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Synthesis, Resolution, and Application of Cyclobutyl- and Adamantyl-Quinazolinap Ligands

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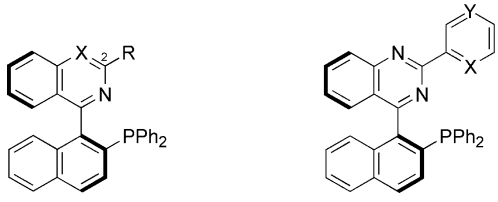
An expedient, seven-step synthesis of two new members of the Quinazolinap ligand family, 2-cyclobutyl- and 2-(1-adamantyl)-Quinazolinaps, has been developed. The racemic ligands have been efficiently resolved by fractional crystallization of their diastereomeric palladacycle complexes. The enantioenriched ligands provide good levels of enantioselection (ee's up to 89%) in a prototypical Pd^{II}-catalyzed allylic alkylation reaction. 2-Cyclobutyl-Quinazolinap has been further functionalized at the 2-position via metalation with a superbase followed by reaction with a range of electrophiles.

Introduction

Axially chiral biaryls are arguably the most versatile class of ligands developed for asymmetric catalysis mediated by transition metals.[1] Following the pioneering work by Dang and Kagan on rational design of their DIOP ligand[2] and, most importantly, the spectacular success of Noyori's BINAP,[3] the notion that C_2-symmetrical molecules are generally more efficient in chiral-information transfer became deeply rooted in the field of homogeneous asymmetric catalysis for over two decades.[4] A seminal report by Achiwa,[5] who demonstrated that desymmetrization of C_2-symmetric ligands can bring about higher levels of enantiocontrol, ushered in a period of intense interest in lower-symmetry ligands in general, and biaryls in particular.[6]

Our research in this arena, inspired by the proven versatility of Brown's Quinap (**1**) (Figure 1),[7] centers on the development of a new class of atropisomeric P,N ligands[8] based on the parent Quinazolinap (**2**) scaffold.[9] To date, we have developed a series of 2-alkyl- and 2-aryl-Quinazolinaps (**3** and **4**, respectively)[10] and applied them, with some success, to asymmetric hydroboration.[10c] Pursuant to our long-term goals, this paper describes the synthesis, resolution, and application of a pair of Quinazolinaps bearing less common 2-substituents, i.e., the sterically miniscule cyclobutyl and extremely bulky 1-adamantyl (Scheme 1, **5a** and **5b**, respectively).[11]



1: X = CH; R = H
2: X = N; R = H
3: X = N; R = Me, *i*Pr, *t*Bu, Bn

4a: X = CH; Y = CH
4b: X = N; Y = CH
4c: X = N; Y = N

Figure 1. Quinap (**1**) and Quinazolinap ligands **2**–**4**.

Results and Discussion

In our previous studies on Quinazolinap ligands, anthranilic acid and alkyl (or aryl) nitriles were used as starting materials in the synthesis of the requisite quinazolines.[10c,12] This method, while superior to older synthetic protocols, is nonetheless operationally tedious and provides the desired products in moderate yield only. Cognizant of this, in the current studies we opted for an alternative approach involving an acylation–cyclocondensation sequence between commercially available and inexpensive anthranilamide (**6**) and an appropriate acyl chloride.[13] W had used a similar strategy for the synthesis of quinazoline–oxazoline-containing (Quinazox) ligands.[10a] Therefore (Scheme 1), the synthesis of ligand **5a** commenced with acylation of **6** with cyclobutanecarbonyl chloride (**7a**) in the presence of Et_3N to give the corresponding amide **8a** that, upon treatment with NaOH in EtOH, underwent cyclocondensation to quinazolinol **9a** in high overall yield (94% from **6**). Chlorination

