1-033

Total synthesis of tiacumicin B aglycone: A DFT-guided strategy

Emmanuel Roulland
Université Paris Descartes, France

Tiacumicin B is an antibiotic endowed with the remarkable ability to interact with a new biological target giving it an inestimable potential in the context of the ever-growing and worrisome apparition of resistances of bacteria and mycobacteria to antibiotics. The development of an efficient synthesis of this complex molecule will allow accessing valuable analogues. We have achieved the total synthesis of the tiacumicin B aglycone featuring the DFT-guided strategy concept. Macrolactone thus obtained is ready for subsequent glycosylation step. Starting from known alcohol (±)-3, this 16 steps synthesis was performed in a 3.6% overall yield, only 4 steps dealing with the installation or the removal of protective groups. Relying on DFT predictions, we dared to use an unprecedented [2,3]-Wittig rearrangement of the propargyl ether of tertiary allylic alcohol to synthesis the most densely functionalized fragment of the target. We also accessed the tetrasubstituted C12-C15 diene stereoselectively using an innovative strategy based on the sequence allene-alkyne Pd/Cu-catalyzed cross-coupling/selective hydrosulfuration/Pd-catalyzed Kumada-Corriu cross-coupling of an alkenyl sulfide function. To end this synthesis the E configuration of the C4=C5 bond was controlled thanks to a selective cross-metathesis of vinyl borate, and a Suzuki cross-coupling was used to install the missing C1-C3 fragment. The final macrolactonization step was found to be ring-size-selective as again predicted by DFT.

Biography

Dr Emmanuel Roulland has completed his PhD at the age of 30 years from University Paris Descartes (France) working on the synthesis of prostaglandins at Institut Curie in Paris under the supervision of Dr Claude Monneret. He made a first post-doc in the team of Henri-Philippe Husson at the Faculty of Pharmacy (Université Paris Descartes) and a second post-doc in the team of Tony Barrett at Imperial College in London in 2003 (UK). He entered CNRS (Centre National pour la Recherche Scientifique) in 2005 as « Chargé de Recherche » at ICSN (Institut de Chimie des Substances Naturelles in Gif-sur-Yvette, France) and he now works at the Faculty of Pharmacie in Paris. He has published 26 papers mainly in the field of the total synthesis of natural products.

emmanuel.roulland@parisdescartes.fr