Tetrahedron: *Asymmetry* 22 (2011) 1680–1686

Contents lists available at SciVerse ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Synthesis of *P*-stereogenic BINAP bissulfide analogues

Eoin Rafter [a], Jimmy Muldoon [b], Helge Müller Bunz [c], Declan G. Gilheany [a,*]

[a] Centre for Synthesis and Chemical Biology, Conway Institute for Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland
[b] NMR Facility, School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland
[c] X-ray Crystallography Laboratory, School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

ARTICLE INFO

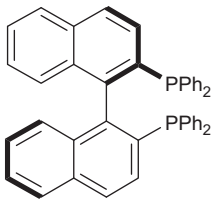
Article history:
Received 12 August 2011
Accepted 13 September 2011
Available online 1 November 2011

ABSTRACT

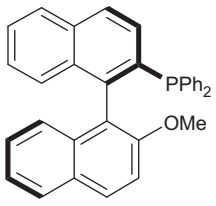
A synthetic route to BINAP disulfide analogues with chirality on one of the phosphorus atoms was developed. The synthesis of these ligands was achieved by step-wise palladium and nickel-catalysed coupling reactions of the precursor binaphthyl triflate with secondary phosphines and phosphine oxides, respectively. C2-Unsymmeric BINAP bissulfide analogues with the same aryl substituents were also synthesized for the sake of comparison. Preliminary studies of the reduction of these sulfides to the free phosphines are also described.

1. Introduction

The presence of an axially chiral backbone on ligands for catalysis is one of the best known ways to induce enantioselectivity.[1–3] Its effectiveness has been proven by the high selectivities achieved by such ligands as BINAP[1,2] and MOP[3,4] for hydrogenations and hydrosilylations, respectively. As a result of the success of these and other axially chiral ligands, at present, the development of novel axially chiral ligands is one of the most significant areas of research in homogeneous catalysis.[2,3,8]



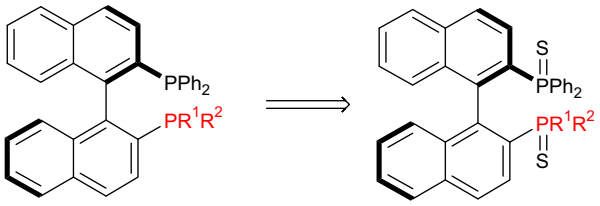
(*R*)-BINAP



(*R*)-MOP

Despite the huge success of such axially chiral phosphine ligands in catalysis, a limiting factor in their usefulness has been their relative air sensitivity, since many of the well known ligands are prone to oxidation under ambient conditions. Thus, another motif in catalysis research has been the search for air-stable ligands for catalysis.[5] A class of possible air stable ligands that is only recently receiving attention are phosphine sulfides.[6,7] These compounds are not strong σ-donating ligands such as phosphines or carbenes and for this reason their use has only been rarely studied. Until recently these ligands were only used in situations where their hemi-labile behaviour was desired. Thus, Aizawa et al. have proven that bis-phosphine sulfide ligands can be active for the Suzuki–Miyaura coupling[8,9] and research by Saigo et al. and Hashimoto et al. have shown that phosphine sulfides can be more active than phosphines for bishydroxycarbonylation.[10] Previously, Faller et al. had also disclosed mixed phosphine/phosphine sulfide ligands and shown them to be useful for asymmetric allylic aminations.[11–13] For these reasons the synthesis of novel phosphine sulfide ligands presents an interesting task for catalysis research.

The use of *P*-stereogenicity to induce enantioselectivity has been used in chiral catalysis with great success for decades with such ligands as DIPAMP achieving exceptional results.[14–17] Despite the known success of these and axially chiral ligands, there are still a few cases where both axial and central chirality have been combined.[18–21] This is due to the difficulty that the synthesis of such ligands and the separation of their diastereomers can present.



BINAP analogues

BINAP sulfide analogues

* Corresponding author. Fax: +353 1 716 21277.
E-mail address: declan.gilheany@ucd.ie (D.G. Gilheany).

0957-4166/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2011.09.007

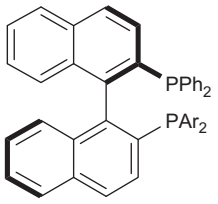
As part of our work towards *P*-stereogenic analogues of axially chiral ligands,[22,23] we herein report the synthesis of a series of disulfide analogues of the BINAP ligand with differing substituents on the two phosphorus atoms and with chirality at one phosphorus. It was our hope that through the procedures that we have developed we could provide not only new phosphine sulfide ligands for catalysis but also a more facile method for the synthesis and separation of ligands combining two forms of chirality.

Therefore we also describe preliminary studies of the desulfurisation to the respective phosphines, some of which would carry both axial and central chirality thereby representing a hybrid of the BINAP ligand and the DIPAMP ligand.[17,14–16]

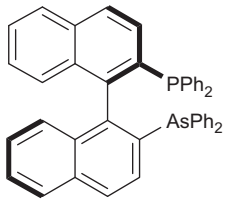
2. Results and discussion

2.1. Synthesis of phosphine sulfides

This was achieved by step-wise palladium and nickel-catalysed coupling reactions of phosphine oxides and secondary phosphines, respectively (Scheme 1). Methods such as this using sequential metal catalysed phosphine oxide and phosphine coupling reactions have been used to synthesise other BINAP analogues, such as BINAPAS and BINAPP′.[24,25]



(*R*)-BINAPP'



