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Preparation and ring-opening reactions of *N*,*O*-bis(diphenylphosphinyl) hydroxymethylaziridine ('Di-Dpp')

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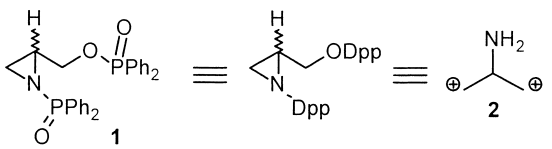
Abstract—*N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine ('DiDpp', **1**) is efficiently prepared from 2-aminoethane-1,3-diol: this activated aziridine undergoes two sequential reactions with copper(I)-modified Grignard reagents, yielding α-branched *N*-Dpp amines in good yield.

1. Introduction

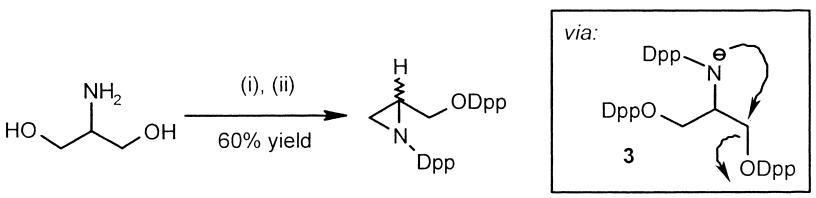
We have, of late, investigated the use of the diphenylphosphinyl (abbreviated in our previous publications to 'Dpp') group as an activating group for ring-opening of aziridines. Accordingly, we have developed such reactions using heteroatom-centred, organometallic[1] and (in the case of vinylaziridines[2]) enolate nucleophiles. We further reported the fruits of our initial labours into the design and utility of *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine ('DiDpp', **1**) as a convenient synthetic equivalent for the 2-aminopropane-1,2-dication synthon **2**.[3] In this paper we describe, in full, the synthesis and some ring-opening reactions of this moiety.[4] We also describe for the first time the preliminary results we have garnered concerning the mechanism of the reaction of **1** with nucleophiles, via the ring-opening reaction of enantiomerically-pure (2*R*)-DiDpp.



2. Results and discussion

We have previously described the synthesis of DiDpp and its reaction with Grignard reagents in the presence of substoichiometric amounts of Cu(I) salts. Thus, we utilized the nucleofugacity of the diphenylphosphinate anion in a 'one-pot' preparation of **1** from commercially-available 2-aminopropane-1,3-diol (Scheme 1) in 60% yield.

The fulcrum of this reaction is the intramolecular displacement of diphenylphosphinate from the intermediate,



Conditions:
(i) $Ph_2P(O)Cl$ (3 eq.), Et_3N (3 eq.), 0°C→rt, THF, 20 hours
(ii) NaH (7.5 eq.), 0°C→rt, 20 hours

Scheme 1. One-pot preparation of (±)-DiDpp.

Keywords: aziridinemethanol; ring-opening; phosphinate.
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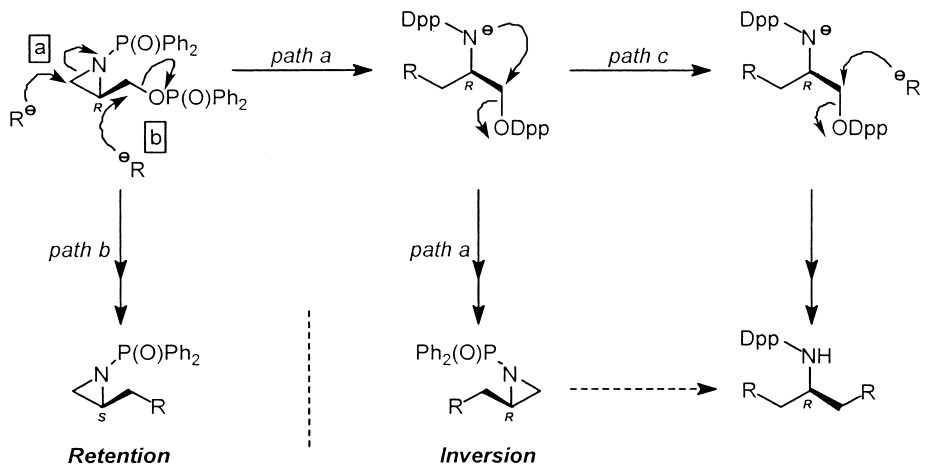


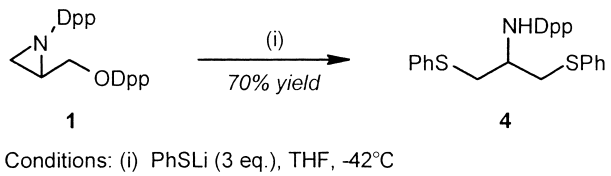
Scheme 2. Mechanistic possibilities in ring-opening of DiDpp.

in situ-generated, trisphosphinylated amide anion **3**, prepared by the introduction of excess sodium hydride to the phosphinylation reaction vessel. The cyclization process is relatively sluggish compared to the phosphinylation, requiring reaction for up to three days at room temperature for complete conversion; elevation of the reaction temperature enhanced the speed of the transformation but at the expense of yield. As might be expected, **1** is extremely polar, but may be purified by standard flash chromatography; using this protocol, gram quantities may be obtained in a few days.

The essence of the proposed reactions of **1** with nucleophiles is captured in Scheme 2. Thus, we anticipated that ring-strain would dominate the synthetic proclivities of DiDpp and, therefore, that **1** would react with a nucleophile firstly by ring-cleavage; the intermediate amide anion thus generated would, we reasoned, react slowly with nucleophiles (due to its negative charge) and would preferentially displace diphenylphosphinate in a manner analogous to that seen in our preparations of a range of *N*-Dpp aziridines, to give a new aziridine (path a). If the diphenylphosphinate leaving group proved more reactive a nucleofuge, then path b would furnish the aziridine antipodal to that generated via path a. There also existed the possibility that the nucleophile might react at least as rapidly with the newly-formed aziridines as with DiDpp, thereby leading to a branched secondary amine as another product of the reaction; such a product would also be observed if the intermediate anion proved amenable to nucleophilic attack (path c). If these reactions were not faster than the initial processes, our proposed method would give entry (if performed upon an enantiomerically-pure sample of DiDpp) to 'non-proteinogenic' (i.e. not derived from naturally-occurring 2-amino-acids) aziridines of high enantiomeric purity, compounds of considerable synthetic potential.

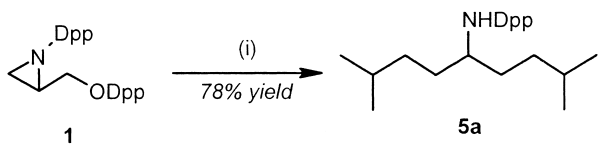
Of course, if ring-cleavage was accompanied by direct displacement of ODpp by a nucleophile as the first step of the reaction, the mechanistic situation would lead to problems in terms of enantiocontrol. Furthermore, convincing data concerning the mechanism would only be forthcoming if enantiomerically-pure DiDpp were employed in the reactions: thus, if either path a or path b were the favoured mechanistic pathways, using an *R*-configured sample we would expect to observe opposite enantiomers depending upon the precise mechanistic course followed.

We first proposed to investigate the reaction of racemic DiDpp with at least 2 equiv. of nucleophiles, assuming that under these conditions double nucleophilic attack would occur, thus avoiding any complication arising from the possibility that the first product of nucleophilic attack might react itself, leading to a range of products. It was, therefore, gratifying to observe that the reaction of DiDpp with an excess of lithium thiophenolate gave a single product, 2-(diphenylphosphinyl)amino-1,3-*bis*(phenylsulfanyl)propane, **4**, in good yield (Scheme 3), demonstrating the validity of our assumption that DiDpp could function effectively as a doubly-electrophilic species.



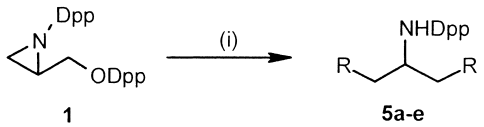
Scheme 3. Reaction of (±)-DiDpp with phenylthiolate.

Of course, it was of more interest to us to assess the reactivity of **1** with carbon-centred nucleophiles and so we proceeded immediately to examine the reaction of DiDpp with Grignard reagents in the presence of sub-stoichiometric amounts of copper(I) bromide, employing the conditions previously developed.[1] When DiDpp reacted in the presence of $CuBr{\cdot}SMe_2$ with 5 equiv. of the Grignard reagent generated from 2-methylbromopropane, a single product (**5a**) was obtained, again arising from double nucleophilic attack, in 78% yield (Scheme 4).



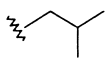
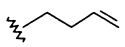
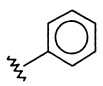
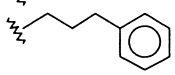
Scheme 4. Reaction of (±)-DiDpp with *iso*butyl magnesium bromide/CuBr.

Table 1. Reaction of (±)-DiDpp with excess copper(I)-modified Grignard reagents



1 5a-e

Conditions:
(i) RMgBr (5 eq.), CuBr•SMe$_2$ (5 mol%), -10°C→reflux , THF

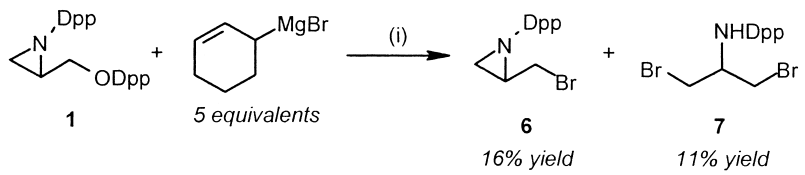
Product	R	Yield (%)
5a		78
5b		75
5c		75
5d[a]		78
5e		70

[a] Chloride used in place of bromide.

nucleophiles. Thus, DiDpp was reacted with a single equivalent of ethylmagnesium bromide in THF, again in the presence of a sub-stoichiometric amount of copper(I), initially at −10°C and subsequently at reflux. After usual aqueous work-up and flash chromatography, a single product, *N*-Dpp-2-propylaziridine, **8a**, was isolated from the reaction, in good yield (Scheme 6).

This reaction demonstrates that there is a pronounced difference in the reactivity of the aziridine and phosphinate electrophilic components, because one might reasonably expect to see a mixture of aziridine and ring-opened products if the two electrophilic centres reacted at a similar rate.

However, since the DiDpp used in the reaction was racemic, no comment could be made concerning the order of events (viz., reaction following path a or path b), but the absence of any other product was, we felt, a very encouraging finding. Similar yields of non-proteinogenic *N*-Dpp aziridines **8b–d** were obtained from reaction of (±)-DiDpp with a range of copper-modified Grignards, as displayed in Table 2. When secondary bromides were used in the reaction, however, the yields of aziridines **8e** and **8f** were significantly lower (by 20–30%) and these products were accompanied by varying



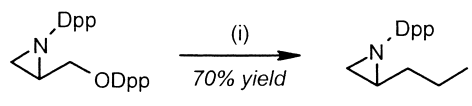
1 5 equivalents 6 7
16% yield 11% yield

Conditions: (i) CuBr•SMe$_2$ (5 mol%), -10°C→reflux , THF

Scheme 5. Reaction of (±)-DiDpp with cyclohex-2-enyl magnesium bromide/CuBr.

The reactions of DiDpp with a range of Grignard reagents proceeded in a similar manner to give amides **5b–e**, summarized in Table 1. Only when the Grignard reagent derived from 3-bromocyclohexene was employed in the process was the reaction not successful (Scheme 5). In this case, bromomethyl aziridine **6** and *N*-Dpp-2-amino-1,3-dibromoethane **7** were obtained from the reaction after column chromatography, in 16 and 11% yields, respectively; when DiDpp was reacted with 1,2-dibromoethane, magnesium and CuBr·SMe$_2$ under identical reaction conditions to those previously employed, **6** was obtained in 60% yield.

