Total Synthesis of (+)-7-Deoxypancratistatin

Lucas Hernandez and David Sarlah

The Amaryllidaceae isocarbostyril alkaloids and their potent antitumor activity have been well documented in the literature. However, their limited availability from natural sources has initiated a number of synthesis campaigns and structure activity relationship (SAR) studies for several of the more potent congeners. Particularly, 7-deoxypancratistatin has been the subject of 11 total syntheses and two formal syntheses, with the asymmetric routes ranging from 11 to 22 steps. While synthetic access to these natural products and their analogues has been achieved, the previous sequences secured only milligram amounts. Herein, we report the asymmetric total synthesis of (+)-7-deoxypancratistatin in six chemical operations, highlighted by the catalytic dearomative desymmetrization of benzene. Our strategy permits the utilization of olefin functionalization chemistry, providing a means for rapid and versatile access to numerous analogues on gram scale.