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Practical Preparation and Resolution of 1-(2′-Diphenylphosphino-1′-naphthyl)isoquinoline: A Useful Ligand for Catalytic Asymmetric Synthesis

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Abstract:

A practical synthesis of the atropisomerically chiral ligand QUINAP is described, followed by its efficient resolution into enantiomers by employing a deficiency of the chloropalladium complex derived from 1′-*(R)*-1′-(dimethylamino)-1-ethylnaphthalene. The X-ray structure of the ligand, which crystallises as a conglomerate, is reported.

Introduction

In 1993 we reported the synthesis and resolution of the atropisomeric ligand 1-(2′-diphenylphosphino-1′-naphthyl)-isoquinoline **1**, prepared by a multistage synthesis from 2-methoxynaphthyl-1-boronic acid and 2-chloroisoquinoline.[1] The racemic ligand was resolved by formation of the corresponding diastereomeric complexes with enantiomerically pure dichlorobis[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]dipalladium(II), and fractional crystallisation. Since our early reports of application of the ligand **1** to catalytic asymmetric hydroboration,[2] and allylic alkylation,[3] a variety of uses in catalysis have been reported. These include application to the Ru complex-catalysed hydrogenation of ketones[4] and the control of sterospecificity in alkene/CO copolymerisation catalysed by Pd complexes.[5] In the Cu-catalysed α-alkynylation of enamines by primary acetylenes, ligand **1** proved to be the most effective in screening studies, affording the addition product in typical yields of ≥80% and up to 90% e.e.[6] For the Diels−Alder reaction between cyclopentadiene and methacrolein, a crystallographically characterised Ru−QUINAP complex (one of a pair of diastereomers) catalysed formation of the *exo* product in 91% de and 99% e.e. with $AgSbF_6$ as co-reactant.[7] Examples of the application of QUINAP to diverse catalytic processses have been reported sporadically.[8] The main application has been in asymmetric hydroboration/oxidation, catalysed by its cationic rhodium complexes. The general tendency for biphosphine and phosphinamine complexes that have been applied to this reaction is to provide a successful outcome with monosubstituted vinylarenes; further substitution at the α- or *β*-position of the alkene affords low enantioselectivities, however.[9] With ligand **1** and its close relatives the reaction may be carried out with α,*β*-disubstituted arylalkenes, including bicyclic reactants. Reaction is not limited to the synthesis of alcohols, despite the fact that the initially formed boronic ester is unreactive towards the range of ambiphiles that are typically reactive towards trialkylboranes.[10] The limitation can be overcome by direct B-alkylation of the boronate ester with R_2Zn or RMgX, followed by reacting the resulting trialkylborane with N-electrophiles. This leads to the corresponding primary or secondary amine with complete chemo- and stereoselectivity.[11] A further development of the protocol lies in the kinetic resolution of chiral 4-substituted 1,2-dihydronaphthalenes.[12] The ligand combination has been successfully applied to clay-supported asymmetric hydroboration.[13]

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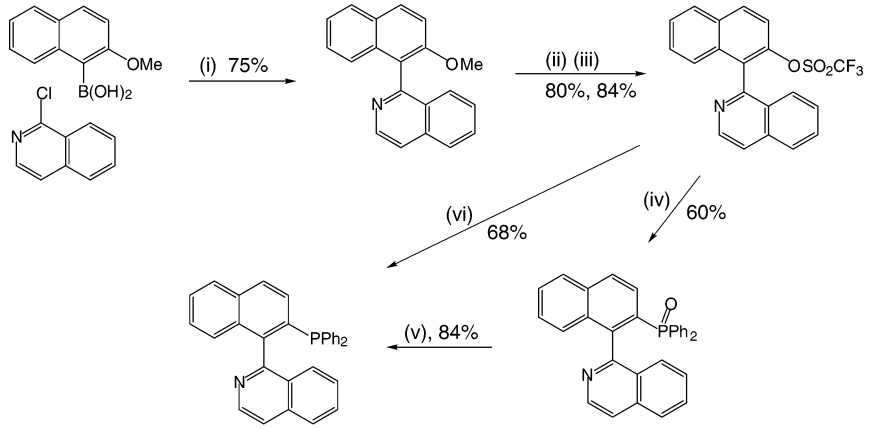
Scheme 1[a]



1 **2**

[a] Conditions: (i) 3 mol% $Pd(Ph_3)_4$ 2 equiv Na_2CO_3; DME reflux. (ii) BBr_3, CH_2Cl_2 (iii) $(CF_3SO_2)O$, xs DMAP, CH_2Cl_2 (iv) 3 mol% Pd(OAc)2 dppp; Ph_2PHO, $NaHCO_3$, DMSO, 85 °C. (v) $HSiCl_3$, NEt_3, C_7H_8, reflux. (vi) Ph_2PH, Cl_2Ni(DPPE), DMF, 100 °C. Current route is (i)−(ii)−(iii)−(vi).

