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Asymmetric Synthesis with Diphenylphosphine Oxides: Bicyclic Aminals and Oxazolidines as Chiral Auxiliaries

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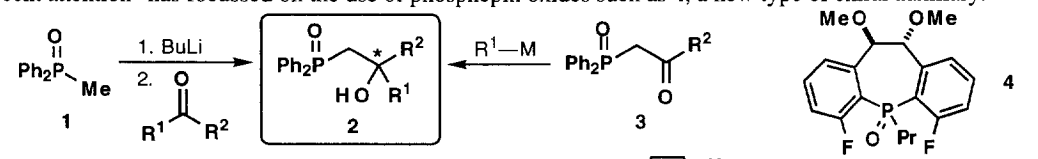
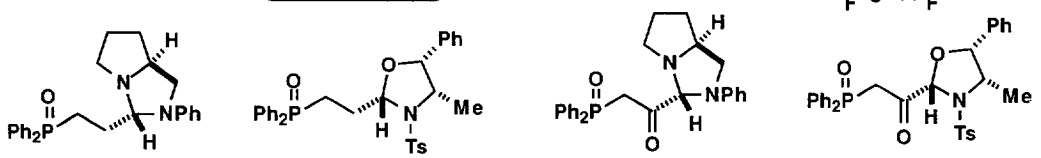
Abstract: Syntheses of six novel phosphine oxide chiral auxiliaries are described. The auxiliaries are composed of the diphenylphosphinoyl (Ph_2PO) group and either proline-derived bicyclic aminals or norephedrine-derived oxazolidines. One auxiliary is used in the synthesis of an optically active β-hydroxy phosphine oxide.

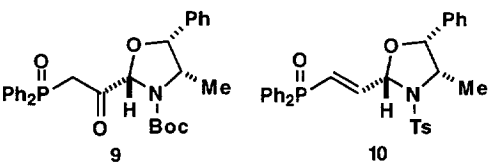
Introduction

Optically active β-hydroxy phosphine oxides like **2** have been used to synthesise enantiomerically enriched unsaturated α-amino acids,[1] allylic alcohols and sulfides,[2,3] alkenyl oxazolidinones[4] and cyclopropyl ketones.[5] Of the many asymmetric methods that we have used to make optically active β-hydroxy phosphine oxides **2** (e.g. epoxidation,[6] dihydroxylation,[7] chiral auxiliary attached to electrophile in **1** → **2**[8]), the one that has received least attention so far is the use of the phosphine oxide as the chiral auxiliary. Our initial contribution[2] in this area utilised a chiral auxiliary which had a stereogenic centre at phosphorus but more recent attention[9] has focussed on the use of phosphepin oxides such as **4**, a new type of chiral auxiliary.





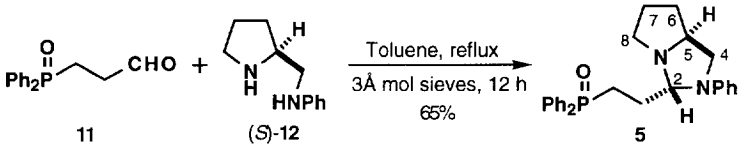
As well as developing modified phosphine oxides as chiral auxiliaries (e.g **4**), we wanted to make *diphenylphosphine oxides* with a chiral auxiliary built in to some other part of the molecule. In this way, we would be able to utilise our acquired synthetic experience with the diphenylphosphinoyl group.[10] We now report syntheses of a number of new diphenylphosphine oxides **5-10** which contain proline-derived aminals[11] or norephedrine-derived oxazolidines[12-15] as masked aldehyde chiral auxiliaries. To date,



oxazolidine **8** has proved to be the most useful compound and its successful application to the synthesis of an optically active β-hydroxy phosphine oxide is also described in this paper.[16]

Synthesis of Diphenylphosphinoyl Aminals

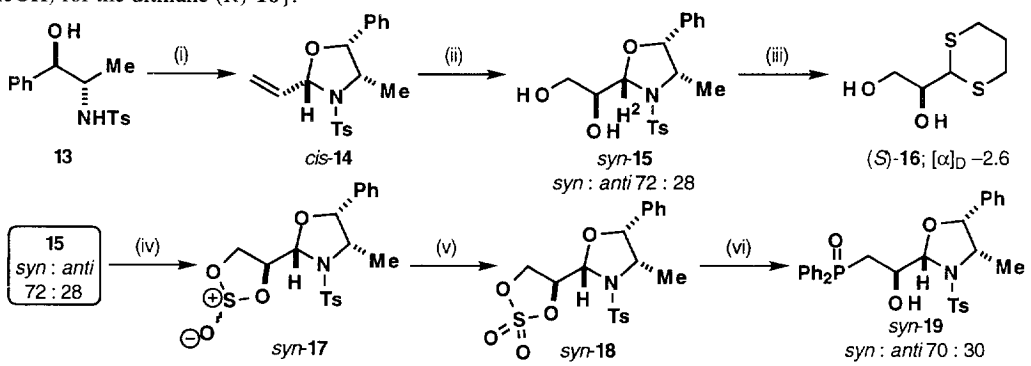
Phosphine oxide **11**, obtained by Dess-Martin periodinane[17] oxidation of the corresponding known[18] alcohol, was condensed with diamine (*S*)-**12** to give a 65% yield of a single diastereomer of phosphine oxide aminal **5**. This was assigned as the *exo* diastereomer by comparison with similar condensations carried out by us[8] and by Mukaiyama.[11] Our synthesis of β-keto phosphine oxide **7** has been described elsewhere.[8c]



11 (*S*)-**12** **5**

Synthesis of Diphenylphosphinoyl *N*-Tosyl Oxazolidines

For the synthesis of each of phosphine oxides **6**, **8** and **10**, we used a different strategy and started with the known[13a] oxazolidine *cis*-**14**. It was synthesised in 83% yield by condensing *N*-tosyl norephedrine **13**[19] with acrolein diethyl acetal using a procedure described by Scolastico;[20] the single alkenyl oxazolidine obtained was identified as *cis*-**14** by 500 MHz NOESY analysis. Alkene *cis*-**14** was dihydroxylated[21] using the Sharpless-style racemic dihydroxylation protocol developed recently in our laboratory[22] to give an 88% yield of a 72:28 mixture of 1,2-diols *syn*- and *anti*-**15**. The relative stereochemistry of 1,2-diols **15** was established by conversion into the dithiane (*S*)-**16** {$[\alpha]_D$ –2.6 (*c* 1.2 in MeOH); lit.,[23] $[\alpha]_D$ +6.0 (*c* 1.08 in MeOH) for the dithiane (*R*)-**16**}.



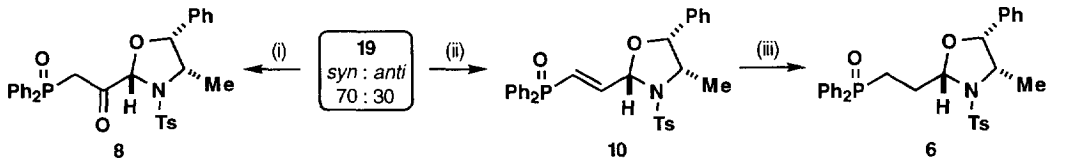
13 *cis*-**14** *syn*-**15** *syn* : *anti* 72 : 28 (*S*)-**16**; $[\alpha]_D$ –2.6

syn-**17** *syn*-**18** *syn*-**19** *syn* : *anti* 70 : 30

Reagents: (i) CH_2=CHCH$(OEt)_2$, cat. PPTS, benzene, reflux, 2.5 h; 83%; (ii) cat. $OsCl_3$, cat. quinuclidine, $K_3Fe(CN)_6$, K_2CO_3, t-BuOH-water (1:1), rt, 20 h; 88%; (iii) propan-1,3-dithiol, BF_3•Et_2O, CH_2Cl_2, rt, 48 h; 34%; (iv) 2 eq Et_3N, $SOCl_2$, CH_2Cl_2, 0 °C → rt, 1 h; 99%; (v) $NaIO_4$, cat. $RuCl_3$, CCl_4-MeOH-water (1:1:1), rt, 12 h; 100%; (vi) (a) Ph_2PLi, THF, –30 °C → rt, 1.5 h (b) cat. conc H_2SO_4, water, 16 h (c) H_2O_2; 82%

Introduction of the diphenylphosphinoyl group was achieved by converting 1,2-diols **15** into their corresponding cyclic sulfates **18**[24] and reacting them with lithium diphenylphosphide (followed by subsequent oxidation). Initially, using Sharpless's conditions,[25] 1,2-diols **15** were transformed into a mixture of four cyclic sulfites **17**. Then, oxidation of these with sodium periodate and ruthenium (III) chloride afforded a 72:28 mixture of cyclic sulfates *syn*- and *anti*-**18** (99% yield over the two steps). When we reacted this mixture of cyclic sulfates with lithium diphenylphosphide (prepared according to the method of Ashby[26]), all of the starting material was consumed (by TLC); treatment of the resulting mixture with water and catalytic concentrated sulfuric acid overnight (according to Sharpless's procedure[27]) and working the reaction up with

hydrogen peroxide gave an 82% yield of hydroxy oxazolidines *syn*- and *anti*-**19** (70:30) after chromatography. The opening of cyclic sulfates with other phosphorus nucleophiles has been described before[28] but this reaction has never been used to synthesise β-hydroxy phosphine oxides. The corresponding epoxide (made using a low yielding *m*-CPBA epoxidation of **14** or starting from 1,2-diols **15**) failed to react with lithium diphenylphosphide even in the presence of boron trifluoride; cyclic sulfites **17** were similarly unreactive.

