Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 62 (2006) 3681–3693

Asymmetric aziridine synthesis by aza-Darzens reaction of *N*-diphenylphosphinylimines with chiral enolates. Part 1: Formation of *cis*-aziridines

J. B. Sweeney,[a,b,*] Alex A. Cantrill,[a] Andrew B. McLaren[b] and Smita Thobhani[b]

[a]*School of Chemistry, University of Bristol, Bristol BS8 1TS, UK*
[b]*School of Chemistry, University of Reading, Whiteknights, Reading RG6 6AD, UK*

Received 27 November 2004; revised 31 December 2005; accepted 19 January 2006

Available online 24 February 2006

Abstract—The aza-Darzens ('ADZ') reactions of *N*-diphenylphosphinyl ('*N*-Dpp') imines with chiral enolates derived from oxazolidinones and camphorsultam have been studied. Whilst oxazolidinone enolates reacted poorly in terms of aziridination, the use of the chiral enolate derived from both antipodes of *N*-bromoacetyl 2,10-camphorsultam, 2*R*-(**5**) and 2*S*-(**5**), with *N*-diphenylphosphinyl aryl and *tert*-butylimines proceeded in generally good yield to give, respectively, (2′*R*,3′*R*)- or (2′*S*,3′*S*)-*cis*-*N*-diphenylphosphinyl aziridinoyl sultams of high de.

1. Introduction

Though aziridines are regarded as valuable synthetic intermediates, there remain few generally applicable methods for the one-step preparation of these compounds in high enantiomeric purity from readily available precursors.[1,2] Furthermore, the methodology previously described is often compromised by the fact that the substituents present on nitrogen (often sulfonyl groups) frequently are not compatible with further immediate synthetic manipulation.

2. Background

We have previously investigated the preparation and ring-opening reactions of *N*-diphenylphosphinyl aziridines,[3] and were keen to devise an asymmetric synthesis of these aziridines; we were especially interested in facilitating the preparation of chiral 2-carboxyaziridines, because of the potential use of such compounds as precursors to related non-proteinogenic 2-amino acids. We report here in detail the results of our preliminary studies[4] into the aza-Darzens (ADZ) reaction[5] of *N*-Dpp imines with chiral, camphorsultam-derived α-bromoenolates, which show that the routine preparation of chiral *N*-Dpp-2-carboxyaziridines with high levels of diastereomeric and enantiomeric purity is indeed feasible.

Keywords: Aza-Darzens; Aziridination; Imine; Camphorsultam.
* Corresponding author. Tel.: +44 118 931 6585; fax: +44 118 378 6331; e-mail: j.b.sweeney@rdg.ac.uk

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.01.068

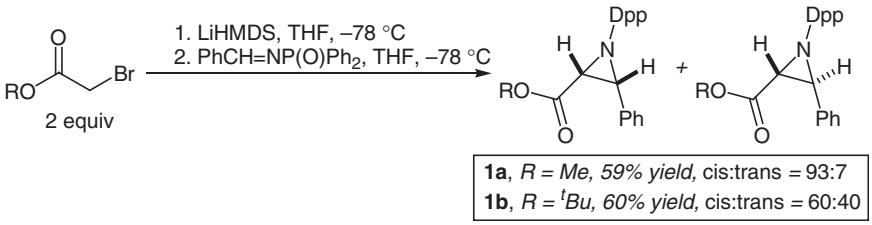
3. Results and discussion

3.1. Feasibility study: reaction of achiral ester enolates with *N*-Dpp imines

ADZ reactions of *N*-Dpp imines had not been reported before we embarked upon our work, which meant that our first task was to assess the feasibility of the proposed reaction using achiral reagents. Thus, when *N*-diphenylphosphinybenzaldimine[6] was added to the lithium enolate of methyl bromoacetate at −78 °C, a diastereoselective reaction was observed, affording methyl *N*-diphenylphosphinyl-2-phenyl aziridine carboxylate **1a** in 60% yield; the product was obtained as 90:10 mixture of cis- and trans-diastereoisomers (J_{cis}=6.5 Hz, J_{trans}=2.8 Hz, Scheme 1). The isomers were separable by flash chromatography; the predominance of the cis-isomer is consistent with results obtained in many other aziridine syntheses.[1]

When a bulkier ester was used in the same procedure, the diastereoselectivity of the reaction was similar (the cis-isomer, *cis*-**1b**, again dominated the product mixture), but lower (cis:trans=60:40, Scheme 1). In this case, a precise measurement of the diastereoselectivity was hampered by the fact that these diastereoisomers could not easily be separated, either by flash chromatography, or by crystallisation.

When NaHMDS was used as base in the preparation of the ^{t}butyl aziridine carboxylate, only *cis*-**1b** was produced, but



Scheme 1.

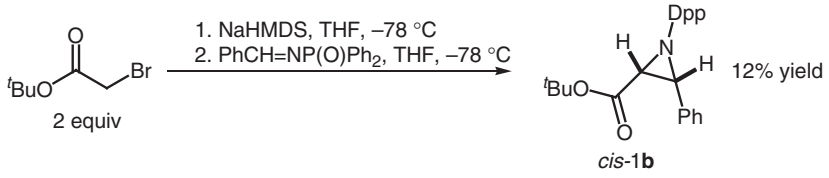
the efficiency of the transformation was greatly reduced (Scheme 2). Under these conditions, the major product of the reaction was the starting imine, even when prolonged reaction time and/or increased temperatures were employed.

Armed with a set of conditions for our new ADZ reaction, we turned to an asymmetric version of these reactions.

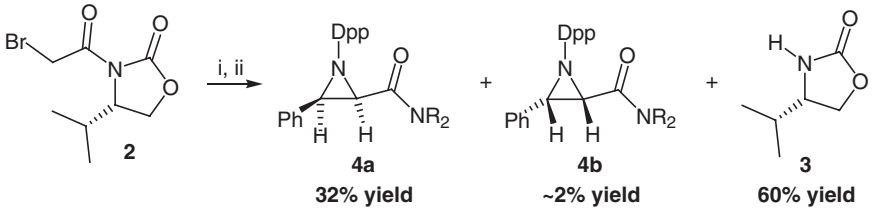
3.2. Aziridination via reaction of 4*S*-*N*-bromoacetyl-4-isopropyloxazolidinone enolates with *N*-Dpp-imines

As a first goal, we sought a reagent-controlled process and chose to examine the use of an Evans' auxiliary. Thus, (4*S*)-*N*-bromoacetyl-4-isopropyloxazolidinone (**2**)[7] was deprotonated at −78 °C in THF by LiHMDS and to the resultant lithium enolate was added a solution of *N*-Dpp benzaldimine. Under these (and a range of other) reaction conditions, no product of Darzens-like reaction were observed: instead, the only product isolated from these reactions was the parent oxazolidinone **3**, its presence presumably resulting from elimination to generate ketene, a reaction pathway known for processes conducted above 0 °C.[8] The use of NaHMDS, thereby furnishing the corresponding sodium enolate, was more encouraging: when the reaction was started at −78 °C and allowed to warm to ambient temperatures, an unequal mixture of two diastereomeric *cis*-aziridines (**4a** and **4b**) was obtained, in mediocre yield (Scheme 3). Again the major reaction pathway furnished oxazolidinone **3**, in 60% yield. These aziridines are non-crystalline, and the analysis of their stereochemistry was carried out using NMR spectroscopy and computer modelling, which led us tentatively to assign the absolute configurations of the new asymmetric centres in the major product **4a** as (2′*R*,3′*R*) (Scheme 3).

In an effort to improve the yield of aziridination at the expense of the elimination pathway, we experimented with many variations of the precise conditions of these reactions, but found little success in these endeavours; noteworthy observations include the obtention of a mixture of **4a** and *trans*-aziridines **4c** and **4d** when using diethyl ether as solvent for the reaction (Scheme 4).

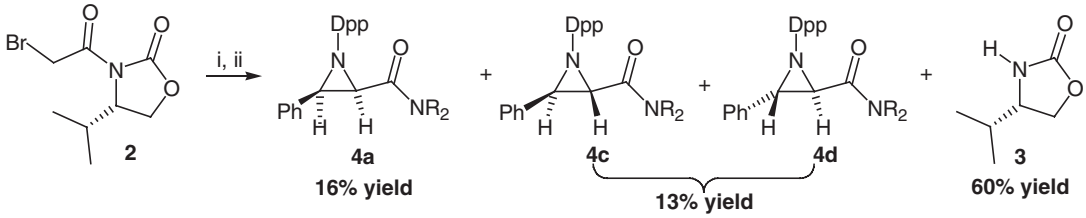


Scheme 2.



Conditions: i. NaHMDS, THF, –78 °C; ii. PhCH=NP(O)Ph2.

Scheme 3.



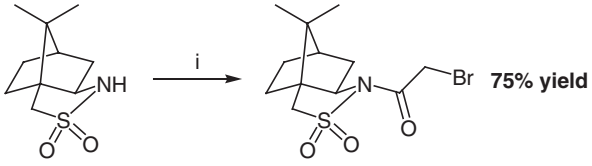
Conditions: i. NaHMDS, Et2O, –78 °C; ii PhCH=NP(O)Ph2.

Scheme 4.

In this case, the *trans*-aziridines were obtained as an inseparable mixture of (2′*R*,3′*R*) and (2′*S*,3′*S*) isomers. Thus, it seemed that the use of chiral oxazolidinones in ADZ reactions was problematic: we turned our attention to another chiral controller.

3.3. Aziridination via reaction of 2*R*-*N*-bromoacetylcamphorsultam enolates with *N*-Dpp-imines

2*R*-*N*-Bromoacetylcamphorsultam (**5**) was prepared in 71% yield in routine fashion (Scheme 5); to our surprise, this compound had not been reported in the literature previously.[9]



Conditions: i. ^{n}BuLi, $BrCH_2C(O)Br$, THF, –78 °C.

Scheme 5.

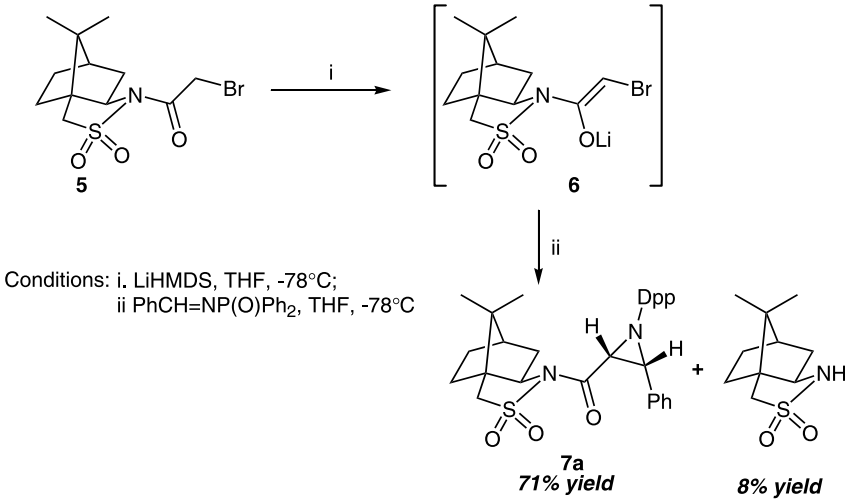
Deprotonation of **5** in THF at −78 °C using LiHMDS gave α-bromo lithioenolate **6**, to which was immediately added a THF solution of *N*-diphenylphosphinylbenzaldimine (Scheme 6). The reaction was allowed to proceed for 3 h at −78 °C, after which aqueous work-up gave aziridinyl sultam **7a**. Spectroscopic examination (^{1}H and ^{13}C NMR) of this crude product indicated that only one, cis-configured (J=6.2 Hz), diastereoisomer had been formed: no evidence of the alternate diastereoisomer could be found. Chromatographic purification subsequently furnished pure (2′*R*,3′*R*)-**7a** in 71% yield, accompanied by a small amount of deacetylated sultam (8%); no trace of any trans-configured aziridine, nor could any of the alternative cis-diastereoisomer be isolated from the reaction.