(*R*)-BINAPAS

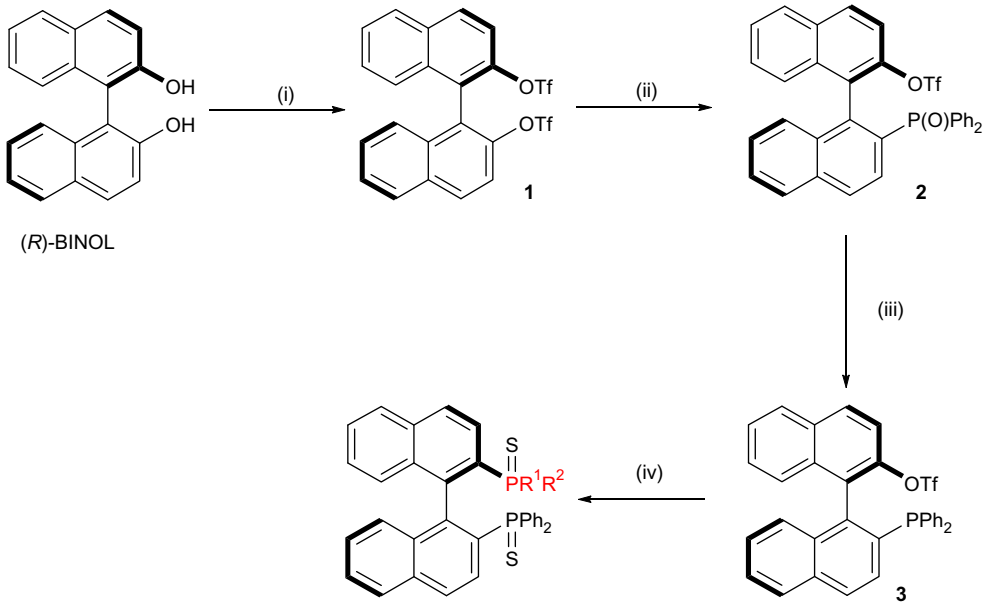
The synthesis, as shown in Scheme 1, begins with the triflation of enantiomerically pure (*R*)-BINOL using triflic anhydride in the presence of a base to give bis-triflate **1** and its coupling to diphenylphosphine oxide using the method reported by Morgans et al.[26] to give phosphine oxide triflate **2**. An advantage of this palladium catalysed method is that, for steric reasons, only one phosphorus moiety is introduced. For the same steric reasons, oxide **2** has then to be reduced to phosphine triflate **3** to allow space for the second (nickel catalysed) coupling to occur. However, this reduction proved to be a difficult task because of degradation of the remaining triflate group in various ways, often occurring as a side reaction. After extensive testing of a number of methods, selective reduction of phosphine was achieved using $PhSiH_3$ under strictly anhydrous conditions.[27]

The nickel catalysed coupling to triflate **3** was then performed with a series of secondary phosphines (Chart 1). The majority of these are known compounds and were made without incident by the addition of the appropriate Grignard reagents to either trichlorophosphine or dichlorophenylphosphine to give the doubly substituted chlorophosphine R^1R^2PCl, which was then reduced with $LiAlH_4$ and the crude material distilled to purity under high vacuum.

Methylphenylphosphine **10** requires a different route because double addition of the methyl Grignard reagent to dichlorophenylphosphine occurs readily even at low temperatures (−78 °C). Instead, again according to the literature, dichlorophenylphosphine was converted to dimethyl phenylphosphonite, rearranged by the Arbuzov reaction with MeI to methyl methylphenylphosphinate,[28] which was reduced with $LiAlH_4$ to give the secondary phosphine.

For the coupling of the secondary phosphines to phosphine triflate **3**, we followed the nickel catalysed procedure originally reported by Cai et al. for the synthesis of BINAP.[29] This has been widely used since it was first reported and has proven a versatile method for the synthesis of novel phosphines.[24,30] We expected many of the resultant bisphosphines to be easily oxidised in air to the bis-phosphine oxides. Although it would be possible to separate the diastereomers as their respective oxides, this was not desired as the subsequent reduction could result in racemisation about the phosphorus centre, as previously observed in our group.[23,22] Since we were targeting phosphine sulfides anyway, we therefore treated the crude products of the coupling reaction directly with sulfur.

The results of the coupling reaction (as measured by the sulfide yields) are given in Table 1 and the resultant isolated products are listed in Chart 2. It can be seen that the efficiency of the coupling, already not very high, is significantly reduced as the bulk of the



(*R*)-BINOL

Scheme 1. Reagents: (i) TfO_2, pyridine, (ii) $Ph_2P(O)H$, $Pd(OAc)_2$, DPPB, EtN^iPr_2, (iii) $PhSiH_3$, (iv) (1) R^1R^2PH, $[NiCl_2(dppe)]$, DABCO, (2) S_8.

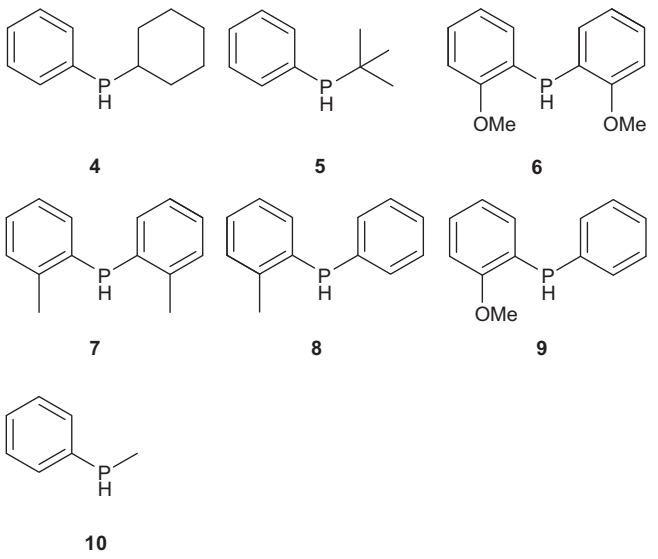


Chart 1. Secondary phosphines synthesised.

Table 1
Yields from nickel coupling reactions to triflate **3** according to Scheme 1(iv) using the secondary phosphines from Chart 1[a]

Phosphines	Yield from coupling reaction[b]
Cyclohexylphenylphosphine **4**	Nil
tert-Butylphenylphosphine **5**	Nil
Di-*o*-tolylphosphine **6**	8%
Di-anisylphosphine **7**	4%
o-Tolylphenylphosphine **8**	29%
Anisylphenylphosphine **9**	32%
Methylphenylphosphine **10**	36%

[a] Reactions carried out under nitrogen in flame dried glassware.
[b] Yields judged by yield of converted phosphine sulfide retrieved.

coupling phosphine increases. Thus, although the introduction of one *ortho*-substituted aryl group in cases **8** and **9** does not have a very detrimental effect, the second *ortho*-substituted group in **6** and **7** causes a large loss of yield. In the cases of cyclohexylphenyl and *tert*-butylphenyl, **4** and **5**, the only observed product was the hydrogenolysed starting material. We can rule out an electronic effect[31–33] in these latter cases because the methylphenyl case **10** gives the best yield and would have similar electronic properties.

The bis-phosphine sulfides were then purified by column chromatography to afford the pure compounds. In the case of **11** and **12**, but not **13**, it was possible to separate the individual diastereomers. For the methylphenyl derivative **11** crystals could be obtained which were suitable for X-ray analysis and assignment of configuration (Fig. 1). However, we were unable to form suitable crystals for any of the other analogues. In the cases of the more hindered analogues **14** and **15**, this was partly because their solubility in most solvents was very poor. This poor solubility was possibly caused by decreased internal freedom of movement. Also heavily arylated compounds in general can be quite insoluble.

