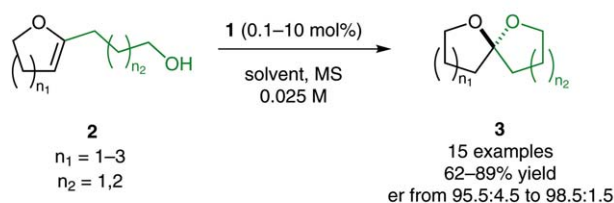
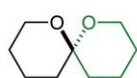


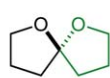
Confined Brønsted Acid Catalysis



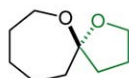
Selected examples:



olean
77% yield
er = 98:2



62% yield
er = 96:4



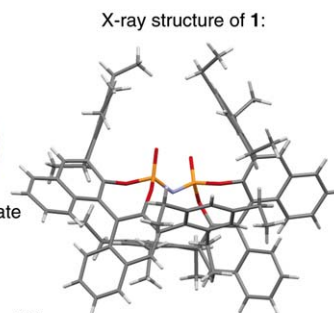
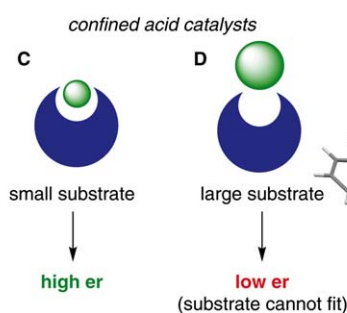
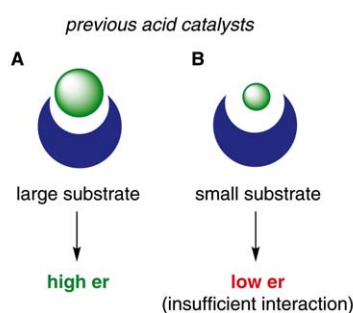
88% yield
er = 98.5:1.5



nonthermodynamic spiroacetal
dr = 7:1
76% yield
(thermodynamic dr = 1:60)



dr = 100:1
86% yield



Significance: Novel confined Brønsted acid catalysts based on a C₂-symmetric imidodiphosphoric acid motif were designed and synthesized. These catalysts possess an extremely sterically demanding chiral microenvironment. With catalyst **1**, an asymmetric spiroacetalization of hydroxyenol ethers **2** to give small spiroacetals **3** has been developed. The spiroacetalization also provides a catalyst-controlled access to nonthermodynamic as well as thermodynamic spiroacetals. Importantly, to access imidodiphosphoric acids **1**, only a single additional step is required compared to the corresponding phosphoric acids.

Comment: Despite numerous reports on Brønsted acid catalysis, particularly with phosphoric acids, reactions of small molecules still present a challenge. As shown schematically above, phosphoric acids typically give good results with relatively large substrates (**A**), while low enantioselectivity is obtained with small substrates due to insufficient interactions with the catalyst (**B**), and a resulting diversity of transition states that can be accommodated. In the case of confined acids, high enantioselectivity can be obtained with small substrates (**C**). In contrast, such catalysts may have difficulties in handling relatively large substrates, which may not fit into the catalytic cavity (**D**).