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Evaluation of bifunctional chiral phosphine oxide catalysts for the asymmetric hydrosilylation of ketimines

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Dedication

This paper is dedicated to the outstanding achievements of Professor Stephen Davies in organic chemistry, for being an incredible mentor and advisor, and for his continual support and friendship over the years.

Keywords

Hydrosilylation; Asymmetric Catalysis; Phosphine Oxide; Organocatalysis

Abstract

A series of bifunctional phosphine oxides have been prepared and evaluated as catalysts for the trichlorosilane mediated asymmetric hydrosilylation of ketimines. *bis*-Phosphine oxides, hydroxy-phosphine oxides, and biaryl phosphine oxides all demonstrated good catalytic activity, but poor to moderate enantioselectivity. A *bis*-*P*-chiral phosphine oxide displayed the highest enantioselectivity of 60%.

Introduction

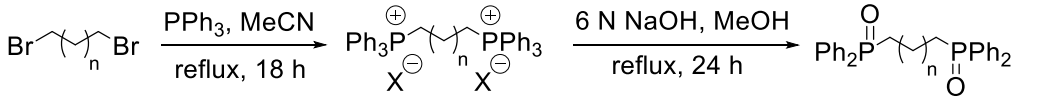
Non-symmetrically substituted phosphorus compounds are commonplace throughout organic chemistry both as chiral ligands and more recently as organocatalysts.[1–5] Despite their prevalence, the majority of examples reported utilise a *P*-chiral phosphine as the catalytic moiety, with very few reports of the application of the analogous *P*-chiral phosphine oxides. The earliest report of the use of a *P*-chiral phosphine oxide detailed the application as a ligand for asymmetric transfer hydrogenation of ketones,[6] and subsequent studies have shown applicability in a number of synthetic applications, including Diels-Alder reactions,[7] enantioselective allylation of α-hydrazono esters,[8] desymmetrisation of diaryl *meso*-epoxides,[9] reductive aldol condensations,[10] and reductive cyclisation of *N*-acylated-β-amino enones.[11] The latter two transformations make use of trichlorosilane as a reductant, a reagent known for susceptibility for activation by Lewis base catalysts, a majority of which are amide based.[12] However, Sun has used *S*-chiral sulfoxides to affect asymmetric hydrosilylation of ketimines,[13] further developing initial disclosures with a second generation *bis*-*S*-chiral sulfoxide that delivered consistently higher reactivity and selectivity.[14] Sun's group also went on to develop an organocatalyst with both carbon and sulfur stereogenic centres to promote the enantioselective hydrosilylation of 1,4-benzooxazines.[15]

Work from our laboratories has developed imidazole derived organocatalysts for the asymmetric hydrosilylation of ketimines that operate very effectively at exceptionally low catalyst loading,[16] and proposed a dual activation model for this behaviour based on catalysts containing both Lewis basic and Brønsted acidic functionality.[17] We have also explored the use of *P*-chiral phosphine oxides as catalysts for this reaction.[18] Although these species displayed potent catalytic activity, they struggled to deliver enantioselectivities of greater than 28% ee. Notably, these phosphine oxides displayed a negative non-linear effect, which is in-line with that observed with *S*-chiral catalysts developed by Sun. In this work we describe efforts to bring together these key design elements; dual activation to provide a catalyst which displays no non-linear effects.

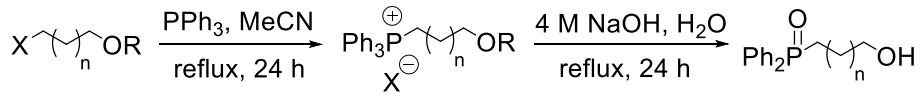
Results and Discussion

Initial studies sought to accrue data to validate the proposed dual activation hypothesis. A series of potential catalysts were targeted bearing phosphine oxide and alcohol functional groups with different length spacers between these. Achiral diphenyl *bis*-phosphine oxide catalysts **1–7** were synthesised with chain lengths varying from two to nine carbon atoms, following

established literature precedent.[19] Thus, the appropriate alkyldihalide was treated with triphenylphosphine to form the *bis*-phosphonium salt, followed by reaction with concentrated sodium hydroxide to afford the desired catalysts in excellent yield (Scheme 1). The hydroxy-phosphine oxides **8**–**10** were prepared adopting a similar route used for the *bis*-phosphine oxides, but instead starting with the appropriate halohydrin or halo-acetate (Scheme 1).



1 n = 0, 95% over 2 steps **5** n = 4, 67% over 2 steps
2 n = 1, 72% over 2 steps **6** n = 5, 64% over 2 steps
3 n = 2, 80% over 2 steps **7** n = 7, 80% over 2 steps
4 n = 3, 80% over 2 steps

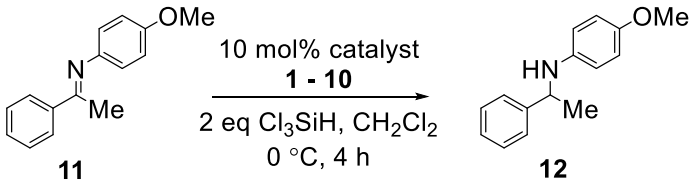


n = 1, X = Cl, R = H
n = 2, X = I, R = Ac
n = 3, X = Br, R = H

8 n = 1, 24% over 2 steps
9 n = 2, 19% over 2 steps
10 n = 3, 39% over 2 steps

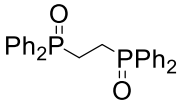
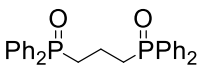
Scheme 1. Synthesis of *bis*-phosphine oxides **1-7** and hydroxy-phosphine oxides **8-10**.

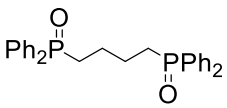
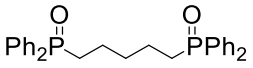
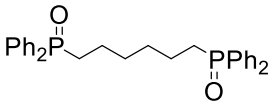
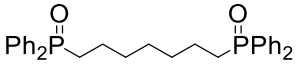
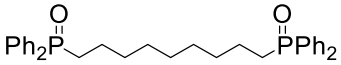
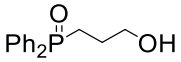
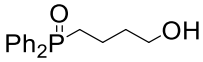
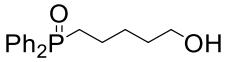
The prepared catalysts **1**–**10** were then trialled in the reduction of a benchmark ketimine substrate **11** to the PMP-amine **12** under standard previously employed reaction conditions (Scheme 2 and Table 1). For the *bis*-phosphine oxides **1**–**7**, there appears to be an optimum chain length of six-carbon atoms that delivers the highest conversion (Table 1, compare entries 1–7). The smaller subset of hydroxy-phosphine oxides provided fairly consistent conversion, with the highest observed with the five-carbon linker (Table 1, entries 8-10).



Scheme 2. Reduction of PMP-ketimine **11** using the achiral phosphine oxide catalysts.

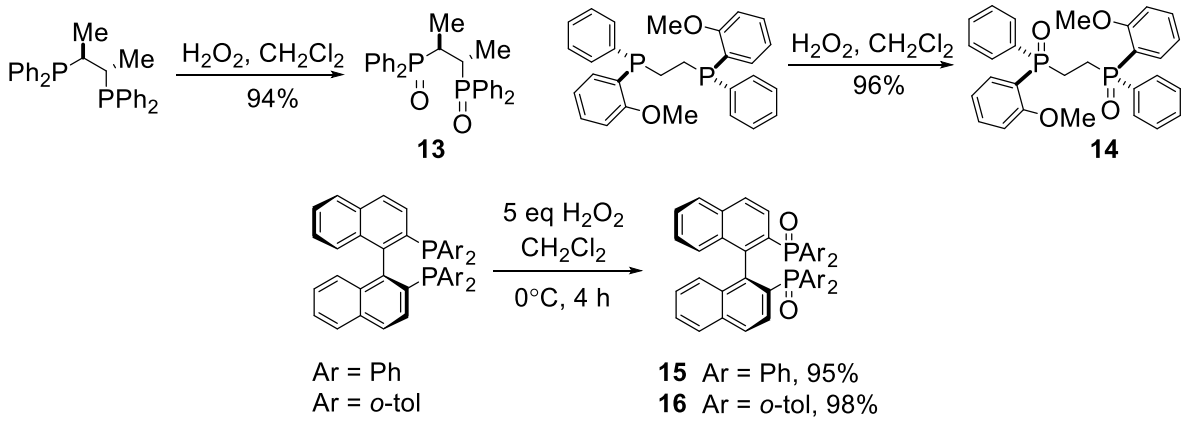
Table 1. Conversion of ketamine **11** to amine **12** according to Scheme 2.[a]

entry	catalyst	conversion / %[b]
1		40
2		55

3		59
4		65
5		81
6		74
7		63
8		75
9		78
10		81

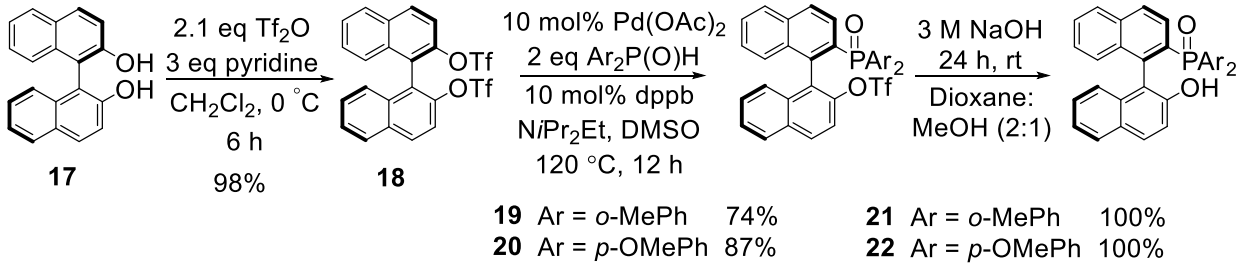
[a] All reactions performed according to Scheme 2 at a 1 mmol scale using 1 mL of solvent; [b] determined by comparison of appropriate integrals of starting material and product in the ^{1}H NMR spectrum of the unpurified reaction mixture. Data refers to the average of two reactions.