Single crystal X-ray analysis of **7a** confirmed the stereochemical analysis, and revealed the absolute configurations of the newly-created asymmetric centres to be (2′*R*,3′*R*). This observation implies that the reaction proceed via a *syn*-selective aza-aldol reaction, involving nucleophilic attack of the *si*-face of the enolate upon the *si*-face of the imine, followed by ring-closure. The obtention of aziridine rather than the intermediate aminobromide is noteworthy, because previously-reported asymmetric Darzens and aza-Darzens reactions using boron-containing asymmetric reagents or catalysts did not proceed directly to the heterocyclic product (epoxide, or aziridine, respectively), relying instead on a subsequent, separate, ring-closing step (Scheme 6).

Encouraged by this result, we immediately turned our attention to an examination of the scope of the reaction. The results of the first part of our study are collated in Table 1.

Thus, a range of aromatic imines was found to undergo ADZ reaction in acceptable yield and with virtually complete diastereo- and enantiocontrol. In all these examples (and despite significant variation in reaction conditions), a small amount of deacetylated sultam (<10%) was always isolated in addition to the desired aziridines; presumably this by-product arises by elimination from the initially formed bromoenolate, or by a self-condensation. As expected, the use of the enantiomeric auxiliary (Table 1, entries 10–16) yielded aziridine products of opposite stereochemistry, with similar selectivity. In most of the reactions the yield of aziridine was good, the only exception being the reaction of the *N*-Dpp imine derived from pivaldehyde (vide infra), and spectroscopic analysis of crude products again did not indicate the presence of other diastereoisomers. In the reaction of *N*-Dpp pivaldehyde imine (Table 1, entry 9) the mediocre yield (40%) of aziridine **7i** was due, in part, to the fact that the precursor 1,2-aminobromide **8** (13%) was also isolated (Scheme 7). It would seem that the additional barrier to rotation caused by the presence of a substituent of considerable steric demand retards the necessary bond rotation, which must occur prior to the second step, cyclization to give the aziridine product.

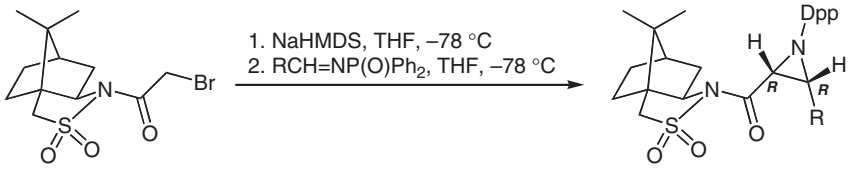
As mentioned above, the identification of *cis*-aziridines as the only products of the reaction was based on analysis of ^{1}H



Conditions: i. LiHMDS, THF, -78°C;
ii PhCH=NP(O)Ph_2, THF, -78°C

Scheme 6.

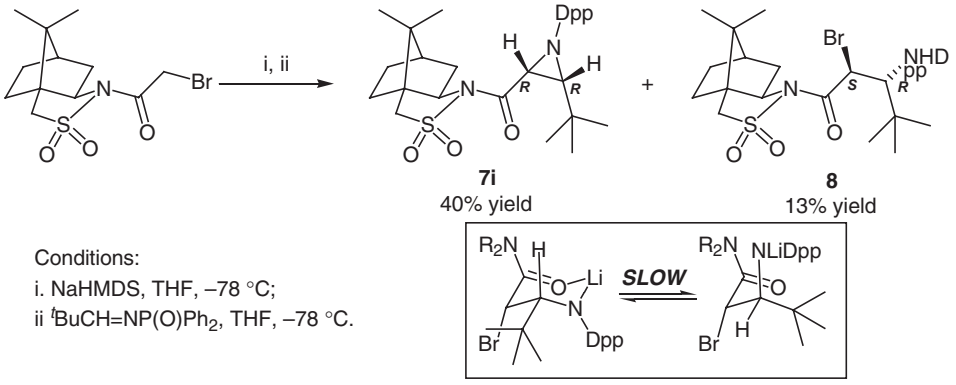
Table 1. Asymmetric aza-Darzens reaction of *N*-bromoacetyl camphorsultams



5 **7a–p**

Entry	R	Yield **7** (%)	cis:trans	dr
1	Ph	**7a** 71	100:0	>95:<5[a]
2	4-O_2N–C_6H_4	**7b** 75	100:0	>95:<5[a]
3	4-MeO–C_6H_4	**7c** 78	100:0	>95:<5[a]
4	2-O_2N–C_6H_4	**7d** 70	100:0	>95:<5[a]
5	4-Br–C_6H_4	**7e** 60	100:0	>95:<5[a]
6	2-Naphthyl	**7f** 72	100:0	>95:<5[a]
7	2-Fluorenyl	**7g** 67	100:0	>95:<5[a]
8	2-Furyl	**7h** 68	100:0	>95:<5[a]
9	^{t}Bu	**7i** 40[b]	100:0	>95:<5[a]
10	Ph[c]	**7j** 71	100:0	>95:< 5[d]
11	4-F–C_6H_4[c]	**7k** 57	100:0	>95:< 5[d]
12	2,6-Cl_2–C_6H_4[c]	**7l** 60	100:0	>95:< 5[d]
13	3-Br–C_6H_4[c]	**7m** 60	100:0	>95:< 5[d]
14	4-MeO–C_6H_4[c]	**7n** 60	100:0	>95:< 5[d]
15	2-Pyridyl[c]	**7o** 67	100:0	>95:< 5[d]
16	CH_2=CH[c]	**7p** 47	100:0	>95:< 5[d]

[a] (2′*R*,3′*R*):(2′*S*,3′*S*).
[b] (2′*S*,3′*R*)-*syn*-(2-Bromo-3-(diphenylphosphinyl)amino)sultam (**8**) also isolated in 13% yield.
[c] (2*S*)-Sultam used as auxiliary.
[d] (2′*S*,3′*S*):(2′*R*,3′*R*).



Scheme 7.

coupling constants (aziridines exhibit $^3J_{cis}$=4.5–7 Hz while $^3J_{trans}$=1.5–3 Hz). In certain cases, however, the relatively restricted rotation induced by the bulky *N*-substituent led to broad and overlapping resonances, which initially precluded assignment of cis- or trans-stereochemistry. Thus, the identification of the product of the reaction of *para*-nitrophenylbenzaldimine **7b** with the camphorsultam enolate (Table 1, entry 5) was complicated by the fact that the ^{1}H resonances of the aziridine protons were not resolved in deuteriochloroform. The signals were, however, resolved in deuteriobenzene, allowing identification of the ^3J coupling constant as 6.4 Hz, again indicative of a cis-configured product (Fig. 1).

A similar situation was encountered in the analysis of the *para*-bromo analogue **7e** (Table 1, entry 2) (Fig. 2): the C_6D_6 spectrum revealed a ^3J value similar in magnitude to the *para*-nitro compound.

3.4. Hydrolytic cleavage of auxiliary from (aziridinyl)acyl sultams

As the utility of the Dpp group as an aziridine activator had already been demonstrated within our group, we next sought to cleave the chiral auxiliary (to give the corresponding *N*-diphenylphosphinyl aziridine carboxylic acids) thereby allowing preparation of simple esters, for use in subsequent synthetic endeavours. Since the acylsultam linkage is labile under basic conditions, whereas the Dpp group is normally removed under acidic conditions, we were confident that this selective hydrolysis would be routine. Reaction of aziridinyl sultams with 1 equiv of lithium hydroxide monohydrate, proceeded smoothly, yielding the corresponding *N*-Dpp aziridine carboxylates **9** in generally good yield (Table 2, Scheme 8). These heterocycles are ideal precursors to a range of aziridine esters or other derivatives, valuable compounds both for synthesis and biological studies.

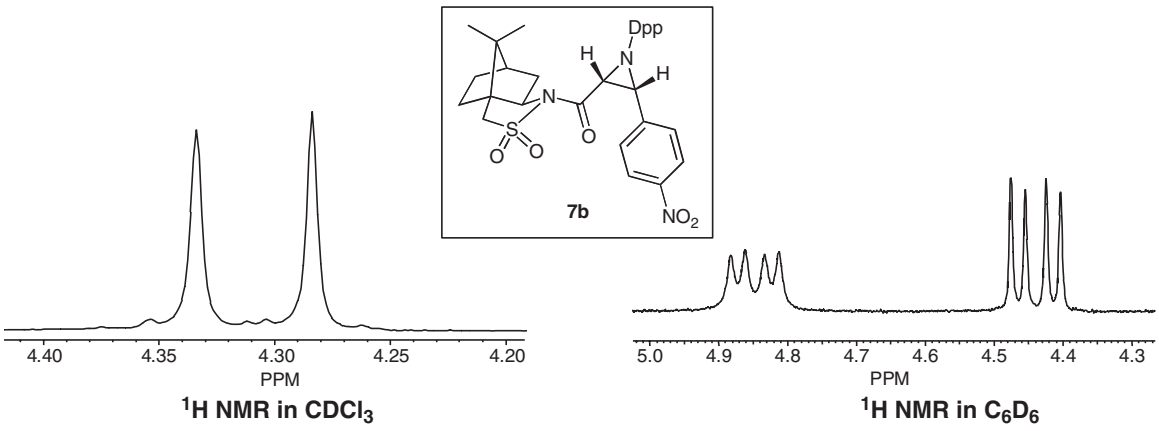


Figure 1.

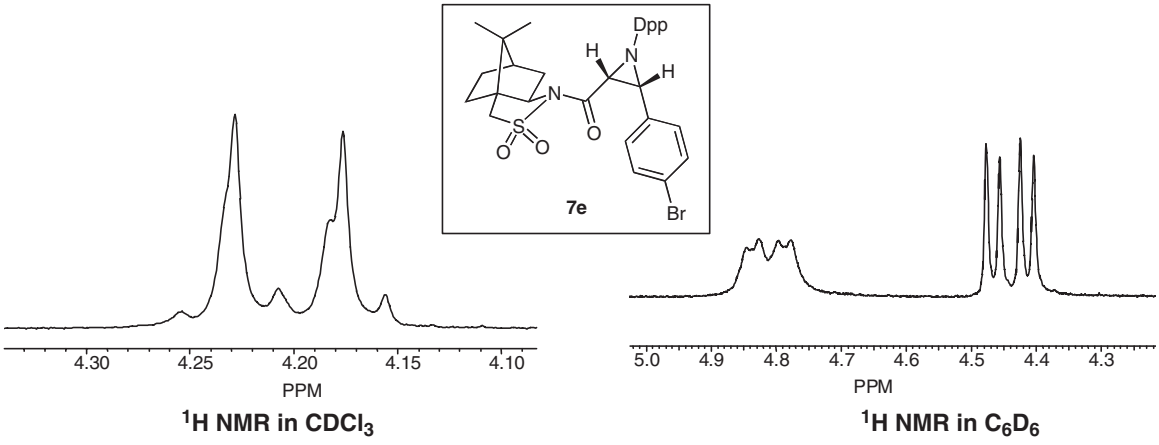
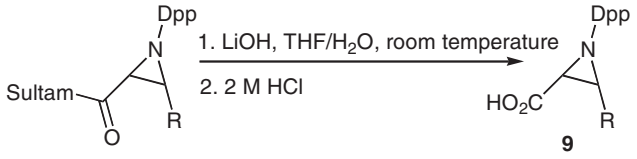


Figure 2.

Table 2. Removal of auxiliary from (aziridinyl)acylcamphorsultams

Entry	R	Sultam configuration	Aziridine configuration	Yield **9** (%)
1	Ph	*R*	(2′*R*,3′*R*)	**9a** 64
2	4-O_2N–C_6H_4	*R*	(2′*R*,3′*R*)	**9b** 60
3	2-O_2N–C_6H_4	*R*	(2′*R*,3′*R*)	**9c** 67
4	4-Br–C_6H_4	*R*	(2′*R*,3′*R*)	**9d** 61
5	2-Naphthyl	*R*	(2′*R*,3′*R*)	**9e** 67
6	^{t}Bu	*R*	(2′*R*,3′*R*)	**9f** 47
7	3-Br–C_6H_4	*S*	(2′*S*,3′*S*)	**9g** 80
8	2,6-Cl_2–C_6H_3	*S*	(2′*S*,3′*S*)	**9h** 45
9	2-Pyridyl	*S*	(2′*S*,3′*S*)	**9i** 100



Scheme 8.

