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A Novel Synthesis of Monosubstituted Sulfines via an Unusual β-Elimination of Chloroform from Allylic and Benzylic Trichloromethyl Sulfoxides.[1]

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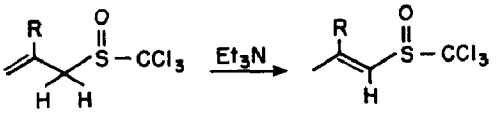
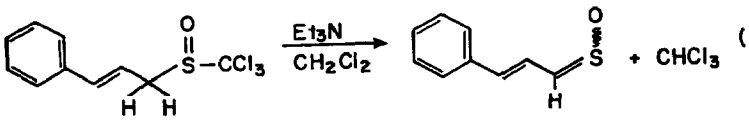
Abstract: *A new method for the synthesis of thioaldehyde S-oxides by base-induced elimination of chloroform from allylic and benzylic trichloromethyl sulfoxides is described. The reaction proceeds smoothly under mild conditions. A mechanism for this remarkable sulfine synthesis and apparently unprecedented β-elimination of chloroform is presented.*

During studies on the rearrangement of allyl trichloromethanesulfinates to allyl trichloromethyl sulfones, we found that these sulfones, unlike the corresponding aryl sulfones, undergo an unusually fast isomerization to vinylic sulfones even in the presence of weak bases such as triethylamine or 2,6-lutidine.[2] This reaction is not only of mechanistic interest but also of synthetic utility due to the growing importance of vinyl sulfones in organic synthesis in recent years.[3]



1a,b **2a,b** (1)

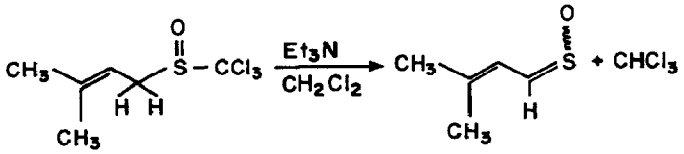
Prompted by these results, we have examined the analogous isomerization of allylic trichloromethyl sulfoxides, which are easily obtained by the well-known [2,3]-sigmatropic rearrangement of allylic trichloromethanesulfenates.[4] We have found that this isomerization (eq. 1) occurs in quantitative yield, but is strongly dependent on the substituents. Thus, while unsubstituted allyl sulfoxide **1a** (R=H) yields the corresponding vinyl sulfoxide **2a** on stirring overnight with one equivalent of Et_3N in CH_2Cl_2 at room temperature, the isomerization of methallyl sulfoxide **1b** (R=Me) to **2b** proceeds only to ~50% when refluxed overnight in CH_2Cl_2 solution. The difference in reactivity between **1a** and **1b**, as well as the reduced rate of isomerization of sulfoxides *vs.* sulfones may be explained by electronic effects on the acidity of the α-hydrogens.[5]



3 **4** (2)

In sharp contrast to the above results, we have found that another allylic derivative, namely cinnamyl trichloromethyl sulfoxide (**3**) under similar conditions (Et_3N, CH_2Cl_2, 25°) undergoes an unexpected and apparently unprecedented β-elimination of chloroform and affords the corresponding thiocinnamaldehyde S-

oxide (**4**, eq. 2). Sulfine **4**, apparently the first published sulfine which is both a conjugated vinyl sulfine and thioaldehyde S-oxide, is best obtained when **3** is treated overnight with 2 equivalents of DABCO, and can be isolated by column chromatography in 95% yield as a yellow solid.[6] The compound shows a characteristic ^1H NMR absorption at δ 8.71 ppm for the sulfinic proton. It should be noted, however, that similar to other (relatively stable) sulfines, compound **4** is stable for extended periods of time only at low temperature and in the dark, while at room temperature it deteriorates and affords a mixture of products, with cinnamaldehyde as the major product. Similar to the reaction of **3**, we have found that γ,γ-dimethylallyl trichloromethyl sulfoxide(5) also undergoes β-elimination of chloroform on treatment with base and affords the corresponding conjugated vinyl sulfine **6** (eq. 3).[6]



5 **6** (3)

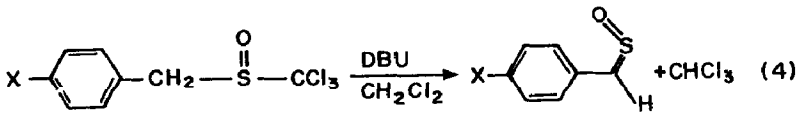
During the past three decades a large variety of substituted sulfines has been reported.[7] However, thus far, conjugated vinyl sulfines have received scarce attention in the literature. They have been prepared by oxidation of the corresponding α,β-unsaturated thiones,[8] by rearrangement of vinylsulfinyl carbenes,[9] by oxidation of 2,5-dimethylthiophene with singlet oxygen[10] and as intermediates in a thermal fragmentation of their formal dimers.[11] A novel synthesis of thiophenes from allenic sulfones involving α,β-unsaturated sulfines as intermediates has also been reported.[12] However, all these routes have a limited scope, and yield disubstituted sulfines, only.