The ability to synthesise functional molecules with a defined stereogenic centre at a benzylic position has potential for considerable application, since that substitution pattern is very common in pharmacology. This provided additional motivation for improvement of the synthesis of compound **1**, so that its catalytic properties could be fully evaluated.[14] The original synthesis is as shown in Scheme 1. Modifications and improvements centered on two aspects—the phosphination step and the resolution. In the course of this work minor changes were made to the preceding steps, and a complete description is therefore recorded in the Experimental Section.

Results and Discussion

The key improvements to the original literature arose from a change in the method of forming the C−P bond and in the details of the resolution procedure. These are recorded in turn.

Phosphination. A particular drawback to the initially published method was that it led initially to the racemic phosphine oxide **2** which then required $HSiCl_3$ reduction to afford the racemic phosphine. With the later advent of direct nickel-catalysed protocols for the phosphination of triflates,[15] a superior alternative was in prospect. The reaction was attempted under the conditions described by Cai and coworkers and initially gave the desired phosphine **1** but was contaminated with up to 15% of the corresponding phosphine oxide **1**. This required careful recrystallisation from $CHCl_3$ or from acetone to remove the impurity. After further experimentation an improved procedure was developed that involved sequential addition of portions of the secondary phosphine PPh_2H to the mixture of triflate, base, and Ni catalyst in hot DMF over several hours. In this way pure ligand **1** was isolated in 68% yield by a simple workup. Following the recommendation that PPh_3 replace dppe in nickel-catalysed reactions of this type, there could be scope for further improvement.[16]

X-ray Structure of Racemic Ligand. In the course of purifying the product from the phosphination reaction, it was observed that the initial reaction product, dissolved in $CHCl_3$, deposited very large single crystals over 7 days (up to 250 mg) that were enantiomerically pure but of random handedness. However, when the recrystallisation process was repeatedly carried out, the number of microscopic crystallisation nuclei increased. As a result the crystals were obtained faster (within 2 days), but their size was greatly decreased. From later batches a crystal suitable for X-ray analysis was grown, and the details are reported in the Experimental Section. The structure is shown in Figure 1, and indicates the chiral space group $P2_1$.

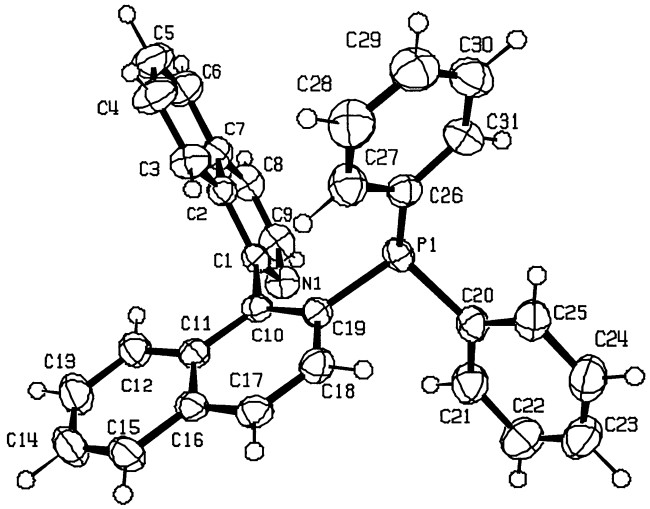


Figure 1. **X-ray structure of (*S*)-1-(2′-diphenylphosphino-1′-naphthyl)isoquinoline, 1. Important bond lengths and angles: P(1)−C(19), 1.8397(15); P(1)−C(20), 1.8403(19); P(1)−C(26), 1.8314(19); N(1)−C(1), 1.319(2); N(1)−C(9), 1.370(3); C(1)−C(10), 1.502(2); C(19)−P(1)−C(20), 98.29(7); C(19)−P(1)−C(26), 102.63(9); C(20)−P(1)−C(26), 103.89(8), P(1)−C(20)−C(21), 115.35(15); P(1)−C(20)−C(25), 125.97(15).**

