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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 19 (2008) 161–166

A practical synthesis of *syn*- and *anti*-α,β-dihydroxyphosphinates via diastereoselective reduction of α-phosphinoyl ketones

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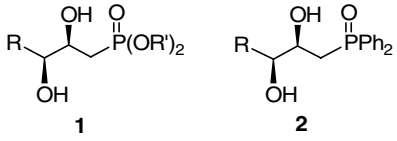
Received 15 August 2007; accepted 19 December 2007

Abstract—Reduction of β-keto-diphenylphosphine oxide (*S*)-**4** derived from (*S*)-mandelic acid with $NaBH_4$ in methanol at −78 °C gave the *anti*-3-diphenylphosphinoyl-1,2-diol **6**, whereas the reduction of (*S*)-**4** with $Zn(BH_4)_2$ in THF at −78 °C afforded the *syn*-1,2-diol **5**, both in high yield and excellent diastereoselectivity. This procedure represents a new approach to the diastereoselective synthesis of diphenylphosphinoyl diols and an example of highly diastereoselective 1,2-induction. A theoretical model to explain the direction and degree of asymmetric induction is proposed.

1. Introduction

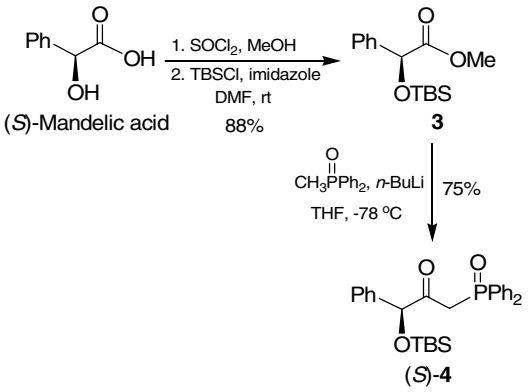
Dihydroxyalkylphosphonates of type **1** and their derivatives have attracted considerable attention in recent years for their role in biologically relevant processes such as the inhibition of imidazole glycerol phosphate (IGP).[1] Additionally, dihydroxyphosphonates **1** have been used in the stereoselective synthesis of γ-amino-β-hydroxyphosphonates,[2] which are key precursors for the preparation of phosphostatine and analogues.[3] Diphenylphosphinoyl diols **2** have also been established as useful intermediates in the synthesis of enantiomerically pure γ-hydroxy vinyl phosphine oxides,[4] allylic alcohols,[5] cyclopropyl ketones,[6] and as ligands.[7]



Synthesis of optically active dihydroxy phosphonates *syn*-**1** and diphenylphosphinoyl diols *syn*-**2** has been achieved by asymmetric dihydroxylation of the allylic phosphonates and phosphine oxides, respectively.[2,5] Herein, we report a new methodology for the synthesis of *syn*- and *anti*-diphenylphosphinoyl-1-phenyl propane-1,2-diols, which involved the diastereoselective reduction of β-keto-diphenylphosphine oxide **4** derived from (*S*)-mandelic acid.[8]

2. Results and discussion

The starting chiral β-keto-diphenylphosphine oxide (*S*)-**4** was readily prepared from (*S*)-mandelic acid (Scheme 1).



Scheme 1.

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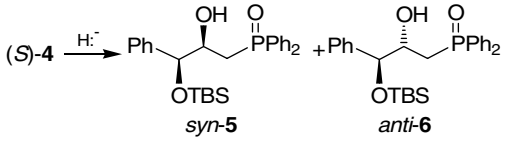
doi:10.1016/j.tetasy.2007.12.016

Esterification of (*S*)-mandelic acid with thionyl chloride in methanol, followed by treatment with *tert*-butyldimethylsilyl chloride (TBSCl) in the presence of imidazole afforded the corresponding methyl ester derivative (*S*)-**3** in 88% yield.[9] Next, reaction of methyl ester (*S*)-**3** with the lithium salt of methyl diphenylphosphine oxide at −78 °C in THF gave the β-keto-diphenylphosphine oxide (*S*)-**4** in 75% yield (Scheme 1).

