The synthesis of alkenyl disulfides

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The disulfide bond is one of the most important structural functionality which plays a crucial role affecting stability, folding, and biological function of proteins and peptides. Disulfides also are important and versatile compounds due to their applications in material and food chemistry. Moreover, the synthesis of unsymmetrical disulfides is an important for preparation of variety of compounds involved in medicinal chemistry and advanced organic synthesis. Although unsymmetrical disulfides can be obtained by several different synthetic methods, the synthesis of unsymmetrical alkenyl disulfides can be accomplished by only five methods (Scheme 1).

A. The reaction of sulfenyl bromide with trityl-alkenyl sulfide C. The reaction of E-alkenyliodonium salt with sodium thiotosylate and thiols

NHBoc
$$R_1$$
 R_2 R_3 R_4 R_4 R_5 R_5 R_6 R_6 R_7 R_8 R_9 R_9

B. The cleavage of an alkenyl thioacetate followed by sulfenylation

D. The reaction of $\alpha\text{-thiophosphorylated}$ ketones with thiosulfonates

E. The conversion of S-vinyl phosphorodithioate and S-vinyl thiosulfonate

$$\begin{array}{c|c}
S & O \\
\hline
R-STs \\
TBAF
\end{array}$$

$$\begin{array}{c}
R-STs \\
TBAF
\end{array}$$

$$\begin{array}{c}
R-SH \\
NEt_3
\end{array}$$

$$\begin{array}{c}
R - SH \\
NEt_3
\end{array}$$

Scheme 1. The available methods for synthesis of alkenyl disulfides.

The synthesis of unsymmetrical Z-alkenyl disulfides with additional functional groups can be accomplished with readily available staring materials under mild conditions with moderate to high yields (Scheme 1C). This method is diastereoselective and exclusive formation of Z-isomer is observed. The developed method includes the reaction of E-alkenyliodonium salt with sodium thiotosylate and thiols in the presence of a base. The another method is based on the base-promoted rearrangement of α-thiophosphorylated ketones followed by thioalkylation with thiotosylates (Scheme 1D). We were interested in the development of an experimentally practical and versatile method to access vinyl disulfides with additional functional groups. The designed method is based on the readily available S-vinyl phosphorodithioate and S-vinyl thiosulfonate (Scheme 1E). The synthetic potential of vinyl disulfides can involve formation of complexes with metals, multicomponent reactions, Heck reaction, olefin metathesis or the variety of cycloaddition reactions. Due to the poor availability of vinyl disulfides, aforementioned transformations were not examined yet.