Tetrahedron Letters, Vol.32, No 39, pp 5393-5396, 1991
Printed in Great Britain

0040-4039/91 $3 00 +
Pergamon Press plc

Control of Diastereofacial Selectivity in the Nucleophilic Epoxidation of γ-Oxygenated-α,β-Unsaturated Sulphones

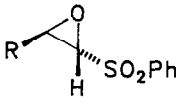
Richard F.W. Jackson,* Stephen P. Standen and William Clegg

Department of Chemistry, Bedson Building, The University, Newcastle upon Tyne, NE1 7RU, U.K.

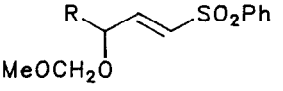
Key Words: Michael Addition; Vinylsulphone; Epoxidation; Allylic Stereochemistry.

Abstract: *Epoxidation of γ-oxygenated-α,β-unsaturated sulphones* ***4-8*** *with lithium t-butyl hydroperoxide proceeds with moderate to high diastereoselectivity to give 2-phenylsulphonyl oxiranes* ***9-13****. The sense of diastereoselectivity is dependent on the steric bulk of the alkyl substituent at the γ-centre.*

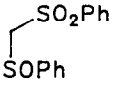
As part of our studies to extend the synthetic utility of 2-phenylsulphonyl oxiranes **1**,[1] we have investigated the diastereofacial selectivity of nucleophilic epoxidation of γ-oxygenated-α,β-unsaturated sulphones using lithium *t*-butyl hydroperoxide. A recent report on the addition of organolithium reagents to γ-methoxymethoxy-α,β-unsaturated sulphones **2**[2] prompts us to report our observations on the stereochemical outcome of the nucleophilic epoxidation of γ-oxygenated-α,β-unsaturated sulphones, especially with regard to the ability to control the sense of diastereofacial selectivity by suitable choice of the alkoxy substituent. Whilst a substantial body of work has addressed the question of stereochemical control by allylic stereocentres in Michael reactions,[3,4] including reactions with cyclic[5] and acyclic[6] vinyl sulphones, reports on analogous stereochemical control in nucleophilic epoxidation processes have been much more limited.[7,8]



1

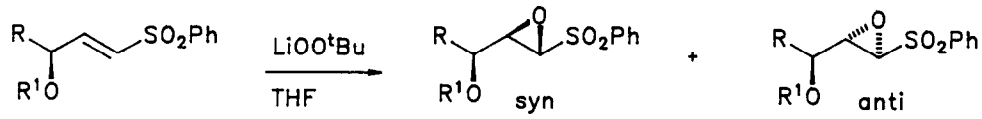


2



3

γ-Hydroxy-α,β-unsaturated sulphones **4a**, **4b** and **4c** are readily available in a one-step process involving the condensation of phenyl phenylsulphinylmethyl sulphone **3** with aldehydes.[9] Protection of the hydroxyl group to give the Ph_3Si (**5a**, **5b** and **5c**), $^tBuPh_2Si$ (**6a**, **6b** and **6c**), $^iPr_3Si$ (**7a**, **7b** and **7c**) and MEM (**8a**, **8b** and **8c**) derivatives was achieved in good yields using standard procedures. We were expecting that use of the MEM protecting group would allow chelation control, whilst use of the silyl protecting groups would reverse the diastereofacial selectivity. Our results for the nucleophilic epoxidation of the vinylsulphones **4**, **5**, **6**, **7** and **8** using lithium t-butyl hydroperoxide to give the oxiranes **9**, **10**, **11**, **12** and **13**, respectively are described in the Table.



4-8 9-13

Table: Epoxidation of Vinylsulphones 4-8

Vinylsulphone	R	R^1	Oxirane	Time, h	Temp, °C	*Syn/Anti* ratio	Yield, %
4a	Me	H	9a	4	-20	3:1	56
5a	Me	Ph_3Si	10a	16	-20	3:1	77
6a	Me	$^tBuPh_2Si$	11a	1	-20 to r.t	4:1	64
7a	Me	$^iPr_3Si$	12a	2	-20 to 0	10:1	94
8a	Me	MEM	13a	2	-20 to 0	1:1.5	63
4b	^nPr	H	9b	3	-20	3:1	80
5b	^nPr	Ph_3Si	10b	1	-20 to 0	2:1	71
6b	^nPr	$^tBuPh_2Si$	11b	4	-20 to r.t	1.5:1	66
7b	^nPr	$^iPr_3Si$	12b	1	-20 to r.t	4:1	92
8b	^nPr	MEM	13b	2	-20 to 0	1:5	65
4c	^iPr	H	9c	3	-20	25:1	46
5c	^iPr	Ph_3Si	10c	1	-20 to r.t	1:25	79
6c	^iPr	$^tBuPh_2Si$	11c	4	-20 to r.t	1:4	89
7c	^iPr	$^iPr_3Si$	12c	16	-20 to r.t	1:40	96
8c	^iPr	MEM	13c	6	-20 to r.t	1:30	55

