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3,3′-Substituted BINAP derivatives containing *C*-bound substituents: applications in asymmetric hydrogenation reactions

Danica A. Rankic, Masood Parvez, Brian A. Keay *

Department of Chemistry, University of Calgary, Calgary, AB, Canada T2N 1N4

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ABSTRACT

The synthesis and resolution of the first 3,3′-disubstituted BINAP ligands containing *C*-bonded substituents are described. An *ortho*-metallation/electrophile capture sequence was used to obtain the key trisubstituted naphthalene intermediate available and this intermediate was successfully converted into the desired ligands. Minor changes in the steric and stereoelectronic components of the 3,3′-substituents on the enantioselectivity and product enantiosense were also assessed in the context of the Rh-catalyzed asymmetric hydrogenation of enamides. A comparison of the absolute stereochemistry of the products derived from 3,3′-disubstituted BINAPs containing *C*-bonded substituents with their *O*-bound counterparts indicated that the product enantiosense could be dictated by increased steric bulk due to the 3 and 3′-substituents.

1. Introduction

The substitution of BINAP to alter not only its size, but also the stereoelectronic properties of the phosphine atoms has been well documented.[1] While elaboration of the 3,3′-positions of BINAP **1a–d** (Fig. 1) and related bisphosphines is challenging, it is highly desirable due to the proximity of the P-atoms in the ligand and therefore the metal center.[1] Elaboration of these positions has an impact on both enantioselectivity and product enantiosense in Rh-catalyzed asymmetric hydrogenations [2] and Pd-catalyzed Heck reactions. [3] Recently, we showed that the effect of 3,3′-substitution could be combined with the 3,5-dialkyl meta effect[4] to afford 3,3′-disubstituted xylBINAP ligands **2**, which were highly enantioselective in both Rh-catalyzed hydrogenations of methyl *N*-acetamido cinnamate **3** (MAC)[5] and the Pd-catalyzed arylation of 2,3-dihydrofuran.[6] With *P*-xylyl-containing BINAP derivatives **2**, a reversal of the enantiosense of the products was observed in both hydrogenation and Heck chemistries.

In all cases of BINAP ligands that were observed to cause enantiosense reversals, oxygen atoms were present at the 3- and 3′-positions of the binaphthyl backbone. In an analogous study with 3,3′-disubstituted MeO-BIPHEP derivatives, we saw that the enantiosense reversal could be suppressed by changing the atom of attachment for the 3,3′-substiutents.[2e] Specifically, going from oxygen-bonded (*O*-bound) to carbon-bonded (*C*-bound) 3,3′-substituents resulted in a reversal of the product enantiosense observed compared with the parent MeO-BIPHEP. Based on these results, we questioned if the oxygen atoms at the 3- and 3′-positions were responsible for the enantiosense reversals seen with ligands **1** and **2**. In order to test this hypothesis, we developed a synthetic route to 3,3′-disubstituted BINAP derivatives in which a carbon atom was directly bonded to the naphthalene ring in the ligands, rather than the oxygen atom currently present in 3,3′-disubstituted BINAP derivatives. Herein we report our synthetic route for the preparation of these ligands and their use in the Rh-catalyzed asymmetric hydrogenations of enamides.

2. Results and discussion

To date, the synthesis of both 3,3′-disubstituted BINAP ligands **1** and xylBINAP derivatives **2** has been limited to ligands containing oxygen-bonded (*O*-bound) groups at the 3- and 3′-positions. The synthesis of these ligands relies on the use of 1-bromo-2-diarylphosphinoyl-3-hydroxy naphthalene **6** (Scheme 1). The free hydroxyl group in this key intermediate allows for covalent chiral auxiliary attachment, essential for the resolution of the chiral axis upon biaryl bond formation.[2a,5] This reliance on naphthol **6** limits the synthesis of BINAP derivatives containing *O*-bonded substituents. Attempts to derivatize **6** or related 3,3′-dihydroxy BINAP via the formation of their corresponding triflates with subsequent cross-coupling reaction conditions have been unsuccessful.[7] Moreover, some elegant work by Widhalm and Mereiter has demonstrated that the direct metallation of the bisphosphine oxide of BINAP leads to intramolecular cyclization products rather than the desired 3,3′-disubstituted BINAP derivatives.[8]

In order to access BINAP ligands containing *C*-bonded substituents at the 3- and 3′-positions, we sought a route to an Ullmann

* Corresponding author. Tel.: +1 403 210 8434; fax: +1 403 282 9154.
E-mail address: keay@ucalgary.ca (B.A. Keay).

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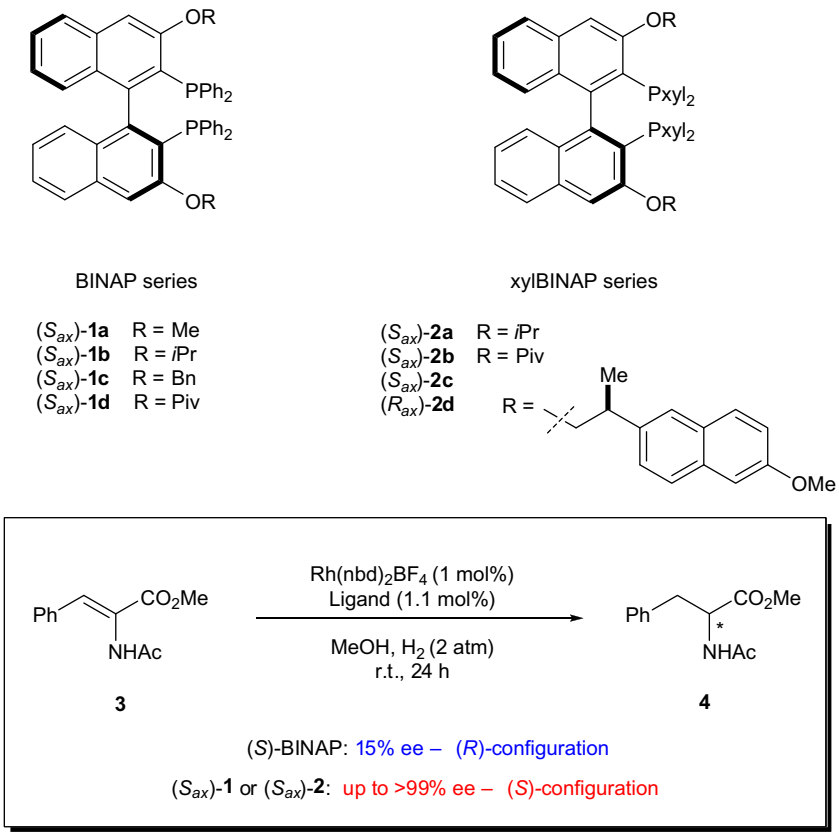
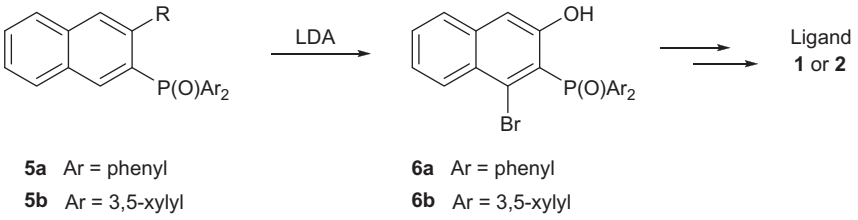
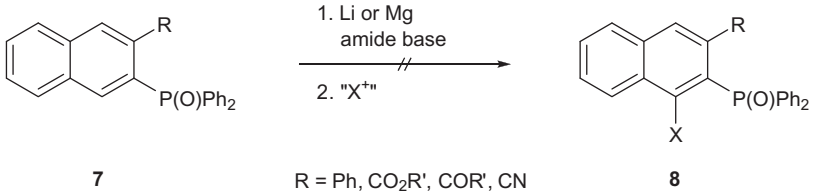


Figure 1. 3,3′-Disubstituted BINAP and xylBINAP ligands, **1** and **2** respectively, and their application in the hydrogenation of MAC (**3**).

