JOC*Article*

Preparation and Resolution of a Modular Class of Axially Chiral Quinazoline-Containing Ligands and Their Application in Asymmetric Rhodium-Catalyzed Olefin Hydroboration

David J. Connolly,[†] Patrick M. Lacey,[†] Mary McCarthy,[†] Cormac P. Saunders,[†] Anne-Marie Carroll,[†] Richard Goddard,[‡] and Patrick J. Guiry*,[†]

Centre for Synthesis and Chemical Biology, Conway Institute of Biomolecular and Biomedical Research, Department of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland, and Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470 Mülheim a. d. Ruhr, Germany

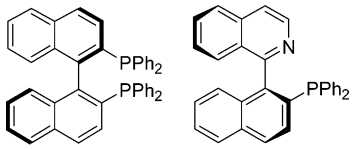
p.guiry@ucd.ie

Received May 13, 2004

The preparation and resolution of a series of axially chiral quinazoline-containing ligands is described in which the key steps are the metal-catalyzed naphthyl-phosphorus bond formation, the naphthalene-quinazoline Suzuki coupling, and the preparation of the Suzuki electrophilic components from the corresponding imidate and anthranilic acid. Diastereomeric palladacycles derived from the racemic phosphinamines and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)-aminato-C_2,N]dipalladium(II) were separated by fractional crystallization. The configuration of the resulting diastereomers was determined by X-ray crystallographic analysis. Displacement of the resolving agent by reaction with 1,2-bis(diphenylphosphino)ethane afforded enantiopure ligand in each case. Their rhodium complexes were prepared and applied in the enantioselective hydroboration of a range of vinylarenes. The quinazolinap catalysts were found to be extremely active, giving excellent conversions, good to complete regioselectivities, and the highest enantioselectivities obtained to date for several members of the vinylarene class, including *cis*-β-methylstyrene (97%), *cis*-stilbene (99%), and indene (99.5%).

Introduction

Much of the success in enantioselective homogeneous catalysis is dependent upon the application of specifically designed chiral ligands to important synthetic transformations. In particular, the development of atropisomeric diphosphine ligands such as Binap **1** have found widespread applicability in asymmetric hydrogenation, olefin isomerization, allylic alkylation, the Heck reaction, and enantioselective hydroboration.[1−5] This axially chiral diphosphine is conformationally flexible about the binaphthyl linkage and can therefore accommodate a variety of transition metals, making it the most versatile ligand ever developed. Subsequently, the development of axially chiral heterobidentate systems has become an active area of research as a result of their ability to induce asymmetry in a variety of reactions. The phosphinamine ligand class has received the most interest due to the combination of steric and electronic effects exerted on substrates at the coordination sphere of the transition metal to which they are bound.[6] The first successful axially chiral phosphinamine ligand, Quinap **2**, was developed by Brown and incorporated a naphthalene-isoquinoline backbone that possessed the necessary steric requirements to raise the energy barrier to rotation around the carbon−carbon bond of the biaryl linkage.



1 **2**

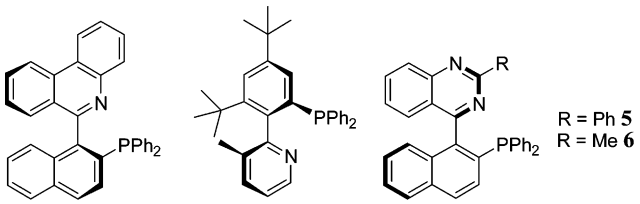
Quinap **2** was subsequently employed in palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate to afford enantiomeric excesses of up to 98%.[7] The ligand also proved to be an extremely active catalyst for the rhodium-catalyzed hydroboration of vinylarenes, with enantioselectivities of up to 97% being achieved.[8,9]

[†] University College Dublin.
[‡] Max-Planck-Institut für Kohlenforschung.

(1) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345.
(2) (a) Ojima, I. *Catalytic Asymmetric Synthesis*, 2nd ed.; VCH: Weinheim, 2000. (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994. (c) Brunner, H.; Zettlmeier, W. *Handbook for Enantioselective Catalysis*; VCH: Weinheim, 1993. (d) Beller, M.; Bolm, C. *Transition Metals for Organic Synthesis*; Wiley/VCH: Weinheim, 1998. (e) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999.
(3) Rosini, C.; Franzini, L.; Raffaelii, A.; Salvadori, P. *Synthesis* **1992**, 503.
(4) McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809.
(5) Kilroy, T. G.; Hennessy, A. J.; Connolly, D. J.; Malone, Y. M.; Farrell, A.; Guiry, P. J. *J. Mol. Catal.* **2003**, *196*, 65.
(6) Guiry, P. J.; McCarthy, M.; Lacey, P. M.; Saunders: C. P.; Kelly, S.; Connolly, D. J. *Curr. Org. Chem.* **2000**, *4*, 821.
(7) Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493.
(8) Doucet, H.; Brown, J. M. *Tetrahedron: Asymmetry* **1997**, *8*, 3775.

10.1021/jo049195+ CCC: $27.50
Published on Web 09/08/2004

A detailed mechanistic investigation of the alkylation process involving both solid-state studies and NMR experiments revealed that the 3-H of the isoquinoline unit was involved in critical ligand-reactant interactions believed to be significant for asymmetric induction. This led to the development of the vaulted analogue Phenap (**3**), which was also screened in Pd-catalyzed allylic alkylation and Rh-catalyzed hydroboration, although the enantioselectivities obtained were slightly lower than those achieved with Quinap.[10,11]



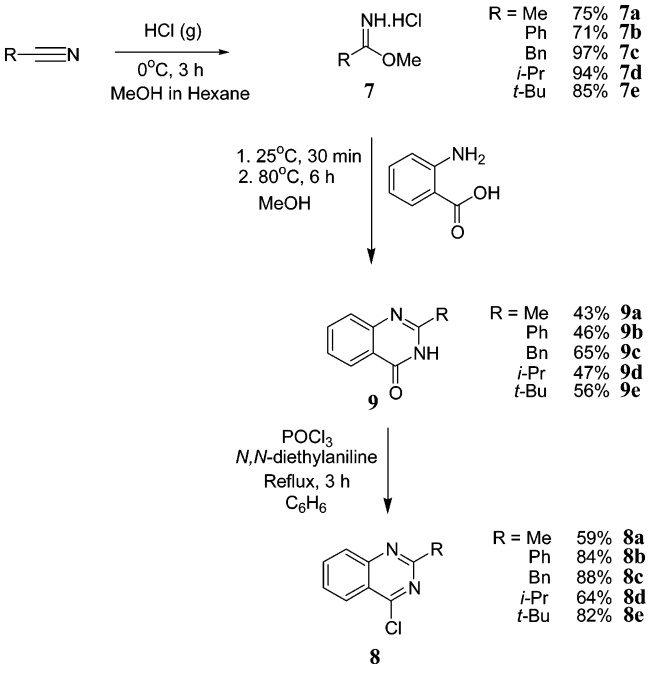
3 **4**

The development and resolution of the atropisomeric ligand Pyphos **4** is also a noteworthy contribution to this area, and its successful application in enantioselective hydroboration has been recently reported.[12−14] Our study into the preparation and application of 2-substituted quinazoline-containing axially chiral phoshinamines in asymmetric catalysis was initiated with 2-phenyl-Quinazolinap (**5**) as the desired target since the naphthalene-quinazoline pivot would be essentially inert to racemisation.[15] In light of the mechanistic observations on related ligand systems, the 2-position of the quinazoline fragment (equivalent to the 3-position of Quinap) is believed to be important for asymmetric induction. Therefore, it was of interest to expand this 2-substituted series in an effort to investigate the effect of steric demand on the degree of enantioselection observed. Additionally, the reduced basicity of the Quinazolinap donor nitrogen (pK_a of ∼3.3 vs pK_a of ∼5.1) relative to that of Quinap **2** could also be investigated, and the variation of this electronic desymmetrization, combined with steric properties, may further aid our understanding of the enantioselection process. We subsequently communicated the preparation of enantiopure 2-methyl-Quinazolinap **6**, and in this article we wish to report the synthesis and resolution of a class of 2-substituted Quinazolinap ligands for asymmetric catalysis and their application in asymmetric rhodium-catalyzed olefin hydroboration.[16]

Ligand Synthesis

To develop this modular ligand series, it was necessary to access a range of 4-chloroquinazolines (R= Me, Ph, Bn, *i*-Pr, *t*-Bu) with different substituents at the 2-position. As these are not commercially available, a convenient synthetic route to the key electrophilic components of the Suzuki coupling was required. We have developed a facile and versatile route to 2-substituted-4-chloroquinazolines **8a**−**e**, the key electrophilic component of the biaryl coupling in the ligand synthesis, Scheme 1.[17]

SCHEME 1

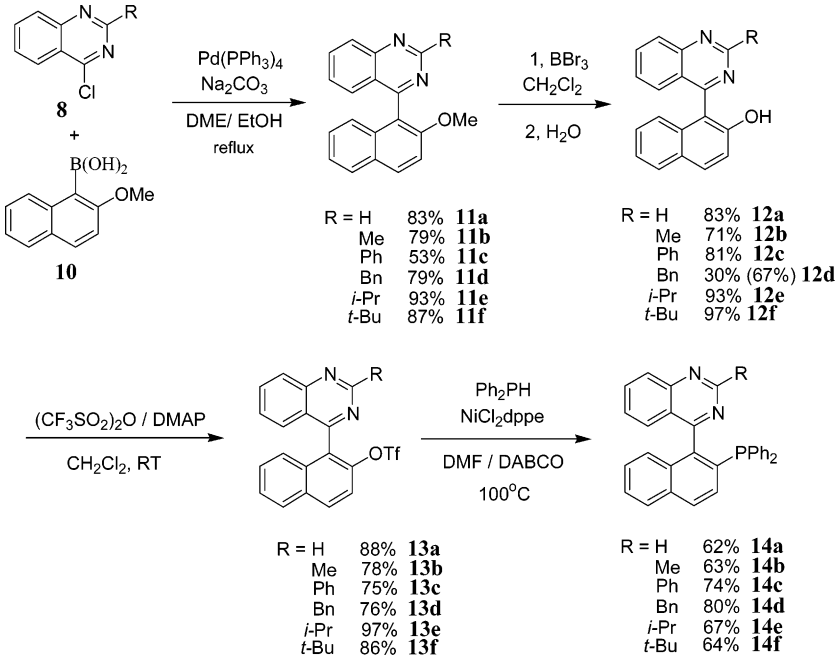


This extremely convenient route afforded the required quinazolinone system **9a**−**e** from the reaction of anthranilic acid with a variety of preformed imidates. Subsequently, the corresponding 4-chloroquinazolines **8a**−**e** could be readily prepared by reaction with phosphorus oxychloride. A significant feature of both reactions was that product isolation could be facilitated by the development of workup procedures that did not include purification by chromatography.

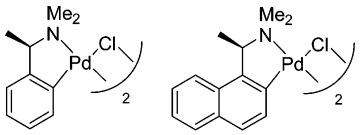
The subsequent synthesis of the Quinazolinap ligands involved two metal-catalyzed couplings, the biaryl cross-coupling and the formation of the naphthyl-phosphorus bond, as the key steps, Scheme 2. The electrophilic component of the Pd-catalyzed Suzuki coupling was the 4-chloro-2-substituted-quinazolines **8a**−**e**, and the nucleophilic component for the reaction was 2-methoxy-1-naphthylboronic acid **10**. This produced the corresponding 2-methoxy-1-(2-substituted-quinazolin-4-yl) naphthalenes **11a**−**f** in moderate to excellent yields. The products were subsequently demethylated using boron tribromide in dichloromethane to afford the appropriate naphthols **12a**−**f** in yields ranging from 71% to 93%. However, a low yield of 30% was obtained in the case of the 2-benzyl variant **12d**, and an alternative method for cleavage of the methyl ether was investigated. Under the optimized conditions of refluxing hydrogen bromide in acetic acid, the demethylation proceeded smoothly to furnish the desired product in an improved yield of 67%.[18] The next step involved treatment of the naphthols with

(9) Doucet, H.; Fernandez, E.; Layzell, T. P.; Brown, J. M. *Chem. Eur. J.* **1999**, *5*, 1320.
(10) Valk, J.-M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2593.
(11) Valk, J.-M.; Claridge, T. D. W.; Brown, J. M.; Hibbs, D.; Hursthouse, M. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2597.
(12) Kwong, F. Y.; Chan, K. S. *Organometallics* **2000**, *19*, 2058.
(13) Kwong, F. Y.; Chan, K. S. *Organometallics* **2001**, *20*, 2570.
(14) Kwong, F. Y.; Yang, Q.; Mak, T. C. W.; Chan, A. S. C.; Chan, K. S. *J. Org. Chem.* **2002**, *67*, 2769.
(15) McCarthy, M.; Goddard, R.; Guiry, P. J. *Tetrahedron: Asymmetry* **1999**, *10*, 2797.
(16) Lacey, P. M., McDonnell, C. M.; Guiry, P. J. *Tetrahedron Lett.* **2000**, *41*, 2475.
(17) Connolly, D. J.; Guiry, P. J. *Synlett* **2001**, *11*, 1707.
(18) Binch, G.; Huisgen, R.; König, H. *Chem. Ber.* **1964**, *97*, 2893.

SCHEME 2



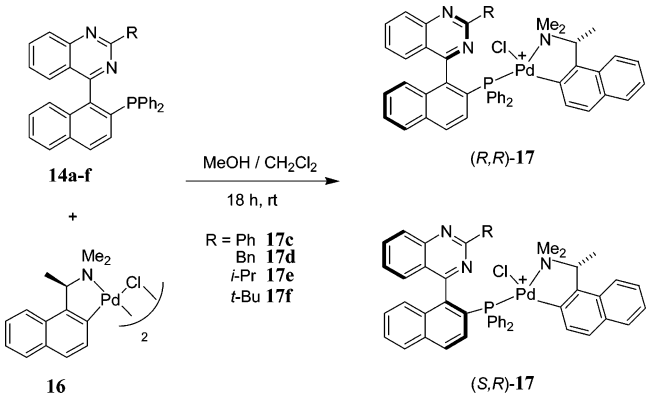
trifluoromethane sulfonic anhydride in the presence of 4-(dimethylamino)pyridine to yield the corresponding triflates **13a**−**f** (75−97%). The final step in the sequence employed the procedure developed by Cai, which utilized [1,2-bis(diphenylphosphino)ethane]dichloronickel(II) as the catalyst and diphenylphosphine as the phosphorus source to give the desired phosphinamines **14a**−**f** as racemates (62−80%).



15 **16**

The resolution of atropisomeric P,N ligands typically involves diastereomeric complexation using chiral palladium amine complexes, followed by fractional crystallization to facilitate the isolation of diastereomerically pure material. In particular, the *ortho*-palladated derivatives of (*R*)-dimethyl(1-phenylethyl) amine **15** and (*R*)-dimethyl(1-(1-naphthyl)ethyl)amine **16** have received significant attention.[19−23] The latter system was applied in the successful resolution of both Quinap **2**, Phenap **3**, 2-phenyl-Quinazolinap **5**, and more recently, Pyphos **4**.[11,24] Because the Quinazolinap ligands are structurally related to the isoquinoline-based systems, the initial resolution attempts focused on the use of naphthylamine palladium dimer **16**.

SCHEME 3



In each case, the palladium dimer, (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-dipalladium(II) **16** and the relevant 2-substituted-Quinazolinap **14a**−**f** were dissolved in dry, degassed methanol under a nitrogen atmosphere and stirred for 18 h at room temperature, Scheme 3. The use of dichloromethane was employed in some cases as solubility problems were encountered with methanol. The diastereomeric complexes **17c**−**f** thus formed as their chloride salts were fractionally crystallized, and in some cases, it was possible to access both hands of the corresponding 2-substituted-Quinazolinap. In those cases where this was not possible, it was necessary to prepare diastereomeric palladacycles in which the ligands were coordinated in a bidentate fashion with hexafluorophosphate as the counterion. For each ligand system, the optimized resolution procedure will be summarized and the ^{31}P NMR signals of the isolated diastereomers will be tabulated for clarity.

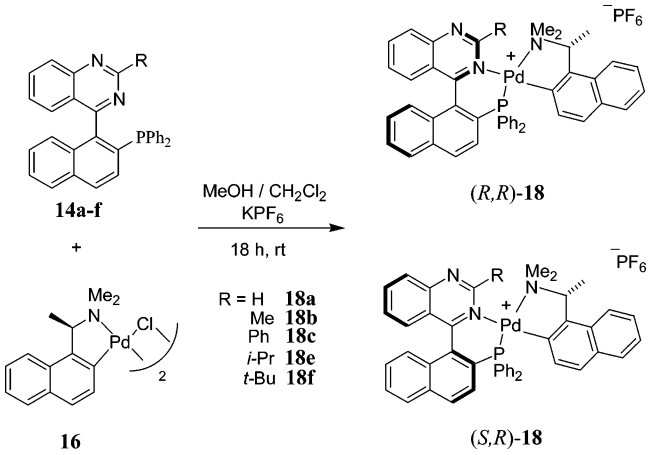
When the resolution of 2-phenyl-Quinazolinap **14c** was attempted, a precipitate of one diastereomer was isolated after the initial mixing period, Scheme 3. This material was recrystallized from chloroform/pentane by isothermal

(19) Otsuka, S.; Nakamura, A.; Kano, T.; Tani, K. *J. Am. Chem. Soc.* **1971**, *93*, 4301.
(20) Tani, K.; Brown, L. D.; Ahmed, J.; Ibers, J. A.; Yokota, M.; Nakamura, A.; Otsuka, S. *J. Am. Chem. Soc.* **1977**, *99*, 7876.
(21) Leung, P. H.; Loh, S.; Mok, K. F.; White, A. J. P.; Williams, D. J. *Tetrahedron: Asymmetry* **1996**, *7*, 45.
(22) Leung, P. H.; Loh, S.; Mok, K. F.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1996**, 591.
(23) Kerr, P. G.; Leung, P. H.; Wild, S. B. *J. Am. Chem. Soc.* **1987**, *109*, 4321.
(24) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743.

