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ELIMINATIVE DEOXYGENATION: A FACILE SYNTHESIS OF α-CYANO AND α-CARBOALKOXY SUBSTITUTED VINYL SULFIDES

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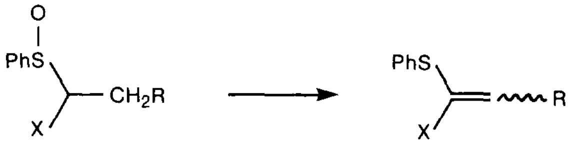
SUMMARY: The facile eliminative deoxygenation of α-cyano and carboalkoxy sulfoxides by trimethylsilyl triflate under mildly basic conditions results in the formation of α-thiophenyl substituted α,β-unsaturated nitriles and esters in high yields.

Vinyl sulfides which are geminally substituted with strongly electron attracting substituents such as cyano and carboalkoxy have been used synthetically as capto-dative radical traps,[1] as potent Michael acceptors[2] as precursors of extended enolates[3] and in a variety of cycloaddition reactions.[4] For these reasons, there has been considerable effort directed toward their synthesis.

α-Alkylthioacrylonitrile derivatives have been prepared by the rearrangement of α-chloro-β-alkylthio nitriles induced by lithium bromide in DMF at elevated temperatures[5] or alternatively by the condensation of alkylthioacetonitrile with aldehydes or ketones in the presence of a strong base.[6] The former procedure has also been employed for the preparation of arylthio derivatives, although a mixture of regioisomers usually results.[5] Similar techniques have been utilized for the preparation of α-carboalkoxyvinyl sulfides.[7] In addition, a number of α-alkyl and arylthio substituted α,β-unsaturated enones and esters have been synthesized by the Pummerer rearrangement of sulfoxides in the presence of strong acid.[3,8]

We were interested in the development of a mild, general procedure for the production of α-thio substituted unsaturated nitriles and esters under neutral or weakly basic conditions. In this regard, we have recently described the preparation of vinyl sulfides from sulfoxides using trimethylsilyl iodide in the presence of tert-amine bases[9,10] and felt that this procedure might also be applicable for the preparation of the desired α,β-unsaturated nitriles and esters as shown in Eq. (1).



(1)

X = CN, CO_2R

I II

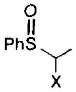
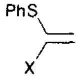
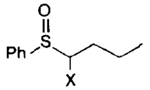
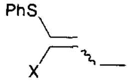
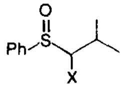
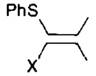
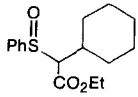
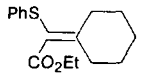
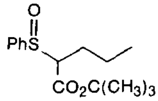
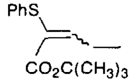
α-Cyano sulfides were prepared as described by Reetz and coworkers[11] and were converted to the desired sulfoxides by oxidation with sodium periodate in ethanol-water. The α-carboalkoxy sulfoxides were produced directly from sulfoxides using two equivalents of lithium diisopropylamide followed by quenching of the resulting anions with diethyl carbonate or di-tert-butyldicarbonate.

Treatment of 1a with trimethylsilyl iodide in the presence of a variety of amine bases failed to produce the desired deoxygenated product. Although a rapid reaction ensued at 0°, ^{1}H NMR examination of the crude reaction mixture showed that 6a was not produced in significant yield. Reaction of 1a at -78°C in the presence of triethylamine also resulted in the rapid disappearance of the starting material, but yielded only an unstable dark oil which rapidly liberated iodine upon standing.[11] No modification of this procedure was discovered which produced the desired product in acceptable yields.

Fortunately, the desired transformation could be effected by substituting trimethylsilyl triflate as the silylating reagent. This highly reactive species generates the weakly nucleophilic triflate moiety upon complexation and reaction. The use of trimethylsilyl triflate in the presence of the weak, sterically hindered base hexamethyldisilazane (HMDS) resulted in the formation of the desired vinyl sulfides in excellent yields (see Table I). Interestingly, previous studies have shown that the use of HMDS and trimethylsilyl iodide with unactivated sulfoxides resulted only in simple deoxygenation without deprotonation.[9] In this regard, the electron attracting cyano and carboalkoxy substituents apparently facilitate subsequent elimination due to the increased acidity of the α-protons.

Examination of Table I shows that the products are produced in good yield under very mild reaction conditions.[13] Although the deoxygenation reaction is usually performed at 25°C, in the case of more sterically hindered sulfoxides such as 3 and 4, the temperature was raised to 35°C to accelerate the reaction without detrimental effects. The mildly basic nature of the reaction medium permits even the preparation of sensitive t-butyl ester derivatives such as 10. In those cases where stereoisomerism is possible, the products are generated as E/Z mixtures. The actual assignment of the stereochemical configuration is based on ^{1}H NMR chemical shift data and is therefore tentative.[14] The procedure is useful for the preparation of a variety of substituent patterns including di, tri and tetrasubstituted olefins. All of the products were easily purified either by distillation or flash column chromatography over silica gel.[15]

Table I

Starting Material	Reaction Conditions	Product	Yield (%)^a	
 1a X=CN 1b X=CO_2Et	1a, 3h, 25°C 1b, 6h, 25°C	 6a 6b	84 83	
 2a X=CN 2b X=CO_2Et	2a, 3h, 25°C 2b, 3h, 25°C	 7a 7b	74 84	1:1^b 6:94^b
 3a X=CN 3b X=CO_2Et	3a, 3h, 35°C 3b, 3h, 35°C	 8a 8b	87 84	
 4	4h, 35°C		73	
	3h, 25°C		76	13:87^b

a. Isolated yield after purification. b. Z/E ratio.

In summary we have described a mild, high yield preparation of synthetically useful α-thiophenyl substituted α,β-unsaturated nitriles and esters under mildly basic reaction conditions from readily available starting materials. The reactivity of other α-substituted sulfoxides is under investigation.

GENERAL PROCEDURE FOR THE PREPARATION OF α-CYANO AND α-CARBOALKOXYVINYL SULFIDES

3 Mmol of the α-substituted sulfoxide was dissolved in 12 mL of anhydrous ether containing 1.58 mL (7.5 mmol) of HMDS, and the mixture was cooled to 0°C. At this point, 1.2 mL (6.6 mmol) of trimethylsilyl triflate was added and the mixture warmed to room temperature. For certain sterically hindered sulfoxides, the mixture was heated to 35°C (see Table I). The disappearance of starting material was monitored by TLC.

When the reaction was complete, the mixture was poured into cold 2N H_2SO_4 and extracted with ether. The organic phase was washed with 5% sodium bicarbonate, saturated brine solution and dried over $MgSO_4$. After removal of the solvent, the crude product was purified either by distillation or by flash column chromatography[15] over silica gel. The yield of the products after purification ranged from 73-87%.

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