

First Examples of Episulfone Substitution Reactions via α -Sulfonyl Carbanion Intermediates

Adriano B. Muccioli and Nigel S. Simpkins*

Department of Chemistry, The University of Nottingham, University Park, Nottingham NG7 2RD, U.K.

Andrew Mortlock

Zeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire SK10 4TG, U.K.

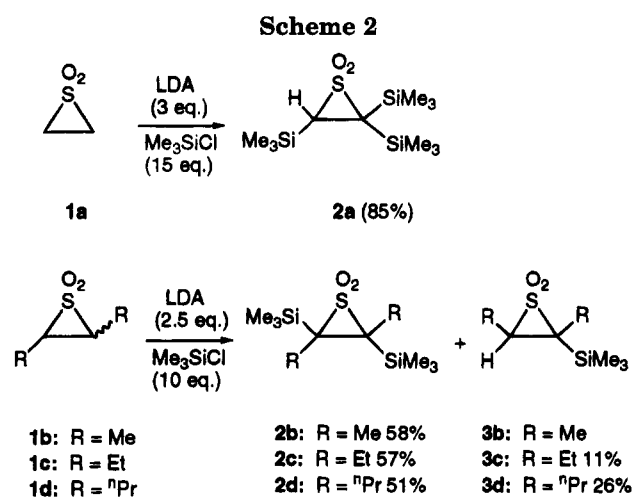
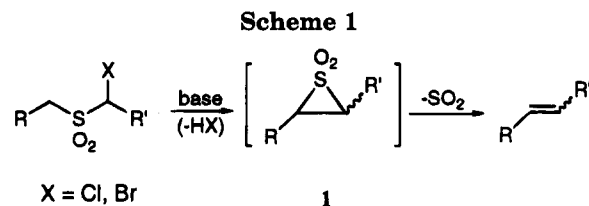
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Summary: Three-membered cyclic sulfones (episulfones) undergo substitution on treatment with base–electrophile mixtures, such as LDA–Me₃SiCl and tBu–P4-phosphazene base–PhCHO, to give either substituted episulfones or the corresponding alkenes following loss of SO₂.

Three-membered cyclic sulfones (episulfones) **1** are well established as intermediates in the classical Ramberg–Bäcklund reaction, which involves the formation of an alkene product by 1,3-elimination from an α -halo sulfone, followed by loss of SO₂, Scheme 1.¹ Although episulfones can be prepared by alternative methods (and have been shown to undergo stereospecific cheletropic loss of SO₂ to give alkenes on heating), they have only recently been isolated from Ramberg–Bäcklund reactions by use of modified mild conditions.²

We were intrigued by the possibility of carrying out substitutions of episulfones via their derived α -sulfonyl carbanions, since this should lead to useful substituted alkenes after SO₂ extrusion and would constitute a new approach to unsaturated products. However, due to their somewhat unwarranted reputation as “unstable intermediates” the chemistry of episulfones has been little explored and no such substitution reactions have been reported.³ Here we describe the first successful substitution reactions of episulfones by the use of hindered bases in the presence of electrophiles such as Me₃SiCl.

A range of simple, symmetrically-substituted episulfones **1a–1d** was prepared by the method of Opitz, involving treatment of sulfonyl chlorides with Et₃N in MeCN.⁴ These products are obtained as mixtures of *cis*- and *trans*-isomers, mostly in the form of colorless oils, which can be stored under refrigeration. If desired, these episulfones can be obtained in isomerically pure form either by fractional crystallization or by flash chromatography. However, in many of the reactions described below, especially the silylation reactions in Scheme 2, such separations are unnecessary (the *cis*- and *trans*-



isomers giving the same products), mixtures of starting isomeric episulfones having been employed.⁵

