Very High Diastereofacial Selectivity in the Nucleophilic Epoxidation of *N*-(*p*-Tolylsulphonyl)vinylsulphoximines

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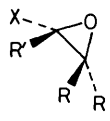
Nucleophilic epoxidation of *N*-(*p*-tolylsulphonyl)vinylsulphoximines (**6**) using lithium t-butyl hydroperoxide proceeds with very high diastereofacial selectivity, the sense of which was established by a single crystal X-ray structure determination, to give *N*-(*p*-tolylsulphonyl)phenylsulphoximino-oxiranes (**5**) in good yield.

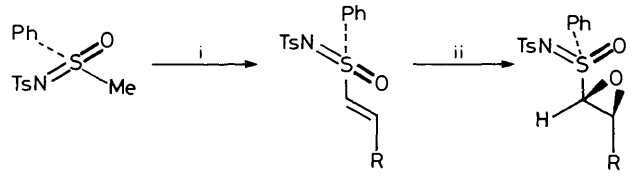
New methods for the synthesis of enantiomerically pure compounds are constantly being sought. We have recently started to investigate the synthetic potential of phenylsulphonyloxiranes,[1] and we now report an approach to asymmetric synthesis using the closely related *N*-(*p*-tolylsulphonyl)phenylsulphoximino-oxiranes. Racemic *N*-methylphenylsulphoximino-oxiranes (**1**) have previously been prepared as mixtures of diastereoisomers by a non-stereoselective Darzens reaction of the *S*-chloromethyl-*N*-methyl-*S*-phenylsulphoximine (**2**) with ketones.[2] Related *p*-tolylsulphinyloxiranes (**3**) have been prepared by Darzens reaction of optically active chloroalkyl *p*-tolyl sulphoxides (**4**) with aldehydes and ketones.[3] In this approach, two diastereoisomeric oxiranes were always obtained with aldehydes and unsymmetrical ketones. We now report a highly diastereoselective synthesis of *N*-(*p*-tolylsulphonyl)phenylsulphoximino-oxiranes (**5**),† which should allow the development of new methods for the asymmetric synthesis of α-substituted carbonyl compounds. We have found that *N*-(*p*-tolylsulphonyl)vinylsulphoximines (**6**)† are easily prepared as pure *E* isomers by reaction of the lithio anion derived from *S*-methyl-*S*-phenyl-*N*-(*p*-tolylsulphonyl)sulphoximine (**7**)† with aldehydes, followed by treatment with methanesulphonyl chloride–triethylamine. This procedure, which is a modification of a method for the synthesis of *N*-alkylvinylsulphoximines,[4] gave comparable yields to those reported for the Peterson synthesis of *N*-(*p*-tolylsulphonyl)vinylsulphoximines.[5] Treatment of the *N*-(*p*-tolylsulphonyl)vinylsulphoximines (**6**)† with lithium t-butyl hydroperoxide in THF led rapidly to the corresponding crystalline phenylsulphoximino-oxiranes (**5**)†,[6] as single diastereoisomers in each case as judged by their 300 MHz ^{1}H NMR spectra (Scheme 1). Our results are shown in the Table. A single crystal X-ray structure determination was performed on the *N*-(*p*-tolylsulphonyl)phenylsulphoximino-oxirane (**5b**) (see Figure).‡ This revealed the *trans* arrangement of substituents on the oxirane, and the sense of stereoselectivity induced by the chiral centre at sulphur. We feel that the relative configurations of the other oxiranes (**5a**), (**5c**), and (**5d**) are, therefore, also established as drawn. The high stereoselectivity in this process suggests that a conformationally locked transition state is involved in the nucleophilic addition of lithium t-butyl hydroperoxide to the vinylsulphoximine (**6b**). A reasonable rationalisation is that in the reactive conformation (**8**), the vinyl group is *anti* to the S=NTs group, and the oxygen of the phenylsulphoximino group then delivers lithium t-butyl hydroperoxide. Further experiments to probe this stereoselectivity are in progress. Initial efforts to deprotonate α to the phenylsulphoximino group in (**5b**) have been unsuccessful, resulting in decomposition. However, the alkene (**6b**) can be deprotonated and the anion quenched with iodomethane to give the methylated vinylsulphoximine (**9**)† (80%).[7] Epoxidation of (**9**) occurs smoothly (91%) on treatment with lithium t-butyl hydroperoxide to give a single diastereoisomeric oxirane (**10**);† a reaction temperature of 20 °C and a reaction time of 12 h is, however, necessary (Scheme 2).

