Orphaned Cyclopropanes

Abstract: Cyclopropanes are strained carbocycles that have fascinated chemists for decades with many established methods for their construction. Unfortunately, many methods struggle to build cyclopropanes containing only alkyl functionality, which limits access to antiviral medicines (e.g., nirmatrelvir), pyrethroid insecticides and sesquiterpenoid natural products. These cyclopropanes have been “orphaned” or left behind by state-of-the-art cycloaddition methods and are typically characterized as arising from the transfer of an unstabilized carbene unit. The goals of the Hill group are to develop new methods to obtain orphaned cyclopropanes and to use these strategies to address the coming “insectocalypse”. To this end, we have developed three cyclopropanation methods that break with traditional paradigms and enable the rational design and facile access to orphaned cyclopropanes. Our most recent approach leverages the high reactivity of lithiosulfones to transfer dialkyl carbene groups to styrenes.