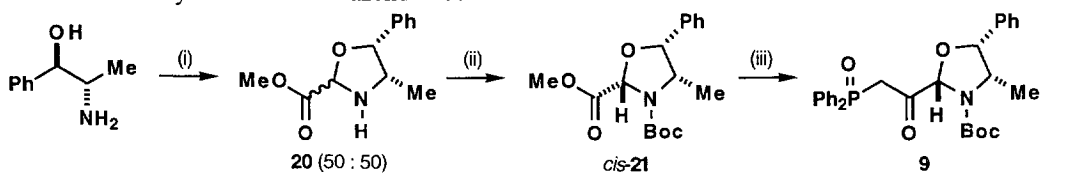


Reagents: (i) Dess-Martin periodinane, CH_2Cl_2, 0 °C, 12 h; 55%; (ii) (a) BuLi, THF, 0 °C, 30 min (b) MsCl (c) BuLi; 52%; (iii) L-selectride®, THF, –78 °C, 2 h; 93%

Dess-Martin periodinane[17] oxidation of the mixture of hydroxy oxazolidines **19** afforded β-keto phosphine oxide **8** in 55% yield which was better than the 18% yield obtained using Swern oxidation.[29] In contrast, sequential treatment of the same mixture with n-butyllithium, mesyl chloride and then n-butyllithium again generated a 52% yield of only one geometric isomer (presumably *E*) of vinyl phosphine oxide **10**. Reduction of vinyl phosphine oxide **10** with L-selectride® gave phosphine oxide **6**.

Synthesis of a Diphenylphosphinoyl *N*-Boc Oxazolidine

In order to synthesise *N*-Boc oxazolidine **9**, we adopted an approach that was similar to our synthesis of aminal **7**[8c] but different from that used to make the *N*-tosyl oxazolidines. First of all, (–)-norephedrine was condensed with methyl glyoxylate[30] to give a 50:50 mixture of oxazolidines **20**. Then, Boc_2O was added slowly over a period of hours to a refluxing ethyl acetate solution of **20** to give an 81% yield of a single diastereomer of *N*-Boc oxazolidine **21**. This was confirmed as the expected *cis* isomer by 500 MHz NOESY analysis and, in any case, the procedure is the same as that used by Agami to make the corresponding ethyl ester.[14] Finally, an acylation reaction between lithiated methyldiphenylphosphine oxide and methyl ester *cis*-**21** afforded a 51% yield of *N*-Boc oxazolidine **9**.



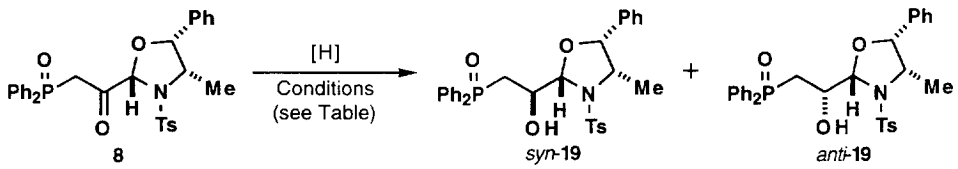
Reagents: (i) $OHCCO_2Me$, toluene, Dean-Stark, reflux, 1 h; 100%; (ii) EtOAc, reflux, addition of Boc_2O over 3 h; 81%; (iii) $Ph_2P(O)Me$, BuLi, THF, –78 °C; 51%

Synthetic Use of *N*-Tosyl Oxazolidines: Stereocontrolled Routes to *R* or *S* β-Hydroxy Phosphine Oxides

Stereoselective reductions of keto oxathianes,[31] keto oxazines,[32] *N*-tosyl keto oxazolidines[13a] and *N*-Boc keto oxazolidines[14,15] have all been reported before. In particular, Scolastico has described the selective reduction of *N*-tosyl keto oxazolidines to each diastereomer of the corresponding alcohols using either chelation controlled reaction conditions (L-selectride® in the presence of magnesium bromide etherate) or non-chelation (Felkin[33]) controlled reaction conditions (L-selectride® in the presence of the crown ether, Kriptofix 211®).[13a] We imagined that we could use such complementary reduction conditions for the selective synthesis of β-hydroxy phosphine oxides *syn*- and *anti*-**19**.

With this in mind, β-keto phosphine oxide **8** was reduced using a variety of conditions (see Table); the sense of asymmetric induction was easily deduced because we had already synthesised hydroxy oxazolidines **19** from 1,2-diols **15** of known relative stereochemistry. In the cases where reduction had occurred (entries 2-5), the reactions were always *syn* selective. Lithium aluminium hydride completely consumed the starting material but the expected hydroxy oxazolidines were not observed in the ^{1}H NMR of the crude reaction mixture (entry 1). With L-selectride® as the reducing agent, the conversion was low (entries 2-3) but with sodium borohydride, all of the starting material reacted (entries 4-5). From the Luche reduction[34] (entry 5), with what became our optimised reduction conditions, we obtained a 60% yield of hydroxy oxazolidine *syn*-**19** after chromatography. In contrast, reductions of the corresponding keto aminal **7** with a range of reducing agents [e.g. $NaBH_4$, $NaBH_4/CeCl_3{\cdot}7H_2O$, $LiAlH_4$, $LiAlH_4/ZnCl_2$, $Zn(BH_4)_2$] failed to generate any hydroxy aminal whatsoever.

Table: Reduction of β-Keto Phosphine Oxide **8** to Hydroxy Oxazolidines **19**

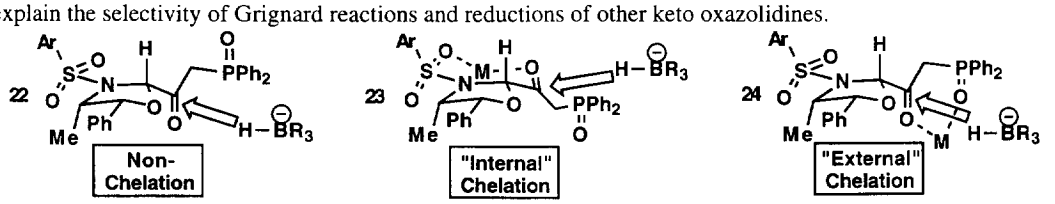


8 *syn*-**19** *anti*-**19**

Entry	Reducing Agent	Solvent	Temp (°C)	SM[a] : Products[b]	*syn*-**19** : *anti*-**19**[b]
1	$LiAlH_4$	THF	0	—[c]	—[c]
2	L-selectride®	THF	–78	44 : 56	95 : 5
3	L-selectride® / $MgBr_2{\cdot}Et_2O$	THF	–78	85 : 15	95 : 5
4	$NaBH_4$	EtOH	rt	No SM	88 : 12
5	$NaBH_4$ / $CeCl_3{\cdot}7H_2O$	EtOH	–78	No SM	95 : 5

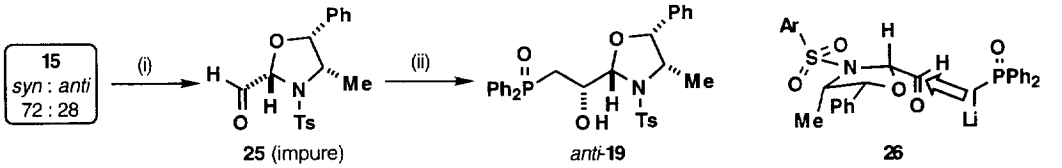
[a] Starting material; [b] By ^{1}H NMR; [c] Expected alcohols **19** were not observed in the ^{1}H NMR of the crude reaction mixture.