Attempted substitution reactions, involving treatment of an episulfone in THF at low temperature with a base such as BuLi, LDA, or LHMDS and subsequent addition of an electrophile such as Me₃SiCl or PhCHO, proved unrewarding, with only destruction of the starting materials evident. Since the problem is most likely to be related to the instability of the intermediate α -sulfonyl carbanion, we turned to the use of *in situ* quench conditions.⁶ Pleasingly, reaction of each of the episulfones **1a–1d** with an excess of LDA in the presence of Me₃SiCl resulted in clean conversion into the silylated episulfone products shown, Scheme 2.⁷

The parent episulfone **1a** is an exceptional case, being efficiently converted into the trisilylated episulfone **2a**

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(1) (a) Ramberg, L.; Bäcklund, B. *Arkiv Kemi, Mineral. Geol.* **1940**, *13A* (27). For reviews, see: (b) Simpkins, N. S. *Sulfones in Organic Synthesis*; Pergamon Press: Oxford, 1993. (c) Clough, J. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, p 861.

(2) (a) Ewin, R. A.; Loughlin, W. A.; Pyke, S. M.; Morales, J. C.; Taylor, R. J. K. *Synlett* **1993**, 660. (b) Jeffery, S. M.; Sutherland, A. G.; Pyke, S. M.; Powell, A. K.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2317.

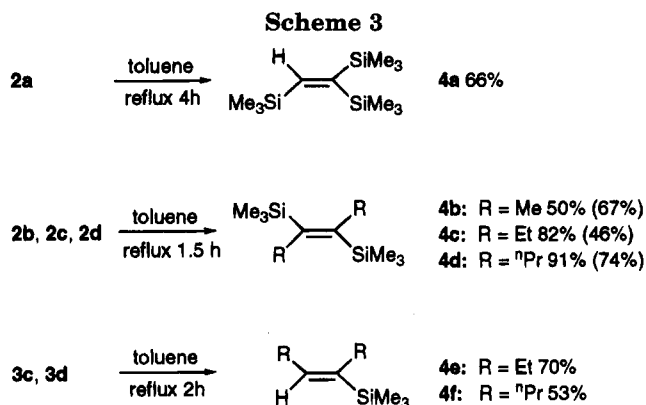
(3) (a) Deuterium incorporation has been observed previously; see: Bordwell, F. G.; Williams, J. M., Jr.; Hoyt, E. B., Jr.; Jarvis, B. B. *J. Am. Chem. Soc.* **1968**, *90*, 429. (b) Prof. R. J. K. Taylor (University of York, U.K.) has informed us of his independent attempts at substitution of episulfones, which have resulted in the formation of low yields of substituted alkene product in one case (poster presented at The First Anglo-Norman Chemistry Colloquium, Rouen, France, 1991).

(4) (a) Opitz, G.; Rieth, K.; Ehliis, T. *Chem. Ber.* **1990**, *123*, 1563 and 1989. (b) Opitz, G.; Ehliis, T.; Rieth, K. *Tetrahedron Lett.* **1989**, *30*, 3131. (c) For a review, see: Fischer, N. H. *Synthesis* **1970**, 393.

(5) In the case of conversion of **1b** into **2b** (Scheme 2) we found that the use of **1b** as a single stereoisomer (either one) or as a mixture gave identical results (see, however, footnote 16).

(6) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

(7) In a typical reaction the starting episulfone, as a solution in THF, was added to a solution of LDA and Me₃SiCl (equivalents shown in the scheme) in THF at –78 °C. The mixture was maintained at this temperature for 2 h before workup (aqueous NH₄Cl and extraction into CH₂Cl₂) and flash chromatography (EtOAc in petroleum ether as eluant) on silica to give the reported products. Episulfones **3c** and **3d** are colorless oils, whereas **2a–d** are solids, mp 69 °C (**2a**), 71 °C (**2b**), 63 °C (**2c**), and 99 °C (**2d**). While the *trans* stereochemistry of **2b–2d** has not been proven, highly selective *cis*-disilylation is highly improbable (especially considering ref 5); the assigned stereochemistry for **3c** and **3d** is supported by NOE experiments.



on treatment with 3 equiv of LDA in the presence of a good excess of Me_3SiCl . Efforts to introduce fewer silicon groups, by using less base, resulted in the formation of rather complex mixtures, while we also failed to prepare the fully silylated episulfone by use of more base or by exposing **2a** to LDA- Me_3SiCl .