The stereochemistry of the major isomer **10a**, *syn* derived from epoxidation of **6a**, with R = methyl, was established by X-ray crystallography (Figure 1).[10] Chemical correlation of all the other compounds **9a**, **11a**, **12a** and **13a** with this material allowed the unambiguous assignment of stereochemistry for these examples. The stereochemistry of the oxiranes **9b-13b**, with R = ^nPr was established by correlation, and by comparison of ^1H and ^{13}C nmr spectra with the methyl series. The stereochemistry of the major isomer **12c**, *anti* derived from epoxidation of **7c**, with R = ^iPr, was also established by X-ray crystallography (Figure 2).[11] This allowed the unambiguous assignment of stereochemistry for **9c**, **10c**, **11c** and **13c**, again by correlation.

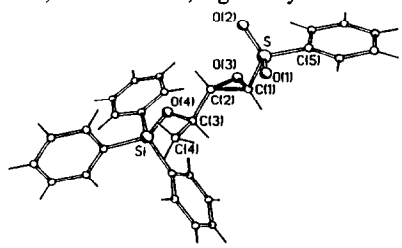


Figure 1

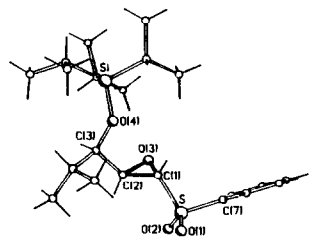
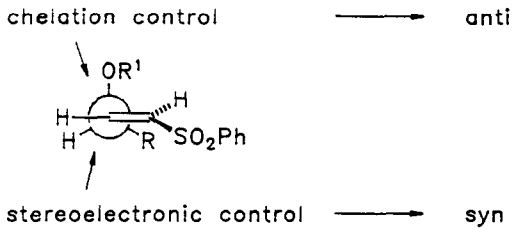


Figure 2

The stereochemical outcome of the nucleophilic epoxidation reaction is clearly dependent on the nature of the alkyl substituent. The results from the epoxidation of the methyl series **4a–7a** and propyl series **4b–7b** can be accounted for using the extended Felkin–Ahn[1,2] model in which the γ-alkoxy substituent is orthogonal to the π-system and *anti* to the direction of nucleophilic attack by lithium t-butyl hydroperoxide, and the alkyl substituent occupies the less hindered inside position (Figure 3). This arrangement leads to the *syn* product. If a similar conformation represents the reactive arrangement in epoxidation of **8a** and **8b**, then chelation control by the MEM group could account for the reversal of diastereofacial selectivity to give the *anti* product.

Figure 3



The stereochemical results obtained from epoxidation of the isopropyl series **4c–8c** are more difficult to rationalise. In the case of the free hydroxyl compound **4c**, the same model used for the epoxidation of the methyl series appears to provide a satisfactory rationalisation, with the *syn* product being favoured. Presumably the requirement for the allylic C–O bond to be *anti* to the direction of nucleophilic attack is particularly marked for the alkoxide anion, which is likely to be formed under the basic conditions of the reaction. However for the remaining examples (**5c–8c**), the presence of two bulky substituents makes the application of simple models rather difficult. If, as seems reasonable, the ^{i}Pr group is now the largest group, a different reactive conformation in which the ^{i}Pr group is *anti* and the oxygen-substituent is inside could now be important (Figure 4). Yamamoto has suggested a similar arrangement for the Lewis acid promoted addition of organocopper reagents to γ-alkoxy-α,β-unsaturated esters.[3a] Nucleophilic attack would occur from below with both non-chelating (**5c–7c**) and chelating substituents **8c**, leading to the *anti* products in all cases. It should be noted that nucleophilic epoxidation of the closely related enone **14** also gave an *anti* product **15** with high diastereoselectivity.[a]

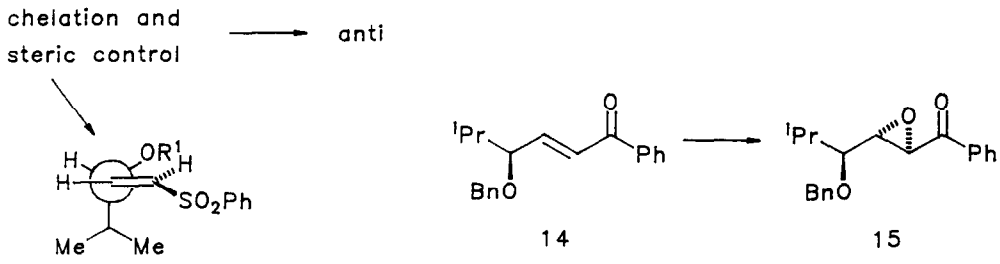


Figure 4

Whatever the rationalisation of the stereochemical outcome of these nucleophilic epoxidation reactions, both *syn* (by silylation of **9c**) and *anti* diastereoisomers of the oxirane **12c** are readily available, and the *syn* diastereoisomer of the oxirane **12a** is also available with reasonable selectivity.

