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Radical Deuteration of α-Selenylated-β-Silylsulfoxides.

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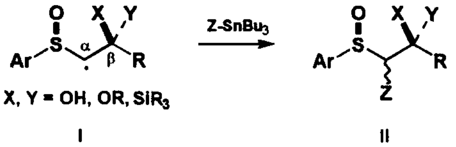
Abstract: The deuteration of α-selenylated-β-silylsulfoxides and α-selenylated-β-*tert*-butylsulfoxides has been shown to lead, with good levels of diastereocontrols to the formation of *syn* isomers irrespective of the stereochemistry of the sulfinyl precursors. Our results have been rationalized using transition state models which parallel the Felkin-Anh model. Copyright © 1996 Elsevier Science Ltd

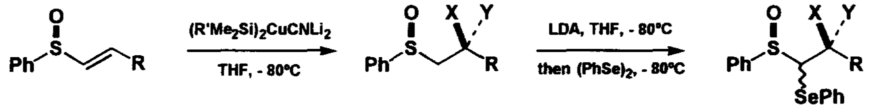
1,2-Stereocontrol in radical reactions has recently attracted a great deal of interest.[1] As a result, several models similar to those proposed earlier for ionic reactions at trigonal centres have been proposed to rationalize the 1,2-transfer of chirality.[1,2] In this context, the use of α-sulfinylated radicals is particularly convenient since sulfoxides are versatile compounds, available in homochiral form,[3] and the transfer of chirality from sulfur to the vicinal prochiral centre is usually efficient depending on the reaction conditions and the substituent on the sulfoxide group.[2l,m] Recent studies have also shown that the incorporation of a second chiral centre in the β-position relative to the sulfoxide group (**I**, Scheme 1) may reinforce the stereocontrol provided by the sulfoxide moiety.[2m] While high diastereoselectivity was observed with the large OTBDMS group, poor stereocontrol was obtained with a OH group at C-β. Therefore, we anticipated that the replacement of the hydroxy in the β-position by its silicon equivalent[4] would introduce a larger steric component as well as an opposite electronic effect compared to that of an oxygenated substituent. It was also anticipated that changes in the degree and of the sense of diastereocontrol might be observed.[5] We report herein our preliminary results on the 1,2-stereocontrol arising from radical deuterations of α-selenylated-β-silylsulfoxides such as **3** (Scheme 2). Transition state models will be proposed along with a discussion of the factors which are likely to control this diastereoselective process.



Scheme 1

α-Selenylated-β-silylsulfoxides **3** were prepared using a two-step protocol starting from vinylsulfoxides **1a-b** as illustrated in Scheme 2. Silyl-cupration of the sulfoxides **1**, using either $(PhMe_2Si)_2CuCNLi_2$ or $(Me_3Si)_2CuCNLi_2$, produced the expected compounds **2a-e** in 45-60% yield.[6] *Anti* and *syn* diastereoisomers were readily separated using flash chromatography and were subsequently selenylated with $(PhSe)_2$ to afford **3a-e** in modest yields and random selectivity.[2f] The selenylated precursors **3a-e** were used as a mixture of diastereoisomers. It should be noted that the deuteration was also carried out on both single diastereoisomers of **3a** affording the deuterated sulfoxides in essentially the same ratio.

The deuteration of **3a-e** with Bu_3SnD was carried out at 10°C under UV irradiation to afford a mixture of **4** and **5** in excellent yield (Scheme 3, Table 1). The diastereomeric ratio were determined from ^1H NMR of the crude reaction mixtures. We were pleased to find that higher levels of diastereoselectivity could be attained compared to that of precursors having a OH group at C-β. Lowering the temperature and changing the solvent had little effect on the selectivity. It is also worthy of note that during deuteration of **3d-e**, 10-20% of the α-dihydrogenated compound was always obtained, even in the presence of a large excess of Bu_3SnD. It is reasonable to assume that the α-dihydrogenation results from a very favourable intramolecular [1,4]-hydrogen abstraction from $SiCH_3$ to the radical centre α to the sulfinyl group.