4. Conclusion

We have demonstrated the use of the previously unreported *N*-bromoacylcamphorsultams as efficient precursors to a range of *cis*-*N*-Dpp-aziridine-2-carboxylates by a two-step process; the subsequent paper in this series will describe our observations of factors controlling the diastereoselectivity of the aziridine-forming reactions, and comments concerning the mechanism of the reaction.

5. Experimental

5.1. General techniques

All organic solvents were distilled prior to use and all reagents were purified by standard procedures.[10] 'Petrol' refers to the fraction of petroleum ether with the boiling range 40 to 60 °C and 'ether' refers to diethyl ether. Ether and THF were distilled from sodium benzophenone ketyl; toluene from sodium; dichloromethane, triethylamine, acetonitrile from calcium hydride, methanol from magnesium methoxide and diisopropylethylamine from potassium hydroxide. Chemicals were purchased from Aldrich Chemical Co. or prepared by literature methods.

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. Spectra were recorded on Perkin Elmer 881 or Paragon 1000 spectrophotometers. Optical rotations were measured using a Perkin Elmer 241 MC polarimeter and are quoted in 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on VG9090 or Fisons Autospec mass

spectrometers. ^{1}H and ^{13}C NMR spectra were recorded on Jeol GX-270, Jeol GX-400, Lambda 300, Bruker DPX-250 or Bruker AX-400 spectrometers. Unless otherwise stated, deuterochloroform was used as solvent and tetramethylsilane was the internal standard. Chemical shifts in ^{1}H NMR spectra are expressed as ppm downfield from tetramethylsilane, and in ^{13}C NMR, relative to the internal solvent standard. Coupling constants (J) are quoted in Hertz.

Reactions involving chemicals or intermediates sensitive to air or moisture were conducted under a nitrogen or argon atmosphere in oven- or flame-dried apparatus. Flash chromatography was performed using Merck Kieselgel 60 or Fluka Kieselgel 60 silica gel. Analytical thin-layer chromatography was performed using either precoated Merck Kieselgel 60 F_{254} glass-backed plates, or precoated Merck Kieselgel 60 F_{254} aluminium backed plates and were visualised under UV at 254 nm and by staining with iodine and/or an acidic ammonium molybdate dip.

^{13}C NMR spectra of *N*-Dpp compounds are complicated by rotameric isomers, which often leads to the appearance of 'excess' resonances in the aromatic region of the spectra; the situation is further complicated by the difficulty in obtaining precise coupling constants. Rather than refer to the entire region of the spectra as being a 'multiplet', the data quoted describes the actual appearance of the spectra.

5.1.1. (±)-Methyl *cis* *N*-diphenylphosphinyl-3-phenylaziridine-2-carboxylate (*cis*-1a). To a solution of methyl 2-bromoacetate (0.18 mL, 1.83 mmol) in THF (10 mL) at −78 °C, was added LiHMDS in THF (1.83 mL, 1.0 M, 1.83 mmol), dropwise. After 30 min, a THF (10 mL) solution of *N*-(phenylmethylene)diphenylphosphinamide (280 mg, 0.92 mmol), cooled to −78 °C, was slowly added. The reaction was then stirred for 2.5 h, before being quenched with water, and diluted with EtOAc at −78 °C. The solution was partitioned between H_2O (10 mL), and EtOAc (2×10 mL), the organic layers separated, washed with brine (15 mL), dried ($MgSO_4$), filtered, and the solvent removed in vacuo to leave a yellow oil. Purification by flash chromatography (EtOAc/petrol 1:1) gave *cis*-**1a** as an oil (190 mg, 55%). R_f 0.7 (EtOAc); IR ν_{max} ($CHCl_3$) 2982, 1751, 1437, 1175, 1126, 729 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 3.48 (3H, s), 3.71 (1H, dd, J_P=14.9 Hz, J=6.5 Hz), 4.16 (1H, dd, J_P=15.8 Hz, J=6.5 Hz), 7.30–7.55 (11H, m), and 7.92–8.18 (4H, m); δ_C (67.5 MHz, $CDCl_3$) 40.7, 41.7, 52.2, 127.5, 128.4, 130.5, 132.4, 137.0, 166.6; *m/z* (CI) 378 (MH^+, 100%), 346 (40), 320 (18), 201 (19), 79 (18); HRMS found: $[MH]^+$378.1260, $C_{22}H_{21}NO_3$ requires 378.1259.

5.1.2. (±)-Methyl *trans* *N*-diphenylphosphinyl-3-phenylaziridine-2-carboxylate (*trans*-1a). *Trans*-**1a** was also isolated from the reaction, as a viscous oil (15 mg, 4%). R_f 0.4 (EtOAc); IR ν_{max} (film) 2924, 1747, 1439, 1211, 1124, 728, 696 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 3.57 (1H, dd, J_P=13.6 Hz, J=2.8 Hz), 3.60 (3H, s), 4.03 (1H, dd, J_P=14.2 Hz, J=2.9 Hz), 7.30–7.46 (11H, m), and 7.65–8.06 (4H, m); *m/z* (CI) 378 (MH^+, 100%), 346 (26), 320 (17), 201 (17), 201 (17), 176 (13); HRMS found: $[MH]^+$378.1274, $C_{22}H_{21}NOP$ requires 378.1259.

5.1.3. (±)-^{t}Butyl *cis*- and *trans*-*N*-diphenylphosphinyl-3-phenylaziridine-2-carboxylate (1b). To a solution of *tert*-butyl 2-bromoacetate (0.08 mL, 0.52 mmol) in THF (10 mL) at −78 °C, was added LiHMDS in THF (0.52 mL, 1.0 M, 0.52 mmol), dropwise. After 30 min, a THF (10 mL) solution of *N*-(phenylmethylene)diphenylphosphinamide (80 mg, 0.26 mmol), was slowly added at −78 °C. The reaction was then stirred for 2.5 h, before being quenched with water, and diluted with EtOAc at −78 °C. The solution was then partitioned between H_2O (10 mL), and EtOAc (2×10 mL), the combined organic layers were then washed with brine (15 mL), dried ($MgSO_4$), filtered, and the solvent removed in vacuo to leave a yellow oil. This was purified by flash chromatography (EtOAc/petrol 1:1) to give a mixture of *cis*-**1b** and *trans*-**1b** (cis:trans=60:40) as a colourless oil (65 mg, 60%). R_f 0.6 (EtOAc); IR ν_{max} ($CHCl_3$) 2985, 1737, 1438, 1369, 1180, 1127, 729, 697 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 1.15 and 1.35 (9H, 2×s), 3.56 (0.4H, dd, J_P=13.3 Hz, $J_{(trans)}$=2.8 Hz), 3.58 (0.6H, dd, J_P=15.2 Hz, $J_{(cis)}$=6.6 Hz), 4.08 (0.4H, dd, J_P=11.5 Hz, $J_{(trans)}$=2.8 Hz), 4.10 (0.6H, dd, J_P=15.4 Hz, $J_{(cis)}$=6.6 Hz), 7.22–8.21 (15H, m), δ_C (67.5 MHz, $CDCl_3$) 27.7, 27.8, 41.2, 41.4, 43.4, 43.5, 44.7, 44.8, 127.6, 127.9, 128.4, 132.4, 135.1, 165.2, 166.8; *m/z* (CI) 420 (MH^+, 5%), 364 (M−^{t}Bu, 27), 320 (M−CO_2^tBu, 100), 201 (17), 120 (48), 79 (72); HRMS found: $[MH]^+$420.1722, $C_{25}H_{27}NO_3P$ requires 420.1729.

5.1.4. (±)-^{t}Butyl *cis*-*N*-diphenylphosphinyl-3-phenylaziridine-2-carboxylate (*cis*-1b). By following the procedure above, *tert*-butyl 2-bromoacetate (0.2 mL, 1.3 mmol), NaHMDS in THF (1.3 mL, 1.0 M, 1.3 mmol), *N*-(phenylmethylene)diphenylphosphinamide (200 mg, 0.66 mmol), were reacted together in THF (15 mL) at −78 °C for 3 h, to give a yellow oil. Purification by flash chromatography (EtOAc/petrol 1:1) gave *cis*-**1b** as a colourless oil (33 mg, 12%). R_f 0.6 (EtOAc); IR ν_{max} ($CHCl_3$) 2976, 1743, 1439, 1368, 1180, 1127, 729, 697 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 1.15 (9H, s), 3.58 (1H, dd, J_P=15.4 Hz, J=6.6 Hz), 4.10 (1H, dd, J_P=15.6 Hz, J=6.6 Hz), 7.23–7.56 (11H, m), 7.91–8.21 (4H, m); δ_C (67.5 MHz, $CDCl_3$) 27.8, 41.4, 43.5, 44.8, 127.6, 127.9, 128.4, 132.4, 135.1, 166.8; *m/z* (CI) 420 (MH^+, 18%), 364 (M−^{t}Bu+H^+, 51), 320 (M−CO_2^tBu+H^+, 100), 218 (15), 120 (14); HRMS found: $[MH]^+$420.1720, $C_{25}H_{27}NO_3P$ requires 420.1729.

5.1.5. (4*S*,2′*R*,3′*R*)-(+)-3-[(1′-Diphenylphosphinyl-3′-phenyl-2′-aziridinyl)carbonyl]-4-(1-methylethyl)oxazolidin-2-one (4a).[11] (4*S*)-(+)-3-Bromoacetyl-4-(1-methylethyl)-2-oxazolidinone (150 mg, 0.6 mmol), was dissolved in THF (15 mL), and cooled to −78 °C. NaHMDS in THF (0.66 mL, 1.0 M, 0.66 mmol) was then added dropwise, and the resulting pale yellow solution stirred for 30 min. *N*-(Diphenylmethylene)diphenylphosphinamide (900 mg, 0.3 mmol), was then added at −78 °C as a solution in THF (5 mL). The reaction mixture was then stirred for 3 h and allowed to reach ambient temperature, at which point the reaction was quenched with saturated ammonium chloride solution (20 mL) and EtOAc (20 mL, 2×10 mL), the organic layers were then combined, washed with brine, dried ($MgSO_4$), filtered, and the solvent removed in vacuo, to afford a yellow oil. Purification by flash chromatography (gradient 20–80% EtOAc in petrol),

provided a clear oil, which was crystallised from EtOAc/Hexane to afford **4a** as colourless needles (40 mg, 32%). R_f 0.5 (EtOAc); mp 183–184 °C; $[\alpha]_D^{20}$ +110.9 (*c* 1.5, CH_2Cl_2); IR ν_{max} (film) 2964, 1785, 1708, 1439, 1209, 1126, 729, 698 cm^{-1}; δ_H (400 MHz, CD_2Cl_2) 0.00 (3H, d, J=7.0 Hz), 0.61 (3H, d, J=7.0 Hz), 1.71–1.74 (1H, m), 3.94–3.98 and 4.05–4.12 (3H, 2×m), 4.33 and 4.38 (2H, 2×dd, J_P=15.2 Hz, J=6.6 Hz), 7.12–8.19 (15H, m); δ_C (67.5 MHz, $CDCl_3$) 13.1, 17.6, 27.9, 42.1, 42.5, 58.1, 63.7, 127.3, 128.5, 131.4, 132.2, 135.2, 153.2, 164.7; *m/z* (CI) 475 ($[MH]^+$, 100%), 346 (56), 320 (43), 275 (28), 201 (23), 130 (63); HRMS found: $[MH]^+$475.1775, $C_{27}H_{28}N_2O_4P$ requires 475.1787; Found: C, 68.3; H, 5.8; N, 6.1; $C_{27}H_{27}N_2O_4P$ requires C, 68.4; H, 5.8; N, 5.9%.