Next, a series of easily accessible enantiopure phosphine oxides were targeted, two being based on a conformationally flexible sidechain **13** and **14**, and the others on a more rigid binaphthyl framework, **15** and **16**. Oxidation of the commercially available enantiopure phosphines with hydrogen peroxide gave the *bis*-phosphine oxides **13**–**16** in excellent yield following known literature precedent.[20,21]



Scheme 3. Synthesis of chiral *bis*-phosphine oxides **13**–**16**.

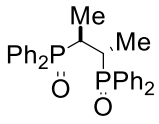
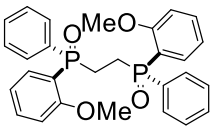
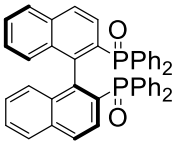
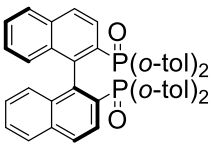
A series of biaryl catalysts were also synthesised incorporating a Brønsted acidic hydroxyl group also based upon a binaphthyl framework. Following known literature precedent, the mono *ortho*-tolyl and *para*-methoxy catalysts **21** and **22** were both successfully synthesised from commercially available (*R*)-BINOL **17** *via* a common *bis*-BINOL triflate **18** (Scheme 4).[22]

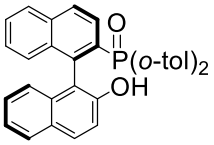
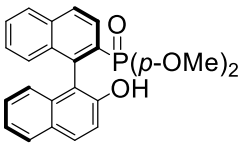


Scheme 4. Synthesis of biaryl-hydroxy BINOL catalysts **21** and **22**.

Analysis of these catalysts under the standard reduction conditions (Scheme 2) demonstrated that all reduced the PMP-ketimine **11** but with varying degrees of efficiency. The catalyst bearing a two carbon linker was more effective than the achiral counterpart (compare Table 1, entry 1 verses Table 2, entry 1) which may be due to the chiral version exhibiting gauche interactions of the methyl groups when the phosphine oxides are *anti*-periplanar, preferring a *syn*-periplanar arrangement that promotes a dual activation mechanism. This effect is also mirrored in the catalyst with stereogenic phosphorus centres; with no methyl groups on the backbone, the reactivity drops (Table 2, entries 1 & 2). Although only small, a better enantioselectivity is observed with stereogenic phosphorus centres rather than carbon centered ones on the backbone. In contrast, (*S*)-BINAPO derived catalysts **21** and **22** both performed excellently as catalysts, but delivered very similar enantioselectivities depending on the nature of the aryl phosphine oxides used (Table 2, entries 3 & 4). In contrast the hydroxy-BINOL phosphine oxides where considerably less reactive, with no significant improvement in enantioselectivity (Table 2, entries 5 & 6).

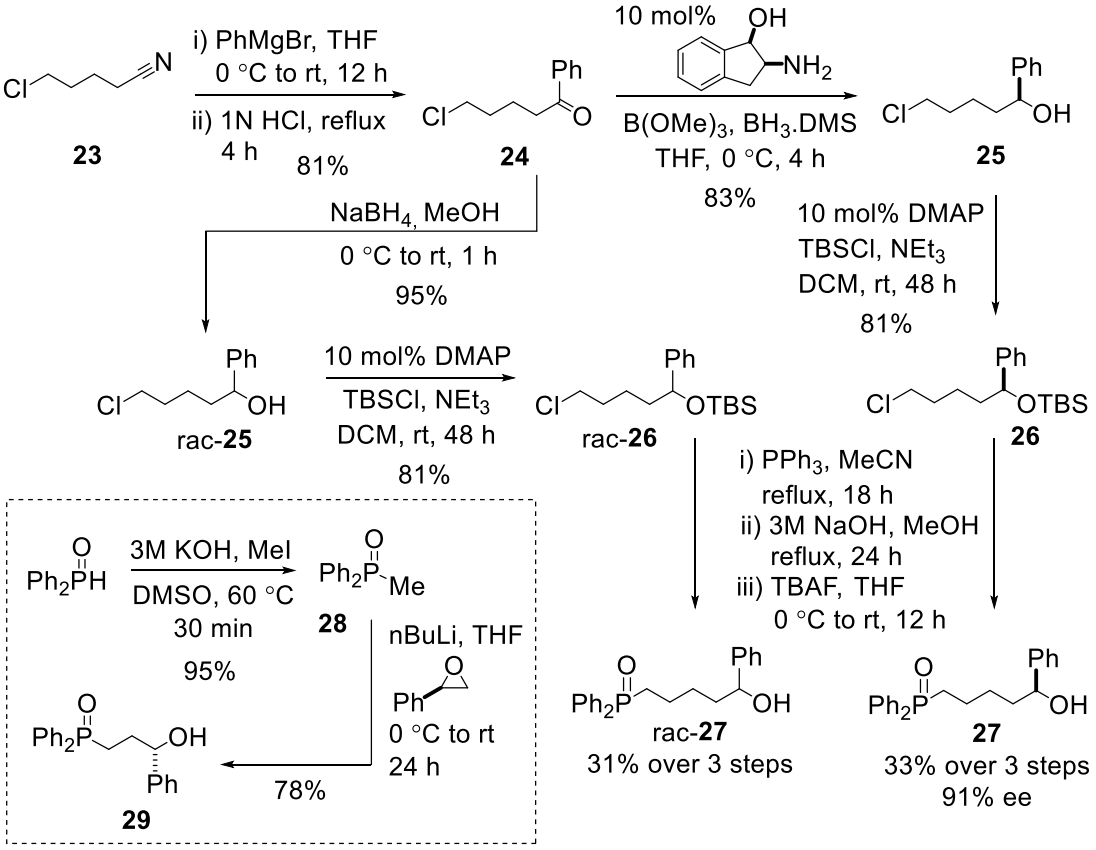
Table 2. Conversion of ketamine **2** to amine **1** according to Scheme 2.[a]

entry	catalyst	conversion / %[b]	ee / %[c]
1		85	3
2		66	16
3		100	15
4		100	19

5		55	13
6		70	11

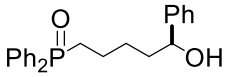
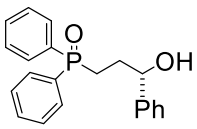
[a] All reactions performed according to Scheme 2 at a 1 mmol scale using 1 mL of solvent; [b] determined by comparison of appropriate integrals of starting material and product in the ^{1}H NMR spectrum of the unpurified reaction mixture. Data refers to the average of two reactions; [c] enantiomeric excess determined by chiral phase HPLC analysis.

Further hydroxy-phosphine oxide catalysts were prepared based on a more conformationally mobile framework bearing a stereogenic alcohol centre. Thus, the commercially available chloro-nitrile **23** was treated with phenylmagnesium bromide to afford the chloro-ketone **24** in excellent yield (Scheme 5).[23] This was reduced using an oxazaborolidine derived from (1*R*, 2*S*)-amino indanol and trimethylborate at 0 °C,[24] and the resulting alcohol **25** protected as a TBS ether **26**. Formation of the phosphonium salt and subsequent oxidation to the phosphine oxide using 3 M NaOH afforded the TBS protected catalyst that was deprotected with TBAF to form the target molecule **27** in six steps. In order to determine the enantioselectivity of catalyst **27**, a racemic version of the catalyst was synthesised in analogous fashion using the racemic alcohol derived from the sodium borohydride reduction of chloro-ketone **24**. Analysis of the enantioselectivity of the catalyst by chiral HPLC analysis showed a 91% ee, which was sufficient to enable its use. A shorter 3-carbon analogue **29** was also synthesised through the ring opening of an enantiomerically pure epoxide with a lithium phosphinate derived from methyl diphenyl phosphine oxide **28**.[25]



Scheme 5. Synthesis of hydroxy-phosphine oxide catalysts **27** and **29**.