The β-keto-diphenylphosphine oxide (*S*)-**4** was reduced using $NaBH_4$, DIBAL-H, catecholborane (CB), $LiBH_4$, and $Zn(BH_4)_2$, to obtain the *syn*-**5** and *anti*-**6** diphenylphosphinoyl-1-phenylpropane-1,2-diols. Conditions,yields, and diastereoisomeric ratios are summarized in Table 1.

Table 1. Reduction of (*S*)-**4** with various reducing agents



Entry	Conditions	Yield (%)	*syn*-**5**:*anti*-**6**
1	$NaBH_4$, MeOH, 0 °C	99	35:65
2	$NaBH_4$, MeOH, −78 °C	95	05:95
3	DIBAL-H, THF, −78 °C	99	50:50[a]
4	CB, THF, −78 °C	90	63:37
5	$LiBH_4$, THF, −78 °C	92	74:26
6	$Zn(BH_4)_2$, THF, −78 °C	90	96:04

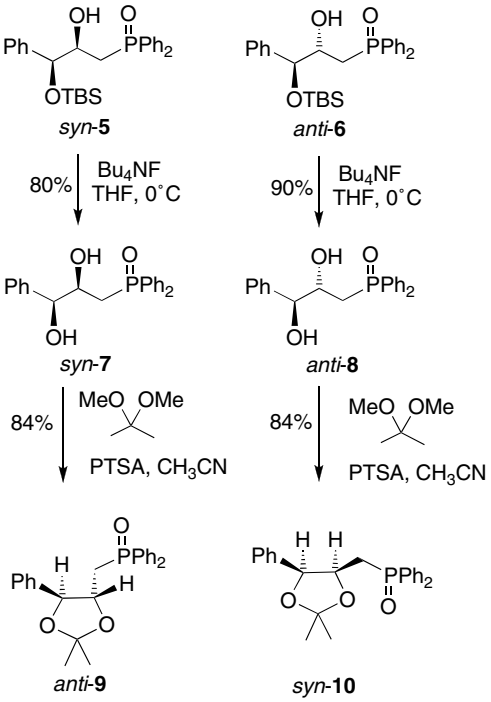
[a] Unprotected products *syn*-**7** and *anti*-**8** were obtained under these conditions.

The reduction of β-keto-diphenylphosphine oxide (*S*)-**4** with $NaBH_4$ in methanol at 0 °C afforded the corresponding hydroxy derivatives *syn*-**5** and *anti*-**6** with high yield and diastereoisomeric ratio 35:65 in the favor of diastereoisomer *anti*-**6** (Table 1, entry 1). A better diastereoselectivity was achieved when the reduction was carried out at −78 °C, when the hydroxy derivatives *syn*-**5** and *anti*-**6** were obtained in 95% yield and diastereoisomeric ratio of 5:95 (Table 1, entry 2). The diastereoisomeric ratio of the reduction of (*S*)-**4** was determinated by means of ^{31}P NMR, with a chemical shift for the diastereoisomer *syn*-**5** at 36.25 ppm and for diastereoisomer *anti*-**6** at 36.60 ppm.

To obtain the diastereoisomer *syn*-**5** as the principal product, we carried out the reduction of (*S*)-**4** using different reducing agents. Thus, the reduction of (*S*)-**4** with DIBAL-H in THF at −78 °C gave *syn*-**5** and *anti*-**6** in quantitative yield but with a poor diastereoselectivity (Table 1, entry 3), additionally under these conditions cleavage of the silyl ether also occurred.

On the other hand, reduction of (*S*)-**4** with catecholborane in THF at −78 °C led to *syn*-**5** and *anti*-**6** with good chemical yield and 63:37 diastereoisomeric ratio in favor of *syn*-**5** (Table 1, entry 4). When $LiBH_4$ was used at −78 °C the corresponding β-hydroxy derivatives were obtained with similar yield and moderate diastereoselectivity in favor of *syn*-**5** (Table 1, entry 5). Finally, the reduction of (*S*)-**4** with $Zn(BH_4)_2$ (obtained from $LiBH_4$ and $ZnCl_2$) at −78 °C afforded the β-hydroxy derivatives *syn*-**5** and *anti*-**6** with good chemical yield and excellent diastereoselectivity with a predominance of the desired diastereoisomer *syn*-**5** (Table 1, entry 6).