Having demonstrated that both the aziridine and phosphinate moieties of DiDpp could act as electrophilic centres, we next turned our attention to the question of which species was more reactive with the cuprates so far employed as

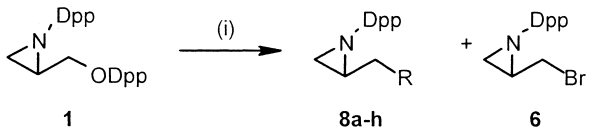


1 8a

Conditions:
(i) EtMgBr (1.1 eq.), CuBr•SMe$_2$ (5 mol%), -10°C→reflux , THF

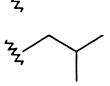
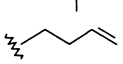
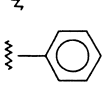
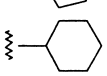
Scheme 6. Reaction of (±)-DiDpp with 1 equiv. of ethyl magnesium bromide in the presence of CuBr.

Table 2. Reaction of (±)-DiDpp with 1 equiv. of copper(I)-modified Grignard reagents



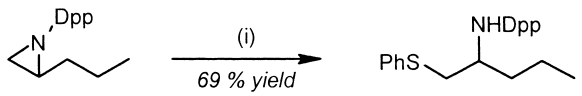
1 8a-h 6

Conditions: (i) RMgBr (1 eq.), CuBr•SMe$_2$ (5 mol%), -10°C→reflux , THF

Aziridine	R	Yield of **8** (%)	Yield of **6** (%)
8a		70	0
8b		52	0
8c		63	0
8d		76	0
8e		42	24
8f		37	25
8g		40	25
8h		31	25

amounts of bromomethylaziridine **6**. A wide variation in reaction conditions was examined in an attempt to minimize the bifurcation in reaction pathway, but the yields shown in Table 2 represent the best attainable in our hands.

Having isolated a range of novel *N*-Dpp aziridines, we next examined their own reactivity with a range of nucleophiles. In the first instance, reaction of aziridine **8a** with phenylthiolate gave the expected ring-opening product (**9**) in good yield (Scheme 7).

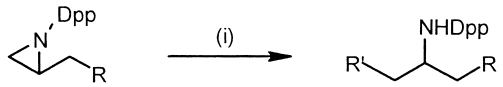


Conditions: (i) PhSLi (3 eq.), THF, -42°C

Scheme 7. Reaction of (±)-**8a** with phenylthiolate.

We next turned our attention to the use of organocuprates; the results of these reactions are gathered in Table 3. Thus, aziridines **8a**–**h** smoothly underwent nucleophilic ring-opening to give a range of secondary amines, **10a**–**i**, in acceptable yield. In these reactions, no side-reactions were observed, even when the nucleophilic component of the reaction was α-branched (entries 2 and 3).

Table 3. Reaction of (±)-DiDpp aziridines **8a**–**h** with copper(I)-modified Grignard reagents



Conditions:
(i) R'MgBr (5 eq.), CuBr•SMe_2 (5 mol%), -10°C→reflux , THF

Entry	Product	R	R′	Yield of **10** (%)
1	**10a**			52
2	**10b**			75
3	**10c**			77
4	**10d**			65
5	**10e**			64
6	**10f**			60
7	**10g**			66
8	**10h**			72
9	**10i**			66

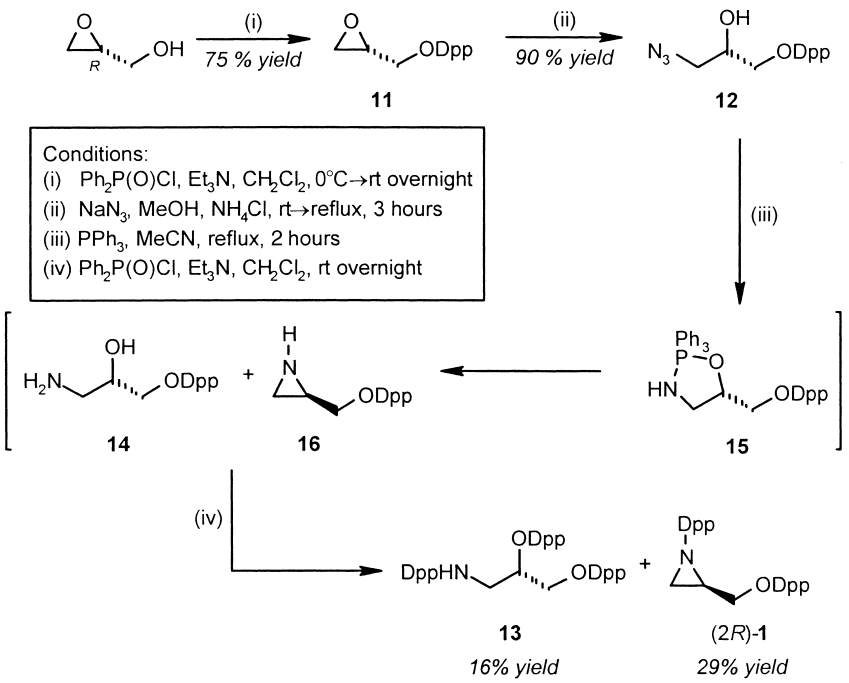
We have referred above to the mechanistic possibilities in the reactions of DiDpp with nucleophiles and have described how these nuances could most easily be revealed by using an enantiomerically-pure DiDpp. Thus, we set out to synthesize (*R*)-DiDpp by the protocol outlined in Scheme 8.

Our synthetic endeavour commenced with the phosphinylation of (*R*)-glycidol; reaction of this commercially-available epoxide with diphenylphosphinic chloride proceeded smoothly to give the corresponding phosphinate (**11**) in 75% yield. We next attempted to ring-open the epoxide with trimethylsilyl azide, using a number of reaction condition reported to effect similar reactions on structurally-related glycidols, but to no avail. Gratifyingly, reaction of **11** with sodium azide proved a very efficient reaction, delivering the desired, ring-opened azide **12** as a colourless solid in excellent yield. Without further purification, this azide was directly converted to (2*R*)-DiDpp by a two-step process; thus, **12** was reacted firstly with triphenylphosphine in refluxing acetonitrile for 2 h and the crude product of this reaction was obtained simply by removal of solvent. This yellow oil was then dissolved in dichloromethane and treated sequentially with triethylamine and diphenylphosphinic chloride and the reaction mixture stirred overnight at room temperature. Following usual work-up and flash chromatography, two highly polar products were obtained from the reaction: these proved to be (2*S*)-*N*,*O*,*O*-tris(diphenylphosphinyl)-1-aminopropane-2,3-diol, **13** (obtained in 16% yield), and (2*R*)-DiDpp (29% yield). Clearly, **13** results from aminodiol **14**, which is itself generated as a by-product of incomplete conversion of oxazaphospholidine **15** to the corresponding aziridine **16**. Despite extensive variation of reaction conditions, little could be done to alter the ratio and yield of these two products.

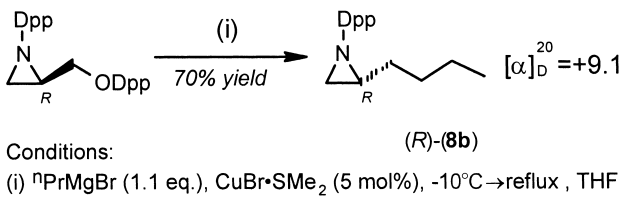
Armed with our enantiomerically-pure aziridine, we next reacted it with the cuprate derived from phenyl magnesium bromide, anticipating that the reaction would furnish 2-benzyl aziridine, whose optical rotation could be compared to the known enantiomerically-pure compound. Unfortunately, the reaction gave a complex mixture of products under a range of conditions; furthermore, this finding was again encountered with other organometallic reagents, thus hindering our mechanistic studies considerably. Finally, we were able to execute an efficient reaction using the cuprate derived from (freshly distilled) 1-bromopropane using the protocol followed for reaction of racemic aziridine; the single product of the reaction was (2*R*)-*N*-Dpp-2-butylaziridine (*R*)-(**8b**), which was obtained in 70% yield after flash chromatography (Scheme 9).

The optical rotation exhibited for this non-aminoacid-derived aziridine was recorded as +9.1 (*c* 5, CH_2Cl_2), which compares well in terms of magnitude with other *N*-Dpp aziridines which had previously been prepared unambiguously from enantiomerically-pure 2-aminoacids (Table 4). The sign of the rotation was, however, the opposite of the values seen for (2*S*)-configured aziridines, suggesting that the product had the opposite absolute stereochemistry of the aminoacid-derived aziridines, i.e. that the aziridine possessed (*R*)-stereochemistry at its single asymmetric centre. Thus we tentatively assigned this stereochemical label to (*R*)-**8b**.

This finding suggests that the mechanistic route followed

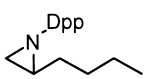
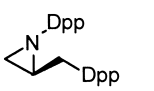
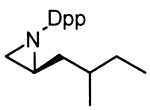
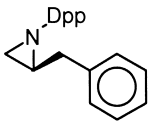
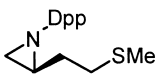


Scheme 8. Synthesis of (2*R*)-DiDpp.



Scheme 9. Ring-opening of (2*R*)-DiDpp.

Table 4. Optical rotation values of optically-active DiDpp aziridines

R	$[\alpha]_D^{23a}$	R	$[\alpha]_D^{23a}$
	+9.1		−1.5
	−15.0[1]		−7.1[1]
	−14.9[1]		−3.7[1]
	−4.6[1]		−10.3[1]

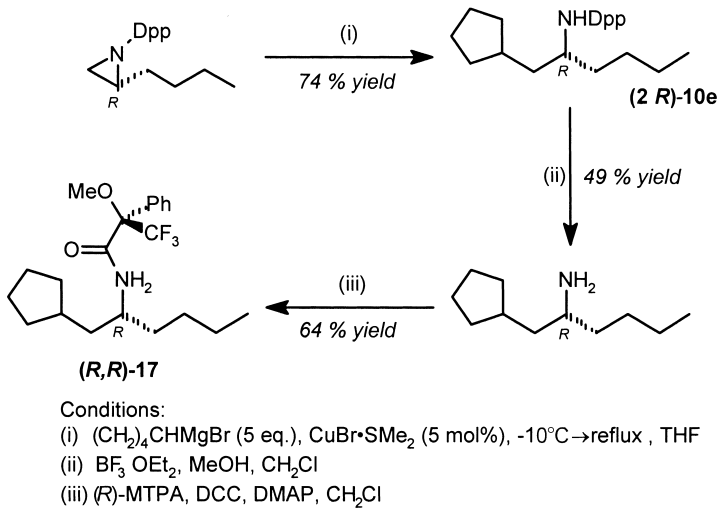
[a] 10^{-1} deg cm^{-2} g^{-1}.

during the reaction is path a, in other words, that the reaction with a single equivalent of Grignard-derived organocuprates proceeds via aziridine ring-opening as the first step; subsequent intramolecular displacement of diphenylphosphinate yields (2*R*)-*N*-Dpp-butylaziridine. As confirmation of this hypothesis (and given that this aziridine was not aminoacid-derived), we next sought to ring-open (*R*)-**8b** and to derivatize the branched primary amine, (2*R*)-**10e**, thus formed in a manner suitable to enable us to ascertain whether the product was enantiomerically-pure. We anticipated that preparation of a Mosher's amide[5] would satisfy our needs, and so we reacted (*R*)-**8b** with an excess of the organocuprate derived from bromocyclopentane: (2*R*)-*N*-Dpp-2-amino-1-(cyclopentyl)hexane, (2*R*)-**10e**, was thus obtained in 74% yield after chromatographic purification. This amine was dephosphinylated and reacted with (*R*)-2-methoxy-2-trifluoromethylphenylacetic acid in the presence of DMAP and DCC, giving (*R*, *R*)-amide **17** (Scheme 10).