The ^{1}H NMR of the di-*o*-tolyl phosphine bissulfide **15** unexpectedly showed a significant difference in the shifts of the methyl peaks along with discernable differences in linewidth. Similar differences in linewidth were observed at lower temperatures in the ^{31}P NMR spectra. Such differences may be attributable to the restricted rotation of substituents about their bonds to phosphorus—the environment around the phosphorus in these compounds is crowded due to the presence of sulfur and large *ortho*-substituted aryl rings (see Fig. 2). Further work is currently being planned to investigate these phenomena.

2.2. Tests of the reduction of phosphine sulfides

The important issue in the reduction of these compounds is that there should be conversion with stereoretention at the *P*-stereogenic centre; hence we sought reductants that did not require heating. We chose Raney nickel and triethylphosphine (Et_3P) and tested both in the reduction of triphenylphosphine sulfide at room temperature. With Raney nickel this proceeded well with a 60% conversion in 16 h (as judged by ^{31}P NMR), while Et_3P gave effectively no reduction after 86 h.

We then tested Raney nickel further on BINAP-S_2.[34] We sought this further test as it has been observed that the reduction of $BINAPO_2$ (bisoxidised BINAP) is far more difficult than a regular triaryl phosphine oxide.[35] Indeed, $BINAPS_2$ desulfurisation was much slower than that of triphenylphosphine sulfide. However, it did still give the half-reduced product (80%) after four days at room temperature.

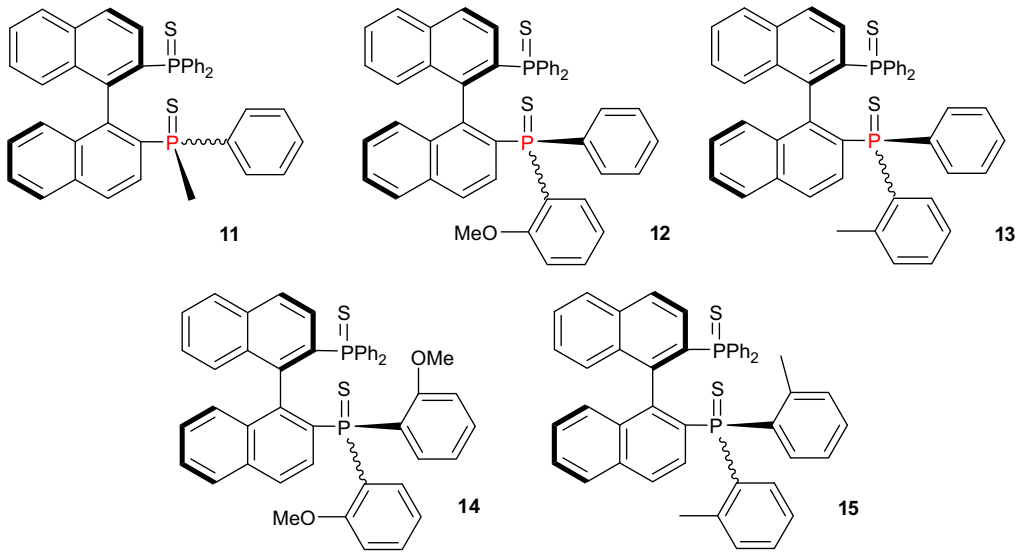


Chart 2. Bis-phosphine sulfides synthesised, *P*-stereogenic centres marked in red.

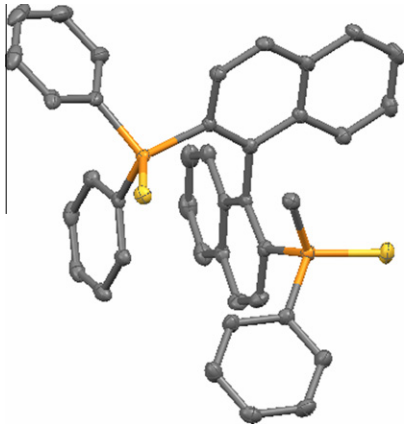


Figure 1. X-ray crystal structure of (*R,R*)-diastereomer of 2-(methylphenyl phosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl **11**. The hydrogen atoms are omitted for clarity.

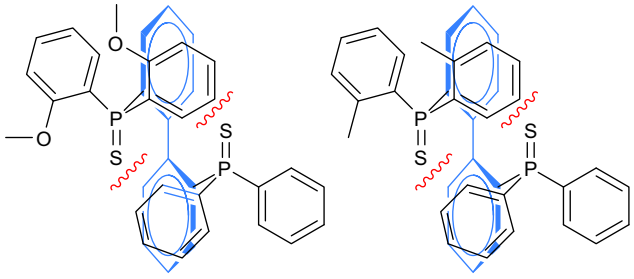


Figure 2. Hindered environment around the phosphine sulfide.

Finally we tested one of the diastereomers of 2-(anisylphenylphosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl **12**. As expected, this reacted similarly to $BINAPS_2$ with a slow desulfurisation over several days. After 96 h, the ^{31}P NMR of the reaction showed both half-reduction products. We are currently investigating this reduction further in our laboratory.

2.3. Investigation of alternative routes

Due to the limitations in the nickel-catalysed coupling of the bulky secondary phosphines, we investigated two other approaches for the synthesis of our target compounds. The first of these involved the palladium-catalysed addition of the unsymmetrically substituted secondary phosphine (as the oxide) as the first coupling in the synthesis (Scheme 2). We hoped then to reduce to phosphine and add the diphenyl-substituted moiety by nickel catalysis. Secondary phosphine oxides were synthesised using the method of Busacca et al. or by direct air oxidation of a secondary phosphine and tested in the palladium coupling step.[39] Indeed the initial palladium-catalysed coupling worked well for the cyclohexylphenyl case (one of the problem cases earlier) and we were also able to achieve chromatographic separation of the diastereomers of phosphine oxide triflate **16** and crystallise for X-ray assignment of the configuration at the phosphorus (Fig. 3). These compounds had previously been reported but their specific stereochemistry has not been fully assigned before.[36]

