Optically Active *N*-Phosphinoyloxaziridines: Preparation and Chiral Oxygen Transfer to Prochiral Sulfides

W. Brian Jennings,*[a] Michael J. Kochanewycz,[b] Carl. J. Lovely[b] and Derek R. Boyd[c]

[a] *Department of Chemistry, University College Cork, Ireland*
[b] *School of Chemistry, The University of Birmingham, Edgbaston, Birmingham, UK B15 2TT*
[c] *School of Chemistry, The Queen's University of Belfast, Belfast, UK BT9 5AG*

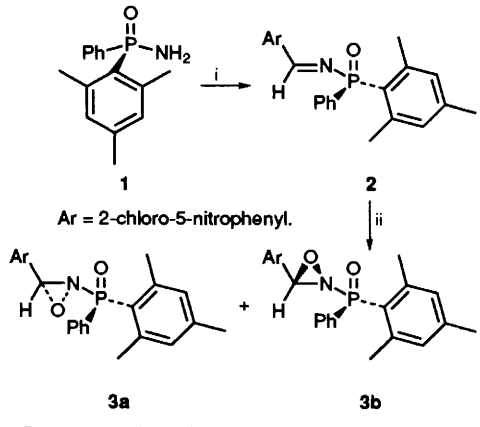
Optically active *N*-phosphinoyloxaziridines **3a** and **3b** containing a chiral phosphorus centre have been prepared; these compounds oxidise aryl alkyl sulfides to chiral sulfoxides with 34–70% enantiomeric excess.

A few years ago we reported the preparation and characterization of *N*-phosphinoyloxaziridines.[1] These initial compounds contained an achiral *N*-diphenylphosphinoyl group and functioned as neutral aprotic oxidants like their better established *N*-sulfonyl analogues.[2] We now report the preparation of optically active *N*-phosphinoyloxaziridines containing a chiral phosphorus centre, and some initial results on enantioselective oxygen transfer.

The original synthetic route of Krzyzanowska and Stec[3] for preparing *N*-phosphinoylimines, the precursors of *N*-phosphinoyloxaziridines, is unsuitable for the incorporation of an optically active phosphorus moiety since it involves a stereolabile chlorophosphorus(III) reagent, PhP(R)Cl, which can readily racemise by chloride exchange.[4] The recent development of an alternative method[5] for preparing *N*-phosphinoylimines from phosphinic amides, which are configurationally stable at phosphorus, enabled the synthesis of optically active *N*-phosphinoyloxaziridines. Thus, treatment of 2-chloro-5-nitrobenzaldehyde with scalemic† (75% ee) *R*-P-mesityl-P-phenylphosphinic amide **1**[6] in the presence of titanium(IV) chloride and triethylamine gave the crude *N*-phosphinoylimine **2** which was oxidised *in situ* with anhydrous 3-chloroperoxybenzoic acid/potassium fluoride complex at 0 °C in dichloromethane (Scheme 1).[1] Flash chromatography of the crude product on silica gel using diethyl ether as eluent gave the oxaziridines **3** in 51% yield. ^{1}H, ^{13}C and ^{31}P NMR analysis indicated that the chromatographed product was a mixture of diastereoisomers **3a** and **3b** in the ratio 2.6:1. ^{1}H NMR spectra of this diastereoisomeric mixture recorded in the presence of a chiral shift reagent indicated an enantiomeric purity of 73 ± 3% for both **3a** and **3b**.‡ This confirmed that the configuration at phosphorus remained intact during the conversion of the phosphinic amide **1** to the oxaziridines **3a** and **3b**.