Since we had carried out reductions using conditions which approximated to Scolastico's chelation (entries 3 and 5) and non-chelation (entries 2 and 4) conditions, we were somewhat surprised to find that hydroxy oxazolidine *syn*-**19** was the major product from all of our reactions (see Table). With L-selectride® and sodium borohydride as the reducing agents (entries 2 and 4), *syn* selective reductions were expected via nucleophilic attack alongside the carbon–hydrogen bond in the Felkin[33] transition state **22** (*N*-tosyl group perpendicular to the carbonyl group[35]). In contrast, when we carried out these reductions in the presence of magnesium bromide etherate and cerium (III) chloride (entries 3 and 5), we expected the reactions to be *anti* selective proceeding via nucleophilic attack on the less hindered face of the carbonyl group in the chelated intermediate **23** (M = Mg or Ce). Hoppe,[12] Scolastico[13] and Agami[14] (*N*-Boc) have used such a model to explain the selectivity of Grignard reactions and reductions of other keto oxazolidines.



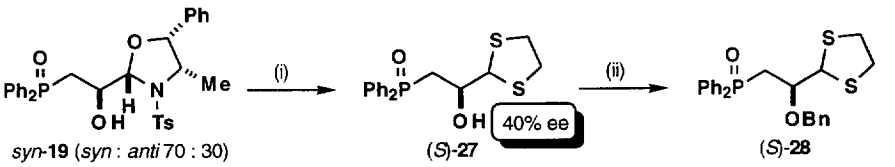
In fact, our reductions of keto oxazolidine **3** in the presence of chelating metals (Mg and Ce) were highly *syn* selective (entries 3 and 5). We suggest that the presence of the diphenylphosphinoyl group

interferes with the usual "internal" chelation of sulfonyl and ketone oxygens (e.g. **23**) – instead, "external" chelation between the ketone and phosphinoyl oxygens[36] occurs and the *syn* selectivity can be rationalised by Felkin control[33] (*N*-tosyl group perpendicular to the carbonyl group; transition state **24**) on an "externally" chelated intermediate.



Reagents: (i) $NaIO_4$ (2 eq), MeOH, rt, 2.5 h; 70%; (ii) $Ph_2P(O)Me$, BuLi, THF, –78 °C; 33%

Unfortunately, we were unable to find a good method for generating hydroxy oxazolidine *anti*-**19** using our reduction strategy. However, by changing our approach, we were able to make hydroxy oxazolidine *anti*-**19** selectively albeit in a low unoptimised yield: 1,2-diol cleavage of a mixture of 1,2-diols **15** with sodium periodate gave aldehyde **25** which could not be obtained completely pure. Then, reaction of aldehyde **25** with lithiated methyldiphenylphosphine oxide afforded a 33% yield of pure *anti*-**19** after chromatography. The *anti* selectivity is rationalised by invoking the Felkin[33] transition state **26** (identical in all respects to transition state **22** except that the diphenylphosphinoylmethyl and hydride groups are added in the opposite order). Perhaps surprisingly, the corresponding known aminal aldehyde[37] failed to react with lithiated methyldiphenylphosphine oxide.



Reagents: (i) ethan-1,2-dithiol, $BF_3{\cdot}Et_2O$, CH_2Cl_2, rt, 5 days; 53%; (ii) NaH, BnBr, THF, TBAI, rt, 16 h; 61%

Finally, to demonstrate the potential of this methodology for the synthesis of optically active β-hydroxy phosphine oxides, we have deprotected a 70:30 mixture of hydroxy oxazolidines *syn*- and *anti*-**19** using ethan-1,2-dithiol and $BF_3{\cdot}Et_2O$.[20,38] A 53% yield of β-hydroxy phosphine oxide (*S*)-**27** was obtained and its enantiomeric excess was confirmed as 40% by ^1H NMR spectroscopy in the presence of Pirkle's chiral shift reagent.[39] Subsequent protection generated benzyl ether (*S*)-**28**, a useful synthetic intermediate.

Summary

We have described the synthesis of six new diphenylphosphine oxide chiral auxiliaries (**5**-**10**). These types of compounds are nucleophilic (e.g. **5** and **6**) or electrophilic (e.g. **7**-**10**) in character; clearly, this allows maximum flexibility when designing subsequent stereoselective reactions. The synthetic potential of these chiral auxiliaries has been demonstrated by selectively synthesising both hydroxy oxazolidines *syn*- and *anti*-**19**, direct precursors of optically pure β-hydroxy phosphine oxides (*S*)- and (*R*)-**27**.

Experimental

General methods have been described previously.[8b] The carbon atoms in the bicyclic aminal are referred to by numbers as depicted on aminal **5**. The symbols $^+$ and $^-$ after the carbon NMR chemical shift indicate odd and even numbers of attached protons respectively. The enantiomeric excess of phosphine oxide (*S*)-**27** was determined by measuring the integration of the 400 MHz ^1H NMR spectrum in the presence of

(*R*)-(–)-2,2,2-trifluoro-1-(9-anthryl)ethanol[39] as a chiral shift reagent[8c] and is referrred to in the experimental section as "by Pirkle".

2-(2'-Diphenylphosphinoylethyl)-3-phenyl-1,3-diazabicyclo[3.3.0]octane 5

Aldehyde **11** (327 mg, 1.3 mmol) was added in one portion to a stirred suspension of diamine (*S*)-**12** (267 mg, 1.5 mmol) and 3Å molecular sieves in toluene (10 cm^3) at room temperature and the resulting suspension was heated under reflux for 12 h. After cooling to room temperature, the mixture was filtered and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with CH_2Cl_2-MeOH (20:1) as eluent gave *phosphine oxide* **5** (350 mg, 65%) as pale yellow plates, m.p. 90-92 °C (from EtOAc); R_f(10:1 CH_2Cl_2-MeOH) 0.5; $\nu_{max}(CDCl_3)/cm^{-1}$ 1599 (Ph), 1424 (P–Ph) and 1240 (P=O); δ_H(200 MHz, $CDCl_3$) 7.88-7.70 (4 H, m, *o*-Ph_2PO), 7.54-7.38 (6 H, m, *m*- and *p*-Ph_2PO), 7.16 (2 H, dd, *J* 7.4 and 8.5, *m*-NPh), 6.65 (1 H, t, *J* 7.3, *p*-NPh), 6.46 (2 H, d, *J* 7.9, *o*-NPh), 4.49 (1 H, dd, *J* 2.75 and 9.4, H^2), 3.80 (1 H, dtd, *J* 3.1, 7.5 and 10.4, H^5), 3.38 (1 H, t, *J* 8.7, $H^{4'}$), 3.08 (1 H, ddd, *J* 4.4, 6.6 and 9.7, $H^{8'}$), 2.96 (1 H, dd, *J* 7.8 and 8.5, H^4), 2.69-2.26 (2 H, m, PCH_2), 2.56 (1 H, q, *J* 5.1, H^8), 2.20-2.00 (2 H, m, PCH_2CH_2) and 1.95-1.55 (4 H, m, CH_2CH_2); δ_C(50 MHz, $CDCl_3$) 145.9$^-$ (*ipso*–NPh), 143.5-128.4 (Ph_2PO and *m*-NPh), 116.1$^+$ (*p*-NPh), 112.3$^+$ (*o*-NPh), 81.4$^+$ (d, *J* 13.8, C^2), 61.1$^+$ (C^5), 54.1$^-$ (C^4 or C^8), 52.1$^-$ (C^4 or C^8), 29.6$^-$ (C^6 or C^7), 25.8$^-$ (d, *J* 72.0, PCH_2), 25.3$^-$ (PCH_2CH_2) and 24.3$^-$ (C^6 or C^7); *m/z* 416 (10%, M^+) and 187 (100, M – $Ph_2POCH_2CH_2$)(Found: M^+, 416.2001. $C_{26}H_{29}N_2OP$ requires *M*, 416.2018).