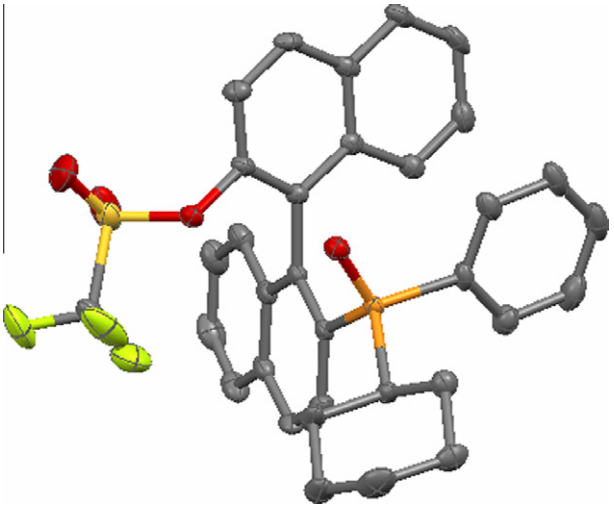
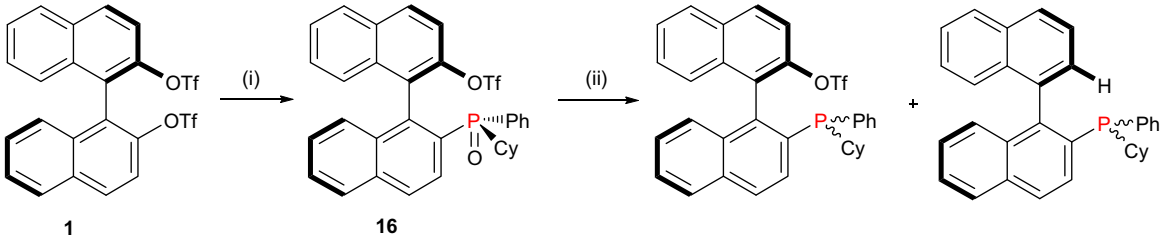


Figure 3. X-ray crystal structure of (*R,R*)-(+)-2-cyclohexylphenylphosphinyl-2′((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl **16**.

However, we subsequently found that these compounds could not be successfully reduced to their phosphines in the same manner as diphenylphosphine oxide/triflate **2**. We were not so worried about epimerisation in the reduction because we could have carried a mixture through to the sulfides, which we were confident we could separate. Much more disappointing was that, in the case of cyclohexylphenylphosphine oxide/triflate **16**, the reduction of the adjacent triflate group always occurred to some degree (Scheme 2). Also in the case of anisylphenyl phosphine oxides, the *P*-stereogenic centre was racemised in the reduction step. These two hindrances in the route meant that any possible advantage achieved by the early addition of the unsymmetrically substituted phosphorus moiety was lost.

Another alternative that we attempted involved purification of the bis-phosphine products from the nickel catalysed coupling as their respective boranes. This was simply achieved by switching to a work up with borane–THF. However two interlinked issues soon became apparent. Firstly and most importantly, the diastereomers of bisphosphine boranes were inseparable by column chromatography. Secondly they were unstable in air, slowly converting to the bisphosphine oxides over time. This was due to the establishment of an equilibrium between phosphine borane and the free phosphine, which was then oxidised to the oxide over



Scheme 2. Alternative route via *P*-stereogenic oxide/triflate. Reagents: (i) CyPhP(O)H, $Pd(OAc)_2$, DPPB, EtN^iPr_2, (ii) $PhSiH_3$.

time; through this dissociation and oxidation, what started out as a clean phosphine borane would become a mixture of phosphine borane, phosphine, and phosphine oxide.

This lability of our phosphine boranes compared to the other known stable phosphine boranes must be due to the reduced Lewis basicity of our phosphines. In the majority of cases where boranes are used to protect a phosphine, there is one or more alkyl (electron donating) substituent on phosphine.[32,37,33] Our tri-arylphosphines would not have as much electron density present on phosphine, reducing their basicity and weakening the P–B bond in the borane.

3. Conclusion

In conclusion, we have shown that the synthesis of certain *P*-stereogenic BINAP sulfide analogues can be achieved through a short synthesis without arduous separation required. This synthesis also presents a possible approach to novel phosphine ligands and potential hybrid DiPAMP/BINAP ligands. However, of particular note are the steric limitations in the use of nickel catalysed phosphine coupling reactions. Several ways to overcome this limitation were investigated with only limited success. Initial tests of the reduction of phosphines sulfides to their respective phosphines have also been carried out, with promising results.

4. Experimental

4.1. General

X-ray diffraction experiments on **11** and **16** were carried out at 100 K, for **16** on a Bruker SMART diffractometer using Mo Kα radiation, λ = 0.71073 Å and for **11** on a SuperNova. A Diffractometer by Agilent Technologies (formerly known as Oxford Diffraction) using Cu Kα radiation, λ = 1.54184 Å. Absorption corrections were based on equivalent reflections and structures refined against all F^2 data. Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre [ref. CCDC 838736 and 838737].

All reactions were carried out under a N_2 atmosphere in dry glassware using Schlenk-line techniques. Air and moisture sensitive liquids and solutions were transferred via syringe. All 'dry' solvents were dried and distilled by standard procedures[38] or through Grubbs dry solvent apparatus. All 'anhydrous' solvents or solutions were purchased dry from chemical suppliers. Solutions were concentrated under reduced pressure by rotary evaporator. Chromatographic purification[38] of products was accomplished on Merck Silica Gel 60 (0.040–0.063 mm).

The standard NMR spectra were recorded at 25 °C on Varian VNMRS 300, 400, and 500 MHz spectrometers. ^{13}C spectra with ^{31}P decoupling were performed at 30 °C on a Varian VNMRS 600 MHz spectrometer equipped with a triple resonance probe. Tetramethylsilane was used as an internal standard for routine ^{1}H and ^{13}C spectra and 85% H_3PO_4 for ^{31}P spectra. ^{31}P and ^{13}C NMRs were performed proton decoupled.

FT-IR data were collected using a Varian 3100 FT-IR spectrometer. Routine electrospray mass spectra were obtained on a Micromass Quattro Spectrometer and high resolution mass spectra were carried out on a Micromass LCT system at UCD.

Compounds **1** and **2** were prepared according to the literature procedures.[26,3]

4.1.1. Synthesis of (*R*)-2-diphenylphosphino-2′ ((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl 3

The procedure of Hiemstra et al. was incorporated.[27] (*R*)-(+)-2-Diphenylphosphinyl-2′-((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl (1.3 g, 2.2 mmol, 1.0 equiv) was added to a 100 mL round bottomed flask equipped with an N_2 inlet and stirring bar. The solid reagent was dissolved in neat phenylsilane (11.7 g, 13.30 mL, 0.108 mol, 50.00 equiv). The solution was heated on a 110 °C oil bath and stirred overnight. The solution was allowed to return to room temperature, and was charged with dry degassed ethyl acetate (30 mL). The solvent was removed in vacuo. The yellow oily residue was redissolved in a 4:1 cyclohexane/ethyl acetate solution (5 mL) and passed through a short pad of silica under a N_2 flow. The pad was washed with 4:1 cyclohexane/ethyl acetate solution (5 mL). The solvent was removed in vacuo to give the crude product (1.26 g, 97% crude yield) as an off-white solid. The product is prone to oxidation, and was therefore carried through to the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 9.1, 1H, ArH), 7.73 (d, J = 8.5, 1H, ArH), 7.68 (d, J = 8.3, 2H, ArH), 7.47–6.85 (m, 17H, ArH), 6.81 (d, J = 8.3, 1H, ArH) ppm; ^{19}F NMR (282 MHz, $CDCl_3$) δ −74.7 ppm; ^{31}P NMR (121 MHz, $CDCl_3$) δ −13.0 ppm.

