A Convenient and Efficient α-Sulfenylation of Carbonyl Compounds

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Abstract: A method for the α-sulfenylation of carbonyl compounds by 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinanane-2-disulfanyl derivatives has been developed. Readily available reagents, mild reaction conditions, and excellent yields with high selectivity make this method quite simple, convenient and practical.

Key words: thioethers, sulfides, sulfenylation, thiols, carbonyl compounds

The development of new reactions that produce convenient and versatile building blocks from simple and readily available reagents is currently one of the most important tasks for contemporary organic synthesis. α-Sulfenylated carbonyl compounds are particularly interesting synthetic intermediates since they have been used for a variety of organic transformations.[1] Preparation of these compounds very often involves S_N2 displacement of α-halogenated carbonyl compounds with sulfides anions.[2] Other methods are based on the reaction of enolates or enamines with various electrophilic sulfenylating reagents such as commercially available dimethyl disulfide, diphenyl disulfide, *N*-(phenylsulfanyl)phthalimide [3] or *S*-methyl methanethiosulfonate, *N*-(phenylsulfanyl)caprolactam, *N*-(phenylsulfanyl)succinimide,[4] and sulfenyl chlorides (e.g., PhSCl).[5] In recent years, some attention has been paid to the enantioselective α-sulfenylation of carbonyl compounds (aldehydes, ketones, lactones, lactams, and 1,3-dicarbonyl compounds) using chiral organocatalysts[6] and also titanium(IV) catalysts.[7] Although a wide range of sulfenylating reagents is available, many of them required multistep sequences for their preparation. Moreover, their reactivity is often compromised by their stability[6b] or the presence of additional functional groups.

We have previously prepared functionalized unsymmetrical dialkyl disulfides, alkyl aryl disulfides,[8] 'bioresistant' disulfides,[9] unsymmetrical disulfides based on L-cysteine and L-cystine derivatives,[10] and diaryl disulfides[11] using of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives in reactions with aliphatic, aromatic thiols and thiol groups from cysteine derivatives. The presence of additional functional groups such as amino, hydroxy, or carboxy did not disturb the unsymmetrical disulfide bond formation.

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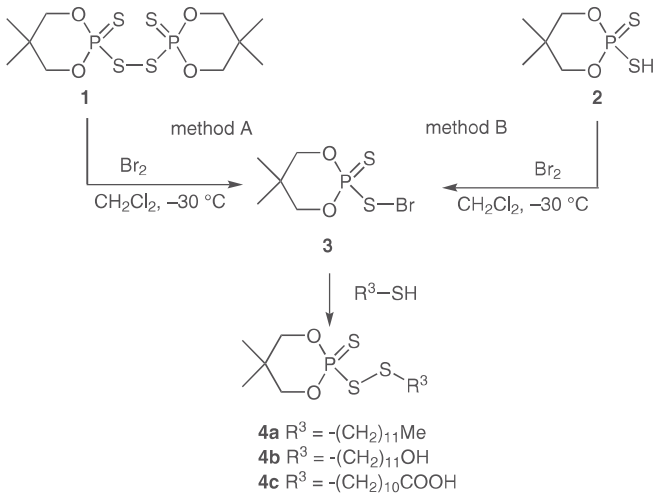
The presence of enolizable C–H bonds in aldehydes, ketones, and α-acidic hydrogens in β-keto esters allows the possibility for reactions with different classes of electrophilic sulfenylating reagents leading to the formation of C–S bonds. Herein, we report a convenient and efficient method for the preparation of α-oxo sulfides from enolizable carbonyl compounds and 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives.

Treatment of the stable and readily available bis(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfide (**1**) (method A) or 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane **2** (method B) with bromine at –30 °C quantitatively affords 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-sulfenyl bromide (**3**) (Scheme 1). Subsequent treatment, without prior isolation, of sulfenyl bromide **3** with dodecane-1-thiol, 11-sulfanylundecan-1-ol, or 11-sulfanylundecanoic acid provides the corresponding 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives **4a–c**, which can be isolated in very good yields[12] (92–100%, Scheme 1).



Scheme 1 The synthesis of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives **4a–c**

These compounds are stable at room temperature for several months; decomposition by moisture or formation of symmetrical disulfides was not observed.

Initially, we attempted the sulfenylation of diethyl malonate (**5a**) with disulfide **4a** using stoichiometric amounts of reagents. After three hours at room temperature, product **6a** was isolated only in 42% yield (54% of starting material **4a** was recovered) (Table 1, entry 1). When the