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Efficient oxidative resolution of a *P*-stereogenic triarylphosphine and asymmetric synthesis of a *P*-stereogenic atropoisomeric biphenyl diphosphine dioxide

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Dedicated to Professor Henri Kagan on the occasion of his 80th birthday

ABSTRACT

Racemic 3-methoxyphenyl(1-naphthyl)phenylphosphine **1** was effectively resolved via an oxidative resolution procedure utilizing L-menthyl bromoacetate as the resolving agent to give enantiopure 3-methoxyphenyl(1-naphthyl)phenylphosphine oxide (*R*)-**2** in 41% yield. Reduction of the resolved (*R*)-**4** with $HSiCl_3/NEt_3$ provided the corresponding phosphine (*R*)-**1** in >97% ee. *Ortho*-iodination of the enantiopure (*R*)-**4** followed by Ullmann coupling of the resulting iodoarylphosphine oxide gave a *P*-stereogenic and atropoisomeric biphenyl diphosphine dioxide as a single diastereoisomer. The latter transformation constitutes the first example of an effective transfer of a *P*-centered chirality to an axial chirality of the atropoisomeric biaryl system. The absolute configurations of the resolved phosphine and the atropoisomeric biaryl system have also been established.

1. Introduction

Over the past three decades, great progress has been made in the field of asymmetric catalysis by using homogeneous catalysts based on transition metal complexes modified by chiral phosphine ligands.[1] These chiral ligands generally fall into three main categories: ligands possessing stereogenic phosphorus centers;[2] ligands containing stereogenic carbon centers;[3] and ligands with axial[4] or planar[5] chirality. A number of hybrid ligands possessing both stereogenic phosphorus and stereogenic carbon centers have been synthesized,[6] but those which bear both axial chirality and a stereogenic phosphorus are still very rare.[7]

Most of the chiral phosphine ligands utilized in asymmetric catalysis have been bidentate ligands. In recent years, however, a growing interest in the use of chiral monophosphine ligands has also been observed.[8] However, phosphines with stereogenic phosphorus centers are relatively difficult to obtain in a nonracemic form.[9] This remains especially true for *P*-stereogenic triarylphosphines which despite their closest structural analogy to the parent icon ligand, triphenylphosphine, have not been yet made accessible in a practical way.[10]

Herein, we report an efficient gram-scale oxidative resolution of a model triarylphosphine, that is, 3-methoxyphenyl(1-naphthyl)phenylphosphine **1**. The use of the derived enantiopure *P*-stereogenic 3-methoxyphenyl(1-naphthyl)phenylphosphine oxide **4** as a chiral substrate for the asymmetric synthesis of an atropoisomeric biphenyl diphosphine dioxide providing the first case of a highly efficient transfer of *P*-centered chirality to an axial chirality of the atropoisomeric biphenyl system will also be described.

2. Results and discussion

Racemic **1** was conveniently synthesized by the sequential treatment of dichlorophenylphosphine with 1-naphthylmagnesium bromide at −5 °C followed by *m*-anisylmagnesium bromide at −5 to 36 °C under an inert atmosphere. Crystallization of the crude, oily product from ethanol afforded crystalline phosphine **1** in 61% yield. For the resolution of *rac*-**1** we decided to use our oxidative resolution protocol which we previously applied successfully for the resolutions of monocyclic and bicyclic phospholenes.[11] The resolution protocol developed for *rac*-**1** is delineated in Scheme 1.

Racemic phosphine **1** was reacted with L-menthyl bromoacetate to give an equimolar mixture of the two *P*-epimeric phosphonium bromides **2** (96%) in the form of an oil. Attempts to crystallize these oily bromides from a variety of solvents were unsuccessful.