Table 3. Reduction of the PMP-ketimine **11** using chiral hydroxy-phosphine oxide catalysts **27** and **29**[a]

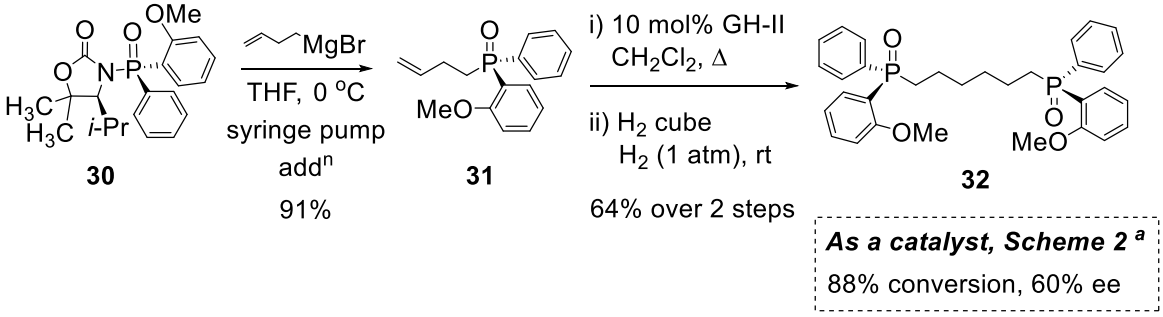
entry	catalyst	conversion / %[b]	ee / %[c]
1[d]		82	10
2		73	10

[a] All reactions performed according to Scheme 1 at a 1 mmol scale using 1 mL of solvent; [b] determined by comparison of appropriate integrals of starting material and product in the ^{1}H NMR spectrum of the unpurified reaction mixture. Data refers to the average of two reactions; [c] enantiomeric excess determined by chiral phase HPLC analysis; [d] Catalyst used was 91% ee.

Screening of the phosphine oxides **27** and **29** under benchmark conditions (Scheme 2) demonstrated very similar conversion to the PMP-amine **12** after 4 hours to those obtained with the achiral linear variant of the catalysts. However, in both cases, the amine **12** was obtained in a 10% ee in both cases. This indicates that a stereogenic centre located at these positions on the carbon chain has only a small effect on the overall enantioselectivity.

As already noted, use of *P*-chiral phosphine oxides demonstrated negative [ML_2] non-linear effects similar to observed by Sun and co-workerswith an analogous *S*-chiral sulfoxide. Thus,

a *P*-chiral phosphine oxide that delivered the highest enantioselectivity was selected and a *bis*-phosphine oxide prepared with an appropriate 6-carbon linker that was shown to be the most effective chain length in earlier experiments (Table 1, entry 5). Controlled addition of the *P*-chiral oxazolidinone **30** to a solution of but-3-enylmagnesium bromide employing previously developed methodology for the synthesis of *P*-chiral phosphine oxides gave the desired *P*-chiral phosphine oxide **31** as a single enantiomer (>99% ee as determined by chiral HPLC analysis).[26] Treatment of this with 10 mol% of Grubbs-Hoveyda second generation catalyst followed by immediate hydrogenation afforded the desired catalyst **32** in good yield over two steps (Scheme 6)



Scheme 6. Synthesis of *P*-chiral *bis*-phosphine oxide catalyst **32**. [a] Reaction performed according to Scheme 1 at a 1 mmol scale using 1 mL of solvent.

The *bis*-phosphine oxide catalyst **32** was evaluated under the standard reduction conditions (Scheme 2), undergoing 88% conversion to the *N*-PMP amine **12**. Analysis of the enantioselectivity of the reduction showed a 60% ee and is consistent with the hypothesis that two phosphine oxide moieties were required to enable high enantiocontrol. To further confirm this, a non-linear relationship study was again undertaken on catalyst **32** (Fig. 1), where scalemic mixtures of the catalyst **32** were accessed by mixing the opposing enantiomer of the *bis*-phosphine oxide, prepared in analogous fashion using the *N*-phosphinoyl oxazolidinone derived from (*R*)-valine. The observation of a direct linear relationship between the enantioselectivity of the catalyst and the enantioselectivity of the resultant *N*-PMP amine **12** confirmed that the reaction now proceeded through a pathway whereby only a single molecule of the catalyst **32** was present in the transition state, and confirms a need to have stereogenic elements at either end of the catalyst system.

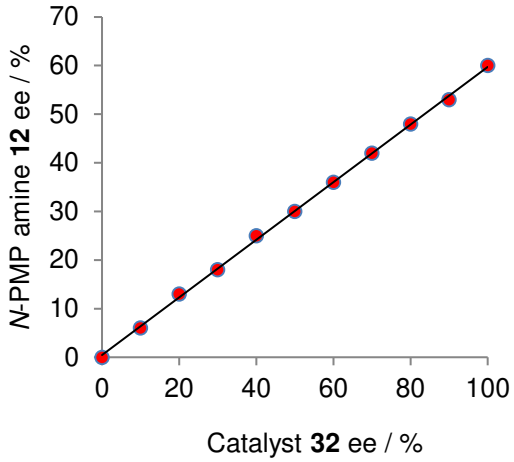


Figure 1. Probing non-linear activity of catalyst **32** using reaction conditions according to Scheme 2.

In the recently disclosed dual activation model with the organocatalyst derived from imidazole, trichlorosilane is coordinated to the Lewis basic amide and the hydroxyl group, whilst the protonated imidazole activates the imine substrate. One can propose a similar model for the *bis*-phosphine oxide **32** where each terminus can act as a Lewis base or a Bronsted acid. The same model overlays well with a catalyst system developed by Sun and co-workers based on chiral sulfoxides that displays similar non-linear effects.

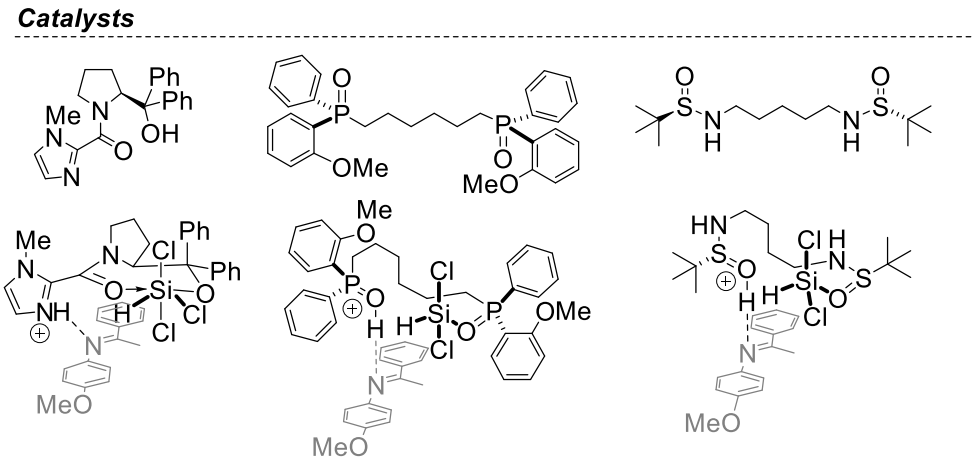


Figure 2. Dual activation models for the imidazole, phosphine oxide, and sulfoxide catalysts.

Conclusion

P-Chiral phosphine oxides offer potential for acting as effective catalysts for the asymmetric reduction of ketimines. Symmetric variants offer good reactivity and selectivity but refinements are needed in order to improve the levels of selectivity further. Potential exists for the synthesis of *P*-chiral omega-hydroxy hybrids that may offer further advantages over those presented here.

Experimental

General procedure A for the preparation of the achiral *bis*-phosphine oxide catalysts

The dibromoalkane (5 mmol) and triphenyl phosphine (2.60 g, 10 mmol) were dissolved in MeCN (20 mL) and the solution heated to reflux for 18 h. Upon cooling to room temperature the solvent was removed *in vacuo* to afford the crude phosphonium salt. The phosphonium salt was redissolved in a solution of MeOH (10 mL) and aqueous 6 M KOH solution (10 mL) and heated at reflux for a further 24 h. The solvent was removed *in vacuo* to afford the crude *bis*-phosphine oxide. Purification of the crude material occurred as described within the individual experimental details.

1,2-*bis*(Diphenylphosphinyl)ethane 1[27]

Prepared according to general procedure **A** from 1,2-dibromoethane (0.4 mL, 5 mmol). Recrystallisation of the crude compound from MeOH: EtOAc afforded the title compound as a white crystalline solid (2.02 g, 95%); m.p. 273–274 °C (lit.[27] 273–276 °C); δ_H (400 MHz, $CDCl_3$) 2.51 (4 H, d, $J_{P\text{-}H}$ 1.8, 2 × CH_2), 7.41–7.53 (12 H, m, ArC*H*), 7.66–7.73 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 32.5. All data is in accordance with that in the literature.

