TOWARDS THE TOTAL SYNTHESIS OF (–)-PULVOMYCIN

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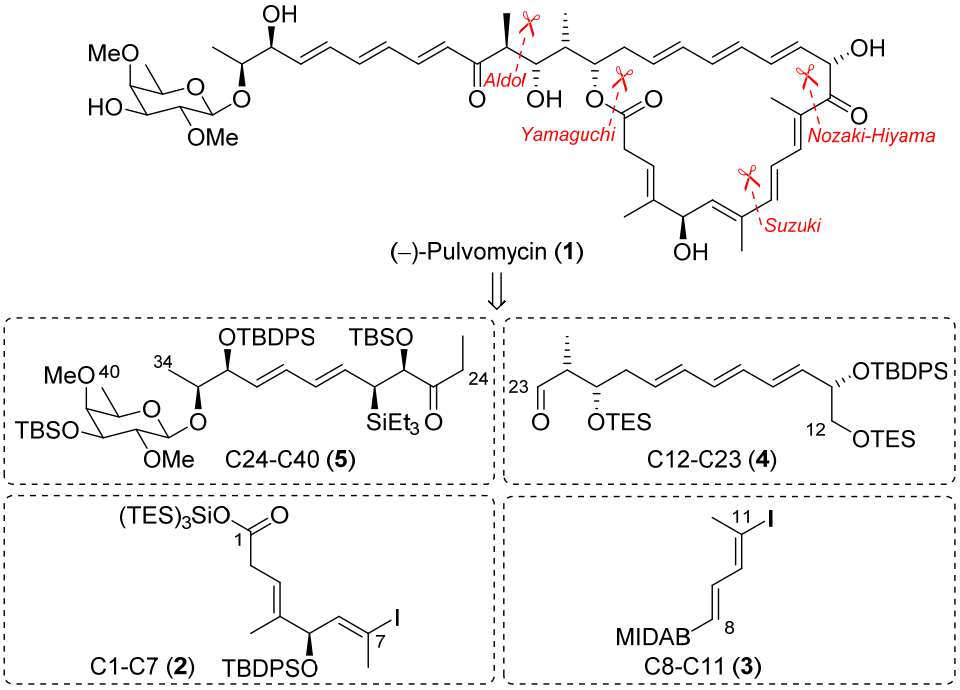
The antibiotic macrolide (–)-Pulvomycin (**1**), which has first been isolated in 1957 and to date has not been synthesized, was targeted in a convergent total synthesis [1]. The molecule was retrosynthetically divided into four building blocks.



Scheme 1. Retrosynthesis into the building blocks C1-C7 (**2**), C8-C11 (**3**), C12-C23 (**4**) and C24-C40 (**5**).

The vinyl iodide **2** bearing a supersilyl protecting group on the carboxylic acid was prepared over twelve linear steps from 1,3-propanediol with 18% overall yield. The literature known stable linchpin diene **3** was synthesized from propynol with 29% yield over seven steps [2]. In a 13-step sequence starting from methyl crotonate, D-mannitol, D-phenylalanine and 1,3-propanediol aldehyde **4** was received with 18% yield. The synthesis involved a *Horner-Wadsworth-Emmons* as well as a *Julia-Kocienski* olefination. Starting from D-galactose, ethyl lactate and propynol the synthesis of ketone **5** could be achieved in a 23-step sequence with 6.8% yield. All four building blocks could be merged into the C1-C40 carbon skeleton of (–)-Pulvomycin (**1**) to provide a precursor for the final macrolactonization.

[1] M. Zief, R. Woodside, H. Schmitz, *Antibiot. Chemother.* **1957**, 384-386.

[2] E. M. Woerly, J. Roy, M. D. Burke, *Nat. Chem.* **2014**, *6*, 484-491.