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Effects of Additional Stereogenic Centres and Cation in the Nucleophilic Epoxidation of Vinylsulfoximines with Metal Alkylperoxides

Andrew D. Briggs,[a] Richard F.W. Jackson,[a]* William Clegg,[a] Mark R.J. Elsegood,[a] Josephine Kelly,[a] and Paul A. Brown[b]

[a] Department of Chemistry, Bedson Building, The University of Newcastle, Newcastle upon Tyne, NE1 7RU, UK

[b] Roche Products Limited, Research Centre, Welwyn Garden City, Hertfordshire, AL7 3AY, UK

Abstract: Epoxidation of vinylsulfoximines using metal alkylperoxides proceeds with varying degrees of stereoselectivity, depending both on the metal cation and the steric bulk of the alkyl group. The stereochemical outcome of the epoxidation of substrates bearing an allylic asymmetric centre is also dependent on the epoxidising agent, and very high levels of stereoselectivity may be obtained in the formation of sulfonyloxirane **6a**. This oxirane was subsequently converted into the sulfonyloxirane **13**, a precursor to a useful chiral functionalised acyl anion equivalent.

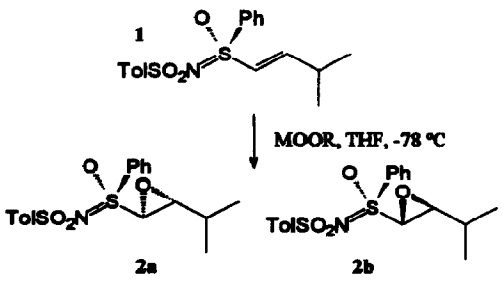
The low-temperature epoxidation of *N*-tosylvinylsulfoximines using lithium *t*-butylperoxide is known to give *N*-tosylsulfoximinooxiranes with high diastereoselectivity.[1] We have now further investigated this process by exploring the use of potassium *t*-butylperoxide,[2] as well as the bulkier reagents lithium and potassium triphenylmethylperoxide,[3] as the epoxidising agents. We have also investigated the diastereoselective epoxidation of both vinylsulfones and *N*-tosylvinylsulfoximines which possess an additional stereogenic centre as a route to useful chiral building blocks.

Epoxidation of the racemic model vinylsulfoximine **1** with potassium *t*-butylperoxide in tetrahydrofuran (THF) proceeded very rapidly at -78 °C to give a mixture of the two stereoisomeric oxiranes **2a** and **2b** (ratio 10:11). This result is in sharp contrast to the results obtained using lithium *t*-butylperoxide, in which oxirane **2a** is formed with high stereoselectivity. The fact that such a markedly different result was obtained under reaction conditions which were closely comparable, provides very strong evidence for interaction between the lithium cation and the sulfoximine group during lithium *t*-butylperoxide epoxidations. Epoxidation with lithium triphenylmethylperoxide proceeded with very high diastereoselectivity to give **2a**, whilst epoxidation with potassium triphenylmethylperoxide gave **2a** and **2b** with moderate selectivity in favour of **2a** (4:1). Our results are summarised in Table 1.

Table 1

Reagent	Ratio 2a:2b	Yield, %
$LiOOBu^t$	25:1	97
$LiOOCPh_3$	25:1	73
$KOOBu^t$	10:11	76
$KOOCPh_3$	4:1	74

Diastereoisomer ratios were obtained from ^1H NMR spectra of crude reaction mixtures. Yields are of purified material.



Having established the significant variation in stereoselectivity available by choice of epoxidising agent, we now set out to investigate the epoxidation of substrates possessing an additional stereogenic centre. As initial substrates, we chose the vinylsulfone **3** derived from (R)-isopropylideneglyceraldehyde, together with the two diastereoisomeric *N*-tosylvinylsulfoximines **4** and **5** derived from (*S*)- and (R)-S-methyl-S-phenyl-N-tosylsulfoximines, respectively. The vinylsulfone **3** was prepared using the general method reported by Oh,[4] and the vinylsulfoximines **4** and **5** were prepared using our previously reported general procedure.[1]

