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Optically active C^3-symmetric triarylphosphines in asymmetric allylations

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Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

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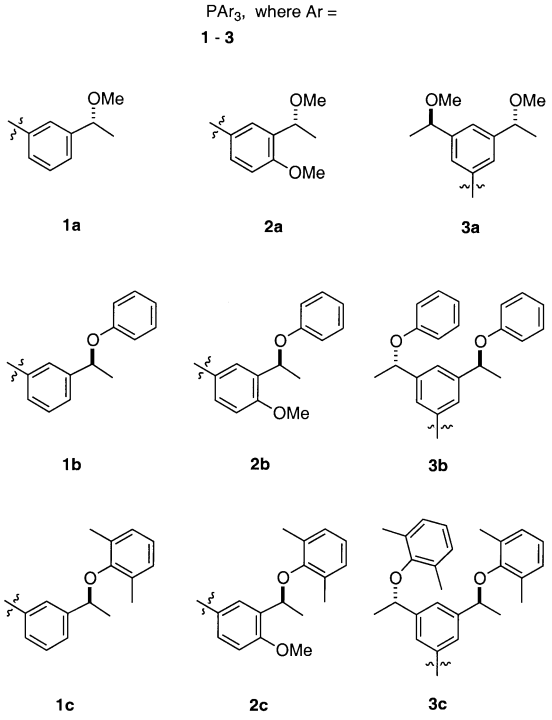
Abstract—A new class of optically active, monodentate, C^3-symmetric ligands for asymmetric catalysis, **1**–**3**, were prepared via routes involving asymmetric reduction of aryl ketones (Schemes 1–3). Single crystal X-ray structures of *trans*-$PdCl_2$(phosphine)$_2$ complexes of ligands **1a**, **2a** and **3a** showed that the ligands do not adopt perfect C^3-symmetric conformations in the solid state; in fact, all three have one aromatic ring lying 'face-on' to the metal. Circular dichroism studies of the same complexes provided some evidence for an aromatic ordering effect for complex **22**, but none for **21** and **23**. Palladium catalyzed allylation reactions using ligands **1**–**3** showed that encouraging enantioselectivities could be obtained, particularly for cyclic, allylic substrates.

1. Introduction

A decade ago, ligand design for asymmetric catalysis focused on bidentate, C^2-symmetric systems.[1] Recent developments, however, have shown ligands that are not C^2-symmetric can also give high enantioselectivities. For instance, optically active phosphine oxazolines with low overall symmetry have been shown to be valuable for several asymmetric transformations.[2] In fact, chiral ligands do not even have to be bidentate for good enantioselectivities to be obtained. Some optically active monodentate ligands, like the 2′-alkoxy-2-(diphenylphosphino)-1,1′-binaphthyl (MOP) systems,[4] can induce excellent enantioselectivities.[3] The MOP ligands are relatively unsymmetrical molecules proving that a high degree of symmetry is not essential for monodentate ligands to be successful in asymmetric catalysis. However, the inverse of this situation has not been investigated thoroughly, i.e. the potential of highly symmetrical monodentate ligands in asymmetric syntheses.

The research described in this paper was designed to explore the importance of symmetry in monodentate ligands for enantioselective catalysis. Specifically, could C^3-symmetric monodentate phosphine ligands be prepared easily, and, if so, how would their structures and solution phase conformations correlate with their performance in asymmetric catalysis? Ligands **1**–**3** were conceived to test this issue.[5] These are fundamentally different to C^3-symmetric phosphines that had been prepared previously.[6,7] The C^3-symmetric phosphines that were known prior to these studies were not particularly suitable for asymmetric catalysis,[8–12] or simply could not be resolved into their enantiomers.[13,14] This paper discusses synthesis, structure, conformations of ligands **1**–**3**, and their performance in asymmetric allylation reactions involving five different π-allyl complex precursors.



Keywords: C^3-symmetric ligands; asymmetric allylations; palladium catalysis.

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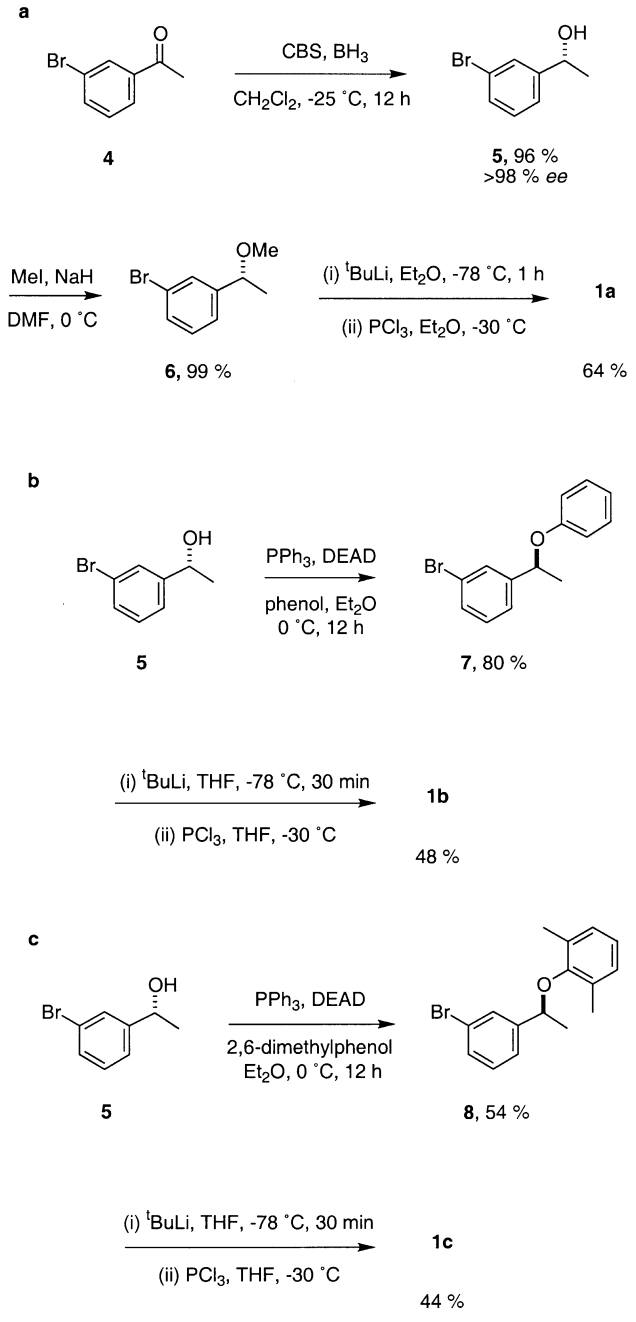
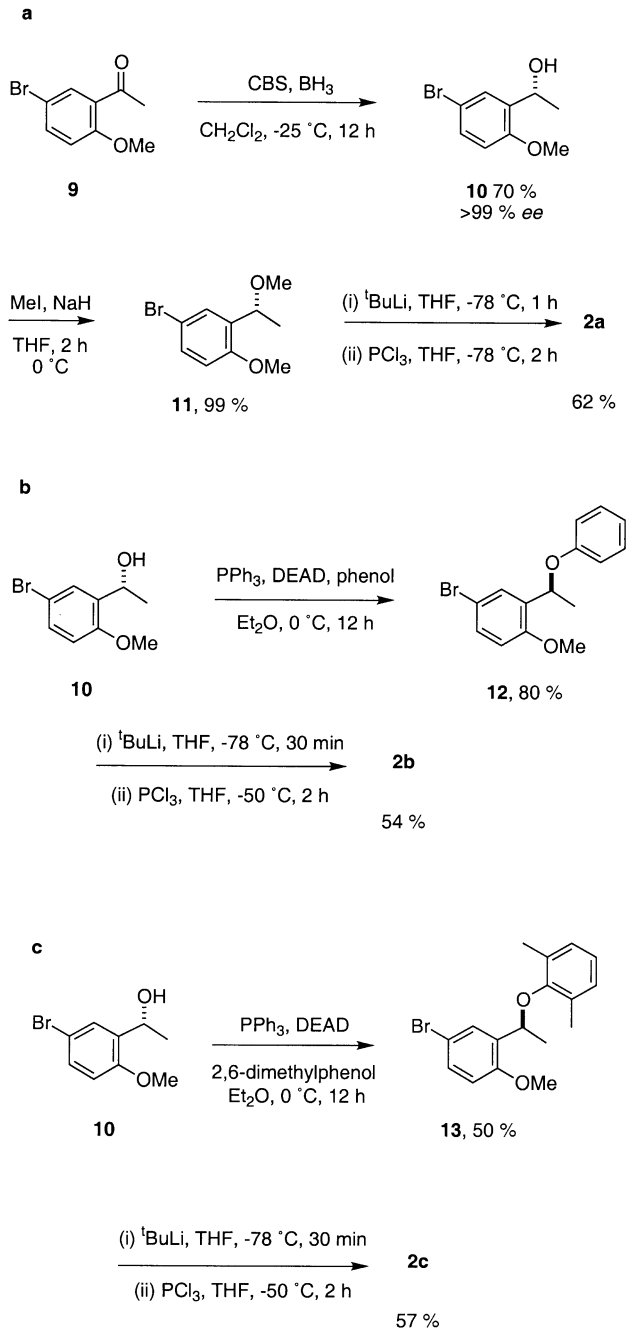


Scheme 1. Syntheses of ligands **1**.



Scheme 2. Syntheses of ligands **2**.