To unequivocally establish the configuration of the new stereogenic center of diphenylphosphinoyl-1-phenylpropane-1,2-diols *syn*-**5** and *anti*-**6**, these were first transformed into the corresponding dioxolanes *anti*-**9** and *syn*-**10**, respectively. Treatment of diastereoisomerically pure *syn*-**5** and *anti*-**6** with *n*-tetrabutylammonium fluoride (TBAF) in THF at 0 °C afforded the diols *syn*-**7** and *anti*-**8** with 80% and 90% yield, respectively. Finally, reaction of diol *syn*-**7** with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid (PTSA) in acetonitrile gave the acetonide *anti*-**9** with 84% yield. In a similar manner, *anti*-**8** gave the acetonide *syn*-**10** with 84% yield (Scheme 2).



Scheme 2.

The ^1H NMR spectra of *anti*-**8** and *syn*-**10** show that the vicinal coupling constants for protons at C2 and C3 are 8.0 and 6.4 Hz, respectively, confirming the relative stereochemistry between these protons.[10] Additionally, the absolute configuration at C-2 for the acetonide *anti*-**9** was confirmed by X-ray crystal structure analysis (Fig. 1).[11]

Therefore, if the reduction of (*S*)-**4** with $NaBH_4$ indeed took place under non-chelation control or a Felkin–Anh model,[12] where the OTBS (largest group) is perpendicular to the plane of the carbonyl group and phenyl (medium group) is gauche, then the approach of hydride should be close to the hydrogen (smallest group) or *Si* face, yielding diastereoisomer *syn*-**5** (Fig. 2). However, experimental data show that diastereoisomer *anti*-**6** is preferentially obtained under these conditions.

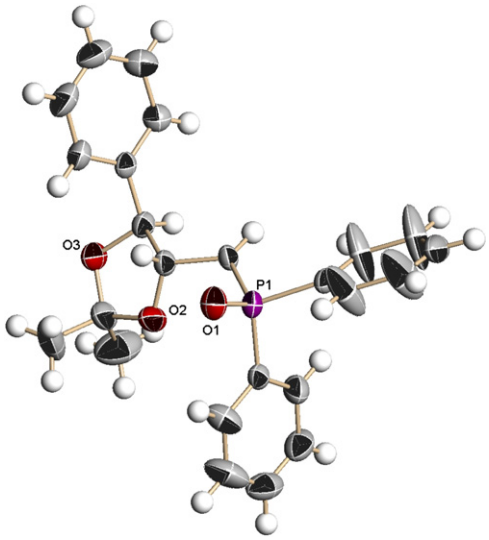


Figure 1. X-ray structure for the acetonide *anti*-**9**.

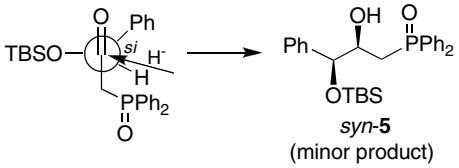


Figure 2. Felkin–Anh model for the reduction of (*S*)-**4** with $NaBH_4$.

A molecular orbital model is proposed to explain the stereochemical outcome in the reduction of (*S*)-**4** with $NaBH_4$ in methanol. We first explored the stability of the conformations of (*S*)-**4** by varying the positions of the relevant OTBS, the phenyl, and the hydrogen groups. This potential energy surface of (*S*)-**4** was explored by ab initio calculations where the O–C(2)–C(3)–H dihedral angle was rotated at 10° increments.

Initial results show two conformations with lowest energy, **A** and **B**. These were then used as starting geometries for further full optimization (all calculations were done at the B3LYP/6-31G* level using the G98 suite of program.[13] Stationary points were confirmed by frequency characterization). For the lower energy conformation **B**, we also varied the orientation of the OTBS group and further optimization yielded conformation **C**. The results are shown in Table 2.