The replacement of the bromide anion in **2** with hexafluorophosphate anion by metathesis with ammonium hexafluorophosphate followed by washing off ammonium bromide resulted in the formation of oily phosphonium hexafluorophosphate salts **3**. This time, however, upon dissolution in warm ethanol the oily phosphonium salts **3** yielded white crystals which consisted mainly of one *P*-epimeric salt **3**. A single recrystallization of the crystals from the same solvent furnished pure *P*-epimer of **3** of practically 100% diastereomeric purity (NMR) and in a remarkable

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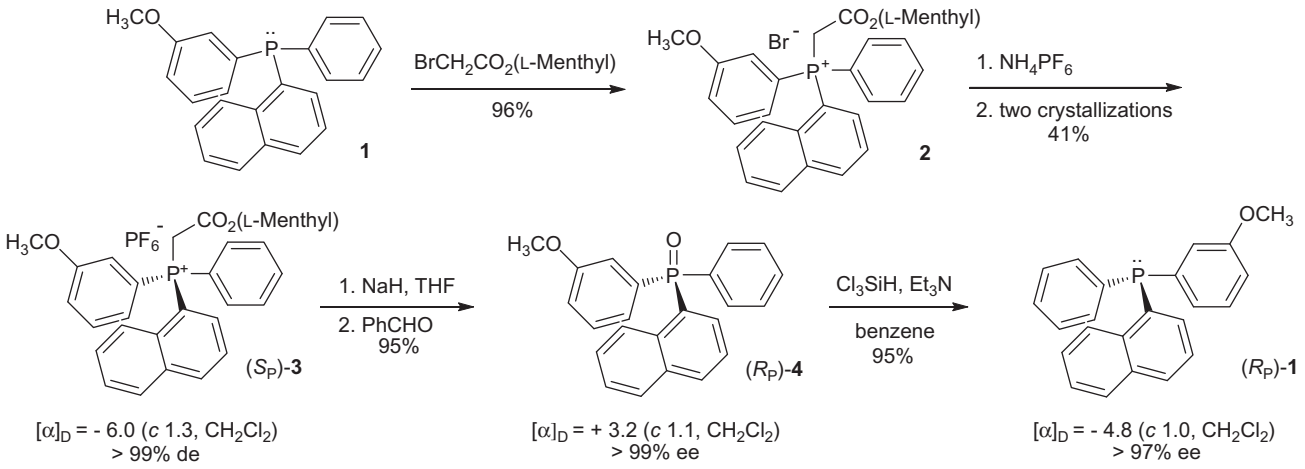


Scheme 1. Resolution of *rac*-**1**.

41% yield (82% calculated for one *P*-epimer). The absolute configurations at *P* in the phosphonium salts **3** were assigned on the basis of the single crystal X-ray diffraction study of the resolved more crystalline *P*-epimer **3**. The X-ray structure of the resolved crystalline **3** showing also its (S_P)-absolute configuration is presented in Figure 1.

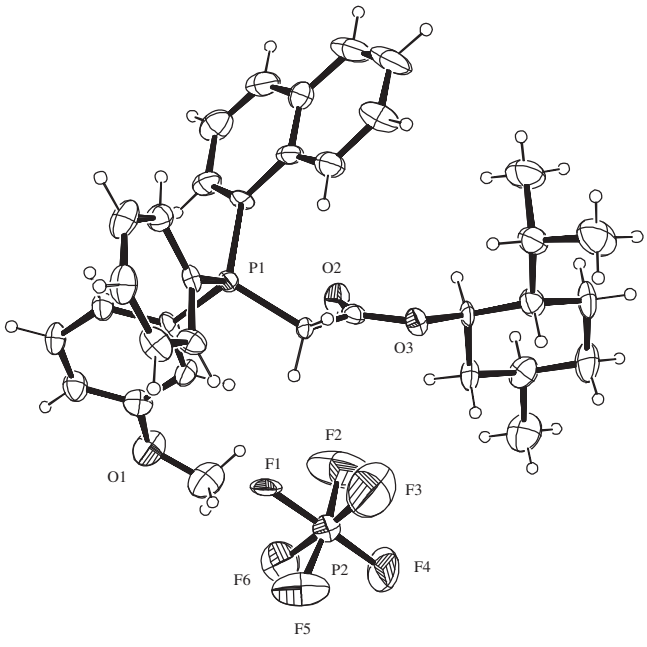
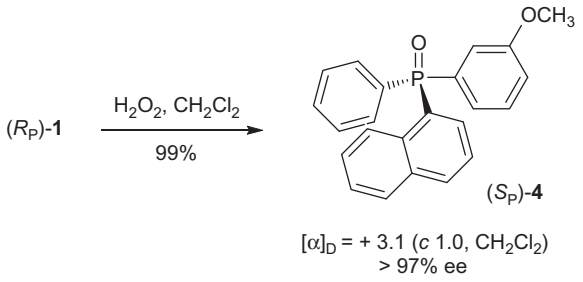


Figure 1. ORTEP drawing of (S_P)-**3** drawn with 30% probability ellipsoids, except for the hydrogen atoms which are represented as spheres of arbitrary size.