TABLE 1. ^{31}P NMR Signals of Isolated Diastereomerically Pure Complexes

entry	R in ligand	compound	X^-	(*R*,*R*)	(*S*,*R*)
1	H	**18a**	PF_6	41.2	39.9
2	Me	**18b**	PF_6		37.5
3[15]	Ph	**17c**	Cl	40.0	
		18c	PF_6		45.1
4	Bn	**17d**	Cl	42.4	45.5
5	*i*-Pr	**17e**	Cl	42.7	45.5
		18e	PF_6		35.2
6	*t*-Bu	**17f**	Cl	43.8	
		18f	PF_6	43.7	42.2

SCHEME 4



diffusion to afford crystals suitable for X-ray crystallographic analysis. The diastereomer was found to have the (*R*,*R*)-configuration **17c**. In this instance, the ligand was bound to palladium in a monodentate fashion and only a single peak at 40.0 ppm was evident by ^{31}P NMR spectroscopy, Table 1, entry 3.[15] Furthermore, it later proved possible to precipitate (*S*,*R*)-**18c** from the residual solution by the addition of KPF_6, which suggests a bidentate coordination of the ligand to palladium, Scheme 4.

In the case of the palladacycle derived from 2-methyl-Quinazolinap, the addition of KPF_6 to the reaction mixture precipitated both diastereomers **18b** in a 1:1 ratio, Scheme 4, and a range of solvent systems were tested to effect their separation. The use of a chloroform/diethyl ether/trace water combination afforded diastereomerically pure material that resonated at 37.5 ppm in the ^{31}P NMR spectrum, Table 1, entry 2, and was shown to have the (*S*,*R*)-configuration by X-ray analysis, Figure 1. Unfortunately all attempts to isolate (*R*,*R*)-**18b** were unsuccessful.

Similarly, the Quinazolinap diastereomers **18a** were formed as their hexafluorophosphate salts, Scheme 4, and fractional crystallization of the mixture from butanone/diethyl ether afforded a palladacycle with a ^{31}P NMR resonance at 39.9 ppm, Table 1, entry 1, which was later assigned as (*S*,*R*)-**18a** by X-ray crystallography (recrystallized from chloroform/diethyl ether), Figure 2.

Palladacycle (*R*,*R*)-**18a** was subsequently isolated from the filtrate with an optimal diastereomeric ratio of 96:4 by recrystallization from chloroform. Interestingly, spectroscopic evidence indicated that an unusual methanolysis had occurred during the initial binding process, resulting from the cleavage of the naphthyl-phosphorus

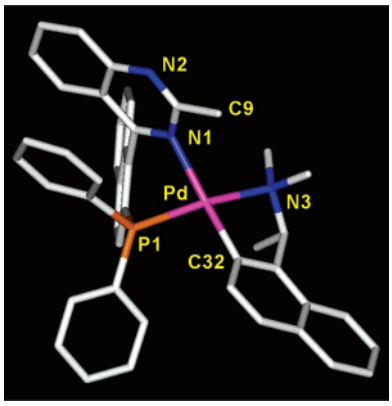


FIGURE 1. Structure of the cation in (*S*,*R*)-**18b**·0.2H_2O. Selected distances (Å) and angles (deg): Pd−P1 2.2423(5), Pd−N1 2.187(2), Pd−N3 2.147(2), Pd−C32 1.978(3), Pd···C9 3.146(3), P1−Pd−N1 82.34(6), N3−Pd−C32 80.2(1), P1−Pd−N3 155.3(1), N1−Pd−C32 171.0(1), plane(Pd, P1, N1)/plane(Pd, N3, C32) 28(2).

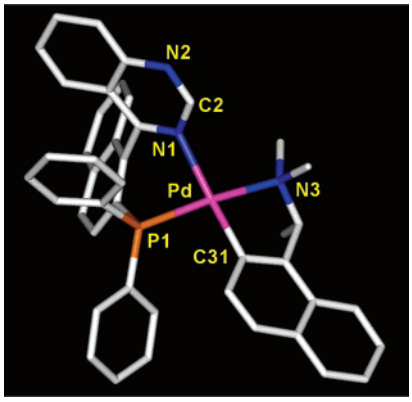
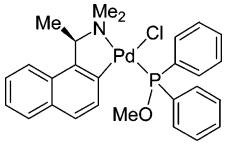


FIGURE 2. Structure of the cation in (*S*,*R*)-**18a**·2$CHCl_3$. Selected distances (Å) and angles (deg): Pd−P1 2.256(2), Pd−N1 2.189(5), Pd−N3 2.132(5), Pd−C31 2.002(6), P1−Pd−N1 84.7(1), N3−Pd−C31 80.4(2), P1−Pd−N3 165.9(2), N1−Pd−C31 171.2(2), plane(Pd, P1, N1)/plane(Pd, N3, C31) 17(2).

bond. A key resonance at 125 ppm in the ^{31}P NMR spectrum, characteristic for bound phosphinites, further supported the structure of this impurity as (*R*)-[dimethyl-(1-(1-naphthyl)ethyl)aminato-C_2,N]-[methyl(diphenyl)-phosphite] palladium(II)chloride **19**. It is significant that there have been no previously reported examples of such behavior with palladium, although Pregosin has reported an analogous P−C bond cleavage in a ruthenium complex.[25]



19

On the other hand, the 2-benzyl-Quinazolinap diastereomers were formed as their chloride salts **17d**, Scheme 3, and were separated as a result of solubility differences. An insoluble precipitate, which corresponded to a single peak at 45.5 ppm by ^{31}P NMR spectroscopy, Table 1,

(25) Geldbach, T. J.; Pregosin, P. S. *Eur. J. Inorg. Chem.* **2002**, 1907.

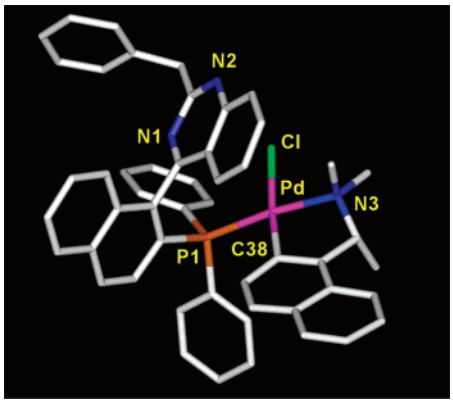


FIGURE 3. Structure of (*S*,*R*)-**17d**. Selected distances (Å) and angles (deg): Pd−P 2.264(1), Pd−Cl 2.374(1), Pd−N3 2.151(4), Pd−C38 2.023(4), P−Pd−C38 95.7(1), N3−Pd−C38 80.9(1), P−Pd−N3 173.2(1), Cl−Pd−C38 168.9(1), mean plane(naphthyl)/mean plane(quinazolinyl) 72(3).

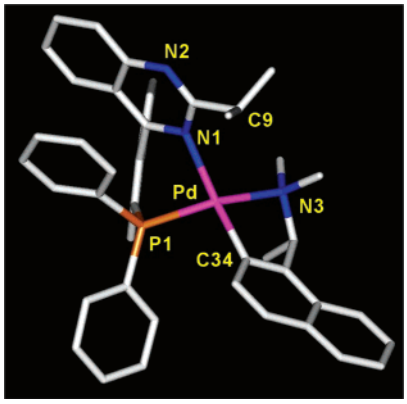


FIGURE 4. Structure of the cation in (*S*,*R*)-**18e**. Selected distances (Å) and angles (deg): Pd−P1 2.238(2), Pd−N1 2.192(5), Pd−N3 2.164(6), Pd−C34 1.993(6), Pd···C9 3.205(6), P1−Pd−N1 84.6(2), N3−Pd−C34 80.9(2), P1−Pd−N3 152.9(2), N1−Pd−C34 166.7(2), plane (Pd, P1, N1)/plane (Pd, N3, C34) 32(2).

entry 4, was isolated after stirring the diastereomeric mixture in diethyl ether. A chloroform/diethyl ether mixture was then employed to form X-ray quality crystals of this complex, which was assigned the (*S*,*R*)-configuration, Figure 3.

The filtrate was subsequently reduced in vacuo to furnish (*R*,*R*)-**17d**, and a singlet at 42.4 ppm was evident in its ^{31}P NMR spectrum.

A 1:1 mixture of the (*R*,*R*)- and (*S*,*R*)-2-isopropyl-Quinazolinap complex **18e** was formed as their hexafluorophosphate salts, Scheme 4. Analogous to the resolution of 2-methyl-Quinazolinap **18b**, a chloroform/diethyl ether mixture was successful for fractional crystallization of the diastereomeric mixture, Table 1, entry 5.

The isolated diastereomer **18e** (crystallized from chloroform/pentane) was shown to have (*S*,*R*)-configuration by X-ray crystallography with bidentate coordination of the ligand to palladium, Figure 4. Interestingly, the introduction of a substituent into the 2-position on the Quinazolinap ligand in the dimethyl(1-(1-naphthyl)ethyl)amine diastereomers results in a change in both the conformation of the ligand and the coordination geometry of the Pd atom. Thus, the conformation of the Quinazolinap ligand is almost identical in both (*S*,*R*)-**18e** (R = *i*-Pr) and (*S*,*R*)-**18b** (R = Me) despite different crystal environments but different from that in (*S*,*R*)-**18a** (R = H). The most likely reason is repulsive steric interaction between the 2-substituent and one of the methyl groups on N3 of the neighboring dimethyl(1-(1-naphthyl)ethyl)-amine ligand, though a weakly attractive C−H···Pd interaction between the H atom on the α-C atom of the 2-substituent and the cationic metal atom center cannot be ruled out. Subsequent recrystallizations to isolate the (*R*,*R*)-palladacycle **18e** were unsuccessful and resulted in the formation of oils rather than crystals. In an attempt to access (*R*)-2-isopropyl-Quinazolinap **14e**, palladacycles **17e** were reformed as their chloride salts, Scheme 3, and were fractionally crystallized using different solvent systems. The chloroform/diethyl ether combination enabled the isolation of diastereomerically pure material as indicated by the existence of one peak at 42.7 ppm in the ^{31}P NMR spectrum. The remaining diastereomer in the filtrate was found to be insoluble in diethyl ether, and a single peak at 45.5 ppm was observed in the ^{31}P NMR spectrum. Subsequent decomplexation of (*S*,*R*)-**18e** and diastereomerically pure **17e** coupled with a comparison of the optical rotation of the isolated ligands would allow for the correct assignments of the parent diastereomers **17e**.

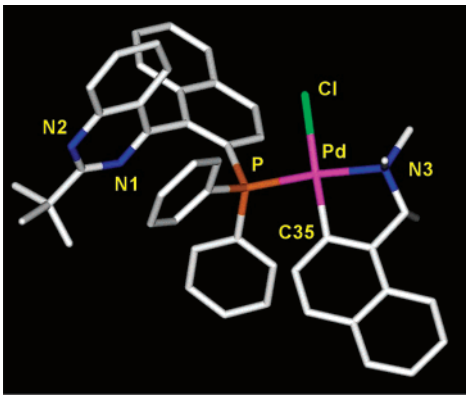
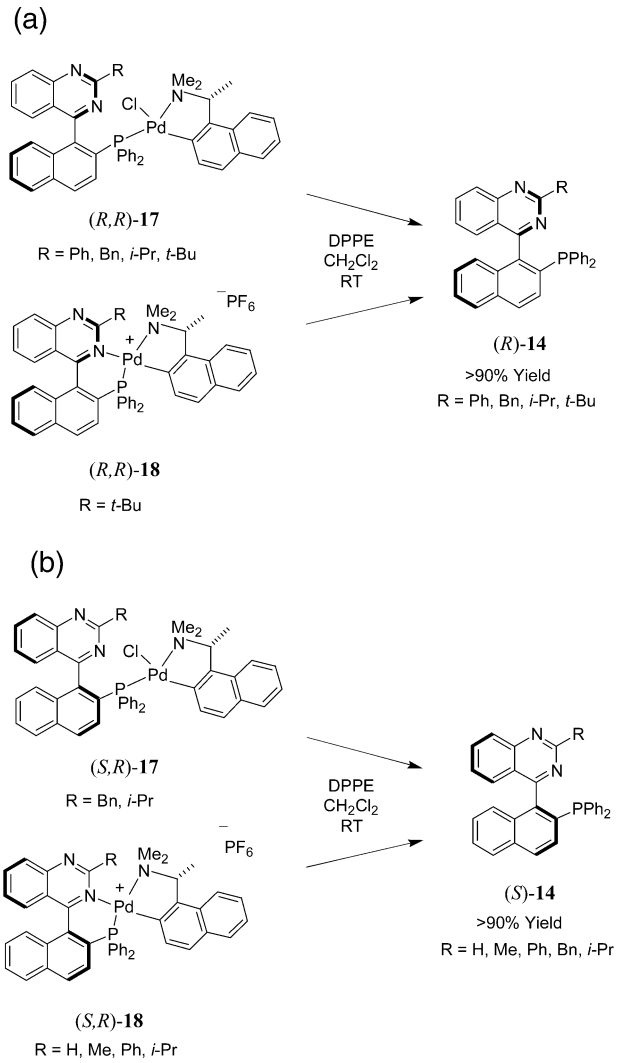


FIGURE 5. Structure of (*R*,*R*)-**17f**. Selected distances (Å) and angles (deg): Pd−P 2.250(1), Pd−Cl 2.390(1), Pd−N3 2.145(2), Pd−C35 2.007(2), P−Pd−C35 94.8(1), N3−Pd−C35 80.8(1), P−Pd−N3 174.1(1), Cl−Pd−C35 167.5(1), mean plane(naphthyl)/mean plane(quinazolinyl) 86(2).

The 2-*tert*-butyl-substituted quinazoline complex **17f** was formed as a 1:1 mixture of diastereomers when dichloromethane was employed as solvent, Scheme 3. Fractional crystallization of the mixture from hot butanone/diethyl ether afforded a yellow solid that was subsequently stirred in methanol. The ^{31}P NMR spectrum had a peak at 43.8 ppm corresponding to a single diastereomer, Table 1, entry 6. Additionally, a sample suitable for X-ray crystallographic analysis was prepared from a dichloromethane/diethyl ether combination and was assigned as (*R*,*R*)-**17f**, Figure 5.

All attempts to isolate the (*S*,*R*)-palladacycle **17f** failed. Therefore, the diastereomers were reformed as their chloride salts, and potassium hexafluorophosphate was added to facilitate counterion exchange, Scheme 4. The corresponding (*R*,*R*)-**18f** and (*S*,*R*)-**18f** were later isolated in a 1:1 ratio. The resultant solid was stirred in methanol and filtered to yield a single diastereomer of unknown

SCHEME 5



configuration (single peak at 43.7 ppm by ^{31}P NMR). Subsequently, the filtrate was recrystallized from hot methanol, and analysis of the ^{31}P NMR spectrum revealed a diastereomeric ratio of 96:4 with the major resonance at 42.2 ppm. Further attempts to isolate diastereomerically pure material proved unsuccessful. To assign the configuration of the 2-*tert*-butyl palladium complexes **18f**, a strategy similar to that employed above for the 2-isopropyl diastereomers **17e** was used, as we had previously isolated (*R,R*)-**17f**.

Decomplexation of Resolved Palladacycles

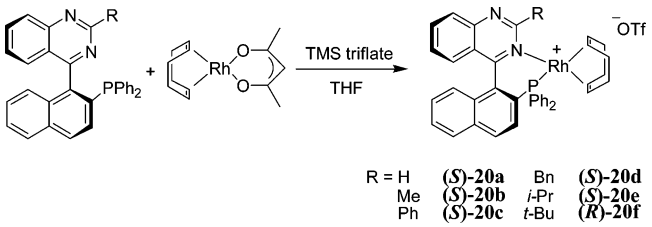
Enantiopure 2-substituted-Quinazolinap ligands **14a**−**f** were obtained by decomplexation of the corresponding diastereomeric palladium complexes using 1,2-bis(diphenylphosphino)ethane in dichloromethane, Scheme 5. In each case, the enantiopure ligand was isolated in excellent yield and was also found to be configurationally stable even after refluxing in toluene for 7 days. This was confirmed by optical rotation and by rebinding the ligand with palladium dimer **16** followed by subsequent analysis of the ^{1}H/^{31}P NMR spectra obtained. Ligands (*R*)-**14c**−**f** were isolated from (*R,R*)-**17c**−**f** and (*R,R*)-**18f**, Scheme 5a, whereas (*S*)-**14a**−**e** were isolated from (*S,R*)-**17c**−**e** and (*S,R*)-**18a**−**c** and **e**, Scheme 5b.

Rhodium-Catalyzed Asymmetric Hydroboration

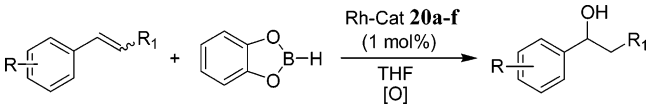
The development of transition-metal-catalyzed hydroboration has been extensively investigated since the initial report by Männing and Nöth, in which catecholborane was found to add to a range of alkenes in the presence of Wilkinson's catalyst.[26] Burgess later demonstrated an enantioselective process based upon the use of chiral transition metal catalysts, which included the application of Binap- and Diop-derived rhodium species with norbornene as the substrate.[27] Hayashi later improved the enantiomeric excesses for the hydroboration of styrenes (up to 96% ee at −78 °C) employing rhodium-Binap complexes.[28] The catalytic variant of hydroboration offered potential advantages in terms of chemo-, regio-, and enantioselectivity. Subsequently, the search for successful catalysts was expanded to include phosphinamines; for example, the ferrocenyl pyrazole ligands (98% ee), the axially chiral Quinap (97% ee), and Phenap (84% ee) ligands were reported by Togni and Brown, respectively.[29,30] As previously mentioned, our research laboratories and the group of Chan have also applied novel axially chiral phosphinamine systems in asymmetric hydroboration with considerable success.[13,14,31] Brown has also extended the standard hydroboration-oxidation sequence to include the synthetically important hydroboration-amination protocol.[32] This methodology has been directed toward a formal synthesis of the antidepressant Sertraline where an efficient kinetic resolution was demonstrated in the Quinap-mediated hydroboration.[33] The construction of carbon−carbon bonds from boronate esters, allowing the preparation of optically active 2-arylpropionic acids, has also received attention since the nonsteroidal antiinflammatory agents such as ibuprofen and naproxen are among this class of compounds.[34−36] In an important contribution, the Fernández group has focused their efforts on the development of a recyclable hydroboration process.[40,41] Attempts to increase the range of substrates to include cyclopropenes have recently been investigated, as well as developments toward the establishment of an iridium-catalyzed asymmetric variant.[39,40] We now wish to report in full our investigations into the

(26) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878.
(27) Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1988**, *53*, 5178.
(28) Hayashi, T.; Matsumoto, Y.; Ito, K. *J. Am. Chem. Soc.* **1989**, *111*, 3426.
(29) Schnyder, A.; Hintermann, L.; Togni, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 931.
(30) Brown, J. M.; Hulmes, D. I.; Layzell, T. P. *J. Chem. Soc., Chem. Commun.* **1993**, 1673.
(31) Guiry, P. J.; Hooper, M. W.; McCarthy, M. *Chem. Commun.* **2000**, 1333.
(32) Fernàndez, E.; Maeda, K.; Hooper, M. W.; Brown, J. M. *Chem. Eur. J.* **2000**, *6*, 1840.
(33) Maeda, K.; Brown, J. M. *Chem. Commun.* **2002**, 310.
(34) Ren, L.; Crudden, C. M. *Chem. Commun.* **2000**, 721.
(35) Chen, A. C.; Ren, L.; Crudden, C. M. *Chem. Commun.* **1999**, 611.
(36) Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704.
(37) Segarra, A. M.; Guerrero, R.; Claver, C.; Fernàndez, E. *Chem. Commun.* **2001**, 1808.
(38) Segarra, A. M.; Guerrero, R.; Claver, C.; Fernàndez, E. *Chem. Eur. J.* **2003**, *9*, 191.
(39) Rubina, M.; Rubin, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2003**, *125*, 7198.
(40) Pérez Luna, A.; Bonin, M.; Micouin, L.; Husson, H.-P. *J. Am. Chem. Soc.* **2002**, *124*, 12098.
(41) Freshly distilled substrate and catecholborane were used for optimum catalytic performance.