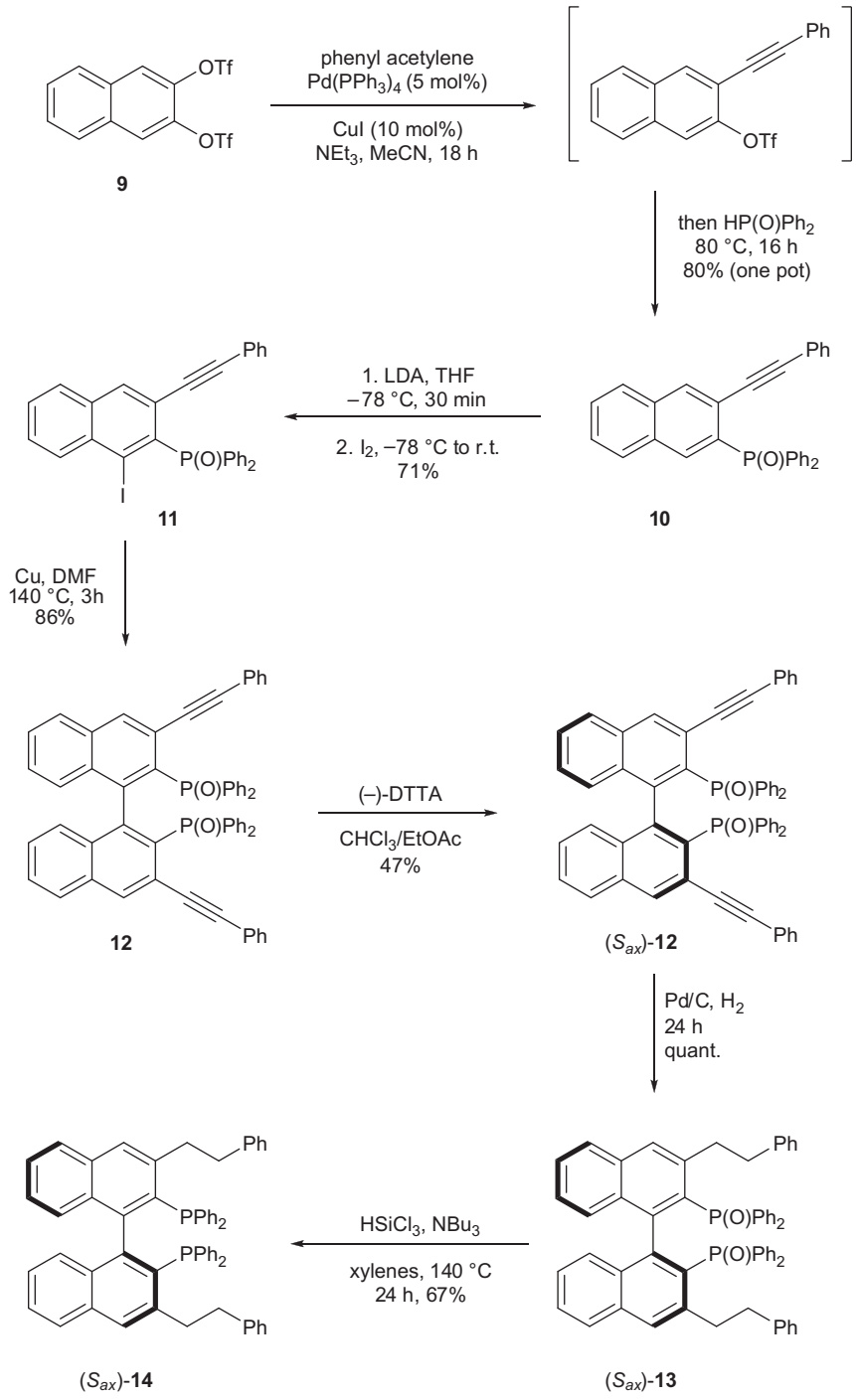


Scheme 1. The synthesis of 1-bromo-2-diarylphosphinoyl-3-hydroxy naphthalene **6**, a key intermediate in the synthesis of 3,3′-disubstituted BINAP and xylBINAP derivatives **1** and **2**.

coupling precursor that already possesses a *C*-bonded substituent. In preliminary investigations, we examined the use of compounds **7**, containing aryl groups, esters, and nitriles, as precursors to trisubstituted naphthalenes **8** (Scheme 2). The *ortho*-metallation/halide capture sequences involving these substrates failed to yield the desired products.[9] It should be noted that while nitrile-substituted naphthalene **8** did provide us with some of the desired Ullmann precursor, a competitive lithiation was observed at the 4-position, along with nucleophilic attack of LDA on the cyano group to afford an amide by-product. We presumed that the successful lithiation of cyano-containing naphthalene **8** was due to its small size and linear projection away from the naphthalene ring. We



Scheme 2. Attempted C-1 metallation of 2-diphenylphosphinoyl naphthalenes **7** to afford Ullman coupling precursors **8**.

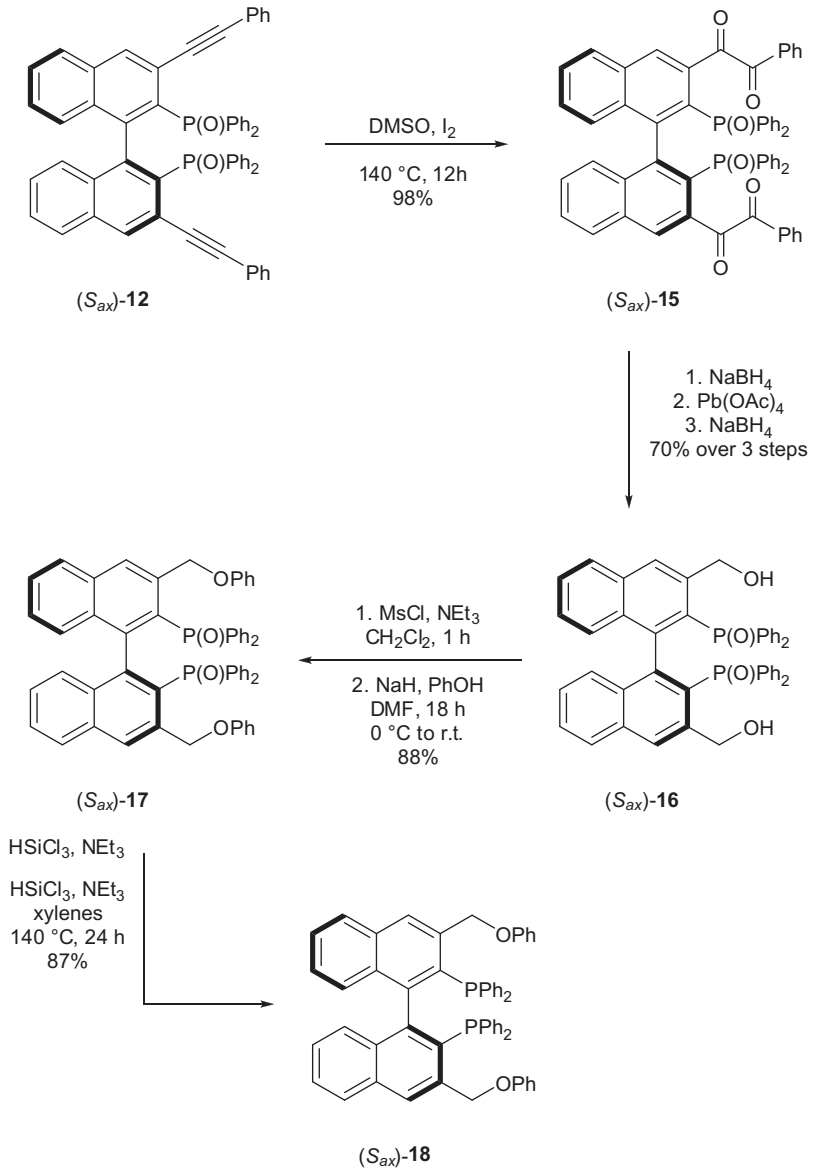


Scheme 3. Synthesis of (S_{ax})-3,3′-(phenethyl)$_2$-BINAP **14.**

hypothesized that an alkyne, linear yet less susceptible to attack by nucleophiles, might be able to undergo lithiation and successful electrophile capture without the formation of by-products.

