Leveraging Key Driving Forces to Access Cyclobutenes

By Daniel Turner

Abstract: Cyclobutenes are valuable handles in synthetic organic chemistry and constitute an important motif in various bioactive compounds. Common methods to access cyclobutenes involve photoexcited or transition metal-mediated [2+2] cycloadditions between an alkyne and an alkene. However, these reactions suffer from practical limitations, including the regioselectivity of the cycloadditions, the requirement for substrate specificity, and the formation of products bearing extraneous functional groups.

This presentation will address recent advances to access cyclobutenes. Introductory material will include an overview of the previous methods to assemble cyclobutenes, as well as a discussion of the high energy, strained structure of cyclobutene. Several new strategies toward the synthesis of cyclobutenes from unconventional precursors will then be examined, each of which relies on leveraging specific driving forces. An enantioselective Brønsted acid-catalyzed isomerization of bicyclobutanes will be discussed. Additionally, an approach leveraging the high energy intermediate cyclobutadiene, which can engage as a diene in [4+2] cycloadditions, will be considered. Another strategy involving a decatungstate-mediated photocatalytic isomerization of cyclobutylidenes to cyclobutenes will also be discussed. The key driving forces, such as strain-release, relief of anti-aromaticity, and light-based excitation, will be considered throughout the talk, highlighting important considerations applicable to the reaction design of strained motifs.