Refinement of the Flack enantiopole parameter[17] gave a value of −0.04(7), showing the crystal to be the *S*-enantiomer. The

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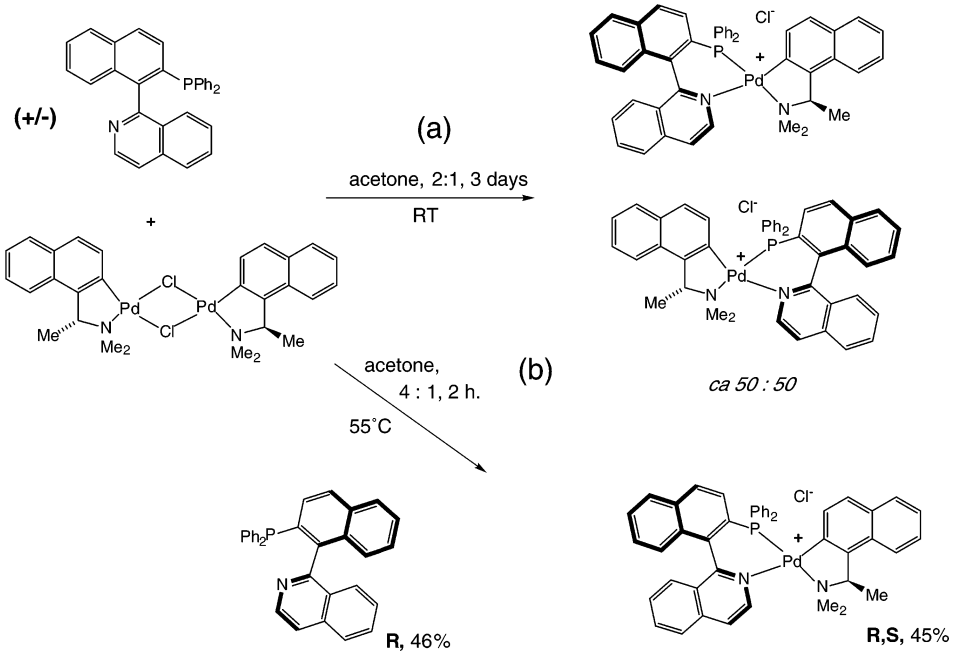
Scheme 2. **Resolution of rac-QUINAP with (*R*)-Pd dimer (a) with 1 equiv of the resolving agent and (b) with 0.5 equiv of the resolving agent as described in the Experimental Section**



dihedral angle between the quinoline and naphthalene rings is 85.3°.

Resolution Procedure. In the course of the original work it was observed that the *R*,*S*-diastereomer of the resolution complex was more stable than the *R*,*R*-diastereomer, an observation reinforced during ES-MS studies.[18] The molecular interactions observed in X-ray structures of the complexes accord with this stability difference.[19] To develop the effect for preparative purposes, excess ligand (2 equiv) was added to the Pd complex and the course of reaction monitored by NMR. In acetone, the isolated product was solely the *R*,*S* diastereomer of complex together with an equivalent of free ligand (Scheme 2). When the solution was made up in CD_2Cl_2 it was observed that both *R*,*R* and *R*,*S* complexes were formed initially in comparable proportions; on standing for 24 h the *R*,*S* isomer gradually became predominant and then exclusive. These experiments defined that the discrimination was due to thermodynamic factors and did not lead to kinetic control of the product ratio. Since the discrimination in favour of the (*R*,*S*)-diastereomer is near-complete and the mass economy of a single-step resolution based on this observation is far greater than one based on complete formation of the Pd complex from both hands of ligand, it was applied in the large-scale procedure using the (*R*)-Pd complex. The recovered phosphine was obtained in 46% yield as pure *R* enantiomer,[20] and the isolated complex was treated with dppe to give pure *S* enantiomer. In this way 20 g of each enantiomer of ligand **1** was obtained in a single synthetic run.

The protocol employed is similar to the "method of half-equivalents" occasionally used in acid−base resolution methodologies and described in detail in standard Stereochemistry texts.[21] Because of the intrinsic dynamic properties of metal complexes, it should find wider application in the resolution of racemic ligands.

