Sulfoxide induced sigmatropic rearrangement (SISR) of methyl 1-methylsulfanylvinyl sulfoxides

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Treatment of methyl 1-methylsulfanylvinyl sulfoxides with sodium thiophenolate in MeOH gives 1-methylsulfanylalk-1-en-3-ols.

The sigmatropic rearrangement of allylic sulfoxides in the presence of a thiophilic reagent leads to allylic alcohols.[1] A special sequence which includes this reaction is the rearrangement of α-arylsulfinylacrylates to 4-hydroxyalk-2-enoate esters.[2] In this sequence a thiophilic base first gives an *in situ* isomerization of the vinyl sulfoxide moiety into an allylic sulfoxide, which then undergoes a 2,3-sigmatropic rearrangement and a subsequent thiophilic cleavage of the thus-formed intermediate sulfenic esters by the same base. A practical variant of this synthesis of γ-hydroxyalkenoic esters is the so-called SPAC (sulfoxide piperidine and carbonyl) reaction[3,4] in which the sulfinylacrylates are prepared by a Knoevenagel-type condensation of an appropriate aldehyde and arylsulfinyl acetates, and subsequently rearranged under the same conditions in a one-pot operation.

Here we report on a new related sulfoxide induced sigmatropic rearrangement (SISR) of methyl 1-methylsulfanylvinyl sulfoxides. The required starting materials were conveniently prepared from the corresponding dithiocarboxylic esters by deprotonation with LDA and subsequent *S*-methylation. The ketene dithioacetals thus prepared were oxidized to the *S*-monoxides with 1 equiv. of MCPBA. In all cases the *E*-isomers were formed preferentially. The dithioesters were prepared from Grignard reagents and carbon disulfide, followed by methylation with methyl iodide[5] (Scheme 1). The products **1**–**3** were characterized by IR, mass and NMR spectroscopy. The various compounds **3** prepared in this manner are listed in the Table 1.

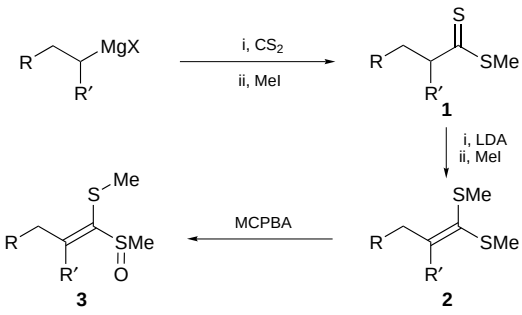
It is of interest to note that an alternative preparation of sulfoxides **3** from the *S*-oxides of dithioesters **1**, by deprotonation and subsequent *S*-alkylation of the intermediate vinylsulfenate anion,[6] was unsuccessful due to the limited stability[7] of the dithioesters of *S*-oxides and the formation of complex mixtures of products.

For the SISR reaction, first the recommended conditions for the SPAC reactions were tried for substrate **3a**. Prolonged treatment of **3a** with a large excess of piperidine in MeCN at room temperature did not give any reaction. Reaction at 85 °C for five days, adding 10 equiv. of piperidine every day, gave a 70% yield of 1-methylsulfanylpent-1-en-3-ol **6a** which had almost exclusively the *E* configuration (*E*:*Z* ratio greater than 95:5). More convenient conditions involved treatment with 5 equiv. of sodium thiophenolate in MeOH at room temperature for four days. In this manner **6a** was obtained in 75% yield almost exclusively in the *E* form. The formation of **6a** from **3a** can readily be explained by invoking an initial base-induced prototropic shift to give allylic sulfoxide **4a**, which then undergoes a 2,3-sigmatropic rearrangement to produce sulfenate ester **5a**. Subsequent thiophilic reaction of **5a** with thiophenolate then leads to product **6a**. It is quite surprising that thiophenoxide serves as thiophilic reagent[1] as well as base. These newly established conditions were also successful for the sequential prototropic shifts and sigmatropic rearrangement reactions of the substrates **3b**–**e**. The corresponding 1-methylsulfanylalk-1-en-3-ols **6b**–**e** were all obtained in yields ranging from 75–98%. The products **6a**–**e** have been characterized by IR, mass and NMR spectroscopic data.† The spectral characteristics revealed that all products **6** predominantly have the *E* configuration with *E*:*Z* ratio exceeding 90:10 (Scheme 2, Table 2).

