Exploring Sulfenate Chemistry: Diastereoselective Alkylations of a Protected Cysteinesulfenate

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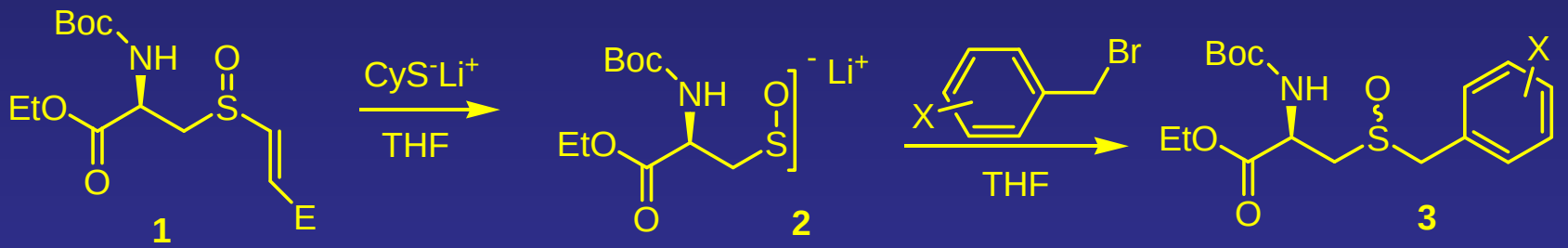
Sulfenate anions represent a underexplored reactive entity in organic chemistry. They have been implicated in the action of the antibiotic leinamycin and their intermediacy in some biochemical oxidations and enzyme mechanisms has recently been recognized. In the laboratory sulfenates can be generated from β-sulfinyl acrylates (e.g., **1**) through a nucleophilic addition-elimination mechanism. Using lithium cyclohexanethiolate, the chemistry is sufficiently mild to permit the release of cysteinesulfenate **2** from base-sensitive sulfinyl compound **1**. Of particular interest is the stereoselective sulfur alkylation chemistry of **2** as a means to learn more about sulfenate reactivity.



Using a selection of benzyl bromides, sulfenate **2** are alkylated with diastereoselectivities ranging from 7.7:1 to 19:1. In the burgeoning field of sulfenate chemistry these values are quite significant. An interesting feature of the cysteine sulfenate chemistry is the rate of the alkylation chemistry. Compared to other sulfenate alkylations, this sulfenate does not readily alkylate at sulfur with benzyl bromide. Indeed, sulfoxide formation is accelerated by exposure of the mixture of water and/or silica gel. It is suggested that an internal complexation or a reversible bond forming event to a proximal functional group is responsible for both the slow and selective alkylation chemistry observed. Some versions of **3** (X = *o*-Br, o-CHO) hold potential for cyclization reactions.

X	% Yield	dr
H	52	11.4:1
p-Me	66	11.7:1
p-Br	76	11.9:1
m-OMe	39	10.1:1
m-NO_2	50	7.8:1
p-CN	44	7.7:1
o-CN	43	8.4:1
o-Br	67	19.0:1
o-CHO	53	13.0:1