Experimental Section

General Details. All reactions were carried out under argon, and HPLC grade solvents were used without further purification. The NMR spectra were recorded on Bruker AM 250 (250 MHz) or 500 (500 MHz), melting points were determined on a Reichert-Kofler block and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter, and elemental analyses were carried out in the Dyson Perrins Laboratory using a Carlo Erba 1106 elemental analyzer. 1-Chloroisoquinoline,[22] tetrakis(triphenylphosphine)-palladium(0),[23] and dichlorobis[(*R*)-dimethyl(1-(1-naphthyl)-ethyl)aminato-C^2,N]dipalladium(II)[24] were prepared according to the literature, the last-named from (*R*)-1-naphthyl-1′-ethylamine purchased from Avocado. Diphenylphosphine and 1,2-bis(diphenylphosphino)ethane were purchased from Strem Chemicals Inc. and used without further purification.

1-Bromo-2-methoxynaphthalene. Bromine (100.7 g, 0.63 mol) in AcOH (125 mL) was added to a solution of 2-methoxynaphthalene (100 g, 0.63 mol) in AcOH (500 mL) at room temperature and stirred overnight. After filtering the white precipitate, the remaining solute was diluted with water

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to give more precipitate which was collected by filtration. The solids were washed with water and dried in vacuo giving 1-bromo-2-methoxynaphthalene; yield: 138.6 g, 93%; mp 83−85 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.25 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 8.9 Hz, 1H), 7.80 (d, J = 8.3 Hz, 1H), 7.59 (t, J = 7.7 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 8.9 Hz, 1H), 4.04 (s, 3H) ppm.

2-Methoxy-1-naphthylboronic Acid. A solution of 1-bromo-2-methoxynaphthalene (137.1 g, 0.58 mol) in THF (800 mL) was added dropwise to Mg (16.9 g, 0.69 mol, activated by stirring overnight under argon at rt).[25] After stirring for 2 h, the reaction mixture was cooled to −78 °C, and trimethylborate (119.2 g, 1.16 mol) was added followed by stirring overnight at room temperature. Water (150 mL) was added with stirring to give a homogeneous solution, and then volatiles were removed in vacuo. The remaining aqueous solution was extracted with CH_2Cl_2 (300 mL × 3), and the organic layers were combined and dried over anhydrous $MgSO_4$, filtered, and concentrated to give a brown solid. The resulting material was stirred for 0.5 h in CH_2Cl_2 (300 mL), filtered, and washed with cold CH_2Cl_2 (3 × 50 mL) to give 2-methoxy-1-naphthylboronic acid as a white solid; yield: 118.7 g, 73%; mp 117−119 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.86 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 9.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.29 (d, J = 9.0 Hz, 1H), 6.30 (br, s, 2H), 4.04 (s, 3H) ppm; ^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 159.3, 136.4, 130.0, 129.2, 128.6, 128.0, 126.5, 123.7, 114.3, 56.5 ppm. Anal. Found: C, 65.2; H, 5.3. Calcd For $C_{11}H_{11}BO_3$: C, 65.4; H, 5.5.

1-(2-Methoxy-1-naphthyl)isoquinoline. To a solution of tetrakis(triphenylphosphine)palladium (0) (13.7 g, 11.9 mmol) in DME (600 mL) was added 1-chloroisoquinoline (64.8 g, 0.4 mol) as a solid and stirred for 0.5 h. 2-Methoxynaphthylboronic acid (100 g, 0.5 mol) in ethanol (50 mL) and sodium carbonate (109 g, 1.03 mol) in water were successively added at room temperature to the solution followed by refluxing for overnight. The solution was cooled to 0 °C and filtered to remove the solid which was washed with CH_2Cl_2 until it was white. The filtrates were concentrated, and the residues were dissolved in CH_2Cl_2 (700 mL), washed with water and brine, dried over $MgSO_4$, filtered, and concentrated to give a brown solid. The solid was stirred in ethyl ether (150 mL), filtered and washed with ethyl ether several times to give 1-(2-methoxy-1-naphthyl)isoquinoline as a colorless solid; yield: 84.6 g, 75%; mp 130−133 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.74 (d, J = 6.0 Hz, 1H), 8.03 (d, J = 9.0 Hz, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.77 (d, J = 6.0 Hz, 1H), 7.68 (t, J = 7.0 Hz, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.45 (d, J = 9.0 Hz, 1H), 7.41 (t, J = 7.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.25 (t, J = 8.5 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 3.78 (s, 3H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 157.9, 154.6, 142.2, 136.1, 133.6, 130.3, 130.3, 130.0, 128.8, 128.6, 127.7, 127.2, 127.0, 126.6, 126.5, 124.5, 123.5, 121.7, 120.0, 113.3, 56.3 ppm.