4.2. General procedure for the synthesis of phosphine sulfides

A dry 100 mL J.Young®'s flask was charged with [$NiCl_2$(dppe)] (30.0 mg, 0.17 mmol, 0.10 equiv) using a glovebox apparatus. The flask was charged with dry degassed DMF (10 mL) and the secondary phosphine (1.0 mmol, 0.6 equiv). The solution was heated for 60 min in a 100 °C oil bath after which the reaction was charged with a solution of (*R*)-(+)-2-diphenylphosphino-2′((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl(0.97 g, 1.65 mmol, 1.00 equiv) and DABCO (0.74 g, 6.60 mmol, 4.00 equiv) in dry degassed DMF (15 mL). The dark red solution was maintained at 100 °C for 60 min and then a second aliquot of phosphine (1.0 mmol, 0.6 equiv) was added. The solution was stirred at 100 °C for 16 h and the final aliquot of phosphine (1.0 mmol, 0.6 equiv) was added. The reaction was maintained in a 100 ° oil bath for 86 h after which it was allowed to cool to 60 °C and then the solvent was removed in vacuo. The residue was dissolved in dry degassed toluene after which sulfur (0.53 g, 16.5 mmol, 10.0 equiv) was added to the mixture. The mixture was stirred for 16 h and the solvent was removed in vacuo. The crude product was purified by column chromatography.

4.2.1. 2-(Methylphenylphosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl 11

(*R,R*)-Diastereomer: 1st elute: 193 mg, 18.2% yield $[\alpha]_D$ = +3 (*c* 1, CH_2Cl_2); IR (KBr, cm^{-1}) 898, 1096, 1433, 1634, 2361, 3050, 3461; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (ddd, J = 13.4, 6.6, 3.2 Hz, 2H, Ar*H*), 8.00 (dd, J = 8.8, 2.0 Hz, 1H, Ar*H*), 7.90 (d, J = 8.2 Hz, 1H, Ar*H*), 7.74–7.63 (m, 3H, Ar*H*), 7.60 (dd, J = 8.8, 1.6 Hz, 1H, Ar*H*), 7.58–7.51 (m, 5H, Ar*H*), 7.46 (td, J = 7.2, 1.6 Hz, 1H, Ar*H*), 7.40 (td, J = 7.5, 3.0 Hz, 3H, Ar*H*), 7.33–7.19 (m, 5H, Ar*H*), 7.11–7.04 (m, 1H, Ar*H*), 6.84 (td, J = 8.0, 3.2 Hz, 2H, Ar*H*), 6.79–6.68 (m, 2H, Ar*H*), 1.65 (d, J = 13.8 Hz, 3H, PC*H*$_3$) ppm;^{13}C NMR (151 MHz, $CDCl_3$) (P–C decoupled) δ 141.4, 136.8, 135.3, 134.4, 134.2, 133.5, 133.2, 133.0, 132.7, 132.19, 132.15, 132.12, 132.07, 132.03, 131.98, 131.3, 131.1, 130.5, 129.9, 129.8, 129.33, 129.29, 129.2, 129.0, 128.7, 128.53, 128.49, 128.4, 128.31, 128.27, 127.7, 127.31, 127.28, 127.2, 127.10, 127.07, 126.0, 110.3, 22.6 (P*C*H$_3$) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.4, 136.8, 135.6, 134.9, 134.6, 134.17, 134.15, 134.0, 133.6, 133.5, 133.3, 133.2, 133.1, 132.8, 132.7, 132.6, 132.24, 132.15, 132.11, 132.06, 132.03, 131.98, 131.30, 131.27, 131.25, 130.5, 130.5, 130.2, 129.9, 129.5, 129.4, 129.3, 129.0, 128.88, 128.7, 128.61, 128.55, 128.5, 128.3, 128.2, 127.72, 127.69, 127.6, 127.3, 127.2, 127.1, 126.9, 126.0, 22.8 (P*C*H$_3$), 22.3 (P*C*H$_3$) ppm; ^{31}P NMR (243 MHz, $CDCl_3$) δ 43.2, 39.8 ppm; *m/z* (% intensity) [**MH**]$^+$ 625.5 (100), [**MH**+1]$^+$ 626.5. (50), [**MH**+2]$^+$ 627.5 (20); HRMS calcd for [**MH**]$^+$ = $C_{39}H_{31}P_2S_2$

625.1342; found 625.1326. X-ray quality crystals were obtained by slow diffusion of hexane into a solution in dichloromethane, see Figure 1.

(*S,R*)-Diastereomer: 2nd elute: 185 mg, 18% yield; $[\alpha]_D = -86$ (*c* 0.25, CH_2Cl_2); IR (KBr, cm^{-1}) 711, 897, 1097, 1434, 1635, 3464. ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 14.0, 8.8 Hz, 1H, Ar*H*), 7.86 (dd, *J* = 8.8, 1.6 Hz, 1H, Ar*H*), 7.81 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.75 (dt, *J* = 12.9, 7.9 Hz, 3H, Ar*H*), 7.65 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.58 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.50–7.35 (m, 5H, Ar*H*), 7.34–7.27 (m, 3H, Ar*H*), 7.18 (dd, *J* = 8.2, 6.7 Hz, 1H, Ar*H*), 7.11–7.02 (m, 5H, Ar*H*), 6.95 (t, *J* = 7.6 Hz, 1H, Ar*H*), 6.91–6.85 (m, 3H, Ar*H*), 6.82 (d, *J* = 8.6 Hz, 1H, Ar*H*), 1.81 (d, *J* = 13.7 Hz, 3H, P*CH*$_3$) ppm;^{13}C NMR (151 MHz, $CDCl_3$) (P–C decoupled) δ 139.7, 136.0, 134.7, 134.0, 133.8, 133.6, 133.42, 132.41, 132.37, 132.33, 132.28, 132.24, 132.19, 131.9, 131.5, 131.0, 130.54, 130.51, 130.4, 130.0, 129.3, 129.1, 128.63, 128.59, 128.2, 128.04, 128.01, 127.9, 127.8, 127.7, 127.6, 127.5, 127.30, 127.26, 127.12, 127.07, 126.4, 90.6, 21.6 (P*CH*$_3$) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.8, 138.72, 138.69, 138.66, 134.99, 134.95, 134.1, 133.4, 132.8, 132.7, 132.6, 132.5, 132.4, 131.5, 131.4, 131.3, 131.2, 130.9, 130.8, 130.2, 130.04, 130.02, 129.7, 129.6, 129.5, 129.44, 129.42, 129.11, 129.07, 129.0, 128.3, 128.2, 128.1, 127.7, 127.6, 127.2, 127.1, 127.0, 126.8, 126.71, 126.69, 126.6, 126.5, 126.28, 126.27, 126.1, 126.0, 125.4, 20.8 (P*CH*$_3$), 20.4 (P*CH*$_3$) ppm; ^{31}P NMR (243 MHz, $CDCl_3$) δ 44.2, 39.8 ppm; *m/z* (% intensity) [**MH**]$^+$ 625.5 (100), [**MH**+1]$^+$ 626.5. (50), [**MH**+2]$^+$ 627.5 (20); HRMS calcd for [**MH**]$^+ = C_{39}H_{31}P_2S_2$ 625.1342; found 625.1326.