5.1.6. (4*S*,2′*S*,3′*S*)-(+)-3-[(1′-Diphenylphosphinyl-3′-phenyl-2′-aziridinyl)carbonyl]-4-(1-methylethyl)oxazolidin-2-one (4b). From the reaction described above a small quantity of a different cis diastereoisomer, **4b**, was also isolated (2–3 mg, ~2%), as a colourless oil. This product could not be satisfactorily separated from (4*S*)-4-(1-methylethyl) oxazolidinone generated by enolate decomposition and only partial physical data were collected: R_f 0.6 (EtOAc); δ_H (400 MHz, $CDCl_3$) 0.74 and 0.78 (6H, 2×d, J=7.1 Hz), 2.13–2.20 (1H, m), 3.86–3.91 and 4.09–4.12 (3H, 2×m), 4.27 and 4.45 (2H, 2×dd, J_P=15.4 Hz, J=6.6 Hz), 7.28–8.26 (15H, m); *m/z* (CI) 475 ($[MH]^+$, 65%), 390 (10), 346 (40), 320 (41), 275 (25), 201 (23), 130 (100); HRMS found: $[MH]^+$475.1796, $C_{27}H_{28}N_2O_4P$ requires 475.1787.

5.1.7. *trans*-(4*S*)-3-[(1′-Diphenylphosphinyl-3′-phenyl-2′-aziridinyl)carbonyl]-4-(1-methylethyl)oxazolidin-2-one (4c and 4d). Following the procedure above, (4*S*)-(+)-3-bromoacetyl-4-(1-methylethyl)-2-oxazolidinone (200 mg, 0.8 mmol), NaHMDS in THF (0.9 mL, 1.0 M, 0.88 mmol), and *N*-(phenylmethylene)diphenylphosphinamide (120 mg, 0.4 mmol) were reacted together in ether (25 mL). Purification by flash chromatography (gradient 20–100% EtOAc in petrol), provided **4a** a yellow oil (20 mg, 16%), and a mixture of *trans*-aziridine diastereoisomers, **4c** and **4d** as a clear oil (25 mg, 13%). R_f 0.2 (EtOAc); $[\alpha]_D^{20}$ +59.8 (*c* 0.5, CH_2Cl_2); IR ν_{max} (film) 2965, 1782, 1704, 1438, 1204, 1124, 727, 696 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.64 and 0.79 (6H, 2×d, J=7.2 Hz), 2.14–2.26 (1H, m), 4.11–4.29 (3H, m), 4.39–4.44 (1H, m), 4.81 (1H, dd, J_P=12.6 Hz, J=2.8 Hz), 7.01–7.46 (11H, m), 7.72–7.95 (4H, m); δ_C (100 MHz, $CDCl_3$) 14.6, 17.9, 28.1, 43.2, 45.3, 58.6, 63.9, 127.6, 132.2, 135.9, 153.8, 166.4; *m/z* (CI) 475 ($[MH]^+$, 100%), 346 (39), 320 (13), 275 (10), 201 (10), 130 (26); HRMS found: $[MH]^+$475.1776, $C_{27}H_{28}N_2O_4P$ requires 475.1787.

5.1.8. (2*R*)-(−)-(*N*-Bromoacetyl)bornane-10,2-sultam (*R*-5). (2*R*)-Bornane-10,2-sultam (200 mg, 9.3 mmol), was dissolved in THF (25 mL), under a nitrogen atmosphere and cooled to −78 °C. *n*-BuLi in hexanes (2.5 M, 0.41 mL, 1.0 mmol), was then added dropwise and the solution stirred for 20 min. Bromoacetyl bromide (0.1 mL, 1.0 mmol), was then dissolved in THF (10 mL), and this was then added dropwise to the anion. The reaction was stirred at −78 °C and was determined to be complete by TLC after 2 h. Water (10 mL) was added to quench the reaction, and EtOAc (20 mL) added. The organic layer was partitioned and the aqueous layer washed with EtOAc (2×10 mL). The combined organic layers were then dried ($MgSO_4$), filtered, and the solvent removed in vacuo. The resulting pale yellow oil was then purified by flash chromatography, (gradient 0–10% EtOAc in hexane), affording (*R*)-**5** as a clear oil, which was crystallised from $CHCl_3$/hexane to provide colourless needles (220 mg, 71%). R_f 0.4 (EtOAc/heptane 3:7); mp 113–114 °C; $[\alpha]_D^{20}$ −118.5 (*c* 1, CH_2Cl_2); IR ν_{max} ($CHCl_3$) 2959, 1705, 1330, 1170 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.98 and 1.16 (6H, 2×s), 1.37–1.43, and 1.90–2.16 (7H, 2×m), 3.44–3.55 (2H, 2×d, J=14.0 Hz), 3.91 (1H, dd, J=7.6, 5.1 Hz), 4.20 and 4.34 (2H, 2×d, J=13.0 Hz); δ_C (100 MHz, $CDCl_3$), 19.9, 20.7, 26.4, 27.5, 32.8, 37.9, 44.5, 47.9, 49.1, 52.7, 65.5, 164.5; *m/z* (CI) 336 ($[MH]^+$, 86%), 258 (16), 192 (42), 135 (100); HRMS found: $[MH]^+$336.0259, $C_{12}H_{19}BrNO_3S$ requires 336.0269; Found: C, 43.0; H, 5.5; N, 4.1; $C_{12}H_{18}BrNO_3S$ requires C, 42.9; H, 5.4; N, 4.2%.

5.1.9. (2*S*)-(+)-(*N*-Bromoacetyl)bornane-10,2-sultam (*S*-5). Bornane-10,2-sultam (1.00 g, 4.7 mmol) was dissolved in anhydrous THF (30 mL) under a nitrogen atmosphere and cooled to −78 °C. *n*-BuLi in hexanes (2.1 mL, 2.5 M, 5.1 mmol) was added dropwise to the solution and left to stir for approximately 1 h. After this time bromoacetyl bromide (0.4 mL, 4.7 mmol) dissolved in anhydrous THF (20 mL) was added dropwise to the reaction mixture. The reaction mixture was allowed to stir for 3 h at −78 °C and the course of the reaction was followed by TLC. Once all starting materials had been consumed, water (20 mL) was added to quench the reaction followed by the addition of ether (20 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed in vacuo. Flash chromatography of the resultant colourless solid (petrol/ether, 6:4), affording the desired product as a colourless needles (1.23 g, 77%). R_f 0.34 (petrol/ether, 1:1); mp 113 °C; $[\alpha]_D^{20}$ +118.5 (*c* 1, $CHCl_3$); IR ν_{max} (CCl_4) 2959, 1705, 1330, 1170 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, s), 1.09 (3H, s), 1.25–1.40 and 1.72–2.11 (7H, 2×m), 3.38–3.48 (2H, 2×d, J=13.7 Hz), 3.90 (1H, dd, J=7.5, 5.0 Hz), 4.14 and 4.27 (2H, 2×d, J=13.2 Hz); δ_C (100 MHz, $CDCl_3$) 19.8, 20.7, 26.4, 28.0, 32.7, 37.9, 44.5, 47.8, 49.0, 52.7, 65.4, 164.5; *m/z* (CI) 36 ($[MH]^+$, 86%), 258 (16), 192 (42), 135 (100); HRMS found: $[MH]^+$336.0259, $C_{12}H_{19}BrNO_3S$ requires 336.0269.

5.2. General procedure for asymmetric aza-Darzens reaction using *R*-5

(2*R*)-(−)-(*N*-Bromoacetyl)bornane-10,2-sultam (*R*-**5**), (1.1 equiv), was dissolved in THF (25 mL) and cooled to −78 °C. LiHMDS in THF (1.2 equiv) was then added dropwise, and the resulting pale yellow solution stirred for 30 min. Phosphinylimine, (typically 0.7 mmol) was then added at −78 °C as a solution in THF (10 mL). The reaction mixture was then stirred for over 2 h at −78 °C, after which time the reaction was judged to have reached completion by TLC and the mixture was quenched with saturated ammonium chloride solution (20 mL). The aqueous layer was extracted with EtOAc (20 mL, 2×10 mL), the organic layers were then combined, washed with brine, dried ($MgSO_4$), filtered, and the solvent removed in vacuo, to afford the crude aziridine.

5.2.1. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-phenyl-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7a). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (490 mg, 1.4 mmol), LiHMDS in THF (1.6 mL, 1.0 M, 1.6 mmol), and *N*-(phenylmethylene)diphenylphosphinamide (400 mg, 1.3 mmol), were reacted together in THF (35 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in petrol containing 0.05% v/v acetic acid) provided a colourless oil. Crystallisation from $CHCl_3$/hexane afforded **7a** as a colourless solid (520 mg, 71%). R_f 0.5 (EtOAc); mp 197–198 °C; $[\alpha]_D^{20}$ −11.3 (*c* 1, CH_2Cl_2); IR ν_{max} ($CHCl_3$) 2961, 1705, 1439, 1336, 1270, 1213, 1137, 837, 654 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, s), 0.95 (3H, s), 1.20–1.32 and 1.79–1.96 (7H, 2×m), 3.27 and 3.38 (2H, 2×d, *J*=13.6 Hz), 3.57–3.61 (1H, m), 4.18 and 4.27 (2H, 2×dd, J_P=14.4 Hz, *J*=6.1 Hz), 7.19–7.55 (11H, m), and 7.93–8.15 (4H, m), δ_C (75 MHz, $CDCl_3$) 19.8, 19.9, 26.3, 32.5, 38.1, 41.6, 44.0, 44.6, 47.7, 49.0, 52.6, 64.7, 127.7, 128.4, 128.7, 130.9, 131.9, 132.7, 163.7; *m*/*z* (CI) 561 ($[MH]^+$, 72%), 483 (11), 361 (42), 346 (44), 320 (70), 216 (100), 135 (67); HRMS found: $[MH]^+$561.1987, $C_{31}H_{34}N_2O_4PS$ requires 561.1977; Found: C, 66.6; H, 6.0; N, 5.0; $C_{31}H_{33}N_2O_4PS$ requires C, 66.4; H, 5.9; N, 5.0%.

5.2.2. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-(4-nitrophenyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7b). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (250 mg, 0.74 mmol), LiHMDS in THF (0.8 mL, 1.0 M, 0.8 mmol), and *N*-(4-nitrophenylmethylene)diphenylphosphinamide (240 mg, 0.7 mmol), were reacted together in THF (35 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in petrol, containing 0.05% v/v acetic acid) provided a colourless oil. Crystallisation from $CHCl_3$/hexane afforded **7b** as a colourless solid (320 mg, 77%). R_f 0.55 (EtOAc); $[\alpha]_D^{20}$ −28.6 (*c* 1, CH_2Cl_2); mp 213 °C (EtOAc/hexane); IR ν_{max} (film) 2960, 1703, 1439, 1347, 1215, 1127, 730, 695 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, s), 0.98 (3H, s), 1.21–1.31 and 1.81–2.05 (7H, 2×m), 3.28 and 3.42 (2H, 2×d, *J*=13.7 Hz), 3.54–3.57 (1H, m), 4.29–4.33 (2H, m), 7.38–7.64 (10H, m) and 7.90–8.15 (4H, m); δ_H (300 MHz, C_6H_6) 0.26 (3H, s), 0.65 (3H, s), 0.53–0.89, 1.07–1.16 and 1.65–1.85 (7H, m), 2.42 and 2.46 (2H, 2×d, *J*=13.9 Hz), 3.14–3.18 (1H, m), 4.44 (1H, dd, J_P=15.4 Hz, *J*=6.4 Hz), 4.85 (1H, dd, J_P=14.8 Hz, *J*=6.4 Hz) 6.93–7.86 and 8.09–8.43 (14H, m); δ_C (75 MHz, $CDCl_3$) 19.8, 20.7, 26.3, 32.5, 38.0, 42.0, 42.8, 44.5, 47.8, 49.1, 52.7, 64.8, 123.0, 128.7, 131.9, 131.9, 131.9, 140.2, 140.2, 147.7, 163.3; *m*/*z* (CI) 606 ($[MH]^+$, 100%), 541 (10), 419 (44), 406 (47), 219 (25), 201 (12), 135 (22); HRMS found: $[MH]^+$606.1824, $C_{31}H_{33}N_3O_6PS$ requires 606.1828; Found: C, 61.8; H, 5.6; N, 6.9; $C_{31}H_{32}N_3O_6PS$ requires C, 61.5; H, 5.3, H, 7.0%.