SCHEME 6



SCHEME 7



application of the Quinazolinap ligands **14a**−**f** in the rhodium-catalyzed hydroboration of vinylarenes.

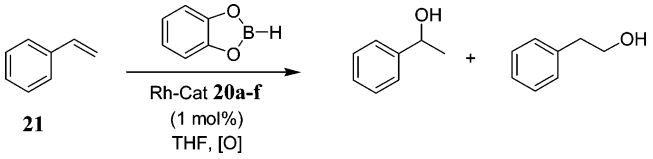
In Situ Formation of 2-Substituted-Quinazolinap Catalysts

The cationic Rh-catalysts (*S*)-**20a**−**e** were prepared from cycloocta-1,5-diene-(pentane-2,4-dionato)rhodium-(I), enantiopure (*S*)-phosphinamines **14a**−**e**, and trimethyl-silyltrifluoromethanesulfonate, Scheme 6. As only enantiopure (*R*)-2-*tert*-butyl-Quinazolinap was available, the corresponding rhodium complex (*R*)-**20f** was prepared in an identical procedure. Because of the susceptibility of these complexes to oxidation, the catalyst was prepared in situ immediately prior to each reaction. A comprehensive study of vinylarenes was undertaken in an attempt to understand the effect of reactivity and enantioselectivity with differing aryl substituents and *β*-substitution on styrene.[41] Furthermore, the cyclic olefins, indene and 1,2-dihydronaphthalene, which are two of the most challenging substrates in the Rh-catalyzed hydroboration, were also screened in the present study.

The procedure involved the addition of 0.5 mmol of catecholborane to a 1 mol % solution of the rhodium-catalyst dissolved in dry THF. The olefin (0.5 mmol) was added, and the reaction was stirred for the required time at either room temperature or 0 °C, Scheme 7. The reaction mixture was cooled in ice, and the product borane was oxidized directly with a H_2O_2/NaOH combination over a 1 h period. After this time, the reaction mixture was extracted into diethyl ether, and the catechol side product was removed by washing with sodium hydroxide and saturated brine. The percent conversion and regioselectivity were calculated by ^{1}H NMR spectroscopy, and the enantiomeric excess was determined by the use of either chiral GC or HPLC. Optical rotation values from the literature were used to assign the absolute configuration of the alcohol products. In all cases the (*S*)-enantiomer was the favored product when rhodium complexes (*S*)-**20a**−**e** were employed. [As expected rhodium complex (*R*)-**20f** furnished the (*R*)-product.]

The 2-substituted-Quinazolinap-derived rhodium complexes proved extremely efficient catalysts for the hydroboration of styrene **21** at room temperature and at 0 °C, Table 2. In all but one case, quantitative conversions were obtained after just 2 h at the relevant temperature.[42] The highest enantioselectivity of 90% and regioselectivity of 88:12 were obtained in the same reaction with complex **20b** (R = Me, entry 3). It is interesting to note that the degree of enantioselection observed with the 2-unsubstituted, 2-benzyl, and 2-isopropyl-Quinazolinap ligands was relatively constant at room temperature (86−87% ee) (entries 1, 7, and 9). However, decreasing the reaction temperature proved detrimental to the regioselectivity and enantioselectivity of hydroboration of styrene as a general trend. In contrast, low temperatures were necessary to obtain high enantioselectivies with Binap **1** (96% ee), although complete regioselectivities were also observed at this temperature. The regioselectivities obtained for the hydroboration of styrene with rhodium complexes of Quinap **2** and Pyphos **4** were superior, and the enantiomeric excesses of 88% and 90%, respectively, mirrored closely those achieved with our quinazoline-containing ligands.[43] Additionally, an attenuated enantiomeric excess of 67% was obtained with the vaulted analogue Phenap **3**, although a respectable α:*β* ratio of 94:6 was produced.

TABLE 2. Hydroboration of Styrene



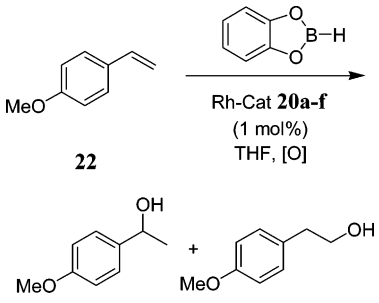
entry	R group	temp (°C)	conversion (%)	α:*β*	ee (%)
1	H	20	100	84:16	86 (*S*)
2	H	0	95	81:19	71 (*S*)
3	Me	20	100	88:12	90 (*S*)
4	Me	0	100	76:24	83 (*S*)
5	Ph	20	100	68:32	63 (*S*)
6	Ph	0	100	80:20	79 (*S*)
7	Bn	20	100	85:15	87 (*S*)
8	Bn	0	100	86:14	87 (S)
9	*i*-Pr	20	100	77:33	87 (*S*)
10	*i*-Pr	0	100	73:27	70 (*S*)
11	*t*-Bu	20	100	80:20	84 (*R*)
12	*t*-Bu	0	100	66:34	68 (*R*)

Almost quantitative conversions were obtained in all cases at room temperature with 4-methoxystyrene **22** as the substrate. As observed with styrene, a maximum enantioselectivity of 95% and regioselectivity of 88:12 was obtained with the 2-methyl catalyst system **20b**, Table 3, entry 3. An enantiomeric excess of 92% was produced on increasing the size of the 2-substituent to an isopropyl group, although this was coupled with a less favorable regiochemistry of 76:24, entry 9. Both Quinazolinap **14a** and 2-*tert*-butyl-Quinazolinap **14f** gave excellent enantioselection (91%) at room temperature, but the effect of the bulky *tert*-butyl group led to a slight decrease in the ratio of α-alcohol formed, entries 1 and 11. Additionally, lowering the reaction temperature had a deleterious effect on the enantio- and regioselectivity of the hydroboration. Clearly, these results demonstrate that an electron-releasing substituent on styrene has a favorable effect

(42) The hydroboration of styrene with both Quinazolinap- and Quinap-derived rhodium complexes was complete after 2 h at ambient temperature, whereas an extended reaction time of 12 h was necessary for complete reaction with Pyphos at this temperature.

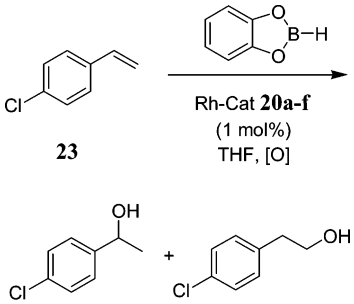
(43) Regioselectivities of 97:3 and 99:1 were obtained with Quinap and Pyphos, respectively.

TABLE 3. Hydroboration of 4-Methoxystyrene



entry	R group	temp (°C)	conversion (%)	α:β	ee (%)
1	H	20	100	81:19	91 (*S*)
2	H	0	93	77:23	90 (*S*)
3	Me	20	99	88:12	95 (*S*)
4	Me	0	97	70:30	91 (*S*)
5	Ph	20	100	75:25	77 (*S*)
6	Ph	0	100	77:23	81 (*S*)
7	Bn	20	100	78:22	89 (*S*)
8	Bn	0	91	75:25	86 (*S*)
9	*i*-Pr	20	100	76:24	92 (*S*)
10	*i*-Pr	0	67	76:24	84 (*S*)
11	*t*-Bu	20	99	78:22	91 (*R*)
12	*t*-Bu	0	100	55:45	65 (*R*)

TABLE 4. Hydroboration of 4-Chlorostyrene

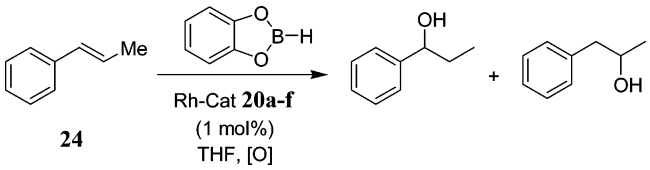


entry	R group	temp (°C)	conversion (%)	α:β	ee (%)
1	H	20	100	83:17	81 (*S*)
2	H	0	100	75:25	64 (*S*)
3	Me	20	99	88:12	77 (*S*)
4	Me	0	98	79:21	70 (*S*)
5	Ph	20	100	78:22	46 (*S*)
6	Ph	0	100	83:17	49 (*S*)
7	Bn	20	100	81:19	71 (*S*)
8	Bn	0	100	79:21	64 (*S*)
9	*i*-Pr	20	100	81:19	73 (*S*)
10	*i*-Pr	0	92	77:23	61 (*S*)
11	*t*-Bu	20	100	84:16	70 (*R*)
12	*t*-Bu	0	99	81:19	70 (*R*)

on the enantioselection, while the regiochemistry can be adversely affected by these electronic differences.

On changing from an electron-releasing to an electron-withdrawing substituent, a marked reduction in the enantioselectivity was observed. The best enantioselection in the hydroboration of 4-chlorostyrene **23** of 81% was achieved with Quinazolinap **14a** coupled with an α:β ratio of 87:13, Table 4, entry 1. Surprisingly, the influence of a 2-phenyl group in the quinazoline ring had a detrimental effect on the enantioselection of the reaction, entries 5 and 6, whereas a comparable effect was not observed with a 2-benzyl substituent, entries 7 and 8. The more sterically encumbered 2-isopropyl and 2-*tert*-butyl substituents produced enantiomeric excesses of 73% and 70% at room temperature, respectively, entries 9 and 11. It appears that the presence of an electron-withdrawing substituent on styrene has a significant impact on the enantioselection but not on the regioselectivity of the hydroboration.

TABLE 5. Hydroboration of Trans-β-methylstyrene



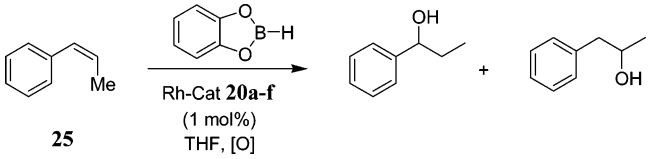
entry	ligand	time	temp (°C)	conversion (%)	α:β	ee (%)
1	H	2	20	54	92:8	89 (*S*)
2	H	24	0	50	93:7	82 (*S*)
3	Me	2	20	93	93:7	94 (*S*)
4	Me	2	0	96	94:6	95 (*S*)
5	Ph	2	20	100	91:9	94 (*S*)
6	Ph	4	0	100	96:4	85 (*S*)
7	Bn	2	20	64	93:7	80 (*S*)
8	Bn	2	0	67	92:8	92 (*S*)
9	*i*-Pr	2	20	100	91:9	88 (*S*)
10	*i*-Pr	4	0	100	87:13	91 (*S*)
11	*t*-Bu	2	20	97	94:6	86 (*R*)
12	*t*-Bu	4	0	100	92:8	91 (*R*)

The effect of varying the electronics on enantioselectivity was less pronounced with Binap, although changing from a 4-methoxy (89% ee) to a 4-chloro (91% ee) substituent did result in a slight increase in enantioselection.[28] 4-Methoxystyrene was hydroborated in 94% ee with Quinap- and Pyphos-derived rhodium complexes, yet a slightly higher regioselectivity was produced in the latter case (98:2 vs 96:4). With 4-chlorostyrene as substrate, lowered enantiomeric excesses of 78% and 79% were obtained with Quinap and Pyphos, accompanied by high regioselectivities of 96:4 and 99:1, respectively. Whereas the enantioselection observed with our modular Quinazolinap series is comparable, if not superior, to other axially chiral systems applied, they are limited in terms of regiochemical control.

However, substitution of the vinylarene double bond results in a marked reduction in the enantioselectivity with Binap and other diphosphines. In contrast, the application of P,N-ligand systems to more sterically demanding substrates leads to an overall increase in enantioselection. Therefore, it is of interest to apply our quinazoline-containing phosphinamines to the hydroboration of β-substituted substrates, as well as those with differing aromatic substitution patterns.

The most obvious benefit of β-substitution, for instance with (*E*)-β-methyl-styrene **24**, was the marked increase in regioselectivity compared to that of the unsubstituted styrene derivatives, Table 5. An optimum enantioselectivity of 95% was obtained with the 2-methyl rhodium complex **20b**, entry 4, while the ee range was 80−94% irrespective of the ligand 2-substitution pattern. A further observation was the reduced conversion obtained with Quinazolinap **14a** at room temperature, which was further exacerbated at low temperature, where an extended reaction period of 24 h was required for a 50% conversion, entries 1 and 2. The effect of the *trans*-alkene stereochemistry on the reaction progress was less pronounced with 2-phenyl, 2-isopropyl, and 2-*tert*-butyl-Quinazolinap, as quantitative conversions were obtained after 4 h at 0 °C, entries 6, 10, and 12. Overall, the

TABLE 6. Hydroboration of *cis*-β-Methylstyrene



25

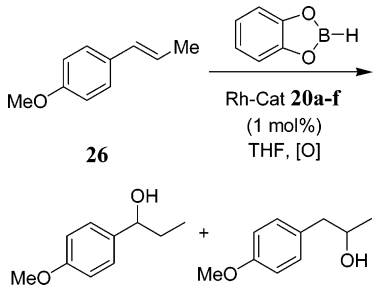
entry	ligand	time	temp (°C)	conversion (%)	α:β	ee (%)
1	H	2	20	96	99:1	94 (*S*)
2	H	2	0	85	99:1	92 (*S*)
3	Me	2	20	97	99:1	95 (*S*)
4	Me	2	0	100	99:1	97 (*S*)
5	Ph	2	20	100	92:8	91 (*S*)
6	Ph	2	0	100	94:6	88 (S)
7	Bn	2	20	100	99:1	90 (S)
8	Bn	2	0	95	98:2	90 (S)
9	*i*-Pr	2	20	100	96:4	96 (*S*)
10	*i*-Pr	2	0	100	93:7	90 (*S*)
11	*t*-Bu	2	20	100	91:9	93 (*R*)
12	*t*-Bu	2	0	100	90:10	71 (*R*)

2-substituted-Quinazolinap series was found to be more effective than Binap (42% ee) for the hydroboration of *trans*-β-methyl styrene and gave results comparable to those of Quinap (95% ee), although complexes of the latter were more regioselective (99:1).

A distinct improvement in regioselectivity was evident on hydroboration of *cis*-β-methylstyrene **25** compared to its *trans*-isomer **24**. The smaller quinazoline 2-substituents proved to be more regioselective catalysts (99:1) compared to the bulkier ligand substituents, Table 6, entries 1−4 vs entries 5−12. In addition, lowering the reaction temperature slightly decreased the α:β ratio when rhodium complexes of 2-benzyl, 2-isopropyl, and 2-*tert*-butyl-Quinazolinap were employed, entries 7−12. An optimum enantiomeric excess of 97% was obtained at 0 °C with the 2-methyl variant **20b**, entry 4, whereas the highest enantioselection (96%) at room temperature was produced with the 2-isopropyl-derived rhodium complex **20e**, entry 9. These are the best results reported to date for the hydroboration of *cis*-β-methylstyrene. Furthermore, a significantly enhanced conversion was observed on changing from a *trans*- to *cis*-alkene stereochemistry with Quinazolinap rhodium complexes **20a,** which highlights the difference in reactivity between the two substrates, Table 5, entries 1 and 2 vs Table 6, entries 1 and 2. In general, our 2-substituted-Quinazolinap series compares most favorably with Binap (18%), whereas the 2-methyl and 2-isopropyl variants **20b** and **20e**, respectively, perform better than Quinap (93%) with this sterically demanding substrate.

