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Stereoselective Nucleophilic Epoxidation of Hydroxy Vinyl Sulfoxide Derivatives.[1]

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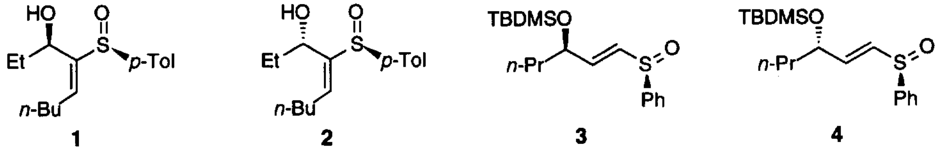
Abstract: The diastereoselectivity of the nucleophilic epoxidation of vinyl sulfoxides bearing oxygenated substituents at allylic positions, **1-4**, with MOO-*t*-Bu (M = Na, K) is primarily controlled by the chiral sulfur atom. Copyright © 1996 Elsevier Science Ltd

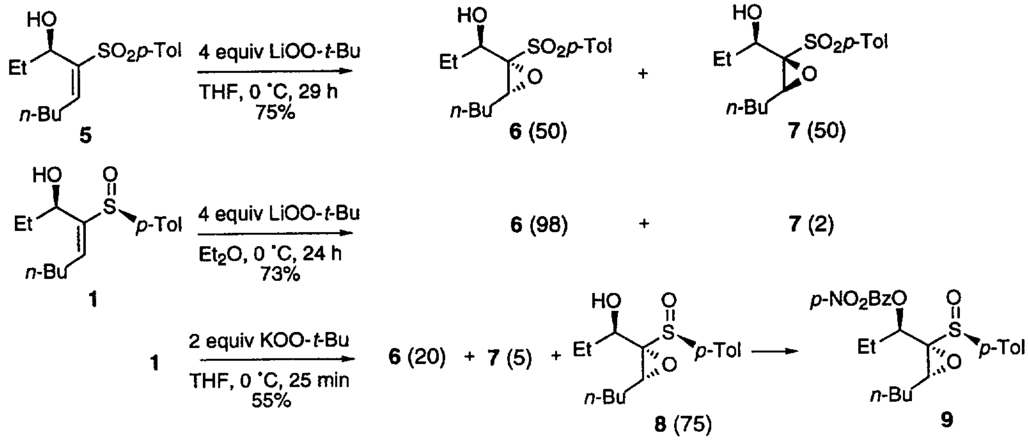
We have recently reported that simple *p*-tolyl vinyl sulfoxides undergo nucleophilic epoxidation with metal alkyl peroxides to generate enantiopure sulfinyl oxiranes.[3] This novel process takes place with good yields and fair to excellent diastereoselectivities. In this paper we describe our preliminary results on the epoxidation of diastereomeric hydroxy vinyl sulfoxides **1-4** (Scheme 1) bearing an additional stereocenter adjacent to the reactive carbon-carbon double bond.



Scheme 1

Jackson has recently shown that α-(1-hydroxyalkyl)- and γ-oxygenated vinyl sulfones undergo nucleophilic epoxidation with good to excellent diastereoselectivity.[4] Similarly, (*E*)-*N*-[(*p*-tolylsulfonyl)vinyl]sulfoximines give rise to the corresponding oxiranes with outstanding selectivity.[5] A subsequent study revealed that a γ-oxygenated substituent was an even more powerful element of stereocontrol than the chiral sulfoximine functionality.[6] Since hydroxy vinyl sulfoxides such as **1-4** are readily available enantiomerically pure,[7] we considered that a study parallel to Jackson's,[4-6] could shed additional insight into the stereochemical outcome of such processes and enhance their synthetic usefulness.

At the initial stage of this project, the behavior of diastereomeric hydroxy sulfoxides **1** and **2** was examined and the results obtained are shown in Schemes 2 and 3. For comparison and characterization purposes, vinyl sulfone **5** was epoxidized under standard conditions to produce a 50:50 mixture of epoxy sulfones **6** and **7**. Apparently, the size of the substituent at the β position plays a crucial role in this epoxidation.[8] The reaction between vinyl sulfoxide **1** and LiOO-*t*-Bu (THF, 0 °C) afforded a 72:28 mixture of epoxy sulfones which indicates that epoxidation is taking place prior to oxidation, at least to some extent. Seeking to improve this selectivity the epoxidation with LiOO-*t*-Bu was carried out in Et_2O and epoxy sulfone **6** was obtained as practically a single diastereomer. In contrast, the use of KOO-*t*-Bu afforded a fair yield of a single isomer of epoxy sulfoxide **8** which produced sulfone **6** upon oxidation with MMPP. It should be pointed out that the epoxidation of **1** should be carefully monitored to avoid overoxidation at sulfur. To establish unequivocally the stereochemical outcome of these epoxidations, *p*-nitrobenzoate **9** was subjected to an X-ray diffraction analysis (Figure 1)[9] which confirmed the structures of these oxiranes to be as shown.