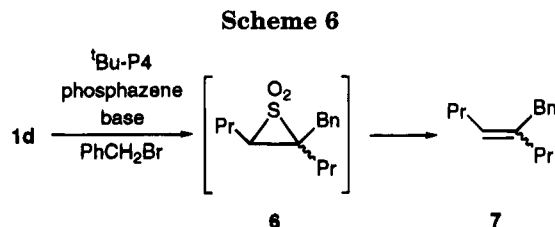
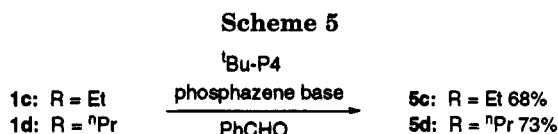
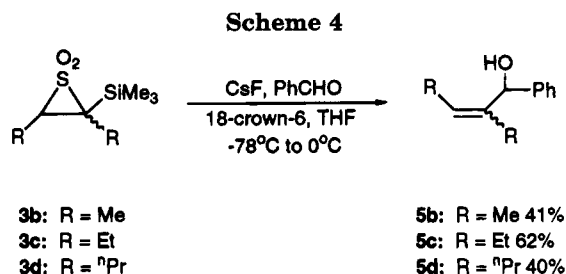
The vicinally-disubstituted episulfones **1b–1d** behaved similarly on exposure to mixtures of LDA- Me_3SiCl , each producing only one stereoisomeric disilylated episulfone **2b–2d** together with minor amounts of monosilylated products. In the cases of **1c** and **1d** significant amounts of monosilylated product **3c** or **3d** were also isolated under our standard conditions.⁸

The substituted episulfones obtained as shown in Scheme 2 proved to be surprisingly stable and could be subjected to column chromatography without serious loss. However, on reflux in toluene (1.5–4 h) each episulfone underwent facile loss of SO_2 to give the corresponding vinylic silane, disilane, or trisilane product in good yield, Scheme 3.⁹

As expected, each pure episulfone gave a single stereoisomeric alkenyl product on thermolysis, the overall yield of alkenes from starting episulfones **1** being somewhat improved in the case of **4b** and **4d** if purification of the intermediate episulfone was avoided (values in parentheses).

Although the above reactions constitute the first efficient substitution reactions of episulfones, and a potentially useful new route to certain silylated alkenes, we were disappointed at our inability to introduce other types of substituent using LDA as base. We therefore examined two alternative protocols with the aim of introducing carbon-centered electrophiles, Schemes 4–6.

Firstly, we found that the use of monosilylated episulfones **3b–3d** in fluoride-mediated reactions with PhCHO, following the type of procedure used previously for simple α -silyl sulfones,¹⁰ gave acceptable yields of allylic alcohols **5b–5d**, Scheme 4.¹¹ Furthermore, simple episulfones **1c** and **1d** were converted into the same allylic alcohols by treatment with an excess of



Schwesinger's tBu-P4-phosphazene base in the presence of PhCHO, Scheme 5.^{12,13} In these reactions no substituted episulfones were observed, and the alkenyl products were isolated directly. However, reaction with benzyl bromide under the same conditions resulted in the formation of an observable trisubstituted episulfone product **6**.¹⁴ Unfortunately, this compound proved unstable to our present workup procedure and rapidly decomposed to give the alkene **7** as a mixture of stereoisomers (30%).

In the reactions shown in Schemes 4 and 5 the allylic alcohol products are formed as stereoisomeric mixtures with the (*Z*)-isomer predominating, regardless of the stereochemistry of the starting episulfone.¹⁵ At present it seems that the product stereochemistry is determined by epimerization of the presumed intermediate α -sulfonyl carbanion to place the alkyl substituents (R) on opposite faces of the episulfone ring, this leading to the observed (*Z*)-isomer.¹⁶

(12) Schwesinger, R.; Hasenfratz, C.; Schlemper, H.; Walz, L.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1361 and references cited therein.