The ^{19}F NMR spectrum of this species exhibited a single resonance (δ_F=−68.41); as expected, the amide derived from the racemic amine showed two ^{19}F resonances in its NMR spectrum (δ_F=−68.37 and −68.41) (Fig. 1). Thus, it is clear that the reaction of (2*R*)-DiDpp with the cuprate derived from 1-bromopropane proceeds to give an enantiomerically-pure compound, whose optical properties strongly support an assignment of (2*R*) to the single asymmetric centre. From this, in turn, can be inferred the notion that the reaction of DiDpp with this nucleophile proceeds via a two-step, ring-opening/ring-closure mechanism, indicating that the aziridine is more reactive than the phosphinate (at least when considering reaction with Grignard-derived propylcuprates).

3. Conclusion

We have investigated the ability of *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (DiDpp) (**1**) and showed it to function as a synthetic equivalent for the 2-aminopropane-1,3-dication (**2**). Preliminary results obtained from the reaction of (2*R*)-DiDpp indicate that the mechanism of the reaction with organocuprates proceed via a ring-opening/ring-closing pathway. We are currently



Scheme 10. Preparation of Mosher's amide **17**.

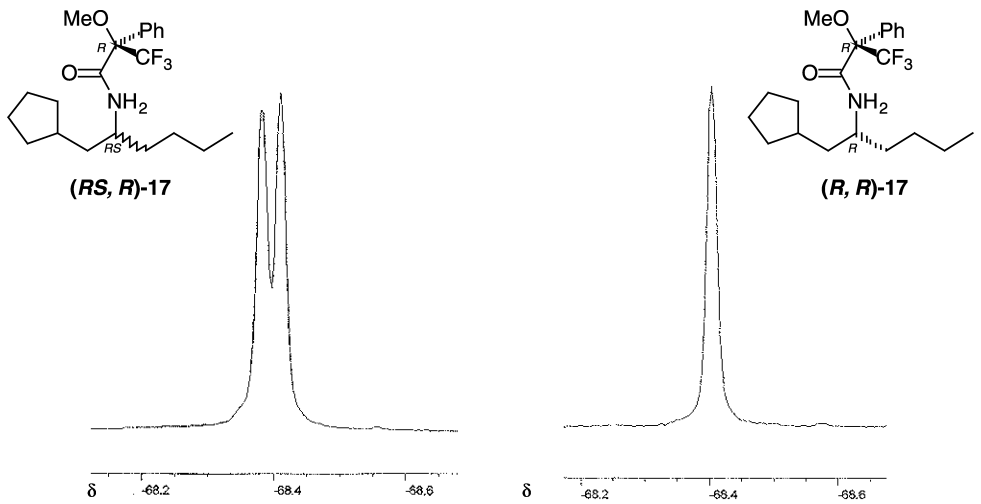


Figure 1. ^{19}F NMR spectra of Mosher's amides (*R*,*R*)-**17** and (*RS*,*R*)-**17**.

engaged in research to strengthen the validity of this conclusion in our laboratory.

4. Experimental

4.1. General

All organic solvents were distilled prior to use and all reagents were purified by standard procedures. Light petroleum refers to the fraction with the boiling range 40–60°C. Diethyl ether and THF were distilled from sodium benzophenone ketyl; toluene from sodium; dichloromethane, triethylamine and acetonitrile from calcium hydride.

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 881 spectrophotometer. Optical rotations were measured at 20°C using the sodium D-line by means of a Perkin–Elmer 241 MC polarimeter and are quoted in 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on a VG9090 mass spectrometer. ^1H and ^{13}C NMR spectra were recorded on Jeol GX-270, Jeol GX-400, and Lambda 300 MHz spectrometers. Unless otherwise stated, deuterochloroform was used as solvent and tetramethylsilane as the internal standard. Chemical shifts in ^1H and ^{13}C NMR spectra are expressed as ppm downfield from tetramethylsilane. ^{13}C Spectra were referenced to $CDCl_3$ when the TMS signal could not be observed. Coupling constants are quoted in Hz. ^{31}P spectra were recorded using a Jeol GX-400 or Lambda 300 MHz spectrometer with chemical shifts reported relative to phosphoric acid. ^{19}F spectra were recorded using a Lambda 300 MHz spectrometer with chemical shifts reported relative to trichlorofluoromethane.

Reactions involving chemicals or intermediates sensitive to air and/or moisture were performed under nitrogen or argon atmosphere in flame or oven dried apparatus. Grignard reagents were prepared in situ, or used as commercially-available solutions in the solvent employed in the reaction. Flash column chromatography was performed using Merck or Fluka Kieselgel 60 silica. Analytical thin layer chromatography (tlc) was performed on precoated Merck kieselgel

60 F_{254} aluminium-backed Plate and visualised under UV light (254 nm) or by staining with an acidic ammonium molybdate spray and acidic potassium permanganate spray.

4.1.1. *N*,*O*-Bis(Diphenylphosphinyl)-2-(hydroxymethyl)-aziridine (1). To a suspension of 2-amino-1,3-propanediol (Aldrich Chemical Co.) (0.5 g, 5.5 mmol), in THF (100 mL), under argon at 0°C was added diphenylphosphinic chloride (3.2 mL, 16.5 mmol), and triethylamine (3.1 mL, 22.0 mmol). A white precipitate of triethylamine hydrochloride was immediately formed. The suspension was stirred for 20 h, after which time sodium hydride (1.0 g, 41.7 mmol), was added at 0°C. This dense grey suspension was stirred at room temperature for a further 72 h. After this time water (1 mL) was added, before filtering through anhydrous magnesium sulfate. The resulting filter cake was washed with 150 mL of ethyl acetate. The solvent was removed under reduced pressure to leave a pale yellow oil. Purification by flash chromatography (1% methanol, EtOAc eluent), afforded a colourless oil. Crystallisation from EtOAc/hexane gave aziridine (**1**) (1.56 g, 60%) as a colourless solid. R_f 0.4 (10% methanol, EtOAc); mp 138–139°C. (Found: C, 68.3; H, 5.4; N, 2.8. $C_{27}H_{25}NO_3P_2$ requires C, 68.5; H, 5.3; N, 3.0%); ν_{max} ($CHCl_3$)/cm^{-1} 2982 (CH), 1438 (PhP), 1132 (P═O), 1022, 834 (aromatic); δ_H (300 MHz, $CDCl_3$), 2.03 (1H, dd, J=3.0, 12.3 Hz, CH of CH_2N), 2.58 (1H, dd, J=6.0, 15.8 Hz, CH of CH_2N) 3.04–3.19 (1H, m, CHN), 3.89–3.97 and 4.19–4.23 (2H, 2×m, CH_2ODpp), 7.27–7.95 (20H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 26.85, (CH_2N), 34.13, (CHN), 65.69, (CH_2ODpp), 128.8 131.5; δ_P (161.9 MHz), 31.91 and 32.68; *m*/*z* (CI), 474 (MH^+, 95%), 419 (9), 274 (M−$Ph_2P(O)$, 9), 219 (100), 201 ($Ph_2P(O)$, 41). (Found: $[MH]^+$ 474.1376. $C_{27}H_{25}NO_3P_2$ requires $[MH]^+$ 474.1387).

4.1.2. 2-(Diphenylphosphinamido)-1,3-bis(thiophenyl)-propane (4). To a solution of thiophenol (0.07 g, 0.6 mmol) in THF (8 mL), under argon at −42°C, was added BuLi (0.26 mL, 2.65 M, 0.6 mmol) dropwise. The solution was stirred at −42°C for 0.5 h, after which time a solution of *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)-aziridine (0.1 g, 0.2 mmol) in THF (2 mL) was added. The solution was gradually allowed to warm to ambient temperature and then stirred overnight. The reaction mixture was partitioned between H_2O (10 mL), and EtOAc (2×15 mL), the organic layer separated and washed with brine (15 mL), dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure to leave a yellow oil. Purification by flash chromatography (EtOAc/light petroleum 1:1), gave (**4**) (0.07 g, 70%) as a colourless solid. R_f 0.5 (EtOAc); mp 142°C. (Found: C, 67.9; H, 5.5; N, 2.85. $C_{27}H_{26}NOPS_2$ requires C, 68.2; H, 5.5; N, 2.95%); ν_{max}/cm^{-1} 2980 (CH), 1438 (PhP), 1124 (P═O) 1056, 844, 696 (aromatic); δ_H (270 MHz, $CDCl_3$), 1.71 (1H, br s, NH), 3.21 (2H, dd, J=6.6, 13.9 Hz, 2×CH of CH_2SPh), 3.47–3.51 (3H, m, 2×CH of CH_2SPh and CHN); δ_C (67.5 MHz, $CDCl_3$), 38.32 and 38.34 (2×CH_2), 50.18 (CHN), 126.09, 128.50 (d, J=13.0 Hz), 129.03, 131.9, 135.35; δ_P (161.9 MHz) 21.96; *m*/*z* (CI), 476.49 (MH^+, 100%), 352.34 (55), 218.21 (66), 201 ($Ph_2P(O)$, 50). (Found: $[MH]^+$ 476.1280. $C_{27}H_{26}NOPS_2$ requires $[MH]^+$ 476.1272).

4.2. General method for copper-modified Grignard reactions using excess of Grignard reagent

To copper(I) bromide dimethylsulfide complex (5 mol%), under argon, at ambient temperature was added a solution of *N*-diphenylphosphinylaziridine in THF, (typically 1.0 mmol in 15 mL). The solution was then cooled to −10°C, and a solution of Grignard reagent (5 equiv.) in THF (5 mL), added dropwise. The resulting yellow solution was then warmed to room temperature, before being refluxed for 30 min, during which time the reaction mixture turned black. Upon cooling to room temperature the reaction was quenched with saturated ammonium chloride solution (30 mL), and partitioned with EtOAc, (30 mL, and then 2×10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The products were purified by flash chromatography.

4.2.1. 2,8-Dimethyl-5-(diphenylphosphinamido)nonane (5a). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (**1**) (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and 2-methylpropylmagnesium bromide (5 equiv.), prepared from magnesium (0.13 g, 5.4 mmol), and 1-bromo-2-methylpropane (0.6 mL, 5.3 mmol), were reacted in THF (20 mL), to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**5a**) (0.31 g, 78%) as a colourless solid. R_f 0.6 (EtOAc); mp 131–132°C. (Found: C, 74.4; H, 9.4; N, 3.6. $C_{23}H_{34}NOP$ requires C, 74.4; H, 9.2, N, 3.8%); ν_{max}/cm^{-1}, 3201 (NH), 2868 (CH), 1435 (PhP), 1187 (P═O), 722 and 694 (aromatics); δ_H (270 MHz, $CDCl_3$) 0.83 and 0.86 (12H, 2×d, J=2.2 Hz, $CH(CH_3)_2$), 1.10–1.26 (4H, m, 2×CH_2-$CH(CH_3)_2$), 1.41–1.52 (6H, m, 2×CH_2CHN, and $CH(CH_3)_2$), 2.62 (1H, dd, J=5.9, 10.6 Hz, NH), 3.01–3.10 (1H, m, CHN), 7.39–7.52 (6H, m, ArH), and 7.87–7.96 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$); 22.30 and 22.90 (4×CH_3), 27.66 and 27.95 (2×$CH(CH_3)_2$), 33.98 and 34.17 (4×CH_2), 51.51 (CH), 128.1 131.5, 133.13 (d, J=128.6 Hz); δ_P (121.4 MHz, $CDCl_3$) 21.49; *m*/*z* (CI) 372 (MH^+, 100%), 300 (57), 294 (26), 201 (12). (Found: $[MH]^+$ 372.2456. $C_{23}H_{34}NOP$ 2456).

