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Intramolecular Cyclization of (Allylthio)sulfines via their Vinylsulfenic Acid Tautomers.

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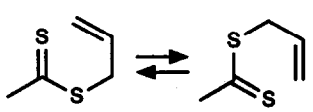
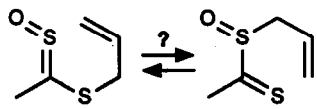
Abstract . Intramolecular cyclization of enethiolizable (allylthio)sulfines afford 2-alkylidene-1,3-dithiolane-1-oxides in good yields. The formation of these compounds can be explained by an initial tautomerization of the sulfine to vinyl sulfenic acid, followed by an intramolecular addition of the sulfenic acid to the allylic double bond. The structures of the products were elucidated by means of ^{1}H-and ^{13}C-NMR spectroscopy as well as LIS effects, deuteriation experiments and an X-ray analysis.

Hetero [3,3]-sigmatropic rearrangements involving a 1S-3S group transfer have been observed for allyl dithioates[1,2] (Scheme 1a). In the context of our continuous interest in the chemistry of sulfines[3] the question arose whether thiono-S-oxides of allyl dithioesters would undergo a similar thio-Claisen rearrangement (Scheme 1b).



Scheme 1.a



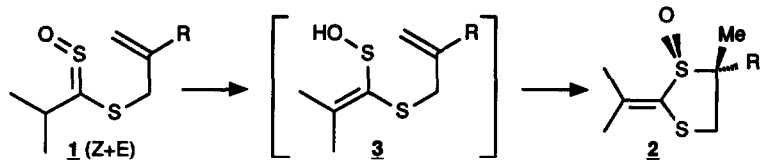
Scheme 1.b

The substrates for this study, viz. (allylthio)sulfines, are readily accessible by oxidation of the corresponding allyl dithioates, which in turn can be prepared by allylation of magnesium dithioates obtained from appropriate Grignard reagents and carbon disulfide[4]. In contrast to our expectation phenyl(allylthio)sulfine[5] did not show the desired thermal rearrangement reaction; only decomposition was observed at about 110°C in $C_6 D_6$ in a sealed NMR tube. The product of rearrangement, viz. an α-thioxosulfoxide, may however not be stable under the conditions of the reaction. Therefore, 2,3-dimethyl-1,3-butadiene was used as reaction medium with the aim to trap the rearrangement product by a [4+2]-cycloaddition reaction. However, at 65°C only the cycloadduct of the sulfine was obtained in 80% yield.

The second substrate that was tested, viz. isopropyl(allylthio)sulfine[6] **1a**, gave on heating at reflux in toluene for 16h, in the presence of PPTS (pyridinium p-toluenesulfonate) as the catalyst (10 mol %), a rearranged product **2a** in 72% yield. In the absence of PPTS the yield decreased to 13%. The same rearrangement was observed for isopropyl(methallylthio)sulfine[7] **1b** producing compound **2b** in 43% yield. The structure of the

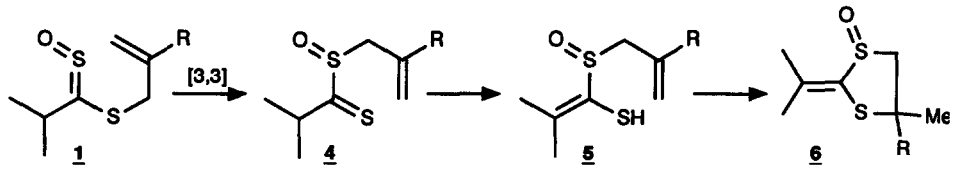
products 2 was based on a correct mass measurement, infrared and especially NMR spectral data[8]. A comparison of ^{1}H- and ^{13}C-NMR spectra[9,10] of 2 a,b with those of methyl-substituted thiolane S-oxides (*cis*-and *trans*-2-Me, *cis*-and *trans*-3-Me and 2,2-diMe), reveals that the methyl substituent in 2 is positioned α to the sulfoxide. Especially, the ^{13}C-resonances at 62 ppm for the methine carbon in 2a and 65.3 ppm for the quaternary carbon in 2b are typical for a carbon atom adjacent to a sulfoxide function[10].

