

# Diastereoselective Synthesis of Z-Alkenyl Disulfides from $\alpha$ -Thiophosphorylated Ketones and Thiosulfonates

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**Abstract:** We developed a simple and efficient method for the synthesis of functionalized unsymmetrical Z-alkenyl disulfides under mild conditions in moderate to good yields. The designed method is based on the reaction of  $\alpha$ -thiophosphorylated carbonyl compounds with thiotosylates in the presence of a base. The developed method allows the preparation of unsymmetrical Z-alkenyl disulfides bearing additional hydroxy, carboxy, or ester functionalities

**Keywords:** Disulfides; alkenes; thiotosylates; diastereoselectivity; phosphorodithioic acid

## Introduction

Organosulfur compounds have been widely investigated for their importance in many chemical and biochemical processes. In this field, oligosulfides, such as disulfides,<sup>[1]</sup> represent important and versatile molecules for their applications in food chemistry and material science. The formation of unsymmetrical disulfides is an important transformation in organic synthesis and medicinal chemistry<sup>[2]</sup> as well. Recent developments in disulfide bond formation reactions have been reviewed.<sup>[3]</sup> Although many different methods exist for the preparation of unsymmetrical disulfides, the most common approach involves substitution of a sulfenyl derivative with a thiol or thiol derivative. To date, the most commonly utilized sulfenyl derivatives are sulfenyl chlorides,<sup>[4]</sup> S-alkyl thiosulfates and S-aryl thiosulfates (Bunte salts),<sup>[5]</sup> S-alkylsulfanyliothioureas,<sup>[6]</sup> benzothiazol-2-yl disulfides,<sup>[7]</sup> benzotriazolyl sulfanes,<sup>[8]</sup> dithioperoxyesters,<sup>[9]</sup> (alkylsulfanyl)dialkylsulfonium salts,<sup>[10]</sup> 2-pyridyl disulfides and derivatives,<sup>[11]</sup> N-alkyltetrazolyl disulfides,<sup>[12]</sup> sulfonamides,<sup>[13]</sup> sulfenyldimesylamines,<sup>[14]</sup> sulfenyl thiocyanates,<sup>[15]</sup> 4-nitroarenesulfenylamides,<sup>[16]</sup> thiolsulfonates and thiosulfonates,<sup>[17]</sup> sulfanylsulfonamides,<sup>[18]</sup>

thionitrites,<sup>[19]</sup> sulfenyl thiocarbonates,<sup>[20]</sup> thioimides,<sup>[21]</sup> and thiophosphonium salts.<sup>[22]</sup> Other practical procedures involve the reaction of a thiol with a sulfenylbenzimidazole,<sup>[23]</sup> a rhodium-catalyzed disulfide exchange,<sup>[24]</sup> an electrochemical method,<sup>[25]</sup> the ring opening of an aziridine using tetrathiomolybdate in the presence of a symmetrical disulfide,<sup>[26]</sup> or the use of diethyl azodicarboxylate (DEAD)<sup>[27]</sup> or a solid support<sup>[28]</sup> in a sequential coupling of two different thiol groups. Recently, the oxidation of a mixture of two different thiols by 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)<sup>[29]</sup> or iridium (III) photoredox catalysis<sup>[30]</sup> to produce an unsymmetrical disulfide have also been reported.

Earlier studies demonstrated the preparation of functionalized unsymmetrical molecules, such as dialkyl disulfides,<sup>[31]</sup> alkyl-aryl disulfides,<sup>[32]</sup> 'bioresistant' disulfides,<sup>[33]</sup> unsymmetrical disulfides of L-cysteine and L-cystine,<sup>[34]</sup> and diaryl disulfides<sup>[35]</sup> based on the readily available 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives. These disulfanyl derivatives of phosphorodithioic acid are convenient for the preparation of  $\alpha$ -sulfenylated carbonyl compounds,<sup>[36]</sup> functionalized phosphorothioates,<sup>[37]</sup> and unsymmetrical alkynyl sulfides<sup>[38]</sup> as well as symmetrical<sup>[39]</sup> and unsymmetrical trisulfides.<sup>[40]</sup>