With this goal in mind, we synthesized alkyne **10** via a one-pot, sequential Sonogashira coupling/P–C bond formation reaction of ditriflate **9** (Scheme 3). Compound **10** was *ortho*-lithiated using LDA and then iodinated to furnish iodonaphthalene **11**. Ullmann coupling of **11** forged the biaryl bond in *rac*-**12** which was resolved by co-crystallization with (−)-DTTA to afford (S_{ax})-**12** in 47% yield.[2a] Hydrogenation of the alkynyl groups in (S_{ax})-**12** followed by phosphine oxide reduction afforded (S_{ax})-**14** in 67% yield. To the best of our knowledge, this synthetic sequence represents the first synthesis and resolution of a BINAP ligand containing carbon bound substituents at the 3- and 3′-positions.

We recognized that phenethyl-substituted BINAP **14** was isostructural to benzyloxy-substituted BINAP **1c**, the former containing a methylene unit in place of the oxygen atom present in the latter. In order to gain access to another analogue of BINAP **1c**, we oxidatively cleaved the alkynyl groups in intermediate (S_{ax})-**12** using a three-step procedure (Scheme 4). This was accomplished by converting bis-alkyne (S_{ax})-**12** to bis(diketone) (S_{ax})-**15** (Scheme 4).[10] Reduction of (S_{ax})-**15** to the corresponding



Scheme 4. Synthesis of (S_{ax})-3,3′-(phenoxymethyl)$_2$-BINAP **18.**

Table 1
Summary of the ^{31}P–^{77}Se coupling constants obtained from diselenides of (*S*)-BINAP, (*S*)-**1c**, (*S*)-**14**, and (*S*)-**18**

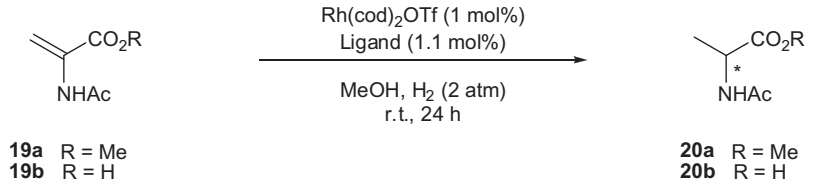
Entry	Ligand	3,3′-Substituent	Diselenide	$^1J(^{31}P–^{77}Se)$ (Hz)
1	(*S*)-BINAP	–H	(*S*)-BINAP(Se)$_2$	739
2	(*S*)-**1c**	–OCH$_2$Ph	(*S*)-**1c**(Se)$_2$	722
3	(*S*)-**14**	–CH$_2$CH$_2$Ph	(*S*)-**14**(Se)$_2$	738
4	(*S*)-**18**	–CH$_2$OPh	(*S*)-**18**(Se)$_2$	727

bis(diol), followed by oxidative cleavage using Pb(OAc)$_4$ and reduction of the resultant dialdehyde afforded diol (S_{ax})-**16** in 70% over three steps. Mesylation of (S_{ax})-**16** and subsequent substitution with NaOPh afforded (S_{ax})-**17**. Phosphine oxide reduction provided BINAP analogue (S_{ax})-**18** in 87% yield.

The electronic properties of BINAP and isostructural 3,3′-ligands were estimated by synthesizing their corresponding diselenides and measuring their $^1J(^{31}P–^{77}Se)$ values (Table 1).[11] The BINAP derivative (S_{ax})-**14** displayed a ^{31}P–^{77}Se coupling constant nearly identical to that of BINAP. This is important, since the change in the steric properties between BINAP and **14** is quite drastic with very little deviation in the electronic properties of the two ligands. The absence, presence, and position of the oxygen atoms in the 3,3′-substituents of **1c**, **14,** and **18** have subtle effects on the electronic properties of the ligands. The phosphorus atoms of the 3,3′-OBn-substituted ligand **1c** were estimated to be the most electron rich, while the phosphorus atoms in ligand **14** were found to be the most electron deficient of the series. Interestingly, **18** had an intermediate basicity, even though the phenoxymethyl-substituent was anticipated to be inductively electron withdrawing.

Ligands **1c**, **14,** and **18** were tested along with BINAP in the Rh-catalyzed hydrogenation of dehydroamino acids **19**. When a Rh/(*S*)-BINAP catalyst system was used for the hydrogenation of olefin **19a**, alanine derivative (*R*)-**20a** was isolated in 21% ee (Table 2, entry 1). However, employing ligand (*S*)-**14** in the same hydrogenation resulted in (*S*)-**20a** being isolated in 98% ee, nearly a 5-fold amplification of the enantiomeric excess and a reversal in product

Table 2
Rh-catalyzed hydrogenations of dehydroamino acids **19** using ligands (*S*)-(BINAP), (*S*)-**1c**, (*S*)-**14**, and (*S*)-**18**



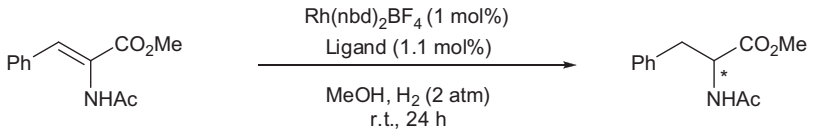
19a R = Me
19b R = H

20a R = Me
20b R = H

Entry[a]	Ligand[b]	3,3′-Substituent	Olefin	%ee (Config)[c]
1	(*S*)-BINAP	–H	**19a**	21 (*R*)
2			**19b**	34 (*R*)[d]
3	(*S*)-**14**	$-CH_2CH_2Ph$	**19a**	98 (*S*)
4			**19b**	95 (*S*)[d]
5	(*S*)-**18**	$-CH_2OPh$	**19a**	83 (*S*)
6			**19b**	69 (*S*)[d]
7[e]	(*S*)-**1c**	$-OCH_2Ph$	**19a**	96 (*S*)
8[e]			**19b**	92 (*S*)[d]

[a] Catalysts formed in situ by stirring $Rh(cod)_2OTf$ and the ligand in MeOH for 30 min at rt. All reactions proceeded with 100% conversion as determined by ^1H NMR.
[b] The results in this table are ordered by increasing $^{31}P–^{77}Se$ coupling constant.
[c] Measured by chiral GC.
[d] Converted to methyl ester for ee determination
[e] Obtained by comparison to the literature.[2a]

Table 3
Rh-catalyzed hydrogenations of methyl cinnamate **3** using ligands (*S*)-BINAP, (*S*)-**1c**, (*S*)-**14**, and (*S*)-**18**



3 **4**

Entry[a]	Ligand[b]	3,3′-Substituent	%ee (Config)[c]
1	(*S*)-BINAP	–H	15 (*R*)
2	(*S*)-**14**	$-CH_2CH_2Ph$	78 (*S*)
3	(*S*)-**18**	$-CH_2OPh$	65 (*S*)
4[d]	(*S*)-**1c**	$-OCH_2Ph$	45 (*S*)

[a] Catalysts formed in situ by stirring $Rh(nbd)BF_4$ and ligand in MeOH for 30 min at rt. All reactions proceeded with 100% conversion as determined by ^1H NMR.
[b] The results in this table are ordered by increasing $^{31}P–^{77}Se$ coupling constant.
[c] Measured by chiral HPLC.
[d] Obtained from the literature[2a] for the sake of comparison.

enantiosense, when compared to the parent BINAP (entry 3). This observation was not restricted to substrate **19a**. When acid **19b** was hydrogenated, (*S*)-BINAP gave (*R*)-**20b** in 34% ee whereas (*S*)-**14** gave amino acid derivative (*S*)-**20b** in 95% ee (entries 2 vs. 4). It should be reiterated that ligand **14** is nearly electronically identical to BINAP, yet sterically different due to the presence of the 3,3′-phenethyl substituents on its binaphthyl skeleton; this suggests that increasing the steric bulk around the Rh center induces both a marked increase in ee as well as a reversal of the absolute configuration of products **20**.

The electronic effects of the ligand were assessed by analyzing the results obtained for the hydrogenations of dehydroamino acids **19** using isostructural 3,3′-BINAP ligands **1c**, **14,** and **18**. No relationship was found between ligand electron density and the ee of the products formed in the hydrogenation of *N*-acetyl alanine **19b** or its methyl ester **19a**. Ligands (*S*)-**1c** and (*S*)-**14** afforded higher ee′s than those obtained from (*S*)-**18** (Table 2). If an electronic effect was present, an increase or decrease in product ee as the electron density of each ligand increased or decreased would be expected.