Since both (+)- and (−) *S*-methyl-*S*-phenyl-*N*-(*p*-tolylsulphonyl)sulphoximine are readily available,[8] access to



(**1**) X = S(O)(NMe)Ph, R′ = H
(**3**) X = S(O)Ph

(**2**) X = S(O)(NMe)Ph, R′ = H
(**4**) X = S(O)Ph



(**7**) (**6**) (**5**)

Scheme 1. *Reagents and conditions:* i, BuLi (1.0 equiv.), −78 °C to room temp. (10 min), RCHO (1.05 equiv.), −78 °C to 0 °C (45 min), Et_3N (1.1 equiv.) 0 °C and $MeSO_2Cl$ (1.4 equiv.), 15 min followed by Et_3N (1.1 equiv.), 0 °C, 15 min; ii, BuLi (1.1 equiv.), Bu^{t}OOH (1.5 equiv.), THF, − 55 °C, 3 min.

† Compounds (**5a–d**), (**6a–d**), (**7**), (**9**), and (**10**) are racemic, but one enantiomer is drawn for clarity.

‡ *Crystal data for compound* (**5b**). $C_{18}H_{21}NO_4S_2$, M = 379.5, monoclinic, a = 10.469(1), b = 10.520(1), c = 18.188(2) Å, β = 94.36(1), V = 1 997.3 Å^3, Z = 4, D_c = 1.262 g cm^{-3}, $F(000)$ = 800, μ = 0.27 mm^{-1} for Mo-K_α radiation (λ = 0.710 73 A), T = 295 K, space group P_1/n. The structure was determined by direct methods [9] and refined to a minimum of $\Sigma w\Delta^2$ ($\Delta = |F_o| - (F_c|$; $w^{-1} = \sigma_c^2(F) + 11 - G + 4G^2 - 30H + 20H^2 + 8GH$; $G = F_o/F_{max}$, $H = \sin\theta/\sin\theta_{max}$) [10] from 2 234 reflections with $2\theta < 50°$ and $F > 4\sigma_c(F)$ (σ_c from counting statistics only) measured with a Stoe-Siemens diffractometer and on-line profile fitting.[11] Final R = 0.049, wR = $(\Sigma w\Delta^2/\Sigma wF_o^2)^{\frac{1}{2}}$ = 0.055 for 236 parameters including anisotropic thermal parameters and constrained hydrogen atoms. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1990, Issue 1.

Table.

R	Vinyl-sulphoximine	Yield (%)	Sulphoximino-oxirane	Yield (%)
Me	(**6a**)	76	(**5a**)	72
Pr^i	(**6b**)	93	(**5b**)	85
Pr	(**6c**)	85	(**5c**)	82
Pe	(**6d**)	86	(**5d**)	86

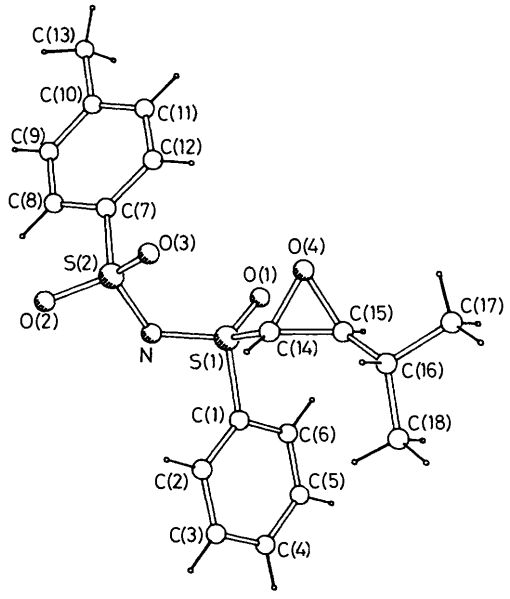
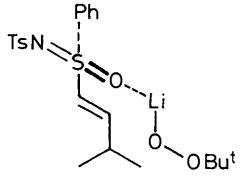
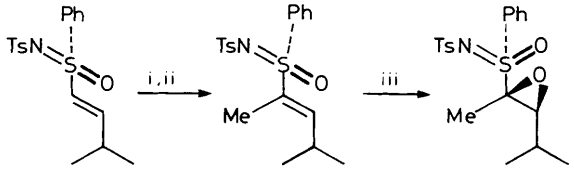