Table 2. Dihedral angle, energy difference ($E(\mathbf{B}) = 0.0$) and dipolar moment of stable conformers of (*S*)-**4**

Conformer	A	B	C
Dihedral angle	104.963	22.19	22.67
ΔE (kcal/mol)	1.00	0.00	1.26
Dipole (D)	2.9772	3.7451	4.2928

Among the three most stable conformations obtained when the O–C(2)–C(3)–H dihedral is varied, we note that in conformers **B** and **C**, the OTBS group is almost perpendicular to the carbonyl plane. However, the smallest functional group (H) finds itself in the gauche position with respect to the carbonyl moiety (Fig. 3). The Felkin–Anh model, instead, suggests that the phenyl group to be in this position. Since the calculated energy difference among the three geometries was only around 1 kcal/mol, even though the reaction was carried out at a rather low temperature, all three conformations are accessible thermally to the molecule.

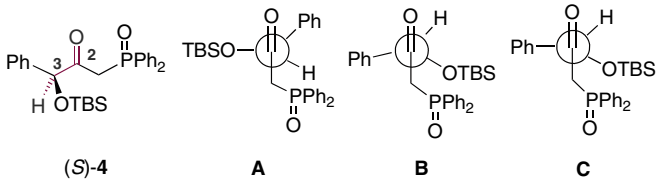


Figure 3. Stable conformers of (*S*)-**4** obtained when the O–C(2)–C(3)–H dihedral is varied.

Table 2 also shows that conformers **B** and **C** have larger dipolar moment than conformer **A**, which suggests that the former two should constitute a larger proportion in a polar solvent such as methanol. Furthermore, upon examination of the orbital coefficients of the three conformers, we observe that in the LUMO, which according to Frontier Orbital Theory is prone to nucleophilic attack, conformers **B** and **C** show a noticeable contribution from the carbonylic carbon, while conformer **A** shows only a negligible contribution from the carbon atom (Fig. 4). Thus, by adopting the gauche position for the phenyl group as suggested by the Felkin–Anh model, conformer **A** in fact provides a less than ideal condition for hydride attack.

These analyses bode well for the model in which (*S*)-**4** reacts with $NaBH_4$ preferably with the H group being eclipsed to the carbonyl group, which leads to the formation of diastereoisomer *anti*-**6** (Fig. 5).

For the reduction of (*S*)-**4** with $Zn(BH_4)_2$ at −78 °C in THF we propose that it took place under chelation control, whereby the $Zn(BH_4)_2$ coordinates with both oxygen of the carbonyl and the phosphinoyl groups, and hydride transfer takes place intramolecularly in a more rigid structure (*Si* face), obtaining the diastereoisomer *syn*-**5** as the major product (Fig. 6), as suggested by Oishi and Nakata.[14]

3. Conclusion

In conclusion, we have found a new methodology for the preparation of *anti*- and *syn*-3-diphenylphosphinoyl-1,2-diols with excellent diastereoselectivity via the reduction of β-keto-diphenylphosphine oxide (*S*)-**4** with $NaBH_4$ and $Zn(BH_4)_2$, respectively. This procedure represents an example of highly diastereoselective 1,2-induction. Theoretical analysis suggests that the nucleophilic attack takes place preferably when the H group is gauche to the carbonyl group contrary to a Felkin–Anh model.

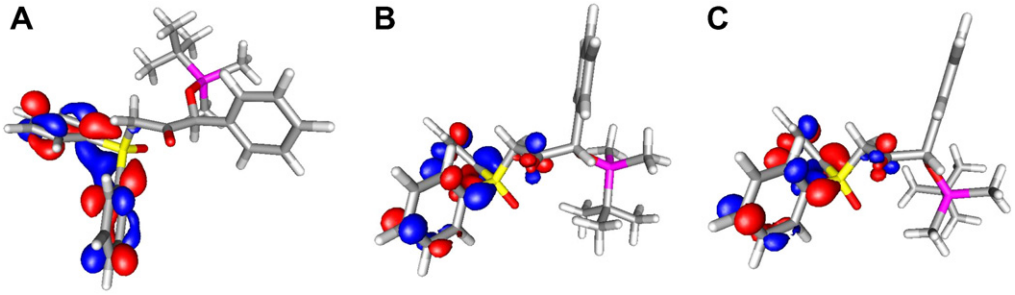


Figure 4. LUMO orbitals of stable conformers of (*S*)-**4**.