Epoxidation of the vinylsulfone **3** with each of the four epoxidising agents under our standard conditions at -20 °C in THF gave a mixture of the *anti* oxirane **6a** and the *syn* oxirane **6b**, with varying selectivity in favour of the *anti* compound (Table 2). Of special note was the excellent diastereoselectivity in favour of **6a** obtained using potassium triphenylmethylperoxide, which allows easy access to a potentially useful chiral building block (*vide infra*). The results for the epoxidation of the vinylsulfoximines **4** and **5** at -78 °C to -55 °C are also indicated in Table 2. The results obtained using both lithium *t*-butylperoxide and lithium triphenylmethylperoxide are complex, and not easily rationalised. Clearly there are several possible sites for lithium coordination in **4** and **5**, and the combination of stereogenic centres in **5** combines to make epoxidation with lithium *t*-butylperoxide poorly stereoselective, whilst the reaction with lithium triphenylmethylperoxide seems completely independent of the sulfoximine stereochemistry. This situation cannot be rationalised on the basis of the Masamune "matched-mismatched" analysis,[5] since it is clear that the effects of the two stereogenic centres in **4** and **5** are not independent of each other. In contrast, epoxidation of all three substrates with potassium *t*-butylperoxide shows clear matched (for **5**) and mismatched (for **4**) situations.

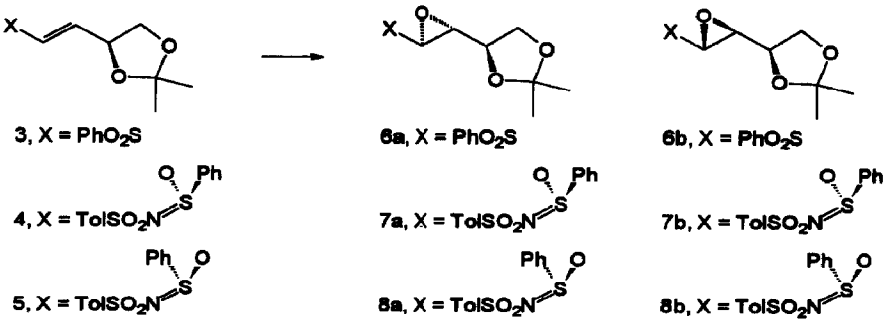
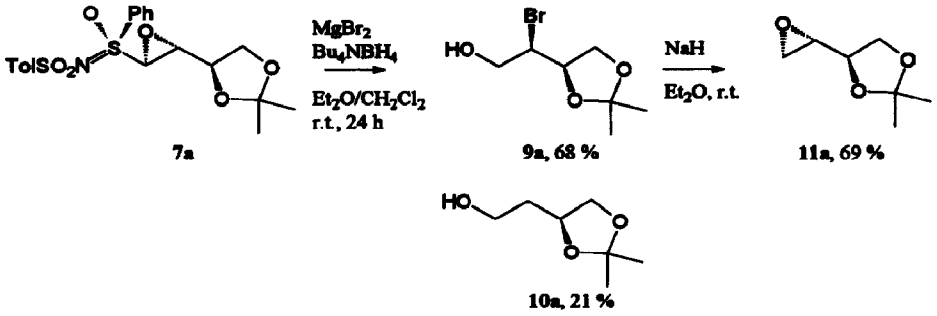


Table 2

Alkene	Oxirane	^{t}BuOOLi	Ph_3COOLi	^{t}BuOOK	Ph_3COOK
3	**6a/6b**	4:3 (85%)	5:4 (78%)	4:1 (68%)	25:1 (76%)
4	**7a/7b**	25:1 (68%)	25:1 (65%)	2:1 (80%)	25:1 (67%)
5	**8a/8b**	2:1 (75%)	25:1 (76%)	6:1 (80%)	7:4 (74%)

The stereochemistry of the *anti* sulfonyloxirane **6a** was established by a single crystal X-ray crystallographic determination of the diol **12** (Figure 1),[6] obtained by cleavage of the isopropylidene acetal (*vide infra*). The *anti* stereochemistry of **7a** was established directly by X-ray crystal structure analysis (Figure 2).[7] Further corroboration of this result was obtained by conversion of the sulfoximinooxirane **7a** to the corresponding bromohydrin **9a** by our recently described method involving ring-opening with magnesium bromide etherate (to give the α-bromoaldehyde) in the presence of tetra-n-butylammonium borohydride as *in situ* reducing agent.[8] Protected butane-1,2,4-triol **10a** was obtained as a by-product in this

process. Treatment of **9a** with sodium hydride in diethyl ether gave the known oxirane **11a**, which was identified by comparison of ^{1}H NMR data with those in the literature.[9]



This result confirms unambiguously that the conversion of **7a** to **9a** occurs with inversion of configuration at C-2. Analogous treatment of the 6:1 mixture of oxiranes **8a** and **8b**, obtained by potassium *t*-butylperoxide epoxidation of **5**, gave a mixture of **9a** and its C-2 epimer (in a ratio of 6:1), thereby establishing that the major isomer had the same configuration at C-2 as **7a**, and therefore had structure **8a**.