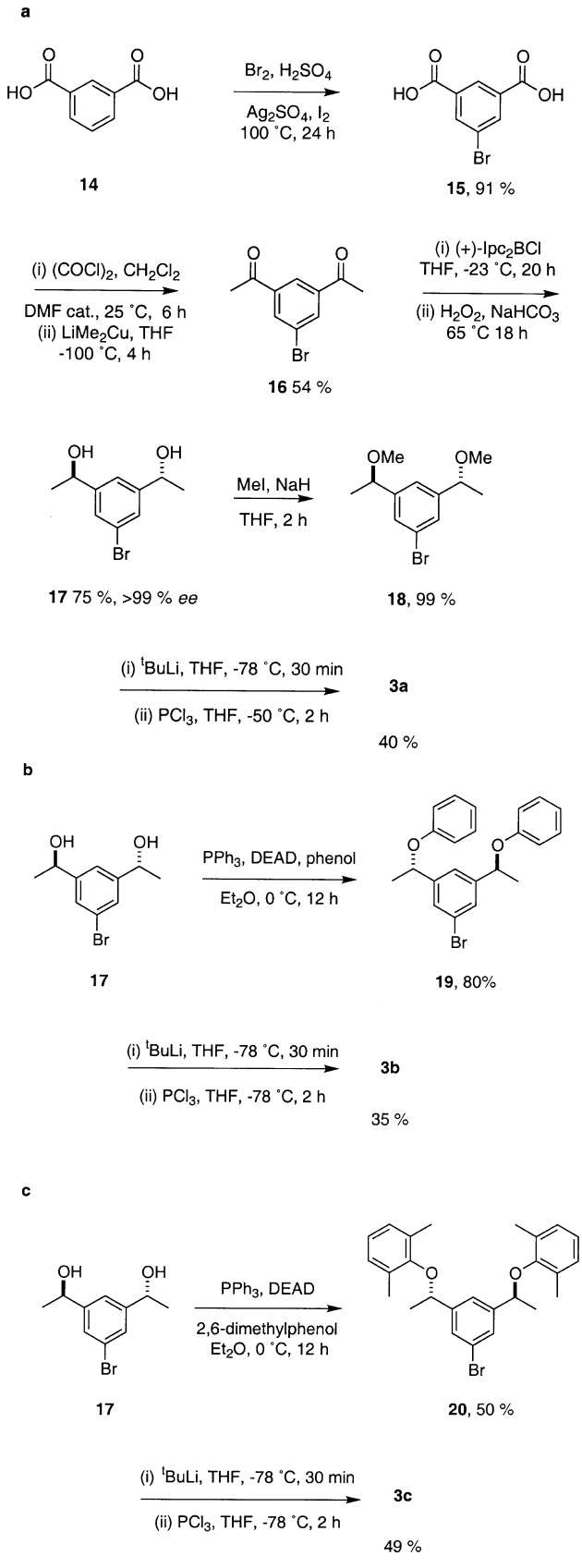
2. Results and discussion

2.1. Syntheses of ligands 1–3

A commercially available aryl ketone was reduced using the CBS reagent (tetrahydro-1-methyl-3,3-diphenyl-1H,3H-pyrrolo-[1,2-*c*]-[1,3,2]-oxazaborole-borane) to give the benzylic alcohol **5** (Scheme 1a).[15,16] This was methylated to the ether **6**, metalated with *tert*-butyl lithium, and the corresponding aryl lithium species was quenched with PCl_3. Throughout this work, temperature control (internal thermometer) and slow addition of the reagents was crucial to obtaining good yields in the metalation/quench procedures (see Section 4).

The synthesis was easily manipulated so that the alcohol **5** could be converted into other phosphine precursors. Thus a Mitsunobu reaction[17,18] was used to introduce aryl ether functionalities in the routes outlined in Scheme 1b and c. The stereochemistry of the benzylic position is not inverted in Scheme 1a, but it is in Scheme 1b and c; this becomes important when comparing induction that results from ligands **1a** and from **1b/1c**.

The synthetic approaches used to obtain ligands **2** were similar to those described above except that the requisite starting material, ketone **9**, was prepared via methylation of a commercially available ketone (Scheme 2). The syntheses shown in Scheme 3 began with the known aryl



Scheme 3. Syntheses of ligands **3**.

bromide **15**; we found this easier to prepare via the bromination route shown[19] than via an alternative route that has been published.[20] Asymmetric reduction of the diketone **16** using Ipc_2BCl (*B*-chlorodiisopinocamphenylborane)[21,22] gave better enantioselectivities than the CBS reagent did for this particular substrate. Overall, ligands **3** were more difficult to obtain than **1** and **2** mainly because the yields in the final metalation step were inferior in the former case.

2.2. Solid state structures of ligand 1–3 derivatives

Three palladium complexes of the general formula *trans*-$PdCl_2(PAr_3)_2$ (**21**, from ligand **1a**; **22**, from **2a**; and **23**, from **3a**) were prepared, crystallized, and examined via single crystal X-ray diffraction. Fig. 1 shows representations of all three with one of the two phosphines omitted, and viewed opposite a Pd–P bond (colloquially referred to here as 'end-on'), and along the Cl–Pd–Cl axis ('side-on').

The design of ligand types **1**–**3** was based on the following considerations. Ligands **1** were conceived as an easy way to potentially induce a C^3-propeller-like conformation of the aromatic rings. Data collected in asymmetric allylation reactions using complexes of ligands **1** were encouraging, but in absolute terms the enantioselectivities obtained were moderate (see below). A 4-methoxy substituent was incorporated into the second generation of phosphines, ligands **2**, to provide some restriction to the free rotation about the aryl-(3-alkoxyethyl) bond, in an attempt to increase the enantioselectivities that could be obtained using these ligands. This change must also perturb the electronic characteristics of the phosphorus center, but the electronic change was not anticipated to be as significant. These modifications did indeed alter the enantioselectivities of the corresponding catalysts (see below), but further optimization was desirable. A strategy for further improvements to the ligand design became apparent from crystallographic studies. Triarylphosphines like **1** and **2** can crystallize with the *meta*-substituent oriented *exo* with respect to the metal phosphine bond, or *endo* to it. In the solid state, ligand **1a** crystallized with two substituents that were clearly *endo* and one that marginally tilts towards an *exo* orientation), but that aryl ring rests in a conformation that is almost 'face-on' with respect to the metal. The more crowded ligand **2a** crystallized with one aryl-substituent *endo*, one *exo*, and again one less clearly *exo* because the aryl ring also adopted a near face-on conformation.

The third generation ligands **3** were designed to avoid ambiguities caused by *exo*/*endo* conformations. A 3,5-disubstituted aryl group with an edge pointing towards the metal must have one *endo*-substituent and one *exo*. Fig. 1c shows crystal structure of a complex formed from a ligand of this type. Like the others in this series, it crystallized with one aryl group in an edge-on orientation, another face-on, and with one aryl unit with its face to the rest of the complex.

2.3. Circular dichroism studies of ligand 1–3 derivatives

Rotational energy barriers about the P–aryl bond in complexes of ligands **1**–**3** are likely to be small enough to

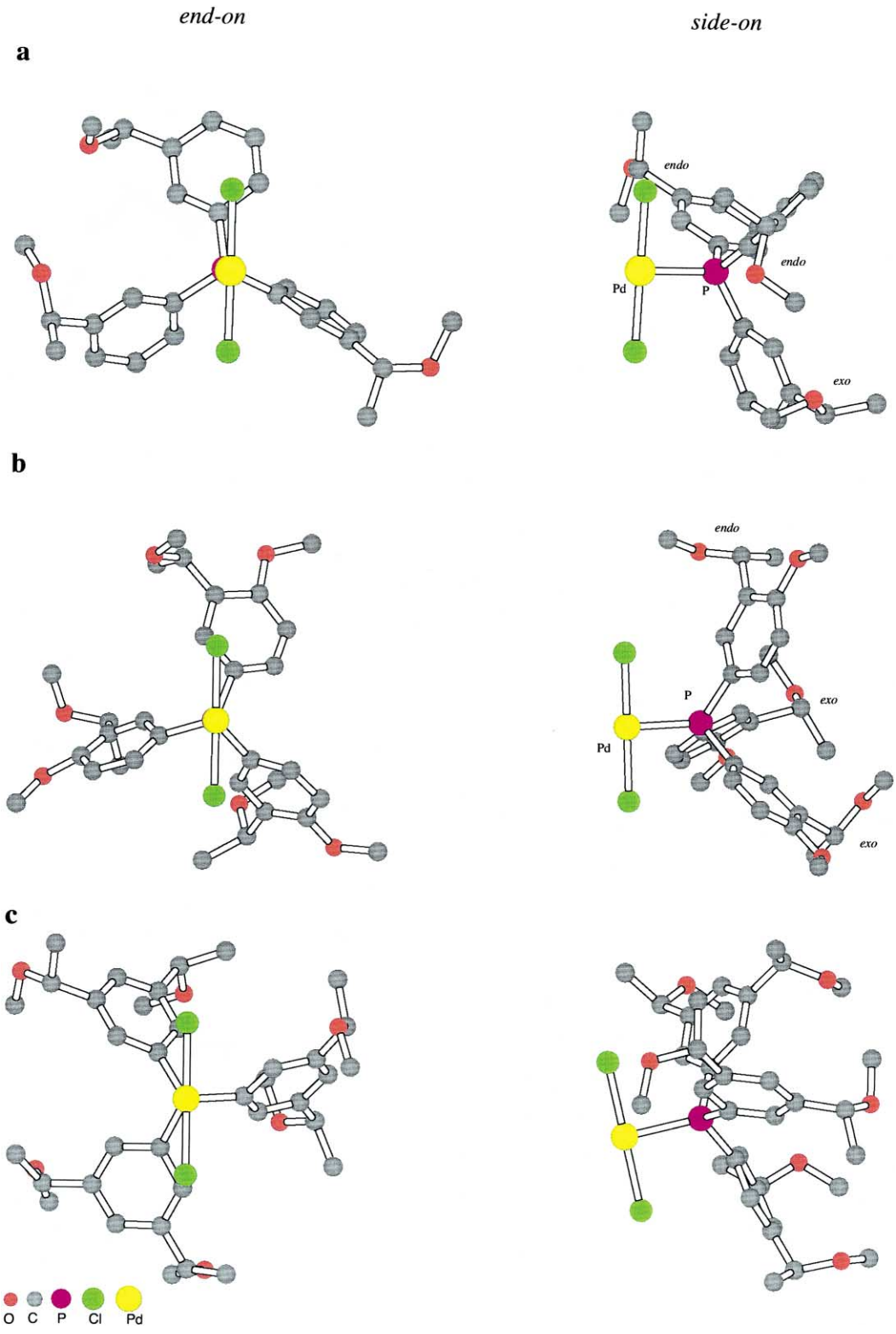


Figure 1. CHEM3D representations of data from solid state single crystal studies of the *trans*-$(Ar_3P)_2PdCl_2$ complexes, shown with one ligand removed for clarity. End-on and side-on views are shown in each case to illustrate the orientation of the aryl rings for clarity: (a) complex **21** from ligand **1a**; (b) complex **22** from ligand **2a**; and (c) complex **23** from ligand **3a**.