1,3-*bis*(Diphenylphosphinyl)propane 2[27]

Prepared according to general procedure **A** from 1,3-dibromopropane (0.5 mL, 5 mmol). Recrystallisation of the crude material from MeOH: EtOAc afforded the title compound as a white solid (1.61 g, 72%); m.p. 140–141 °C (lit.[27] 139–140 °C); δ_H (400 MHz, $CDCl_3$) 1.92–2.08 (2 H, m, CH_2), 2.45–2.56 (4 H, m, 2 × CH_2), 7.39–7.52 (12 H, m, ArC*H*), 7.65–7.72 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 32.2. All data is in accordance with the literature.

1,4-*bis*(Diphenylphosphinyl)butane 3[27]

Prepared according to general procedure **A** from 1,4-dibromobutane (0.6 mL, 5 mmol). Recrystallisation of the crude material from MeOH: EtOAc afforded the title compound as a white crystalline solid (1.81 g, 80%); m.p. 267–268 °C (lit.[27] 267–269 °C); δ_H (400 MHz, $CDCl_3$) 1.67–1.79 (4 H, m, 2 × CH_2), 2.21–2.28 (4 H, m, 2 × CH_2), 7.42–7.53 (12 H, m, ArC*H*), 7.66–7.73 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 31.8. All data is in accordance with the literature.

1,5-*bis*(Diphenylphosphinyl)pentane 4[28,29]

Prepared according to general procedure **A** from 1,5-dibromopentane (0.7 mL, 5 mmol). Recrystallisation of the crude material from MeOH: EtOAc afforded the title compound as a white crystalline solid (1.64 g, 67%); m.p. 119–120 °C (lit.[29] 119–120 °C); δ_H (400 MHz, $CDCl_3$) 1.55–1.69 (6 H, m, 3 × C*H*$_2$), 2.15–2.26 (4 H, m, 2 × C*H*$_2$), 7.44–7.48 (12 H, m, ArC*H*), 7.66–7.74 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 32.2. All data is in accordance with the literature.

1,6-*bis*(Diphenylphosphinyl)hexane 5[28]

Prepared according to general procedure **A** from 1,6-dibromohexane (0.8 mL, 5 mmol). Recrystallisation of the crude material from MeOH : EtOAc afforded the title compound as a white crystalline solid (1.53 g, 64%); m.p. 196–197 °C (lit.[28] 196.9–197.2 °C); δ_H (400 MHz, $CDCl_3$) 1.35–1.42 (4 H, m, 2 × C*H*$_2$), 1.54–1.65 (4 H, m, 2 × C*H*$_2$), 2.19–2.26 (4 H, m, 2 × C*H*$_2$), 7.44–7.56 (12 H, m, ArC*H*), 7.69–7.76 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 32.1. All data is in accordance with that of the literature.

1,7-*bis*(Diphenylphosphinyl)heptane 6[28]

Prepared according to general procedure **A** from 1,7-dibromoheptane (0.9 mL, 5 mmol). Recrystallisation of the crude material from MeOH: EtOAc afforded the title compound as a white crystalline solid (2.01 g, 80%); m.p. 90–91 °C (lit.[28] 90–91 °C); δ_H (250 MHz, $CDCl_3$) 0.84–0.92 (2 H, m, C*H*$_2$), 1.23–1.43 (4 H, m, 2 × C*H*$_2$), 1.50–1.67 (4 H, m, 2 × C*H*$_2$), 2.17–2.30 (4 H, m, 2 × C*H*$_2$), 7.42–7.58 (12 H, m, ArC*H*), 7.68–7.78 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 32.3. All data is in accordance with the literature.

1,9-*bis*(Diphenylphosphinyl)nonane 7[30,31]

Prepared according to general procedure **A** from 1,9-dibromononane (2.62 g, 5 mmol). Recrystallisation of the crude compound from MeOH: EtOAc afforded the title compound as a white crystalline solid (1.80 g, 70%); m.p. 123–125 °C (lit.[30] 123–125 °C); δ_H (250 MHz, $CDCl_3$) 1.10–1.38 (10 H, m, 5 × C*H*$_2$), 1.52–1.68 (4 H, m, 2 × C*H*$_2$), 2.19–2.30 (4 H, m, 2 × C*H*$_2$), 7.43–7.56 (12 H, m, ArC*H*), 7.70–7.78 (8 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 32.4. All data is in accordance with the literature.

General procedure B for the formation of the diphenylphosphine oxide moiety from the halogenated alcohol or ester

The halogenated alcohol or ester (7 mmol) was added dropwise to a suspension of sodium iodide (1.00 g, 7 mmol) and triphenylphosphine (2.00 g, 7.0 mmol) in acetonitrile (20 cm³) and

the reaction mixture heated at reflux for 24 hours. The solution was cooled to room temperature and the solvent removed *in vacuo* to yield the phosphonium salt. The salt was dissolved in a 30% aqueous solution of NaOH (20 cm³) and methanol (10 cm³) and heated at reflux for 12 hours. The reaction mixture was poured into a saturated solution of ammonium chloride (20 cm³) and the aqueous phase extracted with dichloromethane (3 × 30 cm³). The organic layers were combined, washed with brine (10 cm³) and dried over magnesium sulfate. Removal of the solvent *in vacuo* afforded the crude material. Purification of the crude material occurred as described in the individual experimental details.

3-(Diphenylphosphinyl)-1-propanol 8[32]

Prepared in accordance to general procedure **B** using 3-chloro-propan-1-ol (0.7 cm³, 7 mmol). Trituration of the crude material from diethyl ether (20 cm³) gave the title compound as a white crystalline solid (0.60 g, 24%); m.p. 95 °C (lit.[32] 95–96 °C); δ_H (400 MHz, $CDCl_3$) 1.83–1.93 (2 H, m, C*H*$_2$), 2.42 (2 H, dt, *J* 11.5 7.3, PC*H*$_2$), 3.69–3.72 (2 H, m, C*H*$_2$OH), 4.23 (1 H, br s, O*H*), 7.45–7.55 (6 H, m, ArC*H*), 7.72–7.77 (4 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 34.7. All data is in accordance with the literature.

4-(Diphenylphosphinyl)butan-1-ol 9[33]

Prepared according to general procedure **B** using 4-iodobutyl benzoate[33] (2.00 g, 7 mmol). Purification of the crude material by flash column chromatography on silica gel using an eluent of 100% ethyl acetate afforded the title compound as a colourless oil (270 mg, 19%); δ_H (400 MHz, $CDCl_3$) 1.65–1.79 (4 H, m, C*H*$_2$), 2.28–2.38 (2 H, m, C*H*$_2$), 2.90 (1 H, br s, O*H*), 3.65 (2 H, t, *J* 5.8, C*H*$_2$OH), 7.28–7.55 (6 H, m, ArC*H*), 7.67–7.78 (4 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 33.7. All data is in accordance with that of the literature.

5-(Diphenylphosphinyl)pentan-1-ol 10[34]

Prepared according to general procedure **B** using 5-bromopentan-1-ol (1.00 g, 7 mmol). Purification of the crude material by flash column chromatography on silica gel using an eluent of 100% ethyl acetate afforded the title compound as a colourless oil (700 mg, 39%); δ_H (400 MHz, $CDCl_3$) 1.43–1.75 (6 H, m, 3 × C*H*$_2$), 1.95 (1 H, br s, O*H*), 2.21–2.34 (2 H, m, C*H*$_2$), 3.61 (2 H, t, *J* 6.3, C*H*$_2$OH), 7.42–7.54 (6 H, m, ArC*H*), 7.70–7.78 (4 H, m, ArC*H*); δ_H (101 MHz, $CDCl_3$) 32.7. All data is in accordance with that of the literature.

General procedure for the asymmetric reduction of the PMP-ketimine 11

The PMP-ketimine **11** (225 mg, 1.00 mmol) and catalyst (0.1 mmol) were dissolved in CH_2Cl_2 (1 cm³) and the solution cooled to 0 °C. Trichlorosilane (0.20 cm³, 2.0 mmol) was added dropwise and the reaction mixture stirred for 4 hours. The reaction solution was quenched

through addition of 1M aqueous HCl solution (1 cm³), diluted with CH_2Cl_2 (5 cm³) and basified with a 1M aqueous NaOH solution (10 cm³). The organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (3 × 5 cm³). The combined organics were washed with brine (10 cm³), before being dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the crude material. Purification of the crude product by flash column chromatography eluting on silica gel with 10% EtOAc / petroleum ether afforded the desired amine **12** as a golden yellow solid; m.p. 64 °C (lit.[16] 65 °C); δ_H (400 MHz, $CDCl_3$) 1.52 (3H, d, *J* 6.7, C*H*$_3$CHN), 3.80 (3H, s, OC*H*$_3$), 3.83 (1H, bs, NH), 4.42 (1H, q, *J* 6.7, CH_3C*H*N), 6.48 [2H, $(AX)_2$, ArC*H*], 6.70 (2H, $(AX)_2$, ArC*H*], 7.20 – 7.25 (5H, m, ArC*H*); HPLC t_R = 7.9 min. (*R* isomer), 8.6 min. (*S* isomer) (Chiralpak AD, 95/5 hexane/propan-2-ol); All data is in accordance with the literature.