Figure. The molecular structure of (**5b**). Selected distances and bond angles: C(14)–O(4) 1.394(4), C(15)–O(4) 1.452(5), C(14)–C(15) 1.443(5) Å, C(14)–O(4)–C(15) 60.9(2), O(4)–C(14)–C(15) 61.6(2), O(4)–C(15)–C(14) 57.6(2)°.

enantiomerically pure phenylsulphoximino-oxiranes is possible. We are currently exploring the use of phenylsulphoximino-oxiranes for the asymmetric synthesis of α-substituted carbonyl compounds. In an initial experiment, we have found that treatment of racemic (**5b**) with $MgBr_2$ in THF at reflux does yield the expected α-bromo aldehyde.



(**8**)



(**6b**) (**9**) (**10**)

Scheme 2. *Reagents and conditions:* i, BuLi (1 equiv.), THF, −78 °C, 10 min.; ii, MeI (1.5 equiv.) −78 °C, 12 min; iii, BuLi (1.1 equiv.), Bu^{t}OOH (1.5 equiv.), THF, −78°C to 20 °C, 12 h.

Experimental

(E)-S-(3-*Methylbut*-1-*enyl*)-S-*phenyl*-N-(p-*tolylsulphonyl*)*sulphoximine* (**6b**). BuLi (2.3M; 7.0 ml, 16.1 mmol) was added, dropwise, to a stirred solution of *S*-methyl-*S*-phenyl-*N*-(*p*-tolylsulphonyl)sulphoximine (**7**) (5.0 g, 16.18 mmol) in dry THF (80 ml) under N_2 at −78 °C. The reaction mixture was warmed to room temperature and stirred for 5 min at that temperature. During this time the colour of the solution changed from pale yellow to intense yellow–orange. After 5 min the reaction mixture was cooled to −78 °C and 2-methylpropanal (1.51 ml, 16.6 mmol) was added, dropwise. Following the addition of the aldehyde, the reaction mixture was warmed slowly, over 45 min, to 0 °C. Triethylamine (2.5 ml, 17.9 mmol) was added followed by the dropwise addition of methanesulphonyl chloride (1.8 ml, 23.2 mmol) at 0 °C. The reaction mixture was stirred for 15 min during which time a pale yellow precipitate was formed. After 15 min, triethylamine (2.5 ml, 17.9 mmol) was added and the reaction mixture was allowed to warm to room temperature when it was stirred for a further 15 min before being quenched with aqueous NH_4Cl (10%; 10 ml) and extracted with dichloromethane (3 × 20 ml). The dichloromethane extract was then dried (Na_2SO_4), concentrated, and chromatographed on silica gel with 50% ethyl acetate–light petroleum as eluant to give a white crystalline solid (**6b**) (5.48 g, 15.1 mmol, 93%), m.p. 108–110 °C; ν_{max}(KBr) 1 622w; δ_H(200 MHz; $CDCl_3$), 1.05 (3 H, d, *J* 6.8 Hz), 1.06 (3 H, d, *J* 6.9 Hz), 2.39 (3 H, s), 2.53 (1 H, m), 6.34 (1 H, dd, *J* 15.0 and 1.5 Hz), 7.00 (1 H, dd, *J* 15.0 and 6.3 Hz), and 7.21–7.97 (9 H, m); *m/z* (electron impact) 364 (MH^+, 25%), 363 (M^+, 6), and 278 (100) (Found: M^+, 363.0929. $C_{18}H_{21}NO_3S_2$ requires 363.0963).