1-(2-Hydroxy-1-naphthyl)isoquinoline. Boron tribromide (84.3 g, 0.34 mol) was added to a solution of 1-(2-methoxy-1-naphthyl)isoquinoline (80 g, 0.28 mol) in CH_2Cl_2 (1 L) via dropping funnel at room temperature, then refluxed for 1 h. After the resulting dark reddish solution was stirred overnight at room temperature, water (400 mL) was added cautiously at 0 °C. The yellow precipitate was collected by filtration. The filtrate was neutralized with aqueous 2 M NaOH solution, and extracted with CH_2Cl_2 (400 mL × 3). Aqueous 10% HCl solution was added to the organic layer with stirring and more yellow precipitate formed which was collected by filtration. The combined yellow solids were stirred in dichlomethane (600 mL) and 2 M aqueous Na_2CO_3 (200 mL) solution, and the organic layer was separated. The aqueous phase was extracted with CH_2Cl_2 (200 mL × 3), and the organic layers were combined and concentrated to give yellow solid. This was purified by recrystallization with cold CH_2Cl_2 to give 1-(2-hydroxy-1-naphthyl)isoquinoline as a colorless solid; yield: 59.8 g, 79%; mp 244−245 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.65 (d, J = 5.7 Hz, 1H), 7.94 (d, J = 8.3 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.78 (d, J = 5.7 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 8.9 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.13 (d, J = 8.5 Hz, 1H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 157.8, 152.9, 141.7, 136.8, 133.6, 130.7, 130.6, 128.6, 128.0, 127.9, 127.5, 126.9, 126.5, 124.6, 123.1, 120.8, 118.7, 117.9 ppm. Anal. found: C, 84.4; H, 4.65; N, 5.1. Calcd for $C_{19}H_{13}NO$, C, 84.1; H, 4.8; N, 5.5.

1-(2-Trifluoromethanesulfonyloxy-1-naphthyl)isoquinoline. To a mixture of 1-(2-hydroxy-1-naphthyl)isoquinoline (55 g, 0.2 mol) and 4-dimethyl aminopyridine (2.47 g, 20 mmol) in CH_2Cl_2 (1 L) was added CF_3SO_3H (62.9 g, 0.22 mol) at room temperature followed by stirring overnight. The resulting solution was washed with 1 M HCl solution (1 L), water (1 L), and brine (500 mL). The organic phase was dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed in vacuo to give a yellow solid which was purified by stirring in diethyl ether (300 mL) and filtering. This gave 1-(2-trifluoromethanesulfonyloxy-1-naphthyl)isoquinoline as a white solid; yield: 68.4 g, 84%; mp 98−100 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.79 (d, J = 5.7 Hz, 1H), 8.11 (d, J = 9.1 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.85 (d, J = 5.7 Hz, 1H), 7.72 (ddd, J = 2.1, 6.0, 8.2 Hz, 1H), 7.62 (d, J = 9.1 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.49−7.43 (m, 2H), 7.40 (t, J = 7.7 Hz, 1H), 7.29 (d, J = 8.5 Hz, 1H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 154.1, 145.1, 142.7, 136.4, 133.3, 132.6, 131.3, 130.6, 129.5, 128.6, 128.3, 127.9, 127.8, 127.2, 127.2, 126.8, 126.6, 121.3, 119.5 ppm. Anal. found: C, 59.7; H, 2.9; N, 3.6. Calcd for $C_{20}H_{12}NO_3SF_3$, C, 59.6; H, 3.0; N, 3.5.