The formation of these unanticipated compounds 2 can only be reconciled by invoking an initial tautomerization of sulfine 1 to the corresponding vinylsulfenic acid 3 catalyzed by PPTS, followed by an intramolecular addition of the sulfenic acid to the olefinic bond, as is depicted in Scheme 2.



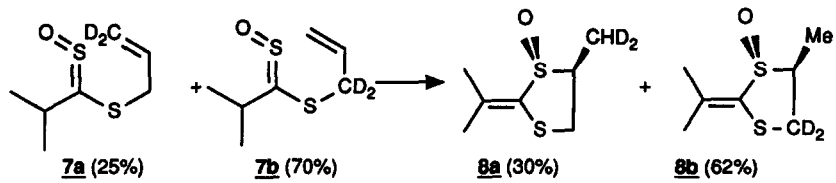
Scheme 2

It should be pointed out however, that a regio-isomeric structure 6 can be envisaged by assuming that substrate 1 undergoes a thio-Claisen rearrangement, initially producing thio-ketone 4 (*cf* Scheme 1b) which subsequently enethiolizes to 5 and then intramolecularly adds to the double bond in a Markownikow fashion, as is shown in Scheme 3.



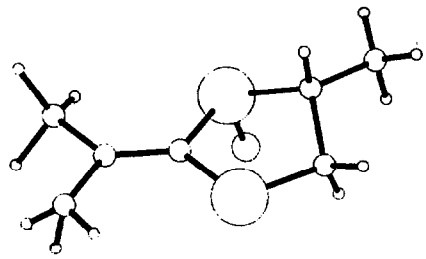
Scheme 3

In order to further confirm the structure of 2, and particularly to rule out the reaction sequence depicted in Scheme 3, d_2-labelled isopropyl(allylthio)sulfine consisting of a mixture[11] of 7a (25%) and 7b (70%), was subjected to the above mentioned cyclization reaction. A mixture of d_2-dithiolane 1-oxides 8a and 8b was obtained in 30 and 62% yield, respectively[12] (Scheme 4). Hence, the mechanism is as put forward in Scheme 2.



Scheme 4

The *cis* relationship of the sulfinyl oxygen and the α-methyl group in 2a was deduced from LIS experiments[13] with Eu $(fod)_3$ on 2a and 2b. The structure of 2a was unambiguously confirmed by an X-ray diffraction analysis[14] (Figure). This *cis* stereochemistry of 2a is in accordance with the stereochemical course of the intramolecular addition of sulfenic acid to olefinic bonds reported in the literature[9,15].



Figure

The results above unequivocally demonstrate that the reaction takes the course as shown in Scheme 2, involving tautomerization of the sulfine as the first step. This finding is of great interest, because the tautomeric form of sulfines received scarce attention in the literature. One of the reasons for this is that most sulfines that have been prepared in recent years do not possess a hydrogen at the α-carbon atom. Explicit mention of vinylsulfenic acids as sulfine tautomers was made when the structure of naturally occurring ethylsulfine, the principal lachrymatory factor in freshly cut onions, was investigated. Actually, Virtanen et al.[16] suggested that the lachrymator, which arises from enzymatic cleavage of propenyl cysteine sulfoxide [MeCH=CHS(O)CH_2CH(NH_2)COOH], is propanesulfenic acid [H_3C-CH=CH-SOH],[16] instead of ethylsulfine as was established later on[17]. In some instances the intermediacy of vinylsulfenic acid has been suggested.[18] Also examples are known in which α-deprotonation of a sulfine leads, after alkylation, to vinylsulfoxides arising from vinylsulfenate anions as intermediates.[19,20] The tautomerization of enethiolisable sulfines to vinylsulfenic acids was also suggested to explain the formation of thiolane 1-oxide derivatives from allylsulfenic acids and alkynes. Currently, we are actively exploring the involvement of vinylsulfenic acid tautomers in reactions of sulfines.