Similarly, the alkene stereochemistry of *trans*-anethole **26** had a detrimental effect on the conversion when Quinazolinap-derived rhodium complexes **20a** were employed, although a sluggish rate of reaction was also observed with the 2-benzyl variant at 0 °C, Table 7, entries 2 and 8. However, excellent conversions of 97% and 100% were obtained using the 2-isopropyl and 2-*tert*-butyl rhodium complexes **20e** and **20f**, respectively, after 24 h at low temperature, entries 10 and 12. An optimum enantioselectivity of 97% was obtained with the 2-methyl complex **20b**, accompanied by a regioselectivity of 88:12, entry 4. Unexpectedly, increased enantioselectivities were produced at 0 °C with the 2-methyl, 2-phenyl, 2-benzyl, and 2-*tert*-butyl complexes. In comparison to

TABLE 7. Hydroboration of *trans*-Anethole



26

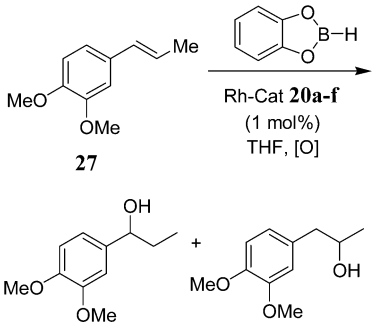
entry	ligand	time	temp (°C)	conversion (%)	α:β	ee (%)
1	H	2	20	51	78:22	88 (*S*)
2	H	2	0	29	80:20	78 (*S*)
3	Me	2	20	78	86:14	92 (*S*)
4	Me	2	0	89	88:12	97 (*S*)
5	Ph	2	20	87	88:12	88 (*S*)
6	Ph	2	0	72	89:11	92 (*S*)
7	Bn	2	20	77	85:15	88 (*S*)
8	Bn	2	0	31	68:32	90 (*S*)
9	*i*-Pr	2	20	51	77:23	93 (*S*)
10	*i*-Pr	24	0	97	68:32	87 (*S*)
11	*t*-Bu	2	20	88	89:11	90 (*R*)
12	*t*-Bu	24	0	100	83:17	91 (*R*)

trans-β-methyl styrene, lower regioselectivities were observed as a consequence of the additional 4-methoxy aromatic substituent. Our highest enantioselectivity of 97% for *trans*-anethole (2-methyl-complex **20b**) equals that reported for Quinap,[30] although a more favorable regiochemistry of 99:1 was achieved with the isoquinoline-derived rhodium complex.

Surprisingly, a more favorable regiochemistry was obtained with *trans*-3,4-dimethoxy-β-methyl styrene **27** relative to that of *trans*-anethole **26**. However, as expected the hydroboration progress was attenuated with the Quinazolinap catalyst **20a** even at room temperature, Table 8, entry 1. The enantiomeric excess and conversion were improved at low temperature, although a 24-h reaction period was required, entry 2. The best enantioselectivity of 98% was obtained using 2-methyl-Quinazolinap at 0 °C, entry 4. In addition, a higher degree of enantioselection and regiocontrol was obtained with the 2-phenyl rhodium complex **20c** compared to that of the 2-benzyl, 2-isopropyl, and 2-*tert*-butyl analogues **20d**−**f**, entries 5−8.

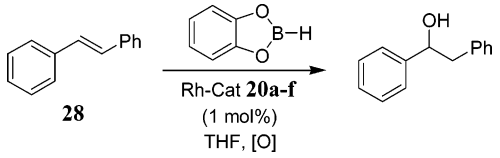
A significantly attenuated conversion was apparent in all cases on application of the more sterically demanding (*E*)-stilbene **28** substrate. This was exemplified by the Quinazolinap-derived rhodium complex **20a**, as there was no reaction even after 24 h at room temperature, Table 9, entry 1. Similarly, there was no evidence of product formation when 2-phenyl-Quinazolinap **14c** was employed, entry 5. Again, the steric influence of 2-methyl variant **20b** proved optimal, and the highest enantioselectivity and conversion of 87% and 50%, respectively, were obtained after 21 h, entry 2. Moderate to good enantiomeric excesses were observed with the 2-benzyl, 2-isopropyl, and 2-*tert*-butyl analogues, although the reactions were also characterized by poor yields, entries 7−12. Additionally, although the hydroboration of *trans*-stilbene **28** was slow with Quinap **2** as ligand (45 turnovers in 20 h), a respectable enantioselectivity of 85% was obtained.

TABLE 8. Hydroboration of *trans*-3,4-Dimethoxy-β-methyl Styrene



entry	ligand	time	temp (°C)	conversion (%)	α:β	ee (%)
1	H	2	20	35	88:12	76 (*S*)
2	H	24	0	68	86:14	93 (*S*)
3	Me	2	20	86	93:7	95 (*S*)
4	Me	2	0	75	92:8	98 (*S*)
5	Ph	2	20	62	93:7	94 (*S*)
6	Ph	24	0	65	91:9	93 (*S*)
7	Bn	2	20	77	90:10	90 (*S*)
8	Bn	2	0	74	85:15	84 (*S*)
9	*i*-Pr	2	20	72	82:18	91 (*S*)
10	*i*-Pr	24	0	72	87:13	85 (*S*)
11	*t*-Bu	2	20	55	90:10	86 (*R*)
12	*t*-Bu	24	0	76	70:30	59 (*R*)

TABLE 9. Hydroboration of *trans*-Stilbene



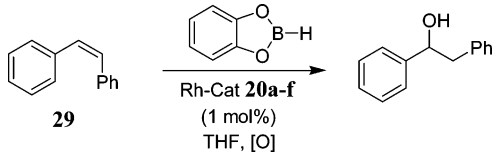
entry	ligand	time	temp (°C)	conversion (%)	ee (%)
1	H	24	20		
2	Me	21	20	50	87 (*S*)
4	Me	21	0	16	80 (*S*)
5	Ph	24	20		
7	Bn	2	20	7	77 (*S*)
8	Bn	24	0	17	69 (*S*)
9	*i*-Pr	2	20	7	64 (*S*)
10	*i*-Pr	24	0	18	59 (*S*)
11	*t*-Bu	2	20	15	65 (*R*)
12	*t*-Bu	24	0	6	53 (*R*)

The hydroboration of *cis*-stilbene **29** occurred rapidly at room temperature and at 0 °C compared to its *trans*-isomer **28**. Excellent enantioselectivities were obtained with the 2-alkyl-substituted rhodium complexes, whereas a sharp decrease in enantiomeric excess was observed with the 2-phenyl complex **20c**, Table 10, entries 5 and 6. An optimal enantioselectivity of 99% was produced on application of the 2-isopropyl complex **20e** and is the best result reported to date for the hydroboration of *cis*-stilbene, entry 9. Furthermore, an enantiomeric excess of 97% was obtained with the 2-methyl and 2-*tert*-butyl rhodium complexes, entries 3, 4, and 12. Quinap **2** was also an effective catalyst with this substrate and afforded (*R*)-1,2-diphenyl ethanol in 91% ee and 86% yield.

An excellent enantioselectivity of 98% was achieved in the hydroboration of indene **30** with the Quinazolinap-derived ligand system **20a**, although the conversion was moderate at low temperature, Table 11, entry 2. The introduction of a 2-methyl group into the ligand framework was striking, as a quantitative conversion, an enantiomeric excess of 99.5%, and complete regioselectivity was observed, entry 3. This represents the highest result reported for the hydroboration of indene. The catalyst system was also highly efficient at 0 °C, affording a 99% enantioselectivity and α:β ratio of 99:1, entry 4. Interestingly, the degree of enantioselection (ca. 81−86% ee) was comparable with that of the 2-phenyl, 2-benzyl, 2-isopropyl, and 2-*tert*-butyl catalyst systems, entries 5−12. The decrease in enantiomeric excess with larger 2-substituents indicates that a less sterically demanding ligand can more easily accommodate the cyclic substrate, and this has a profound effect on the catalytic chemistry observed. On the whole, the Quinazolinap series are superior to all other ligand systems reported for the hydroboration of indene, as an enantiomeric excess of just 19% was obtained with Binap, whereas Quinap and Phenap afforded ee's of 76% and 64%, respectively.

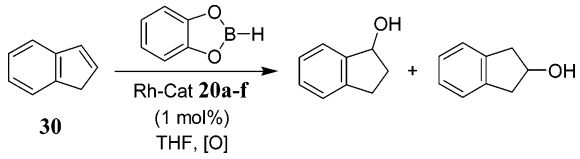
Excellent regioselectivities were obtained in all cases with 1,2-dihydronaphthalene **31** as the substrate. The 2-methyl complex **20b** produced the highest enantiomeric excess of 93% at 0 °C, entry 4, followed by the 2-*tert*-butyl catalyst system **20f**, which afforded an enantioselectivity of 90%, Table 12, entries 4 and 12. In general, lowering the reaction temperature led to a reduction in

TABLE 10. Hydroboration of *Cis*-stilbene



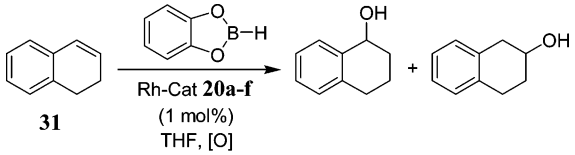
entry	ligand	time	temp (°C)	conversion (%)	ee (%)
1	H	2	20	73	92 (*S*)
2	H	24	0	97	95 (*S*)
3	Me	2	20	96	97 (*S*)
4	Me	2	0	82	97 (*S*)
5	Ph	2	20	100	59 (*S*)
6	Ph	2	0	100	62 (*S*)
7	Bn	2	20	83	89 (*S*)
8	Bn	2	0	81	89 (*S*)
9	*i*-Pr	2	20	84	99 (*S*)
10	*i*-Pr	2	0	60	95 (*S*)
11	*t*-Bu	2	20	71	96 (*R*)
12	*t*-Bu	2	0	80	97 (*R*)

TABLE 11. Hydroboration of Indene



entry	ligand	time	temp (°C)	conversion (%)	α:β	ee (%)
1	H	2	20	83	98:2	90 (*S*)
2	H	2	0	39	97:3	98 (*S*)
3	Me	2	20	100	>99:1	99.5 (*S*)
4	Me	2	0	95	99:1	99 (*S*)
5	Ph	2	20	98	98:2	84 (*S*)
6	Ph	2	0	99	98:2	81 (*S*)
7	Bn	2	20	99	99:1	82 (*S*)
8	Bn	2	0	88	97:3	86 (*S*)
9	*i*-Pr	2	20	100	98:2	84 (*S*)
10	*i*-Pr	2	0	100	97:3	81 (*S*)
11	*t*-Bu	2	20	100	94:6	72 (*R*)
12	*t*-Bu	2	0	100	97:3	80 (*R*)

TABLE 12. Hydroboration of 1,2-Dihydronaphthalene



entry	ligand	time	temp (°C)	conversion (%)	α:β	ee (%)
1	H	2	20	78	>99:1	87 (*S*)
2	H	2	0	64	>99:1	77 (*S*)
3	Me	2	20	98	>99:1	89 (*S*)
4	Me	2	0	90	>99:1	93 (*S*)
5	Ph	2	20	100	>99:1	89 (*S*)
6	Ph	2	0	>99	>99:1	88 (*S*)
7	Bn	2	20	81	>99:1	87 (*S*)
8	Bn	2	0	42	>99:1	78 (*S*)
9	*i*-Pr	2	20	91	>99:1	86 (*S*)
10	*i*-Pr	2	0	50	>99:1	64 (*S*)
11	*t*-Bu	2	20	97	>99:1	83 (*R*)
12	*t*-Bu	2	0	96	>99:1	90 (*R*)

conversion, and a corresponding drop in enantiomeric excess was observed with the 2-unsubstituted, 2-benzyl, and 2-isopropyl variants, entries 1 and 2 and 7−10. The highest reported enantioselection of 96% was obtained with Quinap **2**, although our modular Quinazolinap series compares more favorably with Phenap (84%) for the hydroboration of 1,2-dihydronaphthalene **31**.[11]

In conclusion, rhodium complexes of our 2-substituted-Quinazolinap series were highly efficient catalysts for the hydroboration of vinylarenes. For styrene derivatives, higher enantioselectivities were obtained with a 4-methoxy substituent (up to 95% ee) compared to those of the 4-chloro or 4-unsubstituted analogues. This signifies that the electronic nature of the substrate combined with the inherent steric properties of the catalyst are important for high asymmetric induction. A marked increase in regioselectivity and enantioselectivity was observed when *β*-substituted substrates were employed, which was particularly evident in the hydroboration of *cis*-*β*-methylstyrene (97% ee). Generally, the smaller quinazoline 2-substituents afforded a superior regiochemistry than the bulkier ligands, whereas a *trans*-alkene stereochemistry typically lowered the regiocontrol and hampered the reaction progress. This trend was further highlighted with *trans*-anethole, although the degree of enantiocontrol was comparable to that obtained with *trans*-*β*-methylstyrene. The effect of two methoxy substituents in (*E*)-3,4-dimethoxy-*β*-methylstyrene led to an augmented regio- and enantioselectivity in several cases (up to 98% ee), demonstrating that our 2-substituted-Quinazolinap systems also form highly stereoselective catalysts for the hydroboration of *β*-substituted electron rich vinylarenes. The increased steric demand at the *β*-position in *trans*-stilbene had a detrimental effect on both the enantioselection and chemical yield, although its *cis*-isomer was hydroborated with an optimal enantiomeric excess of 99%. Of the cyclic olefins applied, indene was hydroborated with exceptional enantioselectivity (99.5%) and regioselectivity (>99:1), while the less sterically demanding ligands afforded higher levels of stereocontrol. Overall, the present study has highlighted the potential benefits of ligand−substrate matching in this asymmetric transformation and as a consequence has afforded some of the highest reported enantiomeric excesses for several members of the vinylarene class. Further studies into electronic effects in enantioselective hydroboration are currently underway and will form the basis of future publications from these laboratories.

Experimental Section

General Methods. Melting points were determined using a standard melting point apparatus and are uncorrected. Infrared spectra were recorded on an infrared FT spectrometer. The Microanalytical Laboratory, University College Dublin, performed elemental analyses. Electron impact mass spectra were determined on a mass spectrometer in the EI mode unless otherwise stated. Exact mass ESI mass spectra (HRMS) were measured on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass. ^{1}H NMR spectra were obtained on a 300 and a 500 MHz spectrometer. ^{1}H−^{1}H COSY spectra were recorded on a 300 and a 500 MHz spectrometer. Chemical shifts are quoted in ppm relative to tetramethylsilane, and coupling constants (*J*) are quoted in Hz. $CDCl_3$ was used as the solvent for all NMR spectra unless otherwise stated. 75.4 MHz ^{13}C spectra were recorded on a 300 MHz spectrometer and 125.7 MHz ^{13}C spectra on a 500 MHz spectrometer. Tetramethylsilane was used as the internal standard in all ^{13}C spectra recorded. 121.4 MHz ^{31}P spectra were recorded on a 300 MHz spectrometer, and ^{31}P chemical shifts are reported relative to 85% aqueous phosphoric acid (0.0 ppm). Flash chromatography was performed using Merck Kieselgel 60 (art. 9385) and aluminum oxide 90, standardized (activity II−III). Merck precoated Kieselgel 60F_{254} and alumina (neutral, type E) were used for thin-layer chromatography. GC and HPLC analysis were carried out using a Supelco 2-4304 beta-Dex 120 (30 mm × 0.25 mm, 0.25 mm film) and a Chiralcel OD column (0.46 cm i.d. × 25 cm), respectively. Optical rotation values were measured on a standard polarimeter. All commercially available solvents were purified and dried before use. Diethyl ether and tetrahydrofuran were distilled from sodium/benzophenone, and dichloromethane was distilled from calcium hydride. Where necessary other solvents and reagents used were purified according to the procedures in *Purification of Laboratory Chemicals*.[44] Solvents were degassed using three freeze−thaw cycles. Note: The experimental details for the preparation and resolution of 2-phenyl-Quinazolinap have previously been published.[15]

General Method for the Preparation of Imidate Hydrochloride Salts. Acetimidic Acid Methyl Ester 7a. Hydrogen chloride was bubbled through a solution of acetonitrile (28.57 mL, 0.547 mmol) in dry methanol (26.55 mL, 0.656 mmol) and hexane (160 mL) in a two-necked flask for 4 h at 0−5 °C. The mixture was allowed to stir for 30 min until a white precipitate formed. Further precipitation occurred after storage at −10 °C for 3 days. The product was filtered and dried to give acetimidic acid methyl (44.94 g, 75%) as a white solid: mp 97−100 °C (lit.[45] mp 95−95.5 °C); ν_{max} (KBr) 3687, 3337, 2546, 2365, 2304, 2170, 1517, 1362 1143, 1048, 872 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$) δ 12.5 (1H, br. s), 11.5 (1H, br. s), 4.3 (3H, s), 2.52 (3H, s); ^{13}C NMR (75 MHz; $CDCl_3$) δ 176.78, 59.7, 18.4.

General Method for the Preparation of 2-Substituted-4(3*H*)quinazolinones. 2-Methyl-4(3*H*)quinazolinone 9a. Anthranilic acid (5.00 g, 36.46 mmol) was dissolved in dry methanol (40 mL) under nitrogen on a vacuum line. Acetimidic acid methyl ester (3.54 g, 37.82 mmol) in dry methanol (40 mL) was placed under nitrogen in a separate Schlenk tube to give a cloudy white suspension. Sodium metal (1.04 g, 45.38 mmol) was added carefully in several portions to this suspension, which was precooled over an ice bath. The anthranilic

(44) Perrin, D.; Armarego, W. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon.
(45) Bristol-Myers Co. Patent DE 1806169; *Chem. Abstr.* **1970**, 72.

acid solution was transferred via cannula to the free based imidate in methanol and stirred for 30 min. The reaction mixture was heated at 80 °C for 6 h, the reaction mixture was then cooled to room temperature, and the Schlenk tube was placed in an ice bath to facilitate crystal formation. The solution was filtered, and the white paperlike solid was dried under vacuum. The mother liquor was reduced in volume and allowed to crystallize overnight. The solid was filtered, dried, and combined with the initial crop to furnish 2-methyl-4(3*H*)-quinazolinone (2.52 g, 43%): mp 229−230 °C (lit.[49] mp 230−232 °C); ν_{max} (KBr) 3710, 3192, 3003, 2908, 1826, 1446 cm^{-1}; ^1H NMR (300 MHz; $CDCl_3$) δ 11.5 (1H, br. s), 8.29 (1H, ddd, J = 7.61, 1.47, 0.59 Hz), 7.77 (1H, dt, J = 8.49, 7.03, 1.47), 7.68 (1H, ddd, J = 8.79, 1.17, 0.59 Hz), 7.48 (1H, dt, J = 8.2, 7.03, 1.47), 2.59 (3H, s); ^{13}C NMR (75 MHz; $CDCl_3$) δ 164.2, 154, 149.8, 134.5, 127.3, 126.5, 126.2, 121, 22; EIMS m/z 160 (M^+, 100), 145 (17), 132 (10), 118 (25).