permit the aryl groups to turn through 360°, though, particularly for ligands **3**, rotation of the three aryl rings might be somewhat concerted in a cog-like mechanism. The latter point would be difficult to prove, but circular dichroism experiments provided a convenient way to search for general trends in conformational rigidity. The hypothesis followed was that complexes of the ligands might have preferred conformations that could be detected by increased ellipticities in the aromatic region, relative to the free phosphines and the chiral aryl bromides (e.g. compound **5**) that

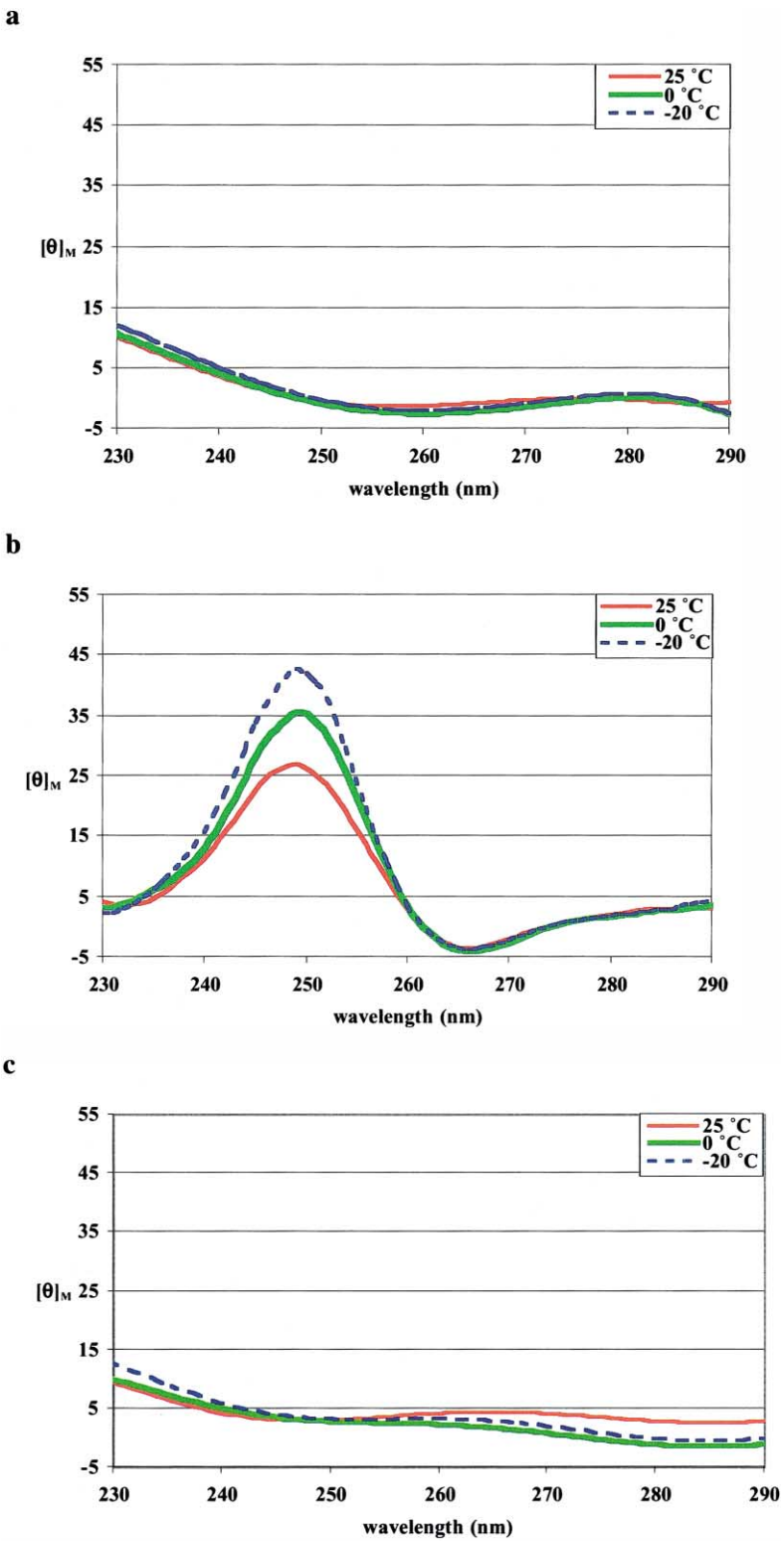


Figure 2. CD spectra recorded in CH_3CN for: (a) the aryl bromide **6**; (b) complex **22** (from ligand **2a**); and (c) complex **23** (from ligand **3a**). Ligand **1a** showed no significant ellipticity in the aromatic absorption region at any of the temperatures indicated (data not shown).

they were prepared from. Moreover, these ellipticity differences should be temperature dependent.

Fig. 2a–c show molar ellipticities per aromatic ring (a correction to enable direct comparison of an aryl bromide with one aromatic ring with triarylphosphines), for the aryl bromide **6**, complex **22** (from ligand **2a**), and complex **23** (from ligand **3a**), respectively. The CD spectrum of the aryl bromide is a negative control; aromatic ellipticity would not be expected for this compound, and none was seen. Complex **21** (from ligand **1a**) also gave no significant ellipticity in this region. For **22**, however, an appreciable

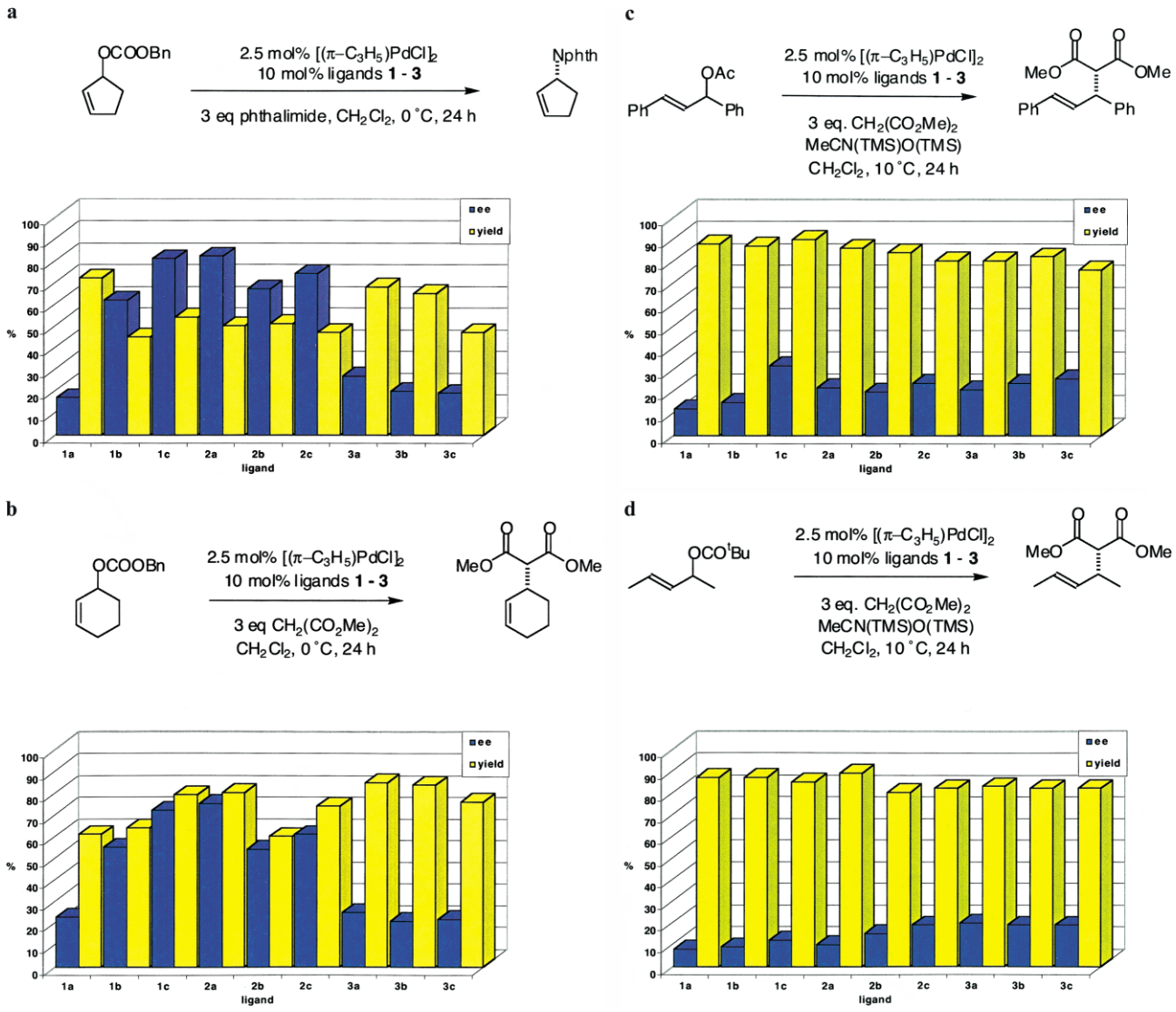


Figure 3. Overall yield (yellow) and enantiomeric purity (blue), for the allylation shown.

ellipticity was observed, and it was shown to be inversely proportional to temperature. Surprisingly, the same effect is not observed for complex **23**. This leads to the conclusion that the ellipticity in this region is not due to some conformational preference in the ordering of the aromatic rings, or that ligand **2a** in **22** adopts a preferred conformation that imparts a chiral ordering of the aromaticity. It is curious that **1a** and **3a** do not show the same effect if the aromatic groups are ordered, but it could be that the complexed form of ligand **1a** undergoes conformational averaging between several states, and ligand **3a** in complex **23** populates two conformers for which the ellipticities cancel.