In contrast, an apparent relationship between the ligand σ-basicity and ee was observed for the hydrogenation of olefin **3** (Table 3). As the ligand σ-basicity (as estimated by $^1J(^{31}P–^{77}Se)$ values) was increased (i.e., **14** to **18** to **1c**), the ee of product **4** decreased. This suggests that subtle electronic changes in the utilized 3,3′-disubstituted BINAP ligand might influence the ee, even with only minor changes in ligand structure.

3. Conclusion

In conclusion, we have demonstrated that the synthesis of 3,3′-disubstituted BINAP ligands containing *C*-bonded substituents could be successfully accomplished using an appropriately trisubstituted naphthalene intermediate **11**. This intermediate was obtained by an *ortho*-lithiation/halide capture sequence. Two new BINAP derivatives were synthesized and tested in Rh-catalyzed

hydrogenation reactions. The ee's of the hydrogenation products derived from these ligands and 3,3′-$(OBn)_2$-BINAP **1c** were compared and this allowed us to study how subtle changes in the structure would influence the ee in the Rh-catalyzed hydrogenations of enamides. It appears as though a reversal in the product enantiosense observed with 3,3′-disubstituted BINAP ligands may arise due to an increase in steric bulk at the 3- and 3′-positions of the ligand backbone. However, further studies are currently underway in order to further supplement the results obtained herein and these will be reported in a full account.

4. Experimental

4.1. General

All glassware used in anhydrous reactions were either flame-dried or dried overnight in a 120 °C oven and subsequently cooled under an argon atmosphere. Moisture or oxygen sensitive reactions were performed under an argon atmosphere or through the use of Schlenk techniques. All solvents and reagents were purified via standard methods, when required. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately prior to use. Dichloromethane and toluene were freshly distilled from calcium hydride. Other reagents/solvents including triethylamine, diethylamine, diisopropylamine, benzene, acetonitrile, methanol, dimethyl sulfoxide (DMSO), and xylenes were distilled from CaH_2 and the stored over 4 Å molecular sieves in Sure/Seal® bottles. *N*,*N*-Dimethyl formamide was purchased as an anhydrous solvent in a Sure/Seal® bottle from the Aldrich Chemical Company. Lithium diisopropylamide (LDA) was purchased as a 1.8 M solution in THF/heptane/ethylbenzene from the Aldrich Chemical Company. *n*-Butyllithium was titrated prior to use with *N*-benzylbenzamide as the indicator. Solutions of NaCl, $NaHCO_3$, and NH_4Cl for washing organic phases were saturated unless specified otherwise.

Melting points were determined using an Electrothermal® melting point apparatus in a sealed capillary tube. Optical rotations were obtained using a Rudolph Research Autopole IV polarimeter at 589 nm using a 1 dm path length cell. HPLC Grade $CHCl_3$ stored over K_2CO_3 was the solvent used for optical rotation measurements. Infrared spectra were recorded on a Nicolet Nexus 470 FT-IR E.S.P spectrophotometer. Liquid samples were analyzed neat between KBr plates while solid samples were handled as chloroform thin films. Characteristic absorptions are listed in wavenumbers followed by the assignment in parentheses.

Proton, carbon, and phosphorus NMR spectra were obtained on either a Bruker DMX 300 (^{1}H 300 MHz, ^{13}C 75 MHz, ^{31}P 121.5 MHz), Bruker Avance DRX 400 (^{1}H 400 MHz, ^{13}C 100 MHz, ^{31}P 162 MHz), Bruker Avance II DRY 400 (^{1}H 400 MHz, ^{13}C 100 MHz, ^{31}P 162 MHz), or a Bruker Avance III RDQ 400 (^{1}H 400 MHz, ^{13}C 100 MHz, ^{31}P 162 MHz). Unless otherwise noted, $CDCl_3$ was used as the NMR solvent. The residual chloroform signal was used as an internal standard for chemical shift referencing in the case of ^{1}H NMR and ^{13}C NMR spectra. A solution of H_3PO_4 in D_2O was used as an external reference when obtaining ^{31}P NMR spectra. ^{1}H NMR spectra are listed in the following format: chemical shift (in ppm), (multiplicity, coupling constant (Hz), number of protons, assignment). For all ^{13}C NMR spectra, the signals were assigned as C, CH, CH_2, or CH_3 by DEPT 135 experiments. ^{13}C NMR spectra are listed in the following format: chemical shift (in ppm), [multiplicity, coupling constant (Hz), methyl (CH3), methylene (CH2), methane (CH), or quaternary (C) assignment].

GC-MS analyses were performed on an Agilent HP5975 gas chromatograph. Low resolution mass spectra on non-volatile samples were obtained on a Thermo Finnigan SSQ7000 mass spectrometer by Mr. J. Li [LRMS(EI) and LRMS(CI)]. Electrospray ionization low resolution mass spectra were obtained on a Bruker Esquire 3000 mass spectrometer by either Ms. Q. Wu or Mr. W. White. High resolution mass spectra were obtained by Ms. D. Fox on a Kratos MS80 mass spectrometer (HRMS(EI) or HRMS(CI)) or by Ms. Q. Wu on a Burker Autoflex III mass spectrometer (MALDI-TOF). Mass spectral data are listed in the following format: mass (m/z), (assignment). Elemental analyses were performed by Mr. J. Li on a Perkin Elmer Model 2400 series II elemental analyzer. X-Ray structure determination was performed by Dr. M. Parvez (University of Calgary) using either a Bruker APEX2 CCD installed on a Nonius Kappa Goniometer diffractometer with graphite monochromated Mo-Kα radiation. Flash column chromatography was performed using silica gel 60 (E. Merck, 0.04–0.063 mm, 230–400 mesh) using the method developed by Still et al.[12] Analytical TLC was carried out on aluminum sheets coated with a uniform thickness of 0.2 mm of Merck silica gel 60 F254. Spots were visualized under UV light or by dipping in a stain solution followed by heat development.

Chiral GC analyses were carried out on a Shimadzu GC-9A gas chromatograph equipped with a widebore column (30 m, 0.32 mm, 0.25 μm I.D.) with a solid phase of β-cyclodextrin and a flame ionization detector. HPLC analyses were carried out using a Waters 1525 Binary HPLC pump equipped with a Daicel Chiralcel OD column and a Waters 2487 detector (UV detection at 254 nm).

4.2. 2-(Diphenylphosphinoyl)-3-phenylethynyl naphthalene 10

Ditriflate **9**[13] (3.796 g, 8.9465 mmol) was dissolved in acetonitrile (50 mL) under an atmosphere of argon. Phenyl acetylene (0.88 mL, 8.0 mmol), $Pd(PPh_3)_4$ (514 mg, 0.445 mmol, 5 mol %), CuI (172 mg, 0.903 mmol, 10 mol %), and NEt_3 (15.5 mL, 108 mmol) were added to the reaction vessel sequentially. The reaction was stirred at ambient temperature for 15 h. TLC analysis revealed complete consumption of the starting material. Diphenyl phosphine oxide (1.842 g, 9.110 mmol) and an additional 5 mol % of $Pd(PPh_3)_4$ were added to the reaction vessel and the mixture was heated to 80 °C. After 18 h, the reaction mixture was cooled to room temperature prior to being poured into a saturated NH_4Cl solution (100 mL) and extracted with EtOAc (3 × 50 mL). The organic layers were combined and washed with $NaCl_{(aq)}$ (1 × 75 mL), dried over $MgSO_4$, filtered, and concentrated to afford a bright yellow solid. Purification by silica gel chromatography (2:1 EtOAc/hexanes) provided a spectroscopically pure product as a yellow solid (2.74 g, 6.39 mmol, 80%). An analytical sample was obtained by recrystallization from hot EtOAc to give pale gold needles. mp 184–185 °C; IR (film) υ_{max} 3043, 2204, 1957, 1891, 1839, 1487, 1439, 1187, 1113, 1030 cm^{-1}; ^{1}H NMR (300 MHz) δ 8.47 (d, J = 14.5 Hz, 1H), 8.12 (d, J = 3.9 Hz, 1H), 7.88–7.78 (m, 6H), 7.59–7.46 (m, 4H), 7.43–7.37 (m, 4H), 7.24–7.19 (m, 3H), 7.01 (dd, J = 7.9 Hz, 1.7 Hz, 2H); ^{13}C NMR (75 MHz) 136.4 (d, J = 8.6 Hz, CH), 134.3 (d, J = 2.1 Hz, C), 134.1 (d, J = 8.7 Hz, CH), 132.4 (d, J = 106 Hz, C), 132.3 (d, J = 10.0 Hz, CH), 131.8 (d, J = 2.8 Hz, CH), 131.6 (d, J = 12.5 Hz, CH), 131.3 (CH), 130.2 (d, J = 101 Hz, C), 129.1 (CH), 128.9 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 127.6 (CH), 127.4 (CH), 122.6 (C), 121.2 (d, J = 8.0 Hz, C), 96.1 (C), 88.97 (d, J = 4.4 Hz, C); ^{31}P{^{1}H} NMR (162 MHz) 29.1; LRMS(EI) 427.2 (base peak), 349.1, 302.1, 226.1; HRMS(TOF-EI) calcd for $C_{30}H_{21}OP$ 428.1330, found 428.1309.