After much experimentation (initially on the racemic material) it was found that careful crystallisation of the diastereoisomeric oxaziridine mixture (1.5 g) from methanol gave the minor diastereoisomer **3b** (0.28 g), mp 183–187 °C (dec.), $[\alpha]_D$ − 25.0° (*c* 4.5, $CHCl_3$), essentially enantiopure (>95% ee).‡ The relative and absolute configuration of the diastereoisomers was established by an X-ray crystal structure determination on **3b**, which established the *S*-configuration of both carbon and nitrogen relative to the known *R*-configuration at phosphorus.[7] *N*-Phosphinoyloxaziridines derived from aromatic aldehydes exclusively prefer *trans* (S_CS_N/R_CR_N) stereochemistry, though previous work on more symmetrically substituted analogues has shown that the nitrogen atom inverts fairly rapidly at ambient temperature, in contrast to the situation in *N*-alkyl oxaziridines.[8]

Recrystallisation of the residue, obtained by rotary evaporation of the mother liquor, from tetrachloromethane/hexane gave the major diastereoisomer **3a** (0.82 g) with an enantiomeric purity‡ of 78%, raised to 90% by further recrystallisations, mp 154–156 °C (dec.), $[\alpha]_D$ + 98.7° (*c* 0.50, $CHCl_3$).§ The availability of these optically active *N*-phosphinoyloxaziridines enables their potential as chiral oxidants to be explored using prochiral sulfides **4–7** as substrates (Scheme 2). These oxaziridines convert sulfides to chiral sulfoxides at 0–20 °C with little or no sulfone formation (Table 1), and in principle the chiral imine co-product **2** can be recycled back to the oxaziridines **3**. The absolute configurations and enantiopurity of the sulfoxides obtained from sulfides **4** and **5** were determined by comparison of the chemical shifts and integrals of the anisochronous S–Me ^{1}H NMR signals observed in the presence of a chiral shift reagent with those of sulfoxide of known enantioenrichment obtained by oxidation of these sulfides using the modified Sharpless procedure of Kagan *et al.*[9] The configuration and enantiopurity of sulfoxides derived from sulfides **6** and **7** were established by their retention times and relative integrals on a D-phenylglycine HPLC column. It has previously been established[10] that the *S* enantiomer of these sulfoxides is eluted before the *R* enantiomer on this type of column.

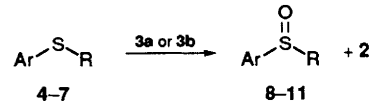


Scheme 1 *Reagents and conditions*: i, $TiCl_4$, Et_3N, ArCHO, CH_2Cl_2, 0 °C; ii, KF–MCPBA, CH_2Cl_2, room temperature

Table 1 Sulfide oxidations by chiral *N*-phosphinoyloxaziridines **3** in dichloromethane at 0 °C

Sulfide	Oxaziridine configuration	Sulfoxide ee %	Predominant sulfoxide configuration
4-MeC$_6$H$_4$–S–Me **4**	$R_CR_NR_P$ **3a**	35 (27)[a]	*R*
	$S_CS_NR_P$ **3b**	34	*S*
9-Anthryl–S–Me **5**	$R_CR_NR_P$ **3a**	56 (44)[a]	*R*
	$S_CS_NR_P$ **3b**	56	*S*
9-Anthryl–S–Bu^n **6**	$R_CR_NR_P$ **3a**	69 (54)[a]	*R*
	$S_CS_NR_P$ **3b**	70	*S*
9-Anthryl–S–Bu^t **7**	$R_CR_NR_P$ **3a**	56 (44)[a]	*R*
	$S_CS_NR_P$ **3b**	48	*S*

[a] Sulfoxide ee values obtained from **3a** have been corrected to allow for the 78% enantiomeric purity of the oxaziridine used; the uncorrected experimental ee values are given in parentheses.



Scheme 2

The results in Table 1 show that there is moderately good reagent controlled enantioselectivity in these oxygen transfer reactions. Two aspects of the results merit further consideration. Firstly, the predominant configuration of sulfoxide products correlates well with the configuration at the oxaziridine ring, *i.e.* R_C oxaziridine **3a** gives *R*-sulfoxides and S_C oxaziridine **3b** gives *S*-sulfoxides.

Secondly, the results in Table 1 indicate that the configuration at phosphorus has little influence on the asymmetric induction. Thus diastereoisomeric oxaziridines **3a** and **3b** which have the same (*R*) configuration at phosphorus produce sulfoxides of opposite configuration in almost equal enantiomeric excess. This result is surprising as it might have been expected that the configuration of the rather bulky mesitylphenylphosphinoyl group would play a significant role in the chiral recognition as it is directly attached to the oxaziridine ring adjacent to the oxygen atom being transferred.