4.2.2. 2-(*o*-Anisylphenylphosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl 12

Diastereomer A 1st elute: 98 mg, 8.3% yield; $[\alpha]_D = +56.6$ (*c* 0.5, CH_2Cl_2); IR (KBr, cm^{-1}) 707, 1095, 1269, 1432, 1470, 1632, 2361, 3950, 3445.; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02–7.90 (m, 3H, Ar*H*), 7.74–7.54 (m, 8H, Ar*H*), 7.45–7.27 (m, 10H, Ar*H*), 7.13 (m, 4H, Ar*H*), 7.01 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.85 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.72 (dd, *J* = 7.8, 5.6 Hz, 1H, Ar*H*), 6.59 (t, *J* = 7.2 Hz, 1H, Ar*H*), 6.35 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.26 (t, *J* = 7.6 Hz, 1H, Ar*H*), 3.43 (s, 3H, OC*H*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) (P–C decoupled) δ 159.8 (*C*OMe), 141.3, 139.5, 136.9, 136.2, 134.5, 134.0, 133.9, 133.7, 133.3, 133.2, 133.11, 133.07, 132.8, 132.50, 132.46, 132.1, 131.6, 131.2, 130.7, 130.5, 130.1, 123.0, 129.6, 128.4, 128.1, 127.9, 127.8, 127.55, 127.45, 127.4, 127.2, 126.9, 126.4, 125.94, 125.90, 125.7, 125.03, 124.99, 121.2, 118.0, 110.3, 110.0, 54.5 (O*CH*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8 (*C*OMe), 141.3, 139.5, 136.9, 136.8, 136.5, 135.9, 134.8, 134.2, 134.00, 133.99, 133.92, 133.90, 133.73, 133.72, 133.5, 133.3, 133.3, 133.2, 133.1, 133.0, 132.9, 132.8, 132.54, 132.47, 131.7, 131.6, 131.3, 131.2, 130.8, 130.7, 130.47, 130.45, 130.3, 130.2, 130.1, 130.04, 129.97, 129.64, 129.56, 128.4, 128.24, 128.17, 128.1, 127.9, 127.83, 127.75, 127.5, 127.4, 127.3, 127.2, 126.88, 126.87, 126.4, 126.0, 125.9, 125.7, 125.0, 121.3, 121.2, 118.3, 117.7, 110.01, 109.97, 105.0, 54.5 (O*CH*$_3$) ppm; ^{31}P NMR (243 MHz, $CDCl_3$) δ 43.5, 41.9 ppm. *m/z* (% intensity) [**MH**]$^+$ 717.6 (100), [**MH+1**]$^+$ 718.5 (50); HRMS calcd for [**MH**]$^+ = C_{45}H_{35}OP_2S_2$ 717.1605; found 717.1605.

Diastereomer B 2nd elute: 131 mg, 11% yield; $[\alpha]_D = -43$ (*c* 0.5, CH_2Cl_2); IR (KBr, cm^{-1}) 707, 1096, 1272, 1470, 1636, 2360, 3052, 3462; ^1H NMR (600 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 12.8, 7.8 Hz, 2H, Ar*H*), 7.73 (m, 3H, Ar*H*), 7.67–7.60 (m, 4H, Ar*H*), 7.55–7.40 (m, 3H, Ar*H*), 7.37 (dd, *J* = 13.5, 7.6 Hz, 2H, Ar*H*), 7.33–7.28 (m, 2H, Ar*H*), 7.23–7.16 (m, 4H, Ar*H*), 7.14 (t, *J* = 7.0 Hz, 1H, Ar*H*), 7.09 (dd, *J* = 7.4, 5.1 Hz, 2H, Ar*H*), 6.99–6.86 (m, 6H, Ar*H*), 6.51 (s, 2H, Ar*H*), 3.65 (s, 3H, OC*H*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$)(P-C decoupled) δ 160.4 (*C*OMe), 139.7, 139.6, 134.7, 134.6, 134.1, 133.7, 133.5, 133.3, 133.2, 132.9, 132.82, 132.77, 132.3, 132.22, 132.18, 132.1, 131.9, 130.6, 130.2, 130.10, 130.06, 123.0, 129.53, 128.45, 128.0, 127.9, 127.7, 127.6, 127.50, 127.48, 127.42, 127.37, 127.3, 127.2, 127.13, 127.08, 126.9, 126.12, 126.08, 125.0, 123.9, 120.8, 112.3, 55.7 (O*CH*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.4 (*C*OMe), 139.7, 139.6, 134.7, 134.6, 134.2, 134.1, 133.72, 133.70, 133.6, 133.50, 133.48, 133.32, 133.30, 133.2, 133.0, 132.9, 132.8, 132.3, 132.2, 132.18, 132.15, 131.6, 130.57, 130.55, 130.5, 130.19, 130.17, 130.07, 130.05, 130.0, 129.9, 129.8, 129.3, 128.5, 128.4, 128.1, 127.98, 127.95, 127.9, 127.7, 127.6, 127.5, 127.4, 127.26, 127.23, 127.14, 127.09, 126.9, 126.1, 125.0, 124.1, 123.6, 120.8, 120.7, 112.29, 112.25, 55.7 (O*CH*$_3$) ppm; ^{31}P NMR (243 MHz, $CDCl_3$) δ 43.8, 40.4 ppm; *m/z* (% intensity) [**MH**]$^+$ 717.6 (100), [**MH+1**]$^+$ 718.5 (50) .

4.2.3. 2-(*o*-Tolylphenylphosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl 13

Crude mixture: ^{31}P NMR (162 MHz, $CDCl_3$) δ 43.61, 42.51, 41.80, 41.05 ppm; *m/z* (% intensity) phosphine oxide/sulfide [**MH**]$^+$ 685.7 (100), bisphosphine sulfide [**MH**]$^+$ 701.4 (100), [**MH+1**]$^+$ 702.7 (50).