(2*R*, 3*R*)-(+)- 2,3-*bis*(Diphenylphosphinyl)butane 13[35]

(2*R*, 3*R*)-(+)-*bis*(Diphenylphosphino)butane (200 mg, 0.5 mmol) was dissolved in CH_2Cl_2 (10 cm³) and the reaction solution cooled to 0 °C. Hydrogen peroxide (35 wt. %, 0.5 cm³) was added dropwise and the reaction mixture stirred for 18 hours. The solution was poured into water (10 cm³) and the organic phase separated. The aqueous layer was extracted with dichloromethane (3 × 10 cm³) and the organic phases combined, washed with a saturated aqueous solution of sodium sulfite (15 cm³) and dried over magnesium sulfate. Filtration, then removal of the solvent *in vacuo* afforded the title compound as a white crystalline solid that required no further purification (203 mg, 94%); m.p. 183 °C (lit.[35] 183–184 °C); $[\alpha]_D^{25}$ +39.0 (*c* 2.0 in CH_2Cl_2, lit.[35] +39.4 *c* 2.0 in CH_2Cl_2); δ_H (250 MHz, $CDCl_3$) 1.29–1.39 (6 H, m, 2 × C*H*$_3$), 2.87 (2 H, qd, *J* 7.1, 5.1, 2 × C*H*), 7.28–7.81 (20 H, m, ArC*H*); δ_P (101 MHz, $CDCl_3$) 36.7. All data is in accordance with the literature.

(1*R*, 1*R*')-(-)-1,1'-(1,2-Ethanediyl)*bis*[1-(2-methoxyphenyl)-1-phenyl-phosphine oxide 14[36]

(1*R*, 1*R*')-(-)-*bis*[(2-Methoxyphenyl)phenylphosphino]ethane (100 mg, 0.2 mmol) was dissolved in anhydrous CH_2Cl_2 (5.0 mL) and the solution cooled to 0 °C. Hydrogen peroxide (35 wt. %, 0.1 mL) was added dropwise and the solution warmed to room temperature and stirred for 12 hours. The reaction was poured into water (3.0 mL) and the organic phase separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the organic phases combined, washed with a saturated aqueous solution of sodium bisulfite (10 mL) and dried with $MgSO_4$. Filtration and removal of the solvent *in vacuo* afforded a white crystalline solid as the title compound which required no further purification (100 mg, 96%); m.p. 206 °C; $[\alpha]_D^{25}$ -44.5 (*c* 1.0 in MeOH); δ_H (400 MHz, $CDCl_3$) 2.57–2.74 (4 H, m, 2 × C*H*$_2$), 3.57 (6 H, s, 2 ×

OC*H*$_3$), 6.79–6.82 (2 H, m, ArC*H*), 7.08 (2 H, t, *J* 7.3, ArC*H*), 7.37–7.49 (8 H, m, ArC*H*), 7.72–7.77 (4 H, m, ArC*H*), 7.97–7.99 (2 H, m, ArC*H*); δ_P (121 MHz, $CDCl_3$) 32.2. All data is in accordance with that of the literature.

(*S*)-2,2'-*Bis*-(Diphenylphosphinyl)-1,1'-binaphthyl 15[37]

(*S*)-2,2'-*bis*-(Diphenylphosphino)-1,1'-binaphthyl (300 mg, 0.5 mmol) was added to dichloromethane (10 cm³) and the solution cooled to 0 °C. Hydrogen peroxide (35 wt.%, 0.2 cm³) was added dropwise and the mixture stirred for 18 hours. The solution was poured into water (10 cm³) and the organic phase separated. The aqueous layer was extracted with diethyl ether (3 × 15 cm³) and the combined organic phases washed with a saturated aqueous solution of sodium sulfite (10 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* afforded a white crystalline solid that required no further purification (290 mg, 95%); m.p. 261 °C (lit.[37] 260.5–261.5 °C); $[\alpha]_D^{25}$ -390 (*c* 1.0 in C_6H_6, lit.[37] -391.2 *c* 0.5 in C_6H_6); δ_H (250 MHz, $CDCl_3$) 6.78–6.85 (4 H, m, ArC*H*), 7.26–7.51 (20 H, m, ArC*H*), 7.69–7.77 (4 H, m, ArC*H*), 7.82–7.89 (4 H, m, ArC*H*); δ_P (250 MHz, $CDCl_3$) 28.3. All data is in accordance with the literature.

(*S*)-2,2'-*bis*(di-*o*-Tolylphosphinyl)-1,1'-binaphthyl 16

(S)-(−)-2,2′-*bis*(di-*o*-Tolylphosphino)-1,1′-binaphthyl (100 mg, 0.1 mmol) was dissolved in dichloromethane (5 cm³) and the solution cooled to 0 °C. Hydrogen peroxide (35 wt. %, 0.2 cm³) was added dropwise and the reaction mixture stirred for 18 hours. The solution was poured into water (10 cm³) and the organic layer separated. The aqueous layer was extracted with diethyl ether (3 × 15 cm³) and the combined organic phases washed with a saturated solution of sodium sulfite (10 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* afforded the title compound as a white crystalline solid that required no further purification (100 mg, 98%); m.p. 268 °C; $[\alpha]_D^{25}$ -421 (*c* 1.0 in C_6H_6); υ_{max} (ATR)/ cm^{-1} 3658, 3379, 3046, 2920, 2865, 1601, 1553. 1501; δ_H (400 MHz, $CDCl_3$) 2.33 (12 H, d, J_{P-H} 23.4, 4 × C*H*$_3$), 6.85–6.91 (4 H, m, ArC*H*), 6.99–7.05 (8 H, m, ArC*H*), 7.27–7.31 (4 H, m, ArC*H*), 7.37–7.55 (8 H, m, ArC*H*), 7.81–7.86 (4 H, m, 4 × ArC*H*), 7.82–7.85 (4 H, m, 4 × ArC*H*); δ_C (100 MHz, $CDCl_3$) 21.5 (d, J_{P-H} 2.1, 4 × *C*H$_3$), 125.9 (Ar*C*H), 127.1 (Ar*C*H), 127.3 (Ar*C*H), 127.4 (Ar*C*H), 127.7 (Ar*C*H), 128.2 (d, J_{P-H} 13.5, Ar*C*H), 128.5 (2 × Ar*C*H), 128.7 (2 × Ar*C*H), 129.6 (Ar*C*), 130.4 (d, J_{P-H} 28.4, Ar*C*), 131.4 (Ar*C*), 132.0 (d, J_{P-H} 10.1, Ar*C*H), 132.5 (d, J_{P-H} 12, Ar*C*H), 133.7 (d, J_{P-H} 11.4, Ar*C*), 133.9 (d, J_{P-H} 2.5, Ar*C*), 141.1 (d, J_{P-H} 7.9, Ar*C*), 141.2 (d, J_{P-H} 7.9, Ar*C*), 142.9 (d, J_{P-H} 6.1, Ar*C*), 143.0 (d, J_{P-H} 6.1, Ar*C*); δ_P (101 MHz, $CDCl_3$) 28.4;

m/z (ESI$^+$) 711.2559 (100%, MH$^+$, $C_{48}H_{41}O_2P$ requires 711.2576).

(*R*)-1,1'-Binaphthyl-2,2'-diyl *bis*(trifluoromethanesulfonate) 18[38]

(*R*)-BINOL **17** (1.00 g, 4 mmol) was dissolved in a solution of dichloromethane (20 cm³) and freshly distilled pyridine (1.0 cm³, 13 mmol) and the mixture cooled to 0 °C. Triflic anhydride (3.00 g, 2.0 cm³, 12 mmol) was added dropwise over a period of 30 minutes and the mixture warmed to room temperature and stirred for six hours. The solution was diluted with ethyl acetate (50 cm³) and the organic phase was separated. The aqueous phase was extracted with ethyl acetate (3 × 10 cm³) and the combined organic layers washed sequentially with an aqueous solution of 5% HCl (20 cm³), aqueous saturated sodium hydrogen carbonate solution (20 cm³) and brine (20 cm³). The organic phase was dried over sodium sulfate, filtered and the solvent removed *in vacuo* to yield an orange oil. Purification of the crude material by column chromatography on silica gel using an eluent of 5% ethyl acetate: petroleum ether 40–60 °C furnished the title compound as a white crystalline solid (3.03 g, 100%); m.p. 75 °C (lit.[38] 76–78 °C); $[\alpha]_D^{25}$ -146.2 (*c* 1.0 in $CHCl_3$, lit.[38] -147.7 *c* 1.01 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.27–7.29 (2 H, m, ArC*H*), 7.41–7.46 (2 H, m, ArC*H*), 7.59–7.65 (4 H, m, ArC*H*), 8.03 (2 H, d, *J* 8.0, ArC*H*), 8.17 (2 H, d, *J* 9.0, ArC*H*); δ_F (235 MHz, $CDCl_3$) -74.57 (2 × C*F*$_3$). All data is in accordance with that of the literature.