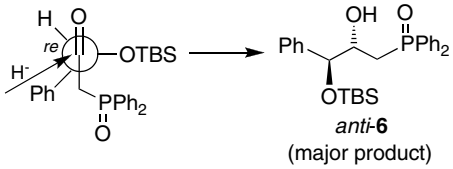


Figure 5. Model for the reduction of (*S*)-**4** with $NaBH_4$.

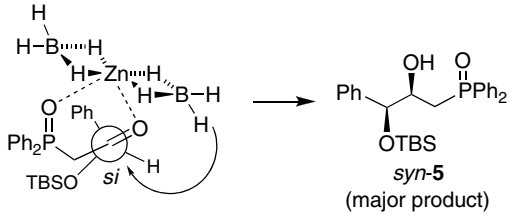


Figure 6. Suggested mechanism for the reduction of (*S*)-**4** with $Zn(BH_4)_2$.

4. Experimental

Optical rotations were taken at 20 °C on a Perkin–Elmer 241 polarimeter in a 1 dm tube; concentrations are given in g/100 mL. For the flash chromatography, silica gel 60 (230–400 mesh ASTM, Merck) was used. ^{1}H NMR spectra were registered on a Varian INOVA 400 (400 MHz), ^{13}C NMR (100 MHz) and ^{31}P NMR on a Varian Mercury 200 (81 MHz). The spectra were recorded in $CDCl_3$ solution using TMS as internal reference. Flasks, stirrings bars and hypodermic needles used for the generation of organometallic compounds were dried for ca. 12 h at 120 °C and allowed to cool in a dessicator over anhydrous $CaSO_4$. Anhydrous solvents (ethers) were obtained by distillation from benzophenone ketyl. HRMS spectra were recorded on a JEOL JMS-700.

4.1. (*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(diphenylphosphinoyl)-1-phenylpropan-2-one (*S*)-4

To a solution of methyl diphenylphosphine oxide (690 mg, 3.2 mmol) in anhydrous THF (100 mL), *n*-BuLi 2.5 M in hexanes (220 mg, 1.35 mL, 3.4 mmol) was added at −78 °C. After 1 h this solution was slowly added to a flask containing (*S*)-**3** (500 mg, 1.78 mmol) in THF (60 mL) at −78 °C. The reaction mixture was stirred for 12 h before the addition of a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 60 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (hexane–ethyl acetate 2:1) to afford 620 mg (75%) of (*S*)-**4** as a colorless oil. $[\alpha]_D = +20.9$ (*c* 2.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.08 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si), 0.87 (s, 9H, $(CH_3)_3CSi$), 3.65 (dd, $J_{gem} = J_{H/P} = 15.2$ Hz, 1H, CH_2P), 3.73 (dd, $J_{gem} = 15.2$, $J_{H/P} = 13.4$ Hz, 1H, CH_2P), 5.27 (s, 1H, CHCO), 7.29–7.70 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.72 (CH_3Si), 0.26 (CH_3Si), 18.5 ($C(CH_3)_3$), 26.0 (($CH_3)_3C$), 40.2 (d, $J = 62.2$ Hz, CH_2P), 81.7 (CHPh), 126.8, 128.4, 128.6 (d, $J = 4.6$ Hz), 128.7 (d, $J = 4.6$ Hz), 128.8, 131.0 (d, $J = 9.1$ Hz), 131.2 (d, $J = 9.1$ Hz), 132.0, 137.8 (CO). ^{31}P NMR (81 MHz, $CDCl_3$) δ 28.32. HRMS (FAB^+) Calcd for $C_{27}H_{34}O_3PSi$ (MH^+) 465.2015; found 465.2021.

4.2. Reduction of (*S*)-4

4.2.1. Reduction with $NaBH_4$ at 0 °C in MeOH. To a solution of (*S*)-**4** (500 mg, 1.1 mmol) in methanol (40 mL) sodium borohydride (203 mg, 5.4 mmol) was slowly added at 0 °C. After 6 h the solvent was evaporated. The residue was diluted with H_2O and extracted with ethyl acetate (3 × 30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to yield 500 mg (99%) of *syn*-**5** and *anti*-**6** in a ratio 35:65, respectively.