2.4. Asymmetric allylation reactions using ligands 1–3

The data illustrated in Fig. 3 for the four allylation reactions shown in parts a–d illustrate that ligands **1**–**3** give the highest enantioselectivities for cyclic substrates. The enantioselectivities observed (up to 82% in Fig. 2a, and 75% in Fig. 2b) compare favorably with those reported for many other ligands, but do not match the best obtained for either substrate category. Cyclic carboxylates, like the one shown in Fig. 3a, are relatively difficult to transform with high enantioselectivities, but ligands from Helmchen[23] and from Trost[24] have been used to give approximately 95% ee in such relations.

1,3-Diphenylpropenyl acetate has been studied in asymmetric allylation reactions by many groups, and enantioselectivities of 99% or more have been reported in several cases.[25] Surprisingly, ligands **1**–**3** gave only modest enantioselection in these processes (up to 32% for ligand **1c**). Similarly, the analogous aliphatic substrates shown in Fig. 3d gave enantioselectivities of 20% (ligand **3a**) or less. It is difficult to rationalize why these two substrates should give inferior results to the cyclic systems.

Ligands **1**–**3**, particularly the ones with bulky substituents at the benzylic position (i.e. in the series **b** and **c**), could be anticipated to be so large that coordination of two *cis*-phosphines and a π-allyl fragment around palladium is disfavored. Hayashi and co-workers have used similarly

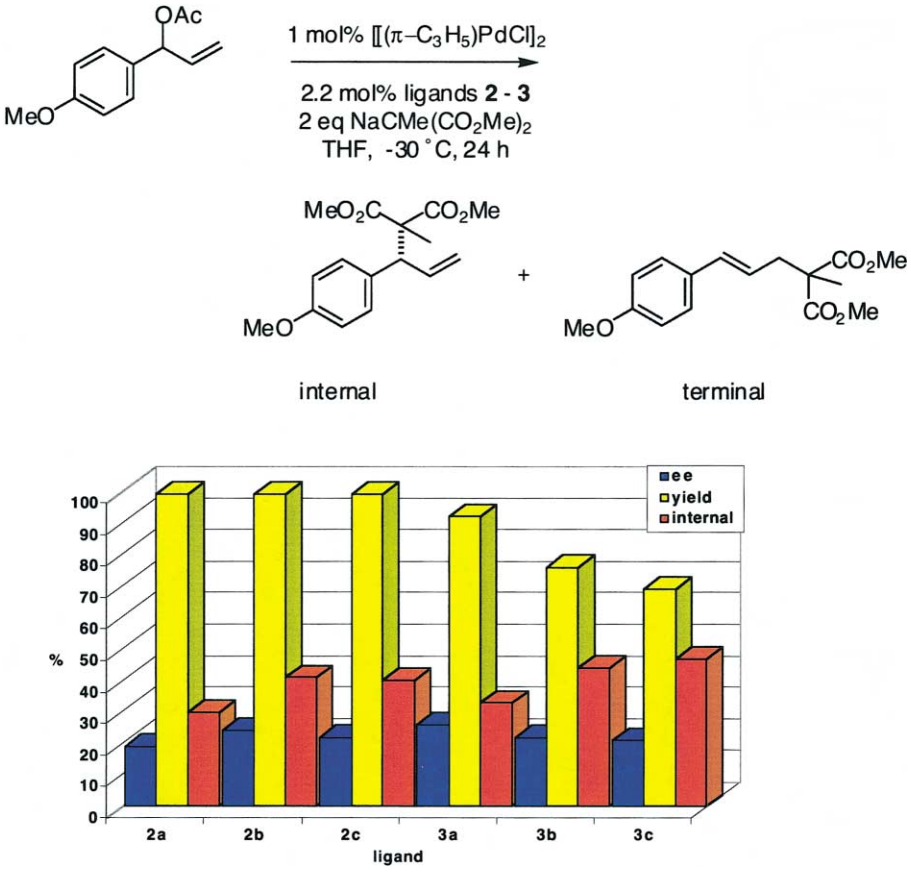


Figure 4. Overall yield (yellow), yield of the internal isomer (red), and enantiomeric purity of that isomer (blue), for the allylation shown.

hindered phosphines to favor formation of (π-allyl)PdCl-(phosphine) complexes in a catalytic cycle over intermediates of the type $[(\pi\text{-allyl})Pd(phosphine)_2]^+$. The *trans*-directing effect of the phosphine then controls the regioselectivity of the allylation leading to high regioselectivities for the branched (or internal) allylation product. In some cases, high enantioselectivities were also obtained for the branched products.[4,26,27] Fig. 4 shows data from an investigation designed to test if the larger ligands prepared in this work, **2** and **3**, could be used in a similar way. An identical reaction was tested using triphenylphosphine as the ligands as a control, and it gave a total yield of 92% of the *internal/terminal* isomers in a ratio of 27:73. Each of the ligands **2** and **3** gave better regioselection for the internal isomer, the best being **3c**, which gave an internal:terminal ratio of 47:53. The maximum ee of the internal isomer was obtained using ligand **3a**, but this was only 26% whereas Hayashi and co-workers have obtained selectivities of more than 90%.

3. Conclusions

Ligands **1**–**3** were prepared via relatively direct routes that involve asymmetric reduction of appropriately functionalized aryl methyl ketones. This type of approach gives a convenient entry into the desired ligands. Free rotation about the aryl–P bonds enables these ligands to populate conformations that are not perfectly C^3-symmetric; this is evident from X-ray crystallographic studies that show the aryl ligands do not adopt perfect propeller-shaped conformations in the solid state. Moreover, the 3-substituted derivatives **1** and **2** can align their *meta*-substituents in *endo* and *exo* orientations relative to the metal. Ligands **3**, having two *meta*-substituents, were designed to nullify that effect but, in solution, all the ligands must have a considerable degree of conformational freedom. Evidence was obtained for structural ordering of the aromatic groups in compound **22** (a ligand **2a** complex), but similar trends were not observed for complexes of ligands **1a** and **3a**.

Overall, these studies indicate that C^3-symmetric triarylphosphines do have the potential to be useful ligands in asymmetric catalysis. Improved enantioselectivities could probably be obtained by introducing more stringent conformational restraints than are present in ligands **1**–**3**.

4. Experimental

4.1. General procedures

High field NMR spectra were recorded on a Varian Unity Plus spectrometer. Chemical shifts of ^1H and ^{13}C spectra were referenced to the NMR solvents; ^{31}P spectra are referenced to H_3PO_4 (85%) external standard (0 ppm). IR spectra were recorded on an FTIR instrument. Melting points are uncorrected. Optical rotations were measured on a Jasco

DIP-360 digital polarimeter. Flash chromatography was performed using silica gel (230–600 mesh). Thin layer chromatography was performed on glass plates coated with silica gel 60 F254 (E. Merck, Darmstadt, Germany). Micro analyses were performed by Atlantic Microlab, Norcross, GA. The CD spectra were recorded in quartz cells of 0.1 mm path length using metal complex concentrations of 0.125 mM in CH_3CN. CH_2Cl_2 was distilled over CaH_2, Et_2O and THF over Na/benzophenone, and acetone over $CaSO_4$. Other solvents and reagents were used as received.

4.1.1. (*R*)-1-(3′-Bromophenyl)-ethanol 5. A solution of **4** (Aldrich; 10.8 g, 64.96 mmol) in CH_2Cl_2 (50 mL) was added dropwise over 2 h to a solution of (*S*)-4,5,6,7-tetrahydro-1-methyl-3,3-diphenyl-1H,3H-pyrrolo-[1,2-*c*]-[1,3,2]-oxazaborole-borane (i.e. CBS, 0.9 g, 3.2 mmol) and $BH_3{\cdot}Me_2S$ (5.1 mL, 51 mmol) in CH_2Cl_2 (30 mL) at −20°C. The solution was allowed to stand at −23°C for 8 h. The cold solution was added slowly to methanol (50 mL) at −20°C. Rapid gas evolution occurred. The solution was concentrated in vacuo, and the oily residue was purified by bulb-to-bulb distillation (94°C, 0.5 mmHg) to yield the title compound as a colorless oil (96%, 98.6% ee). The ee was determined by chiral GC on a column prepared in house.[28] $[\alpha]^{25}_D$=+34.7° (*c* 1.35, CCl_4, 25°C); IR (film) 3350, 2978, 2870, 1677 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52–7.18 (m, 4H), 4.80 (q, *J*=6.3 Hz, 1H), 2.95 (s, 1H), 1.45 (d, *J*=6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 148.2, 130.5, 130.2, 128.6, 124.1, 122.6, 69.7, 25.3.