4.2.2. 6-(Diphenylphosphinamido)undeca-1,10-diene (5b). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (**1**) (0.5 g, 1.06 mmol), copper(I) bromide dimethylsufide complex (0.01 g, 0.05 mmol) and but-4-enyl magnesium bromide (5 equiv.), prepared from magnesium (0.13 g, 5.35 mmol), and 4-bromobutene (0.54 mL, 5.3 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**5b**) (0.30 g, 76%) as a colourless solid. R_f 0.5 (EtOAc); mp 89–90°C. (Found C, 75.3; H, 8.3; N, 3.7. $C_{23}H_{30}NOP$ requires C, 75.2; H, 8.2; N, 3.8%); ν_{max}/cm^{-1} 3191 (NH), 2929 (CH), 1641 (C═C), 1435 (PhP), 1183, 1123 (P═O), 723, 694 (aromatics); δ_H (400 MHz, $CDCl_3$), 1.18–1.63 (8H, m, 4×CH_2), 1.87–2.15 (4H, m, 2×CH_2), 2.69 (1H, dd, J=4.5, 11.5 Hz, CHNH), 3.02–3.18 (1H, m, CHNH), 4.91–5.03 (4H, m, CH═CH_2), 5.64–5.84 (2H, m, CH═CH_2), 7.38–7.98 (10H, m, ArH);

δ_C (67.5 MHz, $CDCl_3$), 24.25 ($CH_2{=}CHCH_2CH_2CH_2$), 32.93 and 35.04 ($CH_2{=}CHCH_2CH_2CH_2$), 51.03 (CHNH), 114.18 ($CH{=}CH_2$), 128.13 (d, J=10.7 Hz), 131.8, 132.9, 138.78 ($CH{=}CH_2$); δ_P (161.7 MHz, $CDCl_3$), 21.32; *m/z* (CI) 368 (MH^+, 43%), 298 (36), 201 (17) 83 (100). (Found: $[MH]^+$ 368.2140, $C_{23}H_{30}NOP$ requires $[MH]^+$ 368.2143).

4.2.3. 1,3-Diphenyl-2-(diphenylphosphinamido)propane (5c). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (**1**), (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and phenyl magnesium bromide (5 equiv.), prepared from magnesium (0.13 g, 5.35 mmol), and bromobenzene (0.52 mL, 5.3 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**5c**) (0.33 g, 75%), as a colourless solid. R_f 0.4 (EtOAc); mp 138–139°C. (Found C, 78.8; H, 6.6; N, 3.4. $C_{27}H_{26}NOP$ requires C, 78.8; H, 6.4; N, 3.4%); ν_{max}/cm^{-1} 3169 (NH), 2924 (CH), 1438 (PhP), 1188, 1123 (P═O), 749, 723 (aromatic); δ_H (400 MHz, $CDCl_3$), 2.73 (1H, br dd, J=5.8, 11.5 Hz, NH), 2.81 (2H, dd, J=6.4, 13.4 Hz, CH of CH_2Ph), 2.93 (2H, dd, J=5.6, 13.4 Hz, CH of CH_2Ph), 3.46–3.54 (1H, m, CHNH) 7.18–7.54 (20H, m, ArH); δ_C (100 MHz, $CDCl_3$), 42.82 and 42.88 (2×CH_2), 42.70 (CH), 126.36, 128.29 (d, J=13.0 Hz), 128.32, 129.93, 131.49 (d, J=3.0 Hz), 132.0, 138.34; δ_P (161.9 MHz, $CDCl_3$), 21.40; *m/z* (CI) 412 (MH^+, 100%), 334 (12), 320 (24), 201 (Ph_2PO). (Found: $[MH]^+$ 412.1817, $C_{27}H_{26}NOP$ requires $[MH]^+$ 412.1830).

4.2.4. 2,6-Dimethyl-4-(diphenylphosphinamido)heptane (5d). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (**1**), (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and 2-(methyl)ethylmagnesium chloride, (2.7 mL, 2.0 M, 5.3 mmol) were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**5d**) (0.26 g, 72%). R_f 0.45 (EtOAc); mp 162°C. (Found C, 73.45; H, 9.0; N, 4.1. $C_{21}H_{30}NOP$ requires C, 73.4; H, 8.8; N, 4.1%); ν_{max}/cm^{-1} 3145 (NH), 2957 (CH), 1437 (PhP), 1186, 1123 (P═O), 727, 696 (aromatic); δ_H (400 MHz, $CDCl_3$), 0.72–0.81 (12H, m, 4×CH_3), 1.25–1.42 (4H, m, 2×$CH(CH_3)_2$, and one CH from each CH_2CH(NHDpp)), 1.71–1.83 (2H, m, 2×CH, CH_2CH(NHDpp)), 2.53 (1H, dd, J=5.1, 10.6 Hz, NH), 2.95–3.10 (1H, m, CH), 7.4–7.55 and 7.85–8.00 (10H, ArH); δ_C (100 MHz, $CDCl_3$), 22.68 and 24.73 (4×CH_3), 24.27 (2×$CH(CH_3)_2$), 47.72 and 47.76 (2×CH_2), 48.47 (CH(NHDpp)), 128.38 (d, J=13.6 Hz), 131.70 (d, J=2.4 Hz), 132.35 (d, J=9.3 Hz), 133.13 (d, J=128.7 Hz); δ_P (100 MHz, $CDCl_3$), 20.82; *m/z* (CI) 344 (MH^+, 100%), 286 (48), 266 (15), 218 (11), 201 (Dpp, 11%). (Found: $[MH]^+$ 344.2149. $C_{21}H_{30}NOP$ requires $[MH]^+$ 344.2143).

4.2.5. 1,9-Diphenyl-5-(diphenylphosphinamido)nonane (5e). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (**1**), (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and 3-phenylpropylmagnesium bromide (5 equiv.), prepared from magnesium (0.13 g, 5.4 mmol), and 1-bromophenylpropane (0.8 mL, 5.3 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), afforded (**5d**) (0.56 g, 70%) as a colourless solid. R_f 0.5 (EtOAc); mp 84–85°C. (Found: C, 80.2; H, 8.0; N, 2.7. $C_{33}H_{38}NOP$ requires C, 80.0; H, 7.7; N, 2.8%); ν_{max}/cm^{-1} 3202 (NH), 2929 (CH), 1434 (PhP), 1188, 1123 (P═O), 748, 697 (aromatic); δ_H (400 MHz, $CDCl_3$), 1.26–1.41 and 1.49–1.59 (12H, m, 6×CH_2), 2.52–2.64 (5H, m, 2×CH_2 and NH), 2.97–3.10 (1H, m, CHNHDpp), 7.10–7.50 (16H, m, ArH), and 7.84–7.90 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$), 25.0 (CH_2CH_2-Ph), 31.2 ($CH(NH)CH_2CH_2$), 35.7 ($CH(NH)CH_2CH_2$), 36.6 (CH_2Ph), 51.4 (CHNH), 125.56, 128.3, 131.5, 132.12 (d, J=9.1 Hz), 133.0 (d, J=129.0 Hz), 142.44; δ_P (121.4 MHz, $CDCl_3$) 21.37; *m/z* (CI) 496 (MH^+, 100%), 418 (8), 362 (28), 201 (Ph_2PO, 9). (Found: $[MH]^+$ 496.2778, $C_{33}H_{38}NOP$ requires $[MH]^+$ 496.2769).

4.2.6. *N*-Diphenylphosphinyl-2-(bromomethyl)aziridine (6) and 1,3-dibromo-2-(diphenylphosphinamido)propane (7). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)-aziridine (**1**) (1.4 g, 3.0 mmol), copper(I) bromide dimethylsulfide complex (0.03 g, 0.15 mmol) and cyclohexenemagnesium bromide (5 equiv.), prepared from magnesium (0.37 g, 15.3 mmol), and 3-bromocyclohexene (1.7 mL, 14.8 mmol), were reacted in THF to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave 1,3-dibromo-2-(diphenylphosphinamido)propane (**7**) (0.16 g, 11%) as a colourless solid. R_f 0.5 (EtOAc); mp 154–156°C. (Found C, 43.3; H, 4.2; N, 3.2. $C_{15}H_{16}NOPBr_2$ requires C, 43.2 H, 3.9 N, 3.4%); ν_{max}/cm^{-1} 3122 (NH), 2872 (CH), 1438 (PhP), 1180, 1125 (P═O), 839, 697 and 691 (aromatic); δ_H (400 MHz, $CDCl_3$), 3.52 (2H, d, broad, J=6.3 Hz, CHNH), 3.61–3.63 (2H, m, CH_2Br), 3.83 and 3.85 (2H, 2×br s, CH_2Br), 7.44–7.56 (6H, m, ArH), and 7.79–7.93 (4H, m, ArH); δ_H D_2O shake, (270 MHz, $CDCl_3$), 3.47–3.57 (1H, m, CHNH), 3.63 (2H, dd, J=6.6, 10.3 Hz, CH of CH_2Br), 3.84 (2H, dd, J=3.4, 10.3 Hz, CH of CH_2Br), 7.41–7.59 (6H, m, ArH), and 7.79–8.05 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$), 36.10 and 36.16 (2×CH_2Br), 51.10 (CHNH), 128.5 131.5; δ_P (161.9 MHz, $CDCl_3$), 22.91; *m/z* (FAB), [calcd(obs.)], 421 [5.4 (5.5)], 420 [31.9 (31.5)], 419 [11.1 (11)], 418[64 (64)], 417[5.7 (5.5)], 416[32.6 (32.5)], 247 (65), 201 (100, Ph_2PO); *m/z* (CI) 418 (MH^+, 5%), 338 (M−Br, 8), 201 (7) 83 (100). (Found: $[MH]^+$ 417.9414. $C_{15}H_{16}NOPBr_2$ requires $[MH]^+$ 417.9394).

Further elution, (gradient 60–100% EtOAc in light petroleum), gave *N*-diphenylphosphinyl-2-(bromomethyl)-aziridine (**6**) (0.11 g, 16%), as an unstable pale yellow oil. R_f 0.4 (EtOAc); ν_{max}/cm^{-1} 3057 (CH), 1203, 1126 (P═O), 727, 695 (aromatic); δ_H (400 MHz, $CDCl_3$), 2.10 (1H, dd, J=3.2, 12.5 Hz, CH of CH_2N), 2.70 (1H, dd, J=5.9, 16.8 Hz, CH of CH_2N), 3.04–3.11 (1H, m, CHN), 3.35 (2H, d, J=6.1 Hz, CH_2Br), 7.45–7.96 (10H, m, ArH); δ_C (67.5 MHz, $CDCl_3$), 30.10 (CH_2Br), 32.88 (CH_2N), 35.45 (CHN), 128.5 131.7; δ_P (161.9 MHz, $CDCl_3$), 31.59; *m/z* (FAB), 338 and 336 (bromine isotope pattern, 79%), 256 (M−Br, 12%), 201 (Ph_2PO, 100%); *m/z* (CI) 338 and 336 (16%), 258 (40), 201 (9) 79 (100). (Found: $[MH]^+$ 336.0148, $C_{15}H_{15}NOPBr$ requires $[MH]^+$ 336.0153).

4.3. General method for copper-modified Grignard reactions using 1 equiv. of Grignard reagent

N,*O*-Bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (typically 1 mmol), and copper(I) bromide dimethylsulfide complex (5 mol%) were dissolved in THF (10 mL), and cooled to approximately −10°C. A solution of freshly prepared Grignard reagent in THF (5 mL), was then added dropwise (1.1 equiv.). The resulting yellow solution was warmed to room temperature over 30 min, and then heated to reflux for 30 min, during which time the reaction mixture often turned black. Upon cooling to room temperature the reaction was quenched with saturated ammonium chloride solution (20 mL), and partitioned with EtOAc (50 mL, and then 2×15 mL) the combined organic layers were then washed with brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The products were purified by flash chromatography.