4.3. 2-(Diphenylphosphinoyl)-1-iodo-3-phenylethynyl naphthalene 11

Phenylethynyl naphthalene **10** (447 mg, 1.043 mmol) was dissolved in THF (7 mL), and cooled to −78 °C after which was added dropwise a solution of lithium diisopropyl amide (0.7 mL in THF/heptane/ethylbenzene, 1.26 mmol). A cherry red anion solution

formed and was stirred for 0.5 h. A solution of iodine (336 mg, 1.32 mmol) in THF (1.3 mL) was prepared and added to the anion solution dropwise. The reaction mixture was stirred at −78 °C for 30 min before being warmed to room temperature and quenched with a 10% sodium thiosulfate solution. The reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with $NaCl_{(aq)}$ (1 × 20 mL), dried over Na_2SO_4, filtered, and evaporated to afford an amber film. Purification by flash column chromatography (2:1 EtOAc/hexanes) afforded an off-white solid (242 mg, 0.436 mmol, 42%). mp 230–231 °C; IR (film) υ_{max} 3052, 2222, 1578, 1483, 1435, 1248, 1191, 1113 cm^{-1}; ^1H NMR (400 MHz) δ 8.56 (d, J = 9.0 Hz, 1H), 8.11 (d, J = 3.2 Hz, 1H), 7.86–7.81 (m, 4H), 7.74 (d, J = 7.1 Hz, 1H), 7.66–7.60 (m, 2H), 7.50–7.34 (m, 6H), 7.00 (d, J = 7.9 Hz, 2H); ^{13}C NMR (100 MHz) δ 136.0 (d, J = 8.0 Hz, CH), 135.5 (d, J = 10.2 Hz, C), 134.7 (CH), 133.8 (d, J = 108 Hz, C), 133.62 (d, J = 102 Hz, C), 133.61 (C), 133.59 (C), 132.0 (d, J = 8.4 Hz, CH), 131.5 (d, J = 2.9 Hz, CH), 131.2 (CH), 129.3 (CH), 129.2 (CH), 128.4 (d, J = 12.4 Hz, CH), 127.9 (CH), 127.8 (CH), 124.1 (d, J = 9.1 Hz, C), 122.7 (C), 110.7 (d, J = 5.2 Hz, C), 98.9 (C), 88.9 (d, J = 4.7 Hz, C); $^{31}P\{^1H\}$ NMR (162 MHz) δ 33.3; ESI-MS 593 $(M+K)^+$, 577 $(M + Na)^+$, 555 $(M+H)^+$, MS/MS of 555: 477, 427, 323; Anal. calcd for $C_{30}H_{20}IOP$ C, 65.00; H, 3.64; found C, 64.90; H, 4.02.

4.4. (S_{ax})-2,2′-Bis-(diphenylphosphinoyl)-3,3′-bis-phenylethynyl-[1,1′]binaphthyl 12

Iodonaphthalene **11** (3.602 g, 6.497 mmol) was dissolved in DMF (35 mL) under argon. To this solution was added Cu powder (1.238 mg, 19.48 mmol) and the reaction mixture was immersed in an oil bath preheated to 140 °C. The reaction was stirred for 3 h before cooling to rt, diluting with $CHCl_3$ (50 mL), and stirring for an additional 10 min. The reaction mixture was filtered and the collected solids were washed with $CHCl_3$ (2 × 25 mL). The filtrate was concentrated under vacuum to afford a light brown solid. This solid was suspended in $CHCl_3$ and passed through a 3 × 1 inch plug of silica gel, eluting with 1:1 CH_2Cl_2/EtOAc, in order to remove any inorganic salts. Upon concentration, a light brown residue was obtained and this solid was suspended in 1:1 EtOAc/Et_2O (~75 mL). After stirring for 10 min, the suspension was filtered and the collected solids were washed with 1:1 EtOAc/Et_2O (5 mL) and then Et_2O (5 mL). The filtrate was concentrated to afford the product as a white solid (2.493 g, 2.916 mmol, 90%). mp 318–319 °C; IR (film) υ_{max} 3052, 2205, 1490, 1438, 1195, 1110 cm^{-1}; ^1H NMR (400 MHz) δ 8.25 (d, J = 3.7 Hz, 2H), 7.88 (d, J = 8.1 Hz, 2H), 7.81–7.73 (m, 4H), 7.68–7.62 (m, 4H), 7.49 (ddd, J = 8.0, 6.9, 1.0 Hz, 2H), 7.37–7.33 (m, 2H), 7.26–7.12 (m, 14H), 7.11–7.01 (m, 6H), 6.82–6.75 (m, 4H); ^{13}C NMR (100 MHz) δ 147.2 (d, J = 4.8 Hz, C), 147.1 (d, J = 4.8 Hz, C), 135.3 (d, J = 9.0 Hz, CH), 134.0 (d, J = 108 Hz, C), 133.8 (d, J = 11.0 Hz, C), 133.51 (C), 133.49 (C), 133.3 (d, J = 104 Hz, C), 132.8 (d, J = 9.7 Hz, CH), 132.4 (d, J = 11.0 Hz, CH), 131.1 (CH), 130.9 (d, J = 2.6 Hz, CH), 130.5 (d, J = 2.6 Hz, CH), 128.3 (C), 128.1 (CH), 127.94 (CH), 127.8 (CH), 127.64 (CH), 127.61 (CH), 127.58 (CH), 127.5 (CH), 127.3 (CH), 127.2 (CH), 126.8 (CH), 123.0 (C), 121.4 (d, J = 10.0 Hz, C), 96.9 (C), 91.2 (d, J = 5.0 Hz, C); ^{31}P NMR (162 MHz) δ 30.4; ESI-MS 855 $(M+H)^+$; HRMS(MALDI-TOF) calcd for $(C_{60}H_{40}O_2P_2 + H^+)$ 855.25763, found 855.2578; Anal. calcd for $C_{60}H_{40}O_2P_2$ C, 84.29; H, 4.72, found C, 83.79; H 4.95.

The racemic bisphosphine oxide 12 (4.158 g, 4.864 mmol) was dissolved in $CHCl_3$ (209 mL) and heated to 60 °C. To this was added a pre-warmed solution of (−)-DTTA (1.879 mg, 4.863 mmol) in EtOAc (139 mL). The solution was refluxed for 1 h before being allowed to cool to room temperature and sit at room temperature for 24 h. An off-white crystalline solid was collected by vacuum filtration. The solid was suspended in CH_2Cl_2 (100 mL) and stirred with 10% $NaOH_{(aq)}$ (75 mL) for 1 h. The layers were separated and the aqueous layers extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with 10% $NaOH_{(aq)}$ (75 mL) and H_2O (75 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford (−)-12 as a white solid (1.270 g, 1.486 mmol, 30.5%): $[\alpha]_D^{20} = -137$ (c 0.225, $CHCl_3$)

The mother liquor of the crystals was also base extracted (vide supra) to afford a scalemic mixture enriched in (+)-12 (2.888 g, 3.378 mmol, 69.5%). This mixture was dissolved in $CHCl_3$ (145 mL) and heated to 60 °C. A preheated solution of (+)-DTTA (1.305 g, 3.378 mmol) in EtOAc (97 mL) was added to the aforementioned solution and the mixture was refluxed for 1 h. The reaction was cooled to r.t. in the absence of stirring and allowed to sit for 18 h. The formed crystals were washed with base and (+)-12 was isolated as a white solid by the procedure outlined above (1.642 g, 1.920 mmol, 39%): $[\alpha]_D^{20} = +137$ (c 0.22, $CHCl_3$).