(*R,S*)-(±)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline. In a dried 1-L three-neck flask, diphenylphosphine (9 g, 48 mmol) was added to a solution of $NiCl_2$(dppe) (8.51 g, 16.1 mmol) in DMF (200 mL) at room temperature, and the resulting dark brown solution was heated for 0.5 h. In

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the other part, a solution of 1-(2-trifluoromethanesulfonyloxy-1-naphthyl)isoquinoline (65 g, 0.16 mol) in DMF (100 mL) was added to the solution of 1,4-diazabicyclo[2,2,2]octane (72.3 g, 0.65 mol) in DMF (200 mL), and it was transferred in one portion to the reaction flask via cannula. The resulting solution was kept at 100 °C, and three additional portions of diphenylphosphine (9 g × 3, 0.14 mol) were added by syringe after 1, 3, and 7 h. After being stirred for 40 h at 100 °C, the reaction mixture was allowed to cool to 0 °C. The mixture was diluted with CH_2Cl_2 (1 L) and then washed with saturated Na_2CO_3, water, and brine successively. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resulting sludge was suspended with acetone (200 mL) and stirred for 1 h under argon and filtered, and the filter cake was washed with acetone and methanol to give (*R*,*S*)-(±)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline as a colorless solid; yield: 48.3 g, 68%; mp 217−219 °C; ^{1}H NMR (500 MHz, benzene-d_6) δ = 8.58 (d, J = 5.7 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.56 (dd, J = 8.5 Hz, $J_{P,H}$ = 2.9 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.35 (d, 1H), 7.30 (m, 2H), 7.28 (d, 1H), 7.26 (d, J = 5.7 Hz, 1H), 7.16 (t, 1H), 7.15 (t, 1H), 7.05−6.98 (m, 6H), 6.95 (dd, J = 8.5, 6.8 Hz, 1H), 6.86 (dd, J = 8.5, 6.8 Hz, 1H) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$) δ = 160.5, 144.4, 142.3, 137.4, 135.9, 134.9, 133.7, 133.6, 133.2, 132.7, 131−126, 120.3 ppm; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ = −13.1 ppm. Anal. found: C, 84.9; H, 5.0; N, 3.0. Calcd for $C_{31}H_{22}NP$, C, 84.7; H, 5.05; N, 3.2.

(*R*)-(+)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline. Dichlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]dipalladium(II) (17.4 g, 25.6 mmol) in acetone (600 mL) was added to a suspension of (*R*,*S*)-(±)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (45 g, 0.1 mol) in acetone (1 L) via cannula at 55 °C and the resulting solution stirred for 2 h. Potassium hexafluorophosphate (9.42 g, 51.2 mmol) in acetone (300 mL) was added via cannula, and the resulting mixture was stirred at 55 °C for 2 h. On cooling to room temperature, a white precipitate was obtained and collected by filtration, saving the orange filtrate for the next step below. The solid was dried in vacuo and dissolved in chloroform, and the resulting solution was filtered through Celite. The filtrate was concentrated in vacuo, and the remaining white solid was washed with acetone (100 mL) and dried to give enantiomerically pure (*R*)-(+)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline ($[\alpha]_D$ = +166 (c = 1, $CHCl_3$) as a white solid; yield: 20.8 g, 46%.

(+)-*cis*-[(*R*)-Dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[(*S*)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]dipalladium (II)Hexafluorophosphate. All of the above solution was combined and evaporated to give an orange solid which was washed with toluene (2 × 100 mL) and $CHCl_3$ (2 × 100 mL). The remaining yellow solid was dried in vacuo to give [(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[(*S*)-1-(2-diphenylphosphino-1-naphthyl) isoquinoline]-dipalladium (II) hexafluorophosphate as a pale yellow powder; yield: 40.7 g, 45%; mp 228−230 °C; ($[\alpha]_D$ = −245.3 (c = 1, acetone); ^{1}H NMR (500 MHz, acetone-d_6) δ = 9.01 (d, J = 6.2 Hz, 1H), 8.32 (dd, J = 8.5 Hz, $J_{P,H}$ = 1.8 Hz, 1H), 8.20 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 6.2 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.79 (d, J = 8.3 Hz, 1H), 7.79 (t, J = 7.6 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 7.6 Hz, 2H), 7.47−7.39 (m, 4H), 7.39−7.33 (m, 4H), 7.26 (d, J = 8.5 Hz, 1H), 7.15 (dd, J = 8.2, 9.1 Hz, 2H), 7.09 (t, 2H), 7.06 (d, J = 8.5 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 6.99 (br, 1H), 6.61 (dd, J = 8.5 Hz, $J_{P,H}$ = 5.8 Hz, 1H), 4.61 (quin, J = 6.0 Hz, 1H), 2.95 (d, J = 2.2 Hz, 3H), 2.81 (d, $J_{P,H}$ = 3.5 Hz, 3H), 1.75 (d, J = 6.3 Hz, 3H) ppm; ^{13}C NMR (125.8 MHz, acetone-d_6) δ = 150.6, 141.9, 137.7, 136.2, 136−123, 74.0, 51.9, 48.1, 24.2 ppm; ^{31}P NMR (101.3 MHz, acetone-d_6) δ = 40.5, −50.7 (heptet, $J_{P,F}$ = 713 Hz) ppm; HRMS (MALDI) found: M^+ = 743.188, Calcd for $C_{45}H_{38}N_2PPd^+$, 743.181.