4.3.1. *N*-Diphenylphosphinyl-2-propylaziridine (8a). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.2 mmol), and bromoethane (0.09 mL, 1.16 mmol) were reacted together in THF to produce a pale yellow oil, which was purified by flash chromatography (gradient 20–60% EtOAc in light petroleum), to give (**8a**) (0.21 g, 70%) as a colourless oil. R_f 0.3 (EtOAc); ν_{max}/cm^{-1} 2929 (CH), 1437 (PhP), 1202, 1125 (P═O), 727, 696 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.80 (3H, t, *J*=7.5 Hz, CH_3), 1.19–1.54 (4H, m, CH_3CH_2-CH_2), 1.92 (1H, dd, *J*=2.2, 12.5 Hz, CH of CH_2N), 2.58 (1H, dd, *J*=5.9, 16.9 Hz, CH of CH_2N), 2.68–2.74 (1H, m, CHN), 7.37–7.51 (6H, m, ArH), and 7.88–7.96 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 14.13 (CH_3), 20.10, 29.56, (2×CH_2), 34.64 (CH_2N), 35.37 (CHN), 128.3 131.7, 133.08 and 133.15 (d, *J*=122.2 Hz); δ_P (161.9 MHz) 31.95; *m*/*z* (CI) 286 (MH^+, 100%), 272 (7), 208 (27), 201 ($Ph_2P(O)$, 9). (Found: $[MH]^+$ 286.1355, $C_{17}H_{20}NOP$ requires $[MH]^+$ 286.1360).

4.3.2. *N*-Diphenylphosphinyl-2-butylaziridine (8b). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (0.75 g, 1.59 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.04 g, 1.9 mmol), and bromopropane (0.16 mL, 1.74 mmol) were reacted together in THF to produce a pale yellow oil, which was purified by flash chromatography (gradient 20–80% EtOAc in light petroleum), to give (**8b**) (0.31 g, 66%) as a colourless oil. R_f 0.4 (EtOAc); ν_{max}/cm^{-1} 2956 (CH), 1438 (PhP), 1203, 1125 (P═O), 727, 696 (aromatic); δ_H (400 MHz, $CDCl_3$), 0.77 (3H, t, *J*=7.1 Hz, CH_3CH_2), 1.17–1.36 (4H, m, $CH_3CH_2CH_2$), 1.47–1.52 (2H, m, CH_2CHN), 1.91 (1H, ddd, *J*=1.2, 3.4, 12.5 Hz, CH of CH_2N), 2.53 (1H, ddd, *J*=1.2, 6.1, 17.4 Hz, CH of CH_2N), 2.65–2.74 (1H, m, CHN), 7.41–7.51 (6H, m, ArH), and 7.90–7.95 (4H, m, ArH); δ_C (75 MHz, $CDCl_3$), 13.72 (CH_3), 22.25, 28.80 ($CH_3CH_2CH_2$) 29.44 (CH_2CHN), 32.06 (CH_2N, d, *J*=4.2 Hz) 35.51 (CHN, d, *J*=6.2 Hz), 128.3 131.4, 132.81 and 132.87 (2×d, *J*=127.1 Hz); δ_P (161.9 MHz, $CDCl_3$) 31.78; *m*/*z* (CI) 300 (MH^+, 100%), 222 (18), 218 (14), 98 (5), 83 (14). (Found: $[MH]^+$ 300.1509, $C_{18}H_{22}NOP$ requires $[MH]^+$ 300.1517).

4.3.3. *N*-Diphenylphosphinyl-2-(3-methylbutyl)aziridine (8c). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.27 mmol), and 1-bromo-2-methylpropane (0.13 mL, 1.16 mmol) were reacted together in THF to produce a yellow oil. Purification by flash chromatography (gradient 20–50% EtOAc in light petroleum), gave (**8c**) (0.21 g, 63%) as a pale yellow oil. R_f 0.5 (EtOAc); ν_{max}/cm^{-1}, 2955 (CH), 1438 (PhP), 1203, 1125 (P═O), 727, 696 (aromatics); δ_H (270 MHz, $CDCl_3$), 0.73–0.75 and 0.77–0.79 (6H, 2×d, *J*=6.6 Hz, $CH(CH_3)_2$), 1.00–1.12 (2H, m, $(CH_3)2CHCH_2CH_2$), 1.37–1.62 (3H, m, $(CH_3)2CHCH_2CH_2$), 1.92 (1H, ddd, *J*=1.1, 3.6, 12.5 Hz, CH of CH_2N), 2.53 (1H, ddd, *J*=1.1, 5.9, 17.6 Hz, CH of CH_2N) 2.61–2.73 (1H, m, CHN), 7.40–7.50 (6H, m, ArH), and 7.89–7.97 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 21.88 and 22.14 (2×CH_3), 27.03 ($CH(CH_3)_2$), 27.60 and 29.13 (2×CH_2), 29.22 (CH_2N), 35.32 (CHN), 128.1, 131.5; δ_P (161.9 MHz, $CDCl_3$), 31.78; *m*/*z* (CI) 314 (MH^+, 100%), 298 (5), 236 (27), 201 (7). (Found: $[MH]^+$ 314.1680. $C_{19}H_{24}NOP$ requires $[MH]^+$ 314.1674).

4.3.4. *N*-Diphenylphosphinyl-2-(pent-4-enyl)aziridine (8d). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.27 mmol), and 4-bromobut-1-ene (0.12 mL, 1.16 mmol) were reacted together in THF to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**8d**) (0.25 g, 76%) as a clear oil. R_f 0.4 (EtOAc); ν_{max}/cm^{-1}, 2931 (CH), 1438 (PhP), 1203, 1125 (P═O), 727, 696 (aromatic); δ_H (400 MHz, $CDCl_3$), 1.22–1.59 (4H, m, CH_2═$CHCH_2CH_2$), 1.86–2.04 (3H, m, CH of CH_2N and CH_2CHN), 2.55 (1H, ddd, *J*=1.4, 6.0, 15.4 Hz, CH of CH_2N), 2.66–2.67 (1H, m, CHN), 4.87–4.93 (2H, m, CH═CH_2), 5.60–5.73 (1H, m, CH═CH_2), 7.41–7.52 (6H, m, ArH), and 7.89–7.95 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$), 25.60, 29.24, 31.84, 35.34 (4×CH_2), 36.35 (CHN, d, *J*=6 Hz), 114.74 (CH═CH_2), 128.30 (d, *J*=12.1 Hz), 131.7, 132.7 and 132.8 (2×d, *J*=122.9 Hz), 138.30 (CH═CH_2); δ_P (121.4 MHz, $CDCl_3$), 32.00; *m*/*z* (CI) 312 (MH^+, 100%), 298 (9), 201 (15) 83 (12). (Found: $[MH]^+$ 312.1512. $C_{19}H_{22}NOP$ requires $[MH]^+$ 312.1517).

4.3.5. *N*-Diphenylphosphinyl-2-benzylaziridine (8e).[1] By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.26 mmol), and bromobenzene (0.12 mL, 1.16 mmol) were reacted together in THF to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**8e**) (0.15 g, 42%) as a colourless solid. Mp 103–104°C (lit.[1] 103–105°C); R_f 0.5 (EtOAc); δ_H

(270 MHz, $CDCl_3$), 2.03 (1H, ddd, J=1.2, 3.3, 12.5 Hz, CH of CH_2N), and 2.58 (1H, ddd, J=1.2, 5.9, 17.3 Hz, CH of CH_2N), 2.82 (2H, d, J=5.6 Hz, $PhCH_2$), 2.95–3.07 (1H, m, CHN), and 7.06–7.56 (11H, m, ArH), and 7.72–8.04 (4H, m, ArH).

4.3.6. *N*-Diphenylphosphinyl-2-(2-methylpropyl)aziridine (8f). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)-aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.27 mmol), and 2-bromopropane (0.11 mL, 1.16 mmol) were reacted together in THF to produce a yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in light petroleum), gave (**8g**) (0.12 g, 37%) as a colourless solid. R_f 0.4 (EtOAc); mp 62–64°C. (lit.[1] 65–66°C); ν_{max}/cm^{-1} 2956 (CH), 1438 (PhP), 1203, 1125 (P═O), 727, 696 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.76 and 0.83 (6H, 2×d, J=6.2 Hz, $CH(CH_3)_2$), 1.22–1.30 (1H, m, $CH(CH_3)_2$), 1.49–1.58 (2H, m, CH_2CHN), 1.93 (1H, ddd, J=1.1, 3.7, 12.5 Hz, CH of CH_2N), 2.72 (1H, ddd, J=1.1, 5.9, 17.8 Hz, CH of CH_2N), 2.68–2.78 (1H, m, CHN), 7.40–7.53 (6H, m, ArH), and 7.88–7.97 (4H, m, ArH).

4.3.7. *N*-Diphenylphosphinyl-2-(cyclopentylmethyl)aziridine (8g). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)-aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.27 mmol), and cyclopentyl bromide (0.12 mL, 1.16 mmol) were reacted together in THF to produce a yellow solid. Purification by flash chromatography (gradient 20–80% EtOAc in light petroleum), gave (**8g**) (0.14 g, 40%) as a colourless solid. R_f 0.5 (EtOAc); mp 80–81°C. (Found: C, 73.7; H, 7.4; N, 4.0. $C_{20}H_{24}NOP$ requires C, 73.8; H, 7.4; N, 4.3). ν_{max}/cm^{-1} 2949 (CH), 1438 (PhP), 1203, 1125 (P═O), 727, 695 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.98–1.64 (11H, m, 4×CH_2, CH, ring, and CH_2), 1.90 (1H, ddd, J=1.3, 3.5, 12.5 Hz, CH of CH_2N) 2.55 (1H, ddd, J=1.3, 5.9, 17.6 Hz, CH of CH_2N), 2.64–2.78 (1H, m, CHN), 7.39–7.52 (6H, m, ArH), and 7.88–7.98 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$), 24.62, 29.82, 31.95, 32.62 (4×CH_2 ring), 34.85 (CH, ring), 38.17 (CH_2N), 38.68 (CHN, d, J=5.2 Hz) 128.21 (d, J=12.8 Hz), 131.5, 132.86 and 132.96 (2×d, J=126.4 Hz); δ_P (121.4 MHz, $CDCl_3$) 31.96; *m*/*z* (CI) 326 (MH^+, 100%), 248 (27), 203 (35), 79 (55). (Found: $[MH]^+$ 326.1680. $C_{20}H_{24}NOP$ requires $[MH]^+$ 326.1674).

4.3.8. *N*-Diphenylphosphinyl-2-(cyclohexylmethyl)aziridine (8h). By following the general procedure described above *N*,*O*-bis(diphenylphosphinyl)-2-(hydroxymethyl)-aziridine (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.27 mmol), and cyclohexylbromide (0.14 mL, 1.16 mmol) were reacted together in THF to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**8h**) (0.11 g, 31%) as a colourless solid. R_f 0.5 (EtOAc); mp 101–103°C. (Found: C, 74.1; H, 7.9; N, 3.9. $C_{21}H_{26}NOP$ requires C, 74.3; H, 7.7; N, 4.1%); ν_{max}/cm^{-1} 2923 (CH), 1438 (PhP), 1203, 1126 (P═O), 727, 696 (aromatic); δ_H (270 MHz, $CDCl_3$) 0.74–1.57 (13H, m, hexyl ring, and CH_2CHN), 1.90 (2H, 2×ddd, J=1.1, 3.3 Hz, 12.5, CH of CH_2N), 2.54 (1H, ddd, J=1.1, 5.9, 17.5 Hz, CH of CH_2N), 2.71–2.80 (1H, m, CHN), 7.40–7.53 (6H, m, ArH), and 7.88–7.97 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 25.57, 25.85, 25.98, 33.38 and 33.57 (5×CH_2 cyclohexyl ring), 29.79 (CH cyclohexyl ring), 32.14 (CH_2), 35.89 (CH_2N), 40.10 (CHN, d, J=5.0 Hz), 128.1 (d, J=12.8 Hz), 131.4, 132.73 and 132.82 (2×d, J=126.4 Hz); δ_P (161.9 MHz, $CDCl_3$), 31.79; *m*/*z* (CI) 340 (MH^+, 100%), 262 (24), 201 (8), 79 (17). (Found: $[MH]^+$ 340.1833. $C_{21}H_{26}NOP$ requires $[MH]^+$ 340.1830).