4.1.2. (*R*)-1-Bromo-3-(1′-methoxyethyl)benzene 6. Neat **5** (1.0 g, 4.9 mmol) was added dropwise to a suspension of NaH (0.18 g, 7.35 mmol) in DMF (4 mL) at 0°C. Gas evolution occurred. The cold suspension was stirred for 30 min whereupon it was treated with neat MeI (0.7 mL, 11.4 mmol added in one portion) and allowed to warm to 25°C and stirred for 12 h. The reaction was quenched with water (25 mL) and diluted with ether (100 mL). The organics were washed with H_2O (2×25 mL), with brine (25 mL), dried (Na_2SO_4), and concentrated to dryness in vacuo. $[\alpha]_D$=+81.8° (*c* 1.33, CCl_4, 25°C); IR (film) 2976, 2932, 2820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47 (m,1H), 7.39 (m, 1H), 4.24 (q, *J*=6.3 Hz, 1H), 3.22 (s, 3H), 1.40 (d, *J*=6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 146.0, 130.5, 130.0, 129.2, 124.7, 122.6, 79.0, 56.6, 23.8.

4.1.3. (*S*)-1-Bromo-3-(1′-phenoxyethyl)benzene 7. Neat DEAD (0.92 mL, 7.5 mmol) was added dropwise over 5 min to a solution of **5**, triphenylphosphine (2.0 g, 7.5 mmol) and phenol (0.71 g, 7.5 mmol) in dry Et_2O (25 mL) at 0°C. The reaction was allowed to warm to 25°C and stirred for 12 h. The reaction was quenched with 1 mL 30% H_2O_2, washed with 1 M NaOH (20 mL), brine (20 mL), and dried (Na_2SO_4). The mixture was filtered and concentrated in vacuo. The crude oil was purified via flash chromatography, using 2% EtOAc/hexanes as the eluting solvent, yielding the title compound (1.18 g, 80% yield). IR (film) 3063, 2982, 2924, 1601, 1493, 1237 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55 (t, *J*=1.5 Hz, 1H), 7.39 (dt, *J*=7.8, 1.5 Hz, 1H), 7.31 (dt, *J*=7.8, 1.2 Hz, 1H), 6.94–6.85 (m, 3H), 5.26 (q, *J*=6.6 Hz, 1H), 1.62 (d, *J*=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 157.6, 145.7, 130.5, 130.2, 129.4, 128.6, 124.1, 122.7, 120.9, 115.8, 75.1, 24.4.

4.1.4. (*S*)-1-Bromo-3-(1′-(2″, 6″-dimethylphenoxy)ethyl)-benzene 8. Neat DEAD (0.92 mL, 7.5 mmol) was added dropwise over 5 min to a solution of **5** (1.0 g, 4.9 mmol), triphenylphosphine (2.0 g, 7.5 mmol), and 2,6-dimethylphenol (0.92 g, 7.5 mmol) in dry Et_2O (25 mL) at 0°C. The reaction was allowed to warm to 25°C and stirred for 12 h. The reaction was quenched with 1 mL of 30% H_2O_2, washed with 1 M NaOH (20 mL), brine (20 mL), and dried over Na_2SO_4. The mixture was filtered and concentrated in vacuo. The crude oil was purified via flash chromatography, using 2% EtOAc/hexanes as the eluting solvent, yielding the title compound (0.89 g, 55% yield). $[\alpha]_D$=−54.3° (*c* 1.32, CCl_4, 25°C); IR (film) 2977, 2925, 1757, 1374, 1253 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59 (t, *J*=1.5 Hz, 1H), 7.43 (ddd, *J*=7.8, 2.1, 1.2 Hz, 1H), 7.32 (dt, *J*=7.5, 1.2 Hz, 1H), 7.21 (t, *J*=8.1 Hz, 1H), 6.99–6.87 (m, 3H), 4.90 (q, *J*=6.6 Hz, 1H), 2.16 (s, 6H), 1.56 (d, *J*=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 154.6, 145.4, 131.1, 130.7, 129.8, 129.4, 125.0, 123.5, 122.4, 79.4, 22.4, 17.2.

4.1.5. Tris [(*R*)-3-(1′-methoxyethyl)phenyl)]-phosphine 1a. Compound **6** (1.0 g, 4.7 mmol) was placed in a dry round bottom flask under nitrogen atmosphere. Et_2O (20 mL) was added and the clear solution was stirred and cooled to −78°C. A solution of ^{t}BuLi (2.75 ml, 1.68 M) in pentane was added dropwise over 10 min using a syringe pump. The reaction was stirred for 1 h at −78°C, then warmed to −30°C. A solution of phosphorus trichloride (0.13 mL, 1.5 mmol) in 2 mL of Et_2O was added dropwise over 10 min using a syringe pump. The reaction was warmed to 25°C, stirred for 12 h, concentrated in vacuo, and purified via flash chromatography to yield the title compound (1.2 g, 59% yield). ^1H NMR ($CDCl_3$) δ 7.48 (m, 3H), 7.43 (m, 2H), 7.27 (m, 9H), 4.30 (q, *J*=10.5 Hz, 3H), 3.27 (s, 9H), 1.44 (d, *J*=10.5 Hz, 9H); ^{13}C NMR ($CDCl_3$) δ 143.7 (d, *J*=6.9 Hz), 137.5 (d, *J*=10.8 Hz), 132.8, (d, *J*=17 Hz), 128.7 (d, *J*=6.5 Hz), 126.7, 79.5, 56.5, 23.9; ^{31}P NMR ($CDCl_3$) δ −4.3.

4.1.6. Tris [(*S*)-3-(1′-phenoxyethyl)phenyl)]-phosphine 1b. Compound **7** (1.0 g, 3.4 mmol) was placed in a dry round bottom flask under nitrogen atmosphere. THF (20 mL) was added and the clear solution was stirred and cooled to −78°C. A solution of ^{t}BuLi (2.75 ml, 1.68 M) in pentane was added dropwise over 10 min using a syringe pump. The reaction was then stirred for 1 h at −78°C, then warmed to −30°C. A solution of phosphorus trichloride (0.13 mL, 1.5 mmol) in 2 mL THF was added dropwise over 10 min using a syringe pump. The reaction was warmed to 25°C, stirred for 12 h, concentrated in vacuo, and purified via flash chromatography to yield the title compound (0.36 g, 48% yield). $[\alpha]_D$=−146.7° (*c* 1.02, $CHCl_3$, 25°C); ^1H NMR ($CDCl_3$) δ 7.50 (s, 3H), 7.38–7.15 (m, 15H), 6.90–6.78 (m, 9H), 5.25 (q, *J*=6.5 Hz, 3H), 1.60 (d, *J*=6.3 Hz, 9H); ^{13}C NMR ($CDCl_3$) δ 157.8, 143.4 (d, *J*=7.1 Hz), 137.3 (d, *J*=11.0 Hz), 132.5 (d, *J*=17.0 Hz), 131.1 (d, *J*=22.0 Hz), 129.3, 128.8 (d, *J*=6.8 Hz), 126.1, 120.7, 116.0, 75.7, 24.3; ^{31}P NMR ($CDCl_3$) δ −4.2.

4.1.7. Tris [(*S*)-3-(1′-(2″,6″-dimethylphenoxyethyl)-phenyl)]-phosphine 1c. Compound **8** (1.0 g, 3.4 mmol) was placed in a dry round bottom flask under nitrogen

atmosphere. THF (20 mL) was added and the clear solution was stirred and cooled to −78°C. A solution of ^{t}BuLi (2.75 ml, 1.68 M) in pentane was added dropwise over 10 min using a syringe pump. The reaction was then stirred for 1 h at −78°C, then warmed to −30°C. A solution of phosphorus trichloride (0.13 mL, 1.5 mmol) in 2 mL THF was added dropwise over 10 min using a syringe pump. The reaction was warmed to 25°C, stirred for 12 h, concentrated in vacuo and purified via flash chromatography to yield the title compound (0.31 g, 44% yield). $[\alpha]_D$=−208.4° (*c* 1.0, $CHCl_3$, 25°C); ^{1}H NMR ($CDCl_3$) δ 7.42–7.38 (m, 6H), 7.35–7.30 (m, 3H), 7.23–7.18 (m, 3H), 6.98–6.90 (m, 9H), 4.92 (q, *J*=6.3 Hz, 3H), 2.10 (s, 18H), 1.55 (d, *J*=6.3 Hz, 9H); ^{31}P NMR ($CDCl_3$) δ −3.9.

4.1.8. 3-Bromo-6-methoxyphenyl-ethanone 9. A solution of 3-bromo-6-hydroxyphenyl-methyl ketone (Aldrich; 2.0 g, 9.3 mmol) in 20 mL acetone was treated with K_2CO_3 (2.6 g, 19 mmol) under a nitrogen atmosphere. The yellow solution was stirred for 1 h, then neat MeI (1.5 g, 10 mmol, 0.64 mL) was added in one portion. The reaction was stirred for 2 h. The reaction was concentrated in vacuo and the oily residue was partitioned between Et_2O (6 mL) and water (20 mL). The organics were separated and the aqueous fraction was washed with Et_2O (2×6 mL). The organic layers were combined and washed with brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo to yield the title compound as a white solid (2.0 g, 95%). Mp 36–37°C; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, *J*=2.7 Hz, 1H), 7.53 (dd, *J*=8.8, 2.7 Hz, 1H), 6.86 (d, *J*=8.8 Hz, 1H), 3.89 (s, 3H), 2.58 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 197.9, 157.8, 135.9, 132.6, 129.2, 113.4, 112.8, 55.6, 31.6; Anal. calcd for $C_9H_9BrO_2$: C, 47.37; H, 3.98. Found: C, 47.20; H, 3.97.