Removal of the auxiliary L-menthyl acetate moiety from the resolved (S_P)-**3** was accomplished by means of the stereochemically well-behaved Wittig reaction by the treatment of (S_P)-**3** with NaH and benzaldehyde, which afforded virtually enantiopure (R_P)-**4**[12] in 95% yield and with the retention of configuration at *P*.[13]

Reduction of (R_P)-**4** by Cl_3SiH/Et_3N proceeded with high stereoselectivity and with inversion of configuration at *P* and eventually gave the resolved phosphine (R_P)-**1** in 95% yield and in >97% ee. The enantiomeric excess of (R_P)-**1** as well as its absolute configuration was established through the correlation with the enantiopure oxide **4** in which the phosphine was converted in a single step by oxidation with H_2O_2, known to occur with complete retention of configuration at *P*.[14] The correlation is shown in Scheme 2 and supports the expected assignment of the R_P configuration to the resolved phosphine **1**.



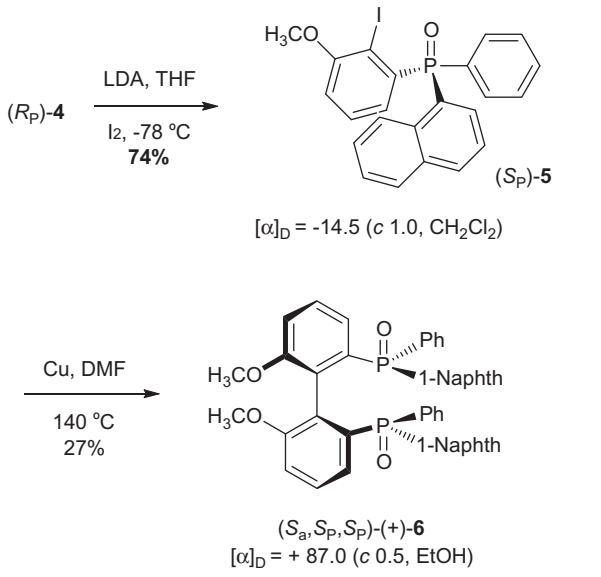
Scheme 2. Correlation of the absolute configuration of (R_P)-(−)-**1** with (S_P)-(−)-**4**.

The successful preparation of the enantiopure *P*-stereogenic triarylphosphine oxide containing an *m*-anisyl substituent at *P* opened the way to the synthesis of the atropoisomeric biaryl diphosphine dioxide system that bears both axial chirality and stereogenic phosphorus centers. Following the procedure described by Schmid et al.[4e] for the synthesis of the MeO-BIPHEP ligand, (R_P)-**4** was *ortho*-metallated by treatment with LDA at a low temperature and then reacted with iodine to furnish aryl iodide (S_P)-**5** in 74% yield (Scheme 3). Coupling of (S_P)-**5** under Ullmann conditions[15] gave the expected biphenyl diphosphine dioxide **6** in only 27% yield, but in the form of a single diastereoisomer.[16] The rest of the isolated material was identified as (R_P)-**4**, which apparently resulted from deiodination of the substrate under the reaction conditions. The observed difficulty of coupling of (S_P)-**6** could be associated with considerable steric crowding of the system bearing very large tertiary 1-naphthylphosphine oxide groups at the *ortho*-positions.

The absolute configuration of the coupled product was assigned by the single crystal X-ray diffraction study, which revealed the (S_a)-absolute chirality of its biphenyl axis (Fig. 2). It is worth stressing that the observed asymmetric coupling of (R_P)-**5** to (S_a,S_P,S_P)-**6** with virtually 100% asymmetric induction is remarkable as it constitutes the first case of an efficient transfer of the *P*-centered chirality to the axial chirality of the atropoisomeric biaryl system.

3. Conclusion

In conclusion, we have developed a practical procedure for the resolution of a *P*-stereogenic 3-methoxy(1-naphthyl)phenylphos-



Scheme 3. Synthesis of atropoisomeric biphenyl diphosphine dioxide (S_a,S_P,S_P)-**6** by means of asymmetric Ullmann coupling.