4.4. Ring-opening of aziridines 8a–h

4.4.1. 2-(Diphenylphosphinamido)-1-(thiophenyl)pentane (9). To a solution of thiophenol (0.15 mL, 2.1 mmol) in THF (8 mL), under argon at −42°C, was added BuLi (0.9 mL, 2.5 M, 2.3 mmol) dropwise. The solution was stirred at −42°C for 0.5 h, after which time a solution of *N*-diphenylphosphinyl-2-propylaziridine (**8a**) (0.2 g, 0.7 mmol) in THF (2 mL) was added. The solution was then gradually warmed to room temperature over 3–4 h, before being partitioned between H_2O (10 mL), and EtOAc (2×10 mL), the combined organic layers washed with brine (15 mL), dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to leave a yellow oil. Purification by flash column chromatography, (gradient 0–50% EtOAc in light petroleum), gave (**9**) (0.19 g, 69%) as a pale yellow oil. R_f 0.6 (EtOAc); ν_{max} ($CHCl_3$)/cm^{-1} 3361 (NH), 2958 (CH), 1439, 1176, 1124 (P═O), 1025, 875 (aromatics); δ_H (400 MHz, $CDCl_3$), 0.82 (3H, t, J=7.1 Hz, CH_3), 1.16–1.78 (4H, m, $CH_3CH_2CH_2$), 3.09–3.14, (2H, m, CH of CH_2SPh and CHNH), 3.27–3.38 (2H, m, CH of CH_2SPh and CHNH), 7.13–7.52 (11H, m, ArH), and 7.79–7.88 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 13.84 (CH_3), 19.05 (CH_2CH_3), 38.0 (CH_2CHNH), 40.95 (CH_2SPh), 50.86 (CHNHDpp), 126.04, 128.48 (d, J=12.8 Hz), 128.96, 129.37, 132.3, 136.26; *m*/*z* (CI) 396 (MH^+, 100%), 272 (86), 218 (32), 201 (40), 111 (44). (Found: $[MH]^+$: 396.1538, $C_{23}H_{25}NOPS$ requires $[MH]^+$ 396.1551).

4.4.2. 2-(Diphenylphosphinamido)octane (10a). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-propylaziridine (**8a**) (0.5 g, 1.8 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and propylmagnesium bromide (5 equiv.), prepared from magnesium (0.22 g, 8.9 mmol), and 1-bromopropane (0.8 mL, 8.8 mmol), were reacted together in THF (20 mL) to produce a yellow solid. Purification by flash chromatography (gradient 20–50% EtOAc in light petroleum), gave (**10a**) (0.30 g, 52%) as a colourless solid. R_f 0.6 (EtOAc); mp 81–82°C. (Found: C, 72.7; H, 8.8; N, 4.3. $C_{20}H_{28}NOP$ requires C, 72.9; H, 8.6; N, 4.25%); ν_{max} (CCl4)/cm^{-1} 3370 (NH), 2966, 2932 (CH), 1124, 1024 (PO), 624 (aromatic); δ_H (270 MHz, $CDCl_3$) 0.78–0.89 (6H, m, 2×CH_3), 1.25–1.54 (10H, m, 5×CH_2), 2.67 (1H, dd, J=5.5, 16.7 Hz, NH), 3.00–3.10 (1H, m, CHN), 7.41–7.51 (6H, m, ArH) and 7.88–7.95 (4H, m,

ArH); δ_C (67.5 MHz, $CDCl_3$), 13.82 and 13.91 (2×CH_3), 18.49, 22.46, 35.19, 36.40, 45.92 (5×CH_2), 128.4, 131.9; δ_P (121.4 MHz, $CDCl_3$), 21.40; *m/z* (CI), 330 (MH^+, 100%), 286 (20), 272 (19), 252 (18), 201 (8), 79 (15). (Found: $[MH]^+$ 330.1978. $C_{20}H_{28}NOP$ requires $[MH]^+$ 330.1987).

4.4.3. 1-Cyclopentyl-2-(diphenylphosphinamido)pentane (10b). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(cyclopentylmethyl)-aziridine (**8g**) (0.4 g, 1.2 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and ethylmagnesium bromide (5 equiv.), prepared from magnesium (0.15 g, 6.2 mmol), and bromoethane (0.5 mL, 6.1 mmol), were reacted together in THF (20 mL) to produce a colourless solid. Purification by flash chromatography (gradient 20–50% EtOAc in light petroleum), provided (**10b**) (0.32 g, 75%) as a colourless solid. R_f 0.4 (EtOAc); mp 105–107°C. (Found C, 74.6; H, 8.8; N, 3.9. $C_{22}H_{30}NOP$ requires C, 74.3; H, 8.5; N, 3.9%); ν_{max}/cm^{-1} 3208 (NH), 1435 (PhP), 1187, 1123 (P═O), 722, 696 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.86 (3H, t, *J*=7 Hz, CH_3), 0.91–0.96, 1.31–1.63 and 1.86–1.94 (15H, m, 7×CH_2 and CH of cyclopentyl), 2.63 (1H, dd, *J*=5.7, 10.9 Hz, NH), 2.98–3.2 (1H, m, CHN), 7.40–7.51 (6H, m, ArH), and 7.88–7.96 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$), 13.94 (CH_3), 18.36 (CH_2CH_3), 24.84, 32.46, and 32.68 (4×CH_2 ring), 36.49 (CH cyclopentyl) 39.39 (CH_2CH_2CH), 43.65 ($CHCH_2$-pentyl), 50.75 (CHNH), 128.1 (d, *J*=12.9 Hz), 132.2; δ_P (121.4 MHz, $CDCl_3$), 21.13; *m/z* (CI) 356 (MH^+, 100%), 312 (21), 272 (27), 218 (8), 203 (15), 79 (52). (Found: $[MH]^+$ 356.2141. $C_{22}H_{30}NOP$ requires $[MH]^+$ 356.2143).

4.4.4. 1-Cyclopentyl-2-(diphenylphosphinamido)-3-phenylpropane (10c). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(cyclopentylmethyl)aziridine (**8g**) (0.32 g, 1.0 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and phenylmagnesium bromide (5 equiv.), prepared from magnesium (0.17 g, 7.1 mmol), and bromobenzene (0.52 mL, 6.9 mmol), were reacted together in THF (20 mL) to produce a pale yellow solid. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), provided (**10c**) as a colourless solid (0.30 g, 77%). R_f 0.4 (EtOAc); mp 125–126°C. (Found: C, 77.3; H, 7.6; N, 3.4. $C_{26}H_{30}NOP$ requires C, 77.4; H, 7.45; N, 3.5%); ν_{max}/cm^{-1}; 3182 (NH), 2946 (CH), 1437 (PhP), 1188, 1122 (P═O), 724, 698 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.85–1.03 and 1.25–1.70 (10H, m, 4×CH_2 cyclopentyl and cyclopentyl-CH_2CHN), 1.94–2.15 (1H, m, CH cyclopentyl); 2.65 (1H, dd, *J*=5.1, 11.2 Hz, CHNH), 2.76–2.98 (2H, 2× dd, *J*=5.9, 13.4 Hz, benzyl CH_2), 3.16–3.31 (1H, m, CHNH), 7.15–7.90 (15H, m, ArH); δ_C (125 MHz, $CDCl_3$); 24.98, 25.05, 32.59, 32.69 (4×CH_2 cyclopentyl), 36.69 (CH cyclopentyl), 43.34 (CH_2cyclopentyl, d, *J*=5.1 Hz), 43.44 (benzyl-CH_2, d, *J*=5.1 Hz), 52.40 (CHN), 126.3, 128.3, 128.38 (d, *J*=12.4 Hz), 130.1, 131.59, and 131.71 (2×d, *J*=2.1 Hz), 132.10 and 132.27 (2×d, *J*=9.3 Hz), 132.48 and 132.95 (2×d, *J*=129.3 Hz), 138.3; δ_P (202 MHz, $CDCl_3$) 21.15; *m/z* (CI), 404 (MH^+, 100%), 312 (68), 218 (25), 201 (35), 91 (20). (Found: $[MH]^+$: 404.2132. $C_{26}H_{30}NOP$ requires $[MH]^+$ 404.2143).

4.4.5. 1-Cyclopentyl-2-(diphenylphosphinamido)-4-methylpentane (10d). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(2-methylpropyl)aziridine (**8f**) (0.33 g, 1.1 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and cyclopentylmagnesium bromide (5 equiv.), prepared from magnesium (0.14 g, 5.6 mmol) and cyclopentyl bromide (0.6 mL, 5.5 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 10–40% EtOAc in light petroleum), gave (**10d**) (0.26 g, 65%) as colourless solid. R_f 0.5 (EtOAc). Mp 132–134°C (lit.[1] 133–134.5); ν_{max}/cm^{-1} 3179 (NH), 2950 (CH), 1437 (PhP), 1188, 1123 (P═O), 721, 696 (aromatics); δ_H (270 MHz, $CDCl_3$), 0.76 and 0.78 (6H, 2×d, *J*=6.4 Hz, $CH(CH_3)_2$), 0.82–1.97 (14H, m, $(CH_3)_2CHCH_2CHCH_2$ and cyclopentyl), 2.58 (1H, dd, *J*=5.2, 10.5 Hz, NH), 2.93–3.06 (1H, m, CH), 7.40–7.52 (6H, m, ArH) and 7.88–7.97 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 22.52 and 22.66 ($(CH_3)_2CH$), 24.62 ($(CH_3)_2CH$), 24.97, 32.67, 32.81 (cyclopentyl CH_2), 36.54 (CH), 44.49 (d, *J*=4.5 Hz, CH_2), 47.42 (d, *J*=5.5 Hz, CH_2), 49.51 ($(CH_3)_2CHCH_2CH$), 128.18, 128.37, 131.54, 131.97, 132.05, 132.13, 132.257, 133.88, 133.97 (ArC); δ_P (161.7 MHz, $CDCl_3$) 20.64; *m/z* (CI) 398 (M+29, 18%), 370 (M+1, 91), 312 (M−Me_2-$CHCH_2$, 84), 286 (M−CH_2cyclopentyl, 100) and 201 ($POPh_2$, 76); Found: 370.2293. $C_{23}H_{33}NPO$ requires 370.2300.

4.4.6. 1-Cyclopentyl-2-(diphenylphosphinamido)hexane (10e). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(n-butyl)aziridine (**8b**) (0.15 g, 0.5 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and cyclopentylmagnesium bromide (5 equiv.), prepared from magnesium (0.06 g, 2.6 mmol), and cyclopentyl bromide (0.3 mL, 2.5 mmol), were reacted together in THF (15 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–50% EtOAc in light petroleum), provided (**10e**) (0.12 g, 64%) as a colourless oil. R_f 0.5 (EtOAc), ν_{max}/cm^{-1} 3218 (NH), 2952 (CH), 1436 (PhP), 1187, 1123 (P═O), 722, 695 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.88 (3H, t, *J*=7.0 Hz, CH_3), 0.91–1.00 and 1.21–2.05 (17H, m, cyclopentyl and 4×CH_2), 2.63 (1H, dd, *J*=5.0, 10.4 Hz, NH), 3.00–3.05 (1H, m, CHN), 7.41–7.53 (6H, m, ArH), and 7.79–7.94 (4H, m, ArH); δ_C (75 MHz, $CDCl_3$), 14.07 (CH_3), 22.67, 24.99, 27.36, 32.66, 32.83 (6×CH_2), 36.64 (CH pentyl), 37.01 (CH_2CH_2CHNH, d, *J*=4.5 Hz), 43.74 (pentyl-CH_2-CHNH, d, *J*=5.2 Hz), 51.03 (CHN, d, *J*=2.5 Hz), 128.3 (d, *J*=12.3 Hz), 132.2; δ_P (121.4 MHz, $CDCl_3$), 21.22; *m/z* (CI) 370 (MH^+, 100%), 292 (14), 201 (8), 218 (7). (Found: $[MH]^+$ 370.2286. $C_{23}H_{32}NOP$ requires $[MH]^+$ 370.2230).

