Macrocyles through fragmentation of fused bicyclic ring systems

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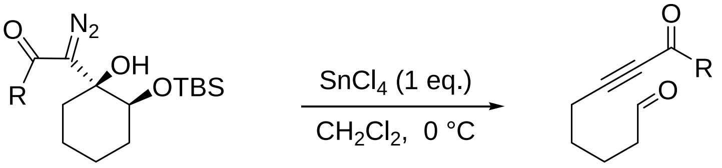
Medium and large sized ring systems are a common structural motif in natural products and pharmaceutically important molecules. However, their synthesis is full of challenges and very few methods are available to make such ring systems.

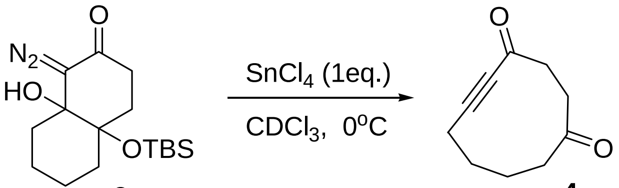
Previously we discovered that cyclic γ-silyloxy-β-hydroxy-α-diazo carbonyls (e.g. **1,** R = OEt, Alkyl, Aryl) undergo efficient *ring fragmentation* upon treatment with Lewis acids to provide tethered aldehyde ynone and ynoate products (e.g. **2**).



1 **2**

R= OEt, Alkyl, Aryl

We are currently investigating the application of this ring fragmentation methodology to the synthesis of medium and large ring systems. We hypothesized that bicyclic γ-silyloxy-β-hydroxy-α-diazo carbonyl compounds (e.g. **3)** fused through the β-γ bond would fragment in the presence of Lewis acids to provide ynones (e.g. **4**) and ynoates contained in medium and large rings.



3 **4**

To test our hypothesis we prepared diazo bicycle[4.4.0] decane (**3**) as a fragmentation precursor. This compound productively fragmented into ten member cyclodec-5-yne-1,4-dione (**4**) in good yield upon treatment with one equivalent of tin tetrachloride. Our results regarding the scope and limitations of this new synthetic method will be discussed.