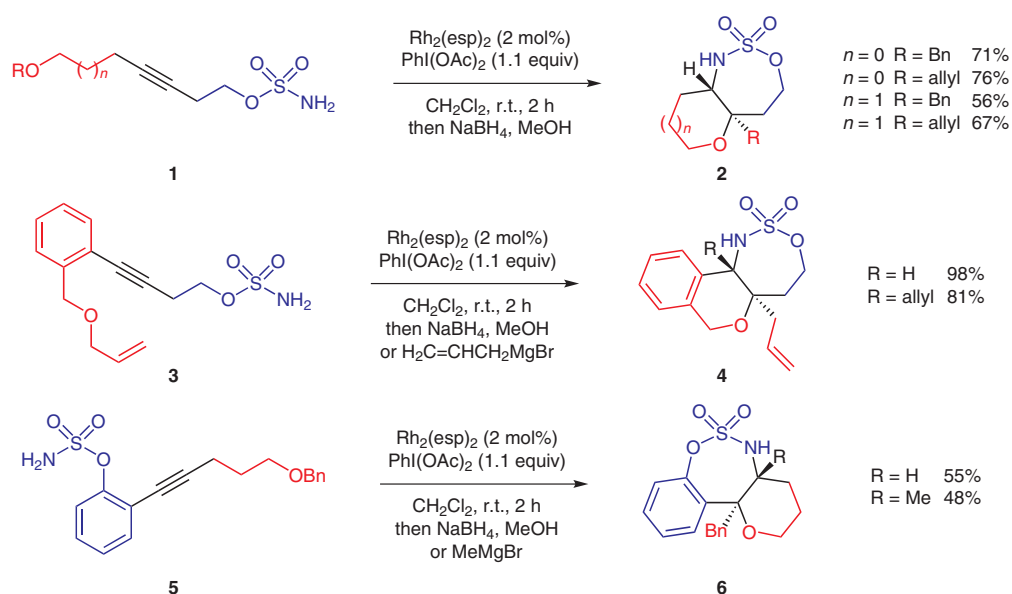


Synthesis of Cyclic Sulfamates by a Cascade Process



Significance: A one-pot synthesis of nitrogen-containing molecules via a rhodium-catalyzed cascade process is described. Treatment of homopropargylic sulfamate esters **1**, **3** and **5** with catalytic dirhodium and a stoichiometric oxidant leads to formation of cyclic *N*-sulfonyl imines. Reductive workup or Grignard addition gives the final products **2**, **4** and **6** in moderate to excellent yields. In all cases, the seven-membered ring is formed exclusively. Geometrical constraints prevent the propargylic sulfamate from undergoing cyclization, whilst extending the chain length further also leads to the seven-membered ring via cyclization onto the proximal alkyne carbon. The reaction conditions were optimized with respect to the rhodium catalyst and solvent. The proposed mechanism involves attack of the alkyne on a generated metallonitrene, followed by cyclization to the oxonium ylide and subsequent rearrangement, as evidenced by several control experiments.

Comment: Many sulfamates have been shown to exhibit important biological activity, including the anticonvulsant topiramate. Steroidal and nonsteroidal sulfamates have also been implicated in the treatment of breast cancer. As initiated by the original observations of du Bois (*Angew. Chem. Int. Ed.* **2001**, *40*, 598), the direct incorporation of a nitrogen functionality into organic hydrocarbons by C–H activation represents an efficient process of potential general synthetic value. The use of metallonitrenes in synthesis has primarily been limited to C–H amination and olefin aziridination, in contrast to the large array of chemistry displayed by metallocarbenes. The current methodology therefore represents an important new development in this field, utilizing a conceptually interesting metallonitrene–alkyne metathesis cascade process to construct bicyclic heterocycles from readily available starting materials.

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