

Stereoelectronic Effects in Vinyl Sulfoxides

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Virtually everything is known about the reactivity and structure of carbonyl compounds and their α,β -unsaturated analogues.^{1,2} Though sulfoxides behave similarly to carbonyl compounds in some respects, much less is known about sulfoxides and especially about their α,β -unsaturated derivatives, the vinyl sulfoxides.³ During examination of nucleophilic additions to dithiane-derived alkylidene bissulfoxides,⁴ we encountered some fundamental questions that have hardly been addressed in the literature.

Alkylidene bissulfoxides³ have repeatedly been used in organic synthesis because of their electron-deficient double bonds.⁵ Aggarwal and co-workers have used dithiane- and dithiolane-derived bissulfoxides in epoxidations, cyclopropanations, and cycloadditions.⁶ Fensterbank, Malacria, and co-workers have reported nucleophilic additions to ditolyl-substituted alkylidene bissulfoxides and observed excellent selectivities and high reactivities in the addition of various nucleophiles.^{7,8} Knowledge about the stereoelectronic effects arising from the S=O bond is essential for understanding and controlling the stereochemical outcome in nucleophilic additions to vinyl sulfoxides. These effects compete with possible steric effects or with a putative precomplexation of the reactants as postulated in the Zimmerman–Traxler transition state. Though stereoelectronic effects in sulfoxides have been studied occasionally,⁹ much less is known about orbital interactions in vinyl sulfoxides.¹⁰ Systems used to date either were not in a fixed (or otherwise unambiguously known) conformation, thus precluding a concise treatment,^{7,11} or were present together with interfering carbonyl groups,^{5a,12} thus hampering an independent examination of the influence of the sulfoxide. Here we discuss stereoelectronic effects in the reactions of conformationally fixed vinyl sulfoxides.

4,6-Dimethyl- and (with reservations) 5-*tert*-butyl-substituted 2-alkylidene-1,3-dithianes should be conformationally rigid enough to allow for the exclusion of competing chair conformations in a mechanistic survey.¹³ These conformationally constrained compounds were prepared according to published methods (Scheme 1, Table 1);¹⁴ oxidation was achieved with *m*-chloroperbenzoic acid (mcpba).^{15,16}

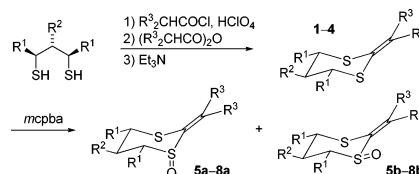
Table 1. Synthesis of 2-Alkylidene-1,3-dithiane-1-oxides

R ¹	R ²	R ³	dithiane	yield (%) ^a	sulfoxides	dr	yield (%) ^a
Me	H	H	1	45	5a/b	42:58	11/22
Me	H	Me	2	67	6a/b	76:24	38/7
H	<i>t</i> Bu	H	3	71	7a/b	34:66	26/32
H	<i>t</i> Bu	Me	4	75	8a/b	80:20	42/14

^a Yields of separated and isolated isomers.

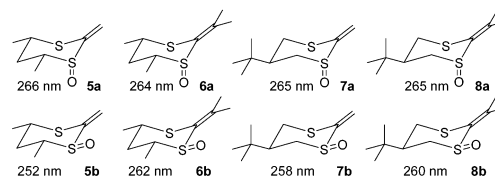
While the stabilizing effect between a C=C double bond and a carbonyl group is strongest when the p orbitals are in a collinear arrangement, X-ray crystallographic data¹⁷ and ab initio calculations¹⁸ suggest that this is not valid for S=O bonds. In fact, a π bond is almost nonexistent between the S and O atoms, and the

Scheme 1. Synthesis of 2-Alkylidene-1,3-dithiane-1-oxides



bond order is significantly smaller than 2.¹⁹ Delocalization of the C=C double bond into an S=O bond is possible when the S=O bond is approximately collinear to the π system of the C=C double bond, as in the case of sulfoxides **5a–8a**. This can be analyzed by inspection of the UV–vis spectra of compounds **5–8** (Chart 1). An axial S=O group leads to a bathochromic shift of 2–14 nm, indicating a stabilizing stereoelectronic interaction in these compounds.

