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Amination and [2,3]-sigmatropic rearrangement of propargylic sulfides using a ketomalonate-derived oxaziridine: synthesis of *N*-allenylsulfenimides

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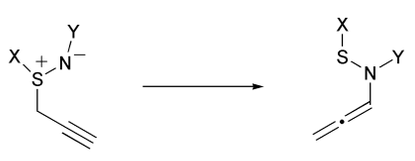
Amination of propargylic sulfides with a ketomalonate-derived oxaziridine under metal free conditions gives *N*-Boc-*N*-allenylsulfenimides *via* [2,3]-sigmatropic rearrangement.

Introduction

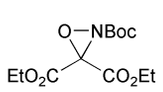
The chemistry of allenes is currently attracting considerable interest, and they are involved in several novel synthetic transformations.[1–3] For example, work by Hsung and co-workers on allenamides[4–7] has demonstrated the widespread synthetic potential of aminoallene derivatives. An important feature of Hsung's work was the use of an electron withdrawing substituent on nitrogen to confer greater stability to the allene moiety. However, methods of synthesis of these compounds remain scarce. The [2,3]-sigmatropic rearrangement of propargylic sulfimides **1** offers an attractive potential route to *N*-allenylsulfenimides **2** (Scheme 1). Evidence for this process was first reported by Tamura *et al.*[8] in 1975 (Y = H), although the compound isolated was a tautomer of the initial allenic product. Tamura later reported a single example of the rearrangement using an ethyl carbamate protecting group on nitrogen[9] (Y = CO_2Et), which facilitated isolation. In this work, the sulfimide intermediate was generated *via* reaction of a sulfide with an aminating reagent. A *tert*-butoxycarbonyl (Boc; Y = $CO_2{}^tBu$) protecting group would afford allenic products with even greater synthetic potential. We recently reported the novel oxaziridine **3** which effects efficient amination of sulfides, allowing [2,3]-sigmatropic rearrangement of allylic sulfimides.[10] We wondered whether this reagent would also allow synthesis and rearrangement of propargylic sulfides. Very recently, while our studies were underway, Van Vranken and co-workers[11] reported the use of Bach's sulfimidation system ($FeCl_2$–$BocN_3$)[12] for this purpose. This prompts us to report our results using oxaziridine **3**, including the synthesis of some novel and highly functionalised allene systems.



1
X= Ar or R

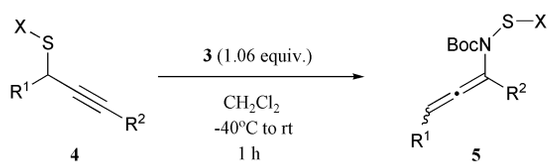
2

Scheme 1



3

Table 1 Conversion of propargylic sulfides to *N*-allenylsulfimides[a]



4 **5**

Entry	Sulfide **4**	X	R^1	R^2	Yield of **5** (%)
1	**a**	Ph	H	H	87
2	**b**	Ph	H	Me	55
3	**c**	Ph	H	$CO_2{}^tBu$	66
4	**d**	Ph	H	Ph	88
5	**e**	Ph	H	I	85
6	**f**	Ph	Me	H	31
7	**g**	*n*-hexyl	Me	H	37
8	**h**	*n*-hexyl	Me	Me	13

[a] Typical amination procedure. To a stirred solution of oxaziridine **3** (100 mg, 0.35 mmol) in CH_2Cl_2 (2 ml) at −40 °C was added dropwise a solution of sulfide (0.33 mmol) in CH_2Cl_2 (2 ml). The resulting solution was allowed to warm to room temperature over 1 h and then the solvent was concentrated under reduced pressure. Chromatography (10% ether–petrol) yielded the required product.