(2*S*,4*S*,5*R*)-2-Ethenyl-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine *cis*-14

Using reaction conditions described by Scolastico,[20] a solution of *N*-tosyl norephedrine **13**[19] (312 mg, 1.0 mmol), acrolein diethyl acetal (170 µl, 1.1 mmol) and pyridinium *p*-toluenesulfonate (95 mg, 0.4 mmol) in benzene (10 cm^3) was heated under reflux via a by-passed dropping funnel containing 4Å molecular sieves. After 2.5 h, the mixture was allowed to cool to room temperature and the solvent was evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with hexane-EtOAc (4:1) as eluent gave *alkenyl oxazolidine cis*-**14** (290 mg, 83%) as a colourless oil, R_f(1:1 EtOAc-hexane) 0.6; $[\alpha]_D^{20}$ –17.6 (*c* 2.5 in $CHCl_3$); (Found: C, 66.3; H, 6.2; N, 4.25%; M^+, 343.1248. $C_{19}H_{21}NO_3S$ requires C, 66.4; H, 6.2; N, 4.1%; *M*, 343.1242); ν_{max}(film)/cm^{-1} 1652 (C=C), 1598 (C_6H_4), 1495 (C_6H_4), 1351 (SO_2N) and 1169 (SO_2N); δ_H(500 MHz, $CDCl_3$) 7.82 (2 H, d, *J* 8.1, *o*-$C_6H_4SO_2$), 7.38 (2 H, d, *J* 8.0, *m*-$C_6H_4SO_2$), 7.32-7.17 (5 H, m, Ph), 6.03 (1 H, ddd, *J* 5.8, 10.3 and 16.6, C*H*=CH_2), 5.63 (1 H, d, *J* 17.1, CH=C$H_A$$H_B$), 5.47 (1 H, d, *J* 5.8, OCHN), 5.39 (1 H, d, *J* 10.3, CH=C$H_A$$H_B$), 4.41 (1 H, d, *J* 5.4, PhCHO), 4.12 (1 H, quin, *J* 6.6, CHN), 2.46 (3 H, s, C_6H_4Me) and 0.83 (3 H, d, *J* 6.8, CH*Me*); δ_C(50 MHz, $CDCl_3$) 144.2$^-$ (*ipso*-$C_6H_4SO_2$), 136.1$^+$ (*C*H=CH_2), 135.3$^-$, 129.9$^+$, 128.2$^+$, 127.9$^+$, 127.7$^+$, 125.9$^+$, 144.2$^-$ (CH=*C*H_2), 90.2$^+$ (OCHN), 81.3$^+$ (PhCHO), 58.3$^+$ (CHN), 21.5$^+$ (C_6H_4Me) and 17.1$^+$ (CH*Me*); *m/z* 343 (20%, M^+), 316 (20, M – CH=CH_2), 91 (40, C_6H_4Me) and 82 (100). The *cis* stereochemistry was confirmed by 500 MHz NOESY analysis. Diagnostic NOEs: NOE between δ_H 5.47 (OCHN) and δ_H 4.41 (PhCHO); NOE between δ_H 4.41 (PhCHO) and δ_H 4.12 (CHN).

(2*S*,4*S*,5*R*)-2-[(2'*S*)-1'-hydroxy-2'-hydroxyethyl]-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine *syn*-15 and (2*S*,4*S*,5*R*)-2-[(2'*R*)-1'-hydroxy-2'-hydroxyethyl]-4-methyl-5-phenyl-3-*p*-toluenesulfonyl-oxazolidine *anti*-15

Osmium (III) chloride (20 mg, 0.07 mmol) was added to a stirred solution of alkenyl oxazolidine *cis*-**14** (8.0 g, 23.3 mmol), potassium ferricyanide (24.5 g, 74.4 mmol), potassium carbonate (9.6 g, 69.6 mmol) and quinuclidine (185 mg, 1.7 mmol) in *tert*-butyl alcohol–water (1:1; 200 cm^3) at room temperature. The resulting orange slurry was stirred vigorously at room temperature for 20 h and sodium sulfite (35 g) was added. After stirring at room temperature for 1 h, CH_2Cl_2 (100 cm^3) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc-hexane (1:1) as eluent gave a 72:28 ratio (by ^1H NMR) of *1,2-diols syn*- and *anti*-**15** (7.75 g, 88%) as a foam which could not be crystallised, R_f(1:1 EtOAc-hexane) 0.2; $[\alpha]_D^{20}$ +18.6 (*c* 0.9 in $CHCl_3$); (Found: C, 60.1; H, 6.3; N, 3.5%; M^+ + H, 378.1378. $C_{19}H_{23}NO_5S$ requires C, 60.5; H, 6.1; N, 3.7%; *M* + H, 378.1375); $\nu_{max}(CHCl_3)/cm^{-1}$ 3692 (OH), 3668 (OH), 1598 (C_6H_4), 1495 (C_6H_4), 1347 (SO_2N) and 1164 (SO_2N); δ_H(400 MHz, $CDCl_3$) 7.84 (2 H, d, *J* 8.3, *o*-$C_6H_4SO_2^{syn}$), 7.83 (2 H, d, *J* 8.5, *o*-$C_6H_4SO_2^{anti}$), 7.42 (4 H, d, *J* 8.0, 2 × *m*-$C_6H_4SO_2$), 7.37-7.07 (10 H, m, 2 × Ph), 5.13 (1 H, d, *J* 3.5, $OCHN^{anti}$), 5.06 (1 H, d, *J* 6.3, $OCHN^{syn}$), 4.24 (1 H, d, *J* 5.6, $PhCHO^{anti}$), 4.18 (1 H, d, *J* 5.4, $PhCHO^{syn}$), 4.14-3.83 (8 H, m, 2 × C*H*N, 2 × C*H*OH and 2 × C*H*$_2$OH), 3.70 (1 H, br s, OH^{anti}), 2.92 (1 H, br s, OH^{syn}), 2.47 (6 H, s, 2 × C_6H_4Me), 0.87 (3 H, d, *J* 6.9, CH*Me*^{syn}) and 0.84 (3 H, d, *J* 6.8, CH*Me*^{anti}); δ_C(50 MHz, $CDCl_3$) 144.9$^-$ (*ipso*-$C_6H_4SO_2^{syn}$), 144.8$^-$ (*ipso*-$C_6H_4SO_2^{anti}$), 134.7$^-$(^{anti}), 134.6$^-$(^{syn}), 133.8$^-$(^{anti}), 133.6$^-$(^{syn}), 130.2-125.7$^+$ (C_6H_4Me and Ph), 90.7$^+$ ($OCHN^{anti}$), 90.6$^+$ ($OCHN^{syn}$), 81.1$^+$ ($PhCHO^{anti}$), 80.9$^+$ ($PhCHO^{syn}$), 74.3$^+$ ($CHOH^{syn}$), 73.35$^+$ ($CHOH^{anti}$), 62.9$^-$ (CH_2OH^{anti}), 62.5$^-$ (CH_2OH^{syn}), 59.0$^+$ (CHN^{syn}), 58.5$^+$ (CHN^{anti}), 21.5$^+$ (2 × C_6H_4Me), 17.1$^+$ (CH*Me*^{syn}) and 17.0$^+$ (CH*Me*^{anti}); *m/z* 378 (60%, M^+ + H), 316 (90, M – $CHOHCH_2OH$) and 91 (100, C_6H_4Me).

Conversion of 1,2-diols *syn* and *anti*-15 into the dithiane (*S*)-16

Boron trifluoride etherate (60 μl, 0.5 mmol) was added dropwise to a stirred solution of a 72:28 ratio of 1,2-diols *syn* and *anti*-**15** (169 mg, 0.45 mmol) and propan-1,3-dithiol (250 μl, 2.5 mmol) in CH_2Cl_2 (7.5 cm^3) under argon at room temperature. After 48 h, water (10 cm^3) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were washed with saturated sodium bicarbonate solution (10 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave the dithiane (*S*)-**16** (27 mg, 34%) as a colourless oil, R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ –2.6 (*c* 1.2 in MeOH)[lit.,[23] $[\alpha]_D^{20}$ +6.0 (*c* 1.08 in MeOH) for the dithiane (*R*)-**16**]; ν_{max}(Nujol)/cm^{-1} 3447 (OH); δ_H(200 MHz, $CDCl_3$) 4.05-3.77 (4 H, m, C*H*$_2$OH, C*H*OH and SCHS), 3.00-2.88 (2 H, m), 2.74-2.66 (2 H) and 2.08-1.99 (2 H, m, CH_2); δ_C(50 MHz, $CDCl_3$) 71.3$^+$ (CHOH), 63.6$^-$ (CH_2OH), 47.3$^+$ (SCHS), 27.45$^-$ (SCH_2), 26.9$^-$ (SCH_2) and 25.4$^-$ (CH_2); *m/z* 180 (100%, M^+), 149 (30, M – CH_2OH) and 45 (90, $CHCH_2OH$)(Found: M^+, 180.0280. $C_6H_{12}O_2S_2$ requires *M*, 180.0279).