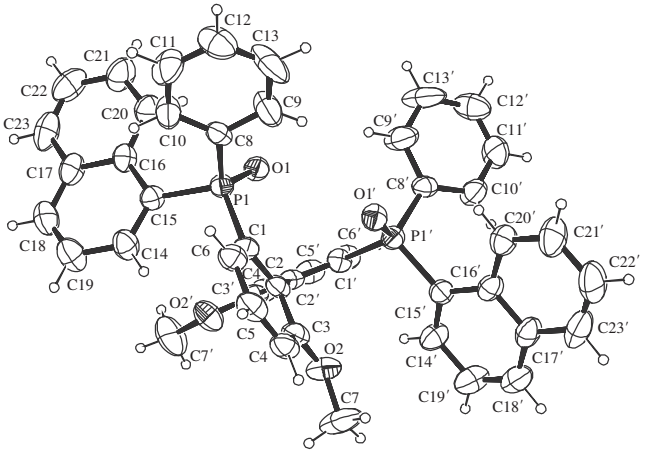


Figure 2. ORTEP drawing of (S_a,S_P,S_P)-**6** drawn with 30% probability ellipsoids, except for the hydrogen atoms which are represented as spheres of arbitrary size.

phine. The resolution was accomplished by fractional crystallization of its diastereomeric L-menthoxycarbonylmethylphosphonium salts. The resolved diastereomerically pure salt, (S_P)-**3**, was then transformed into enantiopure phosphine (R_P)-**1** by the Wittig process followed by silane reduction of the intermediate enantiopure phosphine oxide (R_P)-**4**. The enantiopure (R_P)-**4** was used as a substrate for the highly effective asymmetric synthesis of the atropoisomeric and *P*-stereogenic biphenyl diphosphine by a procedure involving *ortho* iodination of the anisyl ring followed by the Ullmann coupling of the resulting aryl iodide. The first efficient transfer of the *P*-centered chirality to the axial chirality of the atropoisomeric biaryl system was thus accomplished. Efforts to generalize the developed resolution procedure to other triarylphosphines as well as to synthesize other *P*-stereogenic atropoisomeric bidentate ligands are currently in progress.

4. Experimental

4.1. General

The reagents were purchased from commercial suppliers and used without further purification. Solvents were dried and distilled under argon before use. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AV400 (^{1}H 300 MHz, ^{31}P 121.5 MHz, ^{13}C 75 MHz) spectrometer. All spectra were obtained in deuterochloroform solutions, unless mentioned otherwise, and the chemical shifts δ are expressed in ppm using internal reference to TMS and external reference to 85% H_3PO_4 in D_2O for ^{31}P. Coupling constants (J) are given in Hertz. The abbreviations of signal patterns are as follows: s—singlet, d—doublet, t—triplet, q—quartet, m—multiplet, b—broad, i—intensive. Mass spectra (MS) were run on AMD-604 spectrometer with a standard ionization potential 70 eV (EI MS). Infrared spectra were recorded on a Perkin–Elmer Spectrum 2000 spectrometer. Elemental analyses were measured on the Perkin–Elmer CHN 2400. Optical rotations were measured on a Perkin–Elmer 341LC digital polarimeter. Thin-layer chromatography (TLC) was done on silica gel (Kieselgel 60, F254 on aluminum sheet, Merck). All column chromatographic separations and purifications were conducted by using Merck Slica Gel 60 (230–400 mesh), unless noted otherwise.