5.2.3. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-(4-methoxyphenyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7c). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (390 mg, 1.2 mmol), LiHMDS in THF (1.25 mL, 1.0 M, 1.25 mmol), and *N*-(4-methoxyphenylmethylene)diphenylphosphinamide (350 mg, 1.0 mmol), were reacted together in THF (40 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–80% EtOAc in petrol, containing 0.05% v/v acetic acid), provided a colourless oil. Crystallisation from $CHCl_3$/hexane afforded **7c** (460 mg, 74%). R_f 0.5 (EtOAc); mp 138–140 °C; $[\alpha]_D^{20}$ −14.0 (*c* 1, CH_2Cl_2); IR ν_{max} (film) 2964, 3840, 1698, 1439, 1330, 1188, 1275, 1126, 730, 703, 652 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, s), 0.94 (3H, s), 1.21–1.30 and 1.79–1.98 (7H, 2×m), 3.28 and 3.39 (2H, 2×d, *J*=14.0 Hz), 3.61 (1H, m), 3.75 (3H, s), 4.11–4.26 (2H, 2×dd, J_P=15.9, 6 Hz, *J*=0.2 Hz), 6.80 (2H, app. d, *J*=8.5 Hz), 7.34–7.54 (8H, m), and 8.10–8.15 (4H, m); δ_C (75 MHz, $CDCl_3$) 19.8, 20.7, 26.3, 32.5, 38.1, 41.7, 43.8, 44.6, 47.7, 49.0, 52.6, 55.1, 64.7, 113.2, 124.7, 124.8, 128.6, 131.5, 131.7, 131.8, 159.4, 163.9; *m*/*z* (CI) 591 ($[MH]^+$, 100%), 526 (15), 419 (47), 373 (32), 219 (36), 135 (14); HRMS found: $[MH]^+$591.2064, $C_{32}H_{36}N_2O_5PS$ requires 591.2082.

5.2.4. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-(2-nitrophenyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7d). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (320 mg, 0.94 mmol), LiHMDS in THF (1.0 mL, 1.0 M, 1.0 mmol), and *N*-(2-nitrophenylmethylene)diphenylphosphinamide (300 mg, 0.9 mmol), were reacted together in THF (35 mL) at −78 °C to produce a yellow solid. Purification by flash chromatography (gradient 20–70% EtOAc in petrol, containing 0.05% v/v acetic acid) provided a colourless oil. Crystallisation from EtOAc/hexane afforded **7d** (380 mg, 72%). R_f 0.55 (EtOAc); $[\alpha]_D^{20}$ −112.4 (*c* 1, CH_2Cl_2); mp 190–192 °C; IR ν_{max} (film) 2960, 1700, 1438, 1342, 1212, 1136, 730, 696 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.88 (3H, s), 0.89 (3H, s), 1.17–1.32 and 1.79–1.96 (7H, 2×m), 3.28 and 3.36 (2H, 2×d, *J*=13.8 Hz), 3.51–3.55 (1H, m), 4.25 (1H, br dd, J_P=14.9 Hz, *J*=5.8 Hz), 5.05 (1H, dd, J_P=15.2 Hz, *J*=6.2 Hz), 7.38–7.58 (10H, m), and 7.80–8.12 (4H, m); δ_C (75 MHz, $CDCl_3$) 19.8, 20.6, 26.3, 32.5, 38.1, 40.8, 42.2, 44.6, 47.8, 49.0, 52.4, 64.5, 124.9, 128.8, 128.9, 128.7, 128.7, 131.0, 131.2, 131.2, 131.6, 131.8, 132.4, 132.9, 148.7, 164.1; *m*/*z* (CI) 606 ($[MH]^+$, 2.5%), 419 (15), 321 (20), 272 (32), 219 (25), 201 (12), 135 (100); HRMS found: $[MH]^+$606.1832, $C_{31}H_{33}N_3O_6PS$ requires 606.1828; Found: C, 61.4; H, 5.35; N, 6.9; $C_{31}H_{32}N_3O_6PS$ requires C, 61.5; H, 5.3, H, 7.0%.

5.2.5. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(3′-(4-Bromophenyl)-1′-diphenylphosphinyl-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7e). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (270 mg, 0.8 mmol), LiHMDS in THF (0.9 mL, 1.0 M, 0.9 mmol), and *N*-(4-bromophenylmethylene)diphenylphosphinamide (280 mg, 0.73 mmol), were reacted together in THF (25 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–80% EtOAc in petrol, containing 0.05% v/v acetic acid) provided a colourless oil. Crystallisation from $CHCl_3$/hexane afforded **7e** as a colourless crystalline solid (300 mg, 65%); mp 135–136 °C ($CHCl_3$/hexane). R_f 0.55 (EtOAc); $[\alpha]_D^{23}$ −16.0 (*c* 1, CH_2Cl_2); IR ν_{max} (film) 2940, 1708, 1442, 1347 and 1170, 1272, 1137, 750, 720, 684 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.90, (3H, s), 0.97 (3H, s), 1.22–1.33 and 1.80–1.97 (7H, 2×m), 3.28 and 3.41 (2H, 2×d, *J*=3.7 Hz), 3.58–3.62

(1H, m), 4.17–4.22 (2H, 2×m), 7.31–7.56 (10H, m) and 7.89–8.13 (4H, m); δ_C (300 MHz, C_6D_6) 0.28 (3H, s), 0.68 (3H, s), 0.21–0.56, 0.83–0.93, 1.11–1.29 and 1.65–1.88 (7H, m), 2.45 and 2.59 (2H, 2×d, J=13.9 Hz), 3.10–3.14 (1H, m), 4.43 (1H, dd, J_P=15.8 Hz, J=6.2 Hz), 4.81 (1H, br dd, J_P=14.1 Hz, J=6.2 Hz), 6.92–7.16 (6H, m), 7.26 (4H, d, J=8.6 Hz), and 7.47 (4H, d, J=8.6 Hz), 8.09–8.44 (4H, m); δ_C (75 MHz, $CDCl_3$) 19.8, 20.7, 26.3, 32.5, 38.1, 41.4, 43.3, 44.6, 47.8, 49.0, 52.7, 64.8, 122.2, 128.5, 131.9, 163.5; *m/z* (CI) 641 and 639 ($[MH]^+$, Br isotopic pattern, 24%), 576 (19), 574 (19), 561 (5), 424 (20), 358 (15), 219 (70), 201 (100), 135 (55); HRMS found: $[MH]^+$639.1068, $C_{31}H_{33}BrN_2O_4PS$ requires 639.1082.

5.2.6. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-(2-naphthyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7f). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (370 mg, 1.1 mmol), LiHMDS in THF (1.2 mL, 1.0 M, 1.2 mmol), and *N*-(2-naphthylmethylene)diphenylphosphinamide (350 mg, 1.0 mmol), were reacted together in THF (40 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in petrol, containing 0.05% v/v acetic acid), afforded **7f** as a clear oil (440 mg, 73%). R_f 0.55 (EtOAc); $[\alpha]_D^{20}$ −16.6 (*c* 1, CH_2Cl_2); IR ν_{max} (film) 2962, 1702, 1438, 1336, 1214, 1126, 646, 618 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.85 (3H, s), 0.94 (3H, s), 1.15, 1.72–1.93 (7H, 2×m), 3.21 and 3.36 (2H, 2×d, J=13.9 Hz), 3.49–3.51 (1H, m), 4.11 and 4.42 (2H, 2×dd, J_P=15.9 Hz, J=6.2 Hz), 7.31–8.20 (17H, m); δ_C (75 MHz, $CDCl_3$) 19.7, 20.7, 26.2, 32.4, 38.0, 41.8, 44.1, 44.5, 47.6, 48.9, 52.6, 64.6, 125.8, 125.9, 127.2, 127.6, 127.7, 128.4, 131.9, 133.1, 163.6; *m/z* (CI) 611 ($[MH]^+$, 100%), 546 (22), 419 (82), 411 (70), 393 (37), 219 (64), 201 (30), 135 (28); HRMS found: $[MH]^+$611.2126, $C_{35}H_{36}N_2O_4PS$ requires 611.2133.

5.2.7. (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-(2-fluorenyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7g). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (330 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol), and *N*-(fluorenemethylene)diphenylphosphinamide (350 mg, 0.9 mmol), were reacted together in THF (40 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in petrol, containing 0.05% v/v acetic acid), afforded **7g** as a pale yellow oil (390 mg, 68%). R_f 0.5 (EtOAc); $[\alpha]_D^{20}$ −20.0 (*c* 1, CH_2Cl_2); IR ν_{max} (film) 2962, 1702, 1439, 1337, 1217, 1127, 730, 646, 619 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.87 (3H, s), 0.95 (3H, s), 1.19–1.21 and 1.76–1.97 (7H, 2×m), 3.25 and 3.38 (2H, 2×d, J=13.9 Hz), 3.58 (1H, m), 3.85 (2H, d, J=3.7 Hz), 4.22 and 4.38 (2H, 2×dd, J_P=15.9 Hz, J=6.2 Hz), 7.26–7.72 and 7.97–8.20 (17H, 2×m); δ_C (75 MHz, $CDCl_3$) 19.7, 20.6, 26.2, 32.4, 38.0, 36.8, 41.9, 44.3, 44.5, 47.6, 48.9, 52.5, 64.6, 119.0, 119.8, 124.9, 126.6, 127.0, 128.6, 131.9, 141.3, 141.6, 142.6, 143.4, 163.6; *m/z* (CI) 649 ($[MH]^+$, 21%), 585 (7), 449 (43), 419 (100), 219 (60), 135 (22); HRMS found: $[MH]^+$649.2282, $C_{38}H_{38}N_2O_4PS$ requires 649.2290.

5.2.8. (2*R*,2′*R*,3′*S*)-(−)-*N*-[(1′-Diphenylphosphinyl-3′-(2-furyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7h). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (500 mg, 1.49 mmol), LiHMDS in THF (1.6 mL, 1.0 M, 1.6 mmol), and *N*-(2-furylmethylene)diphenylphosphinamide (400 mg, 1.4 mmol), were reacted together in THF (35 mL) at −78 °C to produce a pale yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in petrol, containing 0.05% v/v acetic acid), provided a pale yellow oil. Crystallisation from EtOAc/hexane afforded **7h**, as a colourless crystalline solid (530 mg, 71%). R_f 0.5 (EtOAc); $[\alpha]_D^{20}$ −18.9 (*c* 3, CH_2Cl_2); IR ν_{max} (film) 2961, 1701, 1438, 1336, 1217, 1137, 728, 695 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.91 (3H, s), 0.98 (3H, s), 1.16–1.36 and 1.83–1.89 (7H, 2×m), 3.31 and 3.41 (2H, 2×d, J=13.5 Hz), 3.73–3.76 (1H, m), 4.09–4.22 (2H, 2×dd, J_P=16.1 Hz, J=5.9 Hz), 6.29 (1H, dd, J=3.4, 1.9 Hz), 6.36 (1H, d, J=3.2 Hz), 7.33–7.58 (7H, m), and 7.84–8.12 (4H, m); δ_C (75 MHz, $CDCl_3$) 19.8, 20.6, 26.4, 32.6, 37.6, 38.1, 41.0, 44.6, 47.8, 49.2, 52.5, 64.7, 109.1, 110.5, 128.6, 131.7, 142.8, 148.5, 165.0; *m/z* (CI) 551 ($[MH]^+$, 35%), 487 (15), 447 (10), 419 (70), 351 (100), 219 (80), 201 (12), 135 (30); HRMS found: $[MH]^+$551.1779, $C_{29}H_{32}N_2O_5PS$ requires 551.1770.

