Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship

New Phosphonate Analogs Cyclophostin and Cyclipostins: Synthesis and kinetic evaluation as inhibitors of lipases

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Date: 11/18/15
Time: 1pm-2pm
Venue: AHC2-170

Biography

Dr. Spilling received his BSc (Hons.) degree and PhD degree from the University of Technology, Loughborough, England. He was a Postdoctoral Fellow at Northwestern University before joining the UM-St. Louis faculty in 1989. He was promoted to associate professor in 1995 and professor in 2001. He has served as Chair of the Department of Chemistry and Biochemistry since 2004 and Chair of the faculty senate and university assembly 2012-2014. During his 26 years at UMSL, Professor Spilling returned briefly to the UK for a one-year sabbatical leave at Cambridge University (1996) working in association with Prof. S.V. Ley. He is a Member of the Royal Society of Chemistry (MRSC), a member of the American Chemical Society and a member of the National Academy of Inventors. He has published over 75 peer-reviewed research papers and 6 patents. He was the recipient of the 2009 St. Louis award for Chemistry (ACS), 2009 UM President's Entrepreneur of the Year Award and the 2015 Chancellor's Award for Excellence in Service. In 2006, he co-founded Alkymos with Wesley Harris (UMSL), Robert Yokel (U of Kentucky), Robert Kuhn (UK) and Chang-Guo Zhan (UK). Prof. Spilling's current research involves the design of catalysts for asymmetric phosphonylation, chemistry of hydroxy phosphonates, synthesis of metal chelators, natural products and enzyme inhibitors.

Abstract

Cyclophostin is a natural organophosphate isolated from fermentation broth of Streptomyces levundalae (K90109) and is a potent inhibitor of acetylcholinesterase. The cyclipostins are a family of potent inhibitors of hormone-sensitive lipase (HSL) isolated from fermentation broths of Streptomyces sp. (DSM13381) with nanomolar IC50. Both cyclophostin and cyclipostins share a common core unit which comprises a [5.0.3] bicycle with a 7-membered enol phosphate ring fused with 5-membered lactone and chiral centers both at the bridgehead carbon and the phosphorus atom. Cyclophostin, some cyclipostins and a new series of monocyclic phosphonate and phosphate analogs have been synthesized and tested for their abilities to inhibit lipolytic enzymes from various origins including mammalian lipases (AChE, HSL, rHPL, rDGL & GPLRP2) and microbial lipases (Cutinase, LipY & Rv0183).

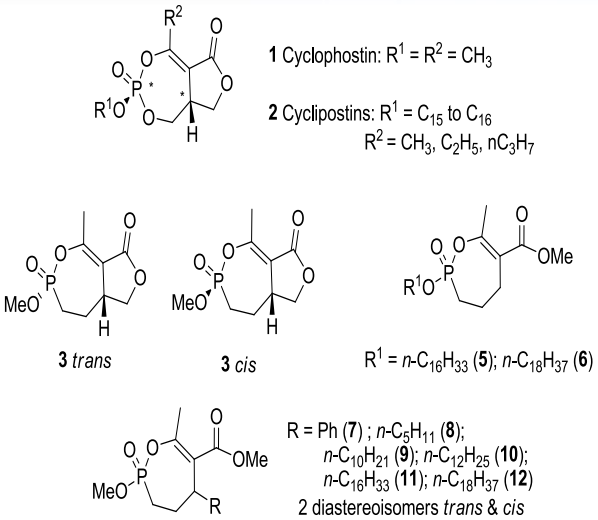

Figure 1Cylophostin, the Cyclipostins and Phosphonate Analogs

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