Conversion of 1,2-diols *syn*- and *anti*-15 into cyclic sulfites 17

Triethylamine (90 μl, 0.65 mmol) was added dropwise to a stirred solution of a 72:28 ratio of 1,2-diols *syn*- and *anti*-**15** (118 mg, 0.3 mmol) and thionyl chloride (35 μl, 0.5 mmol) in CH_2Cl_2 (5 cm^3) under argon at 0

°C. The resulting solution was allowed to warm to room temperature over 1 h and then the solvent was evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with hexane-EtOAc (2:1) as eluent gave a 44:28:17:11 ratio (by ^{1}H NMR) of *cyclic sulfites* **17** (126 mg, 99%) as a foam which could not be crystallised, R_f(1:1 EtOAc-hexane) 0.5; $\nu_{max}(CHCl_3)/cm^{-1}$ 1598 (C_6H_4), 1496 (C_6H_4), 1356 (SO_2N), 1168 (SO_2N) and 1070 (SO); Diagnostic signals for the four diastereomers: δ_H(400 MHz, $CDCl_3$) 5.45 (1 H, d, *J* 2.8, $OCHN^{syn,minor}$), 5.37 (1 H, d, *J* 4.2, $OCHN^{anti,minor}$), 5.19 (1 H, d, *J* 2.8, $OCHN^{syn,major}$), 5.16 (1 H, d, *J* 3.4, $OCHN^{anti,major}$), 4.43 (1 H, d, *J* 5.8, $PhCHO^{syn,minor}$), 4.39 (1 H, d, *J* 5.9, $PhCHO^{syn,major}$), 4.35 (1 H, d, *J* 5.6, $PhCHO^{anti,major}$) and 4.27 (1 H, d, *J* 5.5, $PhCHO^{anti,minor}$); δ_C(100 MHz, $CDCl_3$) 89.1$^+$ ($OCHN^{anti}$), 88.4$^+$ ($OCHN^{syn}$), 88.0$^+$ ($OCHN^{anti}$), 87.5$^+$ ($OCHN^{syn}$), 68.1$^-$ ($CH_2OSO^{syn,minor}$), 67.8$^-$ ($CH_2OSO^{anti,minor}$), 67.0$^-$ ($CH_2OSO^{syn,major}$), 66.8$^-$ ($CH_2OSO^{anti,major}$), 17.6$^+$ ($CHMe^{syn}$), 17.5$^+$ ($CHMe^{syn}$), 16.9$^+$ ($CHMe^{anti}$) and 16.8$^+$ ($CHMe^{anti}$); *m/z* 424 (40%, $M^+ + H$), 423 (10, M^+), 316 (80, $M - CHOSO_2CH_2$) and 91 (100, C_6H_4Me)(Found: M^+, 423.0789. $C_{19}H_{21}NO_6S_2$ requires *M*, 423.0810).

Conversion of cyclic sulfites 17 into cyclic sulfates *syn*- and *anti*-18

Sodium periodate (207 mg, 1.0 mmol) and ruthenium (III) chloride trihydrate (3 mg, 0.01 mmol) were added in one portion to a stirred solution of cyclic sulfites **17** (340 mg, 0.8 mmol) in carbon tetrachloride-water-acetonitrile (1:1:1; 9 cm^3) at room temperature. After 12 h at room temperature, water (10 cm^3) and CH_2Cl_2 (10 cm^3) were added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with EtOAc-hexane (1:1) as eluent gave a 72:28 ratio (by ^{1}H NMR) of *cyclic sulfates syn*- and *anti*-**18** (358 mg, 100%) as a foam which could not be crystallised, R_f(1:1 EtOAc-hexane) 0.5 for *syn*-**18** and 0.4 for *anti*-**18**; $[\alpha]_D^{20}$ −10.3 (*c* 0.9 in $CHCl_3$); (Found: C, 51.8; H, 4.85; N, 3.0%; M^+, 439.0738. $C_{19}H_{21}NO_7S_2$ requires C, 51.9; H, 4.8; N, 3.2%; *M*, 439.0760); $\nu_{max}(CHCl_3)/cm^{-1}$ 1598 (C_6H_4), 1495 (C_6H_4), 1356 (SO_2N), 1174 (SO_2N) and 1128 (SO_2); δ_H(400 MHz, $CDCl_3$) 7.83 (2 H, d, *J* 8.2, *o*-$C_6H_4SO_2^{syn}$), 7.82 (2 H, d, *J* 8.0, *o*-$C_6H_4SO_2^{anti}$), 7.44 (2 H, d, *J* 8.1, *m*-$C_6H_4SO_2^{syn}$), 7.43 (2 H, d, *J* 7.7, *m*-$C_6H_4SO_2^{anti}$), 7.34-7.12 (10 H, m, 2 × Ph), 5.43 (1 H, ddd, *J* 2.3, 6.15 and 7.1, $CHOSO_2^{syn}$), 5.35 (1 H, d, *J* 2.3, $OCHN^{syn}$), 5.30 (1 H, d, *J* 3.45, $OCHN^{anti}$), 5.23 (1 H, dt, *J* 3.4 and 6.2, $CHOSO_2^{anti}$), 5.04 (1 H, dd, *J* 5.8 and 9.2, $SO_2OCH_AH_B^{syn}$), 4.97 (1 H, dd, *J* 6.0 and 9.2, $SO_2OCH_AH_B^{anti}$), 4.86 (1 H, dd, *J* 6.8 and 9.1, $SO_2OCH_AH_B^{syn}$; 1 H, "underneath", $SO_2OCH_AH_B^{anti}$), 4.47 (1 H, d, *J* 5.9, $PhCHO^{syn}$), 4.38 (1 H, d, *J* 5.6, $PhCHO^{anti}$), 4.03 (2 H, quin, *J* 6.7, 2 × CHN), 2.49 (6 H, s, 2 × C_6H_4Me), 0.83 (3 H, d, *J* 6.9, $CHMe^{syn}$) and 0.82 (3 H, d, *J* 6.8, $CHMe^{anti}$); δ_C(50 MHz, $CDCl_3$) 145.5$^-$ (*ipso*-$C_6H_4SO_2^{syn}$), 145.3$^-$ (*ipso*-$C_6H_4SO_2^{anti}$), 133.9-125.6 (C_6H_4Me and Ph), 87.8$^+$ ($OCHN^{anti}$), 87.2$^+$ ($OCHN^{syn}$), 82.4$^+$ ($CHOSO_2^{anti}$), 81.7$^+$ ($CHOSO_2^{syn}$), 80.9$^+$ ($PhCHO^{anti}$), 80.3$^+$ ($PhCHO^{syn}$), 68.6$^-$ ($SO_2OCH_2^{anti}$), 67.5$^-$ ($SO_2OCH_2^{syn}$), 58.8$^+$ (CHN^{syn}), 58.6$^+$ (CHN^{anti}), 23.2$^+$ (2 × C_6H_4Me), 17.4$^+$ ($CHMe^{syn}$) and 16.4$^+$ ($CHMe^{anti}$); *m/z* 440 (10%, $M^+ + H$), 439 (5, M^+), 316 (70, $M - CHOSO_2OCH_2$) and 91 (100, C_6H_4Me).

Reaction of lithium diphenylphosphide with cyclic sulfates 18

n-Butyllithium (3.8 cm^3 of a 1.5 M solution in hexane, 5.7 mmol) was added dropwise to a stirred solution of diphenylphosphine (1.0 cm^3, 5.75 mmol) in THF (60 cm^3) under argon at −30 °C. The resulting orange solution was stirred at this temperature for 4 h and then a solution of a 72:28 ratio of cyclic sulfates *syn*- and

anti-**18** (2.03 g, 4.6 mmol) in THF (20 cm^3) was added dropwise and the resulting yellow solution was allowed to warm to room temperature over 1.5 h. Water (5 cm^3) was then added dropwise followed by the addition of concentrated sulfuric acid (0.5 cm^3). The resulting colourless solution was stirred at room temperature for 12 h. Hydrogen peroxide (100 vol, 5 cm^3) was added and the solution stirred for a further 30 min. The THF was evaporated under reduced pressure and the residue dissolved in CH_2Cl_2-water (1:1; 30 cm^3). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30cm^3). The combined arganic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave a 70:30 ratio of *alcohols syn*- and *anti*-**19** (2.13 g, 82%) as a foam which could not be crystallised.