5.2.9. (2*R*,2′*R*,3′*R*)-(+)-*N*-[(3′-(*tert*-Butyl)-1′-diphenylphosphinyl-2′-aziridinyl)carbonyl]bornane-10,2-sultam (7i). By following the procedure above, (2*R*)-(−)-(*N*-bromoacetyl)bornane-10,2-sultam (260 mg, 0.77 mmol), LiHMDS in THF (0.8 mL, 1.0 M, 0.8 mmol), and *N*-(*tert*-butylmethylene)diphenylphosphinamide (200 mg, 0.7 mmol), were reacted together in THF (40 mL) at −78 °C to produce a yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in petrol, containing 0.05% v/v acetic acid) provided a colourless oil. Crystallisation from ethyl acetate/hexane afforded (**7i**) as a colourless crystalline solid (150 mg, 40%). R_f 0.55 (EtOAc); mp 204 °C (EtOAc/hexane); $[\alpha]_D^{20}$ +11.9 (*c* 1, CH_2Cl_2); IR ν_{max} (film) 2960, 1703, 1439, 1339, 1203, 1127, 1064, 729, 704 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.82 (9H, s), 0.83 and 0.91 (6H, 2×s), 1.26–1.44 and 1.80–2.08 (7H, 2×m), 3.03 (1H, dd, J_P=17.8 Hz, J=6.3 Hz), 3.36 and 3.42 (2H, 2×d, J=13.7 Hz) 3.61 (1H, br dd, J_P=17.3 Hz, J=5.9 Hz), 3.85 (1H, m), 7.40–7.53 (6H, m), and 7.94–8.10 (4H, m); δ_C (75 MHz, $CDCl_3$) 19.8, 20.4, 27.9, 26.4, 32.6, 38.0, 32.4, 39.6, 44.4, 47.8, 49.0, 52.5, 53.5, 65.1, 128.4, 131.8, 131.7, 132.0, 165.5; *m/z* (CI) 541 ($[MH]^+$, 100), 471 (42), 419 (20), 298 (56), 201 (23), 135 (9); HRMS found: $[MH]^+$541.2294, $C_{29}H_{38}N_2O_4PS$ requires 541.2290; Found: C, 64.6; H, 6.9; N, 5.2; $C_{29}H_{37}N_2O_4PS$ requires C, 64.4; H, 6.9, H, 5.2%.

5.2.10. (2*R*)-*N*-[2′-Bromo-4′-dimethyl-3′-(diphenylphosphinamido)-1′-oxopentyl]bornane-10,2-sultam (8). The above reaction also gave compound **8** as a clear oil (60 mg, 13%). R_f 0.65 (EtOAc); IR ν_{max} (film) 3368, 2960, 1706, 1438, 1332, 1216, 1122, 724, 698 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.93 (9H, s), 0.95 (3H, s), 1.24 (3H, s), 1.26–1.41 and 1.80–1.91 (6H, 2×m), 2.37–2.42 (1H, m), 3.37–3.43 and 3.53–3.63 (2H, 27×m), 3.45–3.53 (2H, 2×d, J=13.7 Hz), 3.90 (1H, dd, J=7.8, 4.6 Hz), 5.52 (1H, s), 7.38–7.52 (6H, m), and 7.82–7.94 (4H, m), δ_C (100 MHz, $CDCl_3$) 20.0, 20.8, 27.8, 26.5, 33.1, 37.0, 37.9, 44.6, 47.8, 48.5, 53.1, 53.3, 58.8, 66.4, 128.2, 132.2, 166.2; *m/z* (CI) 623 and 621 ($[MH]^+$, Br isotope pattern, 26%), 543 (14),

485 (27), 326 (17), 270 (100), 216 (20), 57 (54); HRMS found: $[MH]^+$621.1539, $C_{29}H_{39}BrN_2O_4PS$ requires 621.1552.

5.3. General procedure for asymmetric aza-Darzens reactions using *S*-5

Compound *S*-**5** (336 mg, 1.0 mmol) was dissolved in anhydrous THF (20 mL) and cooled to −78 °C under an inert atmosphere. LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) was added dropwise and the resulting yellow solution stirred for approximately 30 min. Phosphinylimine (0.9 mmol) was added as a THF solution (15 mL) to the reaction mixture. The reaction mixture was then left stirring at −78 °C for approximately 3–4 h and followed by TLC. After this time the reaction was quenched via addition of a saturated ammonium chloride solution (20 mL). The aqueous layer was then extracted with ether (3×20 mL) and the organic layers combined, washed with brine, dried ($MgSO_4$), filtered and the solvent removed in vacuo to afford the crude aziridine.

5.3.1. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(phenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7j). Following the general procedure described above, *S*-**5** (336 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) and *P*,*P*-diphenyl-*N*-(phenylmethylene)phosphinic amide (275 mg, 0.9 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:9), affording **7j** as a colourless solid (358 mg, 71%). R_f 0.53 (EtOAc); mp 198 °C; $[\alpha]_D^{20}$ +11.3 (*c* 1, CH_2Cl_2); IR ν_{max} (CCl_4) 2961, 1705, 1439, 1336, 1270, 1213, 1137, 837, 654 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, s), 0.94 (3H, s), 1.21–1.26 and 1.78–1.96 (7H, 2×m), 3.27, 3.39 (2H, 2×d, J=13.9 Hz), 3.58 (1H, m), 4.25 and 4.29 (2H, 2×dd, J_P=15.8 Hz, J=6.2 Hz), 7.23–7.52 (11H, m), 7.93–7.98 and 8.11–8.15 (4H, m); δ_C (100 MHz, $CDCl_3$) 19.6, 20.5, 26.2, 32.3, 37.9, 41.5, 43.8, 44.4, 47.6, 48.8, 52.5, 64.6, 127.6, 127.9, 128.2, 128.3, 128.4, 128.6, 128.7, 130.9, 131.0, 131.4, 131.5, 131.6, 131.7, 132.0, 132.1, 132.2, 132.3, 132.5, 132.6, 163.5; *m*/*z* (CI) 561 ($[MH]^+$, 60%), 483 (11), 361 (42), 346 (44), 320 (70), 216 (100), 135 (67); HRMS found: $[MH]^+$561.1987, $C_{31}H_{34}N_2O_4PS$ requires 561.1977.

5.3.2. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(4-fluorophenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7k). Following the general procedure described above, *S*-**5** (336 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) and *P*,*P*-diphenyl-*N*-(4-fluorophenylmethylene)-phosphinic amide (323 mg, 1.0 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:9), affording **7k**, as a colourless solid (328 mg, 57%). R_f 0.51 (EtOAc); mp 197 °C; $[\alpha]_D^{20}$ +8.5 (*c* 1, $CHCl_3$); IR ν_{max} (CCl_4) 3056, 2968, 1705, 1441, 1338, 1188, 1267, 1127, 740, 705 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, s), 0.96 (3H, s), 1.20–1.29, 1.79–1.81 and 1.95–1.97 (7H, m), 3.28 and 3.40 (2H, 2×d, J=13.6 Hz), 3.57–3.60 (1H, m), 4.19–4.26 (2H, 2×dd, J_P=16.1 Hz, J=6.2 Hz), 6.92–6.97 and 7.35–7.54 (10H, m), 7.91–7.96 and 8.09–8.14 (4H, m); δ_C (100 MHz, $CDCl_3$) 19.7, 20.6, 26.3, 32.4, 37.9, 41.6, 43.2, 44.4, 47.6, 48.9, 52.5, 64.6, 114.5, 114.8, 128.3, 128.5, 128.6, 129.9, 129.9, 130.9, 131.4, 131.4, 131.6, 131.7, 131.9, 132.2, 161.2, 163.6; *m*/*z* (CI) 579 ($[MH]^+$, 14%), 515 (12), 419 (32), 379 (7), 297 (19), 219 (100), 77 (17); HRMS found: $[MH]^+$579.1870, $C_{31}H_{33}FN_2O_4PS$ requires 579.1883.

5.3.3. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(2,6-dichlorophenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7l). Following the general procedure described above, *S*-**5** (336 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) and *P*,*P*-diphenyl-*N*-(2,6-dichlorophenylmethylene)phosphinic amide (337 mg, 0.9 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:1), affording **7l**, as a colourless solid (493 mg, 87%). R_f 0.18 (petrol/EtOAc 1:1); mp 192 °C; $[\alpha]_D^{20}$ +6.2 (*c* 1, $CHCl_3$); IR ν_{max} (CCl_4) 3057, 2964, 1704, 1441, 1333, 1168, 1274, 1125, 737, 708, 698 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 0.70–0.83 (6H, m), 1.18 and 1.74–1.93 (7H, m), 3.33 (1H, m), 3.45 and 3.50 (2H, 2×d, J=14.0 Hz), 4.18 and 4.21 (2H, 2×dd, J_P=15.6 Hz, J=5.3 Hz), 7.00–7.10 (3H, m), 7.34–7.44 (6H, m), 7.90–7.96 (3H, m); δ_C (60 MHz, $CDCl_3$) 19.7, 21.1, 26.2, 32.8, 38.2, 38.9, 42.6, 44.7, 47.7, 48.9, 52.7, 65.2, 128.1, 128.2, 128.3, 128.7, 129.1, 131.6, 131.7, 132.1, 132.2, 132.5, 132.6, 135.6, 165.2; *m*/*z* (CI) 629 ($[MH]^+$, 18%), 565 (12), 419 (12), 219 (100), 151 (26), 78 (39); HRMS found: $[MH]^+$629.1197, $C_{31}H_{32}Cl_2N_2O_4PS$ requires 629.1197.

5.3.4. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(3-bromophenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7m). Following the general procedure described above, *S*-**5** (300 mg, 0.89 mmol), LiHMDS in THF (1.0 mL, 1.0 M, 1.0 mmol) and *P*,*P*-diphenyl-*N*-(3-bromophenylmethylene)-phosphinic amide (346 mg, 0.89 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:9), affording **7m**, as a colourless solid (343 mg, 60%). R_f 0.75 (EtOAc); $[\alpha]_D^{20}$ +16.5 (*c* 1, $CHCl_3$); IR ν_{max} (CCl_4) 3057, 2964, 1705, 1441, 1339, 1188, 1267, 1128, 740, 705 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 0.90 (3H, s), 0.97 (3H, s), 1.20–1.34 and 1.67–1.98 (7H, 2×m), 3.30 and 3.41 (2H, 2×d, J=13.9 Hz), 3.61–3.64 (1H, m), 4.18 and 4.22 (2H, 2m), 7.11–7.15 and 7.30–7.60 (10H, m), 7.92–7.97 and 8.09–8.14 (4H, m); δ_C (60 MHz, $CDCl_3$) 19.7, 20.6, 26.3, 32.4, 38.0, 41.6, 43.0, 44.5, 47.7, 49.0, 52.6, 64.6, 121.7, 126.6, 127.0, 128.0, 128.1, 128.4, 128.6, 128.7, 129.2, 129.8, 130.7, 130.8, 130.9, 131.1, 131.4, 131.4, 131.5, 131.7, 131.8, 131.9, 132.0, 132.1, 132.2, 135.1, 135.1, 141.0, 163.4; *m*/*z* (CI) 639 ($[MH]^+$, 23%), 573 (28), 419 (57), 359 (10), 219 (100), 135 (24); HRMS found: $[MH]^+$639.1187, $C_{31}H_{33}BrN_2O_4PS$ requires 639.1182.