S-[trans-3-(1-*Methylethyl*)*oxiran*-2-*yl*]-S-*phenyl*-N-(p-*tolylsulphonyl*)*sulphoximine* (**5b**).—To a stirred solution of t-butyl hydroperoxide (3.41M in toluene; 2.4 ml, 8.2 mmol) and BuLi (1.33M; 4.47 ml, 5.9 mmol) in dry THF (60 ml) under N_2 at −78 °C was added the vinylsulphoximine (**6b**) (1.98 g, 5.45 mmol) in THF (10 ml). The addition was done very quickly such that the temperature of the reaction mixture rose to −55 °C; it dropped to −65 °C when the mixture was stirred for 3 min. After 3 min the reaction mixture was quenched with sodium sulphite (1 g) and stirred for a further 15 min before being diluted with dichloromethane (20 ml) and filtered through Celite. Evaporation of the solvent and filtration of the crude product in dichloromethane through a small pad of silica gave a white crystalline solid (**5b**) (1.75 g, 4.62 mmol, 85%), m.p. 98–100 °C (Found: C, 56.7; H, 5.65; N, 3.5. $C_{18}H_{21}NO_4S_2$ requires C, 57.0; H, 5.5; N, 3.7%); ν_{max}(KBr) 1 242m, 910w, 815w, and 802w; δ_H(200 MHz; $CDCl_3$) 0.91 (3 H, d, *J* 7.0 Hz), 0.95 (3 H, d, *J* 7.0 Hz), 2.40 (3 H, s), 3.21 (1 H, dd, *J* 1.6 and 6.4 Hz), 4.42 (1 H, d, *J* 1.6 Hz), and 7.26–8.00 (9 H, m); *m/z* (electron impact) 380 (MH^+, 25%), 296 (50), 278 (80), 155 (94), and 139 (100).

Acknowledgements

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References

1 M. Ashwell and R. F. W. Jackson, *J. Chem. Soc., Chem. Commun.*, 1988, 645; C. T. Hewkin, R. F. W. Jackson, and W. Clegg, *Tetrahedron Lett.*, 1988, **29**, 4889; M. Ashwell and R. F. W. Jackson, *J. Chem. Soc., Perkin Trans. 1*, 1989, 835.

2 H. G. Corkins, L. Veenstra, and C. R. Johnson, *J. Org. Chem.*, 1978, **43**, 4233.

3 T. Satoh, T. Oohara, Y. Ueda, and K. Yamakawa, *Tetrahedron Lett.*, 1988, **29**, 313; T. Satoh, T. Oohara, and K. Yamakawa, *Tetrahedron Lett.*, 1988, **29**, 2851; T. Satoh, T. Oohara, Y. Ueda, and K. Yamakawa, *J. Org. Chem.*, 1989, **54**, 3130.

4 S. G. Pyne, *J. Org. Chem.*, 1986, **51**, 81.
5 I. Erdelmeier and H.-J. Gais, *Tetrahedron Lett.*, 1985, **26**, 4359; H.-J. Veith, H.-J. Gais, and I. Erdelmeier, *Helv. Chim. Acta*, 1987, **70**, 1041.
6 For a preliminary example, see: O. Meth-Cohn, C. Moore, and H. C. Talijaard, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2663.
7 For the deprotonation of *N*-methyl-*S*-phenyl-*S*-vinylsulphoximines, see: I. Erdelmeier and H.-J. Gais, *J. Am. Chem. Soc.*, 1989, **111**, 1125; we thank Prof. Dr. H.-J. Gais for providing further details.
8 C. R. Johnson and C. W. Schroeck, *J. Am. Chem. Soc.*, 1973, **95**, 7418.
9 G. M. Sheldrick, SHELXTL, an integrated system for solving, refining and displaying crystal structures from diffraction data. Revision 5. University of Göttingen, 1985.
10 H. Wang and B. E. Robertson, 'Structure and Statistics in Crystallography,' edited by A. J. C. Wilson, p. 125, Adenine Press, New York, 1985.
11 W. Clegg, *Acta Crystallogr., Sect. A*, 1981, **37**, 22.

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