General Method for the Preparation of 2-Substituted-4-chloroquinazolines. 4-Chloro-2-methyl-quinazoline 8a. A solution of 2-methyl-4(*3H*)quinazolinone (6.0 g, 37.5 mmol), *N*,*N*-diethylaniline (8.9 mL, 56.1 mmol), and dry benzene (100 mL) was refluxed for 5 min. Phosphorus oxychloride (2.9 mL, 31.2 mmol) was added by syringe, and the resultant mixture was refluxed for 3 h [a clear orange color developed after 1 h at reflux and turned deep red after 1.5 h] maintaining anhydrous conditions by use of a $CaCl_2$ drying tube attached to the condenser. The solution was cooled to room temperature and filtered. The insoluble precipitate was washed with dry benzene (40 mL). The combined filtrate was rapidly washed sequentially with ice water (100 mL), ice-cooled 20% sodium hydroxide (2 × 100 mL), ice water (100 mL), and saturated sodium chloride (100 mL). The organic layer was immediately washed with a HCl solution (1 M, 100 mL) and water (100 mL) and dried over sodium sulfate. The solvent was removed in vacuo at 30 °C to give 4-chloro-2-methyl-quinazoline (4.0 g, 59%) as a light yellow solid: mp 85−86 °C (lit.[54] mp 81.5−83 °C); ν_{max} (KBr) 3158, 3010, 1870, 1662, 1477, 1143, 744 cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ 8.22 (1H, ddd, J = 8.2, 1.46, 0.59 Hz), 8.0−7.88 (2H, m) 7.65 (1H, dt, J = 8.2, 6.44, 1.46 Hz), 2.86 (3H, s); ^{13}C NMR (75 MHz; $CDCl_3$) δ 163.6, 162.2, 151.5, 134.9, 128.1, 128, 125.7, 121.8, 26.1; EIMS m/z 178 (M^+, 21), 143 (100), 116 (7). Anal. Calcd for $C_9H_7N_2Cl$: C, 60.52; H, 3.95; N, 15.68. Found: C, 60.43; H, 3.98; N, 15.40.

Note: 4-Chloroquinazoline was prepared from the commercially available 4-hydroxyquinazoline employing an identical procedure: white powder (76%), mp 94−96 °C; ν_{max} (KBr) 3078, 1582, 1489, 1325, 761 cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 9.06 (1H, s), 8.29 (1H, d, J = 8.4 Hz), 8.09 (1H, d, J = 8.5 Hz), 7.99 (1H, t, J = 7.0 Hz), 7.76 (1H, t, J = 7.0 Hz); EIMS (70 eV) m/z 166 (M^+, 18%), 164 (55), 130 (12), 129 (100), 102 (47), 76 (20), 75 (37), 74 (15).

General Method for the Preparation of 2-Substituted-4-(2-methoxy-naphthalen-1-yl)-quinazolines 11a−f. 2-Substituted-4-chloroquinazoline (31.40 mmol) was added as a solid to a solution of tetrakis(triphenylphosphine)palladium(0) (0.94 mmol) in DME (40 mL) and stirred for 10 min under a nitrogen atmosphere. 2-Methyloxy-1-naphthylboronic acid (31.40 mmol), dissolved in the minimum amount of degassed ethanol (∼50 mL), was then added to the 2-substituted-chloroquinazoline solution. Sodium carbonate solution (35 mL, 2M) was added, and the solution was refluxed under nitrogen for 4 d. The solution was cooled to room temperature and filtered to remove any solid, which was washed with dichloromethane. The solvent was removed in vacuo to give a brown oil, which was redissolved in dichloromethane (50 mL), washed with brine (3 × 30 mL), dried over magnesium sulfate, and reduced in vacuo to give a brown solid.

2-Hydrogen-4-(2-methoxy-naphthalen-1-yl)-quinazoline 11a. Purified by stirring in pentane to give 2-hydrogen-4-(2-methoxy-naphthalen-1-yl)-quinazoline (79%). The pentane filtrate was concentrated to an oi,l which was then purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give further product (4%): mp 180−182 °C; ν_{max} (KBr) 3007, 1590, 1489, 1280, 1249, 1069 and 769 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.52 (1H, s), 8.16 (1H, d, J = 8.4 Hz), 8.05 (1H, d, J = 9.1 Hz), 7.90 (2H, m), 7.52 (1H, d, J = 8.4 Hz), 7.45 (1H, dt, J_1 = 7.1 Hz, J_2 = 1.3 Hz), 7.44 (1H, d, J = 9.1 Hz), 7.35 (1H, dt, J_1 = 6.8 Hz, J_2 = 1.3 Hz), 7.29 (1H, dt, J_1 = 7.1 Hz, J_2 = 1.3 Hz), 7.07 (1H, d, J = 8.4 Hz) and 3.78 (3H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 167.7, 155.4, 154.8, 150.7, 134.2, 133.1, 131.6, 129.2, 128.9, 128.3, 127.9, 127.6, 127.3, 125.9, 124.5, 124.2, 119.6, 113.4 and 56.53; EIMS (70 eV) m/z 286 (M^+, 34%), 285 (47), 271 (11), 270 (22), 269 (11), 242 (15), 114 (10) and 76 (12); Found C, 79.54; H, 5.04; N, 9.51. $C_{19}H_{14}N_2O$ requires C, 79.69; H, 4.93; N, 9.78.

General Method for the Preparation of 1-(2-substituted-quinazolin-4-yl)-naphthalen-2-ols 12a−f. 2-Substituted-4-(2-methoxy-naphthalen-1-yl)-quinazoline (26.81 mmol) was dissolved in dry dichloromethane (130 mL) in a 250 mL Schlenk tube. Boron tribromide (53.6 mmol, 1 M solution in dichloromethane) was added slowly via syringe, and the reaction was stirred overnight (16 h) under an atmosphere of nitrogen. Because of the light-sensitive nature of boron tribromide the reaction vessel was covered with aluminum foil for the duration of the reaction. Distilled water (80 mL) was added slowly to the solution, and some vigorous fizzing was observed. An orange precipitate formed after 15 min and was allowed to stir for an additional 1 h. This precipitate was isolated by filtration giving pure 1-(2-substituted-quinazolin-4-yl)-naphthalen-2-ol. The filtrate was neutralized with 1 M NaOH and extracted with dichloromethane, and the organic layer was then stirred with 10% HCl for 30 min. Dichloromethane was added to dissolve any additional solid that precipitated from solution, and the organic layer was isolated once again and reduced in vacuo. All solid was combined and dissolved in dichloromethane (orange color), and 2 M Na_2CO_3 solution was added and allowed stir for 1 h. The organic layer was isolated from the black solution, the aqueous layer was extracted twice with dichloromethane, and the combined solutions were dried over $MgSO_4$ and reduced in vacuo. 1-(2-Substituted-quinazolin-4-yl)-naphthalen-2-ol was isolated as a light orange powder.

1-(Quinazolin-4-yl)naphthalen-2-ol 12a: 83%, mp 195−197 °C; ν_{max} (KBr) 3629, 3043, 1585, 1347, 1276, 814 and 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.36 (1H, br s), 9.24 (1H, s), 8.04 (1H, d, J = 8.4 Hz), 7.85 (2H, m), 7.84 (1H, d, J = 9.7 Hz), 7.63 (1H, d, J = 8.4 Hz), 7.45 (1H, dt, J_1 = 6.8 Hz, J_2 = 1.3 Hz), 7.34 (1H, dt, J_1 = 6.8 Hz, J_2 = 1.0 Hz), 7.26 (1H, dt, J_1 = 8.1 Hz, J_2 = 1.3 Hz), 7.25 (1H, d, J = 9.1 Hz) and 7.13 (1H, d, J = 8.7 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.8, 154.1, 153.9, 150.8, 134.6, 132.7, 132.3, 128.7, 128.6, 128.3, 127.9, 127.9, 127.0, 124.7, 124.6, 123.7, 119.2 and 115.1; EIMS (70 eV) m/z 272 (M^+, 32%), 271 (53), 243 (7), 122 (7) and 76 (8). Found: C, 78.97; H, 4.38; N, 10.08. $C_{18}H_{12}N_2O$ requires C, 79.38; H, 4.44; N, 10.29.

General Method for the Preparation of 1-(2-Substituted-quinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonates 13a−f. To a solution of 1-(2-substituted-quinazolin-4-yl)-naphthalen-2-ol (14.0 mmol) and 4-(dimethylamino)pyridine (42.0 mmol) in dry dichloromethane (130 mL) was added trifluoromethanesulfonic anhydride (15.4 mmol), dropwise

(46) Hunter, M. J.; Ludwig, M. L. *J. Am. Chem. Soc.* **1962**, *84*, 3491.
(47) Ganapathiplackal M.; Shafi, P. M. *Indian J. Chem.* **1986**, *25*, 204.
(48) Pattenden, G.; Thom, S. M. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1629.
(49) Mori, M.; Uozumi, Y.; Shibasaki, M. *J. Organomet. Chem*, **1990**, *3*, 225.
(50) Scheiner, P.; Frank, L.; Giusti, I.; Arwin, S.; Pearson, S. A. *J. Heterocycl. Chem.* **1984**, *21*, 1817.
(51) Xu, X.; Lu, P.; Zhang, Y. *Synth. Commun.* **2001**, *31*, 323.
(52) Bogert, M. T.; Hand, W. F. *J. Am. Chem. Soc.* **1902**, *24*, 1042.
(53) Goerdeler, J.; Richter, R. *Synthesis* **1978**, 760.
(54) Scarborough, H. C., Lawes, B. C., Minielli, J. L., Compton, J. L. *J. Org. Chem.* **1962**, *27*, 957.

with stirring, to give an orange solution. The reaction was stirred overnight (16 h). The dark orange solution was then washed with 1 M HCl (3 × 50 mL), water (2 × 60 mL), and brine (1 × 60 mL) and dried over magnesium sulfate. The solvent was reduced in vacuo to give an orange solid, which was purified by column chromatography (silica gel, 2:1 petroleum ether/ethyl acetate) to give 1-(2-substituted-quinazolin-4-yl)-2-naphthyl(trifluoromethyl) sulfonate.

1-(Quinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate 13a. Purified by chromatography (silica gel, 2:1 petrol ether/ethyl acetate) to give 1-(quinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonate (88%): mp 110−112 °C; ν_{max} (KBr) 3064, 1492, 1423, 1219, 1140 and 830 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.56 (1H, s), 8.21 (1H, d, J = 8.4 Hz), 8.15 (1H, d, J = 9.1 Hz), 8.02 (1H, d, J = 8.4 Hz), 7.96 (1H, dt, J1 = 6.8 Hz, J2 = 1.6 Hz), 7.62 (1H, d, J = 9.1 Hz), 7.60 (1H, t, J = 7.1 Hz), 7.52 (1H, dt, J1 = 7.1 Hz, J2 = 1.0 Hz), 7.45 (2H, m) and 7.27 (1H, dd, J = 9.1 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.3, 154.9, 150.7, 144.6, 134.5, 132.4, 132.3, 132.1, 129.1, 128.4, 128.3, 128.3, 127.5, 126.9, 126.4, 126.0, 125.0, 119.4 and 121.9−119.4−116.9−114.4 (q, J_{C-F} = 320 Hz); EIMS (70 eV) m/z 404 (M$^+$, 13%), 272 (23), 271 (100), 243 (53), 242 (37), 214 (14) and 69 (24). Found: C, 56.16; H, 2.72; N, 6.74; S, 8.2; F, 14.1. $C_{19}H_{11}N_2O_3SF_3$ requires C, 56.43; H, 2.74; N, 6.93; S 7.91; F 14.11.

1-(2-Methylquinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonate 13b. Purified by silica gel column chromatography (petroleum ether/ethyl acetate 2:1) to give 1-(2-methylquinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate as a white solid (78%): mp 124−126 °C. ν_{max} (KBr) 3065, 1612, 1558, 1512, 1428, 1214 (s), 1140 (s) and 831 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (1H, d, J = 10.1 Hz), 8.10 (1H, d, J = 9.2 Hz), 8.00 (1H, d, J = 8.3 Hz), 7.89 (1H, dt, J_1 = 7.7 Hz, J_2 = 1.6 Hz), 7.61 (1H, d, J = 9.2 Hz), 7.59 (1H, t, J = 7.6 Hz), 7.44−7.39 (3H, m), 7.27 (1H, d, J = 8.6 Hz) and 3.01 (3H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.6, 163.5, 151.3, 144.9, 134.6, 132.6, 132.5, 132.2, 128.6, 128.6, 128.5, 127.6, 127.5, 127.4, 126.6, 126.3, 122.9, 119.7, 118.4 (q, J = 320.3 Hz) and 26.6; EIMS (70 eV) m/z 418 (M$^+$, 9%), 285 (100), 257 (53), 243 (12) and 69 (13). Found: C, 57.1; H, 3.2; N, 6.5; S, 8.1; F, 13.8. $C_{20}H_{13}N_2O_3SF_3$ requires C, 57.4; H, 3.1; N, 6.7; S, 7.7; F, 13.6.

1-(2-Phenylmethyl-quinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonate 13d: 77% as beige solid; mp 136−138 °C; ν_{max} (KBr) 3065, 2935, 1615, 1552, 1425, 1214, 1136, 950 and 834 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (1H, d, J = 8.55 Hz), 8.10 (1H, d, J = 8.95 Hz), 7.98 (1H, d, J = 8.15 Hz), 7.88 (1H, dt, J = 8.55, 6.56, 1.99 Hz), 7.60 (1H, d, J = 8.95 Hz), 7.57 (1H, dt, J = 8.15, 6.96, 1.19 Hz), 7.45 (1H, dt, J = 7.36, 1.39 Hz), 7.47−7.36 (4H, m), 7.31−7.19 (3H, m), 7.19 (1H, d, J = 8.35 Hz), 4.57 (1H, d, J = 13.91 Hz) and 4.56 (1H, d, J = 13.91 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 163.7, 151.5, 144.8, 138.7, 134.5, 132.7, 132.2, 129.5, 129.0, 128.6, 128.5, 128.4, 127.7, 127.6, 127.3, 126.6, 126.5, 126.4, 123.2, 119.7, 119.6 and 46.5; EIMS (70 eV) m/z 494 (M$^+$, 10%), 361 (100), 180 (41), 165 (25), 114 (10), 91 (84) and 65 (17). Anal. Calcd for $C_{26}H_{17}N_2O_3SF_3$: C, 63.15; H, 3.47; N, 5.67; S, 6.48; F, 11.53. Found: C, 62.83; H, 3.51; N, 5.53; S, 6.66; F, 11.14.

1-(2-Isopropyl-quinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonate 13e. Purified by silica gel column chromatography (petroleum ether/ethyl acetate 2:1) to give 1-(2-isopropyl-quinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate as a yellow solid (97%): mp 117−118 °C; ν_{max} (KBr) 3059, 2978, 2929, 1616, 1491, 1434, 1229, 1135 and 847 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (1H, d, J = 8.49 Hz), 8.11 (1H, d, J = 8.78 Hz), 8.0 (1H, d, J = 8.2 Hz), 7.88 (1H, dt, J = 8.5, 6.74, 1.78 Hz), 7.6 (1H, d, J = 9.08 Hz), 7.58 (1H, dt, J = 8.2, 7.03,1.47 Hz), 7.44 (1H, dt, J= 8.49, 7.03, 1.17 Hz), 7.41−7.33 (2H, m) and 7.28 (1H, d, J = 8.5 Hz), 3.52 (1H, sept, J = 7.03) and 1.50 (6H, d, J = 6.74 Hz); ^{13}C (75 MHz, $CDCl_3$) δ 170.6, 162.1, 150, 143.6, 133, 131.5, 130.8, 127.7, 127.3, 127.2, 126.4, 126.3, 126.1, 125.2, 125.1, 122, 119.2, 118.5, 37.1, 20.6; EIMS (70 eV) m/z 446 (M$^+$, 6%), 313 (39), 297 (14), 285 (9), 243 (5) and 214 (4). Found: C, 59.01; H, 3.76; N, 6.11. $C_{23}H_{19}F_3N_2O_3S$ requires C, 59.19; H, 3.84; N, 6.27.

1-(2-*tert*-Butyl-quinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonate 13f. Purified by column chromatography (silica gel, 2:1 petroleum ether/ethyl acetate) to give 1-(2-*tert*-butyl-quinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate as a yellow solid (86%): mp 115−117 °C; ν_{max} (KBr) 3070, 2963, 2921, 2885, 1612, 1559, 1420, 1280, 1140 and 875 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (1H, d, J = 8.49 Hz), 8.11 (1H, d, J = 9.1 Hz), 8.0 (1H, d, J = 8.5 Hz), 7.85 (1H, dt, J = 6.74, 1.78 Hz), 7.6 (1H, d, J = 9.08 Hz), 7.58 (1H, dt, J = 8.2, 1.78 Hz), 7.42 (1H, dt, J= 9.37, 1.17 Hz), 7.38−7.31 (2H, m), 7.28 (1H, d, J = 8.79 Hz) and 1.56 (9H, s); ^{13}C (75 MHz, $CDCl_3$) δ 172.3, 161.5, 149.8, 143.5, 132.7, 131.6, 131.5, 130.6, 128, 127.3, 127, 126.7, 126.3, 126, 125.2, 124.9, 121.6, 118.5, 38.8, 28.5; EIMS (70 eV) m/z 460.2 (M$^+$, 15%), 327.3 (100), 311.2 (46), 285.3 (11), 272.1 (14), 242.2 (14), 214.2 (8) and 189.2 (7). Found: C, 59.66; H, 4.00; N, 5.98. $C_{24}H_{21}F_3N_2O_3S$ requires C, 59.99; H, 4.16; N, 6.08.

General Method for the Preparation of (*R*,*S*)-Diphenyl(1-(2-substituted-quinazolin-4-yl)(2-naphthyl)phosphines 14a−f. To a solution of [1,2 bis(diphenylphosphino)-ethane]dichloronickel(II) (0.53 g, 1.0 mmol) in anhydrous DMF (30 mL) was added diphenyl phosphine (5.75 mmol) at room temperature. The dark orange solution was heated at 100 °C for 30 min under nitrogen. 1-(2-Substituted-quinazolin-4-yl)-2-naphthyl(trifluoromethyl) sulfonate (10 mmol) and 1,4-diazabicyclo[2.2.2.]octane (DABCO) (40.0 mmol) in DMF (40 mL) were subsequently added. The dark green solution was maintained at 100 °C, and a further portion of diphenyl phosphine (5.75 mmol) was added after 1 h. The reaction was then heated at 100 °C, under an atmosphere of nitrogen for 6 days. The reaction was cooled, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, 2:1 petrol ether/ethyl acetate) to give (*R*,*S*)-diphenyl(1-(2-substituted-quinazolin-4-yl)(2-naphthyl)phosphine.