4.1.9. (*R*)-1-(3′-Bromo-6′-methoxyphenyl)-ethanol 10. A solution of **9** (15 g, 65 mmol) in CH_2Cl_2 (50 mL) was added dropwise over 5 h to a solution of (*S*)-4,5,6,7-tetrahydro-1-methyl-3,3-diphenyl-1H,3H-pyrrolo-[1,2-*c*]-[1,3,2]-oxazaborole-borane (0.90 g, 3.2 mmol) and $BH_3{\cdot}Me_2S$ (6.5 mL, 65 mmol) in CH_2Cl_2 (50 mL) at −25°C. The solution was allowed to stand at −23°C for 12 h. The cold solution was added slowly to methanol (50 mL) at −20°C. Rapid gas evolution occurred. The solution was concentrated in vacuo and the oily residue was recrystallized from hexanes to yield 10.5 g (70%) of the alcohol in >99% ee (GC) as white needles. $[\alpha]^{25}_D$=+71.6° (*c* 0.5, $CHCl_3$); IR (film) 3600–3150, 2967, 2935, 2846 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47 (d, *J*=2.4 Hz, 1H), 7.31 (dd, *J*=8.5, 2.4 Hz, 1H), 6.72 (d, *J*=8.5 Hz, 1H), 4.66 (q, *J*=6.0 Hz, 1H), 3.79 (s, 3H), 1.34 (d, *J*=6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 157.8, 138.0, 130.7, 128.9, 112.1, 65.6, 55.5, 22.9 Anal. calcd for $C_9H_{11}BrO_2$: C, 47.37; H, 3.98; Br, 34.62. Found: C, 47.24; H, 3.96; Br, 34.75.

4.1.10. (*R*)-1-Bromo-3-methoxy-5-(1′-methoxyethyl)benzene 11. A solution of **10** (2.2 g, 9.5 mmol) in THF (5 mL) was added dropwise over 5 min to a suspension of NaH (0.27 g, 11.4 mmol) in THF (15 mL) at 0°C. Gas evolution occurred. The cold suspension was stirred for 30 min whereupon neat MeI (0.7 mL, 11.4 mmol) was added in one portion. The reaction was allowed to warm to 25°C. The reaction was quenched with water (25 mL) and diluted with ether (100 mL). The organics were washed with H_2O (2×25 mL), with brine (25 mL), dried (Na_2SO_4), filtered, and concentrated to dryness in vacuo. The crude oil was purified by bulb-to-bulb distillation to give 2.1 g (90%) of the ether as a clear oil. $[\alpha]_D$=+105.5° (*c* 1, MeOH, 25°C); IR (film) 3050, 2976, 2929, 2837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47 (d, *J*=2.4 Hz, 1H), 7.31 (dd, *J*=8.5 Hz, *J*=2.4 Hz, 1H), 6.72 (d, *J*=8.5 Hz, 1H), 4.66 (q, *J*=6.0 Hz, 1H), 3.79 (s, 3H), 3.25 (s, 3H), 1.34 (d, *J*=6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 155.6, 134.2, 130.5, 128.7, 113.3, 112.0, 72.9, 56.7, 55.4, 22.3; HRMS (EI) *m/z* calcd for [M+H] 244.0098, found 244.0088.

4.1.11. (*S*)-1-Bromo-3-methoxy-5-(1′-phenoxyethyl)benzene 12. Neat DEAD (1.0 mL, 6.5 mmol) was added dropwise over 5 min to a solution of **10** (1 g, 4.35 mmol), triphenylphosphine (1.7 g, 6.5 mmol), and phenol (0.61 g, 6.5 mmol) in dry Et_2O (40 mL) at 0°C. The reaction was allowed to warm to 25°C and stirred for 12 h. The reaction was quenched with 1 mL 30% H_2O_2, washed with 1 M NaOH (20 mL), brine (20 mL), and dried over Na_2SO_4. The mixture was filtered and concentrated in vacuo. The crude oil was purified via flash chromatography, using 0.5% EtOAc/hexanes as the eluting solvent, yielding the title compound (1.06 g, 80% yield). $[\alpha]_D$=−32.4° (*c* 0.5, $CDCl_3$, 25°C); IR (film) 3444, 2978, 2933 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (d, *J*=2.4 Hz, 1H), 7.30 (dd, *J*=7.5, 2.4 Hz, 1H), 7.24–7.17 (m, 2H), 6.90 (t, *J*=1 Hz, 1H), 6.88 (d, *J*=2.0 Hz, 1H), 6.75 (d, *J*=7.5 Hz, 1H), 5.63 (q, *J*=9.4 Hz, 1H), 3.87 (s, 3H), 1.55 (d, *J*=9.4 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 157.7, 154.8, 133.8, 130.9, 129.3, 128.9, 120.6, 115.5, 113.5, 112.0, 69.3, 55.6, 22.6; Anal. calcd for $C_{15}H_{15}BrO_2$: C, 58.65; H, 4.92. Found: C, 58.82; H, 4.86.

4.1.12. (*S*)-1-Bromo-3-methoxy-5-(1′-(2″,6″-dimethylphenoxy)ethyl)benzene 13. Neat DEAD (5.08 mL, 32.4 mmol) was added dropwise over 5 min to a solution of **10** (5.0 g, 22 mmol), triphenylphosphine (8.50 g, 32.5 mmol), and phenol (3.96 g, 32.4 mmol) in dry diethyl ether (200 mL) at 0°C. The reaction was allowed to warm to 25°C and stirred for 18 h. The reaction was quenched with 5 mL 30% H_2O_2, washed with 1N NaOH (80 mL), brine (80 mL), and dried over Na_2SO_4. The mixture was filtered and concentrated in vacuo. The crude oil was purified via flash chromatography, using hexanes as the eluting solvent, yielding the title compound (3.1 g, 42% yield). Mp 45–46°C; IR (film) 3006, 1487, 1261 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, *J*=2.7 Hz, 1H), 7.35 (dd, *J*=8.6, 2.7 Hz, 1H), 6.99–6.86 (m, 3H), 6.73 (d, *J*=8.6 Hz, 1H), 5.31 (q, *J*=6.3 Hz, 1H), 3.72 (s, 3H), 2.20 (s, 6H), 1.45 (d, *J*=6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 155.1, 154.6, 134.5, 131.1, 130.8, 129.7, 128.8, 123.3, 113.2, 112.0, 74.0, 55.6, 21.7, 17.2; Anal. calcd for $C_{17}H_{19}BrO_2$: C, 61.07; H, 5.73. Found: C, 60.88; H, 5.68.

4.1.13. Tris [(*R*)-3-methoxy-5-(1′-methoxyethyl)phenyl)]-phosphine 2a. Compound **11** (1.0 g, 4.1 mmol) was placed in a dry round bottom flask under nitrogen atmosphere. THF (5 mL) was added and the clear solution was stirred and cooled to −78°C using a dry ice/acetone bath. A solution of ^{t}BuLi (2.42 ml, 1.68 M) in pentane was added dropwise over 10 min using a syringe pump. The reaction was then stirred for 30 min more at −78°C. A solution of phosphorus trichloride (0.19 g, 0.118 mL, 1.4 mmol) in 5 mL

dry THF was then added dropwise over 10 min using a syringe pump. The reaction was warmed to room temperature and stirred for 12 h. The reaction was quenched with 1 mL of a degassed solution of 0.5 M HCl. The reaction was concentrated in vacuo and purified via flash chromatography using a column of silica that was 4 cm high and 4 cm in diameter and 20% EtOAc/hexanes as the eluent to yield the title compound (439 mg, 62% yield). $[\alpha]_D$=138.0° (*c* 1.5, $CHCl_3$, 25°C); IR (film) 3001, 2956, 2834, 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (d, *J*=2.5 Hz, 3H), 7.27–7.25 (m, 3H), 6.83 (d, *J*=7.25 Hz, 3H), 4.71 (q, *J*= 6.8 Hz, 3H), 3.83 (s, 9H), 3.19 (s, 9H), 1.32 (d, *J*=6.8 Hz, 9H); ^{13}C NMR ($CDCl_3$) δ 157.4, 133.7 (d, *J*=10.1 Hz), 131.8 (d, *J*=3.6 Hz), 131.4, 110.4 (d, *J*=4.1 Hz), 73.3, 56.5, 55.3, 22.4; ^{31}P NMR ($CDCl_3$) δ −7.3; HRMS (MALDI) calcd for [M+H] 526.2438, found [M+H]=526.2439.

4.1.14. Tris [(*S*)-3-methoxy-5-(1′-phenoxyethyl)phenyl)]-phosphine 2b. Compound **12** (0.48 g, 1.6 mmol) was placed in a dry round bottom flask under nitrogen atmosphere. THF (5 mL) was added and the clear solution was stirred and cooled to −78°C using a dry ice/acetone bath. A solution of ^{t}BuLi (0.94 ml, 1.68 M) in pentane was added dropwise over 10 min using a syringe pump. The reaction was then stirred for 30 min more at −78°C. The reaction was warmed to −50°C and phosphorus trichloride (0.07 g, 0.04 mL, 0.52 mmol) was added dropwise. The reaction was warmed to room temperature. The reaction was quenched with 1 mL of a solution of 0.5 M HCl, which had been previously degassed. The reaction was concentrated in vacuo and purified via flash chromatography using a column of silica that was 15 cm high and 4 cm in diameter, and using 3% EtOAc/hexanes as the eluent to yield the title compound (200 mg, 54% yield). $[\alpha]_D$=−122.0° (*c* 1.5, $CHCl_3$, 25°C); IR (film) 2939, 1475, 1014 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (dd, *J*=6.6, 1.7 Hz, 2H), 7.16–7.08 (m, 6H), 6.85–6.57 (m, 16H); 5.61 (q, *J*=6.3 Hz, 3H), 3.86 (s, 9H), 1.51 (d, *J*=6.3 Hz, 9H); ^{13}C NMR ($CDCl_3$); δ 157.6, 133.0 (d, 6 Hz), 131.3 (d, 22 Hz), 130.2 (d, 16 Hz), 129.5, 129.1, 120.3, 115.7, 115.5, 110.5, 69.6, 55.5, 22.5; ^{31}P NMR ($CDCl_3$) δ −3.8.