Scheme 2

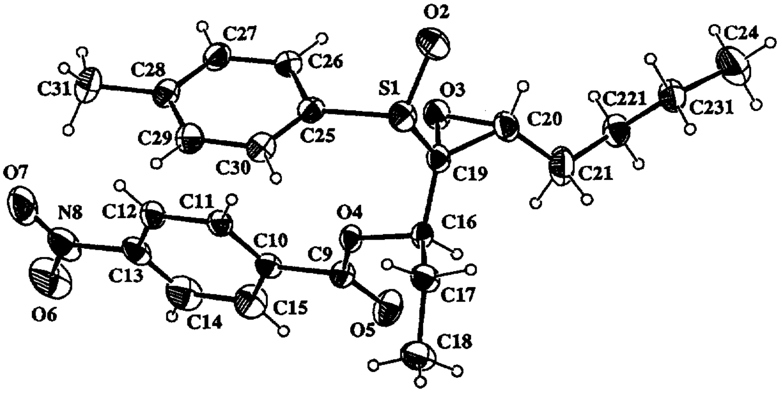
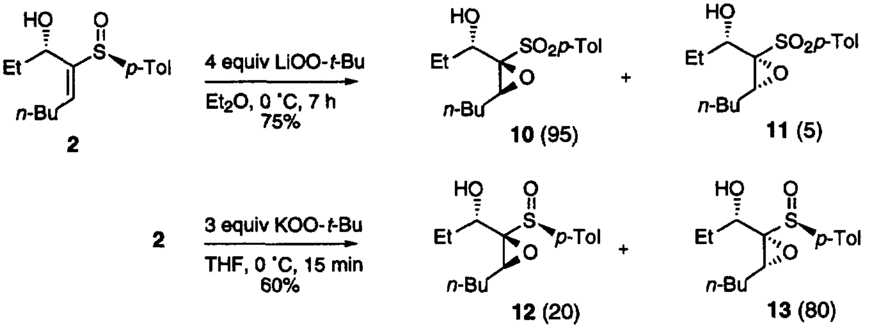


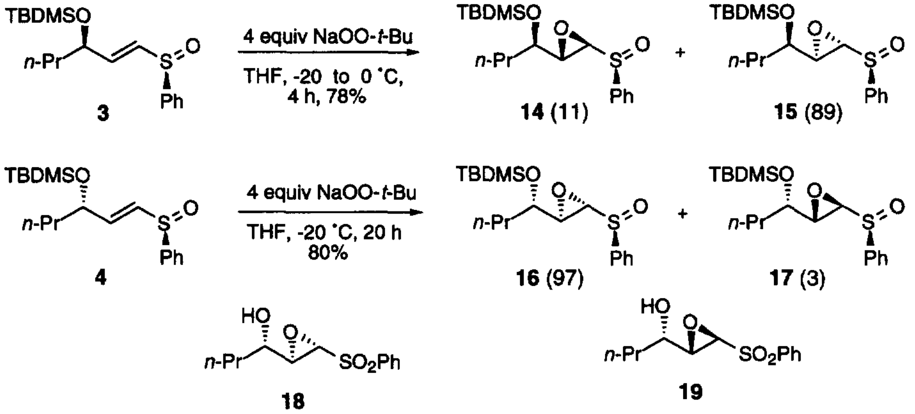
Figure 1. Final X-ray model of **9**.

Diastereomeric sulfoxide **2** (Scheme 3), under similar reaction conditions, showed very different reactivity and selectivity. Indeed, standard conditions afforded a complex mixture of starting material, vinyl sulfone, epoxy sulfones and trace amounts of epoxy sulfoxides **12** and **13**. In contrast, switching to Et_2O as a solvent resulted in fast epoxidation and oxidation to produce epoxy sulfone **10** as practically a single isomer. While NaOO-*t*-Bu was not very effective in this case, KOO-*t*-Bu afforded a fair yield of a separable 20:80 mixture of diastereomeric sulfoxides **12** and **13** whose relative configurations were assigned by oxidation of **13** to the corresponding sulfone **11**.