(2*S*,4*S*,5*R*)-2-(1'-Diphenylphosphinoylethyl-2'-keto)-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine 8
A solution of a 72:28 ratio of alcohols *syn*- and *anti*-**19** (679 mg, 1.2 mmol) in CH_2Cl_2 (5 cm^3) was added dropwise by means of a canula to a stirred solution of Dess-Martin periodinane (974 mg, 2.6 mmol) in CH_2Cl_2 (10 cm^3) under argon at 0 °C. The resulting solution was allowed to warm to room temperature and stirred for 12 h. Then, the mixture was carefully poured into a solution of sodium thiosulfate (20 mmol) in saturated sodium bicarbonate (20 cm^3). After 30 min, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts were washed with saturated sodium bicarbonate (20 cm^3) and saturated brine (20 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by chromatography on silica with EtOAc as eluent gave the *ketone* **8** (373 mg, 55%) as a foam which could not be crystallised, R_f(EtOAc) 0.5; $[\alpha]_D^{20}$ –63.5 (*c* 1.4 in $CHCl_3$); (Found: M^+ – TsH, 403.1345. $C_{31}H_{30}NO_5PS$ requires *M* – TsH, 403.1337); $\nu_{max}(CHCl_3)/cm^{-1}$ 1734 (C=O), 1598 (Ph and C_6H_4), 1495 (C_6H_4), 1438 (P–Ph), 1355 (SO_2N), 1213 (P=O) and 1167 (SO_2N); δ_H(200 MHz, $CDCl_3$) 7.97-7.72 (4 H, m, *o*-Ph_2PO), 7.87 (2 H, d, *J* 8.0, *o*-$C_6H_4SO_2$), 7.58-7.44 (6 H, m, *m*- and *p*-Ph_2PO), 7.37 (2 H, d, *J* 8.1, *m*-$C_6H_4SO_2$), 7.25-7.10 (5 H, m, Ph), 5.72 (1 H, s, OCHN), 4.46 (1 H, dd, *J* 14.0 and 15.6, PCH_AH_B), 4.25 (1 H, d, *J* 5.7, PhCHO), 4.13 (1 H, quin, *J* 7.1, CHN), 3.76 (1 H, t, *J* 13.3, PCH_AH_B), 2.40 (3 H, s, C_6H_4Me) and 0.69 (3 H, d, *J* 6.85, CH*Me*); δ_C(50 MHz, $CDCl_3$) 196.4^- (d, *J* 6.0, C=O), 144.9^- (*ipso*-$C_6H_4SO_2$), 134.8-125.9 (Ph_2PO, C_6H_4Me and Ph), 89.8^+ (OCHN), 82.5^+ (PhCHO), 58.6^+ (CHN), 41.4^- (d, *J* 58.6, PCH_2), 21.5^+ (C_6H_4Me) and 16.3^+ (CH*Me*); *m/z* 403 (40%, M^+ – TsH), 201 (100, Ph_2PO), 91 (50, C_6H_4Me) and 77 (40, Ph).

(2*S*,4*S*,5*R*)-2-Diphenylphosphinoylethenyl-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine 10
n-Butyllithium (70 μl of a 1.5 M solution in hexane, 0.1 mmol) was added dropwise to a stirred solution of a 72:28 ratio of alcohols *syn*- and *anti*-**19** (59 mg, 0.1 mmol) in THF (4 cm^3) under argon at 0 °C. The resulting red solution was stirred at 0 °C for 10 min and then methanesulfonyl chloride (10 μl, 0.1 mmol) was added dropwise. After 1 h at 0 °C, n-butyllithium (80 μl of a 1.5 M solution in hexane, 0.1 mmol) was added dropwise and the reaction mixture was allowed to warm to room temperature and stirred for 2 h. Saturated ammonium chloride (1 cm^3) was added, the THF evaporated under reduced pressure and the residue dissolved in CH_2Cl_2-water (1:1; 10 cm^3). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined arganic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with EtOAc as eluent gave *vinyl phosphine oxide* **10** (31 mg, 52%) as an oil, R_f(EtOAc) 0.5; $\nu_{max}(CHCl_3)/cm^{-1}$ 1598 (Ph and C_6H_4), 1496 (Ph and C_6H_4), 1438 (P–Ph), 1354 (SO_2N), 1237 (P=O) and 1167 (SO_2N); δ_H(200 MHz, $CDCl_3$) 7.80-

7.70 (6 H, m, *o*-Ph_2PO and *o*-$C_6H_4SO_2$), 7.55-7.46 (6 H, m, *m*- and *p*-Ph_2PO), 7.36-7.10 (7 H, m, Ph and *m*-$C_6H_4SO_2$), 6.89 (1 H, d, *J* 22.6, PCH), 6.89 (1 H, dd, *J* 1.0 and 19.0, PCH=C*H*), 5.71 (1 H, dd, *J* 1.6 and 3.9, OCHN), 4.41 (1 H, d, *J* 5.3, PhCHO), 4.14-4.06 (1 H, m, *J* 6.7, CHN), 2.44 (3 H, s, C_6H_4Me) and 0.75 (3 H, d, *J* 6.8, CH*Me*); δ_C(100 MHz, $CDCl_3$) 146.7$^+$ (d, *J* 2.6, PCH=*C*H), 144.6$^-$ (*ipso*-$C_6H_4SO_2$), 135.2-125.9 (Ph_2PO, C_6H_4Me and Ph), 126.65$^+$ (d, *J* 121.0, PCH), 92.7$^+$ (d, *J* 14.2, OCHN), 81.8$^+$ (PhCHO), 58.5$^+$ (CHN), 21.7$^+$ (C_6H_4Me) and 17.0$^+$ (CH*Me*); *m/z* 543 (40%, M^+), 426 (100), 201 (50, Ph_2PO), 91 (100, C_6H_4Me) and 77 (40, Ph)(Found: M^+, 543.1661. $C_{31}H_{30}NO_4PS$ requires *M*, 543.1633).

(2*S*,4*S*,5*R*)-2-Diphenylphosphinoylethenyl-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine 6

L-Selectride® (0.05 cm^3 of a 1.0 M solution in hexane, 0.05 mmol) was added dropwise to a stirred solution of the vinyl phosphine oxide **10** (31 mg, 0.05 mmol) in THF (2 cm^3) under argon at –78 °C. After 2 h at –78 °C, the solution was allowed to warm to room temperature and water (1.0 cm^3) was added. The THF was evaporated under reduced pressure and the residue dissolved in CH_2Cl_2-water (1:1; 20 cm^3). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were washed with 3 M hydrochloric acid (3 × 10 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave *phosphine oxide* **6** (30 mg, 93%) as an oil, R_f(EtOAc) 0.35; ν_{max}($CHCl_3$)/cm^{-1} 1598 (Ph and C_6H_4), 1496 (Ph and C_6H_4), 1438 (P–Ph), 1350 (SO_2N), 1246 (P=O) and 1165 (SO_2N); δ_H(400 MHz, $CDCl_3$) 7.83-7.75 (6 H, m, *o*-Ph_2PO and *o*-$C_6H_4SO_2$), 7.54-7.47 (6 H, m, *m*- and *p*-Ph_2PO), 7.35 (2 H, d, *J* 8.15, *m*-$C_6H_4SO_2$), 7.30-7.23 (3 H, m, Ph), 7.09-7.05 (2 H, m, Ph), 5.14 (1 H, dd, *J* 3.7 and 5.2, OCHN), 4.24 (1 H, d, *J* 5.6, PhCHO), 4.01-3.94 (1 H, m, *J* 6.7, CHN), 2.65-2.20 (4 H, m, PCH_2CH_2), 2.44 (3 H, s, C_6H_4Me) and 0.77 (3 H, d, *J* 6.8, CH*Me*); δ_C(100 MHz, $CDCl_3$) 144.4$^-$ (*ipso*-$C_6H_4SO_2$), 135.1-125.8 (Ph_2PO, C_6H_4Me and Ph), 90.4$^+$ (d, *J* 16.8, OCHN), 80.9$^+$ (PhCHO), 58.5$^+$ (CHN), 28.6$^-$ (PCH_2CH_2), 24.2$^-$ (d, *J* 73.15, PCH_2), 21.7$^+$ (C_6H_4Me) and 17.6$^+$ (CH*Me*).