(*R*)-2-[*bis*-(*o*-Tolylphosphinyl)]- 2'-[(trifluoromethanesulfonoyl)oxy]-1,1'-binaphthyl 19[39]

(*R*)-1,1'-Binaphthyl-2,2'-diyl-*bis*-trifluoromethanesulfonate **18** (0.60 g, 1 mmol) was added to a stirred solution of *bis*-(2-methylphenyl)-phosphine oxide (0.60 g, 3 mmol), palladium acetate (0.06 g, 0.3 mmol) and diphenylphosphoryl butane (0.10 g, 0.3 mmol) under an atmosphere of argon. *N*,*N*-Diisopropylethylamine (0.70 g, 1.0 cm³, 6 mmol) was added dropwise and the reaction mixture heated to 120 °C for 12 hours. Upon cooling to room temperature, the solution was diluted with ethyl acetate (50 cm³) and washed successively with water (3 × 20 cm³), 1*N* HCl (20 cm³) and an aqueous saturated solution of $NaHCO_3$ (20 cm³). The organic layer was dried over magnesium sulfate, filtered, and the solvent removed *in vacuo* to yield an orange oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 40% ethyl acetate: petroleum ether 40–60 °C afforded the title compound as a white crystalline solid (630 mg, 74%); m.p. 78 °C (lit.[39] 123–125 °C); $[\alpha]_D^{25}$ +62.2 (*c* 0.5 in $CHCl_3$, lit.[39] +9.1 (*c* 0.99, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 2.15 (3 H, s, C*H*$_3$), 2.48 (3 H, s, C*H*$_3$), 6.90–7.13 (7 H, m, ArC*H*), 7.25–7.31 (3 H, m, ArC*H*), 7.35–7.45 (5 H, m, ArC*H*), 7.61 (1 H, app. t, *J* 7.1, ArC*H*), 7.87 (1 H, app. d, *J* 8.1, ArC*H*), 7.97–8.01 (3 H, m, ArC*H*); δ_F (235 MHz,

$CDCl_3$) -75.0; δ_P (101 MHz, $CDCl_3$) 33.9. Data is in general agreement with the literature.

(*R*)-2-[*bis*-(4-Methoxyphenyl)phosphinyl]-2'-[(trifluoromethanesulfonyl)oxy]-1,1'-binaphthyl 20[40]

(*R*)-1,1'-Binaphthyl-2,2'-diyl-*bis*-trifluoromethanesulfonate **18** (0.60 g, 1 mmol) was added to a stirred solution of *bis*(4-methoxyphenyl)phosphine oxide (0.60 g, 3 mmol), palladium acetate (0.06 g, 0.3 mmol) and 1,4-*bis*(diphenylphosphino)butane (0.10 g, 0.3 mmol) under an atmosphere of argon. *N*,*N*-Diisopropylethylamine (0.70 g, 1.0 cm³, 6 mmol) was added dropwise and the reaction mixture heated to 120 °C for 12 hours. Upon cooling, the solution was diluted with ethyl acetate (50 cm³) and washed successively with water (3 × 20 cm³), 1N HCl (20 cm³) and a 1M aqueous solution of $NaHCO_3$ (20 cm³). The organic layer was dried over magnesium sulfate, filtered, and the solvent removed *in vacuo* to yield an orange oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 40% ethyl acetate: petroleum ether 40–60 °C afforded the title compound as a white crystalline solid (700 mg, 87%); m.p. 81 °C (lit.[40] 80–81 °C); $[\alpha]_D^{25}$ +66.1 (*c* 0.7 in $CHCl_3$, lit.[40] +66.2 *c* 0.7 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 3.79 (3 H, s, OC*H*$_3$), 3.81 (3 H, s, OC*H*$_3$), 6.66–6.69 (2 H, m, ArC*H*), 6.77–6.80 (2 H, m, ArC*H*), 7.01 (1 H, d, *J* 8.6, ArC*H*), 7.12 (1 H, d, *J* 8.6, ArC*H*), 7.18–7.23 (1 H, m, ArC*H*), 7.30–7.39 (6 H, m, ArC*H*), 7.45 (1 H, ddd, *J* 8.2, 6.9, 1.2, ArC*H*), 7.56–7.60 (1 H, m, ArC*H*), 7.78 (1 H, dd, *J* 11.4, 8.6, ArC*H*), 7.84 (1 H, d, *J* 8.3, ArC*H*), 7.90 (1 H, d, *J* 9.0, ArC*H*), 7.96 (1 H, d, *J* 8.3, ArC*H*), 8.04 (1 H, dd, *J* 8.8, 2.2, ArC*H*); δ_F (235 MHz, $CDCl_3$) -75.0; δ_P (101 MHz, $CDCl_3$) 27.9. All data is in accordance with the literature.

(*R*)-2'-[*bis*-(*o*-Tolylphosphinyl]-[1,1'-binapthalen]-2-ol 21[39]

(*R*)-2-[*bis*-(*o*-tolylphosphinyl)]- 2'-[(trifluoromethanesulfonoyl)oxy]-1,1'-binaphthyl **19** (0.30 g, 0.4 mmol) was added to a solution of dioxane (10 cm³) and methanol (5.0 cm³) at room temperature. A 3 M solution of NaOH (3.0 cm³) was introduced in a single portion and the solution stirred at room temperature for 24 hours. The reaction was acidified to pH 1 using concentrated HCl (5.0 cm³) and the aqueous phase extracted with ethyl acetate (3 × 10 cm³). The organic phases were combined, washed with brine (10 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* yielded a yellow oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 50% ethyl acetate: petroleum ether 40–60 °C afforded the title compound as a white crystalline solid (210 mg, 96%); m.p. 162 °C, lit.[39] 150–152 °C; $[\alpha]_D^{25}$ +135.0 (*c* 0.7 in $CHCl_3$, lit.[39] -59.8 *c* 1.11, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 2.03 (3 H, s, C*H*$_3$), 2.72 (3 H, s, C*H*$_3$), 6.21 (1 H, d, *J* 8.5,

ArC*H*), 6.52–6.63 (2 H, m, ArC*H*), 6.74–6.81 (2 H, m, ArC*H*), 7.03–7.25 (6 H, m, ArC*H*), 7.47–7.52 (6 H, m, ArC*H*), 7.70 (1 H, d, *J* 8.5, ArC*H*), 7.91–8.00 (2 H, m, ArC*H*), 9.33 (1 H, s, O*H*); δ_P (121 MHz, $CDCl_3$) 37.3. All data is in general agreement with the literature.

(*R*)-2'-[*bis*-(4-Methoxyphenyl)phosphinyl]-[1,1'-binapthalen]-2-ol 22[22]

(*R*)-2-[*bis*(4-Methoxyphenyl)phosphinyl]-2'-[(trifluoromethanesulfonyl)oxy]-1,1'-binaphthyl **20** (0.30 g, 0.4 mmol) was added to a solution of dioxane (10 cm³) and methanol (5.0 cm³) at room temperature. A 3 M solution of NaOH (3.0 cm³) was introduced in one portion and the solution stirred at room temperature for 24 hours. The reaction was acidified to pH 1 using concentrated HCl (5.0 cm³) and the aqueous phase extracted with ethyl acetate (3 × 10 cm³). The organic phases were combined, washed with brine (10 cm³) and dried over magnesium sulfate. Removal of the solvent *in vacuo* yielded a yellow oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 50% ethyl acetate: petroleum ether 40 60 °C afforded the title compound as a white crystalline solid (215 mg, 100%). m.p. 178 °C; $[\alpha]_D^{25}$ -126.0 (*c* 0.7 in $CHCl_3$, lit.[22] +126.3 *c* 0.7 in $CHCl_3$ for the (*S*)-enantiomer); δ_H (400 MHz, $CDCl_3$) 3.55 (3 H, s, OC*H₃*), 3.89 (3 H, s, OC*H₃*), 6.21–6.24 (2 H, m, ArC*H*), 6.43 (1 H, app. d, *J* 8.6, ArC*H*), 6.92–6.96 (1 H, m, ArC*H*), 7.05 (2 H, app. dd, *J* 8.6, 2.3, ArC*H*), 7.10–7.16 (4 H, m, ArC*H*), 7.20–7.24 (1 H, m, ArC*H*), 7.38–7.45 (2 H, m, ArC*H*), 7.50–7.56 (2 H, m, ArC*H*), 7.67 (1 H, app. d, *J* 8.6, ArC*H*), 7.81–7.92 (4 H, m, ArC*H*) 9.40 (1 H, s, O*H*); δ_P (121 MHz, $CDCl_3$) 31.3. No melting point data is reported within the literature, all other data is in accordance.