5.3.5. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(4-methoxyphenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7n). Following the general procedure described above, *S*-**5** (336 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) and *P*,*P*-diphenyl-*N*-(4-methoxyphenylmethylene)phosphinic amide (337 mg, 1.0 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:9), affording **7n**, as a colourless solid (355 mg, 60%). R_f 0.45 (EtOAc); mp 139 °C; $[\alpha]_D^{20}$ +11.4

(c 1, $CHCl_3$); IR ν_{max} (CCl_4) 2964, 1698, 1439, 1330, 1188, 1275, 1126, 730, 703, 652 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, s), 0.95 (3H, s), 1.22–1.30, 1.79–1.81 and 1.96–1.97 (7H, m), 3.28 and 3.39 (2H, 2×d, J=13.7 Hz), 3.61 (1H, m), 3.76 (3H, s), 4.11 and 4.25 (2H, 2×dd, J_P=16.1 Hz, J=5.9 Hz), 6.79–6.81 and 7.36–7.52 (10H, m), 7.91–7.96 and 8.10–8.15 (4H, m); δ_C (100 MHz, $CDCl_3$) 19.7, 20.6, 26.3, 32.5, 38.1, 41.6, 43.7, 44.5, 47.7, 48.9, 52.6, 55.1, 64.6, 113.2, 124.7, 124.7, 128.4, 128.5, 128.7, 129.4, 131.1, 131.2, 131.5, 131.6, 131.8, 131.9, 132.1, 132.1, 132.4, 132.5, 159.3, 163.9; m/z (CI) 591 ($[M]^+$, 18%), 419 (37), 219 (92), 148 (100), 77 (49); HRMS found: $[M]^+$591.2089, $C_{32}H_{36}N_2O_5PS$ requires 591.2083.

5.3.6. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(2-pyridinyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7o). Following the general procedure described above, *S*-**5** (336 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) and *P*,*P*-diphenyl-*N*-(2-pyridinylmethylene)phosphinic amide (306 mg, 1.0 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:9), affording **7o**, as a colourless solid (376 mg, 67%). R_f 0.37 (EtOAc); mp 195 °C; $[\alpha]_D^{20}$ +11.8 (c 1, $CHCl_3$); IR ν_{max} (CCl_4) 3059, 2965, 1703, 1440, 1342, 1171, 1268, 1129, 776, 738, 705 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 0.89 (6H, 2s), 1.21–1.29 and 1.82–2.04 (7H, m), 3.25 and 3.34 (2H, 2×d, J=13.9 Hz), 3.72 (1H, m), 4.11 and 4.34 (2H, 2×dd, J_P=15.8 Hz, J=6.6 Hz), 7.14–7.17 (1H, m), 7.37–7.64 (8H, m), 7.91–7.96 and 8.13–8.18 (4H, m), 8.50–8.51 (1H, m); δ_C (60 MHz, $CDCl_3$) 19.8, 20.5, 26.3, 32.7, 38.2, 41.5, 44.3, 44.8, 47.7, 49.2, 52.2, 64.4, 122.2, 123.1, 128.4, 128.6, 128.6, 128.8, 130.8, 131.4, 131.5, 131.8, 131.9, 132.1, 132.2, 132.3, 136.2, 150.3; m/z (CI) 562 ($[MH]^+$, 100%), 498 (75), 419 (97), 362 (34), 319 (50), 280 (73), 219 (93), 119 (31); HRMS found: $[MH]^+$562.1942, $C_{30}H_{33}N_3O_4PS$ requires 562.1930.

5.3.7. *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-Diphenylphosphinyl-3-(ethenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (7p). Following the general procedure described above, *S*-**5** (336 mg, 1.0 mmol), LiHMDS in THF (1.1 mL, 1.0 M, 1.1 mmol) and *P*,*P*-diphenyl-*N*-(ethenylmethylene)phosphinic amide (255 mg, 1.0 mmol) were reacted to produce the crude aziridine. The resulting colourless solid was purified by flash chromatography (petrol/EtOAc 1:9), affording **7p**, as a colourless solid (239 mg, 47%). R_f 0.49 (EtOAc); $[\alpha]_D^{20}$ +10.2 (c 1, $CHCl_3$); IR ν_{max} (CCl_4) 3056, 2966, 1704, 1440, 1338, 1168, 1267, 1129, 735, 703 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.85 (3H, s), 0.93 (3H, s), 1.08–1.36, 1.77–1.81 and 1.97–2.02 (7H, m), 3.30 and 3.38 (2H, 2×d, J=13.7 Hz), 3.52–3.60 (1H, m), 3.77–3.95 (2H, m), 5.19 (1H, d, $J_{(cis)}$=10.5 Hz), 5.36 (1H, d, $J_{(trans)}$=17.4 Hz), 5.65 (1H, ddd, J=17.4, 10.5, 7.3 Hz), 7.33–7.43 (6H, m), 7.81–7.86 and 7.92–8.00 (4H, m); δ_C (100 MHz, $CDCl_3$) 19.8, 20.3, 26.3, 32.7, 38.2, 39.7, 42.9, 44.6, 47.7, 49.2, 52.7, 64.8, 121.4, 128.3, 128.4, 128.6, 128.7, 130.7, 130.8, 131.2, 131.4, 131.5, 131.6, 131.7, 131.7, 131.8, 132.0, 132.3, 132.4, 132.4, 164.7; m/z (CI) 511 ($[MH]^+$, 30%), 419 (18), 268 (100), 201 (76), 77 (22); HRMS found: $[MH]^+$511.1820, $C_{27}H_{32}N_2O_4PS$ requires 511.1820.

5.4. General procedure for the removal of the sultam auxiliary

(2′*R*,3′*R*)-*N*-Sultamoyl-*N*-diphenylphosphinylaziridines (typically 0.2 mmol) were dissolved in a mixture of THF and water (4:1), 5 mL. Lithium hydroxide monohydrate (0.4 mmol) was then added. The resulting suspension was then stirred vigorously overnight, after which the THF was removed in vacuo, the aqueous layer basified to pH 10 with saturated $NaHCO_3$, and extracted with $CHCl_3$ (30 mL and 2×20 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (10 mL) dried ($MgSO_4$), filtered and the solvent removed in vacuo. The aqueous layer was then combined with the base washings and acidified to pH 2 with 2 M HCl. Further $CHCl_3$ was added (3×45 mL), the layers separated, the organic layers combined, dried ($MgSO_4$), filtered and the solvent removed in vacuo, to afford the *N*-diphenylphosphinyl-2-substituted-3-carboxyaziridines.

5.4.1. (2′*R*,3′*R*)-*N*-Diphenylphosphinyl-2-carboxy-3-phenylaziridine (9a). By following the general procedure described above (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-diphenylphosphinyl-3′-phenyl-2′-aziridinyl)carbonyl]bornane-10,2-sultam (90 mg, 0.15 mmol) afforded **9a** as a colourless oil (33 mg, 64%). $[\alpha]_D^{20}$ −6.0 (c 1, MeOH); IR ν_{max} (film) 1717, 1438, 1128, 1025, 727, 691 cm^{-1}; δ_H (300 MHz, d_6-DMSO) 3.40 (1H, dd, J_P=15.4 Hz, J=6.6 Hz), 3.97 (1H, dd, J_P=15.9 Hz, J=6.7 Hz), 7.04–8.00 (15H, m); δ_C (75 MHz, d_6-DMSO) 40.5, 40.7, 127.5, 128.6, 131.9, 133.5, 166.9; m/z (CI) 364 ($[MH]^+$, 0.5%), 320 (83), 242 (9), 218 (20), 201 (12), 89 (47), 61 (100); HRMS found: $[MH]^+$364.1113, $C_{21}H_{19}NO_3P$ requires 364.1102.

5.4.2. (2′*R*,3′*R*)-*N*-Diphenylphosphinyl-2-carboxy-3-(4-nitrophenyl)aziridine (9b). By following the general procedure described (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-diphenylphosphinyl-3′-(4-nitrophenyl)-2′-aziridinyl)carbonyl]-bornane-10,2-sultam (100 mg, 0.17 mmol) afforded **9b** as a colourless oil (40 mg, 60%). $[\alpha]_D^{20}$ −4.4 (c 2, DMSO); IR ν_{max} (film) 1719, 1517, 1347, 1437, 1128, 1025, 727, 691 cm^{-1}; δ_H (300 MHz, d_6-DMSO) 3.59 (1H, dd, J_P=15.2 Hz, J=6.8 Hz), 4.49 (1H, dd, J_P=15.0 Hz, J=6.8 Hz), 7.47–8.31 (14H, m); δ_C (75 MHz, d_6-DMSO) 39.5, 124.6, 128.5, 131.9, 135.9, 148.1, 167.2; m/z (CI) 409 ($[MH]^+$, 1%), 365 (1.5), 335 (2), 219 (100), 201 (8) 141 (23); HRMS found: [M−CO_2] 365.1050, $C_{20}H_{18}N_2O_3P$ requires 365.1056.

5.4.3. (2′*R*,3′*R*)-*N*-Diphenylphosphinyl-2-carboxy-3-(2-nitrophenyl)aziridine (9c). By following the general procedure described (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-diphenylphosphinyl-3′-(2-nitrophenyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (100 mg, 0.17 mmol) afforded **9c** as a colourless oil (45 mg, 67%). $[\alpha]_D^{20}$ +2.3 (c 4, DMSO); IR ν_{max} (film) 1718, 1516, 1343, 1436, 1123, 1024, 727, 691 cm^{-1}; δ_H (300 MHz, d_6-DMSO) 3.61 (1H, dd, J_P=15.2 Hz, J=6.6 Hz), 4.26 (1H, dd, J_P=15.4 Hz, J=6.8 Hz), 7.40–8.20 (14H, m); δ_C (75 MHz, d_6-DMSO) 39.5, 123.2, 128.5, 131.4, 134.1, 135.8, 147.4, 167.3; m/z (CI) 409 ($[MH]^+$, 7%), 365 (10), 347 (45), 219 (100), 201 (70), 120 (60); HRMS found: $[MH]^+$409.0956, $C_{21}H_{18}N_2O_5P$ requires 409.0953.

5.4.4. (2′*R*,3′*R*)-*N*-Diphenylphosphinyl-3-(4-bromophenyl)-2-carboxyaziridine (9d). By following the general procedure described (2*R*,2′*R*,3′*R*)-(−)-*N*-[(3′-(4-bromophenyl)-1′-diphenylphosphinyl-2′-aziridinyl)carbonyl]bornane-10,2-sultam (55 mg, 0.09 mmol) afforded **9d** as a colourless oil (26 mg, 61%). $[\alpha]_D^{20}$ −6.6 (*c* 1.5, DMSO); IR ν_{max} (film) 1735, 1437, 1131, 1011, 730, 692 cm^{-1}; δ_H (300 MHz, d_6-DMSO) 3.49 (1H, dd, J_P=15.3 Hz, J=6.6 Hz), 4.08 (1H, dd, J_P=15.8 Hz, J=6.8 Hz), 7.44–8.07 (14H, m); δ_C (75 MHz, d_6-DMSO) 39.5, 122.2, 128.4, 131.7, 167.4; *m/z* (CI) 442 and 444 ($[MH]^+$, bromine isotope pattern, 3.3%) 398 (31), 400 (31), 320 (26), 219 (100), 201 (35), 141 (12); HRMS found: $[MH]^+$442.0201, $C_{21}H_{18}BrNO_3P$ requires 442.0208.

5.4.5. (2′*R*,3′*R*)-*N*-Diphenylphosphinyl-2-carboxy-3-(2-naphthyl)aziridine (9e). By following the general procedure described (2*R*,2′*R*,3′*R*)-(−)-*N*-[(1′-diphenylphosphinyl-3′-(2-naphthyl)-2′-aziridinyl)carbonyl]bornane-10,2-sultam (100 mg, 0.16 mmol) afforded **9e** as a yellow oil (35 mg, 51%). $[\alpha]_D^{20}$ −10.0 (*c* 2, DMSO); IR ν_{max} (film) 1719, 1437, 1129, 1034, 727, 692 cm^{-1}; δ_H (300 MHz, d_6-DMSO) 3.57 (1H, dd, J_P=15.4 Hz, J=6.6 Hz), 4.21 (1H, dd, J_P=15.7 Hz, J=6.6 Hz), 7.44–8.11 (17H, m); δ_C (75 MHz, d_6-DMSO) 39.5, 125.1, 126.1, 126.2, 127.4, 127.6, 128.4, 131.9, 167.3; *m/z* (CI) 414 ($[MH]^+$, 0.5%), 370 (17), 247 (16), 219 (100), 201 (8), 141 (14); HRMS found: $[M-CO_2]$ 370.1350, $C_{24}H_{21}NOP$ requires 370.1361.

