



Significance: Hygromycin A is a broad-spectrum antibiotic produced by *Streptomyces*. It was recently rediscovered as a potential therapy for the treatment of Lyme Disease (*Cell* 2021, 184, 5405). In mouse models, Hygromycin A was active against *B. burgdorferi* without disturbing the microbiome.

Comment: The first total synthesis of Hygromycin A was reported by Ogawa and co-workers in 1991. Key transformations included a Ferrier carbocyclization and a Sharpless dihydroxylation to form building block A. The furanose and aminocyclitol fragments were pieced together using a Wittig reaction followed by a Yamada peptide coupling.