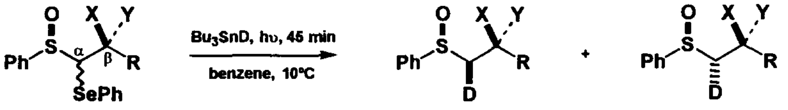
1a, R = Me
1b, R = H

2a, R = Me; X = $SiMe_2Ph$; Y = H
2b, R = Me; X = H; Y = $SiMe_2Ph$
2c, R = H; X = H; Y = $SiMe_2Ph$
2d, R = Me; X = $SiMe_3$; Y = H
2e, R = Me; X = H; Y = $SiMe_3$

3a, R = Me; X = $SiMe_2Ph$; Y = H
3b, R = Me; X = H; Y = $SiMe_2Ph$
3c, R = H; X = H; Y = $SiMe_2Ph$
3d, R = Me; X = $SiMe_3$; Y = H
3e, R = Me; X = H; Y = $SiMe_3$

Scheme 2

The syn diastereomer 4 was always obtained as the major product whatever the stereochemistry of the β-silyl precursor 3 (Scheme 3).[7] However, *syn*-silylsulfoxides afforded substantially higher levels of diastereoselectivity compared with the respective *anti* compounds (entry 1 and 4). The size of the silicon group appeared to have no effect on the diastereocontrol as shown by the similar ratio obtained with $SiMe_2Ph$- and $SiMe_3$-substituted sulfoxides (entry 1-4 and 2-5). More relevant perhaps is the level of diastereocontrol obtained with model **3c** having only one chiral centre located on the sulfur (entry 3). Similarly, in the absence of chirality at sulfur, *i.e.* performing the reaction on the thioether analogue of **3a** (or **3b**) (PhS), we observed a 67:33 *syn*/*anti* ratio. This suggested that both chiral centres equally influence the stereochemical outcome. The higher d.e. observed when both chiral centres are present suggests that there is a co-operativity between the chirality at sulfur and the chirality at C-β. The small difference of d.e. and the same direction in the diastereocontrol observed with *syn* **3a** and *anti* **3b** also suggest ***that the co-operativity overwhelms the expected "matched" and "mismatched" effects***. This is further supported by the fact that the same topicity is observed with *syn* compounds having a OH and a SiR_3 group at C-β.[5]



3a-e

Scheme 3

4a-e

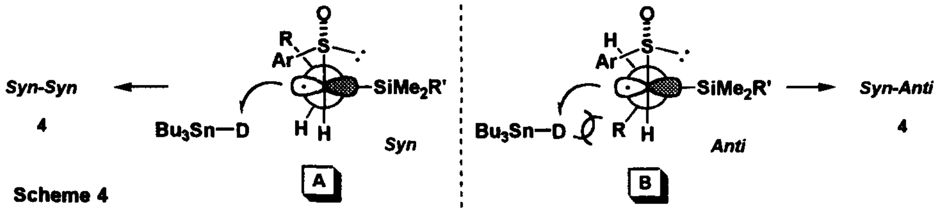
5a-e

Table 1. Radical deuterations of α-selenylated-β-silylsulfoxides 3 (Scheme 3).

Entry	precursor	R	X	Y	Yield (%)^a	4/5 ratio^b
1	3a	Me	$SiMe_2Ph$	H	91	**83 : 17**
2	3b	Me	H	$SiMe_2Ph$	84	**78 : 22**
3	3c	H	$SiMe_2Ph$	H	95	**67 : 33**
4	3d	Me	$SiMe_3$	H	95	**80 : 20^c**
5	3e	Me	H	$SiMe_3$	93	**75 : 25^c**

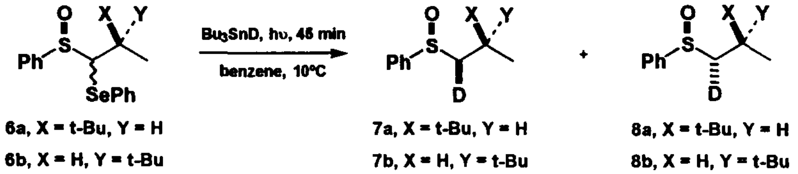
[a] Yield of isolated product after purification. [b] Ratio measured using 360MHz ^1H NMR. [c] Isolated along with 10-20% of dihydrogenated product.