5-Chloro-1-phenyl-pentan-1-one 24[41]

5-Chlorovaleronitrile **23** (5.00 g, 5.0 cm³, 43 mmol) was added to THF (20 cm³) and the solution cooled to 0 °C. Phenyl magnesium bromide (29.0 cm³, 3 M in THF, 86 mmol) was added dropwise over a period of 90 minutes and the reaction mixture warmed to room temperature and stirred overnight. A 10% aqueous solution of HCl (25 cm³) was added and the resulting suspension heated at reflux for 3 hours. The mixture was cooled to room temperature and the aqueous phase extracted with dichloromethane (3 × 30 cm³). The organic layers were combined, washed with 1M NaOH solution (20 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* yielded a yellow solid. Recrystallisation of the crude material from *n*-hexane afforded the title compound as a white crystalline material (7.05 g, 81%); m.p. 50–51 °C (lit.[41] 50 °C); δ_H (400 MHz, $CDCl_3$) 1.90–1.93 (4 H, m, C*H₂*), 3.03 (2 H, t, *J* 6.8, C*H₂*CO), 3.60 (2 H, t, *J* 6.1, C*H₂*Cl), 7.48 (2 H, t, *J* 7.5, ArC*H*), 7.58 (1 H, t, *J* 7.5, ArC*H*), 7.96 (2 H, d, *J* 7.5, ArC*H*). All data is in accordance with that of the literature.

(*S*)-5-Chloro-1-phenyl-pentan-1-ol 25[41]

Trimethyl borate (0.1 cm³, 0.5 mmol) was added dropwise to a solution of (1*R*, 2*S*)-(+)-1-amino-2-indanol (0.80 g, 0.5 mmol) in THF (2.0 cm³) at 0 °C and the mixture stirred for 30 minutes. BH_3.DMS (0.50 cm³, 5 mmol) was added dropwise and stirring continued for a further 45 minutes. The ketone 159 (900 mg, 4 mmol) dissolved in THF (5 cm³) was introduced by syringe pump (1.8 cm³ / hr) at 0 °C and the mixture warmed to room temperature and stirred for a further 90 minutes following complete addition of the ketone **24**. Methanol (5.0 cm³) was added in a single portion and the aqueous phase extracted with dichloromethane (3 × 15 cm³). The organic layers were combined, washed with 1M HCl (10 cm³), brine (10 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* yielded a yellow oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 3% ethyl acetate: petroleum ether 40–60 °C afforded the title compound as a white fluffy solid (800 mg, 83%). A racemic version of the alcohol rac-**25** was prepared through treatment of the ketone **24** with sodium borohydride. m.p. 37 °C; $[\alpha]_D^{25}$ -17.4 (*c* 1.0 in C_6H_6, lit.[41] -14.16 *c* 1.90, C_6H_6, 94% ee for (*S*)-enantiomer); δ_H (400 MHz, $CDCl_3$) 1.40–1.51 (1 H, m, C*H*H), 1.51–1.57 (1 H, m, C*H*H), 1.70–1.87 (5 H, m, 2 × CH_2 and O*H*), 3.54 (2 H, t, *J* 6.8, CH_2Cl), 4.70 (1 H, t, *J* 6.8, C*H*OH), 7.28–7.41 (5 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 23.3 (CH_2), 32.5 (*C*H_2), 38.2 (*C*H_2), 44.9 (*C*H_2Cl), 74.4 (CHOH), 125.9 (2 × Ar*C*H), 127.7 (Ar*C*H), 128.6 (2 × Ar*C*H), 144.6 (Ar*C*). No melting point or ^{13}C NMR data is reported within the literature for this enantiomer, otherwise all other data is in accordance. The enantioselectivity of this compound could not be assayed at this stage.

(*S*)-*tert*-Butyl(5-chloro-1-phenylpentyloxy)dimethylsilane 26

(*S*)-5-Chloro-1-phenyl-pentan-1-ol **25** (1.00 g, 5 mmol) was added to a solution of 4-diaminomethylpyridine (0.20 g, 2 mmol) and triethylamine (2.00 g, 2.0 cm³, 15 mmol) in dichloromethane (20 cm³). The solution was cooled to 0 °C and *tert*-butyl(chloro)dimethylsilane (2.00 g, 10 mmol) added in a single portion. The reaction mixture was stirred for 18 hours before being poured into water (10 cm³). The organic phase was separated and aqueous layer extracted with diethyl ether (3 × 15 cm³). The organic layers were combined, washed with 1M NaOH (10 cm³), brine (10 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* yielded a yellow oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 10% ethyl acetate: petroleum ether 40–60 °C afforded the title compound as a colourless oil (936 mg, 60%). A racemic version of the molecule rac-**26** was prepared in analogous fashion from the racemic

alcohol **25**; $[\alpha]_D^{25}$ -33.0 (*c* 0.5 in $CHCl_3$); υ_{max} (ATR)/ cm^{-1} 3121, 3061, 1515; δ_H (400 MHz, $CDCl_3$) -0.12 (3 H, s, SiC*H*$_3$), 0.05 (3 H, s, SiC*H*$_3$), 0.91 [9 H, s, (C*H*$_3$)$_3$], 1.37–1.55 [6 H, m, (C*H*$_2$)$_3$], 3.52 (2 H, t, *J* 6.9, C*H*$_2$Cl), 4.66 (1 H, dd, *J* 7.5 4.8, C*H*), 7.22–7.34 (5 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) -5.0 (Si*C*H$_3$), -4.6 (Si*C*H$_3$), 18.3 (*C*[CH$_3$]$_3$), 23.0 (*C*H$_2$), 25.7 (3 × *C*H$_3$), 32.6 (*C*H$_2$), 40.1 (*C*H$_2$), 44.9 (*C*H$_2$), 74.8 (*C*H), 125.8 (2 × Ar*C*H), 126.9 (2 × Ar*C*H), 128.0 (Ar*C*H), 145.5 (Ar*C*); *m/z* (TOF) 317.1751 (100%, MH^+, $C_{17}H_{29}{}^{35}ClOSi$ requires 313.1754).

(*S*)-5-(Diphenylphosphinyl)-1-phenylpentan-1-ol 27

(*S*)-t*ert*-Butyl(5-chloro-1-phenylpentyloxy)dimethylsilane **26** (0.10 g, 0.4 mmol) was added to a stirred suspension of triphenylphosphine (0.10 g, 0.4 mmol) and sodium iodide (0.06 g, 0.4 mmol) in acetonitrile (5.0 cm³) and the solution heated to reflux for 18 hours. The solvent was removed *in vacuo* to afford the crude phosphonium salt that was immediately dissolved in a 30% NaOH solution (10 cm³) and heated to reflux for a further 24 hours. The aqueous phase was extracted with dichloromethane (3 × 10 cm³), washed with an aqueous solution of $NaHCO_3$ (10 cm³) and dried over magnesium sulfate. Removal of the solvent *in vacuo* yielded a yellow oil. The crude material was dissolved in THF (10 cm³) and cooled to 0 °C. TBAF (1.5 cm³, 1M in THF, 0.8 mmol) was added dropwise and the solution warmed to room temperature and stirred for 24 hours. The reaction mixture was poured into water (5.0 cm³) and ethyl acetate (10 cm³) and the organic layer separated. The aqueous phase was extracted with ethyl acetate (3 × 10 cm³) and the organic layers combined, washed with 1M NaOH (10 cm³), brine (10 cm³) and dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* yielded a yellow oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 50% ethyl acetate: petroleum ether 40–60 °C afforded the title compound as a colourless oil (45 mg, 33%). A racemic version of the catalyst rac-**27** was prepared in analogous fashion from the TBS ether rac-**26**; t_R 10.5 min (*S* isomer) and 13.2 min (*R* isomer) (Celluose-1, 1: 1 hexane: propan-2-ol); $[\alpha]_D^{25}$ -4.0 (91% ee from HPLC, *c* 0.2 in $CHCl_3$); υ_{max} (ATR) / cm^{-1} 3430, 1641, 1515; δ_H (400 MHz, $CDCl_3$) 1.41–1.85 (5 H, m, C*H*$_2$), 2.18–2.30 (3 H, m, C*H*$_2$), 4.64–4.67 (1 H, m, C*H*OH), 7.26–7.36 (4 H, m, ArC*H*), 7.46–7.56 (6 H, m, ArC*H*), 7.71–7.75 (4 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 21.3 (d, $J_{C\text{-}P}$ 4.0, *C*H$_2$), 27.0 (d, $J_{C\text{-}P}$ 14.0, *C*H$_2$), 29.5 (d, $J_{C\text{-}P}$ 71.0, *C*H$_2$), 38.6 (*C*H$_2$P), 73.7 (*C*HOH), 125.9 (2 × Ar*C*H), 127.1 (Ar*C*H), 128.2 (2 × Ar*C*H), 128.5 (2 × Ar*C*H), 128.7 (2 × ArCH), 130.6 (d, $J_{C\text{-}P}$ 4.0, 2 × Ar*C*H), 130.7 (d, $J_{C\text{-}P}$ 4.0, 2 × Ar*C*H), 131.65 (Ar*C*H), 131.68 (Ar*C*H), 132.3 (d, $J_{C\text{-}P}$ 8.4, Ar*C*), 133.4 (d, $J_{C\text{-}P}$ 8.4, Ar*C*), 145.2 (Ar*C*); δ_P (121 MHz, $CDCl_3$) 32.4; *m/z* (TOF ES$^+$) 365.1671 (100%, MH^+, $C_{23}H_{26}O_2P$ requires 365.1670), 347 (35, M^+-H_2O).

