## Studies Towards the Total Synthesis of Cervinomycin Natural Products

R. Lombardi<sup>1</sup>, M. Wheatley<sup>1</sup>, O. Baudoin<sup>1</sup>\*

<sup>1</sup>University of Basel, Department of Chemistry

Cervinomycins are aromatic polyketides which exhibit antibiotic activity against gram-positive bacteria and high cytotoxicity. <sup>[1]</sup> Herein we report our studies towards the total synthesis of these natural products, in which multiple C-H functionalization steps allow for a convergent route. Retrosynthetically, we aim to construct cervinomycins from functionalized xanthone and isoquinolinone fragments, which will be joined through a reductive Heck coupling and a cross-dehydrogenative coupling. <sup>[2]</sup>

$$\begin{array}{c} \textit{reductive Heck coupling} \\ \textit{cross-} \\ \textit{dehydrogenative} \\ \textit{coupling} \\ \textit{OH} \\ \textit{O$$

The isoquinolinone fragment was accessed in 5 steps from salicylic acid, using two strategic C-H activation reactions. A rhodium-catalyzed C-H annulation of 2-hydroxy-*N*-methoxybenzamide with chloroacetone gave the corresponding isoquinolinone product. [3] After protection of the phenol, an iridium-catalyzed C-H borylation furnished the meta-borylated isoquinolinone as a single isomer. [4] Suzuki-Miyaura coupling with vinyl tosylate gave the corresponding 6-vinylisoquinolinone intermediate. Currently, we are examining different C-H activation-based routes towards the xanthone fragment.

- [1] a) Satoshi Omura, Yuzuru Iwai, Kiyoizumi Hinotozawa, Yoko Takahashi, Junko Kato, Akira Nakagawa, Atsushi Hirano, Hideki Shimizu, Katsuji Haneda, *J. Antibiotics*, **1982**, *35*, 645-652. b) Xiaowen Hu, Xinwin Hu, Xiaomin Hu, Shufen Li, LinLi Li, Liyan Yu, Hongyu Liu, Xuefu You, Zhen Wang, Li Li, Beibei Yang, Bingya Jiang, Linzhuan Wu, *J. Nat. Prod.*, **2019**, *82*, 2337-2342. c) Xiaowen Hu, Wei Sun, Shufen Li, LinLi Li, Liyan Yu, Hongyu Liu, Xuefu You, Bingya Jiang, Linzhuan Wu, *J. Antibiotics*, **2020**, *73*, 812-817.
- [2] Kuanwei Chen, Tao Xie, Yanfang Shen, Haibing He, Xiaoli Zhao, Shuanhu Gao, *Org. Lett.*, **2021**, 23, 1769-1774.
- [3] Da-Gang Yu, Francisco de Azambuja, Frank Glorius, *Angew. Chem. Int. Ed.* **2014**, *53*, 2754-2758.
- [4] Ibraheem A. I. Mkhalid, Jonathan H. Barnard, Todd B. Marder, Jaclyn M. Murphy, John F. Hartwig, *Chem. Rev.*, **2010**, *110*, 890-931.