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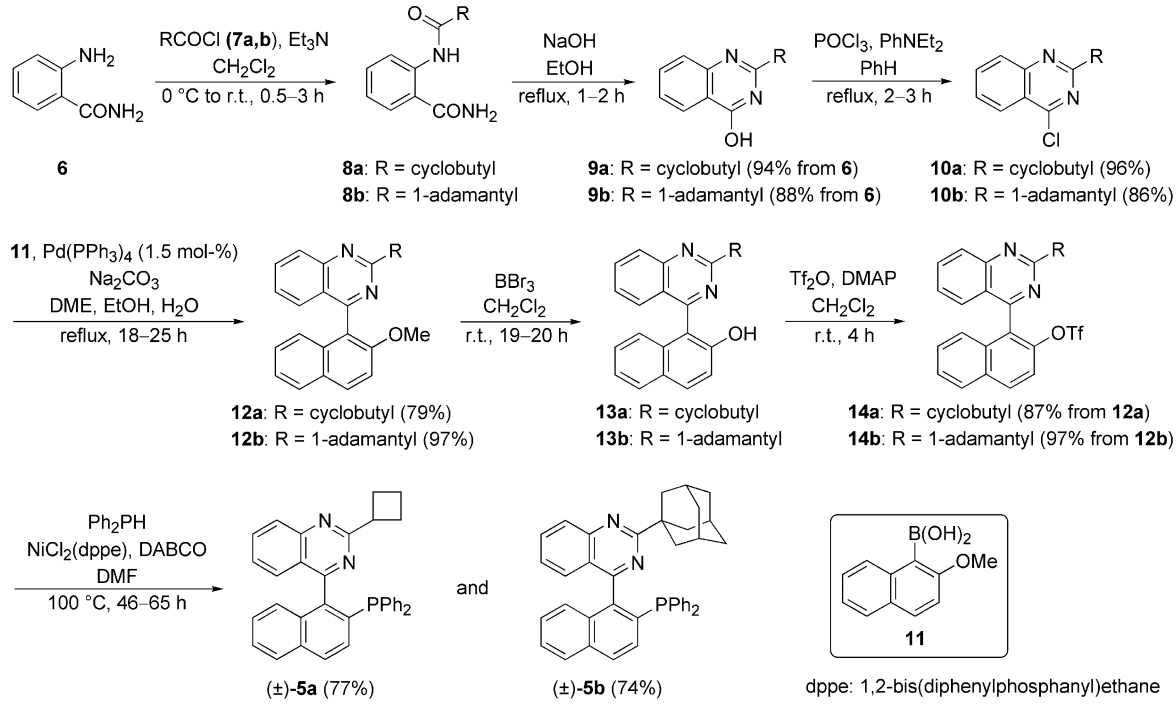
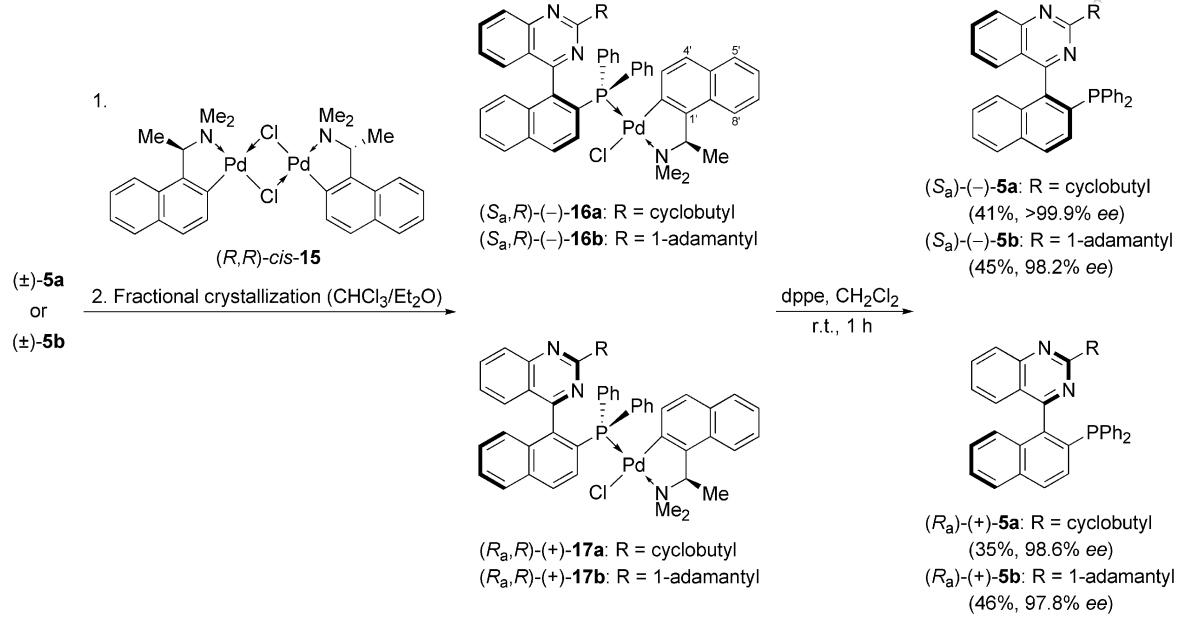