The stereoselectivities can be rationalized by assuming that conformations **A** and **B** in the transition state are those with the C-Si bond in the plane of the radical orbital and perpendicular to the C-S→O system (Scheme 4).[2j,8] The R group would be in a *s-cis* conformation in the *syn* isomer and *s-trans* in the *anti* isomer. The steric interactions between $SiMe_2R'$ and Ar, and those between R and the incoming Bu_3SnD, would then predominate. From these locked conformations, the deuterium would then attack *anti* relative to the silicon moiety. A repulsive interaction between R and Bu_3SnD, as predicted by the Felkin-Anh model,[1,2m] may explain the slightly lower diastereoselectivities observed with *anti* β-silylsulfoxides (through TS **B**) compared to *syn* β-silylsulfoxides (through TS **A**). When R is a hydrogen (*i.e.* **3c**), the diastereofacial selectivity is controlled by the sulfoxide group and reasonable 1,2-stereocontrol is observed.[2j] Similarly, with the thioether precursor, C-β controls the configuration at the new chiral centre following a Felkin-Anh model as in **3c**.



Scheme 4

As suggested above, we assume that the silicon group prefers the position depicted in conformations **A** and **B**. This seems to minimize the steric interactions with bulky groups (Ar) and to maximize the overlapping between the C-Si bond and the nascent C-D bond. In order to evaluate the electronic effect involved in the radical deuteration of β-silylsulfoxides, we extended our studies to the radical deuteration of β-*tert*-butylsulfoxides **6**,[9] assuming a similar steric hindrance between a *tert*-butyl and a trimethylsilyl group.[10] The deuterations were performed as above and the results are summarized in table 2 (Scheme 5). The configuration of the *tert*-butyl substrates **7-8** was confidently assigned by comparison with the ^1H NMR spectra of their silylated analogues.



Scheme 5

Table 2. Radical deuterations of α-selenylated-β-*tert*-butylsulfoxides 6 (Scheme 5).

Entry	precursor	X	Y	Yield (%)[a]	7/8 ratio[b]
1	6a	t-Bu	H	78	82 : 18
2	6b	H	t-Bu	70	60 : 40

[a] Yield of isolated product after purification. [b] Ratio measured using 360MHz ^1H NMR.

The deuteration of the *syn* isomer **6a** gave the *syn-syn* isomer **7a** with good diastereoselectivity (entry 1) probably through a conformation at the transition state closely resembling to **A** where both t-Bu↔Ar and R↔Bu_3SnD interactions are minimized. On the other hand, an almost random stereoselectivity is observed with *anti* **6b** (entry 2). The small but noticeable difference of diastereoselectivity between **6b** and its silylated analogue **3e** is more difficult to rationalize and could be attributed to the occurrence of a β-silyl stabilizing effect on the carbon-centered radical. Such a stabilization may be as large as 4.5 kcal/mol.[11] However, the development of a partial positive charge on the radical centre at the transition state during these deuterations might not be so pronounced and therefore the β-silyl stabilizing effect is likely to be weak. This is reflected by the small difference in diastereoselectivity between **3e** and **6b**.

In summary, we have described in this Letter the deuteration of α-selenylated-β-silyl- and α-selenylated-β-*tert*-butylsulfoxides which led mainly to the formation of *syn*-isomers **4** and **7** **whatever** the stereochemistry of the precursors. Our results have been rationalized by transition state models which parallel the Felkin-Anh model. Comparison of the selectivity obtained during deuteration of β-silyl- and β-*tert*-butylsulfoxides might suggest that weak electronic effects are involved with β-silyl radicals. However more experiments and calculations will be required to provide further insight into this problem and allow for definitive conclusions.

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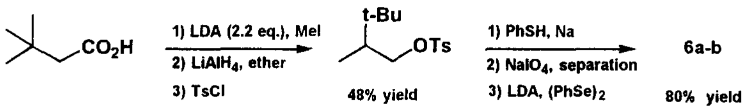
7. The stereochemistry of sulfoxides **4-5** has been unambiguously determined through *syn* elimination of arylsulfenic acid, eventually leading to the known corresponding deuteriated vinylsilanes.[6]
8. These conformations have been obtained from semi-empirical calculations which will be reported in a forthcoming article. Recent calculations on similar models effectively suggested a conformation at the transition state having a S=O bond perpendicular to the radical orbital.[2j] See also: Pasto, D.J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.*, **1987**, *52*, 3062-3072.
9. **6a-b** were prepared from commercial 3,3-dimethylbutanoic acid, according to the following sequence :



10. In fact, a *t*-Bu group may induce slightly more steric hindrance than a SiR_3 group since the C-C bond (1.54Å) is shorter than the C-Si bond (1.9Å).
11. On the opposite, a *t*-Bu group was found to provide no stability to open chain carbon-centered radicals, see : Zhang, S.; Bordwell, F.G. *J. Org. Chem.*, **1996**, *61*, 51-54 and references cited therein.

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