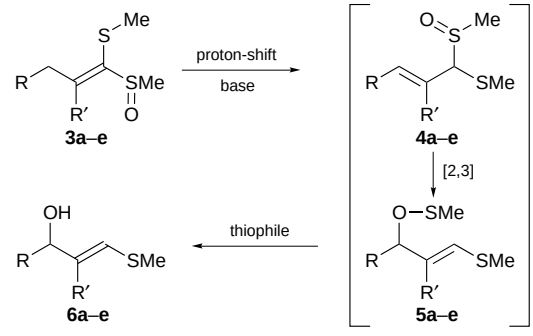
Table 1 Synthesis of compounds **3**

	Substituents		Product yields (%)[a]			
	R	R′	**1**	**2**	**3**	*E*:*Z* ratio[b]
a	Et	H	95	95	72	95:5
b	Pr	H	98	98	82	92:8
c	Bn	H	85	83	78	92:8
d	$PhO(CH_2)_2$	H	30	98	60	91:9
e	$-(CH_2)_3-$	—	75	98	80	—

[a] Yields of pure isolated products. [b] Determined by NMR spectroscopy.



Scheme 1



Scheme 2

Table 2 Synthesis of **6** using thiophenoxide as thiophile

	Substituents		Yield of **6**	
	R	R′	(%)[a]	*E* : *Z* ratio[b]
a	Et	H	75	95 : 5
b	Pr	H	75	92 : 8
c	Bn	H	89	95 : 5
d	$PhO(CH_2)_2$	H	90	97 : 3
e	$-(CH_2)_3-$		90	—

[a] Yields of pure isolated products. [b] Determined by NMR spectroscopy.

It is worth noting that the yield is also high for the formation of **6e**, where the initial isomerization is accompanied by a considerable increase of torsional strain.

The SISR reaction of sulfoxides **3**, of which no precedent is known in the literature, leads to γ-hydroxyvinyl sulfides, which can serve as a synthetic equivalent for β-hydroxy aldehydes[8,9] The synthetic potential of this new SISR reaction is currently under investigation, including chirality transfer from sulfur to carbon when optically active sulfoxides are used as the substrates. Furthermore, the SISR reaction will be investigated for vinyl sulfoxides with other heteroatoms at the geminal position of the sulfoxide group.

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Footnote

† *Selected data* for *E*-**6a**: yellow oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3620 (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 0.90 (3 H, t, *J* 7.0 Hz), 1.50–1.65 (2 H, m), 1.70 (1 H, br s), 2.25 (3 H, s), 4.05 (1 H, q, *J* 7.0 Hz), 5.36 and 5.45 (1 H, dd, *J* 15.0 and 7.5 Hz), 6.30 (1 H, d, *J* 15.0 Hz); *m/z* 132 (M^+), 114 (M^+-H_2O).

For *E*-**6b**: yellow oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3620 (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 0.88 (3 H, t, J 7.5 Hz), 1.20–1.75 (5 H, m), 2.20 (3 H, s), 4.10 (1 H, br q, *J* 6.5 Hz), 5.33 and 5.40 (1 H, dd, *J* 14.5 and 7.3 Hz), 6.25 (1 H, d, *J* 14.5 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.78, 14.31, 18.53, 39.38, 72.64, 126.25, 128.00; *m/z* 146 (M^+), 129 (M^+-H_2O).

For *E*-**6c**: yellow oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3610 (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 2.00 (1 H, br s), 2.26 (3 H, s), 2.80 and 2.90 (2 H, ABq, *J* 13.6, 7.8 and 5.8 Hz), 4.40 (1 H, br q, *J* 4.4 Hz), 5.45 and 5.52 (1 H, dd, *J* 15.6 and 7.0 Hz), 6.33 (1 H, d, *J* 15.6 Hz), 7.40–7.60 (5 H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.30, 44.02, 73.35, 126.32, 126.64, 128.25, 129.39, 137.40; *m/z* 194 (M^+), 176 (M^+-H_2O).

For *E*-**6d**: yellow oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3620 (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 1.99 (2 H, q, *J* 6.0 Hz), 2.15 (1 H, br s), 2.22 (3 H, s), 3.95–4.20 (2 H, m), 4.35–4.50 (1 H, m), 5.42 and 5.47 (1 H, dd, *J* 15.7 and 6.7 Hz), 6.35 (1 H, d, *J* 15.7 Hz), 6.85–6.95 (3 H, m), 7.20–7.35 (2 H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 13.98, 36.33, 64.24, 69.62, 114.12, 120.37, 126.37, 126.82, 129.05, 158.31; *m/z* 224 (M^+).

For **6e**: yellow oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3615 (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 1.30–1.50 (2 H, m), 1.50–1.70 (2 H, m), 1.85–1.95 (1 H, br s), 2.05 (3 H, s), 3.70–3.95 (2 H, m), 4.10–4.20 (1 H, m), 5.70–5.80 (1 H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 16.27, 21.25, 28.06, 35.14, 74.45, 119.78, 142.73; *m/z* 144 (M^+).

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