The Selective Generation of *trans*-Substituted Lithium and Sodium Ethenesulfenate Anions

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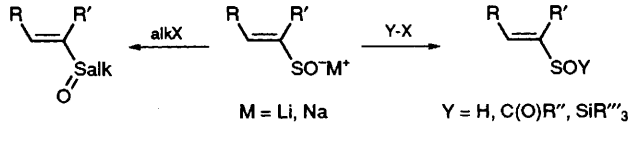
The reaction of *anti*-alkyl thiirane *S*-oxides **1** with hindered amide bases affords *trans*-substituted ethenesulfenate anions *via* a deprotonation–ring-opening sequence.

Bonini *et al.*[1] have demonstrated that the treatment of aryl substituted thiirane *S*-oxides with lithium diisopropylamide (LDA) and organolithium reagents may afford alkenes or lithium sulfenate anions. The alkenes arise from base attack at sulfur and eventual extrusion of that sulfur. The sulfenate anions are formed by way of base attack of a ring hydrogen. Deprotonation is rapidly followed by ring opening to afford the sulfenate, which is methylated at sulfur to afford vinyl sulfoxides.

A general source of simple ethenesulfenate anions would be of interest as it is expected that the ions could be alkylated at sulfur to yield vinyl sulfoxides or they could be functionalized at oxygen to afford ethenesulfenic acid derivatives (Scheme 1) which are of interest to both the synthetic and the mechanistic chemist.[2,3] It was our goal to develop a reliable, efficient route to alkenesulfenate anions in order to evaluate their properties and synthetic value.

The work of Bonini *et al.*[1] and our own work[4] suggested that alkyl substituted thiirane *S*-oxides may prove to be a viable source of the sulfenates. Hence, the required starting materials, *anti*-alkyl thiirane *S*-oxides **1**, were prepared by established procedures[5] from commercially available alkenes,

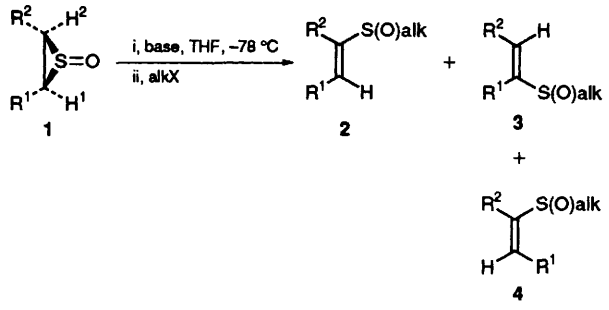


Scheme 1

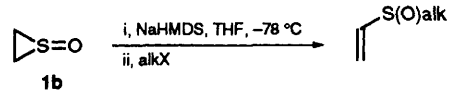
Table 1 Reactions of thiirane *S*-oxides **1** with amide bases[a,b]

	R^1	R^2	Base	Electrophile	Products (% yields)
1a	Me	H	LDA	*p*-TolCH$_2$Br[c]	**2a**(58); **3a**(12)
1a	Me	H	$(C_6H_{11})_2$NLi	*p*-TolCH$_2$Br	**2a**(58); **3a**(22)
1a	Me	H	LiTMP[c]	*p*-TolCH$_2$Br	**2a**(62); **3a**(18)
1a	Me	H	LiHMDS[c]	*p*-TolCH$_2$Br	**2a**(72)
1a	Me	H	NaHMDS	*p*-TolCH$_2$Br	**2a**(69); **4a**(2)
1a	Me	H	KHMDS	*p*-TolCH$_2$Br	**2a**(58); **4a**(3)[d]
1b	H	H	NaHMDS	PhCH$_2$Br	**2b**(80)
1c	$C_{11}H_{23}$	H	LiHMDS	MeI	**2c**(79)
1d	PhOCH$_2$	H	NaHMDS	MeI	**2d**(43); **3d**(24)
1e	But-4-enyl	H	LiHMDS	PhCH$_2$Br	**2e**(75)
1f	cyclo-C_6H_{11}	H	NaHMDS	PhCH$_2$Br	**2f**(68)
1g	$Pr^i_3SiCH_2$	H	LiHMDS	PhCH$_2$Br	**2g**(60)
1h	Et	Et	LDA	PhCH$_2$Br	**2h**(66)
1i	$-[CH_2]_4-$		LDA	PhCH$_2$Br	**2i**(75)

[a] The reaction is as shown in Scheme 2. [b] All yields are of chromatographically pure material. All new compounds gave spectroscopic data consistent with their assigned structure. [c] TMP = 2,2,6,6-tetramethylpiperidide; HMDS = hexamethyldisidazide; *p*-Tol = *p*-tolyl. [d] This mixture contained an additional product (12%). It was assigned the structure allyl *p*-tolylmethyl sulfoxide based on spectroscopic data and independent synthesis.



