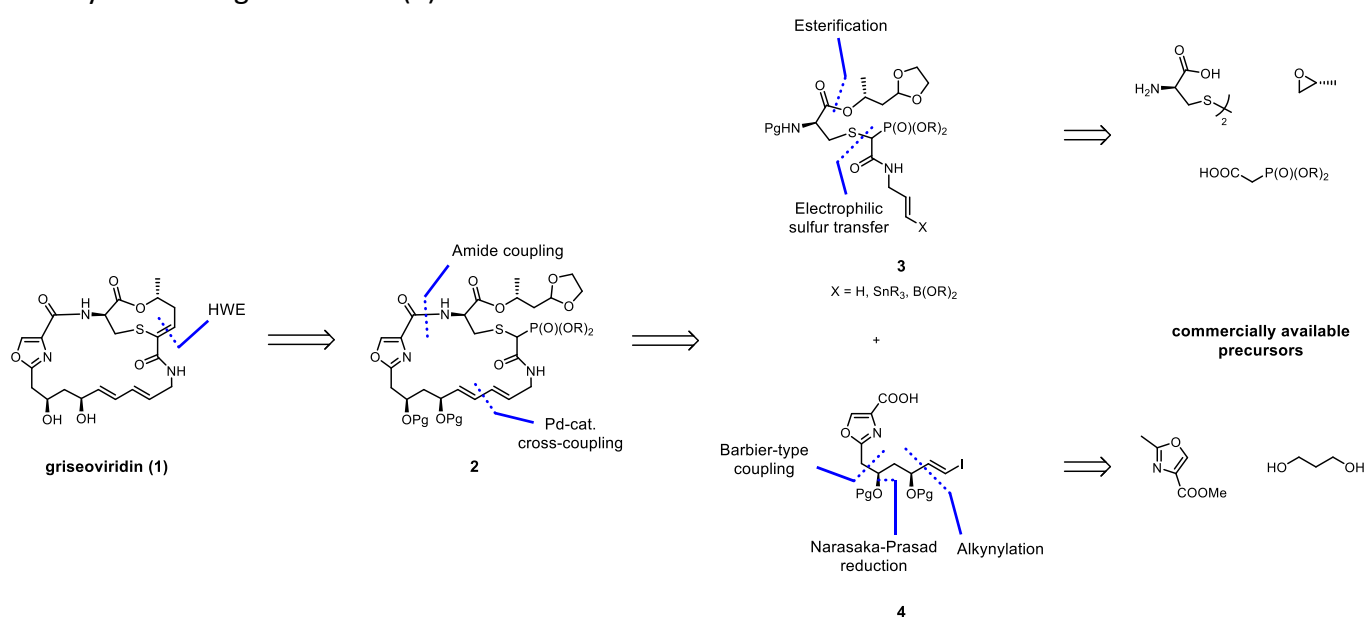


Studies Towards the Total Synthesis of Griseoviridin

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Griseoviridin (**1**) is a natural product of mixed polyketide-non-ribosomal peptide origin, which was first isolated from culture broths of *Streptomyces griseus* in 1955 by Bartz and co-workers. [1] The compound belongs to the streptogramin A class of antibiotics and exerts its antibacterial activity through binding to the ribosome and the inhibition of protein synthesis. [2] Among the various type A streptogramins, griseoviridin (**1**) is the structurally most complex, featuring an additional thio-vinyl ether containing 9-membered lactone ring, and the one whose chemistry and biology has been least studied. [3] Its challenging chemical structure combined with its antibacterial activity prompted us to embark on the total synthesis of griseoviridin (**1**).



We envision to access the natural product via late-stage construction of the macrolactone domain by an intramolecular HWE reaction; we hypothesize that conducting this key step with the macrolactam system already installed could provide a favorable pre-organization effect for the closure of the strained 9-membered ring. The macrocycle **2** is traced back to the two major building blocks **3** and **4** via a Pd-catalyzed cross-coupling / amide coupling sequence. Herein, we present the current state of our efforts towards the total synthesis of griseoviridin (**1**), including the successful synthesis of vinyl iodide **4**, phosphonate **3** and the results of model studies investigating the feasibility of the envisioned intramolecular HWE reaction.

[1] Q. R. Bartz, J. Standiford, J. D. Mold, D. W. Johannessen, A. Ryder, A. Marezki, T. H. Haskell, *Antibiotics Annu.* **1**, **1955**, 777-783.

[2] M. Barbacid, A. Contreras, D. Vazquez, *Biochimica et Biophysica Acta* **1975**, 395, 347-354

[3] F. Ahmed, W. A. Donaldson P., *Mini-Rev. Org. Chem.* **2007**, **4**, 159-181