4.2. 3-Methoxyphenyl(1-naphthyl)phenylphosphine *rac*-1

At first, 3.4 g (0.14 mol) of magnesium was suspended in 100 mL of dry diethyl ether under argon in a 2 L four-necked flask equipped with a condenser, thermometer, mechanical stirrer, and a dropping funnel with pressure compensation. A solution of 29 g (0.14 mol) of 1-bromonaphthalene in 150 mL of diethyl ether was added dropwise to the suspension within 0.5 h. After completion of the addition, the solution was stirred at 35–40 °C for the next 2 h. The reaction mixture was cooled to room temperature and treated dropwise under argon with a solution of 25.1 g (0.14 mol) of dichlorophenylphosphine in 100 mL of diethyl ether at about −5 °C within 1 h. In a separate flask a solution of 31.4 g (0.168 mol) of 3-bromoanisole in 150 mL of diethyl ether was added dropwise to the suspension of 4.1 g of magnesium in 100 mL of diethyl ether under argon within 0.5 h. After the addition the reaction mixture was stirred at 35–40 °C for further 2 h. The resulting Grignard solution was cooled to room temperature and added dropwise within 1 h at −5 °C to the solution of chloro(1-naphthyl)phenylphosphine obtained above. After an additional stirring period of 1 h at about 0 °C the reaction mixture was heated at 35–40 °C for a further 2 h. Subsequently, 350 mL of 30% aq NH_4Cl was added through a dropping funnel with vigorous stirring. The aqueous phase was separated and extracted with 200 mL of dichloromethane. The combined organic phases were washed with 200 mL of water and dried over anhydrous magnesium sulfate, filtered, and evaporated to yield a yellow oil. The oil was dissolved in 300 mL of a mixture of warm ethanol and hexane and cooled in a refrigerator. The white crystals obtained were filtered and washed twice with 50 mL of ethanol and dried in vacuum, The overall yield of 3-methoxyphenyl(1-naphthyl)phenylphosphine was 29.4 g (61.3%). Mp = 107–109 °C. Anal. Calcd for $C_{23}H_{19}OP$ (342.37): C, 80.69; H, 5.59. Found: C, 80.59; H, 5.55. ^{31}P NMR (121.5 MHz) δ −13.10 (s). ^{1}H NMR (300 MHz) δ 3.69 (s, 3H), 6.85–8.49 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ) 159.7 (d, J = 7.5 Hz); 138.0 (d, J = 7.5 Hz); 136.3 (d, J = 7.5 Hz); 135.4 (d, J = 15 Hz); 134.5 (d, J = 15 Hz); 134.3 (d, J = 22.5 Hz); 133.5 (d, J = 7.5 Hz); 132.2; 129.7 (d, J = 7.5 Hz); 129.6; 128.8 (d, J = 15 Hz); 128.7 (d, J = 7.5 Hz); 126.7; 126.5; 126.4; 126.3; 126.1; 126.1; 125.7; 125.7; 119.6 (d, J = 22.5 Hz); 114.6; 55.2.

4.3. (2-Isopropyl-5-methylcyclohexyloxycarbonylmethyl) (methoxyphenyl) (naphthalen-1-yl)phenylphosphonium bromide 2 and (2-isopropyl-5-methylcyclohexyloxy carbonylmethyl) (3-methoxyphenyl) (naphthalen-1-yl)phenyl phosphonium hexafluorophosphate (S_P)-3

A solution of 15.25 g (0.055 mol) of L-menthyl bromoacetate in 50 mL of dry benzene was added dropwise to 18.5 g (0.054 mol) of

3-methoxyphenyl(1-naphthyl)phenylphosphine suspended in 200 mL of dry benzene under argon in a Schlenk-type flask. After the addition, the reaction mixture was stirred at 60 °C for further 22 h. Then, 9.6 g (0.06 mol) of ammonium hexafluorophosphate was added portionwise to the reaction mixture cooled to room temperature. After an additional stirring period of 22 h, the reaction mixture was evaporated and 150 mL of CH_2Cl_2 was added. The organic phase was washed twice with 50 mL of water, separated, dried over anhydrous magnesium sulfate, filtered, and evaporated. The resulting yellow oil was dissolved in 250 mL of warm ethanol and slowly cooled to room temperature. The white crystals obtained were filtered, washed twice with 50 mL of ethanol, and dried in vacuum. Additional recrystallization from ethanol gave 14.1 g (41%) of diastereomerically pure (>99% de by NMR) (S_P)-**3**. Mp = 178–179 °C. Anal. Calcd for $C_{35}H_{40}F_6O_3P_2$ (684.63): C, 61.40; H, 5.89. Found: C, 61.31; H, 5.85. $[\alpha]_D = -6.0$ (*c* 1.3, $CHCl_3$). ^{31}P NMR (121.5 MHz) δ 21.29 (s), −144.0 (sept, J = 713 Hz, PF_6^-). ^1H NMR (300 MHz) δ 0.42 (d, J = 7 Hz, 3H), 0.71 (d, J = 7 Hz, 6H), 0.56–1.57(m, 9H), 3.85 (s, 3H), 4.40, 4.41 (dt, J = 11 Hz, J = 4 Hz, 1H), 4.62–4.79 (m, 2H), 7.20–8.32 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ) 163.9; 161.0 (d, J = 22.5 Hz); 138.8 (d, J = 7.5 Hz); 137.4; 135.6; 134.2 (d, J = 15 Hz); 133.9 (d, J = 7.5 Hz); 132.2 (d, J = 15 Hz); 132.0 (d, J = 15 Hz); 130.8 (d, J = 15 Hz); 130.6 (d, J = 7.5 Hz); 129.5; 128.1; 125.8; 125.7 (d, J = 7.5 Hz); 125.2; 121.8 (d, J = 7.5 Hz); 119.9; 118.8 (d, J = 7.5 Hz); 118.2 (d, J = 15 Hz); 117.6; 113.5; 112.3; 78.0; 56.1; 46.4; 39.6; 33.8; 33.6; 32.9; 31.2; 25.7; 22.8; 21.8; 20.8; 15.6.