4.2.2. Reduction with $NaBH_4$ at −78 °C in MeOH. To a solution of (*S*)-**4** (500 mg, 1.1 mmol) in methanol (40 mL) sodium borohydride (203 mg, 5.4 mmol) was slowly added at −78 °C. After 6 h the solvent was evaporated. The residue was diluted with H_2O and extracted with ethyl acetate (3 × 30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to yield 500 mg (99%) of *anti*-**6** and *syn*-**5** in a ratio 95:5, respectively. The crude product was purified by column chromatography (hexane–ethyl acetate 1:1) obtaining 465 mg (93%) of *anti*-**6** as a white solid.

4.2.2.1. (1*S*,2*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(diphenylphos-phinoyl)-1-phenylpropan-2-ol *anti*-6. Mp 78–80 °C, $[\alpha]_D = +49.7$ (*c* 4.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.10 (s, 3H, CH_3Si), 0.10 (s, 3H, CH_3Si), 0.91 (s, 9H, $(CH_3)_3Si$), 2.44 (d, $J = 9.5$ Hz, 1H, CH_2P), 2.45 (dd, $J = 9.5$, 4.4 Hz, 1H, CH_2P), 3.59 (s, 1H, OH), 4.03–4.16 (m, 1H CHOH), 4.76 (d, $J = 4.4$ Hz, 1H, CHPh)

7.18–7.70 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ −4.5 (CH_3Si), −4.5 (CH_3Si), 18.5 (($CH_3)_3CSi$), 26.1 (($CH_3)_3CSi$), 30.6 (d, $J = 72.7$ Hz, CH_2P), 72.5 (d, $J = 4.0$ Hz, CHOH), 78.1 (CHPh), 126.7, 127.5, 128.2, 128.8 (d, $J = 11.7$ Hz), 130.5 (d, $J = 9.5$ Hz), 130.9 (d, $J = 9.1$), 131.9 (d, $J = 9.1$ Hz), 132.0 (d, $J = 9.1$ Hz), 141.4. ^{31}P NMR (81 MHz, $CDCl_3$): δ 36.60. HRMS (FAB^+) Calcd for $C_{27}H_{36}O_3PSi$ (MH^+) 467.2171; found 467.2174.

4.2.3. Reduction with $Zn(BH_4)_2$. To a solution of (*S*)-**4** (1.0 g, 2.2 mmol) in anhydrous THF (80 mL) freshly prepared[15] $Zn(BH_4)_2$ 0.14 M (410 mg, 30 mL, 4.3 mmol) was slowly added at −78 °C. The reaction mixture was stirred for 7 h before the addition of a saturated solution of NH_4Cl, and extracted with ethyl acetate (3 × 40 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to yield 1.0 g (99%) of *syn*-**5** and *anti*-**6** in a ratio of 96:4, respectively. The crude product was purified by column chromatography (hexane–ethyl acetate 1:2) obtaining 900 mg (90%) of *syn*-**5** as a white solid.

4.2.3.1. (1*S*,2*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(diphenylphos-phinoyl)-1-phenylpropan-2-ol *syn*-5. Mp 140–142 °C, $[\alpha]_D = +33.4$ (*c* 2.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.08 (s, 3H, CH_3Si), 0.14 (s, 3H, CH_3Si), 0.97 (s, 9H, $(CH_3)_3CSi$), 2.13 (ddd, $J = 15.0$, 4.1 Hz, 1H, CH_2P), 2.56 (ddd, $J = 15.0$, 8.3, 1.6 Hz, 1H, CH_2P), 4.27 (s, 1H, OH), 4.28–4.34 (m, 1H, C*H*OH), 4.93 (d, $J = 4.8$ Hz, 1H, CHPh), 7.40–7.88 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.0 (CH_3Si), −4.7 (CH_3Si), 18.3 (($CH_3)_3CSi$), 25.9 (($CH_3)_3CSi$), 30.8 (d, $J = 71.3$ Hz, CH_2P), 71.4 (d, $J = 4.6$ Hz, CHOH), 76.7 (d, $J = 13.7$ Hz, CHPh), 127.4, 127.7, 128.0, 128.8 (d, $J = 9.1$ Hz), 128.9 (d, $J = 10.6$ Hz), 130.6 (d, $J = 10.7$ Hz), 131.2 (d, $J = 9.1$ Hz), 140.1. ^{31}P NMR (81 MHz, $CDCl_3$): δ 36.25. HRMS (FAB^+) Calcd for $C_{27}H_{36}O_3PSi$ (MH^+) 467.2171; found 467.2162.

