Synthesis of Oxacyclic Scaffolds via Dual Ruthenium Hydride/Brønsted Acid-Catalyzed Isomerization/Cyclization of Allylic Ethers

A ruthenium hydride/Brønsted acid-catalyzed tandem sequence is reported for the synthesis of 1,3,4,9-tetrahydropyrano[3,4-b]indoles (THPIs) and related oxacyclic scaffolds. The process was designed on the premise that readily available allylic ethers would undergo sequential isomerization, first to enol ethers (Ru catalysis), then to oxocarbenium ions (Brønsted acid catalysis) amenable to endo cyclization with tethered nucleophiles. This methodology provides not only an attractive alternative to the traditional oxa-Pictet–Spengler reaction for the synthesis of THPIs, but also convenient access to THPI congeners and other important oxacycles such as acetals.