Results and discussion

The initial test substrate, sulfide **4a**, was readily prepared by reaction of propargyl bromide with thiophenol, promoted by K_2CO_3 in refluxing acetone. Pleasingly, we were quickly able to establish that by addition of a solution of **4a** to 1.06 equiv. of oxaziridine **3** in dichloromethane at −40 °C, followed by warming to room temperature over 1 hour, allene **5a** could be isolated in excellent yield by flash chromatography (Table 1, entry 1). Having established the feasibility of the process, a range of sulfides were synthesised in order to evaluate its scope. Sulfide **4b** was prepared in a similar manner to **4a**. Sulfides **4f**–**h** were prepared by analogous reactions between the appropriate thiols and propargylic mesylates. Phenyl-substituted sulfide **4d** was obtained similarly from the tosylate of 3-phenyl-2-propyn-1-ol. Sulfides **4c** and **4e** were accessed *via* the acetylide anion of **4a** (Scheme 2), by reaction with either CO_2 or I_2 as appropriate. Carboxylic acid intermediate **6** was esterified using *tert*-butyl trichloroacetimidate to give **4c**. A room temperature, Lewis acidic method of esterification[13] was chosen in view of the sensitivity of propynoates and the known base-induced isomerisation of related compounds to allenes.[14]

The sulfides were reacted with oxaziridine **3** under the same conditions as those used for amination of **4a** (Table 1). Yields of allenes **5a**–**e** (entries 1–5) from sulfide substrates unbranched α- to sulfur (**4a**–**e**) were moderate to high. The metal-free nature of the reaction conditions may facilitate the isolation of

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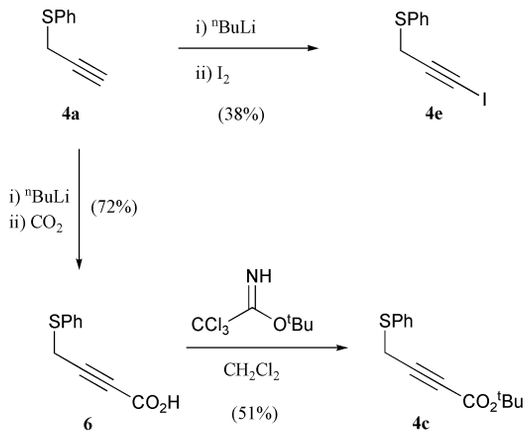

Scheme 2

particularly sensitive allenes or those derived from sensitive sulfides. Of particular note are the unusual iodo-allene **5e** and the formation of **5c** from propynoate ester **4c**. The rearrangement has not been previously reported for sulfides bearing a halogen or carbonyl group at the migration terminus. Indeed, propynoate esters have proved poor substrates for the Fe-catalysed Kirmse reaction,[15] which is mechanistically related to the Bach $FeCl_2$–$BocN_3$ system, due to substrate lability. Compounds like **4c** are therefore likely to give poor results with those reaction conditions.

Branching α- to sulfur led to lower yields. For example, amination of sulfide **4f** resulted in a significantly reduced yield of chiral allene **5f** (31%; entry 6). This was accompanied by formation of sulfoxides by *O*-transfer from the oxaziridine. The two pairs of diastereomeric sulfoxides were isolated in 44% overall yield (ratio 2.5 : 1 by ^{1}H NMR analysis). Competing *O*-transfer had not been observed with substrates **4a**–**e** and it was postulated that increased steric hindrance around sulfur was inhibiting the amination reaction. This led to the synthesis of substrates **4g** and **4h**, in which it was hoped that an *n*-hexyl group would reduce steric demand as well as increasing the sulfide's nucleophilicity. Unfortunately, this strategy did not lead to the desired improvement in yield. The yield of allene **5h** was particularly low (entry 8). However, this compound is of note as the first trisubstituted allene prepared *via* the rearrangement.

In summary, we have discovered that oxaziridine **3** can give good to excellent yields of aminoallene derivatives by amination of propargylic sulfides and subsequent rearrangement. Yields are reduced by branching α- to sulfur. However, the method still gives a useful, metal-free preparation of chiral allenes. The metal-free reaction conditions allow synthesis of allenes (*e.g.* **4c**) that are likely to be difficult to obtain using metal-mediated sulfimidation systems. Synthetic applications of these interesting and highly functionalised allenes are under investigation.

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