Although oxidation of thiocarbonyl compounds is the most general route to sulfines, this method cannot be applied to the synthesis of thioaldehyde S-oxides, because the former are not stable. For this reason, this type of sulfines has been studied to a much smaller extent, and their synthesis involves alternative methods.[13,14] For example, Bonini and coworkers[14] have recently demonstrated that silylthioketones can serve as synthetic equivalents of thioaldehydes, as the silicon substitution can be easily replaced by a proton at a latter stage. By application of this concept the synthesis of various thioaldehyde S-oxides, including some aromatic derivatives, could be accomplished. However, as pointed out above, the method described in this paper provides an easy and direct access to α,β-unsaturated thioaldehyde S-oxides, which have never been reported before. It is worthwhile noting, that although allylic trichloromethyl sulfoxides played an essential role in the discovery and elucidation of the mechanism of the reversible allylic sulfenate-sulfoxide rearrangement a quarter of a century ago, their synthetic potential has been ignored since then. This observation is in sharp contrast to the great synthetic utility enjoyed by allylic aryl sulfoxides in the past.[4]

In order to check the generality of the new method of sulfine synthesis, we have tested the reactivity of benzyl (**7a**, X=H) and *p*-methoxybenzyl (**7b**, X=OMe) trichloromethyl sulfoxides under basic conditions. Interestingly, with these sulfoxides, Et_3N or DABCO are not sufficiently basic to bring about elimination of $CHCl_3$. However, the use of a stronger base such as DBU results in a fast reaction at room temperature and affords the expected phenyl and *p*-methoxyphenylsulfines (**8a,b**, respectively) within less than 15 min and in high yield. It is worthwhile noting that in all cases studied we could only detect one of the two possible

stereoisomers. In the case of the aromatic derivatives **8a,b**, the Z stereochemistry has been determined by comparison of the NMR spectral data with those previously reported by Bonini, who obtained both isomers.[14]

A preliminary mechanistic study indicates that, as expected, the conversion of sulfoxide to sulfine proceeds by a reversible E1cB mechanism and not by a concerted E2 elimination. Thus, on treatment of **3** with Et_3N in the presence of D_2O, the rate of hydrogen-deuterium exchange is faster than the rate of sulfine formation. The observed stereospecifity is therefore quite striking.



7 a,b **8a,b**

Although elimination of HCl is one of the oldest approaches to sulfine synthesis,[13a] the present study on the elimination of chloroform (pKa=24)[15] is rather surprising not only in the context of sulfine formation, but of β-elimination reactions in general. However, the elegant and detailed studies by Kice in recent years[16] have demonstrated that methoxide-induced eliminations of other weak acids such as alcohols, amines, sulfones and fluorene from the corresponding sulfinyl derivatives, are also suitable for sulfine formation.

It is interesting to add, that in spite of the apparent lack of previous documented examples of β-elimination of chloroform in the literature, the α-elimination of chloroform has been thoroughly studied and extensively used for the generation of dichlorocarbene in the past.[17] Similarly, the leaving group ability of the trihalomethyl anion is well demonstrated by the old haloform reaction, whereby the trihalomethyl group of a trihalomethyl ketone is substituted by a two-step nucleophilic addition-elimination mechanism.[18] However, for those ketones which have both a trihalomethyl group and an α-hydrogen, this generally accepted mechanism may require some modification in view of the results reported in this paper. Thus, an alternative mechanism involving β-elimination of haloform and formation of a ketene intermediate, which is then trapped by base to give the observed product is presently under investigation. In addition to this obvious analogy, we are also exploring the application of chloroform and haloform eliminations in general, for the synthesis of various other heterocumulenes, including sulfenes, as well as for the synthesis of disubstituted sulfines (thioketone S-oxides).

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References and Notes

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5. Further details of this study will be published subsequently.
6. All new compounds gave ir, nmr and mass spectral data in accord with the assigned structures. **Sulfine 4**, Mp 67-69°; IR (neat) 1078 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.04 (bd, J = 15.8, 1H), 7.38 (m, 3H, *m* + *p* - H's), 7.57 (m, 2H, *o*-H's), 7.77 (dd, J = 15.8, 11.2 Hz, 1H, H_α), 8.71 (dd. J = 11.2, 0.9 Hz, 1H of CHSO), ^{13}C NMR ($CDCl_3$), δ 118.0 (C_β), 128.15, 128.45, 129.05, 130.20 (Ph), 137.41 (C_α), 171.56 (C=S=O); MS (CI/i-Bu) m/e 165 (M^+ + 1). **Sulfine 6**: IR (neat) 1096 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.89 (m, 3H), 1.95 (m, 3H), 6.99 (dm, J = 11.8 Hz), 8.7 (d, J = 11.8 Hz, 1H of CHSO). ^{13}C NMR ($CDCl_3$): δ 20.30 (CH_3), 26.48 (CH_3), 116.86 (C_β), 146.23 (C_α), 168.26 (C=S=O); MS (EI) m/e 116 (M^+, 69%), 99 (M-OH, 100%), 101 (M-CH_3, 76%), 67 (M-HSO, 26%. **Sulfine 7a**: ^1H NMR ($CDCl_3$) δ 7.1-7.6 (m, 3H, *m* + *p* -H's), 8.08 (dd, J = 9.4, 2.0 Hz, 2H *o*-H's), 8.34 (s, 1H, of CHSO); **Sulfine 7b**; ^1H NMR ($CDCl_3$) δ 3.86 (s, 3H), 6.92 (d, J = 8.8 Hz, 2H, *m*-H's), 8.09 (d, J = 8.8 Hz, 2H, *o*-H's), 8.24 (s, 1H, of CHSO).
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