(*S*)-3-(Diphenylphosphinyl)-1-phenylpropan-1-ol 29[33]

Methyl diphenylphosphine oxide[42] **28** (0.50 g, 2 mmol) was dissolved in anhydrous THF (10 cm³) and the solution cooled to 0 °C. *n*-Butyl lithium (2.0 cm³, 2M in hexanes, 4 mmol) was added dropwise and the reaction mixture stirred for 90 minutes. (*S*)-2-Phenyloxirane (0.3 cm³, 2.5 mmol) was introduced and the solution warmed to room temperature and stirred overnight. The mixture was poured into a saturated ammonium chloride solution (10 cm³) and the aqueous phase extracted with diethyl ether (3 × 15 cm³). The organic layers were combined, washed with brine (15 cm³) and dried over magnesium sulfate. Removal of the solvent *in vacuo* afforded a yellow oil. Purification of the crude material by flash column chromatography on silica gel using an eluent of 10% methanol: ethyl acetate afforded the title compound as a white solid (604 mg, 78%). m.p. 127 °C (lit.[33] 144–145 °C for racemate); $[\alpha]_D^{25}$ -11.5 (*c* 0.7 in $CHCl_3$); δ_H ($CDCl_3$, 400 MHz) 1.99–2.20 (2 H, m, C*H*$_2$), 2.33–2.50 (2 H, m, C*H*$_2$), 2.65 (1 H, br s, O*H*), 4.86 (1 H, dd, *J* 7.3, 4.2, C*H*), 7.25–7.35 (5 H, m, ArC*H*), 7.46–7.57 (6 H, m, ArC*H*), 7.70–7.77 (4 H, m, ArC*H*); δ_P ($CDCl_3$, 101 MHz) 32.7. No data is reported on the enantiomerically pure compound.

(*S*$_P$)-Phenyl-(2-anisyl)-but-3-ene phosphine oxide 31[42]

N-Phosphinyl oxazolidinone[26] **30** (120 mg, 0.3 mmol) was dissolved in THF (2.0 mL) and added by syringe pump (1.0 mL / hr) to a solution of but-3-enylmagnesium bromide (4 mL, 1 M in THF, 4 mmol) and THF (4.0 mL). Once addition was complete the reaction mixture was quenched through addition of a saturated aqueous solution of ammonium chloride (5.0 mL) and the aqueous phase extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (10 mL) and dried over $MgSO_4$. Filtration and removal of the solvent *in vacuo* yielded a crude yellow oil. Purification of the crude material by flash column chromatography on silica gel using a gradient eluent of 75% EtOAc: petroleum ether 40–60 °C to 5% MeOH: CH_2Cl_2 afforded the oxazolidinone (44 mg, 91%) as a white solid and the phosphine oxide **31** as a colourless oil (63 mg, 77%); t_R 10.5 (minor isomer) and 18.8 (major isomer) (Celluose-1, 90: 10 hexane: propan-2-ol, 210 nm); $[\alpha]_D^{25}$ +23.0 (*c* 1.0 in $CHCl_3$); υ_{max} / cm^{-1} (ATR) 3076, 2976, 1640, 1590; δ_H (400 MHz, $CDCl_3$) 2.22–2.60 (4 H, m, 2 × C*H*$_2$), 3.76 (3 H, s, OC*H*$_3$), 4.93–5.04 (2 H, m, CH=C*HH*), 5.84 (1 H, ddt, *J* 16.8, 10.2, 6.4, C*H*=CHH), 6.88 (1 H, dd, *J* 8.3 5.4, ArC*H*), 7.08–7.12 (1 H, m, ArC*H*), 7.39–7.52 (4 H, m, ArC*H*), 7.75–7.81 (2 H, m, ArC*H*), 7.97–8.03 (1 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 25.7 (d, $J_{C\text{-}P}$ 3.0, *C*H_2), 28.5 (d, $J_{C\text{-}P}$ 73.0, *C*H_2), 55.3 (O*C*H_3), 110.8 (d, $J_{C\text{-}P}$ 6.6, Ar*C*H), 114.8 (CH=*C*HH), 119.3 (d, $J_{C\text{-}P}$ 95.7, Ar*C*), 121.2 (d, $J_{C\text{-}P}$ 10.6, Ar*C*H), 128.2 (d, $J_{C\text{-}P}$ 11.8, 2 × Ar*C*H), 130.6 (d, $J_{C\text{-}P}$ 9.7,

2 × Ar*C*H), 131.3 (d, $J_{C\text{-}P}$ 2.4, Ar*C*H), 133.5 (Ar*C*), 133.9 (*C*H=CHH), 134.5 (d, $J_{C\text{-}P}$ 5.2, Ar*C*H), 137.8 (d, $J_{C\text{-}P}$ 16.3, Ar*C*H), 159.7 (d, $J_{C\text{-}P}$ 5.0, Ar*C*); δ_P (101 MHz, $CDCl_3$) 31.4; *m/z* (TOF ES^+) 287.1195 (100%, MH^+, $C_{17}H_{20}O_2P$ requires 287.1201). No data is reported in the literature.

1,6-*bis*[(*S*P)-(2-Methoxyphenyl)(phenyl)phosphinyl]hexane 32

Phosphine oxide **31** (90 mg, 0.3 mmol) was added to a solution of CH_2Cl_2 (3 mL) and Hoveyda-Grubbs II catalyst (18 mg, 0.03 mmol) and the solution heated at reflux for 18 h. Upon cooling to room temperature, the volatiles were removed *in vacuo* and the residue purified by flash column chromatography on silica gel using a gradient eluent of 100% EtOAc to 5% MeOH: CH_2Cl_2 to afford a yellow oil. The oil (54 mg, 0.1 mmol) was dissolved in MeOH (2 mL) and subjected to a single cycle through a Pd/C Thalesnano Catcart H-Cube™ under 1 atmosphere of hydrogen at 30 °C. Removal of the solvent *in vacuo* afforded the title compound as a colourless oil (50 mg, 61% over 2 steps); $[\alpha]_D^{25}$ +42.0 (*c* 1.0 in $CHCl_3$); υ_{max} / cm^{-1} (ATR) 3062, 2929, 1588, 1575; δ_H (400 MHz, $CDCl_3$) 1.30–1.65 (8 H, m, 4 × C*H*$_2$), 2.22–2.47 (4 H, m, 2 × C*H*$_2$), 3.72 (6 H, s, 2 × OC*H*$_3$), 6.82–6.90 (2 H, m, ArC*H*), 7.07–7.10 (2 H, m, ArC*H*), 7.40–7.50 (8 H, m, ArC*H*), 7.72–7.77 (4 H, m, ArC*H*), 7.95–8.00 (2 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 21.4 (d, $J_{C\text{-}P}$ 3.0, *C*H_2), 28.7 (*C*H_2), 29.4 (*C*H_2), 30.5 (d, $J_{C\text{-}P}$ 3.0, *C*H_2), 55.3 (2 × O*C*H_3), 110.7 (d, $J_{C\text{-}P}$ 6.6, 2 × Ar*C*H), 120.5 (d, $J_{C\text{-}P}$ 95.9, 2 × Ar*C*), 121.1 (d, $J_{C\text{-}P}$ 10.6, 2 × Ar*C*H), 128.1 (d, $J_{C\text{-}P}$ 11.7, 4 × Ar*C*H), 130.5 (d, $J_{C\text{-}P}$ 9.6, 4 × Ar*C*H), 131.2 (2 × Ar*C*H), 133.8 (2 × Ar*C*H), 134.1 (d, $J_{C\text{-}P}$ 75.3, 2 × Ar*C*), 134.5 (d, $J_{C\text{-}P}$ 5.2, Ar*C*H), 159.7 (d, $J_{C\text{-}P}$ 5.0, 2 × Ar*C*); δ_P (101 MHz, $CDCl_3$) 32.0; *m/z* (TOF ES^+) 547.2190 (100%, MH^+, $C_{32}H_{37}O_4P_2$ requires 547.2167).

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