The mother liquor of these crystals was treated in a similar fashion with the same relative proportions of $CHCl_3$, EtOAc, and (−)-DTTA to afford a second batch of (−)-**12** (674 mg, 0.788 mmol, 16.2%): $[\alpha]_D^{20} = -127$ (c 0.220, $CHCl_3$). It should be noted that in all instances, the spectroscopic data of the resolved material matched those reported for the racemic material (vide supra).

4.5. (S_{ax})-2,2′-Bis-(diphenylphosphinoyl)-3,3′-bis-phenylethynyl-[1,1′]binaphthyl 13

Bisalkyne (−)-**13** (221 mg, 0.259 mmol) was dissolved in MeOH. To this was added 10% Pd/C (222 mg) and the flask was evacuated and purged with H_2 gas three times. The reaction was placed under an atmosphere of H_2 gas (2 atm) for 24 h with adequate stirring. The reaction mixture was filtered through a pad of Celite and the Celite was washed with MeOH (3 × 5 mL). The filtrate was concentrated in vacuo and the residue was purified by silica gel chromatography (2:1 EtOAc/hexanes) to afford the product as a white foamy solid (223 mg, 0.259 mmol, 100%): $[\alpha]_D^{20} = +95.5$ (c 0.225, $CHCl_3$); mp 138–139 °C; IR (film) υ_{max} 3062, 1438, 1186, 1114, 1095 cm^{-1}; ^1H NMR (400 MHz) δ 7.75–7.73 (m, 4H), 7.58 (dd, J = 12.2, 7.0 Hz, 4H), 7.44–7.37 (m, 6H), 7.27–7.21 (m, 6H), 7.19–7.07 (m, 16H), 6.81 (d, J = 6.8 Hz), 3.02–2.90 (m, 4H), 2.68–2.60 (m, 2H), 2.46–2.39 (m, 2H); ^{13}C NMR (100 MHz) δ 145.6 (C), 141.6 (C), 140.14 (d, J = 10.7 Hz, C), 135.2 (d, J = 103 Hz, C), 134.9 (d, J = 102 Hz, C), 134.1 (d, J = 2.3 Hz, C), 133.2 (d, J = 11.5 Hz, CH), 132.3 (d, J = 10.0 Hz, CH), 131.7 (d, J = 10.0 Hz, CH), 130.7 (d, J = 2.3 Hz, CH), 130.3 (d, J = 3.1 Hz, CH), 129.7 (d, J = 10.0 Hz, CH), 128.2 (CH), 128.1 (d, J = 21.5 Hz, CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 127.36 (CH), 127.28 (CH), 125.6 (CH), 125.4 (CH), 37.2 (CH_2), 37.1 (CH_2), 37.0 (CH_2); $^{31}P\{^1H\}$ NMR (162 MHz) δ 29.3; ESI-MS 901 $(M+K^+)^+$; 885 $(M+Na^+)^+$; 863 $(M + H^+)^+$; HRMS(MALDI-TOF) calcd for $(C_{60}H_{48}O_2P_2 + H^+)$ 863.3208, found 863.3195.

4.6. (S_{ax})-2,2′-Bis-(diphenylphosphino)-3,3‘-bis-phenylethynyl-[1,1′]binaphthyl 14

Bisphosphine oxide (*S*)-(+)-**13** (213 mg, 0.247 mmol) was combined with xylenes (3.9 mL) and NBu_3 (1.05 mL, 4.42 mmol). To this was added $HSiCl_3$ (0.37 mL, 3.67 mmol) dropwise and the reaction mixture was heated at 140 °C for 22 h. The reaction was cooled to 60 °C and aqueous NaOH (30%, 3.9 mL) was added dropwise. After 1 h of stirring at 60 °C, the reaction was cooled to room temperature, diluted with $CHCl_3$ (10 mL) and the layers separated. The aqueous layer was diluted with 30% NaOH (10 mL) and extracted with $CHCl_3$ (2 × 10 mL). The combined organic layers were washed with H_2O (2 × 10 mL) and were then dried over Na_2SO_4, filtered, and the solvent removed in vacuo to afford a white semi-solid. Purification by silica gel chromatography (20:1 hexanes/EtOAc)

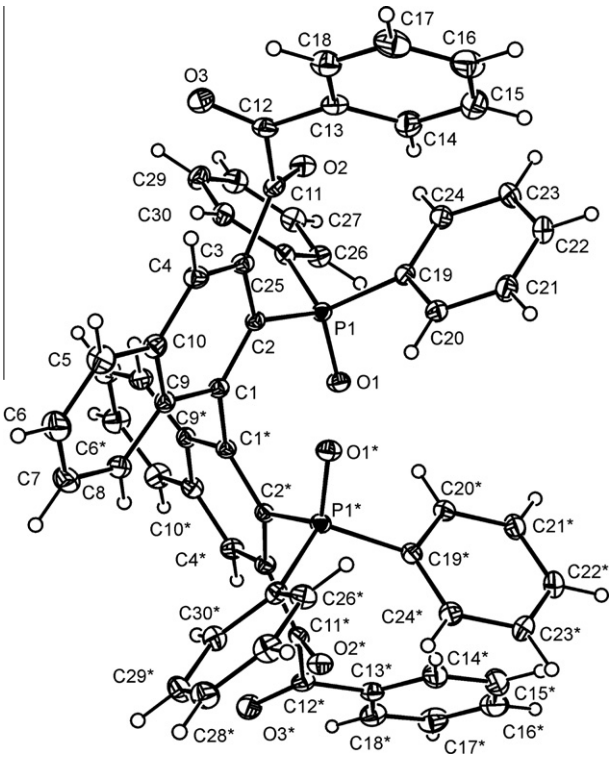
followed by trituration with MeOH afforded the product as an off-white powder (129 mg, 155 mmol, 63%): $[\alpha]_D^{20} = -137.1$ (0.275, $CHCl_3$); mp 196–197 °C; IR (film) ν_{max} 3047, 2929, 1481, 1433, 742, 695 cm^{-1}; ^1H NMR (400 MHz) δ 7.94 (s, 2H), 7.85 (d, J = 8.2 Hz, 2H), 7.43 (ddd, J = 1.6, 6.2, 8.1 Hz, 2H), 7.26–7.20 (m, 4H), 7.18–7.01 (m, 21H), 6.98–6.87 (m, 6H), 6.75–6.69 (m, 4H), 2.86–2.78 (m, 4H), 2.58–2.46 (m, 2H), 2.45–2.33 (m, 2H); ^{13}C NMR (100 MHz) δ 151.1 (d, J = 10.7 Hz, C), 150.6 (d, J = 10.7 Hz, C), 144.1 (s, 2H, C), 141.8 (C), 137.2 (d, J = 19.2 Hz, C), 135.6 (d, J = 14.6 Hz, C), 134.1 (C), 133.5 (d, J = 4.6 Hz, C), 133.4 (d, J = 4.6 Hz, C), 132.62 (d, J = 14.6 Hz, C), 131.9 (d, J = 19.9 Hz, CH), 131.4 (d, J = 19.2 Hz, CH), 129.1 (CH), 128.5 (CH), 128.3 (CH), 128.1 (d, J = 2.3 Hz, CH), 128.0 (CH), 127.9 (CH), 127.8 (d, J = 2.3 Hz, CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 126.8 (CH), 125.5 (CH), 125.3 (CH), 36.8 (CH_2), 36.7 (CH_2); $^{31}P\{^1H\}$ NMR (162 MHz) δ −12.6; ESI-MS 831 (M + H)$^+$; Anal. calcd for $C_{60}H_{48}P_2$ C, 86.72; H, 5.82, found C, 86.49; H, 5.81.