These results have implications in regard to any proposed transition state for oxygen transfer to sulfur involving *N*-phosphinoyloxaziridines and possibly by analogy for oxygen transfer from related *N*-sulfonyloxaziridines.[2] Seemingly in the transition state the bulky phosphinoyl moiety is remote from the newly-created chiral centre at sulfur.

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Footnotes

† 'Scalemic' is a useful term proposed by Heathcock to describe a compound which is enantiomerically enriched but not enantiopure (C. H. Heathcock, *Chem. Eng. News*, 1991, Feb. 4, 3).

‡ ^{1}H NMR determinations of enantiomeric purity were carried out in deuteriochloroform solution at 270 MHz using 1–2 equiv. of the chiral auxiliary *R*-(−)-1-(9-anthryl)-2,2,2-trifluoroethanol to render the enantiomeric C(3)-H signals (oxaziridines) or *S*-alkyl signals (sulfoxides) anisochronous.

§ *Selected spectroscopic data*, **3a**: δ_H ($CDCl_3$) 2.30 (3H, s, mesityl 4′-Me), 2.45 (6H, s, mesityl 2′- and 6′-Me), 6.21 [1H, d, $^3J_{PH}$ 8.7 Hz, C(3)-H], 6.91 (2H, d, $^4J_{PH}$ 3.8 Hz, mesityl 3′- and 5′-H), 7.64 (4H, m, aromatic), 7.7–7.9 (2H, m, aromatic), 8.1–8.2 (2H, m, aromatic); δ_P 41.0. **3b**: δ_H ($CDCl_3$) 2.35 (3H, s, mesityl 4′-Me), 2.62 (6H, s, mesityl 2′- and 6′-CH_3), 6.34 [1H, d, $^3J_{PH}$ 8.5 Hz, C(3)-H], 6.98 (2H, d, $^4J_{PH}$ 4.0 Hz, mesityl 3′- and 5′-H), 7.4–7.5 (2H, m, aromatic), 7.5–7.6 (2H, m, aromatic), 7.65–7.8 (2H, m, aromatic), 8.15–8.3 (2H, m, aromatic); δ_P 40.5. Both **3a** and **3b** gave satisfactory elemental analyses.

References

1 D. R. Boyd, J. F. Malone, M. R. McGuckin, W. B. Jennings, M. Rutherford and B. M. Saket, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1145.
2 For a review of *N*-sulfonyloxaziridines see F. A. Davis and A. C. Sheppard, *Tetrahedron*, 1989, **45**, 6703.
3 B. Krzyzanowska and W. J. Stec, *Synthesis*, 1978, 521; 1982, 270.
4 B. Fontal and H. Goldwhite, *Tetrahedron*, 1966, **22**, 3275; D. Imbery and H. Friebolin, *Z. Naturforsch.*, 1968, **23b**, 759; J. Omelanczuk, *J. Chem. Soc., Chem. Commun.*, 1992, 1718.
5 W. B. Jennings and C. J. Lovely, *Tetrahedron*, 1991, **47**, 5561.
6 T. A. Hamor, W. B. Jennings, C. J. Lovely and K. A. Reeves, *J. Chem. Soc., Perkin Trans. 2*, 1992, 843.
7 T. A. Hamor, C. J. Lovely and W. B. Jennings, unpublished results.
8 W. B. Jennings, S. P. Watson and D. R. Boyd, *Tetrahedron Lett.*, 1989, **30**, 235.
9 P. Pitchen, E. Dunach, M. N. Deshmukh and H. B. Kagan, *J. Am. Chem. Soc.*, 1984, **106**, 8188; E. Dunach and H. B. Kagan, *Nouv. J. Chim.*, 1985, **9**, 1.
10 W. H. Pirkle, J. M. Finn, B. C. Hamper, J. Schreiner and J. R. Pribish, *ACS Symp. Ser.*, 1982, **185**, 245; F. A. Davis, J. P. McCauley, Jr., S. Chattopadhyay, M. E. Harakal, J. C. Towson, W. H. Watson and I. Travanaiepour, *J. Am. Chem. Soc.*, 1987, **109**, 3370.