Diastereoselective Synthesis of Z-Alkenyl Disulfides from α-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 α-thiophosphorylated carbonyl compounds with thiosulfonates 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; thiosulfonates; 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,[1] 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[2] as well. Recent developments in disulfide bond formation reactions have been reviewed.[3] 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,[4] S-alkyl thiosulfates and S-aryl thiosulfates (Bunte salts),[5] S-alkylsulfanylisoniouracils,[6] benzothiazol-2-yl disulfides,[7] benzotriazolyl sulfanes,[8] dithioperoxysters,[9] (alkyl)sulfanyl(dialkyl)sulfonium salts,[10] 2-pyridyl disulfides and derivatives,[11] N-alkylmercaptothiazolyl disulfides,[12] sulfonamides,[13] sulfenylidimesylamines,[14] sulfenyl thiocyanates,[15] 4-nitroaranesulfenamides,[16] thiolsulfonates and thiosulfonates,[17] sulfonylsulfonamidines,[18] thionitrites,[19] sulfenyl thiocarbonates,[20] thioimides,[21] and thiophosphonium salts.[22] Other practical procedures involve the reaction of a thiol with a sulfanylbenzimidazole,[23] a rhodium-catalyzed disulfide exchange,[24] an electrochemical method,[25] the ring opening of an aziridine using tetrathiomolybdate in the presence of a symmetrical disulfide,[26] or the use of diethyl azodicarboxylate (DEAD)[27] or a solid support[28] 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)[29] or iridium (III) photoredox catalysis[30] to produce an unsymmetrical disulfide have also been reported.

Earlier studies demonstrated the preparation of functionalized unsymmetrical molecules, such as dialkyl disulfides,[31] alkyl-aryl disulfides,[32] ‘bioreistant’ disulfides,[33] unsymmetrical disulfides of L-cysteine and L-cystine,[34] and diaryl disulfides[35] based on the readily available 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-disulfanyl derivatives. These sulfanyl derivatives of phosphorodithioic acid are convenient for the preparation of α-sulfenylated carbonyl compounds,[36] functionalized phosphorothioates,[37] and unsymmetrical alkenyl sulfides[38] as well as symmetrical[39] and unsymmetrical trisulfides.[40]