4.7. Bis(diketone) 15

Bisalkyne (*S*)-(−)-**12** (1.235 g, 1.445 mmol) was dissolved in DMSO (23 mL), after which I_2 (367 mg, 1.446 mmol) was added and the reaction was heated at 140 °C for 16 h. The reaction mixture was cooled to rt, diluted with CH_2Cl_2 (100 mL), and washed with 1% $Na_2S_2O_3$ (100 mL). The layers were separated and the aqueous portion was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with water (5 × 30 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to afford the product as a yellow solid (1.297 g, 1.411 mmol, 98%): $[\alpha]_D^{20} = -528$ (*c* 0.195, $CHCl_3$); mp 305–306 °C; ^1H NMR (400 MHz) δ 8.52 (d, J = 3.7 Hz, 2H), 7.90–7.80 (m, 6H), 7.52 (dd, J = 12.6, 7.3 Hz, 6H), 7.42 (t, J = 7.4 Hz, 2H), 7.39–7.19 (m, 21H), 7.16 (dt, J = 7.7, 2.9 Hz, 4H), 7.09 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz) δ 193.5 (C═O), 192.8 (C═O), 150.2 (C), 137.8 (d, J = 7.7 Hz, CH), 136.0 (d, J = 11.5 Hz, C), 134.4 (CH), 132.8 (C), 132.7 (d, J = 10.0 Hz, CH), 132.4 (d, J = 1.5 Hz, C), 131.3 (d, J = 10.7 Hz, CH), 130.7 (d, J = 2.3 Hz, CH), 130.0 (CH), 129.8 (CH), 129.5 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.7 (CH), 127.3 (d, J = 13.0 Hz, CH), 126.1 (d, J = 92.8 Hz, C); $^{31}P\{^1H\}$NMR (162 MHz) δ 35.9; ESI-MS 919 (M + H)$^+$; HRMS(MALDI-TOF) calcd for ($C_{68}H_{40}O_6P_2$ + H)$^+$ 919.23729, found 919.23671.

4.7.1. Crystal structure of 15

The X-ray quality crystals were obtained by recrystallization from a solution of **15** in 1:1 $CH_2Cl_2/CHCl_3$ layered with EtOAc. X-ray crystallographic analysis was performed by Dr. Masood Parvez. A colorless prismatic crystal of $C_{60}H_{40}O_6P_2{\cdot}CHCl_3{\cdot}CH_2Cl_2$ was coated with Paratone 8277 oil (Exxon) and mounted on a glass fiber. All measurements were made on a Bruker APEX2 CCD installed on a Nonius Kappa Goniometer diffractometer with graphite monochromated Mo-K radiation. The data were collected[14] and were corrected for Lorentz and polarization effects and for absorption using multi-scan method.[15] The structure was solved by direct methods using SHELXS.[16] The asymmetric unit contains half of the complex molecule and one half of each of the solvent molecule occupying the same location exhibiting positional disorder. The H-atoms were included at geometrically idealized positions and were not refined. The final cycle of full-matrix least-squares refinement using SHELXL[16] converged with unweighted and weighted agreement factors, R = 0.0483 and wR = 0.11732 (all data), respectively, and goodness of fit, S = 1.027. The absolute structure was established by the Flack method[17] and is presented herein; the inverted structure gave a Flack parameter of 0.80(8) and was therefore, rejected as the structure present in the crystal. The Friedel pairs of reflections were not merged. The weighting scheme was based on counting statistics and the final difference Fourier map was essentially featureless. The figure was plotted with the aid of ORTEPII.[18] The following crystal parameters were obtained: monoclinic C2; a = 25.3676(9) Å, b = 9.2100(5) Å, c = 12.8530(4) Å, α = 90°, γ = 90°, β = 117.724(2), V = 2658.18(19) Å3; Z = 2.



4.8. (S_{ax})-2,2′-Bis-(diphenylphosphinoyl)-3,3′-bis-(hydroxymethyl)-[1,1′]binaphthyl 16

Bis(diketone) (−)-**12** (1.297 g, 1.411 mmol) was suspended in CH_2Cl_2 (4 mL) and 95% EtOH (16 mL). To this stirring yellow slurry was added $NaBH_4$ (107 mg, 2.828 mmol) and the reaction was stirred for 1 h to give a red solution. TLC analysis revealed that all of the starting material had been consumed. The reaction was quenched by adding 5% $HCl_{(aq)}$ dropwise at 0 °C until the color of the solution went from red to pale yellow. This was diluted with H_2O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic fractions were washed with H_2O (50 mL) and $NaCl_{(aq)}$ (50 mL) before being dried over Na_2SO_4, filtered, and concentrated in vacuo to afford an orange foam.

The crude orange foam was dissolved in CH_2Cl_2 (20 mL) and to this was added $Pb(OAc)_4$ (1.314 g, 2.964 mmol). The reaction was stirred for 4 h at rt before being quenched with H_2O (60 mL) and extracted into CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with H_2O (30 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to afford an orange solid. This solid was suspended in CH_2Cl_2 (4 mL) and EtOH (16 mL) and treated with $NaBH_4$ (107 mg, 2.828 mmol) for 16 h at rt. The reaction was quenched by adding 5% $HCl_{(aq)}$ dropwise at 0 °C until evolution of H_2 gas ceased. The mixture was diluted with H_2O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic fractions were washed with H_2O (50 mL) and $NaCl_{(aq)}$ (50 mL) before being dried over Na_2SO_4, filtered, and concentrated in vacuo to afford a yellow foam. The crude material was purified by silica gel chromatography (9:1 EtOAc/MeOH) to afford the product as an off-white solid (704 mg,

0.985 mmol, 70% over three steps): $[\alpha]_D^{20} = +759$ (*c* 0.205, $CHCl_3$); mp 255–256 °C; IR (film) υ_{max} 3324 (O–H), 3052, 2923, 1438, 1157, 1105, 1095, 1019 cm^{-1}; ^1H NMR (400 MHz) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 3.5 Hz, 2H), 7.46 (t, *J* = 7.0 Hz, 2H), 7.42–7.30 (m, 6H), 7.29–7.20 (m, 8H), 7.13–7.09 (m, 2H), 7.02–6.85 (m, 8H), 5.18 (br d, *J* = 6.4 Hz, 2H), 4.68 (d, *J* = 11.9 Hz, 2H), 4.29 (dd, *J* = 13.3, 9.5 Hz, 2H); ^{13}C NMR (100 MHz) δ 141.3 (d, *J* = 9.2 Hz, C), 140.6 (d, *J* = 5.4 Hz, C), 140.5 (d, *J* = 5.4 Hz, C), 136.1 (d, *J* = 103 Hz, C), 134.3 (d, *J* = 2.3 Hz, C), 133.2 (d, *J* = 10.0 Hz, CH), 133.0 (d, *J* = 12.3 Hz, C), 132.4 (d, *J* = 10.7 Hz, CH), 131.9 (C), 131.7 (C), 131.4 (d, *J* = 3.1 Hz, CH), 130.7 (d, *J* = 2.3 Hz, CH), 130.6 (d, *J* = 9.2 Hz, CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 127.0 (CH), 65.6 (d, *J* = 4.6 Hz, CH_2–O); $^{31}P\{^1H\}$NMR (162 MHz) δ 31.8; ESI-MS 737 (*M* + Na)$^+$; HRMS(MALDI-TOF) calcd for ($C_{46}H_{36}O_4P_2$ + Na^+) 737.1981, found 737.1989.

4.9. (S_{ax})-2,2′-Bis-(diphenylphosphinoyl)-3,3′-bis-(phenoxymethyl)-[1,1′]binaphthyl 17

Diol (+)-**16** (704 mg, 0.985 mmol) was dissolved in CH_2Cl_2 (7.5 mL). To this was added NEt_3 (0.63 mL, 4.40 mmol) and the solution was cooled to 0 °C. Next, MsCl (0.17 mL, 2.20 mmol) was added dropwise and the reaction was stirred for 1 h. TLC analysis indicated that all of the starting material had been consumed. The reaction was quenched with saturated $NaHCO_3$ (10 mL) and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic fractions were washed with H_2O (10 mL), dried over Na_2SO_4, filtered, and concentrated to afford a yellow foam. This material was dissolved in DMF (5 mL) and set aside.