4.2.4. (*R*)-2-(Bisanisylphosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl 14

$[\alpha]_D = -61$ (*c* 1, CH_2Cl_2); IR (KBr, cm^{-1}) 470, 500, 6923, 7477, 1020, 1959, 2278, 2929, 3051, 5446; (very broad peaks were observed in all NMRs, notably some peaks were not visible in ^{13}C as a result) ^1H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.84–6.10 (m, 29H, Ar*H*), 3.95 (s, 3H, OC*H*$_3$), 3.40 (s, 3H, OC*H*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) (P–C decoupled) δ 159.8 (*C*OMe), 136.7, 133.9, 133.6, 133.2, 133.1, 133.0, 132.6, 132.0, 131.3, 130.5, 130.2 129.83, 127.82, 127.6, 127.4, 127.3, 127.1, 127.0, 126.7, 125.0, 124.9, 123.2, 121.1, 120.4, 110.2, 109.8, 54.5 , 29.7 ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8, 140.9, 136.7, 134.8, 133.91, 133.89, 133.7, 133.6, 133.1, 133.01, 132.94, 132.7, 132.1, 132.0, 131.4, 131.3, 130.6, 130.5, 130.2, 129.9, 129.8, 128.1, 127.9, 127.74, 127.66, 127.5, 127.4, 127.14, 127.05, 126.7, 125.5, 125.4, 124.9, 123.6, 123.0, 121.1, 120.4, 119.7, 119.6, 113.0, 109.82, 109.78, 54.5 (O*CH*$_3$), 29.7 (O*CH*$_3$) ppm; ^{31}P NMR (243 MHz, $CDCl_3$) δ 42.0, 39.0 ppm; *m/z* (% intensity) [**MH**]$^+$ 747.6 (100) [**MH +1**]$^+$ 748.6 (50); HRMS calcd for [**MH**]$^+ = C_{46}H_{37}O_2P_2S_2$ 747.1710; found 747.1689.

4.2.5. (*R*)-2-(Bis-*o*-tolylphosphinothioyl)-2′-(diphenylphosphinothioyl)-1,1′-binaphthyl 15

Analysis of the crude material: $[\alpha]_D = +26.5$ (*c* 1, CH_2Cl_2); IR (KBr, cm^{-1}) 713, 1096, 1434, 1630, 2342, 3050, 3435.; ^1H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.2 Hz, 2H, Ar*H*), 7.85–7.65 (m, 5H), 7.58 (d, *J* = 10.2 Hz, 1H, Ar*H*), 7.53–7.42 (m, 3H, Ar*H*), 7.41–7.26 (m, 6H, Ar*H*), 7.22 (d, *J* = 5.9 Hz, 3H, Ar*H*), 7.15 (d, *J* = 24.8 Hz, 2H, Ar*H*), 6.96 (dd, *J* = 25.1, 19.2 Hz, 3H, Ar*H*), 6.74 (s, 1H, Ar*H*), 6.60 (s, 1H, Ar*H*), 6.53–6.29 (m, 3H, Ar*H*), 3.02 (s, 3H, C*H*$_3$), 1.98 (s, 3H, C*H*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) (P–C decoupled) δ 144.0, 143.0, 140.9, 140.5, 137.1, 135.8, 134.7, 134.0, 133.77, 133.2, 133.1, 132.8, 132.71, 132.65, 132.2, 131.9,131.4, 131.3, 131.1, 130.6, 130.4, 129.8, 129.5, 129.4, 128.5, 128.3, 128.21, 128.16, 127.83, 127.79, 127.75, 127.4, 127.3, 127.12, 127.10, 126.8, 126.4, 126.1, 125.6, 125.36, 125.31, 110.3, 107.4, 24.7 (*C*H$_3$), 24.0 (*C*H$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.2, 153.1, 144.0, 143.0, 140.9, 140.8, 140.5, 137.3, 136.7, 135.7, 134.72, 134.66, 134.2, 134.0, 133.7, 133.2, 132.8, 132.7, 132.66, 132.2, 132.2, 131.3, 131.1, 131.0, 130.6, 130.5, 130.4, 129.8, 129.7, 128.8, 128.23, 128.15, 127.8, 127.7, 127.39, 127.37, 127.34, 127.28, 127.1, 126.8, 126.4, 126.0, 125.6, 125.5, 125.4, 125.3, 105.0, 24.7 (*C*H$_3$), 24.0 (*C*H$_3$) ppm; ^{31}P NMR (121 MHz, $CDCl_3$) δ 43.6, 41.1 ppm; *m/z* (% intensity) [**MH**]$^+$ 715.6 (100), [**MH+1**]$^+$ 716.6 (50,), [**MH+2**]$^+$ 717.6 (20); HRMS calcd for [**MH**]$^+ = C_{46}H_{37}P_2S_2$ 715.1812; found 715.1834.

4.2.6. Synthesis of (+)-2-cyclohexylphenylphosphinyl-2′ ((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl 16

A modified version of the procedure reported by Hayashi et al. was employed.[3] The solid reagents (*R*)-2,2′-bis((trifluoromethanesulfonyl)oxy)-1,1′-binaphthyl (1.0 g, 1.8 mmol, 1.0 equiv), cyclohexylphenylphosphine oxide (0.75 g, 3.63 mmol, 2.00 equiv), palladium diacetate (31 mg, 0.2 mmol, 0.1 equiv), and bis(diphenylphosphino)butane (78.0 mg g, 0.73 mmol, 0.10 equiv) were charged to a flame dried 250 mL round bottomed flask under a N_2 atmosphere. The flask was charged with dry degassed dimethyl sulfoxide (30 mL). Next, N_2 was bubbled through the solution for 30 min after which diisopropylethylamine (1.25 mL, 0.93 g, 7.23 mmol, 4.00 equiv) was added. This was stirred for 16 h on a 100 °C oil bath. The solution turned a dark red colour. The progress of the reaction was monitored by ^{19}F NMR. When the reaction was deemed complete, it was allowed to cool to 60 °C and the solvent was removed in vacuo. The dark red residue was dissolved in diethyl ether (30 mL) and was washed with H_2O (3 × 10 mL). The aqueous layers were combined and extracted with diethyl ether (20 mL). The organic layers were combined and dried over Mg_2SO_4. The solvent was removed in vacuo to give the crude product as a yellow solid. This was purified by column chromatography (2:1 ethyl acetate: cyclohexane) to give the product diastereomers as an off-white solid. Crystals were obtained of the (*R,R*)-diastereomer by slow evaporation of DCM from a solution of the diastereomer.

