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Synthetic methods to 2-hydroxy fatty acids and lipolytic enzyme inhibitors

2-Hydroxy fatty acids are important components of a subset of mammalian sphingolipids. Current evidence clearly shows that 2-hydroxy ceramides and 2-hydroxy complex sphingolipids have unique functions in membrane homeostasis and cell signaling. The biosynthesis of 2-hydroxy fatty acids is accomplished by the enzyme fatty acid 2-hydroxylase (FA2H), which stereospecifically produces the (*R*)-enantiomers. On the other hand, 2-hydroxy oleic acid has been identified as potent antitumor compound (minerval) acting against cancer by inducing cell cycle arrest, followed by apoptosis in human leukemia cells or differentiation and autophagy in the case of human glioma cells. In 2011, the European Medicines Agency designated 2-hydroxy oleic acid as an orphan medicinal product for the treatment of glioma. We have been previously involved in the asymmetric organo-catalytic α-functionalization of carbonyl compounds. In this presentation, we will discuss our most recent application of these methodologies, as well as the development of novel synthetic approaches for the synthesis of enantioenriched α-substituted fatty acids. We will present the successful application of this methodology in the α-functionalization of fatty acids with hydroxyl, fluoro and sulfenyl moieties. Having in hand a methodology for the fast assembly of chiral and racemic α-functionalized fatty acids, their properties as enzyme inhibitors and signaling-molecules will be pursued. In addition, organo-catalytic methodologies for the synthesis of phospholipase A_2 inhibitors will be presented.

Biography

Christoforos G Kokotos is an Assistant Professor of Organic Chemistry in the Department of Chemistry at the National and Kapodistrian University of Athens, Greece. He has studied Chemistry at the University of Athens and moved to the University of Bristol, UK to obtain his PhD. He then conducted Post-doctoral work in the Department of Chemistry of Princeton University, USA. He has authored over 45 publications in peer-reviewed journals and has been selected in prestigious rising star events of Organic Chemistry including EuCheMS Young Investigators Workshop 2014, 9th Young Academic Investigators Award, 248th ACS Meeting 2014 and Burgenstock Conference 2016.

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