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5. Yield: 75% δ_H ($CDCl_3$) 3.2 and 3.8 (d, 2H, H_2CS; E:Z=45:55), 4.7-5.2 (m, 2H), 5.5-5.9 (m, 1H), 7.4-8.3 (m, 5H, Ph) ppm. ν_{max} (CCl_4) 1125 cm^{-1} (CSO).
6. Yield: 90% δ_H ($CDCl_3$) 1.23 (d, 6H), 2.92 and 4,1 (m, 1H_Z and 1 H_E; E:Z=80:20 on the crude), 3.47 and 4.2 (d, 2H_E and 2H_Z), 5.15=5.4 (m, 2H), 5.65-5.95 (m, 1H) ppm. ν_{max} CCl_4 1125 cm^{-1} (CSO). This compound was previously reported by Metzner, P. and Pha, T.H., J.Chem.Soc., Chem. Commun. **1988**, 380.
7. Yield: 87% δ_H ($CDCl_3$) 1.25 (d, 6H), 1.85 (b.s, 3H), 2.9 and 3.6 (m, H_Z and lH_E, 3.4 and 4.2 (b.s, 2H_E and 2H_Z, 5.0 (m, 2H) ppm. ν_{max} (CCl_4) 1105 cm^{-1} (CSO).
8. 2a: δ_H ($CDCl_3$) 1.55 (d, 3H, J 6.5 Hz), 1.87 (s, 3H), 2.25 (s,3H), 2.98 (m, lH), 3.31 (dd, lH, J 11.5 and 5.5 Hz), 3.70 (td, lH, J 11.5 and 1.5 Hz) ppm. δ_C ($CDCl_3$) 11.21 (CH_3), 23.17 (CH_3), 23.47 (CH_3), 36.69

(CH_2), 62.01 (CH), 138.16 (C), 139.43 (C). ν_{max} (CCl_4) 1045 cm^{-1} (SO); m/e 176 (M^+), 159, 86, 71.
2b: δ_H ($CDCl_3$) 1.23 (s, 3H), 1.54 (s, 3H), 1.87 (s, 3H), 2.25 (s, 3H), 2.98 (d, lH; J 11.5 Hz), 3.84 (d, lH, J 11.5 Hz ppm. δ_C ($CDCl_3$) 19.62 (CH_3), 19.95 (CH_3), 23.45 (CH_3), 23.86 (CH_3), 42.75 (CH_2), 65.35 (C), 138.36 (C), 139.90 (C). ν_{max} (CCl_4) 1050 cm^{-1} (SO); m/e 190 (M^+), 173, 161, 100, 71.

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11. Obtained by reaction of i-PrMgCl with CS_2 followed by alkylation with allyl-l-d_2-bromide and oxidation with MCPBA. Deuterium incorporation was determined by ^{1}H-NMR analysis of the dithioester: δ_H ($CDCl_3$) 1.35 (d, 6H), 3.42 (m, lH), 3.9 (d, 2H, 30% CH_2 +70% CD_2), 5.15-5.4 (m, 2H, 75% CH_2 +25% CD_2), 5.75-5.95 (m, lH) ppm.
12. 8a + 8b: δ_H ($CDCl_3$) 1.45 (d, 30% CD_2H +70% CH_3), 1.87 (s, 3H), 2.25 (s, 3H), 2.9-3.1 (m, lH), 3.31 (dd, 62% CD +38% CH), 3.70 (td, 62% CD +38% CH) ppm.
13. 2a: upon addition of Eu(fod)$_3$ 8 mol% the signal of the 2-Me, originally at 1.55 ppm, was shifted 85 Hz downfield; by comparison, 2b, upon addition of Eu(fod)$_3$ 8 mol%, showed a downfield shift of 77 Hz for the 2-Me syn to SO, originally at 1.54 ppm, and a downfield shift of 45 Hz for the 2-Me anti to SO, originally at 1.23 ppm.
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