Table 1. **Crystal data and refinement details**

crystal identification	ARC107
empirical formula	$C_{31}H_{22}NP$
formula weight	439.50
temperature (K)	293
wavelength (Å)	0.71073
crystal system	monoclinic
space group	$P\,2_1$
a (Å)	9.3582(3)
b (Å)	11.2325(3)
c (Å)	11.0655(4)
α (deg)	90
β (deg)	94.2238(12)
γ (deg)	90
cell volume (Å^3)	1160.0
Z	2
calculated density (Mg/m^3)	1.258
absorption coefficient (mm^{-1})	0.138
F_{000}	460.248
crystal size (mm)	0.30 × 0.60 × 0.60
description of crystal	colorless fragment
absorption correction	semiempirical from equivalent reflections
transmission coefficients (min,max)	0.92, 0.96
θ range for data collection (deg)	$5.0 \le \theta \le 27.5$
index ranges	$-12 \le h \le 12$, $-14 \le k \le 13$, $0 \le l \le 14$
reflections measured	7688
unique reflections	4727
R_{int}	0.032
observed reflections ($I > 3\sigma(I)$)	3870
refinement method	full-matrix least-squares on F
parameters refined	298
weighting scheme	Chebychev 3-term polynomial
goodness of fit	1.0648
R	0.0327
ωR	0.0331
residual electron density (min,max) (e Å^{-3})	−0.213, 0.263

(*S*)-(−)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline. A mixture of [(*R*)-dimethyl(1-(1-naphthyl) ethyl)-aminato-C^2,N]-[(*S*)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]dipalladium (II) hexafluorophosphate (40 g, 45 mmol) and 1,2-bis(diphenylphosphino)ethane (19.7 g, 49.4 mmol) in CH_2Cl_2 (400 mL) was stirred for 3 h at room temperature. The solvent was removed under reduced pressure to give a pale yellow solid. The solid was stirred for 30 min in acetone (200 mL) and collected by filtration; washing

several times with acetone gave pure (*S*)-(−)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline ($[\alpha]_D = -165$ (c = 1, $CHCl_3$) as a white solid; yield: 19.2 g, 97%.

X-ray Structure of (*S*)-(−)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline, $C_{31}H_{22}NP$. A large single crystal from $CHCl_3$ was cut to give a fragment with dimensions approximately 0.3 mm × 0.6 mm × 0.6 mm. This was mounted on a glass fibre using cyanoacrylate adhesive. Diffraction data were measured at ambient temperature using an Enraf-Nonius KappaCCD diffractometer (graphite-monochromated Mo *K*α radiation, $\lambda = 0.71073$ Å). Intensity data were processed using the DENZO-SMN package.[26]

Examination of the systematic absences of the intensity data showed the space group to be either $P2_1$ or $P2_1/m$. The structure was solved in the space group $P2_1$ using the direct-methods program SIR92,[27] which located all non-hydrogen atoms. Examination of the structure clearly showed no mirror plane to be present, confirming the assignment of space group. Subsequent full-matrix least-squares refinement was carried out using the CRYSTALS program suite.[28] Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined. Hydrogen atoms were positioned geometrically after each cycle of refinement. A three-term Chebychev polynomial weighting scheme was applied. Refinement converged satisfactorily to give $R = 0.327$, $\omega R = 0.0331$. The crystal data is displayed in Table 1, and the full CIF file is provided as Supporting Information.

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Supporting Information Available

Tables of crystallographic data (PDF). X-ray crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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