Scheme 1. Synthesis of racemic ligands **5a** and **5b**.

of **9a** with $POCl_3$/$PhNEt_2$ in boiling benzene provided the electrophilic partner **10a** for the subsequent Suzuki–Miyaura cross-coupling. The entire synthetic sequence (exemplified herein by the conversion of **6** to **10a** and **10b**) requires only one chromatographic purification, and can be easily scaled up even in the laboratory setting. When coupled with the arylboronic acid **11**[14] in the presence of $Pd(PPh_3)_4$ (1.5 mol-%), aryl chloride **10a** furnished biaryl **12a** in good yield. The methyl ether cleavage with BBr_3, followed by treatment of the resulting naphthol **13a** with Tf_2O in the presence of DMAP gave triflate **14a**. Finally, nickel-catalyzed cross-coupling between **14a** and Ph_2PH in the presence of $NiCl_2$(dppe)/DABCO according to Cai's protocol[15] provided the racemic triarylphosphane **5a**.[16] All in all, **5a** was obtained in seven operationally simple steps (four chromatographic purifications, 48% yield) from **6**. The racemic adamantyl-based ligand **5b** was prepared in a similar manner (Scheme 1) from **6** in 53% overall yield.

The racemic phosphanes **5a** and **5b** were resolved via formation and separation of their diastereomeric Pd^{II} complexes.[17] Thus, when (±)-**5a** was treated with one equivalent of the chloro-bridged resolving agent (*R*,*R*)-*cis*-**15**,[18] an equimolar mixture of the diastereomeric mononuclear palladacycles (S_a,*R*)-(–)-**16a** and (R_a,*R*)-(+)-**17a** was formed (Scheme 2). Separation of the isomers was accomplished via fractional crystallization from $CHCl_3$/Et_2O. Subsequent treatment of the resolved complexes with dppe in CH_2Cl_2 brought about the ligand exchange with concomitant liberation of the enantioenriched phosphanes (S_a)-(–)-**5a** (41%, >99.9% *ee*) and (R_a)-(+)-**5a** (35%, 98.6% *ee*). Optical resolution of phosphane (±)-**5b** was carried out in an analogous fashion to provide its enantiomers (S_a)-(–)-**5b** (45%, 98.2% *ee*) and (R_a)-(+)-**5b** (46%, 97.8% *ee*). The optical purity of the enantioenriched ligands was determined by CSP HPLC (see Supporting Information).

The assignment of the absolute stereochemistry for each enantiomer of the two newly prepared ligands **5a** and **5b** was cogently secured by single-crystal X-ray analysis of the Pd^{II} complexes (S_a,*R*)-(–)-**16a** and (R_a,*R*)-(+)-**17b** (Figure 2).[19] In the two palladacycles, biaryls (S_a)-(–)-**5a** and (R_a)-(+)-**5b**, respectively, act as monodentate ligands with their soft phosphorus atoms positioned *trans* relative to the hard nitrogen donors of the *ortho*-palladated sub-unit. Steric constraints within these molecules result in a distorted square-planar geometry around the palladium as evident by contraction (to 80.9° and 80.5°, respectively) of the N–Pd–C angles with concomitant enlargement of the other angles (in particular, the P–Pd–C angles to 100.0° and 95.4°, respectively). There are also significant tetrahedral-like out-of-plane deviations of the coordinated atoms (up to 0.31 Å and 0.15 Å, respectively) from their corresponding mean planes. The *C*-methyl substituent of the chiral auxiliary occupies a pseudo-axial position to minimize unfavorable interactions with the H(8′) (see Scheme 2 for numbering); the very feature that is deemed crucial for the creation of a conformationally locked and rigid asymmetric envelope that, in turn, is prerequisite for efficient resolution with the *ortho*-palladate **15**.[20] In (R_a,*R*)-(+)-**17b**, the naphthalene ring system of the chiral auxiliary protrudes in between the two aromatic rings of the PPh_2 group. It positions the H(3′) within the shielding cones of the phenyl rings in accordance with Pople's ring-current model (RCM).[21] As the H(3′) signal in the ^{1}H NMR spectrum is found significantly upfield [at δ = 6.03 ppm; cf. 6.59 ppm for (S_a,*R*)-(–)-**16b**] relative to



Scheme 2. Optical resolution of ligands **5a** and **5b**.

the remaining aromatic protons,[22] it strongly indicates that the conformations of (R_a,*R*)-(+)-**17b** in the solid state and in solution are not dissimilar.