4.1.15. Tris [(*S*)-3-methoxy-5-(1′-(2″, 6″-dimethylphenoxyethyl)phenyl)]-phosphine 2c. Compound **13** (0.60 g, 1.9 mmol) was placed in a dry round bottom flask under nitrogen atmosphere. THF (6 mL) was added and the clear solution was stirred and cooled to −78°C using a dry ice/acetone bath. A solution of ^{t}BuLi (1.11 ml, 1.68 M) in pentane was added dropwise over 10 min using a syringe pump. The reaction was then stirred for 30 min more at −78°C. The reaction was warmed to −50°C and phosphorus trichloride (0.082 g, 0.052 mL, 0.62 mmol) was added dropwise. The reaction was warmed to room temperature. The reaction was quenched with 1 mL of degassed 0.5 M HCl. The reaction was concentrated in vacuo and purified via flash chromatography using a column of silica that was 15 cm high and 4 cm in diameter using 3% EtOAc/hexanes as the eluent to yield the title compound (281 mg, 57% yield). Mp 57–62°C; $[\alpha]_D$=−149.0° (*c* 1.75, $CHCl_3$, 25°C); IR (film) 2954, 2852, 1496, 1245 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (dd, *J*=7.1, 2.0 Hz, 2H), 7.20 (td, *J*=7.8, 2.2 Hz), 6.94–6.79 (m, 14H), 5.37 (q, *J*=6.3 Hz, 3H), 3.71 (s, 9.0 Hz), 2.1 (s, 18H), 1.46 (d, *J*= 9.0 Hz, 9H); ^{13}C NMR ($CDCl_3$) δ 156.7, 155.5, 134.1 (d, 18 Hz), 133.0 (d, 23 Hz), 132.2 (d, 8.0 Hz), 131.5, 129.4, 128.8, 123.2, 110.9, 74.3, 55.8, 21.8, 17.4; ^{31}P NMR δ −3.9; Anal. calcd for $C_{51}H_{57}O_6P$: C, 75.75; H, 7.55. Found: C, 75.82; H, 7.48.

4.1.16. 1-(3-Acetyl-5-bromo-phenyl)ethanone 16. 5-Bromoisophthalic acid (Aldrich; 5 g, 21 mmol) was suspended in 100 mL CH_2Cl_2 and stirred. The white suspension was treated with DMF (0.1 mL), then neat oxalyl chloride (8.8 g, 6 mL, 57 mmol) was added dropwise over 1 h. Then the reaction was stirred for 1 h until it became clear. The clear yellow solution was concentrated in vacuo and the oily residue was distilled (110°C, 0.27 mmHg) to yield a yellow solid which was dissolved in Et_2O and treated with a solution of $LiMe_2Cu$ (7.68 g, 32.8 mmol) in 100 mL Et_2O at −100°C. The reaction was stirred for 30 min and then quenched with a saturated solution of NH_4Cl (50 mL) in water, warmed to 25°C, filtered, and extracted with Et_2O (3×30 mL). The organics were combined and dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was recrystallized from *n*-pentane to yield the title compound[29] (2.8 g, 58%), mp 80–82°C; ^1H NMR ($CDCl_3$) δ 8.39 (s, 1H), 8.24 (s, 2H), 2.63 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 195.8, 138.9, 135.3, 126.4, 123.5, 26.7; Anal. calcd for $C_{10}H_9O_2$: C, 49.82; H, 3.76. Found: C, 50.22; H, 3.90; HRMS (FAB) calcd for [M+H] 240.9864, found 240.9886.

4.1.17. 1-Bromo-3,5-bis-((*R*)-1′-hydroxyethyl)benzene 17. (+)-Ipc_2BCl (Aldrich; 1.61 g, 4.98 mmol) was dissolved in THF (10 mL) and cooled to −30°C. A solution of **16** (0.5 g, 2.1 mmol) in THF (2 mL) was added dropwise over 15 min. The yellow solution was allowed to stand at −22°C for 12 h. The reaction was concentrated in vacuo, then treated with 16 mL of saturated aqueous $NaHCO_3$ and 30% aqueous hydrogen peroxide (3:1) at 50°C for 12 h. The reaction was cooled to 25°C and diluted with water (10 mL). The product was extracted with CH_2Cl_2 (3×50 mL). The organics were washed with brine (100 mL) and dried with Na_2SO_4, filtered, and concentrated. The title compound was purified via recrystallization from Et_2O/pentane (1:1) (75% yield, >99% ee, GC). Mp 77–78°C; $[\alpha]_D$=+50.2° (*c* 1.0, MeOH, 25°C); IR (film) 3351, 2973, 1573 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (s, 2H), 7.25 (s, 1H), 4.82 (q, *J*=6.6 Hz, 2H), 2.09 (s, 2H), 1.45 (d, *J*=6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 148.1, 127.3, 122.4, 121.0, 69.5, 25.1; HRMS (EI) calcd for [M+H]=244.0098, found 244.0099.

4.1.18. 1-Bromo-3,5-bis-((*R*)-1′-methoxyethyl)benzene 18. A solution of **17** (0.31 g, 1.2 mmol) in THF (5 mL) was added dropwise over 5 min to a suspension of NaH (0.67 g, 2.7 mmol) in THF (5 mL) at 0°C. Gas evolution occurred. The cold suspension was stirred for 30 min whereupon it was treated with neat MeI (0.17 mL, 2.7 mmol) in one portion and allowed to warm to 25°C. The reaction was quenched with water (25 mL) and diluted with ether (100 mL). The organics were washed with water (3× 25 mL), with brine (25 mL), dried (Na_2SO_4), and concentrated to dryness in vacuo. The crude oil was purified by flash chromatography using 5% EtOAc/hexane as the eluent to give 0.27 g (80%) of the ether as a clear oil. $[\alpha]_D$=+119.1° (*c* 1.0, $CDCl_3$, 23°C); IR (film) 2976, 2929, 2854, 1117 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (s, 2H),

7.15 (s, 1H), 4.25 (q, J=6.4 Hz, 2H), 3.23 (s, 6H), 1.40 (d, J= 6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 146.2, 128.3, 122.6, 79.0, 56.7, 23.8; HRMS (EI) calcd for [M+H] 272.0411, found 272.0412.

4.1.19. 1-Bromo-3,5-bis-(*S*-1′-phenoxyethyl)benzene 19. Neat DEAD (0.92 mL, 5.82 mmol) was added dropwise over 5 min to a solution of **17**, triphenylphosphine (1.5 g, 5.82 mmol), and phenol (0.55 g, 5.82 mmol) in dry Et_2O (10 mL) at 0°C. The reaction was allowed to warm to 25°C and stirred for 12 h. The reaction was quenched with 1 mL 30% H_2O_2, washed with 1 M NaOH (5 mL), brine (5 mL), and dried over Na_2SO_4. The mixture was filtered and concentrated in vacuo. The crude oil was purified via flash chromatography, using hexanes as the eluent, yielding the title compound (0.62 g, 80% yield). IR (film) 2979, 1574, 1236 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53 (s, 2H), 7.41 (s,1H), 7.29 (t, J=7.5 Hz, 4H), 7.01 (t, J=7.5 Hz, 2H), 7.01 (t, J= 7.6 Hz, 2H), 6.91 (d, J=7.8 Hz, 4H), 5.32 (q, J=6.6 Hz, 2H), 1.70 (d, J=6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 157.5, 145.9, 129.3, 127.7, 123.0, 121.6, 121.0, 115.8, 75.1, 24.2; HRMS (FAB) m/z calcd for [M+H] 396.0725, found 396.0725.

4.1.20. 1-Bromo-3,5-bis-((*S*)-1′-(2″,6″-dimethyl)-phenoxyethyl)benzene 20. Neat DEAD (4.6 mL, 29.4 mmol) was added dropwise over 5 min to a solution of **16** (2.4 g, 9.8 mmol), triphenylphosphine (7.7 g, 29.4 mmol), and 2,6-dimethylphenol (3.6 g, 29.4 mmol) in dry THF (20 mL) at 0°C. The reaction was allowed to warm to 25°C and stirred for 24 h. The reaction was quenched with 5 mL 30% H_2O_2, washed with 1N NaOH (10 mL), brine (10 mL), and dried over Na_2SO_4. The mixture was filtered and concentrated in vacuo. The crude oil was purified via flash chromatography, using hexanes as the eluting solvent, yielding the title compound (1.9 g, 42% yield). Mp 75–76°C; IR (film) 2977, 1475, 1199 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.67 (s, 2H), 7.47 (s, 1H), 7.10–6.98 (m, 6H), 5.01 (q, J=6.3 Hz, 2H), 7.01 (t, J=7.6 Hz, 2H), 6.91 (d, J=7.8 Hz, 4H), 2.28 (s, 12H), 1.68 (d, J=6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 154.6, 145.3, 131.0, 128.5, 123.5, 123.2, 122.2, 79.4, 22.5, 17.2; HRMS (FAB) m/z calcd for [M+H] 453.1298, found 453.1256.