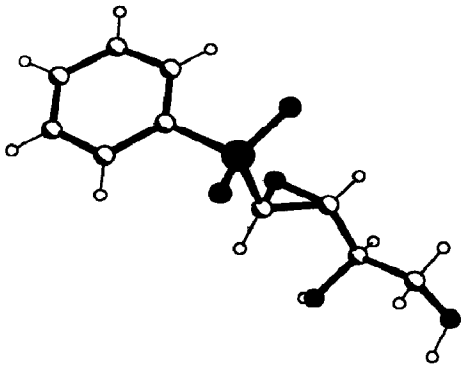


Figure 1
The molecular structure of compound **12**

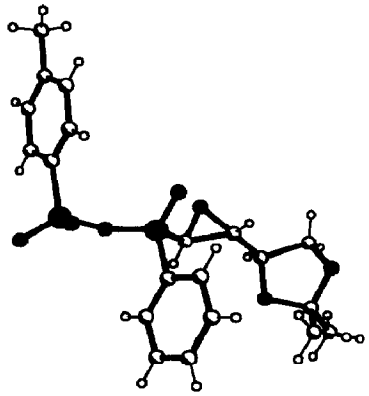
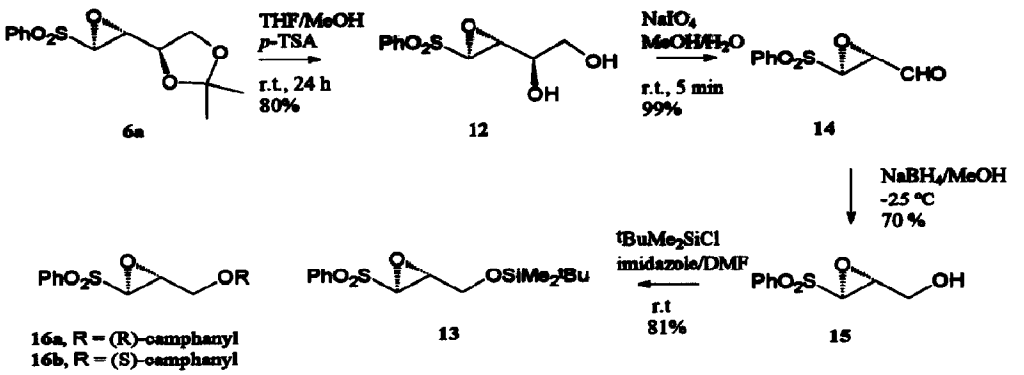


Figure 2
The molecular structure of compound **7a**

To illustrate one potential synthetic application of the sulfonyloxirane **6a**, we have established a method for its conversion to (2S,3R)-2-phenylsulfonyl-3-*t*-butyldimethylsilyloxymethyloxirane **13**. We have previously established that the lithio-derivative of this compound, in racemic form, is a versatile functionalised acyl anion equivalent,[10] and may be used for the preparation of unsubstituted epoxyketones,[11] for example. Thus, treatment of the diol **12** with sodium metaperiodate gave the aldehyde **14**, which was reduced with sodium borohydride to the alcohol **15**. The enantiomeric purity of the alcohol **15** was established by conversion to the (R) and (S) camphanate esters **16a** and **16b**, which were shown to be diastereoisomerically pure within the limits of detection by ^{1}H NMR. Finally, protection of the alcohol **15** as the *t*-butyldimethylsilyl ether gave the target **13**, identical by comparison of spectroscopic data with the racemic compound.[10]



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6. Compound **12** crystallises in the orthorhombic space group $P2_12_12_1$ with a = 5.527(2), b = 7.723(3), c = 25.356(9) Å, Z = 4. The structure was solved from 1908 independent diffractometer reflections ($2\theta < 50°$, MoKα radiation) collected at 160 K and refined on F^2 values to R_w = 0.1963 (conventional R for 1669 observed F values = 0.0481).
7. Compound **7a** crystallises in the orthorhombic space group $P2_12_12_1$ with a = 5.8078(12), b = 14.749(3), c = 25.078(7) Å, Z = 4. The structure was solved from 3251 independent diffractometer reflections ($2\theta < 50°$, MoKα radiation) collected at 293 K and refined on F^2 values to R_w = 0.1425 (conventional R for 2587 observed F values = 0.0422).
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