(13) In a typical reaction a solution of tBu-P4-phosphazene base (Fluka) was added dropwise to a mixture of starting episulfone and PhCHO in THF at -78°C , until consumption of the episulfone was complete by TLC. The reaction mixture was then allowed to warm to room temperature before removal of the solvent, extraction of the solid residue with Et_2O ($\times 3$), and purification of the ethereal extract by flash chromatography.

(14) The episulfone **6** has not been characterized, but was observed as a slightly higher-running component, compared to **1c**, on TLC examination of the reaction mixture (10% EtOAc in petroleum ether eluent), and which was replaced by a much less polar component (solvent front) due to alkene **7** on workup.

(15) Stereochemical assignment has been made by ^1H NMR; in a typical mixture of allylic alcohol products **5** irradiation of the signal corresponding to the vinylic $\text{C}=\text{CH}$ in the *minor* stereoisomer gives rise to a substantial NOE enhancement for the signal corresponding to the benzylic CHOH . Irradiation of the corresponding $\text{C}=\text{CH}$ in the *major* isomer gives no enhancement, indicating the *trans* orientation of the $\text{C}=\text{CH}$ and CHOH groups in this (*Z*) isomer. We assume that the major component of alkene **7** is also the (*Z*)-isomer.

(16) Under the *in situ* quench conditions used it appears that partial equilibration of the intermediate α -sulfonyl carbanion is taking place, so the predominance of (*Z*)-**5** actually observed is dependent on the ratio of isomers in the starting episulfone. Thus, in the reaction of **1c** to give **5c** (Scheme 5), the use of pure (*Z*)-**1c** results in a product ratio of only 1.2–1.5:1, whereas if an epimeric mixture of **1c** (ca. 60% *E*) is reacted in the same way the product ratio is increased to ca. 6:1.

(8) Each of the monosilylated products **3b–d** could also be obtained in higher yield, either by using less LDA (for **1d** use of only 1.5 equiv of LDA gave **3d** in 45% yield) or by employing an inverse quench procedure (addition of 1 equiv of LDA to a mixture of starting episulfone and Me_3SiCl gave 28% of **3b** and 42% of **3c**); however, in such inverse addition reactions the monosilylated products are obtained as stereoisomeric mixtures.

(9) Some of the silanes have been prepared previously; see: (a) Suzuki, T.; Lo, P. Y. *J. Organomet. Chem.* **1990**, *391*, 19 (**4a**). (b) Tamao, K.; Miyake, N.; Kiso, Y.; Kumada, M. *J. Am. Chem. Soc.* **1975**, *97*, 5603 (**3c**). (c) Hudrlík, P. F.; Kulkarni, A. K.; Hudrlík, A. M. *Tetrahedron* **1983**, *39*, 877 (**3d**).

(10) Lamothe, M.; Anderson, M. B.; Fuchs, P. L. *Synth. Commun.* **1991**, *21*, 1675.

(11) For a previous synthesis of **5c**, see: Sato, F.; Ishikawa, H.; Sato, M. *Tetrahedron Lett.* **1981**, *22*, 85.

In summary, we have shown for the first time that substitution of episulfones is possible with both silicon- and carbon-centred electrophiles and that these reactions provide a novel access to unsaturated products. Further studies are underway to explore the range of electrophiles compatible with this approach and to examine in more detail the degree of stereocontrol possible.

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4TG, UK) for support of A.B.M. under the CASE scheme. We would also like to thank Dr. P. J. Cox for preliminary studies of silylation reactions of episulfone **1b**.

Supplementary Material Available: Copies of ^1H NMR spectra of **2a–2d**, **3c**, **3d**, **4a–4f**, and **5b–5d**. Copies of ^{13}C NMR spectra of **2a**, **2c**, **2d**, **3d**, and **4a–4f** (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.