4.4. 3-Methoxyphenyl(1-naphthyl)phenylphosphine oxide (R_P)-4

A 50% dispersion in oil of 0.75 g (0.155 mol) of sodium hydride was added portionwise to the solution of 10.5 g (0.153 mol) of phosphonium salt in 100 mL dry tetrahydrofurane under argon in a Schlenk-type flask. After completion of the addition to the reaction solution was added dropwise 3.2 g (0.031 mol) of benzaldehyde. After an additional stirring period of 22 h, the reaction mixture was evaporated and 100 mL of CH_2Cl_2 was added. The organic phase was washed twice with 30 mL of water. The organic phase was separated, dried over anhydrous magnesium sulfate, filtered, and evaporated. The resulting crude product was purified by silica gel chromatography with acetone (20%)–dichloromethane (80%) as an eluent to give 5.2 g (95% yield) of >99% enantiomericaly pure[14] 3-methoxyphenyl(1-naphthyl)phenylphosphine oxide (R_P)-**4**. Mp = 143–145 °C. Anal. Calcd for $C_{23}H_{19}O_2P$ (358.37): C, 77.08; H, 5.34. Found: C, 76.71; H, 5.29. $[\alpha]_D = +3.2$ (*c* 1.0, CH_2Cl_2). ^{31}P NMR (121.5 MHz) (δ 32.82 (s). ^1H NMR (300 MHz) (δ 3.79 (s, 3H), 7.05–8.61 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ) 159.8 (d, J = 15 Hz); 134.0; 133.8 (d, J = 15 Hz); 133.4; 132.2 (d, J = 7.5 Hz); 132; 129.7; 128.6 (d, J = 7.5 Hz); 128.7 (d, J = 7.5 Hz); 127.4; 126.6; 124.4 (d, J = 15 Hz); 124.2 (d, J = 15 Hz); 118.3 (d, J = 7.5 Hz); 116.8 (d, J = 15 Hz); 55.5.

4.5. 3-Methoxyphenyl(1-naphthyl)phenylphosphine (R_P)-1

To a solution of 3-methoxyphenyl(1-naphhthyl) phenylphosphine oxide 0.36 g (1 mmol) in dry benzene (25 mL) was added pirydine 0.25 g (3 mmol) followed by dropwise addition of trichlorosilane 0.41 g (3 mmol). The mixture was heated at reflux for 3 h. After cooling to room temperature 30% aq NaOH (12 mL) was added carefully to the opaque mixture, until the organic and aqueous layers became clear. After the separation, the aqueous layer was washed with benzene (2 × 15 mL), combined organic layers were washed with H_2O (3 × 10 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated. The crude product was purified by silica gel chromatography with hexane (40%)–dichloromethane (60%) as eluent to give 0.33 g (95% yield) of (R_P)-**1** of >97% enantiomeric purity (as assigned by stereoretentive reoxidation experiment shown in Scheme 2). Mp = 112 °C. Anal. Calcd for $C_{23}H_{19}OP$ (342.37): C, 80.69; H, 5.59. Found: C, 80.56; H, 5.45. $[\alpha]_D = -4.8$ (*c* 1.0, CH_2Cl_2). ^{31}P NMR (121.5 MHz) δ −13.15 (s). ^1H NMR (300 MHz) δ 3.70 (s, 3H), 6.84–8.43 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ) 159.7 (d, J = 7.5 Hz); 138.0 (d, J = 7.5 Hz); 136.3 (d, J = 7.5 Hz); 135.4 (d, J = 15 Hz); 134.5 (d, J = 15 Hz); 134.3 (d, J = 22.5 Hz); 133.5 (d, J = 7.5 Hz); 132.2; 129.7 (d, J = 7.5 Hz); 129.6; 128.8 (d, J = 15 Hz); 128.7 (d, J = 7.5 Hz); 126.7; 126.5; 126.4; 126.3; 126.1; 126.1; 125.7; 125.7; 119.6 (d, J = 22.5 Hz); 114.6; 55.2.