Scheme 3

The epoxidation of γ-alkoxy vinyl sulfoxides **3** and **4** was then addressed, and as expected, these substrates were less prone to oxidation than **1** and **2**. In fact, the use of NaOO-*t*-Bu led to smooth epoxidation to afford good yields of **15** and **16**, along with small amounts of the minor isomers and the corresponding sulfones (<10%) (Scheme 4). The relative configuration of these sulfinyl oxiranes was determined by simple chemical correlations with the known **18** and **19**.[4b]



Scheme 4

The high *anti* selectivity found for **1** and **2** with LiOO-*t*-Bu in Et_2O supports Jackson's proposal of a hydroxyl directed process.[4a] The epoxidation of γ-silyloxy vinyl sulfoxide **4** displays an enhanced *syn* selectivity with respect to related sulfones.[4b] On the other hand, the remarkable reversal of facial selectivity found for **2** and especially **3**[10] may be understood in terms of "mismatched" situations and underlines that a sulfinyl functionality is an extremely powerful chiral controller.[11]

To summarize, we have shown that hydroxy vinyl sulfoxide derivatives may undergo highly stereoselective nucleophilic epoxidation to produce enantiopure sulfonyl and sulfinyl oxiranes.[12] In some cases, the stereochemical outcome of the process may be controlled by simply changing the reaction conditions. Studies to define the scope of this protocol and apply these sulfinyl oxiranes in synthesis are currently underway in our laboratory.

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References and Notes

1. Taken in part from the M.S. Theses of P.M. and J.P., Instituto de Química Orgánica, CSIC.
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7. Hydroxy vinyl sulfoxides **1** and **2** were prepared in two steps from (-)-menthyl sulfinate. See: (a) Marino, J. P.; Viso, A.; Fernández de la Pradilla, R.; Fernández, P. *J. Org. Chem.* **1991**, *56*, 1349-1351. Early experiments involving these substrates, including the X-ray diffraction analysis, were carried out on racemic material; the more significant experiments were then reproduced with enantiomerically pure compounds. Racemic γ-silyloxy vinyl sulfoxides **3** and **4** were prepared by straightforward modifications of the procedures of Rayner for diastereo- and enantiopure materials. See: (b) Westwell, A. D.; Rayner, C. M. *Tetrahedron: Asymmetry* **1994**, *5*, 355-358. All new products reported here have been fully characterized and yields are based on purified compounds obtained by unoptimized procedures. Ratios of products measured by integration of the 300 MHz ^{1}H NMR spectra of crude reaction mixtures are in parentheses.
8. A related substrate bearing a Ph substituent at the β carbon displayed excellent selectivity (1:20). See ref 4a. For a similar observation see ref 7a.
9. Crystal data for **9**: $C_{23}H_{27}NO_6S$, triclinic, P-1, a=9.475(1), b=10.225(1), c=12.332(1) Å, α=77.812(9), β=97.613(7), γ=98.550(8)°, Z=4, D_C=1.288 gr cm^{-3}, $\lambda(MoK\alpha)$=0.7107 Å, μ=0.179 mm^{-1}, Philips PW1100 diffractometer, graphite monochromator, colorless crystal (0.50 x 0.60 x 0.40 mm), 5016 Friedel pairs collected ($2<\theta<27°$), 3374 reflexions with $I>2\sigma I$. R=0.064, Rw=0.171, data/parameters 5017/298, GOF 1.055, largest diff. peak and hole 0.229 and -0.299 eÅ^{-3}.
10. As a result of this study, our tentative stereochemical assignments for epoxides derived from simple *E*-1-hexenyl *p*-tolyl sulfoxide (ref 3) are being reevaluated.
11. For leading references see: (a) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717-1760. (b) Walker, A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 961-968.
12. For leading references on synthetic applications of these oxiranes, see : (a) Satoh, T.; Horiguchi, K. *Tetrahedron Lett.* **1995**, *36*, 8235-8238. (b) Mori, Y.; Yaegashi, K.; Iwase, K.; Yamamori, Y.; Furukawa, H. *Tetrahedron Lett.* **1996**, *37*, 2605-2608.

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