(2*S*,4*S*,5*R*)-2-Methoxycarbonyl-4-methyl-5-phenyl-3-*tert*-butoxycarbonyloxazolidine *cis*-21

A solution of (–)-norephedrine (1.0 g, 6.6 mmol) and methyl glyoxylate[30] (729 mg, 8.3 mmol) in toluene (25 cm^3) was heated under reflux with continuous removal of water by means of a Dean-Stark head. After 1 h, the mixture was allowed to cool to room temperature and the toluene was evaporated under reduced pressure to give a 50:50 ratio (by ^1H NMR) of oxazolidines *cis*- and *trans*-**20** (1.45 g, 100%) as a yellow oil which was dissolved in EtOAc (25 cm^3) and heated to 50 °C. Then, a solution of di-*tert*-butyl dicarbonate (1.47 g, 7.9 mmol) in EtOAc (25 cm^3) was added dropwise over a period of 3 h. Water (10 cm^3) was added, the layers separated and the aqueous layer extracted with EtOAc (3 × 20 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with EtOAc-hexane (1:1) as eluent gave *oxazolidine cis*-**21** (1.7 g, 81%) as a colourless oil, R_f(EtOAc) 0.6; $[\alpha]_D^{20}$ –68.3 (*c* 1.1 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1758 (C=O, CO_2Me), 1713 (C=O, $NCO_2{}^tBu$), 1607 (Ph) and 1498 (Ph); δ_H(200 MHz, $CDCl_3$) 7.39-7.26 (5 H, m, Ph), 5.42 (1 H, br s, OCHN), 5.24 (1 H, d, *J* 5.6, PhCHO), 4.26 (1 H, br m, CHN), 3.86 (3 H, s, MeO), 1.46 (9 H, br s, CMe_3) and 0.91 (3 H, d, *J* 6.6, CH*Me*); δ_C(50 MHz, $CDCl_3$) 168.9$^-$ (C=O), 135.4$^-$ (*ipso*–Ph), 128.2$^+$, 128.0$^+$, 126.1$^+$, 85.0$^+$ (OCHN), 83.2$^+$ (PhCHO), 81.0$^-$ (O*C*Me_3), 55.3$^+$ (CHN), 52.6$^+$ (MeO), 28.3$^+$ (OC*Me*$_3$) and 14.7$^+$ (CH*Me*); *m/z* 321 (5%, M^+), 320 (10, M – H), 262 (60, M – CO_2Me), 206 (80, M – $CO_2{}^tBu$) and 57 (100, CMe_3)(Found: M^+, 321.1581. $C_{17}H_{23}NO_5$ requires *M*, 321.1576).

(2*S*,4*S*,5*R*)-2-(1'-Diphenylphosphinoylethyl-2'-keto)-4-methyl-5-phenyl-3-*tert*-butoxycarbonyl-oxazolidine 9

n-Butyllithium (2.2 cm^3 of a 1.6 M solution in hexane, 3.5 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (751 mg, 3.5 mmol) in THF (15 cm^3) under argon at –78 °C. After 30 min at –78 °C, a solution of methyl ester **21** (868 mg, 2.7 mmol) in THF (10 cm^3) was added dropwise and the resulting solution was stirred at –78 °C for 1 h. Saturated ammonium chloride (1 cm^3) was added and the mixture allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue dissolved in CH_2Cl_2-water (1:1; 20 cm^3). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with EtOAc as eluent gave *ketone* **9** (699 mg, 51%) as plates, m.p. 167-169 °C (from EtOAc); R_f(EtOAc) 0.5; $[\alpha]_D^{20}$ –48.1 (*c* 0.24 in $CHCl_3$); (Found: C, 69.1; H, 6.4; N, 2.7; P, 6.2%; M^+, 505.2025. $C_{29}H_{32}NO_5P$ requires C, 68.9; H, 6.4; N, 2.8; P, 6.1%; *M*, 505.2018); ν_{max}(Nujol)/cm^{-1} 1740 (C=O, CO_2Me), 1707 (C=O, $NCO_2{}^tBu$), 1459 (P–Ph) and 1186 (P=O); δ_H(200 MHz, $CDCl_3$) 7.89-7.76 (4 H, m, *o*-Ph_2PO), 7.56-7.45 (6 H, m, *m*- and *p*-Ph_2PO), 7.34-7.17 (5 H, m, Ph), 5.52 (1 H, s, OCHN), 5.20 (1 H, d, *J* 5.7, PhCHO), 4.4-3.6 (3 H, br m, PCH_AH_B, PCH_AH_B and CHN), 1.35 (9 H, br s, CMe_3) and 0.75 (3 H, d, *J* 6.7, CH*Me*); δ_C(50 MHz, $CDCl_3$) 135.3-125.9 (Ph_2PO and Ph), 89.0$^+$ (OCHN), 82.7$^+$ (PhCHO), 81.2$^-$ ($OCMe_3$), 55.4$^+$ (CHN), 41.8$^-$ (d, *J* 61.8, PCH_2), 28.1$^+$ ($OCMe_3$) and 15.1$^+$ (CH*Me*); *m/z* 505 (10%, M^+), 432 (40, M – $OCMe_3$), 262 (60, M – Ph_2POCH_2CO), 215 (80, Ph_2POCH_2), 206 (100) and 57 (60, CMe_3).

Luche reduction of ketone 8: (2*S*,4*S*,5*R*)-2-[(2'*S*)-1'-Diphenylphosphinoylethyl-2'-hydroxy]-4-methyl-5-phenyl-3-*p*-toluenesulfonyl-oxazolidine *syn*-19

Sodium borohydride (47 mg, 1.2 mmol) was added in one portion to a stirred solution of ketone **8** (500 mg, 0.9 mmol) and $CeCl_3$•$7H_2O$ (580 mg, 1.6 mmol) in EtOH (10 cm^3) under argon at –78 °C. After 2 h at –78 °C, water (5 cm^3) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 40 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a 95:5 ratio (by ^1H NMR) of alcohols *syn*- and *anti*-**19** (500 mg, 100%) as an oil. Purification by chromatography on silica with EtOAc as eluent gave *alcohol syn*-**19** (300 mg, 60%) as a foam which could not be crystallised, R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ –1.4 (*c* 0.5 in $CHCl_3$); (Found: C, 65.7; H, 5.7; N, 2.25; P, 5.6%; M^+ – Ts, 406.1570. $C_{31}H_{32}NO_5PS$ requires C, 66.3; H, 5.75; N, 2.5; P, 5.5%; *M* – Ts, 406.1572); ν_{max}($CHCl_3$)/cm^{-1} 3373 (OH), 1598 (Ph and C_6H_4), 1495 (Ph and C_6H_4), 1438 (P–Ph), 1353 (SO_2N), 1166 (SO_2N) and 1122 (P=O); δ_H(400 MHz, $CDCl_3$) 7.87-7.73 (4 H, m, *o*-Ph_2PO), 7.79 (2 H, d, *J* 8.3, *o*-$C_6H_4SO_2$), 7.56-7.48 (6 H, m, *m*- and *p*-Ph_2PO), 7.36 (2 H, d, *J* 8.0, *m*-$C_6H_4SO_2$), 7.27-7.24 (3 H, m, Ph), 7.10-7.09 (2 H, m, Ph), 5.07 (1 H, d, *J* 3.6, OCHN), 4.60 (1 H, br s, OH), 4.55 (1 H, ddt, *J* 1.8, 3.5 and 9.8, C*H*OH), 4.26 (1 H, d, *J* 5.7, PhCHO), 4.02 (1 H, quin, *J* 6.7, CHN), 2.84 (1 H, ddd, *J* 1.8, 9.0 and 14.85, PCH_AH_B), 2.70 (1 H, td, *J* 11.5 and 14.85, PCH_AH_B), 2.44 (3 H, s, C_6H_4Me) and 0.83 (3 H, d, *J* 6.8, CH*Me*); δ_C(100 MHz, $CDCl_3$) 144.7$^-$ (*ipso*-$C_6H_4SO_2$), 134.9-125.9 (Ph_2PO, C_6H_4Me and Ph), 91.9$^+$ (d, *J* 15.2, OCHN), 81.0$^+$ (PhCHO), 69.2$^+$ (CHOH), 58.9$^+$ (CHN), 30.3$^-$ (d, *J* 72.7, PCH_2), 21.6$^+$ (C_6H_4Me) and 17.5$^+$ (CH*Me*); *m/z* 406 (10%, M^+ – Ts), 316 (40, M – $Ph_2P(O)CH_2CHOH$), 201 (70, Ph_2PO), 91 (100, C_6H_4Me) and 77 (50, Ph).