4.3. (1*S*,2*S*)-3-(Diphenylphosphinoyl)-1-phenylpropane-1,2-diol *anti*-8

To a solution of *anti*-**6** (800 mg, 1.7 mmol) in anhydrous THF (40 mL) *n*-tetrabutylammonium fluoride 1.0 M (896 mg, 3.4 mL, 3.4 mmol) was added at 0 °C. The reaction mixture was stirred for 4 h before the addition of a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 25 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (ethyl acetate–hexane 3:1) to afford 544 mg (90%) of *anti*-**8** as a white solid. Mp 164–165 °C, $[\alpha]_D = +45.7$ (*c* 2.4, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 2.19 (ddd, $J = 15.4$, 8.2, 1.8 Hz, 1H, CH_2P), 2.57 (ddd, $J = 15.4$, 12.0, 10.4 Hz, 1H, CH_2P), 4.19–4.25 (m, 1H, C*H*OH), 4.42 (s, 2H, OH), 4.93 (d, $J = 2.8$ Hz, 1H, CHPh), 7.28–7.60 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.5 (d, $J = 72.1$ Hz, CH_2P), 71.6 (d, $J = 4.6$ Hz, CHOH), 76.2 (d, $J = 12.2$ Hz, CHPh), 126.1, 127.5, 128.4, 128.7 (d, $J = 3.8$ Hz), 128.8 (d, $J = 3.0$ Hz), 130.5 (d, $J = 9.8$ Hz), 130.9 (d, $J = 9.1$ Hz), 132.0 (d, $J = 2.3$ Hz), 140.0. ^{31}P NMR (81 MHz, $CDCl_3$): δ 37.43 HRMS (CI^+) Calcd for $C_{21}H_{22}O_3P$ (MH^+) 353.1307; found 353.1321.

4.4. (1*S*,2*R*)-3-(Diphenylphosphinoyl)-1-phenylpropane-1,2-diol *syn*-7

The procedure is the same as for *anti*-**6**, using the diastereoisomer *syn*-**5** as a starting material (900 mg, 1.93 mmol), obtaining 544 mg (80%) of *syn*-**7** as a white solid. $[\alpha]_D = -1.8$ (*c* 0.7, $CHCl_3$): lit.[10] $[\alpha]_D = -1.8$ (*c* 0.7, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 2.3 (ddd, $J = 15.0$, 8.6, 2.4 Hz, 1H, CH_2P), 2.45 (ddd, $J = 15.0$, 12.0, 10.0 Hz, 1H, CH_2P), 4.11–4.19 (m, 1H, C*H*OH), 3.76 (b, 2H, OH), 4.60 (d, $J = 6.0$ Hz, 1H, CHPh), 7.25–7.65 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.7 (d, $J = 69.8$ Hz, CH_2P), 71.6 (d, $J = 3.0$ Hz, CHOH), 78.0 (d, $J = 13.7$ Hz, CHPh), 127.3, 128.2, 128.6, 128.9 (d, $J = 12.1$ Hz), 130.6 (d, $J = 9.2$ Hz), 130.9 (d, $J = 9.1$ Hz), 132.2, 140.0. ^{31}P NMR (81 MHz, $CDCl_3$): δ 36.00. HRMS (CI^+) Calcd for $C_{21}H_{22}O_3P$ (MH^+) 353.1307; found 353.1270.