4.1.21. Tris [3,5-bis-((*R*)-1′-methoxyethyl)phenyl]-phosphine 3a. Compound **18** (0.19 g, 0.68 mmol) was placed in a dry Schlenk flask under nitrogen atmosphere. THF (3 mL) was added and the clear solution was stirred and cooled to −60°C. A solution of ^{t}BuLi (0.40 ml, 1.7 M) in pentane was added dropwise using a syringe pump. The reaction was then warmed to −50°C. A solution of phosphorus trichloride (0.03 g, 0.02 mL, 0.23 mmol) in THF (2 mL) was added dropwise using a syringe pump. The reaction was warmed to room temperature and stirred for 12 h. The reaction was quenched with 1 mL of a solution of 0.5 M HCl. The reaction was concentrated in vacuo and purified via flash chromatography using 20% EtOAc/hexanes as the eluent to yield the title compound (56 mg, 40% yield). $[\alpha]_D$=261.3° (c 1.0, $CHCl_3$, 25°C); IR (film) 2976, 2819, 1115 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.32–7.17 (m, 9H), 4.30–4.19 (m, 6H), 1.32 (d, J=6.3 Hz, 18H); ^{13}C NMR ($CDCl_3$) δ 143.9 (d, J=7 Hz), 137.9 (d, J=13 Hz), 130.6 (d, J=19 Hz), 124.6, 79.4, 56.3, 23.6; ^{31}P NMR ($CDCl_3$) δ −3.7; HRMS m/z calcd for [M+H] 611.343, found 611.344.

4.1.22. Tris [3,5-bis-((*S*)-1′-phenoxyethyl)phenyl]-phosphine 3b. Compound **19** (0.28 g, 0.71 mmol) was placed in a dry Schlenk flask under nitrogen atmosphere. THF (3 mL) was added and the clear solution was stirred and cooled to −78°C. A solution of ^{t}BuLi (0.49 ml, 1.6 M) in pentane was added dropwise using a syringe pump. A solution of phosphorus trichloride (0.03 g, 0.02 mL, 0.24 mmol) in THF (2 mL) was added dropwise using a syringe pump. The reaction was warmed to 25°C and stirred for 12 h. The reaction was quenched with 1 mL of a solution of 0.5 M HCl. The reaction was concentrated in vacuo and purified via flash chromatography using 10% EtOAc/hexanes as the eluent to yield the title compound (83 mg, 35% yield). $[\alpha]_D$=−270.7° (c 1.0, $CHCl_3$, 25°C); IR (film) 2973, 2834, 1592, 1245; ^{1}H NMR ($CDCl_3$) δ 7.49 (s, 8H), 7.22–7.17 (m, 12H), 6.88–6.85 (m, 18H), 5.50 (q, J= 6.3 Hz, 6H), 1.51 (d, J=6.3 Hz, 18H); ^{13}C NMR ($CDCl_3$) δ 156.8, 143.9 (d, J=7 Hz), 137.6 (d, J=11 Hz), 131.4, 130.8 (d, J=18 Hz), 128.8, 125.4, 123.4, 81.4, 17.2.

4.1.23. Tris [3,5-bis-(S-1′-(2″, 6″-dimethyl)-phenoxyethyl)-phenyl]-phosphine 3c. Compound **20** was placed in a dry Schlenk flask under nitrogen atmosphere. THF (2.5 mL) was added and the clear solution was stirred and cooled to −78°C. A solution of ^{t}BuLi (0.53 ml, 1.7 M) in pentane was added dropwise using a syringe pump. The reaction was warmed to −60°C and stirred for 20 min. A solution of phosphoros trichloride (0.04 g, 0.02 mL, 0.27 mmol) in THF (2 mL) was added dropwise using a syringe pump. The reaction was warmed to 25°C and stirred for 12 h. The reaction was quenched with 1 mL of a solution of 0.5 M HCl, concentrated in vacuo, then purified via flash chromatography using 5% EtOAc/hexanes as the eluent to yield the title compound (0.131 g, 49% yield). $[\alpha]_D$=−266° (c 1.24, $CHCl_3$, 25°C); IR (film) 2974, 2835, 1593, 1246 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.46–7.42 (m, 9H), 6.98–6.86 (m, 18H), 4.91 (q, J=8.5 Hz, 6H), 2.11 (s, 36H), 1.45 (d, J=8.5 Hz, 18H); ^{13}C NMR ($CDCl_3$) δ 154.9, 143.5 (d, J=7 Hz), 137.7 (d, J=10 Hz), 131.1, 130.8 (d, J=20 Hz), 128.8, 125.4, 123.4, 80.0, 22.7, 17.2; ^{31}P NMR ($CDCl_3$) δ −3.0; HRMS (MALDI) calcd [M+H]=1151.6219, found 1151.6090.

4.1.24. Allylic alkylation reactions. Fig. 3a. Allylpalladium chloride dimer (Strem; 2.5 mg, 0.0069 mmol), the ligand (0.0138 mmol), and CH_2Cl_2 (0.5 mL) were placed in a half-dram vial. A glass bead was added to agitate the yellow mixture and the vial was shaken at 0°C for 30 min. Neat carbonic acid cyclopent-2-enyl ester benzyl ester (30 mg, 0.14 mmol) and phthalimide (61 mg, 0.41 mmol) were added and the reaction was shaken for 24 h. Each reaction was passed through a silica plug and analyzed by chiral HPLC using a Chiralcel OD column (ligand, yield, ee, configuration): **1a** 72% yield, 17% ee, *R*; **1b** 45% yield, 54% ee, *S*; **1c** 54% yield, 81% ee, *S*; **2a** 50% yield, 82% ee, *R*; **2b** 51% yield, 67% ee, *S*; **2c** 47% yield, 74% ee, *S*; **3a** 68% yield, 27% ee, *R*; **3b** 20% yield, 65% ee, *S*; **3c** 47% yield, 19% ee, *S*. Fig. 3b. Was performed in a similar manner to reaction 1 using allylpalladium chloride dimer (3.5 mg, 0.0096 mmol), the ligand (0.0194 mmol), CH_2Cl_2

(0.5 mL), carbonic acid cyclohex-2-enyl ester methyl ester (30 mg, 0.19 mmol), and dimethyl malonate (84 mg, 0.58 mmol). Each reaction was passed through a silica plug and analyzed by chiral GC[28] (ligand, yield, ee, configuration): **1a** 61% yield, 23% ee, *R*; **1b** 64% yield, 55% ee, *S*; **1c** 79% yield, 72% ee, *S*; **2a** 80% yield, 75% ee, *R*; **2b** 60% yield, 54% ee, *S*; **2c** 74% yield, 61% ee, *S*; **3a** 85% yield, 25% ee, *R*; **3b** 83% yield, 21% ee, *S*; **3c** 76% yield, 22% ee, *S*. Fig. 3c. Was performed in a similar manner to reaction 1, but at 10°C. Allylpalladium chloride dimer (3.5 mg, 0.0096 mmol), the ligand (0.0194 mmol), and CH_2Cl_2 (0.5 mL) were mixed first, then 1,3-diphenylpropenyl acetate (48 mg, 0.19 mmol), dimethyl malonate (84 mg, 0.58 mmol), and *N*,*O*-bis(trimethylsilyl)acetamide (0.38 mmol) were added. Each reaction was passed through a silica plug and analyzed by chiral HPLC using a Chiralpak AD column (ligand, yield, ee, configuration): **1a** 88% yield, 12% ee, *S*; **1b** 87% yield, 15% ee, *R*; **1c** 90% yield, 32% ee, *R*; **2a** 86% yield, 22% ee, *S*; **2b** 84% yield, 20% ee, *R*; **2c** 80% yield, 24% ee, *R*; **3a** 80% yield, 21% ee, *S*; **3b** 82% yield, 24% ee, *R*; **3c** 76% yield, 26% ee, *R*. Fig. 3d. Was performed in a similar manner to reaction 1 but at 10°C using allylpalladium chloride dimer (3.5 mg, 0.0096 mmol), the ligand (0.0194 mmol), and CH_2Cl_2 (0.5 mL) first, then *trans*-4-pivaloxy-2-pentene (31 mg, 0.19 mmol), dimethyl malonate (84 mg, 0.58 mmol), and *N*,*O*-bis(trimethylsilyl)acetamide (0.38 mmol) were added and the reaction was shaken for 24 h. The reaction was passed through a silica plug and analyzed by chiral GC (ligand, yield, ee, configuration): **1a** 87% yield, 8% ee, *R*; **1b** 87% yield, 9% ee, *S*; **1c** 85% yield, 12% ee, *S*; **2a** 89% yield, 10% ee, *R*; **2b** 80% yield, 15% ee, *S*; **2c** 82% yield, 19% ee, *S*; **3a** 83% yield, 20% ee, *R*; **3b** 82% yield, 19% ee, *S*; **3c** 82% yield, 19% ee, *S*. Fig. 4. A mixture of allylpalladium chloride dimer (1.1 mg, 0.006 mmol), the ligand (0.0066 mmol), and THF (0.5 mL) was shaken at −30°C for 30 min and then treated with 3-acetoxy-3-(4-methoxyphenyl)-1-propene (41 mg, 0.20 mmol) and sodium dimethylmethyl malonate (58 mg, 0.40 mmol), and the reaction was shaken for 24 h. The reaction was passed through a silica plug and analyzed by chiral HPLC using a Chiralpak AD column (ligand, yield, % internal, ee, configuration): **2a** 99% yield, 30%, 19% ee, *R*; **2b** 99% yield, 41%, 24% ee, *S*; **2c** 99% yield, 40%, 22% ee, *S*; **3a** 99% yield, 33%, 26% ee, *R*; **3b** 76% yield, 44%, 22% ee, *S*; **3c** 69% yield, 47%, 21% ee, *S*.

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