4.6. 3-Methoxyphenyl(1-naphthyl)phenylphosphine oxide (S_P)-4 from the correlation experiment

To the solution of 3-methoxyphenyl(1-naphthyl)phenylphosphine (R_P)-**1** 0.21 g (0.6 mmol) in CH_2Cl_2 (20 mL) was added 30% aq H_2O_2 (2 mL). The mixture was stirred at room temperature for 24 h. The phases were separated and the organic phase was washed twice with 15 mL of water. The organic phase was separated, dried over anhydrous magnesium sulfate, filtered, and evaporated. The crude product was purified by silica gel chromatography with acetone (20%)–dichloromethane (80%) as eluent to give 0.21 g (99% yield) of >97% enantiomerically pure 3-methoxyphenyl(1-naphthyl)phenylphosphine oxide (S_P)-**4**. Mp = 143–145 °C. Anal. Calcd for $C_{23}H_{19}OP$ (358.37): C, 77.08; H, 5.34. Found: C, 76.71; H, 5.29. $[\alpha]_D = +3.1$ (*c* 1.0, CH_2Cl_2).^{31}P NMR (121.5 MHz) δ 32.82 (s). ^1H NMR (300 MHz) δ 3.79 (s, 3H), 7.05–8.61 (m, 16H). ^{31}P NMR (121.5 MHz) (δ 32.82 (s). ^1H NMR (300 MHz) (δ 3.79 (s, 3H), 7.05–8.61 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ) 159.8 (d, J = 15 Hz); 134.0; 133.8 (d, J = 15 Hz); 133.4; 132.2 (d, J = 7.5 Hz); 132; 129.7; 128.6 (d, J = 7.5 Hz); 128.7 (d, J = 7.5 Hz); 127.4; 126.6; 124.4 (d, J = 15 Hz); 124.2 (d, J = 15 Hz); 118.3 (d, J = 7.5 Hz); 116.8 (d, J = 15 Hz); 55.5.

4.7. 2-Iodo-3-methoxyphenyl(1-naphthyl)phenylphosphine oxide (S_P)-5

To a solution of (i-Pr)$_2$NH 0.31 g (3.05 mmol) in dry THF (2.5 mL) was added n-BuLi (2 mL, 1.6 M solution in hexane) at −78 °C within 15 min. After stirring for 15 min at −78 °C to −40 °C, the LDA solution was cooled again to −78 °C and added, at −78 °C over 20 min, to a flask containing a solution of 3-methoxyphenyl(1-naphthyl)phenylphosphine oxide (R_P)-**4** 1.0 g (2.8 mmol) in dry THF (6 mL). During the addition the mixture turned reddish-brown and eventually a beige suspension was formed. After stirring for an additional 15 min at −78 °C, a solution of I_2 0.77 g (3.03 mmol) in THF (2.8 mL) was added dropwise at −70 °C. Toward the end of the addition, the formation of a reddish-brown viscous paste began. At this point, the mechanical stirrer was stopped, the cooling bath was removed, and the mixture was allowed to the warm to 0 °C to obtain a clear red solution. The reaction was quenched by the addition of an aq $Na_2S_2O_3$ solution. The aqueous phase was washed with ethyl acetate and the combined organic phases were washed with saturated aq NaCl, dried over anhydrous magnesium sulfate, filtered, and evaporated. The crude product was purified by silica gel chromatography with acetone (4%)–dichloromethane (96%) as eluent to give 1.0 g (74% yield) of pure 2-iodo-3-methoxyphenyl(1-naphthyl)phenylphosphine oxide (S_P)-**5**. Mp = 138–140 °C. Anal. Calcd for $C_{23}H_{18}IO_2P$ (484.27): C, 57.04; H, 3.75. Found: C, 57.07; H, 4.21. $[\alpha]_D = -14.5$ (*c* 1.0, CH_2Cl_2). ^{31}P NMR (121.5 MHz) δ 37.30 (s). ^1H NMR (300 MHz) δ 3.91 (s, 3H), 6.76–8.77 (m, 15H). IR (ATR): 3433 (w), 2924 (m), 1562 (s), 1436 (m), 1266 (s), 1188 (s) cm^{-1}.