4.5. (4*S*,5*S*)-2,2-Dimethyl-4-phenyl-5-(diphenylphosphinoyl methyl)-1,3-dioxolane *syn*-10

To a solution of *anti*-**8** (500 mg, 1.42 mmol) in acetonitrile (30 mL) *p*-toluenesulfonic acid (81 mg, 0.42 mmol) and 2,2-dimethoxypropane (295 mg, 0.35 mL, 2.8 mmol) were added at room temperature. After 12 h, triethylamine (43 mg, 0.1 mL, 0.42 mmol) was added. The volatiles were eliminated under reduced pressure and the residue was purified by column chromatography (ethyl acetate–hexane 1:1) to afford 466 mg (84%) of *syn*-**10** as a white solid. Mp 137–139 °C. $[\alpha]_D = +66.6$ (*c* 1.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.85 (ddd, $J = 15.4$, 3.0 Hz, 1H, CH_2P), 2.19 (ddd, $J = 15.4$, 9.4, 5.8 Hz, 1H, CH_2P), 4.89–4.96 (m, 1H, C*H*CH_2P), 5.29 (d, $J = 6.4$ Hz, CHPh), 7.28–7.75 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1 (CH_3), 27.2 (CH_3), 33.0 (d, $J = 71.3$ Hz, CH_2P), 73.5 (d, $J = 4.5$ Hz, *C*HCH_2P), 80.2 (d, $J = 10.6$ Hz, CHPh), 108.8 ($C(CH_3)_2$), 126.9, 128.1, 128.2 (d, $J = 12.1$ Hz), 128.5 (d, $J = 12.1$ Hz), 128.6, 130.7 (d, $J = 9.1$ Hz), 131.4 (d, $J = 10.6$ Hz), 131.6 (d, $J = 12.1$ Hz), 137.4. ^{31}P NMR (81 MHz, $CDCl_3$): δ 31.56. HRMS (FAB^+) Calcd for $C_{24}H_{26}O_3P$ (MH^+) 393.1620; found 393.1633.

4.6. (4*S*,5*R*)-2,2-Dimethyl-4-phenyl-5-(diphenylphosphinoyl methyl)-1,3-dioxolane *anti*-9

The procedure is the same as for *syn*-**10**, using the diastereoisomer *syn*-**7** as starting material, obtaining 466 mg (84%) of *anti*-**9** as a white solid. Mp 144–145 °C. $[\alpha]_D = +5.5$ (*c* 1.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.52 (ddd, $J = 14.8$, 2.8 Hz, 1H, CH_2P), 2.65 (ddd, $J = 14.8$, 9.2 Hz, 1H, CH_2P), 4.08–4.15 (m, 1H, C*H*CH_2P), 4.76 (d, $J = 8.0$ Hz, CHPh), 7.31–7.71 (m, 15H, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.1 (CH_3), 27.3 (CH_3), 32.5 (d, $J = 71.3$ Hz, CH_2P), 77.8 (d, $J = 5.3$ Hz, **C**HCH_2P), 84.2 (d, $J = 12.9$ Hz, CHPh), 109.6 ($C(CH_3)_2$), 127.1, 128.3 (d, $J = 11.4$ Hz), 128.6 (d, $J = 12.1$ Hz), 128.7,

128.8, 130.9 (d, $J = 9.1$ Hz), 131.2 (d, $J = 9.9$ Hz), 131.8 (d, $J = 9.9$ Hz), 136.4. ^{31}P NMR (81 MHz, $CDCl_3$): δ 30.76. HRMS (FAB^+) Calcd for $C_{24}H_{26}O_3P$ (MH^+) 393.1620; found 393.1624.

Acknowledgments

We gratefully acknowledge CONACYT-Mexico for financial support via Grant 41657-Q and 62271-Q and graduate fellowship by H.R.C. (170296). We also thank the valuable technical help of Victoria Labastida for carrying out all MS spectra and M. A. Muñoz-Hernández for the X-ray crystallographic analysis.

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10. ^{1}H NMR spectrum for diol (*S,R*)-**7** or *syn*-**7** was identical to that reported by Nelson, A. and Warren, S. See Ref. 5.
11. X-ray crystal data of *anti*-**9** were collected at 298 K using a Bruker APEX CCD instrument (Mo Kα radiation $\gamma = 0.71073$ Å). The SHELXTL v. 6.1 program package was used for structure solution and refinement. Compound *anti*-**9**: $C_{24}H_{25}O_3P$, $M = 392.42$, orthorhombic, space group $P2_12_12$, $a = 17.588(3)$ Å, $b = 21.118(4)$ Å, $c = 5.8506(10)$ Å, $V = 2173.0(6)$ Å^3, $Z = 4$, $D_c = 1.196$ mg/m^3, $R = 0.0412$ over 3822 independent reflections.
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