4.4.7. 8-(Diphenylphosphinamido)-2-methyldec-9-ene (10f). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(3-methylbutyl)aziridine (**8c**) (0.3 g, 0.9 mmol), copper(I) bromide dimethylsulfide complex (0.02 g, 0.1 mmol) and 5 equiv. of Grignard reagent, prepared from magnesium (0.11 g, 4.3 mmol), and 4-bromobut-1-ene (0.4 mL, 4.1 mmol), were reacted in THF to produce a yellow oil. Purification by flash

chromatography (gradient 20–60% EtOAc in light petroleum), gave (**10f**) (0.19 g, 60%), as a colourless solid. R_f 0.6 (EtOAc); mp 101–103°C; ν_{max}/cm^{-1} 3200 (NH), 2929 (CH), 1435 (PhP), 1185, 1123 (P═O), 722, 694 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.83–0.87 (6H, 2×d, J=1.7 Hz, $CH(CH_3)_2$), 1.14–1.25, and 1.38–1.56, and 1.96–2.03 (11H, m, $CH(CH_3)2$ and 5×CH_2), 2.70 (1H, dd, J=6.3, 10.3 Hz, NH), 3.02–3.08 (1H, m, CHNH), 4.91–5.02 (2H, m, CH═CH_2), 5.70–5.83 (1H, m, CH═CH_2), 7.39–7.51 (6H, m, ArH), and 7.86–7.95 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$), 22.01 and 22.33 (2×CH_3), 24.52 ($CH_2CH(CH_3)_2$), 27.72 ($CH(CH_3)_2$), 30.01 and 33.41 (CH_2CH_2CH═CH_2), 34.20 and 35.92 (CH_2-$CH(NHDpp)CH_2$), 51.32 (CHNH), 114.37 (CH═CH_2), 128.31 (d, J=12.9 Hz), 132.2, 138.64 (CH═CH_2); δ_P (161.9 MHz, $CDCl_3$), 21.38; m/z (CI) 370 (MH^+, 100%), 300 (23), 292 (19), 218 (15), 83 (76). (Found: $[MH]^+$ 370.2306. $C_{23}H_{32}NOP$ requires $[MH]^+$ 370.2300).

4.4.8. 1-Cyclohexyl-2-(diphenylphosphinamido)-5-methylhexane (10g). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(3-methylbutyl)aziridine (**8c**) (0.23 g, 0.72 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and cyclohexylmagnesium bromide (5 equiv.), prepared from magnesium (0.09 g, 3.7 mmol), and bromocyclohexane (0.4 mL, 3.6 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–40% EtOAc in light petroleum), gave (**10g**) (0.19 g, 66%) as a colourless solid. R_f 0.6 (EtOAc); mp 120–121°C. (Found: C, 75.8; H, 9.4; N, 3.5. $C_{25}H_{36}NOP$ requires C, 75.5; H, 9.1; N, 3.5%); ν_{max}/cm^{-1} 3210 (NH), 2921 (CH), 1436 (PhP), 1190, 1122 (P═O), 720, 696 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.84 and 0.86 (6H, 2×d, J=1.9 Hz, $CH(CH_3)_2$), 1.12–1.63 (18H, m, $CH(CH_3)_2$, 3×CH_2, and cyclohexyl ring), 2.62 (1H, dd, J=5.8, 10.6 Hz, NH), 3.04–3.16 (1H, m, CHNH), 7.40–7.50 (6H, m, ArH) and 7.86–7.94 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$), 22.54 ($CH(CH_3)_2$), 26.21, 26.44, 33.50, 34.06 and 34.13, (5×CH_2 hexyl), 27.91 ($CH(CH_3)_2$), 34.29 (CH hexyl), 34.32 and 45.05 ($CH_2CH(NH)CH_2$hexyl), 49.13 (CHNH), 128.3, 132.0, 132.93 and 133.18 (2×d, J=129.0 Hz); δ_P (161.9 MHz, $CDCl_3$), 21.14; m/z (CI) 398 (MH^+, 100%), 326 (24), 300 (24), 218 (10), 201 (9). (Found: $[MH]^+$ 398.2632, $C_{25}H_{36}NOP$ requires $[MH]^+$ 398.2613).

4.4.9. 5-(Diphenylphosphinamido)-8-methyl-1-phenylnonane (10h). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised. *N*-Diphenylphosphinyl-2-(3-methylbutyl)-aziridine (**8c**) (0.43 g, 1.31 mmol), copper(I) bromide dimethylsulfide (0.01 g, 0.05 mmol) and 3-phenylpropylmagnesium bromide (5 equiv.), prepared from magnesium (0.16 g, 6.67 mmol), and 1-bromo-3-phenylpropane (1.0 mL, 6.5 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–50% EtOAc in light petroleum), gave (**10h**) (0.4 g, 72%) as a colourless solid. R_f 0.6 (EtOAc); mp 99–101°C. (Found C, 77.5; H, 8.25; N, 3.1. $C_{28}H_{36}NOP$ requires C, 77.6; H, 8.4; N, 3.2%); ν_{max}/cm^{-1}, 3188 (NH), 2932 (CH), 1437 (PhP), 1188, 1122 (P═O), 722, 697 (aromatics); δ_H (270 MHz, $CDCl_3$), 0.83–0.87 (6H, 2×d, J=3.2 Hz, $(CH_3)_2CH$) 1.08–1.24 and 1.28–1.60 (11H, m, $Ph(CH_2)_3CH(NH)(CH_2)_2$-$CH(CH_3)_2$), 2.57–2.61 (2H, m, $PhCH_2$), 2.65 (1H, dd, J=6.1, 10.8 Hz, NHCH), 3.00–3.07 (1H, m, CHNH), 7.15–7.28 (5H, m, $PhCH_2$), 7.40–7.50 (6H, m, ArH), and 7.87–7.92 (4H, m, ArH); δ_C (67.5 MHz, $CDCl_3$), 22.23 ($(CH_3)_2CH$), 27.51 ($(CH_3)_2CH$), 24.58, 30.83, 34.04, 34.14, 35.28, 36.04, ($(CH_2)_6$), 51.15 (CHNH), 125.19, 128.4 (d, J=12.9 Hz), 128.9, 131.9, 142.08; δ_P (121.4 MHz, $CDCl_3$), 21.45; m/z (CI) 434 (MH^+, 100%), 362 (20), 201 (17). (Found: $[MH]^+$ 434.2610. $C_{28}H_{36}NOP$ requires $[MH]^+$ 434.2613).

4.4.10. 2-(Diphenylphosphinamido)-1-phenylhept-6-ene (10i). The general method for copper-modified Grignard reactions using excess Grignard reagent as above was utilised.

N-Diphenylphosphinyl-2-(pent-4-enyl)aziridine (**8d**) (0.2 g, 0.65 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol) and phenylmagnesium bromide (5 equiv.), prepared from magnesium (0.08 g, 3.28 mmol), and bromobenzene (0.3 mL, 3.21 mmol), were reacted together in THF (20 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–80% EtOAc in light petroleum), gave (**10i**) (0.17 g, 66%) as a colourless solid. R_f 0.5 (EtOAc); mp 118–119°C. (Found: C, 77.1; H, 7.2; N, 3.5. $C_{25}H_{38}NOP$ requires C, 77.1; H, 7.25; N, 3.6%); ν_{max}/cm^{-1}, 3181 (NH), 2927 (CH), 1437 (PhP), 1186, 1122 (P═O), 723, 698 (aromatics); δ_H (270 MHz, $CDCl_3$), 1.44–1.60 and 1.96–2.05 (6H, m, $CH(NH)(CH_2)_3$) 2.68 (1H, dd, J=4.9, 11.0 Hz, NH), 2.80 (1H, dd, J=6.1, 13.4 Hz, CH of CH_2Ph), 2.91 (1H, dd, J=6.1, 13.4 Hz, CH of CH_2Ph), 3.25–3.30 (1H, m, CHNH), 4.91–4.97 (2H, m, CH═CH_2), 5.71–5.81 (1H, m, CH═CH_2), 7.15–7.89 (15H, m, ArH); δ_C (67.5 MHz, $CDCl_3$), 24.87 (CH_2CH_2CH═CH_2), 33.25 (CH_2CH═CH_2), 35.88 ($CH(NH)CH_2$), 42.81 ($PhCH_2$), 52.77 (CHNH), 114.40 (CH═CH_2), 126.08, 128.05 128.2, 129.67, 131.4, 132.83 and 132.91 (2×d, J=124.3 Hz), 128.19, 138.24 (CH═CH_2); δ_P (161.9 MHz, $CDCl_3$), 21.23; m/z (CI) 390 (MH^+, 100%), 298 (37), 201 (18) 79 (67). (Found: $[MH]^+$ 390.1975, $C_{25}H_{38}NOP$ requires $[MH]^+$ 390.1986).

4.5. Preparation of (2*R*)-DiDpp

4.5.1. (2*R*)-(+)-(*O*-Diphenylphosphinyl)-2-(hydroxymethyl)oxirane (11). (*R*)-(+)-Glycidol (1 mL, 15.1 mmol) was dissolved in dichloromethane (100 mL), and cooled to 0°C, under an argon atmosphere. Triethylamine (3.1 mL, 22.6 mmol), and diphenylphosphinic chloride (3.2 mL, 16.6 mmol) were then added to the clear solution, which was stirred overnight. The solution was then quenched with water (20 mL), and acidified to pH 2 with 1 M hydrochloric acid, and partitioned. The aqueous layer washed with dichloromethane (2×10 mL), and the combined organic layers washed with brine, and dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The resulting pale yellow oil was then purified by flash chromatography (gradient 40–60% EtOAc in hexane), which afforded oxirane (**11**) (3.08 g, 75%) as a colourless oil. R_f 0.5 (EtOAc); $[\alpha]$=+17.9 (c 5, CH_2Cl_2); ν_{max}/cm^{-1} 2934 (CH),

1440 (P═O), 1226 (C–O epoxide), 1162, 1130 (P═O), 732, 698 (aromatic); δ_H (400 MHz, $CDCl_3$), 2.64 and 2.81 (2H, 2×dd, J=1.6, 4.4 Hz, $CH(O)CH_2$), 3.25–3.30 (1H, m, CH), 3.89–3.98 (1H, m, CH of $DppOCH_2$), 4.31 (1H, ddd, J=3.2, 8.0, 13.2 Hz, CH of $DppOCH_2$), 7.38–7.59 (6H, m, ArH), and 7.75–7.97 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$), 44.61 ($CH(O)CH_2$), 50.40 ($CH(O)CH_2$), 65.33 ($DppOCH_2$), 128.4, 131.9; δ_P (161.9 MHz, $CDCl_3$), 32.90; *m/z* (CI) 275 (MH^+, 100%), 219 (25), 141 (9), 79 (9). (Found: $[MH]^+$ 275.0836, $C_{15}H_{15}O_3P$ requires $[MH]^+$ 275.0837).

4.5.2. (2*R*)-(+)-1-Azido-3-(*O*-diphenylphosphinyl)-propane-2,3-diol (12). Oxirane (**11**), (2.8 g, 10.2 mmol), was dissolved in methanol (100 mL) under an atmosphere of nitrogen. Ammonium chloride (1.64 g, 30.7 mmol), and sodium azide (2.00 g, 30.7 mmol), were then added to the clear solution. The resulting suspension was then heated to reflux for 3 h. After cooling the solution was diluted with EtOAc (100 mL), and water (50 mL). The organic layer was partitioned and the aqueous layer washed with EtOAc (2×20 mL). The combined organic layers were then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Often the colourless solid isolated was found to still contain water, and so the product was redissolved in chloroform (40 mL), and partitioned with brine (2×10 mL). The organic layer dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Azide (**12**) (2.93 g, 90%) was afforded as a colourless solid. R_f 0.4 (EtOAc); mp 97–98°C; $[\alpha]$=+23.8 (*c* 5, CH_2Cl_2), ν_{max} ($CHCl_3$)/cm^{-1} 3545 (OH), 2107 (N3), 1437, 1180, 1125 (P═O), 727, 696 (aromatic); δ_H (400 MHz, $CDCl_3$), 3.42 (2H, dd, J=2.6, 5.8 Hz, $CH(OH)CH_2N_3$), 3.99–4.05 (1H, m, CH), 4.10–4.14 (2H, ddd, J=1.0, 4.1, 11.7 Hz, $CH(OH)CH_2ODpp$), 7.26–7.58 and 7.78–7.84 (10H, m, ArH); δ_C (100 MHz, $CDCl_3$), 51.45 ($CH(OH)CH_2N_3$) 66.68 (CH) 68.34 ($DppOCH_2CH(OH)$) 128.8, 131.5; δ_P (161.5 MHz, $CDCl_3$), 36.09; *m/z* (CI) 318 (MH^+, 100%), 275 ($M-N_3$, 21), 261 (35), 219 (68), 201 (Dpp,10). (Found: $[MH]^+$ 318.0996. $C_{15}H_{16}N_3O_3P$ requires $[MH]^+$ 318.1008).