4.8. (6,6′-Dimethoxybiphenyl-2,2′-diyl)bis(1-naphthyl) phenylphosphine oxide (S_a,S_P,S_P)-6

A mixture of 2-iodo-3-methoxyphenyl(1-naphthyl) phenylphosphine oxide (S_P)-**5** 1 g (2.05 mmol), activated Cu powder 0.4 g (6.2 mmol), and DMF (4 mL) was stirred at 140 °C for 2 h. The cooled mixture was evaporated to dryness on a rotary evaporator. The residue was treated for a few minutes with hot CH_2Cl_2, the solid parts were removed by filtration, and the filtrate was washed with saturated NH_4Cl solution, dried over anhydrous magnesium sulfate, filtered, and evaporated. The crude product was purified by silica gel chromatography with ethyl alcohol (1%)–chloroform (96%) as eluent to give 0.2 g (27% yield) of pure (6,6′-3-dimethoxybiphenyl-2,2′-dyil)bis(1-naphthyl)phenylphosphine oxide (S_a,S_P,S_P)-**6**. Mp = 189–191 °C. Anal. Calcd for $C_{46}H_{36}O_4P_2$ + MeOH (746.77): C, 75.59; H, 5.40. Found: C, 75.43; H, 5.36. MS *m*/*z*: 737 (M^++Na^+). $[\alpha]_D$ = +87.6 (*c* 0.5, EtOH). ^{31}P NMR (121.5 MHz) δ 32.98 (s). ^1H NMR (300 MHz) δ 1.64 (s, 3H), 3.29 (s, 3H), 6.71–8.62 (m, 30H). IR (ATR): 3392 (w), 3005 (m), 1568 (s), 1435 (m) 1259 (s), 1188 (s) cm^{-1}.

4.9. X-ray crystallography

4.9.1. General information

Data sets were collected with a Bruker Kappa Appex II diffractometer using CuKα radiation. CCDC 767605 (S_P)-**3** and CCDC 767838 (S_a,S_P,S_P)-**6** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retriving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44(1223)336 033, E-mail: deposit@ccdc.cam.ac.uk].

4.9.2. X-ray crystal structure analysis of (S_P)-3

Formula $C_{35}H_{40}F_6O_3P_2$, M = 684.63, colorless crystal 0.49 × 0.385 × 0.315 mm, a = 8.945(1), b = 20.195(1), c = 9.932(1) Å, β = 107.25, monoclinic, space group $P2_1$, V = 1713.3(2) $Å^3$, ρ_{calcd} = 1.324 Mg/m^3, μ = 1.733 mm^{-1}, Z = 2, λ = 1.54184 Å, T = 293(2) K, 3786 reflections collected, 2451 independent (R_{int} = 0.054), 2451 observed reflections, 416 refined parameters, R_1 = 0.0757, wR_2 = 0.1898, Flack parameter 0.01(7), residual electron density 0.565 (−0.260) e$Å^{-3}$.

4.9.3. X-ray crystal structure analysis(S_a,S_P,S_P)-6

Formula $C_{46}H_{36}O_4P_2{\cdot}3(CH_2Cl_2)$, M = 969.52, colorless crystal 0.42 × 0.42 × 0.42 mm, orthorhombic, space group $P2_12_12$, a = 15.304(3), b = 18.190(4), c = 8.725(2) Å, V = 2428.9(9) $Å^3$, ρ_{calcd} = 1.326 Mg/m^3, μ = 4.187 mm^{-1}, Z = 2, λ = 1.54178 Å, T = 293(2) K, 3163 reflections collected, 2808 independent (R_{int} = 0.065), 1310 observed reflections, 277 refined parameters, R_1 = 0.0888, wR_2 = 0.2178, Flack parameter −0.09(6), residual electron density 0.345 (−0.430) e$Å^{-3}$.

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