Acknowledgements: We thank the SERC for a postgraduate studentship (S.P.S.) and for a research grant (W.C.), and Dr. M. Ashwell for some preliminary experiments.

References

1. Ashwell, M.; Clegg, W.; Jackson, R.F.W. *J. Chem. Soc., Perkin Trans. 1* **1991**, 897-908.
2. Alcaraz, C.; Carretero, J.C.; Dominguez, E. *Tetrahedron Lett.* **1991**, *32*, 1385-1388.
3. For some representative recent experimental work, see: (a) Yamamoto, Y.; Nishii, S.; Ibuka, T. *J. Chem Soc., Chem. Commun.* **1987**, 464-466. (b) Larcheveque, M.; Tamagnan, G.; Petit, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 31-33. (c) Reetz, M.T.; Röhrig, D. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1706-1709. (d) Bernardi, A.; Cardani, S.; Scolastico, C.; Villa, R. *Tetrahedron* **1990**, *46*, 1987-1998. (e) Leonard, J.; Ryan, G.; Swain, P.A. *Synlett* **1990**, 613-614. (f) Barrett, A.G.M.; Lebold, S.A. *J. Org. Chem.* **1990**, *55*, 3853-3857. For earlier references, see those cited in 4a and 4b below.
4. For theoretical discussions, see: (a) Dorigo, A.E.; Morokuma, K. *J. Am. Chem. Soc.* **1989**, *111*, 6524-6536; (b) Bernardi, A.; Capelli, A.M.; Gennari, C.; Scolastico, C. *Tetrahedron: Asymmetry* **1990**, *1*, 21-32.
5. Fuchs, P.L.; Braish, T.F.; *Chem. Rev.* **1986**, *86*, 903-917.
6. (a) Kitamura, M.; Isobe, M.; Ichikawa, Y.; Goto, T. *J. Org. Chem.* **1984**, *49*, 3517-3527; (b) Isobe, M.; Ichikawa, Y.; Funabashi, Y.; Mio, S.; Goto, T. *Tetrahedron* **1986**, *42*, 2863-2872; (c) Ichikawa, Y.; Isobe, M.; Bai, D.; Goto, T. *Tetrahedron* **1987**, *43*, 4737-4748.
7. Cardani, S.; Bernardi, A.; Colombo, L.; Gennari, C.; Scolastico, C.; Venturini, I. *Tetrahedron* **1988**, *44*, 5563-5572.
8. Yamamoto, K.; Yamamoto, N. *Chemistry Lett.* **1989**, 1149-1152.
9. (a) Dominguez, E.; Carretero, J.C. *Tetrahedron* **1990**, *46*, 7197-7206. (b) Trost, B.M.; Grese, T.A. *J. Org. Chem.* **1991**, *56*, 3189-3192. We had independently discovered this reaction in 1988: Ashwell, M.; Hindley, N.G.; Jackson, R.F.W. presented at the symposium in honour of Prof. R.A. Raphael, Cambridge, 22nd July, 1988.
10. Compound **10a** forms monoclinic crystals, a = 11.642(1), b = 7.852(1), c = 28.092(3) Å, β = 91.37(1)°, Z = 4, space group $P2_1/c$. The structure was solved from 2699 diffractometer reflections with $F > 4\sigma(F)$ and $2\theta < 50°$ (MoKα radiation) and refined to R = 0.0564 and R_w = 0.0565.
11. Compound **12c** forms triclinic crystals, a = 8.192(2), b = 11.734(3), c = 13.236(3) Å, α = 109.15(2), β = 100.83(1)°, γ = 95.65(1)°, Z = 2, space group $P\bar{1}$. The structure was solved from 2976 diffractometer reflections with $F > 4\sigma(F)$ and $2\theta < 50°$ (MoKα radiation) and refined to R = 0.0386 and R_w = 0.0470.
12. Chérest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199-2204. Chérest, M; Felkin, H. *Tetrahedron Lett.* **1968**, 2205-2208. Anh, N.T.; Eisenstein, O. *Nouv. J. Chem.* **1977**, *1*, 61-70.

(Received in UK 26 June 1991)