4.5.3. (2*R*)-*N*,*O*,*O*-Tris(diphenylphosphinyl)-1-amino-propane-2,3-diol (13) and (2*R*)-(−)-*N*,*O*-bis(diphenyl-phosphinyl)-2-(hydroxymethyl)aziridine (1). Azide (**12**), (2.73 g, 8.61 mmol) was dissolved in acetonitrile (100 mL), to which triphenylphosphine (2.48 g, 9.47 mmol) was added. The resulting suspension was heated to reflux for 2 h, after which time the azide was judged to have been consumed using infra-red analysis. The solvent was then removed under reduced pressure, affording a yellow oil. This oil was then dissolved in dichloromethane (100 mL), under an atmosphere of argon. Triethylamine (1.8 mL, 12.9 mmol) and diphenylphosphinic chloride (1.8 mL, 9.50 mmol) were then added, and the mixture stirred overnight. The solution was then quenched with brine (20 mL), and acidified to pH 2 with 1 M hydrochloric acid. The organic layer was partitioned and the aqueous layer washed with dichloromethane (2×10 mL). The combined organic layers were then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The resulting pale yellow oil was then purified by flash chromatography (gradient 0–10% methanol in EtOAc), which afforded (2*R*)-**1** (5% methanol/95% ethyl acetate eluent), as a pale yellow oil. Crystallisation from ethyl acetate/hexane afforded (221) (1.2 g, 29%) as a colourless solid. R_f 0.4 (10% methanol/EtOAc); mp 140°C (racemic 138–139°C); $[\alpha]$=−1.5 (*c* 5, CH_2Cl_2). Other physical data was identical to that recorded for (±)-**1**.

Further elution furnished (**13**) (0.95 g, 16%) as a white foam. R_f 0.1 (5% methanol/95%EtOAc); ν_{max} ($CHCl_3$)/cm^{-1} 3057 (NH) 2966, 1418, 1060, 1167 (P═O) 828, 650 (aromatics); δ_H (400 MHz, $CDCl_3$), 3.29–3.32 (2H, m, CH_2NHDpp), 4.12–4.22 (2H, m, $DppOCH_2$), 4.58–4.64 (1H, m, CH), 4.96–4.98 (1H, br m, NHDpp), 7.28–7.85 (30H, m, ArH); δ_C (100 MHz, $CDCl_3$), 41.77 (CH_2NHDpp), 64.16 (CH_2ODpp), 75.96 (CH), 128.5, 132.4; δ_P (161.9 MHz, $CDCl_3$), 24.36 (NP), 33.44, and 33.66 (OP); *m/z* (CI) 692 (MH^+, 82%), 474 (M−ODpp, 92), 256 (28), 219 (HODpp,11). (Found: $[MH]^+$ 692.1903. $C_{39}H_{36}NO_5P_3$ requires $[MH]^+$ 692.1884).

4.6. Ring-opening of (2*R*)-DiDpp

4.6.1. (2*S*)-(+)-*N*-(Diphenylphosphinyl)-2-butylaziridine (8b). By following the general procedure for copper-modified Grignard reactions using 1 equiv. of Grignard reagent described earlier (2 *S*)-(−)-*N*,*O*-bis(diphenyl-phosphinyl)-2-(hydroxymethyl)aziridine (2*R*)-**1** (0.5 g, 1.06 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and 1.1 equiv. of Grignard reagent formed from magnesium (0.03 g, 1.27 mmol), and 1-bromo-propane (0.11 mL, 1.16 mmol) were reacted together in THF to produce a pale yellow oil. Purification by flash chromatography (gradient 20–70% EtOAc in light petroleum), gave (2*R*)-**8b** (0.22 g, 62%) as a clear oil. R_f 0.3 (EtOAc); $[\alpha]$=+9.1 (*c* 5, CH_2Cl_2); ν_{max} ($CHCl_3$)/cm^{-1} 2968 (CH), 1438 (PhP), 1173, 1130 (P═O), 990, 729, 698 (aromatic); δ_H (270 MHz, $CDCl_3$), 0.77 (3H, t, J=7.1 Hz, CH_3CH_2), 1.15–1.23 (4H, m, $CH_3CH_2CH_2$), 1.48–1.52 (2H, m, CH_2CHN), 1.92 (1H, ddd, J=1.2, 3.4, 12.5 Hz, CH of CH_2N), 2.53 (1H, ddd, J=1.2, 6.1, 17.3 Hz, CH of CH_2N), 2.65–2.74 (1H, m, CH_2CHN), 7.41–7.51 (6H, m, ArH), and 7.89–7.95 (4H, m, ArH); *m/z* (CI), 300 (MH^+, 100%), 286, (10%), 258, (34%), 201 ($Ph_2P(O)$,19%). (Found: $[MH]^+$ 300.1516 $C_{18}H_{22}NOP$ requires $[MH]^+$ 300.1517). Other data as for (±)-**8b**.

4.7. MTPA amide of (2*R*)-(−)-2-amino-1-cyclopentylhexane (17)

4.7.1. (2*R*)-1-Cyclopentyl-2-(diphenylphosphinamido)-hexane (10e). By following the general procedure for copper-modified Grignard reactions using excess Grignard reagent as described earlier, (2*R*)-(+)-*N*-diphenylphosphinyl-2-butylaziridine (**8b**) (0.22 g, 0.7 mmol), copper(I) bromide dimethylsulfide complex (0.01 g, 0.05 mmol), and cyclopentylmagnesium bromide (5 equiv.) prepared from magnesium (0.08 g, 3.4 mmol) and cyclopentyl bromide (0.4 mL, 3.3 mmol) were reacted in THF (10 mL) to produce a yellow oil. Purification by flash chromatography (gradient 20–60% EtOAc in light petroleum), gave (**10e**) (0.2 g, 74%), as a colourless oil. R_f 0.45 (EtOAc); ν_{max}/cm^{-1} 3217 (NH) 2952, 2831 (CH), 1436 (PhP), 1187 (P═O), 1123, 749, 722, 695 (aromatics); δ_H (400 MHz, $CDCl_3$), 0.90 (3H, t, J=7.0 Hz, CH_2CH_3), 0.92–1.00 and 1.22–1.96 (17H, m, cyclopentyl and 4×CH_2), 2.63 (1H, dd,

J=4.9, 10.4 Hz, CHNH), 3.01–3.05 (1H, m, CHNH), 7.41–7.53 (6H, m, ArH), and 7.79–7.94 (4H, m, ArH); *m/z* (CI) 370 (MH^+, 100%), 312 (10), 292 (12), 218 (7). (Found: $[MH]^+$ 370.2289. $C_{23}H_{32}NOP$ requires $[MH]^+$ 370.2230). Other data as for (±)-**10e**.

4.7.2. (2*R*)-(−)-2-Amino-1-cyclopentylhexane. To (2*R*)-1-cyclopentyl-2-(diphenylphosphinamido)hexane (**10e**) (0.2 g, 0.5 mmol) in CH_2Cl_2 (2 mL) under argon was added methanol (2 mL) followed by boron trifluoride etherate (0.1 mL). The solution was stirred overnight, after which time H_2O (2 mL) was added. The aqueous layer was then extracted with CH_2Cl_2 (3×10 mL), basified ($NaHCO_3$), and extracted with further CH_2Cl_2 (10 mL). The organic layers were combined, washed with brine (10 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to yield the free amine (0.045 g, 49%), as a colourless oil. [α]=−7.1 (*c* 4.5, CH_2Cl_2); ν_{max}/cm^{-1} 2953 and 2867 (CH br by NH_2), 1604, 1517; δ_H (400 MHz, $CDCl_3$), 0.92 (3H, t, J=7.0 Hz, CH_2CH_3), 1.03–2.05 (17H, m, cyclopentyl and 4×CH_2), 3.13–3.19 (1H, m, $CHNH_2$), 7.82 (2H, br s, NH_2); δ_C (75 MHz, $CDCl_3$), 13.86 (CH_3), 22.35, 25.00, 25.07, 27.31, 32.45, 32.66, 32.78 (7×CH_2), 36.10 (CH pentyl), 39.26 (pentyl-$CH_2CH(NH_2)$, d, J=5.2 Hz), 51.95 ($CH(NH_2)$); *m/z* (CI) 170 (MH^+, 37%), 168 (27), 112 (29), 83 (100), 57 (98). (Found: $[MH]^+$ 170.1905. $C_{11}H_{23}N$ requires $[MH]^+$ 170.1909).

4.7.3. MTPA amide of (2*S*)-(−)-2-amino-1-cyclopentylhexane (17). DCC (0.035 g, 0.2 mmol), was added to a solution of (2S)-(-)-2-Amino-1-cyclopentylhexane (0.035 g, 0.2 mmol) and methoxytrifluoromethylphenylacetic acid (0.049 g, 0.2 mmol) in dichloromethane (5 mL). *N*,*N*-4-(Dimethylamino)pyridine (ca. 1 mg) was then added. Within 1 h a precipitate had formed. The reaction was stirred for 10 h after which time dicyclohexylurea was filtered off and the filtrate concentrated under reduced pressure. The residual oil was purified by flash chromatography (ethyl acetate/hexane 1:4) to give (*R*,*R*)-**17** (0.054 g, 64%) as a colourless oil. R_f 0.35; ν_{max}/cm^{-1} 3324 (NH) 2930, 2854 (CH), 1600 (C=O), 1164, 804, 716 (aromatic); δ_H (300 MHz, $CDCl_3$), 0.83 (3H, t, J=7.0 Hz, CH_2CH_3), 1.07–1.91 (17H, m, cyclopentyl and 4×CH_2), 2.98 (3H, s, OCH_3), 3.98–4.03 (1H, m, CHNH), 6.48 (1H, d, J=10.0 Hz, NHCO), 7.41–7.57 (5H, m, ArH); δ_F (282 MHz, $CDCl_3$), 68.41; *m/z* (CI) 386 (MH^+, 20%), 306 (10), 253 (9), 225 (100), 98 (48), 83 (56). (Found: $[MH]^+$ 386.2313 $C_{21}H_{30}NO_2F_3$ requires $[MH]^+$ 386.2307).

4.7.4. MTPA amide of (2*RS*)-(−)-2-amino-1-cyclopentylhexane (17). By following the procedure directly above, using racemic amine, (*RS*,*R*)-**17** (0.029 g, 34%) was obtained, as a colourless oil. δ_H (300 MHz, $CDCl_3$), 0.84 (3H, t, J=7.0 Hz, CH_2CH_3), 1.07–1.96 (17H, m, cyclopentyl and 4×CH_2), 3.01 (3H, s, OCH_3), 3.99–4.05 (1H, m, CHNH), 6.51 (1H, br d, J=6.0 Hz, NHCO), 7.38–7.54 (5H, m, ArH); δ_F (282 MHz, $CDCl_3$), 68.37 and 68.41 (ratio=1:1); *m/z* (CI) 386 (MH^+, 74%), 379 (28), 316 (27), 253 (31), 225 (100), 207 (24), 123 (32), 98 (48), 83 (56). (Found: $[MH]^+$ 386.2315 $C_{21}H_{30}NO_2F_3$ requires $[MH]^+$ 386.2307).

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