In another flask, phenol (927 mg, 9.85 mmol) was dissolved in DMF (5 mL) and cooled to 0 °C. Next, NaH (355 mg, 60% dispersion in mineral oil) was added to this solution portionwise. Once added, the mixture was allowed to warm to rt over 30 min. The previously prepared solution of **16** in DMF (vide supra) was added dropwise to the solution of sodium phenoxide using a canula. The flask containing **16** was then rinsed with DMF (2 × 1 mL) and these washings were added to the reaction mixture along with NaI (59 mg, 0.39 mmol, 20 mol% per hydroxyl group). The reaction was stirred at rt for 18 h before being cooled to 0 °C and quenched with saturated NH_4Cl (5 mL) dropwise. The quenched reaction was diluted with EtOAc (15 mL) and $NaCl_{(aq)}$ (15 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with $NaCl_{(aq)}$ (30 mL), dried over Na_2SO_4, filtered, and concentrated to afford a thick yellow oil. The crude material was purified by silica gel chromatography (100% EtOAc) to afford the product as a white foam (756 mg, 0.872 mmol, 88%). An analytical sample was obtained by recrystallizing from Et_2O to afford the product as a white, crystalline solid (580 mg, 0.669 mmol, 68%): $[\alpha]_D^{20} = +228$ (*c* 0.265, $CHCl_3$); mp 218–219 °C; IR (film) υ_{max} 3057, 1590, 1581, 1495, 1433, 1238, 1186, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 3.7 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.57 (dd, *J* = 12.0, 7.0 Hz, 4H), 7.47–7.39 (m, 2H), 7.35–7.29 (m, 2H), 7.28–7.07 (m, 20H), 6.96 (dt, *J* = 7.9, 3.1 Hz, 4H), 6.92–6.87 (m, 2H), 6.66–6.63 (m, 4H), 5.12 (d, *J* = 13.9 Hz, 2H), 4.95 (d, *J* = 13.9 Hz, 2H); ^{13}C NMR (100 MHz) δ 158.40 (C), 142.1 (d, *J* = 5.4 Hz, C), 142.0 (d, *J* = 5.4 Hz, C), 136.6 (d, *J* = 13.0 Hz, C), 136.5 (C), 135.7 (C), 134.0 (d, *J* = 1.5 Hz, C), 133.2 (d, *J* = 104 Hz, C), 133.0 (d, *J* = 10.7 Hz, C), 132.5 (d, *J* = 10.0 Hz, CH), 131.2 (d, *J* = 2.3 Hz, CH), 130.9 (d, *J* = 10.0 Hz, CH), 130.6 (d, *J* = 3.1 Hz, CH), 129.2 (CH), 128.9 (d, *J* = 9.2 Hz, CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.95 (C), 127.8 (CH), 127.6 (CH), 127.1 (CH), 127.0 (CH), 126.4 (CH), 120.7 (CH), 114.6 (CH), 68.6 (d, *J* = 3.8 Hz, CH_2); $^{31}P\{^1H\}$NMR (162 MHz) δ 27.8; ESI-MS 867 (*M* + Na)$^+$; HRMS(MALDI-TOF) calcd for ($C_{58}H_{42}O_4P_2$ + Na^+) 889.2670, found 889.2598.

4.10. (S_{ax})-2,2′-Bis-(diphenylphosphino)-3,3′-bis-(phenoxymethyl)-[1,1′]binaphthyl 18

Bisphosphine oxide (+)-**17** (571 mg, 0.659 mmol) was dissolved in xylenes (11 mL). To this was added NBu_3 (4.00 mL, 16.8 mmol) and then $HSiCl_3$ (1.40 mL, 13.9 mmol). The reaction was heated to 140 °C in an oil bath over 15 minutes and this reaction temperature was maintained for 21 h. The reaction was cooled to 60 °C and 30% $NaOH_{(aq)}$ (11 mL) was added slowly. After 1 h of stirring at 60 °C, the reaction was cooled to room temperature, diluted with $CHCl_3$ (10 mL), and the layers separated. The aqueous layer was diluted with 30% $NaOH_{(aq)}$ (10 mL) and extracted with $CHCl_3$ (2 × 10 mL). The combined organic layers were washed with distilled water (2 × 10 mL) and then dried over Na_2SO_4, filtered, and the solvent removed *in vacuo* to afford a white semi-solid. Purification by silica gel chromatography (20:1 hexanes/EtOAc) followed by trituration with MeOH afforded the product as an off-white powder (481 mg, 0.577 mmol, 87%): $[\alpha]_D^{20} = +129$ (*c* 0.200, $CHCl_3$); mp 224–225 °C; IR (film) υ_{max} 3048, 2917, 1602, 1579, 1492, 1429, 1237, 1028 cm^{-1}; ^1H NMR (400 MHz) δ 8.38 (s, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.26–7.22 (m, 4H), 7.19–6.98 (m, 26H), 6.85 (t, *J* = 7.3 Hz, 2H), 6.54 (d, *J* = 7.9 Hz, 4H), 4.56 (d, *J* = 13.8 Hz, 2H), 4.52 (d, *J* = 13.8, 2H); ^{13}C NMR (100 MHz) δ 158.6 (C), 150.0 (d, *J* = 11.5 Hz, C), 149.6 (d, *J* = 11.5 Hz, C), 139.0 (d, *J* = 4.6 Hz, C), 136.2 (d, *J* = 16.1 Hz, C), 135.7 (d, *J* = 17.6 Hz, C), 133.8 (C), 133.3 (d, *J* = 3.1 Hz, C), 133.3 (C), 133.2 (d, *J* = 3.1 Hz, C), 132.2 (d, *J* = 19.9 Hz, CH), 131.2 (d, *J* = 1.5 Hz, CH), 131.1 (d, *J* = 2.3 Hz, CH), 130.9 (d, *J* = 4.1 Hz, C), 130.8 (d, *J* = 4.6 Hz, C), 129.2 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.20 (CH), 128.0 (d, *J* = 6.9 Hz, CH), 127.3 (d, *J* = 6.1 Hz, CH), 127.1 (CH), 125.9 (CH), 120.5 (CH), 114.5 (CH), 69.5 (CH_2–O); $^{31}P\{^1H\}$NMR (162 MHz) δ −14.4; ESI-MS 835 (*M* + H)$^+$; HRMS(MALDI-TOF) calcd for ($C_{58}H_{42}O_2P_2$ + H^+) 835.28893, found 835.28657.

4.11. General procedure for the synthesis of bisphosphine-diselenides

Bisphosphine (20 mg) was dissolved in $CHCl_3$ (2 mL). To this solution was added elemental selenium (10 equiv). The reaction was stirred at rt and monitored by TLC for the disappearance of bisphosphine. For sluggish reactions (>4 h at rt), the mixtures were heated at 60 °C for 16 h. Once completed, the reaction was cooled to rt and filtered through a plug of Celite. The Celite was washed with $CHCl_3$ (3 × 2 mL) and the filtrate was concentrated. The crude material was then analyzed by ^{31}P NMR spectroscopy without further purification.

4.12. General procedure for Rh-catalyzed asymmetric hydrogenations

At first, $Rh(nbd)_2BF_4$ (3.7 mg, 0.01 mmol), ligand (0.011 mmol), and MeOH (1 mL) were combined under an inert atmosphere and stirred for 30 min at room temperature. Olefin (1 mmol) was added with an additional volume of MeOH (1 mL). The reaction mixture was then subjected to three consecutive freeze/pump/thaw cycles on a double manifold (pump time = 10 min). Upon warming to room temperature, the reaction was placed under a hydrogen atmosphere (2 atm) for 24 h. Upon completion, the volatiles were removed in vacuo and the remaining residue was passed through a plug of silica gel (hexanes–EtOAc, 1:1). Upon solvent evaporation, the isolated products were used directly for either chiral GC or

chiral HPLC analysis. Chiral GC data for methyl 2-acetamidopropanoate **20a**: Chiral GC, Cyclodex B, isothermal 90 °C,: t_{R1} [(*R*)-**20a**] = 31.8 min, t_{R2} [(*S*)-**20a**] = 32.8 min.

Chiral data for methyl α-acetamide cinnamate **4**: Chiral HPLC, chiralcel OD; hexane–iPrOH, 9:1; 1.0 mL/min: t_{R1}[(*R*)-**4**] = 12.4 min, t_{R2} [(*S*)-**4**] = 16.3 min.

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