TOWARDS THE TOTAL SYNTHESIS OF TIACUMICIN B: PREPARATION OF GLYCOSIDIC FRAGMENTS AND GLYCOSYLATION

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During the last decades, bacterial resistance to antibiotics has re-emerged as a serious biomedical risk impacting our quality of life. Tiacumicin B (**1**) is an atypical macrolide antibiotic that was approved by the U.S. *FDA* in 2011 for the treatment of nosocomial diarrhea associated with Clostridium difficile. Tiacumicin B inhibits RNA polymerase by interacting with the "switch" region blocking RNA synthesis and then by killing bacteria.[1] Despite this promising biological activity, only one synthetic access to Tiacumicin B, has been reported to date.[2]

This project aims at providing an efficient synthetic access to Tiacumicin B (**1**) and its analogues through the development of novel synthetic strategies and methodologies. While the synthesis of the aglycon core was studied by our partner (Dr. Emmanuel Roulland) and is beyond the scope of this poster, [3] our efforts focused on the elaboration of both rhamnoside (S1) and novioside (S2) fragments, as well as the subsequent key 1,2-*cis* glycosylations required to link them to the core structure (Figure 1).

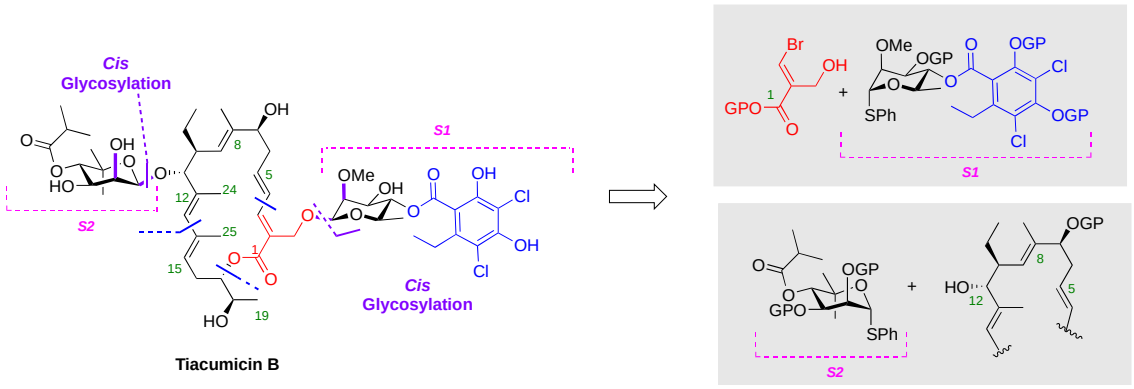

Figure 1

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[1] A. Srivastava, M. Talaue, S. Liu, D. Degen, R. Y. Ebright, E. Sineva, A. Chakraborty, S. Y. Druzhinin, S. Chatterjee, J. Mukhopadhyay, Y. W. Ebright, A. Zozula, J. Shen, S. Sengupta, R. R. Niedfeldt, C. Xin, T. Kaneko, H. Irschik, R. Jansen, S. Donadio, N. Connell, R. H. Ebright, *Curr Opin Microbiol* **2011**, *14*, 532-543. [2] K. Gademann *et al.*, *Org. Lett.* **2015**, *17*, 3514-3517.

[2] F. Glaus, K. H. Altmann, *Angew Chem Int Ed Engl* **2015**, *54*, 1937-1940.

[3] a) L. Jeanne-Julien, G. Masson, E. Astier, G. Genta-Jouve, V. Servajean, J.-M. Beau, S. Norsikian, E. Roulland, *Org. Lett.* **2017**, *19*, 4006-4009. b) L. Jeanne-Julien, G. Masson, E. Astier, G. Genta-Jouve, V.Servajean, J. M. Beau, S. Norsikian, E. Roulland, *J. Org. Chem.* **2018**, *83*, 921-929.