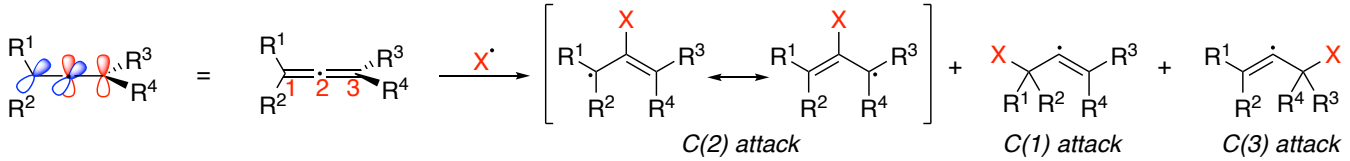
RADICAL ADDITIONS TO ALLENES

Reported by Charlie Dixon Thursday, February 25, 2021

INTRODUCTION

Allenes are interesting species owing to their structural properties and their employment in constructing complex molecules. However, their unique set of orthogonal π-systems makes predicting their reactivity with radicals difficult. Allenes are composed of two cumulated π-bonds in which the central carbon is *sp* hybridized. The site of radical attack on allenes may occur at C(1), C(2), or C(3) (Scheme 1).

Scheme 1. Possible Radical Intermediates Generated from Allenes.



Therefore, site-selectivity is influenced by a number of factors including the substituents on the allene, the attacking radical, and the length between the radical and the proximal carbon.[1]

CHLORINE AND BROMINE RADICALS

The addition of chlorine radicals to allenes can follow two possible routes. In propadiene, chlorine radical attack at the central carbon (C(2)) is thermodynamically favored.[2] Bromine radicals often attack at the central carbon as well. For bromine radicals, attack at the terminal carbons is reversible whereas attack at the central carbon is irreversible owing to the formation of a stable allyl radical.[3]

CARBON CENTERED RADICALS

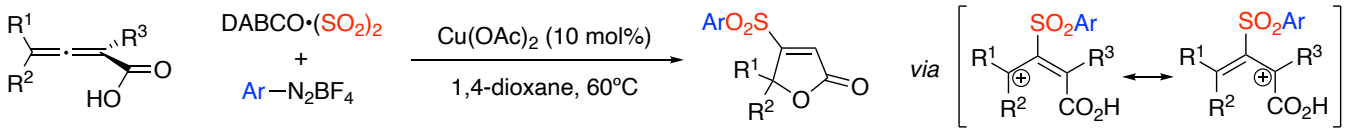
With simple allenes such as propadiene and 1,3-dimethylallene, trifluoromethyl radicals add to the terminal carbon.[7] Using perfluoroalkyl iodides as the radical source, attack at the terminal carbon is favored with the radical adding to the least substituted allene double bond.[4,5] Additionally, the geometry of the addition products is often dictated by substituents on the allene precursor.[1,4-6] In general, radical addition is dictated by substrate control. Interestingly, methyl radicals and CF_3 radicals behave very similar.[7] However, for larger carbon centered radicals such as malonitriles, steric hindrance influences the selectivity in favor of attack at C(2).[8]

NITROGEN AND SULFONYL RADICALS

Nitro radicals are the most heavily studied nitrogen-centered radicals owing to the importance of nitro groups in pharmaceutical settings and their easy transformation into different functional groups.[9,10] Generally, nitro radicals attack the central carbon on most substrates in favor of generating allyl or benzylic radicals and have been employed to convert allenes into interesting units such as isoxazolidinone derivatives.[9,10] For sulfonyl radicals, attack at a terminal carbon is favored with unhindered allenes.

However, in more substituted allenes, sulfonyl radicals tend to attack the central carbon owing to steric restraints and have been employed to synthesize heterocycles.[9,11] Sulfonyl radicals have also been employed to synthesize butenolides by functionalization of 2,3-allenoic acids and subsequent cyclization (Scheme 2).[11]

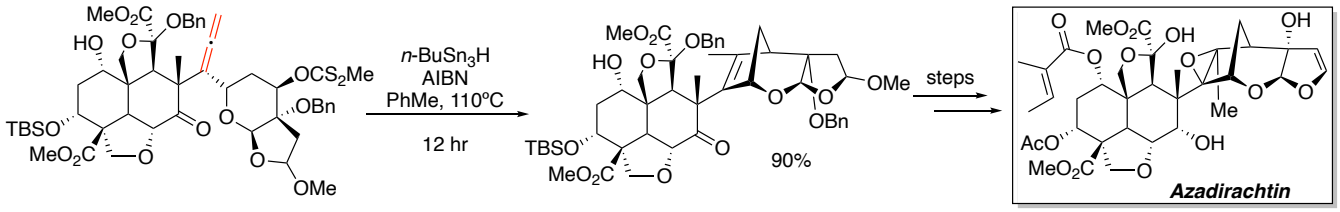
Scheme 2. Butenolide Synthesis from 2,3-Allenoic Acids.



DIRADICAL INTERMEDIATES IN ALLENE CYCLOADDITIONS

Allenes engage in thermal [2+2] cycloadditions with other allenes, alkenes, and alkynes.[1] Generally, [2+2] cycloadditions are concerted. However, there is evidence of radical intermediates in allene cycloadditions.[12,13] Intermolecular cycloadditions usually afford poor regioselectivity whereas intramolecular cycloadditions provide improved regioselectivity.[1] Allene cycloadditions have also been used in the synthesis of natural products by effecting regioselective attack at C(2) (Scheme 3).[14]

Scheme 3. Allene Cyclization in the Synthesis of Azadirachtin.



Radical cyclizations of allenes with other π-systems have revealed mechanistic insight that may be used to highlight the challenges associated with developing regio- and stereoselective reactions using allenes. Overall, many opportunities are available to advance the field of allene chemistry with modern catalysis, radical generation, and synthesis of complex molecules.

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