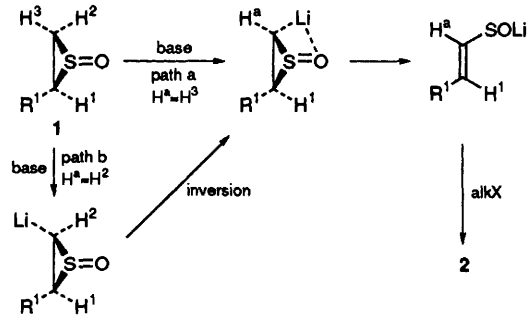
Scheme 2 THF = tetrahydrofuran



alkX = MeI (excess)	71%
alkX = PhCH$_2$Br	80%
alkX = PhCH(Me)Br (excess)	75%[a]
alkX = Bu^{n}I (excess)	72%

[a] 3:2 Mixture of diastereoisomers.

Scheme 3



Scheme 4

oxiranes or thiiranes. Methyl thiirane *S*-oxide **1a** was used as a model compound and was treated with several different hindered bases. Each mixture was quenched with 4-methylbenzyl bromide to capture any sulfenates. It is known that some alkyl halides can capture ethenesulfenates at sulfur; the substitution proceeds without changing the structural makeup of the carbon-containing portion of the molecule.[1,4,6] LiHMDS and NaHMDS were found to be the preferred bases. Indeed LiHMDS afforded only one product from **1a** (Table 1). On the basis of the results with **1a**, these two amide bases were the principal focus for the analysis of the reactions with base of other thiirane *S*-oxides **1**. The results are presented in Table 1.† For the more substituted compounds **1h** and **1i**, the ring hydrogens are equivalent and the need for regioselective deprotonation is precluded. LDA was found to be the preferred base in those instances. The geometry of the products was determined by measuring the ^{1}H NMR coupling constants of the vinyl hydrogens. In the case of **2h** which possesses only one vinyl hydrogen, the double bond geometry was ascertained by performing lanthanide shift reagent experiments.‡ Several *trans*-substituted sulfenate anions were generated (and captured) in good yield by this approach.

A preliminary analysis of the use of the sulfenates as precursors to vinyl sulfoxides was carried out. Sodium ethenesulfenate was captured with different electrophiles (Scheme 3). Benzyl bromides and alkyl iodides are suitable electrophiles, affording the sulfoxides in reasonable yield. Furthermore, in most of the cases in Table 1, the *trans*-isomer was the only product formed. This approach to *E*-vinyl sulfoxides is a particularly rare achievement as other vinyl sulfoxide syntheses usually afford mixtures of *E*- and *Z*-isomers.[7] The alkyl alkenyl sulfoxides synthesized herein are part of a larger family of vinyl sulfoxides that are useful in organic synthesis as reactive substrates in various sorts of Pummerer reactions[8,9] and as willing partners in ene reactions,[10] Michael additions[9,11] and cycloadditions.[12]

From a mechanistic point of view, the deprotonation and ring opening may be a stereospecific process in that only removal of H^2 affords only the *trans*-sulfenate (Scheme 4; path a).[1,13] On the other hand, that process may be accompanied by the removal of H^3 (≡R^2) followed by inversion of the anion before ring opening (Scheme 4; path b),[1,13] a pathway that would lead to some *trans*-sulfenate. We are currently investigating the deprotonation–ring-opening sequence by computational and experimental methods.§ We will report our results in due course.

† *General procedure*: To THF (10 ml) cooled to −78 °C was added the amide base (1.1 molar equiv.; 1.0–1.4 mol dm^{-3} solution from Aldrich or prepared from the amine and BuLi). The substrate (*ca.* 1 mmol in 5 ml of THF) was added dropwise *via* a syringe. The mixture was stirred for 5–10 min at −78 °C (longer and higher temp. for **1i**). The alkyl halide (1.0–3.5 molar equiv.) in THF (5 ml) was then added and the mixture stirred with warming for 12 h. Addition of NH_4Cl (aq) followed by workup, drying and concentration gave the crude material. Flash chromatography or simply filtration through a plug of silica gel afforded pure alkenyl sulfoxide.

CAUTION: Use of an old bottle of BuLi (low volume, sediment evident) leads to decreased yields and significant amounts of byproducts.

‡ Eu(fod)$_3$ [Resolve-Al EuFOD (Aldrich)] was the shift reagent. For practical details see: B. F. Bonini, G. Maccagnani, G. Mazzanti and P. Piccinelli, *Tetrahedron Lett.*, 1979, 3987.

§ The deprotonation/ring opening reaction of **1b** has been theoretically evaluated before (see ref. 13). We are reassessing that work using different methods, assumptions and constraints.

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