(2*S*,4*S*,5*R*)-2-Formyl-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine 25

Sodium periodate (136 mg, 0.6 mmol) was added in one portion to a stirred solution of a 72:28 ratio of 1,2-diols *syn*- and *anti*-**15** (120 mg, 0.3 mmol) in MeOH (5 cm^3) at room temperature. After 2.5 h at room temperature, water (10 cm^3) and EtOAc (10 cm^3) were added and the layers separated. The aqueous layer was extracted with EtOAc (3 × 20 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc-hexane (1:1) as eluent gave impure *aldehyde* **25** (77 mg, 70%) as a colourless oil, R_f(1:1 EtOAc-hexane) 0.4; δ_H(200 MHz, $CDCl_3$) 9.55 (1 H, d, *J* 2.85, CHO), 7.84 (2 H, d, *J* 8.3, *o*-$C_6H_4SO_2$), 7.42 (2 H, d, *J* 8.1, *m*-$C_6H_4SO_2$), 7.36-7.17 (5 H, m, Ph), 5.19 (1 H, d, *J* 2.9, OCHN), 4.50 (1 H, d, *J* 5.6, PhCHO), 4.20-4.00 (1 H, m, CHN), 2.47 (3 H, s, C_6H_4Me) and 0.83 (3 H, d, *J* 6.8, CH*Me*).

(2*S*,4*S*,5*R*)-2-[(2'*R*)-1'-Diphenylphosphinoylethyl-2'-hydroxy]-4-methyl-5-phenyl-3-*p*-toluenesulfonyloxazolidine *anti*-19

n-Butyllithium (0.12 cm^3 of a 1.5 M solution in hexane, 0.2 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (38 mg, 0.2 mmol) in THF (2.5 cm^3) under argon at –78 °C. After 30 min at –78 °C, a solution of the impure aldehyde **25** (77 mg, 0.2 mmol) in THF (2 cm^3) was added dropwise and the resulting solution was stirred at –78 °C for 1 h. Saturated ammonium chloride (0.5 cm^3) was added and the mixture allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue dissolved in CH_2Cl_2-water (1:1; 10 cm^3). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave *alcohol anti*-**19** (33 mg, 33%) as a foam which could not be crystallised, R_f(EtOAc) 0.45; $[\alpha]_D^{20}$ +0.8 (*c* 0.4 in $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3373 (OH), 1598 (Ph and C_6H_4), 1495 (Ph and C_6H_4), 1438 (P–Ph), 1353 (SO_2N), 1166 (SO_2N) and 1122 (P=O); δ_H(400 MHz, $CDCl_3$) 7.83-7.77 (6 H, m, *o*-Ph_2PO and *o*-$C_6H_4SO_2$), 7.55-7.44 (6 H, m, *m*- and *p*-Ph_2PO), 7.38 (2 H, d, *J* 8.1, *m*-$C_6H_4SO_2$), 7.26-7.20 (3 H, m, Ph), 7.10-7.08 (2 H, m, Ph), 5.18 (1 H, d, *J* 4.5, OCHN), 4.32 (1 H, ddd, *J* 3.1, 5.6 and 9.8, C*H*OH), 4.15 (1 H, d, *J* 5.6, PhCHO), 4.02 (1 H, quin, *J* 6.7, CHN), 2.86 (1 H, ddd, *J* 3.5, 10.2 and 15.0, PCH_AH_B), 2.77 (1 H, td, *J* 9.9 and 15.3, PCH_AH_B), 2.44 (3 H, s, C_6H_4Me) and 0.70 (3 H, d, *J* 6.85, CH*Me*); δ_C(100 MHz, $CDCl_3$) 144.8^- (*ipso*-$C_6H_4SO_2$), 135.2-126.0 (Ph_2PO, C_6H_4Me and Ph), 92.7^+ (d, *J* 13.7, OCHN), 81.2^+ (PhCHO), 69.3^+ (CHOH), 58.8^+ (CHN), 32.7^- (d, *J* 71.9, PCH_2), 21.7^+ (C_6H_4Me) and 17.1^+ (CH*Me*); *m/z* 406 (10%, M^+ – Ts), 316 (40, M – $Ph_2P(O)CH_2CHOH$), 201 (70, Ph_2PO), 91 (100, C_6H_4Me) and 77 (50, Ph)(Found: M^+ – Ts, 406.1570. $C_{31}H_{32}NO_5PS$ requires *M* – Ts, 406.1572).

Conversion of hydroxy oxazolidines *syn*- and *anti*-19 into the dithiolane (*S*)-27

Boron trifluoride etherate (6 μl, 0.05 mmol) was added dropwise to a stirred solution of a 72:28 ratio of 1,2-diols *syn* and *anti*-**15** (30 mg, 0.05 mmol) and ethan-1,3-dithiol (30 μl, 0.3 mmol) in CH_2Cl_2 (2 cm^3) under argon at room temperature. After 48 h, water (5 cm^3) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 cm^3) and the combined organic extracts were washed with saturated sodium bicarbonate solution (5 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc-hexane (1:1) and then EtOAc as eluent gave the *dithiolane* (*S*)-**27** (10 mg, 53%) as a foam which could not be crystallised, R_f(EtOAc) 0.3; $[\alpha]_D^{20}$ –23.2 (*c* 1.0 in $CHCl_3$; 40% ee by Pirkle); ν_{max}(Nujol)/cm^{-1} 3364 (OH), 1593 (Ph), 1438 (P–Ph) and 1171 (P=O);

δ_H(200 MHz, $CDCl_3$) 7.84-7.67 (4 H, m, *o*-Ph_2PO), 7.58-7.37 (6 H, *m*- and *p*-Ph_2PO), 4.65 (1 H, br s, OH), 4.58 (1 H, d, *J* 6.4, SCHS), 4.14-3.99 (1 H, m, C*H*OH), 3.17 (4 H, br s, CH_2CH_2), 2.75 (1 H, ddd, *J* 2.3, 9.1 and 14.7, PCH_AH_B) and 2.58 (1 H, ddd, *J* 10.0, 11.5 and 14.7, PCH_AH_B); δ_C(50 MHz, $CDCl_3$) 132.1-128.6 (Ph_2PO), 71.5$^+$ (d, *J* 3.1, CHOH), 59.4$^+$ (d, *J* 15.2, SCHS), 38.6$^-$ (SCH_2), 38.4$^-$ (SCH_2) and 33.7$^-$ (d, *J* 70.45, PCH_2); *m/z* 332 (60%, $M^+ - H_2O$), 245 (100, $Ph_2P(O)CH_2CHOH$), 201 (90, Ph_2PO) and 77 (20, Ph)(Found: $M^+ - H_2O$, 332.0462. $C_{17}H_{19}O_2PS_2$ requires $M - H_2O$, 332.0458).

Conversion of the dithiolane (*S*)-27 into benzyl ether (*S*)-28

The dithiolane (*S*)-**27** (20 mg, 0.06 mmol) was added in one portion to a stirred suspension of sodium hydride (2.5 mg of a 60 wt% dispersion in mineral oil, 0.06 mmol) and tetra-n-butylammonium iodide (1 mg, 0.02 mmol) in THF (2 cm^3) under argon at room temperature. After 5 min, benzyl bromide (10 μl, 0.1 mmol) was added dropwise and the resulting suspension stirred at room temperature for 16 h. Water (5 cm^3) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave *benzyl ether* (*S*)-**28** (16 mg, 61%) as a colourless oil, R_f(EtOAc) 0.5; $[\alpha]_D^{20}$ –7.8 (*c* 1.6 in $CHCl_3$; 40% ee); ν_{max}(Nujol)/cm^{-1} 1593 (Ph), 1438 (P–Ph) and 1171 (P=O); δ_H(200 MHz, $CDCl_3$) 7.85-7.67 (4 H, m, *o*-Ph_2PO), 7.50-7.37 (6 H, *m*- and *p*-Ph_2PO), 7.19-7.16 (3 H, m, Ph), 6.98-6.93 (2 H, m, Ph), 4.78 (1 H, d, *J* 5.4, SCHS), 4.64 (1 H, d, *J* 10.6 PhCH_AH_BO), 4.44 (1 H, d, *J* 10.6, PhCH_AH_BO), 4.24-4.10 (1 H, m, C*H*OBn), 3.29-3.10 (4 H, m, CH_2CH_2) and 2.94-2.68 (2 H, m, PCH_2); δ_C(50 MHz, $CDCl_3$) 137.7$^-$ (*ipso*-Ph), 131.6-127.4 (Ph_2PO and Ph), 78.2$^+$ (d, *J* 2.9, *C*HOBn), 73.5$^-$ ($PhCH_2O$), 57.9$^+$ (d, *J* 12.4, SCHS), 38.7$^-$ (SCH_2), 38.6$^-$ (SCH_2) and 33.7$^-$ (d, *J* 72.2, PCH_2); *m/z* 335 (50%, $M^+ - CH(SCH_2)_2$), 201 (50, Ph_2PO) and 91 (100, $PhCH_2$)(Found: $M^+ - CH(SCH_2)_2$, 335.1220. $C_{24}H_{25}O_2PS_2$ requires $M - CH(SCH_2)_2$, 335.1201).

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