Chart 1. Maximum Absorbance Wavelength Values (λ_{\max}) for 2-Alkylidene-1,3-dithiane-1-oxides

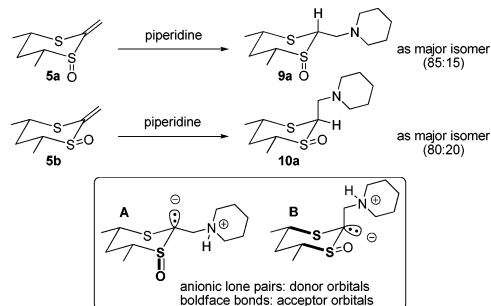


Further evidence comes from ab initio calculations. A generally applicable tool for the quantification of hyperconjugative interactions is the natural bond orbital (NBO) method,^{20,21} which transforms the canonical delocalized Hartree–Fock MOs into localized hybrid orbitals (NBOs). The interactions between filled and antibonding orbitals quantify the energetic contribution of a distinct hyperconjugation. We calculated selected delocalization energies^{16,22} that revealed a contribution of 12.8 kJ/mol from the $\pi_{C=C} \rightarrow \sigma^*_{S-O}$ stereoelectronic interaction in compound **5a** bearing an axial sulfoxide group, while the corresponding interaction in isomer **5b** is virtually nonexistent (0.3 kJ/mol).¹⁶

A significantly more effective stereoelectronic interaction should be possible between an S=O bond and an antiperiplanar lone pair ($n_C \rightarrow \sigma^*_{S-O}$) evolving during nucleophilic attack on 2-alkylidene-1,3-dithiane-1-oxides (Scheme 2). To some extent, this stabilizing effect should already be at work in the transition state. In fact, amine **9a** formed by trans protonation from betaine **A** was isolated as the major isomer (85:15 dr) when sulfoxide **5a** bearing an axial S=O bond was reacted with piperidine. When sulfoxide **5b** bearing an equatorial S=O bond was subjected to the analogous reaction, isomer **10a** evolving from betaine **B** was formed as the major isomer (80:20 dr). Here the dominant stereoelectronic effect is caused by the participation of σ^*_{S-C} rather than σ^*_{S-O} as the acceptor orbital (Scheme 2, bottom).²³ This stabilizing interaction is significantly less effective. Diastereomeric ratios were determined by analysis

of NMR spectra; kinetic control in the additions was confirmed by resubjection of the purified isomers to the reaction conditions, which did not affect their stereointegrity.

Scheme 2. Nucleophilic Attack of Piperidine on 2-Alkylidene-1,3-dithiane-1-oxides



To allow for a quantitative comparison of these stereoelectronic effects, we performed a competition experiment monitored by ^1H NMR spectroscopy (Scheme 3, Figure 1).^{16,24} Addition of piperidine to a 1:1 mixture of sulfoxides **5a** and **5b** was expected to allow for differentiation of these electrophiles' reactivities. In fact, sulfoxide **5a** reacted significantly faster ($k_{\text{ax}} = 6.2 \times 10^{-2} \text{ L mol}^{-1} \text{ min}^{-1}$) than isomer **5b** ($k_{\text{eq}} = 6 \times 10^{-4} \text{ L mol}^{-1} \text{ min}^{-1}$).

Scheme 3. Competitive Addition of Piperidine to a Mixture of Diastereomeric 2-Alkylidene-1,3-dithiane-1-oxides

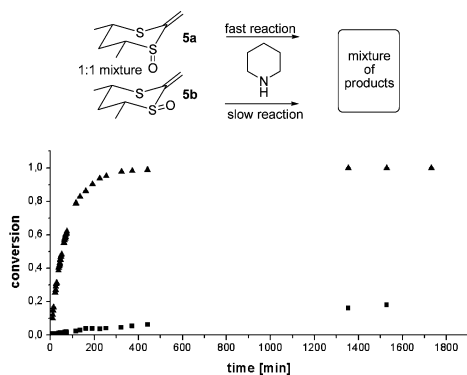


Figure 1. Competitive conversion of vinyl sulfoxides: (▲) **5a**; (■) **5b**.

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Supporting Information Available: Complete ref 22; experimental details, spectroscopic data, and spectra for all new compounds; results of NBO calculations; details of kinetic experiments; and X-ray data for compounds **5a** and **6a** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(24) A kinetic experiment using sulfoxides **7a** and **7b** that had a similar outcome is described in the Supporting Information. Isopropylidene derivatives **6** and **8** were not reactive enough, most probably because of steric hindrance.

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