(*R,R*)-Diastereomer: 0.32 g 33% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 8.21–8.07 (m, 2H, ArH), 8.01 (d, J = 9.1 Hz, 1H, ArH), 7.98–7.89 (m, 2H, ArH), 7.51 (dd, J = 11.1, 3.9 Hz, 1H, ArH), 7.48–7.40 (m, 1H, ArH), 7.36 (d, J = 9.1 Hz, 1H, ArH), 7.32–7.21 (m, 2H, ArH), 7.17–6.97 (m, 6H, ArH), 6.74 (d, J = 8.5 Hz, 1H, ArH), 1.42 (s, 10H, CH2) ppm; ^{31}P NMR (121 MHz, CDCl) δ 33.4 ppm (lit.[13] 34.6); ^{19}F NMR (282 MHz, $CDCl_3$) δ −75.2 ppm.

(*R,S*)-Diastereomer: 0.25 g 23% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (t, J = 9.2 Hz, 1H, ArH), 7.99 (d, J = 7.6 Hz, 1H, ArH), 7.87 (d, J = 9.1 Hz, 1H, ArH), 7.79 (d, J = 8.0 Hz, 1H, ArH), 7.69 (d, J = 8.2 Hz, 1H, ArH), 7.36 (d, J = 9.1 Hz, 2H, ArH), 7.22 (ddd, J = 12.8, 11.7, 7.6 Hz, 3H, ArH), 7.14–7.05 (m, 1H, ArH), 7.05–6.83 (m, 5H, ArH), 6.76 (d, J = 8.5 Hz, 1H, ArH), 1.90 (s, 10H, ArH) ppm; ^{31}P NMR (121 MHz, $CDCl_3$) δ 34.5 ppm (lit.[13] 35.7); ^{19}F NMR (282 MHz, $CDCl_3$) δ −74.8 ppm.

Acknowledgement

This research was partly supported by the Science Foundation Ireland under grant 06/RFP/CHO013.

References

1. Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345–350.
2. Noyori, R. *Acta Chem. Scand.* **1996**, *50*, 380–390.
3. Uozumi, Y.; Tanahashi, A.; Lee, S. Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945–1948.
4. Uozumi, Y.; Kawatsura, M.; Hayashi, T. *Org. Synth.* **2002**, *78*, 1–7.
5. Imamoto, T.; Sugita, K.; Yoshida, K. *J. Am. Chem. Soc.* **2005**, *127*, 11934–11935.
6. Pellissier, H. *Tetrahedron* **2007**, *63*, 1297–1330.
7. Lam, F. L.; Kwong, F. Y.; Chan, A. S. C. *Chem. Commun.* **2010**, *46*, 4649–4667.
8. Sen-ichi, A.; Mitsuyoshi, T.; Sakuma, M.; Kubo, A. *Chem. Lett.* **2007**, *36*, 130.
9. Aizawa, S.-i.; Majumder, A.; Yokoyama, Y.; Tamai, M.; Maeda, D.; Kitamura, A. *Organometallics* **2009**, *28*, 6067–6072.
10. Hayashi, M.; Takezaki, H.; Hashimoto, Y.; Takaoki, K.; Saigo, K. *Tetrahedron Lett.* **1998**, *39*, 7529–7532.
11. Faller, J. W.; Wilt, J. C.; Parr, J. *Org. Lett.* **2004**, *6*, 1301–1304.
12. Faller, J. W.; Wilt, J. C. *Org. Lett.* **2005**, *7*, 633–636.
13. Faller, J. W.; Wilt, J. C. *Organometallics* **2005**, *24*, 5076–5083.
14. Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2567–2568.
15. Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946–5952.
16. Knowles, W. S.; Sabacky, M. J.; Vinyard, B. D. *J. Chem. Soc., Chem. Commun.* **1972**, 10–11.
17. Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998–2007.
18. Taylor, A. M.; Altman, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 9900–9901.
19. Hamada, T.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 999–1001.
20. Rubio, M.; Vargas, S.; Suárez, A.; Álvarez, E.; Pizzano, A. *Chem. Eur. J.* **2007**, *13*, 1821–1833.
21. Rubio, M.; Suarez, A.; Alvarez, E.; Bianchini, C.; Oberhauser, W.; Peruzzini, M.; Pizzano, A. *Organometallics* **2007**, *26*, 6428–6436.
22. Higham, L. J.; Clarke, E. F.; Muller-Bunz, H.; Gilheany, D. G. *J. Organomet. Chem.* **2005**, *690*, 211–219.
23. Kerrigan, N. J.; Dunne, E. C.; Cunningham, D.; McArdle, P.; Gilligan, K.; Gilheany, D. G. *Tetrahedron Lett.* **2003**, *44*, 8461–8465.
24. Gladiali, S.; Dore, A.; Fabbri, D.; Medici, S.; Pirri, G.; Pulacchini, S. *Eur. J. Org. Chem.* **2000**, 2861–2865.
25. Cho, S. Y.; Shibasaki, M. *Tetrahedron Lett.* **1998**, *39*, 1773–1776.
26. Kurz, L.; Lee, G.; Morgans, D.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321–6324.
27. Botman, P. N. M.; Fraanje, J.; Goubitz, K.; Peschar, R.; Verhoeven, J. W.; van Maarseveen, J. H.; Hiemstra, H. *Adv. Synth. Catal.* **2004**, *346*, 743–754.
28. Michaelis, A.; Kaehne, R. *Ber. Deut. Chem. Gesell.* **1898**, *31*, 1048–1055.
29. Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180–7181.
30. Shimizu, H.; Nagasaki, I.; Saito, T. *Tetrahedron* **2005**, *61*, 5405–5432.
31. Mitterhofer, F.; Schindlbauer, H. *Monatsh. Chem.* **1967**, *98*, 206–213.
32. Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.
33. Strohmeier, W.; Müller, F.-J. *Chem. Ber.* **1967**, *100*, 2812–2821.
34. Chapman, C. J.; Frost, C. G.; Gill-Carey, M. P.; Kociok-Köhn, G.; Mahon, M. F.; Weller, A. S.; Willis, M. C. *Tetrahedron: Asymmetry* **2003**, *14*, 705–710.
35. Wu, H.-C.; Yu, J.-Q.; Spencer, J. B. *Org. Lett.* **2004**, *6*, 4675–4678.
36. Lei, Z.-Y.; Ma, G.-N.; Shi, M. *Eur. J. Org. Chem.* **2008**, *2008*, 3817–3820.
37. Mitterhofer, F.; Schindlbauer, H. *Monatsh. Chem.* **1967**, *98*, 206–213.
38. Harwood, L. M.; Moody, C. J.; Percy, J. M. *Experimental Organic Chemistry*, 2nd ed.; Blackwell Science Ltd: England, 1999.
39. Busacca, C. A.; Lorenz, J. C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; Shen, S.; Varsolona, R.; Wei, X.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 4277–4280.