Synthesis of Alsmaphorazine B

Significance: Alsmaphorazine B is an indole alkaloid endowed with an isoxazolidine embedded in the hexacyclic skeleton. Biosynthetically, this natural product is believed to originate from the related alkaloid akuammicine. Hong and Vanderwal present a short synthetic route employing an oxidation/Cope elimination/cycloaddition sequence to enable the transformation of akuammicine into alsmaphorazine B.

Comment: A previously employed intramolecular Heck reaction provided high-yielding access to akuammicine from D. Oxidation followed by SmI₂-mediated deoxygenation gave alstolucines B and F. Oxidation with DMDO followed by base induced Cope elimination yielded hydroxylamine G, which upon oxidation to the nitrone underwent 1,3-dipolar cycloaddition to H. Finally, α-hydroxylation furnished alsmaphorazine B in 15 steps and 11% overall yield.