5.4.6. (2′*R*,3′*R*)-*N*-Diphenylphosphinyl-3-(*tert*-butyl)-2-carboxyaziridine (9f). By following the general procedure described (2*R*,2′*R*,3′*R*)-(+)-*N*-[(3′-(*tert*-Butyl)-1′-diphenylphosphinyl-2′-aziridinyl)carbonyl]bornane-10,2-sultam (50 mg, 0.1 mmol) afforded **9f** as a colourless oil (15 mg, 47%). $[\alpha]_D^{20}$ +3.7 (*c* 1.5, DMSO); IR ν_{max} (film) 2960, 1718, 1438, 1129, 1027, 730, 675 cm^{-1}; δ_H (300 MHz, d_6-DMSO) 0.72 (9H, s), 2.56 (1H, dd, J_P=16.8 Hz, J=6.8 Hz), 3.06 (1H, dd, J_P=16.6 Hz, J=6.8 Hz), 7.40–8.10 (10H, m); δ_C (75 MHz, d_6-DMSO) 26.7, 39.5, 128.5, 128.6, 131.8, 167.4; *m/z* (CI) 344 ($[MH]^+$, 62%), 298 (22), 274 (23), 219 (100), 201 (54), 141 (12); HRMS found: $[MH]^+$344.1414, $C_{19}H_{23}N_2O_3P$ requires 344.1416.

5.4.7. (2′*S*,3′*S*)-2-Carboxy-*N*-diphenylphosphinyl-3-(3-bromophenyl)aziridine (9g). Following the general procedure described above, *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-diphenylphosphinyl-3-(2-bromophenyl)-2-aziridinyl)carbonyl]-bornane-10,2-sultam (128 mg, 0.2 mmol) afforded **9g** as a colourless oil (70 mg, 80%). $[\alpha]_D^{20}$ −12.8 (*c* 1, $CDCl_3$); IR ν_{max} (CCl_4) 1718, 1439, 1131, 1028, 751, 695 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 3.51 and 3.98 (2H, 2×dd, J_P=15.6 Hz, J=6.6 Hz), 7.06–8.05 (14H, m); δ_C (60 MHz, $CDCl_3$) 42.3, 42.6, 123.5, 128.1, 129.8, 130.1, 130.3, 130.4, 130.5, 130.6, 131.4, 132.0, 132.6, 132.8, 132.8, 133.0, 133.2, 133.4, 134.6, 134.6, 137.4, 169.2; *m/z* (CI) 444 ($[MH]^+$, 10%), 398 (7), 236 (67), 219 (100); HRMS found: $[MH]^+$444.0214, $C_{21}H_{18}BrNO_3P$ requires 444.0188.

5.4.8. (2′*S*,3′*S*)-2-Carboxy-*N*-diphenylphosphinyl-3-(2,6-dichlorophenyl)aziridine(9h). Following the general procedure described above *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-diphenylphosphinyl-3-(2,6-dichlorophenyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (126 mg, 0.2 mmol) afforded **9h** as a colourless oil (37 mg, 45%). $[\alpha]_D^{20}$ −10.8 (*c* 1, $CHCl_3$); IR ν_{max} (CCl_4) 1718, 1439, 1131, 1028, 751, 714, 695 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 3.39 and 4.08 (2H, 2×dd, J_P=16.0 Hz, J=6.0 Hz), 7.11–7.92 (13H, m); δ_C (60 MHz, $CDCl_3$) 40.9, 42.6, 129.9, 130.0, 130.1, 130.5, 130.7, 131.2, 132.6, 132.8, 133.2, 133.3, 133.7, 133.8, 134.4, 134.4, 134.6, 134.7, 137.2, 170.7; *m/z* (CI) 432 ($[MH]^+$, 100%), 388 (40), 354 (10), 236 (91), 201 (21), 66 (36); HRMS found: $[MH]^+$432.0303, $C_{21}H_{17}Cl_2NO_3P$ requires 432.0323.

5.4.9. (2′*S*,3′*S*)-2-Carboxy-*N*-diphenylphosphinyl-3-(2-pyridinyl)aziridine (9i). Following the general procedure described above *cis*-2*S*,2′*S*,3′*S*-*N*-[(1-diphenylphosphinyl-3-(2-pyridinyl)-2-aziridinyl)carbonyl]bornane-10,2-sultam (105 mg, 0.187 mmol) afforded **9j** as a yellow oil (68 mg, 99%). $[\alpha]_D^{20}$ −25.8 (*c* 1, $CHCl_3$); IR ν_{max} (CCl_4) 1718, 1439, 1130, 757, 695 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 3.58 and 4.06 (2H, 2×dd, J_P=15.6 Hz, J=6.6 Hz), 7.22–8.35 (14H, m); δ_C (60 MHz, $CDCl_3$) 42.1, 43.4, 124.5, 125.4, 129.8, 130.0, 130.3, 130.5, 130.6, 130.7, 132.6, 132.8, 132.9, 133.0, 133.1, 133.2, 133.4, 134.5, 134.6, 134.7, 139.3, 149.9, 154.5, 169.1; *m/z* (CI) 321 ($[MH-CO_2]^+$, 13%), 236 (63), 218 (100), 150 (17), 121 (23); HRMS found: $[MH-CO_2]^+$321.1171, $C_{19}H_{17}N_2OP$ requires 321.1157.

Acknowledgements

We acknowledge the financial support of the EPSRC (A.McL. and A.A.C.) and Parke Davis Neuroscience Research Centre (A.A.C.); J.B.S. thanks Zeneca for an award from the Strategic Research Fund.

References and notes

1. For reviews, see: Kemp, J. E. G. In Trost, B. M., Fleming, I., Eds.; Comprehensive Organic Synthesis; Oxford: Pergamon, 1991; Vol. 7, p 467. Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. Pearson, W. H.; Lian, B. N.; Bergmeier, S. C. In Katritzky, A. R., Rees, C. W., Scriven, E. F., Padwa, A., Eds.; Comprehensive Heterocyclic Chemistry II; Oxford: Pergamon, 1996; Vol. 1A, p 1. (d) Rai, K. M. L.; Hassner, A. In Katritzky, A. R., Rees, C. W., Scriven, E. F., Padwa, A., Eds.; Comprehensive Heterocyclic Chemistry II; Oxford: Pergamon, 1996; Vol. 1A, p 61. Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693. Padwa, A.; Murphree, S. S. In Gribble, G. W., Gilchrist, T. L., Eds.; Progress in Heterocyclic Chemistry; Pergamon Elsevier Science: Oxford, 2000; Vol. 12, Chapter 4.1, p 57. Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247.
2. For reviews of aziridine syntheses, see: Kemp, J. E. G. In Trost, B. M., Fleming, I., Eds.; Comprehensive Organic Synthesis; Oxford: Pergamon, 1991; Vol. 7, p 467. Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. Pearson, W. H.; Lian, B. N.; Bergmeier, S. C. In Katritzky, A. R., Rees, C. W., Scriven, E. F., Padwa, A., Eds.; Comprehensive Heterocyclic Chemistry II; Oxford: Pergamon, 1996; Vol. 1A, p 1. Rai, K. M. L.; Hassner, A. In Katritzky, A. R., Rees, C. W., Scriven, E. F., Padwa, A., Eds.; Comprehensive Heterocyclic Chemistry II; Oxford: Pergamon, 1996; Vol. 1A, p 61. Osborn,

H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693. Padwa, A.; Murphree, S. S. In Gribble, G. W., Gilchrist, T. L., Eds.; Progress in Heterocyclic Chemistry; Pergamon Elsevier Science: Oxford, 2000; Vol. 12, Chapter 4.1, p 57. Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247. Huang, D.; Yan, M.; Shen, Q. *Chin. J. Org. Chem.* **2004**, *24*, 1200. For recent reports of aziridination reactions, see: Padwa, A.; Flick, A. C.; Leverett, C. A.; Stengel, T. *J. Org. Chem.* **2004**, *69*, 6377. Omura, K.; Uchida, T.; Irie, R.; Katsuki, T. *Chem. Commun.* **2004**, 2060. Xu, J. X.; Ma, L. G.; Jiao, P. *Chem. Commun.* **2004**, 1616. Weller, R. L.; Rajski, S. R. *Tetrahedron Lett.* **2004**, *45*, 5807. Kim, S. K.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 3952. Avenier, F.; Latour, J. M. *Chem. Commun.* **2004**, 1544. Morton, D.; Pearson, D.; Field, R. A.; Stockman, R. A. *Org. Lett.* **2004**, *6*, 2377. Vyas, R.; Gao, G. Y.; Harden, J. D.; Zhang, X. P. *Org. Lett.* **2004**, *6*, 1907. Kumar, G. D. K.; Baskaran, S. *Chem. Commun.* **2004**, 1026. Watson, I. D. G.; Styler, S. A.; Yudin, A. K. *J. Am. Chem. Soc.* **2004**, *126*, 5086. Siu, T.; Yudin, A. K. *J. Am. Chem. Soc.* **2002**, *124*, 530.

3. Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. *Tetrahedron* **1998**, *54*, 2181–2208. Cantrill, A. A.; Jarvis, A. N.; Osborn, H. M. I.; Ouadi, A.; Sweeney, J. *Synlett* **1996**, 847. Cantrill, A. A.; Sweeney, J. B. *Synlett* **1995**, 1277. Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. B.; Howson, W. *Tetrahedron Lett.* **1994**, *35*, 3159. Osborn, H. M. I.; Sweeney, J. B.; Howson, W. *Tetrahedron Lett.* **1994**, *35*, 2739. Osborn, H. M. I.; Sweeney, J. B.; Howson, W. *Synlett* **1994**, 145. *N*-Phosphorylated aziridines have also been reported to undergo efficient ring-opening reactions: Zwierzak, A.; Napieraj, A. *Tetrahedron* **1996**, *52*, 8789. Osowskapacewicka, K.; Zwierzak, A. *Pol. J. Chem.* **1994**, *68*, 1263.
4. McLaren, A. B.; Sweeney, J. B. *Org. Lett.* **1999**, *1*, 1339. Cantrill, A. A.; Hall, L. D.; Jarvis, A. N.; Osborn, H. M. I.; Raphy, J.; Sweeney, J. B. *J. Chem. Soc., Chem. Commun.* **1996**, 2631.
5. Asymmetric aza-Darzens and Darzens-like reactions: Abdel-Magid, A. F.; Pridgen, L. N.; Eggleston, D. S.; Lantos, I. *J. Am. Chem. Soc.* **1986**, *108*, 4595. Corey, E. J.; Choi, S. *Tetrahedron Lett.* **1991**, *32*, 2857. Fujisawa, T.; Hayakawa, R.; Shimizu, M. *Tetrahedron Lett.* **1992**, *33*, 7903. Pridgen, L. N.; Abdelmagid, A. F.; Lantos, I.; Shilcrat, S.; Eggleston, D. S. *J. Org. Chem.* **1993**, *58*, 5107. Gennari, C.; Pain, G. *Tetrahedron Lett.* **1996**, *37*, 3747. Davis, F. A.; Zhou, P.; Reddy, G. V. *J. Org. Chem.* **1994**, *59*, 3243. Davis, F. A.; Zhou, P.; Liang, C. H.; Reddy, R. E. *Tetrahedron: Asymmetry* **1995**, *6*, 1511. Florio, S.; Troisi, L.; Capriati, V. *J. Org. Chem.* **1995**, *60*, 2279.
6. All *N*-diphenylphosphinyl imines were prepared according to: Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561.
7. Pridgen, L. N.; Abdel-Magid, A. F.; Lantos, I.; Shilcrat, S.; Eggleston, D. S. *J. Org. Chem.* **1993**, *58*, 5107.
8. Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.
9. For pertinent leading references as to the synthetic utility of the camphorsulfonyl group as a chiral auxiliary, see: Spivey, A.C. *Encyclopaedia of Reagents for Organic Synthesis*; Wiley: Chichester, UK, 1995; p 975.
10. Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561.
11. The absolute configuration of the aziridine asymmetric centres were tentatively assigned from computer modelling.