(*R*,*S*)-Diphenyl[1-(quinazolin-4-yl)(2-naphthyl)]phosphine 14a. Purified by chromatography (silica gel, 2:1 petroleum ether/ethyl acetate) to give (*R*,*S*)-diphenyl[1-(quinazolin-4-yl)(2-naphthyl)]phosphine as a white solid (62%): mp 212−214 °C; ν_{max} (KBr) 3058, 1611, 1545, 1433, 744 and 698; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.40 (1H, s), 8.13 (1H, d, J = 8.4 Hz), 7.92 (1H, d, J = 8.7 Hz), 7.89 (1H, d, J = 8.4 Hz), 7.82 (1H, app septet, J = 8.4, 5.5, 2.9 Hz), 7.49 (1H, dt, J1 = 6.8 Hz, J2 = 1.3 Hz), 7.43 (1H, dd, J1 = 8.4 Hz, J_{P-H} = 2.9 Hz), 7.31−7.18 (12H, m), 7.15 (2H, dt, J1 = 7.8 Hz, J2 = 1.6 Hz) and 7.06 (d, J = 8.4 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 169.6, 154.9, 150.3, 141.7, 136.9, 134.8, 134.0, 133.9, 133.8, 133.6, 133.5, 133.3, 132.0, 131.0, 130.0, 129.5, 128.9−128.5, 128.3, 127.7, 127.3, 127.2, 126.1 and 125.2; ^{31}P NMR (121 MHz, $CDCl_3$) δ −12.9 ppm; EIMS (70 eV) m/z 440 (M$^+$, 39%), 363 (100), 284 (18), 258 (8), 220 (13), 157 (8) and 77 (20). Found: C, 81.55; H, 4.88; N, 6.28; P, 6.95. $C_{30}H_{21}N_2P$ requires C, 81.80; H, 4.81; N, 6.36; P, 7.03.

(*R*,*S*)-Diphenyl[1-(2-methylquinazolin-4-yl)(2-naphthyl)]phosphine 14b. Purified by silica gel column chromatography (petroleum ether/ethyl acetate) to give (*R*,*S*)-diphenyl[1-(2-methylquinazolin-4-yl)(2-naphthyl)] phosphine as a white solid (63%): mp 195−197 °C; ν_{max}(KBr) 3058, 1637, 1556, 1429, 743 and 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, 1H, J = 8.5 Hz), 7.93 (1H, d, J = 8.5 Hz), 7.91 (1H, d, J = 8.5 Hz), 7.81 (1H, t, J = 7.5 Hz), 7.51 (1H, t, J = 7.6 Hz), 7.43 (1H, dd, $J_{H,H}$ = 8.6 Hz, $J_{P,H}$ = 3.2 Hz), 7.34−7.17 (13H, m), 7.13 (1H, d, J = 8.5 Hz) and 2.82 (3H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 169.5, 164.1, 150.8, 141.8, 137.1, 137.0, 135.0, 134.1−133.7, 132.1, 130.1, 129.4, 128.8−128.6, 128.3, 128.3, 127.3, 127.2, 127.2, 126.9, 126.3, 123.6 and 26.6; ^{31}P NMR (101.3 MHz, $CDCl_3$) δ −12.6; EIMS (70 eV) m/z 454 (M$^+$, 29%), 377 (100), 300 (19) and 77 (16). Found: C, 81.5; H, 5.1; N, 6.1. $C_{31}H_{23}N_2P$ requires C, 81.9; H, 5.1; N, 6.2.

(*R*,*S*)-Diphenyl(1-(2-phenylmethyl-quinazolin-4-yl)(2-naphthyl)phosphine 14d. Purified by silica gel column

chromatography (4:1 petrol ether/ethyl acetate) to give (*R,S*)-diphenyl[1-(2-phenylmethylquinazolin-4-yl)(2-naphthyl)]phosphine (0.76 g, 80%) as a white solid: mp 218−220 °C; ν_{max} (KBr) 3054, 2939, 1612, 1583, 1546, 1485, 1433, 746 and 693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (1H, d, J = 8.64 Hz), 7.94 (1H, d, J = 8.35 Hz), 7.92 (1H, d, J = 7.91 Hz), 7.82 (1H, dt, J = 8.49, 6.44, 1.90 Hz), 7.53 (1H, dt, J = 8.05, 6.88, 1.03 Hz), 7.45 (1H, dd, J = 8.49 Hz, J_{P-H} = 1.03 Hz), 7.35−7.20 (16H, m), 7.15 (2H, dt J = 7.18, 6.30, 1.90 Hz), 7.10 (1H, d, J = 8.49 Hz), 4.44 (1H, d, J = 13.76 Hz) and 4.41 (1H, d, J = 13.62 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 164.4, 149.7, 140.9, 137.6, 135.9, 133.5, 132.7, 132.7, 132.5, 132.4, 132.4, 132.1, 130.8 (d, J_{P-C} = 8.63 Hz), 129.0, 128.2, 128.1, 127.5−127.0, 126.1, 125.9, 125.9, 125.8, 125.2, 125.2, 125.1, 122.7, 122.7 and 45.1; ^{31}P NMR (121 MHz, $CDCl_3$) δ −12.9 ppm; EIMS (70 eV) *m/z* 494 (M^+, 10%), 361 (100), 180 (41), 165 (25), 114 (10), 91 (84) and 65 (17). Found: C, 83.55; H, 5.24; N, 5.26; P, 5.64. $C_{37}H_{27}PN_2$ requires C, 83.75; H, 5.13; N, 5.28; P, 5.84.

(*R,S*)-Diphenyl(1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)phosphine 14e. Purified by chromatography (silica gel, 2:1 petrol ether/ethyl acetate) to give (*R,S*)-diphenyl(1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)phosphine as a white solid (67%): mp 220−221 °C; ν_{max} (KBr) 3064, 2970, 2963, 1772, 1614, 1566 and 1470; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (1H, d, J = 8.49 Hz), 7.91 (1H, d, J = 8.5 Hz), 7.89, (1H, d, J = 7.32 Hz), 7.8 (1H, dt, J = 8.2, 6.44, 1.46 Hz), 7.5 (1H, dt, J = 7.91, 6.73, 1.17 Hz), 7.39 (1H, ddd, J = 8.2, 1.17 Hz), 7.36−7.19 (11H, m), 7.18 (2H, dt, 7.33, 5.57, 1.47 Hz), 7.10 (1H, d, J = 8.79 Hz), 3.28 (1H, sept, J = 7.03), 1.25 (6H, d, J = 6.74 Hz); ^{13}C (75 MHz, $CDCl_3$) δ 172, 169, 150.8, 141.7, 138, 136.3, 133.9, 133.7, 133.5, 130.3, 129.3, 128.8, 128.6, 128.5, 128.3, 127.3−127, 126.9, 126.8, 126.5, 126.4−125.2, 125.1, 38.2, 22; ^{31}P NMR (121 MHz, $CDCl_3$) δ −12.5 ppm; EIMS (70 eV) *m/z* 483 (M^+, 8%), 482 (27), 405 (88), 334 (6), 258 (9) and 233 (25); HRMS 483.2000, $C_{33}H_{28}N_2P$ requires 483.1990.

(*R,S*)-Diphenyl(1-(2-*tert*-butyl-quinazolin-4-yl)(2-naphthyl)phosphine 14f. Purified by chromatography (silica gel, 2:1 petrol ether/ethyl acetate) to give (*R,S*)-diphenyl(1-(2-*tert*-butyl-quinazolin-4-yl)(2-naphthyl)phosphine as a white solid (64%): mp 217−219 °C; ν_{max} (KBr) 3059, 2954, 2918, 1613, 1549, 1480 and 685; ^1H NMR (300 MHz, $CDCl_3$) δ 8.08 (1H, d, J = 8.2 Hz), 7.89 (2H, app d, J = 7.91 Hz), 7.78 (1H, dt, J = 8.49, 6.15, 1.78 Hz), 7.49 (1H, dt, J = 8.2, 5.86, 1.17 Hz), 7.37 (1H, d, J = 8.25 Hz), 7.34−7.21 (11H, m), 7.18 (2H, dt, 8.79, 6.15, 1.47 Hz), 7.08 (1H, d, J = 8.49), 1.31 (9H, s); ^{13}C (75 MHz, $CDCl_3$) δ 169, 160.3, 150.1, 150, 138, 137.7, 133.9, 133.6, 133.5, 133.4, 132.0, 131.0, 129.5, 129.3, 129.2, 129, 128.7−128.3, 127.5−127.1, 126.9, 126.8, 122, 120.1, 40, 29.6; ^{31}P NMR (121 MHz, $CDCl_3$) δ −12.6 ppm; HRMS (ES) *m/z* 497.2162, $C_{34}H_{30}N_2P$ requires 497.2147.

(+)-Di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)-aminato-C_2,N]dipalladium(II). Palladium(II)chloride (1.78 g, 10.03 mmol) and lithium chloride (0.85 g, 20.06 mmol) were placed in a 250 mL Schlenk tube under an atmosphere of nitrogen.[57,58] Dry degassed methanol (40 mL) was added, and the mixture was refluxed until the palladium dissolved (∼30 min) to give a brown solution. This was allowed to cool, and (*R*)-*N,N* dimethyl-1-(1-naphthyl)ethylamine (2.00 g, 10.03 mmol) was added dropwise over a 15 min period to give a yellow precipitate. Triethylamine (1.4 mL, 10.03 mmol) was then added slowly, and the solution was stirred overnight (18 h) to give a yellow suspension. The mixture was filtered, and the solid was washed with methanol followed by ether. The yellow solid was dried on a vacuum line to give-(+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]dipalladium(II) **16** as a bright yellow solid (3.2 g, 94%). Alternatively, the crude solution was reduced in vacuo, dissolved in dichloromethane, and filtered through a column of silica gel to give an identical bright yellow solid (3.29 g, 96%): mp 182−184 °C (lit.[59] mp 183 °C); ^1H NMR 300 MHz δ ($CDCl_3$) 7.8−7.32 (12H, m), 4.2 (2H, q, J = 6.15 Hz), 2.98 (6H, d, J = 9.96 Hz), 2.76 (6H, d, J = 14.35 Hz) and 1.91 (6H, d, J = 6.3 Hz).

Resolution of (*R,S*)-Diphenyl(1-(2-substituted-quinazolin-4-yl)(2-naphthyl) phosphine 14a−f. (*R,S*)-Diphenyl-[1-(quinazolin-4-yl)(2-naphthyl)]phosphine 14a. Diphenyl-[1-(quinazolin-4-yl)(2-naphthyl)]phosphine **14a** (1.23 g, 2.38 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-*C*2,*N*]dipalladium(II) **16** (0.81 g, 1.19 mmol) were placed under an atmosphere of nitrogen in a Schlenk tube. Dry degassed MeOH (70 mL) was added, and the mixture was stirred for 2 h. As all the solid had not dissolved, more methanol (70 mL) was added. The mixture was stirred overnight. The white precipitate was isolated by filtration. However upon analysis this proved to be unbound diphenyl-[1-(quinazolin-4-yl)(2-naphthyl)] phosphine contaminated with a small amount of an unusual impurity, (*R*)-[dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[methyl(diphenyl)phosphite]palladium(II)chloride **19**, which was isolated by column chromatography and characterized: mp 116−119 °C; $[\alpha]^{21}_D$ = −155 (*c* 0.11, $CHCl_3$); ν_{max} (KBr) 2933, 1583, 1436, 1107, 1030 and 748; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24−8.19 (2H, m), 7.84−7.80 (2H, m), 7.72 (2H, d, J = 9.6 Hz), 7.53−7.51 (3H, m), 7.43−7.34 (5H, m), 7.32−7.28 (2H, m), 4.36 (1H, quin, J = 6.4 Hz), 3.30 (3H, d, J = 13.4 Hz), 2.97 (3H, s), 2.61 (3H, s) and 2.09 (3H, d J = 6.4 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 149.9, 149.6, 135.2, 134.8, 134.5 (d, J_{P-C} = 11 Hz), 133.4, 133.3, 133.0, 132.9, 132.4, 132.3, 131.6, 131.4, 131.3, 129.0, 128.8, 128.6, 128.0 (d, J_{P-C} = 11 Hz), 125.7, 125.4 (d, J_{P-C} = 5.8 Hz), 124.3, 123.2, 72.7, 55.0, 50.7, 47.9 and 23.8; ^{31}P NMR (121 MHz, $CDCl_3$) δ 125.1 ppm; ESI/pos (CH_3OH) cation *m/z* 520 = M − Cl; HRMS (ES) *m/z* 520.1019 $C_{27}H_{29}NOPPd$, cation requires 520.1022.

To the filtrate was added potassium hexafluorophosphate (0.736 g, 4.0 mmol) in water (70 mL). Further addition of water (100 mL) precipitated a yellow solid, which was collected by filtration and dried. NMR analysis showed a 1:1 mixture of (*R,R*)- and (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[1-(quinazolin-4-yl(2-naphthyl)diphenylphosphine]palladium(II)hexafluorophosphate **18a**. Recrystallation of the mixture from butanone/diethyl ether gave (*S,R*)-**18a** (0.56 g, 85%): mp 238−241 °C; $[\alpha]^{21}_D$ = −245 (*c* 0.204, $CHCl_3$); ν_{max} (KBr) 3045, 1613, 1569, 1438 and 842; ^1H NMR (300 MHz, $CDCl_3$) δ 9.43 (1H, s), 8.18 (1H, d, J = 8.6 Hz), 8.09 (1H, d, J = 8.3 Hz), 7.97−7.91 (2H, m), 7.72 (1H, d, J = 6.7 Hz), 7.70 (1H, d, J = 6.7 Hz), 7.67 (1H, d, J = 8.3 Hz), 7.54 (1H, t, J = 7.7 Hz), 7.49−7.42 (3H, m), 7.38 (1H, t, J = 7.0 Hz), 7.32−7.24 (5H, m), 7.21 (1H, d, J = 8.6 Hz), 7.10−7.04 (4H, m), 7.01 (1H, d, J = 8.6 Hz), 6.98 (2H, d, J = 8.3 Hz), 6.51 (1H, dd, J1 = 8.3 Hz, J2 = 6.1 Hz), 4.46 (1H, quin, J = 6.1 Hz), 2.92 (3H, s), 2.80 (3H, s) and 1.79 (3H, d, J = 6.4 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.8 (d, J_{P-C} = 6.7 Hz), 151.5, 150.5, 149.7, 149.3, 137.1, 136.7 (d, J_{P-C} = 12.2 Hz), 136.4 (d, J_{P-C} = 11.4 Hz), 135.4 (d, J_{P-C} = 11.4 Hz), 134.2, 133.0, 132.9, 132.8, 132.2, 132.1 (d, J = 11.0 Hz), 131.7, 130.3, 129.3−128.7, 128.2, 127.9, 127.6, 126.6, 126.1 (d, J = 6.7 Hz), 126.0 (d, J = 5.9 Hz), 125.4, 125.1, 124.4, 124.0, 123.7, 123.3, 122.3, 121.9, 73.6, 52.4, 48.4, 24.5; ^{31}P NMR (121 MHz, $CDCl_3$) δ 39.9, −143 (septet, J_{P-F} = 712.6 Hz) ppm; ESI/pos (CH_3OH) *m/z* cation 744 = M − PF_6, *m/z* (HRMS, ES) found 744.1758, $C_{44}H_{37}N_3PPd$ cation requires 744.1760.

Crystal data for (*S,R*)-18a: $[C_{44}H_{37}N_3PPd]^+[PF_6]^-\cdot 2CHCl_3$, from chloroform/diethyl ether, M_r = 1128.84, crystal size: 0.09 × 0.16 × 0.26 mm^3; a = 13.2070(7), b = 13.9716(8), c = 25.669-

(55) Trepanier, D. L.; Sunder, S. *J. Heterocycl. Chem*. **1975**, *12*, 321.
(56) Bowie, R. A.; Thomason, D. A. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1842.
(57) Martin, J. W. L.; Palmer, J. A. L.; Wild, S. B. *Inorg. Chem*. **1984**, *23*, 2664.
(58) Martin, J. W. L. *J. Am. Chem. Soc.* **1988**, *110*, 4346.
(59) Allen, D. G.; McLaughlin, G. M.; Robertson, G. B.; Steffen, W. L.; Salem, G.; Wild, S. B. *Inorg. Chem*. **1982**, *21*, 1007.

(1) Å, $V = 4736.4(5)$ Å^3, $T = 100$ K, orthorhombic, space group $P2_12_12_1$ (No. 19), $Z = 4$, $\rho_{calcd} = 1.583$ g cm^{-3}, $F(000) = 2272$, Siemens SMART diffractometer, λ (Mo Kα) = 0.71073 Å, $\mu = 0.86$ mm^{-1}, 42281 measured and 10666 independent reflections ($R_{int} = 0.148$), 6413 with $I > 2\sigma(I)$, $\theta_{max} = 27.48°$, $T_{min} = 0.874$, $T_{max} = 0.920$, direct methods (*SHELXS-97*) and least-squares refinement (*SHELXL*-97) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 577 parameters, H atoms riding, absolute configuration established (Flack parameter −0.05(3)) and confirmed by chiral reference, Chebyshev weights, $R_1 = 0.060$ ($I > 2\sigma(I)$), $wR_2 = 0.1149$ (all data), $\Delta\rho_{max/min} = 0.906/-0.546$ e Å^{-3}.

The filtrate from the recrystallation was reduced in vacuo. The solid obtained was recrystallized from dichloromethane/2-propanol to afford 97% diastereomerically pure (*R,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C$_2$,N]-[1-(quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II) hexafluorophosphate **18a** in the filtrate: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.61 (s, 1H), 8.21 (1H, d, $J = 8.3$ Hz), 8.09 (1H, d, $J = 8.3$ Hz), 7.92 (2H, m), 7.76 (1H, d, $J = 8.3$ Hz), 7.73−7.68 (2H, m), 7.65 (1H, d, $J = 8.3$ Hz), 7.57 (1H, dt, J1 = 7.5 Hz, J2 = 2.4 Hz), 7.50−7.40 (6H, m), 7.37 (1H, d, $J = 8.0$ Hz), 7.35−7.22 (3H, m), 7.13−6.92 (5H, m), 6.41 (1H, dd, J1 = 8.6 Hz, J2 = 7.0 Hz), 4.67 (1H, quin, $J = 6.3$ Hz), 3.01 (3H, s), 2.94 (3H, s) and 1.92 (3H, d, $J = 6.3$ Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 42.1, −143 (septet, $J_{P-F} = 712.6$ Hz) ppm.

Diphenyl[1-(2-methylquinazolin-4-yl)(2-naphthyl)]phosphine 14b. (+)-Di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)-ethyl)aminato-C$_2$,N]dipalladium(II)**16** (0.56 g, 0.82 mmol) and (*R,S*)-diphenyl[1-(2-methylquinazolin-4-yl)(2-naphthyl)] phosphine **14b** (0.75 g, 1.65 mmol) were placed in a Schlenk tube under nitrogen. Dry, degassed methanol (56 mL) was added via syringe, and the solution was stirred for 12 h. Potassium hexafluorophosphate (0.334 g, 1.83 mmol) was added in water (52 mL) with vigorous stirring, and a cream precipitate formed. A further 40 mL of water was added. The precipitated solid was collected by filtration to give a 50:50 mixture of diastereomers, (*S,R*)- and (*R,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)-aminato-C$_2$,N]-[diphenyl[1-(2-methylquinazolin-4-yl)(2-naphthyl)]phosphine]palladium(II) hexafluorophosphate **18b** (1.21 g, 81%). Fractional crystallization of the mixture from chloroform/diethyl ether gave (*S,R*)-**18b** (0.248 g, 41%): mp 216−218 °C; $[\alpha]_D = 247.4$ (*c* 0.365,CH_2Cl_2); ν_{max} ($CHCl_3$) 3019, 1571, 1521, 1479, 1438 and 760 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (1H, d, $J = 8.5$ Hz), 8.09 (1H, d, $J = 8.5$ Hz), 7.88 (1H, dt, $J_1 = 7.6$ Hz, $J_2 = 1.3$ Hz), 7.80−7.77 (2H, m), 7.72 (1H, t, $J = 6.9$ Hz), 7.69 (1H, d, $J = 7.2$ Hz), 7.64 (1H, d, $J = 7.9$ Hz), 7.53 (1H, t, $J = 7.8$ Hz), 7.51 (1H, t, $J = 7.0$ Hz), 7.46−7.19 (8H, m), 7.13 (1H, t, $J = 7.6$ Hz), 7.10 (1H, d, $J = 8.2$ Hz), 6.93 (1H, d, $J = 8.5$ Hz), 6.89−6.78 (3H, m), 6.64 (1H, d, $J = 8.5$ Hz), 6.62 (1H, d, $J = 8.2$ Hz), 4.28 (1H, quin, $J = 5.9$ Hz), 3.55 (3H, s), 2.76 (3H, d, $J = 2.6$ Hz), 2.49 (3H, d, $J = 3.5$ Hz) and 1.28 (3H, d, $J = 6.4$ Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.6 (d, $J_{P,C} = 6.2$ Hz), 161.4, 150.9, 150.0 (d, 1H, $J_{P,C} = 1.6$ Hz), 149.6 (d, $J_{P,C} = 2.3$ Hz) 136.9 (d, $J_{P,C} = 12.1$ Hz), 136.9, 136.6 (d, $J_{P,C} = 11.7$ Hz), 135.9 (d, $J_{P,C} = 10.9$ Hz), 134.2 (d, $J_{P,C} = 26.9$ Hz), 134.3 (d, $J_{P,C} = 1.6$ Hz), 129.8, 129.6, 129.5−128.9, 128.6, 128.4 (d, $J_{P,C} = 6.6$ Hz), 125.5 (d, $J_{P,C} = 7.0$ Hz), 125.3 (d, $J_{P,C} = 12.5$ Hz), 124.3, 124.0, 123.3, 122.6 (d, $J_{P,C} = 1.2$ Hz), 121.8, 121.4, 73.8 (d, $J_{P,C} = 3.1$ Hz), 52.6 (d, $J_{P,C} = 2.3$ Hz), 48.4 (d, $J_{P,C} = 2.3$ Hz), 27.2 and 22.8; ^{31}P NMR (121.4 MHz, $CDCl_3$) δ 37.7 ppm; ESI/pos (CH_3OH) *m/z* cation 759 M − PF_6^-. Found C, 59.5; H, 4.2; N, 4.5, $C_{45}H_{39}N_3F_6P_2Pd$ requires C, 59.8; H, 4.4; N, 4.7.

Crystal data for (*S,R*)-18b: $[C_{45}H_{39}N_3PPd]^+[PF_6]^-\cdot 0.2H_2O$, from chloroform/diethyl ether/trace water, $M_r = 907.74$, crystal size: 0.07 × 0.10 × 0.25 mm^3; $a = 11.4972(1)$, $b = 15.6101(1)$, $c = 21.7615(2)$ Å, $V = 3905.59(6)$ Å^3, $T = 100$ K, orthorhombic, space group $P2_12_12_1$ (No. 19), $Z = 4$, $\rho_{calcd} = 1.544$ g cm^{-3}, $F(000) = 1848$, Nonius KappaCCD diffractometer, λ (Mo Kα) = 0.71073 Å, $\mu = 0.62$ mm^{-1}, 31043 measured and 14658 independent reflections ($R_{int} = 0.062$), 12379 with $I > 2\sigma(I)$, $\theta_{max} = 33.15°$, $T_{min} = 0.886$, $T_{max} = 0.966$, direct methods (*SHELXS*-97) and least-squares refinement (*SHELXL*-97) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 536 parameters, PF_6^- anion rotationally disordered, residual electron density in a void in the crystal suggested additional solvent, the size of the void indicates trace water, which was modeled by an O atom (0.2 refined occupancy), otherwise H atoms riding, absolute configuration established (Flack parameter −0.05(2)) and confirmed by chiral reference, Chebyshev weights, $R_1 = 0.0428$ ($I > 2\sigma(I)$), $wR_2 = 0.0943$ (all data), $\Delta\rho_{max/min} = 0.955/-0.619$ e Å^{-3}.

(*R,S*)-Diphenyl(1-(2-benzyl-quinazolin-4-yl)(2-naphthyl)phosphine 14d. A solution of (*R,S*)-diphenyl[1-(2-phenylmethylquinazolin-4-yl)(2-naphthyl)] phosphine **14d** (0.58 g, 1.09 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)-ethyl)aminato-C$_2$,N]dipalladium(II) **16** (0.37 g, 0.55 mmol) in dry, degassed dichloromethane (60 mL) was stirred overnight (22 h) at room temperature under an atmosphere of nitrogen. The bright yellow solution was reduced in vacuo and vacuum-dried to give (*R,R*)- and (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)-ethyl) aminato-C$_2$,N]-[1-(2-phenylmethylquinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium (II)chloride **17d** (0.94 g, 99%) as a pale yellow solid, which was a 1:1 mixture of diastereomers by NMR.

Diethyl ether was added to the mixture at room temperature. An insoluble solid remained, while the mother liquor was yellow in color. The solid was removed by filtration and dried on a vacuum line to give (*S,R*)-**17d** as a pale yellow solid: mp 200−202 °C; $[\alpha]_D = -121.6$ (*c* 0.25, $CHCl_3$); ν_{max} (KBr) 3057, 2976, 2889, 1614, 1552, 1501, 1434, 1094 and 809 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (1H, d, $J = 9.08$ Hz), 8.04 (1H, d, $J = 8.64$ Hz), 7.94 (1H, d, $J = 8.20$ Hz), 7.93−7.85 (2H, m), 7.84 (1H, d, $J = 8.05$ Hz), 7.72 (1H, app d, $J = 7.03$ Hz), 7.65 (1H, d, $J = 8.64$ Hz), 7.57 (1H, t, $J = 7.76$ Hz), 7.54−7.49 (2H, m), 7.37 (1H, t, $J = 6.15$ Hz), 7.36−7.28 (9H, m), 7.30 (1H, d, $J = 8.20$ Hz), 7.17−7.06 (3H, m), 6.95 (1H, app s), 6.82 (1H, d, $J = 8.49$ Hz), 6.62 (1H, d, $J = 9.67$ Hz), 6.59 (2H, d, $J = 8.35$ Hz), 6.43 (1H, app s), 4.17 (1H, d, $J = 13.62$ Hz), 4.15 (1H, quin, $J = 9.67$ Hz), 4.07 (1H, d, $J = 13.18$ Hz), 2.89 (3H, s), 2.51 (3H, s) and 1.76 (3H, d, $J = 4.25$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 163.7, 149.4, 149.3 (d, $J_{P-C} = 22.23$ Hz), 147.9, 137.5, 136.1 (d, $J_{P-C} = 12.08$ Hz), 135.2, 135.0, 133.0, 132.6, 131.9, 131.7, 131.4 (d, $J_{P-C} = 8.70$ Hz), 129.9, 129.9, 129.8, 129.3, 128.8, 128.2, 128.2−127.2, 127.5, 127.2, 127.2, 127.1, 127.0, 126.8, 126.6 (d, $J = 10.15$ Hz), 125.9, 125.7, 125.6, 125.2, 125.1, 124.5, 123.0, 122.9, 122.6, 122.2, 72.1 (*C*HMe), 49.7, 47.5, 45.3 and 22.3; ^{31}P NMR (121 MHz, $CDCl_3$) δ 45.5 ppm; ESI/pos (CH_3OH) *m/z* cation 834 = M − Cl; HRMS (ES) *m/z* found 834.2227, $C_{47}H_{43}N_3PPd$ cation requires 834.2229.

Crystal data for (*S,R*)-17d: $[C_{51}H_{43}ClN_3PPd]$, from chloroform/diethyl ether, $M_r = 870.70$, crystal size: 0.10 × 0.11 × 0.11 mm^3; $a = 10.6243(1)$, $b = 16.1488(2)$, $c = 23.9876(4)$ Å, $V = 4115.6(1)$ Å^3, $T = 100$ K, orthorhombic, space group $P2_12_12_1$ (No. 19), $Z = 4$, $\rho_{calcd} = 1.405$ g cm^{-3}, $F(000) = 1792$, Nonius KappaCCD diffractometer, λ (Mo Kα) = 0.71073 Å, $\mu = 0.60$ mm^{-1}, 37966 measured and 15577 independent reflections ($R_{int} = 0.086$), 11181 with $I > 2\sigma(I)$, $\theta_{max} = 33.19°$, $T_{min} = 0.937$, $T_{max} = 0.947$, direct methods (*SHELXS-97*) and least-squares refinement (*SHELXL-97*) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 514 parameters, H atoms riding, absolute configuration established (Flack parameter −0.01(3)) and confirmed by chiral reference, Chebyshev weights, $R_1 = 0.0605$ ($I > 2\sigma(I)$), $wR_2 = 0.1503$ (all data), $\Delta\rho_{max/min} = 0.827/-1.249$ e Å^{-3}.

The mother liquor was reduced in vacuo to give (*R,R*)-**17d** as a pale yellow solid which was dried on the vacuum line: mp 196−198 °C; $[\alpha]_D = +168.8$ (*c* 0.25, $CHCl_3$); ν_{max} (KBr) 3054, 2974, 2916, 1614, 1560, 1501, 1435, 1100 and 812 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (1H, d, $J = 7.40$ Hz), 8.05 (1H, d, $J = 7.16$ Hz), 7.92 (1H, d, $J = 8.35$ Hz), 7.89−7.85 (2H, m), 7.83 (1H, d, $J = 7.87$ Hz), 7.74 (1H, app d, $J = 7.88$ Hz), 7.68 (1H, d, $J = 6.68$ Hz), 7.62 (2H, d, $J = 8.35$ Hz), 7.56−7.47

(4H, m), 7.42 (1H, d, J = 8.35 Hz), 7.38−7.19 (9H, m), 7.14 (1H, t, J = 8.35 Hz), 7.05 (1H, t, J = 7.16 Hz), 6.74 (1H, d, J = 8.83 Hz), 6.69 (2H, t, J = 7.16 Hz), 6.56 (1H, d, J = 8.35 Hz), 5.90 (1H, dd, J = 8.35, 6.20 Hz), 4.35 (1H, d, J = 13.60 Hz, CH_2Ph), 4.30 (1H, d, J = 14.08 Hz), 4.18 (1H, quin, J = 6.20 Hz), 2.88 (3H, s), 2.19 (3H, s) and 2.02 (3H, d, J = 6.44 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2 (d, J_{P-C} = 4.83 Hz), 163.7, 149.6, 147.6 (d, J_{P-C} = 22.23 Hz), 137.5, 136.9 (d, J_{P-C} = 12.56 Hz), 134.6 (d, J_{P-C} = 12.57 Hz), 134.2 (d, J_{P-C} = 10.63 Hz), 132.7, 132.3, 131.3 (d, J_{P-C} = 8.70 Hz), 130.2, 130.0, 129.4, 129.0, 128.7, 128.5, 128.5−127.4, 128.1, 127.6, 127.5, 127.4, 127.1, 127.0, 127.0, 126.9, 126.5, 126.0 (d, J = 11.12 Hz), 125.8, 125.6 (d, J = 11.12 Hz), 125.5, 125.1, 124.4, 123.0, 123.0, 122.9, 122.1, 71.8, 49.6, 47.5, 45.5 and 22.5; ^{31}P NMR (121 MHz, $CDCl_3$) δ 42.4 ppm; ESI/pos (CH_3OH) m/z cation 834 = M − Cl. Alternatively, this diastereomerically pure material, (*R*,*R*)-**17d**, was also isolable as a pale yellow solid by recrystallization of the mixture from hot methanol.

(*R*,*S*)-Diphenyl(1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)phosphine 14e. A solution of (*R*,*S*)-diphenyl(1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)phosphine **14e** (1.0 g, 2.07 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl) aminato-C_2,N]dipalladium(II) **16** (0.71 g, 1.04 mmol) in dry, degassed dichloromethane (80 mL) was stirred for 18 h under an atmosphere of nitrogen. The bright yellow solution was reduced in vacuo and vacuum-dried to give (*R*,*R*)- and (*S*,*R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)diphenyl phosphine]palladium-(II)chloride **17e** as a light yellow solid.

Recrystallization of the mixture from hot chloroform/diethyl ether gave (*R*,*R*)-**17e**: mp 239−241 °C; $[\alpha]_D$ = 269.2 (*c* 0.25, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (1H, d, J = 7.03 Hz), 8.09 (1H, d, J = 7.03 Hz), 7.94 (1H, d, J = 7.62 Hz), 7.9−7.85 (2H, m), 7.83 (1H, d, J = 7.76 Hz), 7.73 (1H, app d, J = 8.93 Hz), 7.7−7.59 (4H, m), 7.58 (1H, app d, J = 7.91 Hz), 7.47−7.13 (9H, m), 7.04 (1H, t, J = 8.2 Hz), 6.8 (1H, t, J = 6.44 Hz), 6.76 (1H, d, J = 8.64 Hz), 5.7 (1H, d, J = 6.44 Hz), 4.22 (1H, quin, J = 6.15 Hz), 3.32 (1H, sept, J = 6.88 Hz), 2.94 (3H, s), 2.33 (3H, s), 2.08 (3H, d, J = 6.3 Hz), 1.42 (6H, d, J = 6.88 Hz); ^{13}C NMR (75 MHz) δ ($CDCl_3$) 168, 150.7, 149.1, 148.9, 138.2, 138, 135.5, 133.8, 133.6, 132.8, 132.3, 132, 131.4, 130.7, 130.3, 129.6, 128.9, 128.4, 128.3, 128.2, 128, 127.9, 127.4, 128.2, 126.9, 125.7, 124.5, 124.3, 124.2, 123.4, 73.2, 51.1, 48.8, 38.2, 23.8, 22; ^{31}P NMR (121 MHz, $CDCl_3$) δ 42.7 ppm.

The filtrate from the hot chloroform/diethyl ether recrystallization was stirred in cold diethyl ether for 15 min. The solid was filtered and dried under vacuum to give (*S*,*R*)-**17e** as a light yellow powder: $[\alpha]_D$ = −169.6 (*c* 0.25, $CHCl_3$); mp 244−246 °C; ν_{max} (KBr) 3058 (Ar−H), 2967 (C−H), 2915 (C−H), 2867 (C−H), 1614 (C═N), 1551 (C═C), 1434 (P−Ph) and 1092 (Ar−H); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.3 (1H, t, J = 8.93 Hz), 8.0 (1H, d, J = 8.64 Hz), 7.91 (1H, d, J = 8.2 Hz), 7.86−7.73 (m, 4H), 7.71−7.61 (3H, app t, J = 8.35 Hz), 7.55 (1H, d, J = 7.9 Hz), 7.48 (1H, t, J = 7.47 Hz), 7.44−7.37 (1H, m), 7.35 (7H, app dt, J = 6.59 Hz), 7.19 (1H, t, J = 7.32 Hz), 6.91 (1H, t, J = 6.59 Hz), 6.8 (1H, d, J = 7.32 Hz), 6.67 (1H, t, J = 8.93 Hz), 6.62 (1H, d, J = 8.64 Hz), 6.44 (1H, t, J = 6.15 Hz), 4.22 (1H, quin, J = 6.0 Hz), 3.04 (1H, sept, J = 7.03 Hz), 2.99 (3H, s), 2.55 (3H, s), 1.77 (3H, d, J = 6.15 Hz), 1.26 (6H, d, J = 6.74 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 167.5, 150.8, 150.5, 149.1, 137.4, 137.3, 136.4, 136.1, 135.9, 134.4, 133.6, 132.8, 131.2, 130.9, 129.9, 129.1, 128.8, 128.8, 128.5, 128.3, 128.2, 128, 127.7, 127.2, 127.0, 126.9, 126.3, 125.8, 124.2, 123.5, 73.4, 51.1, 48.7, 37.8, 23.6, 22.2; ^{31}P NMR (121 MHz, $CDCl_3$) δ 45.5 ppm; HRMS (ES) m/z 786.2231, $C_{47}H_{43}N_3PPd$ cation requires 786.2229.

Formation of (*R*,*R*)- and (*S*,*R*)-18e. A solution of (*R*,*S*)-diphenyl(1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)phosphine **14e** (1.0 g, 2.07 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl) ethyl)aminato-C_2,N]dipalladium(II) **16** (0.71 g, 1.04 mmol) in dry, degassed methanol (80 mL) was stirred for 18 h under an atmosphere of nitrogen. The yellow solution was filtered to remove a small amount of white precipitate that had formed overnight. Potassium hexafluorophosphate (0.42 g, 2.28 mmol) in 80 mL of distilled water was added, a yellow suspension was seen to form in the solution, and the mixture was stirred for a further 1 h. The solution was filtered, and the resulting cream precipitate was dried on the vacuum line to give (*R*,*R*)- and (*S*,*R*)-*cis*-[dimethyl-(1-(1-naphthyl)ethyl)aminato-C_2,N]-[1-(2-isopropyl-quinazolin-4-yl)(2-naphthyl)diphenyl phosphine]palladium(II) hexafluorophosphate **18e** as a 1:1 mixture of diastereomers (1.364 g, 71%).

Recrystallization of the mixture from hot chloroform/diethyl ether gave (*S*,*R*)-**18e**: mp 244−246 °C; $[\alpha]_D$ = −205 (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (1H, d, J = 8.49 Hz), 8.10 (1H, d, J = 7.9 Hz), 7.88 (1H, dt, J = 8.47, 6.44, 1.17 Hz), 7.85 (2H, app dt, J = 9.96, 8.49, 1.46 Hz), 7.74 (1 H, app t, J = 7.90 Hz), 7.68 (3H, app t, J = 8.2 Hz), 7.53 (1H, dt, J = 9.67, 8.49, 1.17 Hz), 7.48−7.22 (8H, m), 7.19−7.12 (3H, m), 7.07 (1H, d, J = 8.49 Hz), 6.92 (1H, d, J = 8.79 Hz), 6.75 (1H, d, J = 7.62 Hz), 6.70 (1H, t, J = 6.74 Hz), 6.65 (1H, d, J = 6.74 Hz), 4.25 (1H, quin, J = 6.0 Hz), 2.7 (1H, sept, J = 7.0 Hz), 2.46 (3H, s), 1.92 (3H, s), 1.59 (3H, d, J = 6.20 Hz), 1.26 (6H, d, J = 6.74 Hz); ^{31}P (121 MHz, $CDCl_3$) δ 35.2 ppm, −143.3 (sept., J = 712.2 Hz); HRMS (ES) m/z 786.2230, $C_{47}H_{43}N_3PPd$ cation requires 786.2229.

Crystal data for (*S*,*R*)-18e: $[C_{47}H_{43}N_3PPd]^+[PF_6]^-$, from chloroform/pentane, M_r = 932.18, crystal size: 0.08 × 0.13 × 0.17 mm^3; a = 11.250(1), b = 16.167(2), c = 11.379(1) Å, β = 92.273(2), V = 2068.0(4) Å^3, T = 100 K, monoclinic, space group $P2_1$ (No. 4), Z = 2, ρ_{calcd} = 1.497 g cm^{-3}, $F(000)$ = 952, Siemens SMART diffractometer, λ (Mo Kα) = 0.71073 Å, μ = 0.59 mm^{-1}, 8039 measured and 4573 independent reflections (R_{int} = 0.054), 3976 with $I > 2\sigma(I)$, θ_{max} = 23.26°, T_{min} = 0.907, T_{max} = 0.956, direct methods (*SHELXS-97*) and least-squares refinement (*SHELXL-97*) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 532 parameters, absolute configuration established (Flack parameter −0.05(3)) and confirmed by chiral reference, Chebyshev weights, H atoms riding, Chebychev weights, R_1 = 0.0416 ($I > 2\sigma(I)$), wR_2 = 0.0868 (all data), $\Delta\rho_{max/min}$ = 0.434/−0.467 e Å^{-3}.

All attempts to isolate (*R*,*R*)-**18e** were unsuccessful.

(*R*,*S*)-Diphenyl(1-(2-*tert*-butyl-quinazolin-4-yl)(2-naphthyl)phosphine 14f. A solution of (*R*,*S*)-diphenyl(1-(2-*tert*-butyl-quinazolin-4-yl)(2-naphthyl)phosphine **14f** (1.54 g, 3.10 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl) aminato-C_2,N]dipalladium(II) **16** (1.05 g, 1.55 mmol) in dry, degassed dichloromethane (100 mL) was stirred for 18 h under an atmosphere of nitrogen. The clear yellow solution was filtered, reduced in vacuo, and dried on a vacuum line to yield (*R*,*R*)- and (*S*,*R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[1-(2-*tert*-butyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride **17f** as a light yellow solid (2.55 g, 98%).

Recrystallization of the mixture from hot butanone/diethyl ether afforded a yellow solid, which was stirred in cold methanol for 10 min and filtered, producing (*R*,*R*)-**17f**: mp 237−239 °C; $[\alpha]_D$ = 254.4 (*c* 0.25, $CHCl_3$); ν_{max} (KBr) 3056 (Ar−H), 2959 (C−H), 2905 (C−H), 2863 (C−H), 1614 (C═N), 1565 (C═C), 1480 (P−Ph) and 1163 (Ar−H); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (1H, d, J = 8.05 Hz), 8.06 (1H, d, J = 7.91 Hz), 7.98−7.83 (3H, m), 7.82 (1H, d, J = 8.79 Hz), 7.80 (1H, d, J = 8.2 Hz), 7.74 (1H, app d, J = 8.2 Hz), 7.7−7.59 (4H, m), 7.54 (1H, d, J = 7.76 Hz), 7.46−7.22 (6H, m), 7.15 (2H, app t, J = 7.18 Hz), 7.69 (1H, t, J = 7.12 Hz), 6.79−6.67 (2H, app d, J = 8.49 Hz), 6.52 (1H, d, J = 8.64 Hz), 6.01 (1H, t, J = 7.76 Hz), 4.26 (1H, quin, J = 6.0 Hz), 2.98 (3H, s), 2.44 (3H, s), 2.10 (3H, d, J = 6.15 Hz), 1.53 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 167.5, 150.6, 149.2, 148.9, 143.1, 138, 137.9, 135.5, 135.3, 133.6, 132.9, 132.8, 131.4, 130.6, 130.3, 129.2, 128.9, 128.4, 128.3, 128.1, 127.3, 127.1, 126.9, 126.3, 125.8, 124.4, 124.2, 123.4, 123.7, 123.3, 122.3, 121.9, 73.2, 51.2, 48.8, 39.9,

30.1, 23.8; ^{31}P NMR (121 MHz, $CDCl_3$) δ 43.8 ppm; HRMS (ES) m/z 800.2390, $C_{48}H_{45}N_3PPd$ cation requires 800.2386.

Crystal data for (*R,R*)-17f: [$C_{48}H_{45}ClN_3PPd$], from dichloromethane/diethyl ether, $M_r = 836.69$, crystal size: $0.19 \times 0.24 \times 0.26$ mm^3; $a = 13.2921(1)$, $b = 14.3043(2)$, $c = 21.8897(2)$ Å, $V = 4162.0(1)$ Å^3, $T = 293$ K, orthorhombic, space group $P2_12_12_1$ (No. 19), $Z = 4$, $\rho_{calcd} = 1.335$ g cm^{-3}, $F(000) = 1728$, Nonius KappaCCD diffractometer, λ (Mo Kα) = 0.71073 Å, $\mu = 0.59$ mm^{-1}, 27470 measured and 10281 independent reflections ($R_{int} = 0.037$), 9106 with $I > 2\sigma(I)$, $\theta_{max} = 28.28°$, $T_{min} = 0.877$, $T_{max} = 0.909$, direct methods (*SHELXS-97*) and least-squares refinement (*SHELXL-97*) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 487 parameters, H atoms riding, absolute configuration established (Flack parameter −0.04(2)) and confirmed by chiral reference, Chebyshev weights, $R_1 = 0.0312$ ($I > 2\sigma(I)$), $wR_2 = 0.0750$ (all data), $\Delta\rho_{max/min} = 0.443/-0.300$ e Å^{-3}.

Formation of (*R,R*)- and (*S,R*)-18f. An identical procedure was followed to form (*R,R*)- and (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]-[1-(2-*tert*-butyl-quinazolin-4-yl)-(2-naphthyl)diphenyl phosphine]palladium(II)chloride **17f**. Potassium hexafluorophosphate (0.62 g, 3.39 mmol) in distilled water (40 mL) was added to a solution of (*R,R*)- and (*S,R*)-**17f** (2.5 g) in dichloromethane (40 mL) and was allowed stir overnight (18 h). The organic layer was isolated, filtered, and reduced in vacuo to give (*R,R*)- and (*S,R*)-*cis*-[dimethyl (1-(1-naphthyl)ethyl)aminato-C_2,N]-[1-(2-*tert*-butyl-quinazolin-4-yl)-(2-naphthyl) diphenylphosphine]palladium(II) hexafluorophosphate **18f**. The yellow solid was stirred in cold methanol for 15 min and filtered to give (*R,R*)-**18f**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (1H, app d, $J = 7.61$ Hz), 8.06 (1H, app d, $J = 7.61$ Hz), 8.0−7.81 (4H, m), 7.74 (3H, app d, $J = 8.23$ Hz), 7.58 (1H, d, $J = 8.02$ Hz), 7.46−7.09 (10H, m), 7.01 (1H, t, $J = 6.99$ Hz), 6.76 (3H, app d, $J = 8.64$ Hz), 6.52 (1H, d, $J = 8.64$ Hz), 6.02 (1H, t, $J = 6.79$ Hz), 4.27 (1H, quin., $J = 6.17$ Hz), 2.98 (3H, s), 2.44 (3H, s), 2.10 (3H, d, $J = 6.17$ Hz), 1.53 (9H, s); ^{31}P NMR (121 MHz, $CDCl_3$) δ 43.7 ppm; HRMS (ES) m/z 800.2387, $C_{48}H_{45}N_3PPd$ cation requires 800.2386.

The filtrate was recrystallized from methanol to give 96% diastereomerically pure (*S,R*)-**18f**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (1H, d, $J = 8.93$ Hz), 7.98 (3H, app d, $J = 8.07$ Hz), 7.82 (1H, app d, $J = 5.74$ Hz), 7.74 (1H, m), 7.68 (1H, d, $J = 7.86$ Hz), 7.62 (2H, app t, $J = 9.98$ Hz), 7.52 (3H, d, $J = 8.5$ Hz), 7.41 (1H, t, $J = 7.01$ Hz), 7.37−7.19 (7H, m), 7.0 (1H, d, $J = 8.3$ Hz), 6.93 (2H, t, $J = 6.8$ Hz), 6.71 (1H, d, $J = 8.5$ Hz), 6.56 (1H, d, $J = 8.5$ Hz), 6.23 (1H, t, $J = 7.65$ Hz), 4.42 (1H, quin, $J = 5.95$ Hz), 2.86 (6H, app d, $J = 9.77$ Hz), 2.11 (3H, br. s), 1.68 (9H, s); ^{31}P NMR (121 MHz, $CDCl_3$) δ 42.2 ppm.

Decomplexation of Enantiopure 2-Substituted-quinazolinap Ligands. (*S,R*)-**17c−e** and (*S,R*)-**18a,b,e** (0.32 mmol) and 1,2-bis(diphenylphosphino)ethane (0.32 mmol) were dissolved in dry, degassed dichloromethane (5 mL). The light yellow solution was stirred for 3 h at room temperature under an atmosphere of nitrogen. The CH_2Cl_2 was removed in vacuo and the resulting solid was purified by silica gel chromatography (CH_2Cl_2 or petroleum ether/ethyl acetate) to give (*S*)-2-substituted-Quinazolinap **14a−e** as a white solid (>90%), identical in allother respects to the previously prepared racemic samples. An analogous procedure was employed for the decomplexation of the (*R,R*)-2-*tert*-butyl palladium complexes **17f** and **18f** to give enantiopure (*R*)-**14f**. (*S*)-Quinazolinap $[\alpha]^{21}_D = -119.3$ (*c* 0.17, $CHCl_3$). (*S*)-2-methyl-Quinazolinap $[\alpha]^{23}_D = -94.1$ (*c* 1.06, CH_2Cl_2); (*S*)-2-phenyl-Quinazolinap $[\alpha]^{18}_D = -93.6$ (*c* 0.25, $CHCl_3$); (*R*)-2-phenyl-Quinazolinap $[\alpha]^{18}_D = +91.2$ (*c* 0.25, $CHCl_3$); (*S*)-2-benzyl-Quinazolinap $[\alpha]^{21}_D = -147.0$ (*c* 0.24, $CHCl_3$); (*R*)-2-benzyl-Quinazolinap $[\alpha]^{21}_D = +155.6$ (*c* 0.25, $CHCl_3$); (*S*)-2-isopropyl-Quinazolinap $[\alpha]^{21}_D = -112.0$ (*c* 0.25, $CHCl_3$); (*R*)-2-isopropyl-Quinazolinap $[\alpha]^{21}_D = +118.2$ (*c* 0.25, $CHCl_3$); (*R*)-2-*tert*-butyl-Quinazolinap $[\alpha]^{21}_D = +86.4$ (*c* 0.25, $CHCl_3$).

Catalyst Formation for Rhodium-Catalyzed Asymmetric Hydroboration. (*S*)-Diphenyl[1-(2-substituted-quinazolin-4-yl)(2-naphthyl)]phosphine Rhodium(1,5-cyclooctadiene)trifluoromethanesulfonate. (1,5-Cyclooctadiene)(2,4-pentanedionato)rhodium (3.1 mg, 0.01 mmol) and(*S*)-diphenyl[1-(2-substituted-quinazolin-4-yl)(2-naphthyl)]-phosphine (0.01 mmol) were dissolved in dry THF (2 mL) under an atmosphere of nitrogen to give a clear yellow solution. Trimethylsilyltrifluoromethanesulfonate (2 μL, 1.11 equiv) was added via syringe, and an orange color developed. The reaction mixture was stirred for 20 min, and the volume was then reduced in vacuo to 0.5 mL. Pentane (10 mL) was added via syringe to produce a light orange precipitate. This was stirred for 5 min before the pentane was removed. The precipitate was washed with fresh pentane (2 × 10 mL), which was syringed from the Schlenk tube to leave (*S*)-**20a−e** as light orange powders. The catalyst was dried under vacuum for 40 min prior to use in rhodium-catalyzed hydroboration. Dry THF (4 mL) was added to the Schlenk tube, and 2 mL portions of the catalyst precursor (1 mol %) were transferred to two oven-dried Schlenk tubes under nitrogen. Note: An identical procedure was followed to form the corresponding 2-*tert*-butyl complex (*R*)-**20f**.

General Procedure For Asymmetric Hydroboration. (*R*)- or (*S*)-Diphenyl[1-(2-substituted-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium (1,5-cyclooctadiene) trifluoromethanesulfonate (5 μmol) in THF (2 mL) was placed under nitrogen in a Schlenk tube. Freshly distilled catecholborane (53 μL, 0.5 mmol) was added via microliter syringe, and the light brown solution was stirred for 5 min at the required temperature. The substrate olefin (0.5 mmol) was injected, and the reaction mixture was stirred for 2 h at room temperature or at 0 °C (in some cases extended reaction times were necessary). The reaction was then cooled to 0 °C, and ethanol (1 mL) was added followed by 1 M NaOH (3 mL) and H_2O_2 (3 mL). The ice bath was removed, and the solution was stirred for 1 h at room temperature. The reaction mixture was transferred to a separatory funnel and diethyl ether (10 mL) was added. The organic layer was washed with 1 M NaOH (10 mL), brine (10 mL) and dried with $MgSO_4$. The solution was filtered, and the solvent was removed in vacuo to give the hydroborated product as an oil. Percent conversion and regioselectivity were determined by ^{1}H NMR. The percent ee was calculated by chiral GC or HPLC analysis.

Experimental Details for Chromatographic Determination of Optical Purities

substrate	conditions	(*R*)	(*S*)
styrene	120 °C, β-Dex 120 column, 16 psi	10.98 min	11.24 min
p-methoxystyrene	125 °C, β-Dex 120 column, 16 psi	36.93 min	37.85 min
p-chlorostyrene	130 °C, β-Dex 120 column, 16 psi	24.1 min	25.35 min
β-methylstyrenes	120 °C, β-Dex 120 column, 16 psi	17.1 min	17.38 min
trans-anethole	130 °C, β-Dex 120 column, 16 psi	45.69 min	47.15 min
3,4-dimethoxy-1-propenylbenzene	135 °C, β-Dex 120 column, 16 psi	115.09 min	118.15 min
stilbenes	HPLC, Daicel OD, 99:1 hexane/^{i}PrOH, 1 mL/min	70.5 min	89.53 min
indene	HPLC, Daicel OD, 99:1 hexane/^{i}PrOH, 1 mL/min	40.9 min	33.9 min
dihydronaphthalene	120 °C, β-Dex 120 column, 16 psi	57.89 min	59.67 min

Acknowledgment. We thank Enterprise Ireland for a Basic Research Award (SC/94/565) to support our initial work in this area and for awarding Research Scholarships to the following students: M.McC. (BR/94/158), P.M.L. (BR/96/108), C.P.S. (BR/97/047), and D.J.C. (BR/99/238). A.M.C. is thankful for an IRCSET scholarship (RS/2002/907-1). The award of the 1997 BOC Gases Postgraduate Bursary and 1999 UCD Open Postgraduate Scholarship to M.McC. and P.M.L., respectively, are gratefully acknowledged. D.J.C. thanks Schering-Plough Corporation for their support and Enterprise Ireland for a postdoctoral award (Sc/2002/349).

Supporting Information Available: Physical data for **7b**−**e, 9b**−**e, 8b**−**e, 11b**−**f, 12b**−**f, 13b**−**f, 14b**−**f**; ^{1}H NMR spectra for **11a**−**f**, **12a**−**f**, **13a**−**f**, **14a**−**f**, **17d**−**f**, **18a**−**b**, **18e**−**f**, and **19**; ^{13}C NMR spectra for **11a**−**f**, **12a**−**f**, **13a**−**f**, **14a**−**f**, and **19**; and ^{31}P NMR spectra for **14a**−**f**, **17d**−**f**, **18a**−**b**, **18e**−**f**, and **19**. X-ray crystallographic files for (*S*,*R*)-**17d**, (*R*,*R*)-**17f**, (*S*,*R*)-**18a**, (*S*,*R*)-**18b**, and (*S*,*R*)-**18e**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049195+