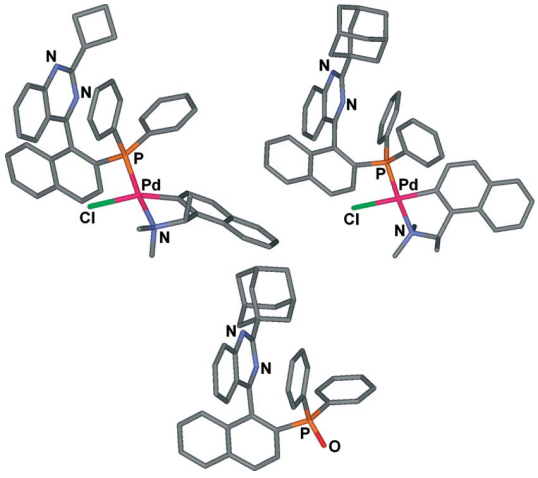
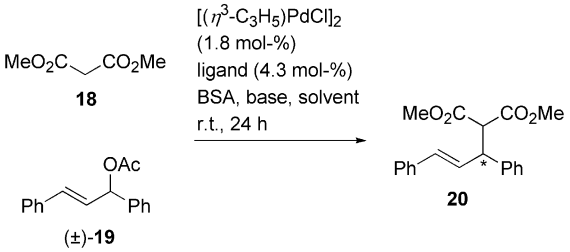


Figure 2. Single-crystal X-ray structures of Pd^{II} complexes (S_a,*R*)-(–)-**16a** (top left) and (R_a,*R*)-(+)-**17b** (top right), and phosphane oxide (S_a)-**5b**-(O) (bottom). Hydrogen atoms and solvent molecules (when applicable) omitted for clarity.

Ligands **5a** and **5b** were initially tested in the asymmetric allylic alkylation (AAA) of the racemic acetate **19** with dimethyl malonate (**18**) (Scheme 3). Because of its synthetic importance, combined with the detailed understanding of the catalytic cycle, the AAA is frequently employed for preliminary screening of new ligand candidates.[23] The results (Table 1) clearly show that the cyclobutyl-based ligand **5a** is superior to its adamantyl analog **5b** in terms of the levels of enantioselectivity that can be reached (entry 1 vs. entry 11). Furthermore, it is apparent that the steric size of the ligand 2-substituent plays, under certain reaction conditions, an important role in the sense of the asymmetry induced {entry 4 [40% *ee* (*R*)] and entry 7 [47% *ee* (*S*)]}. We have observed similar trends when comparing Quinap (**1**) to our 2-phenyl-Quinazolinap ligand **4a**.[10e] It can also be noted that the stereochemical outcome of the reaction is strongly dependent on the alkali metal salt used as the additive. For ligand **5a**, the larger counterions (K^+ and Cs^+, entries 1 and 2) provide **20** in high optical purity (89% *ee*



Scheme 3. Asymmetric allylic alkylation (AAA) with cyclobutyl- and adamantyl-Quinazolinap ligands **5a** and **5b**.

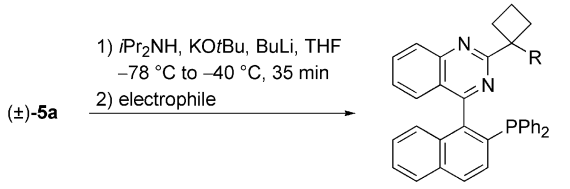
Table 1. AAA with ligands **5a** and **5b**.

Entry	Ligand	Base	Solvent	Yield (%)[a]	*ee* (%)[b]
1	(S_a)-(–)-**5a**	KOAc	CH_2Cl_2	>95	89 (*R*)
2	(S_a)-(–)-**5a**	Cs_2CO_3	CH_2Cl_2	>95	87 (*R*)
3	(S_a)-(–)-**5a**	NaOAc	CH_2Cl_2	>95	82 (*R*)
4	(S_a)-(–)-**5a**	LiOAc	CH_2Cl_2	>95	40 (*R*)
5	(S_a)-(–)-**5a**	KOAc	THF	>95	41 (*R*)
6	(S_a)-(–)-**5a**	KOAc	PhMe	47	59 (*R*)
7	(S_a)-(–)-**5b**	LiOAc	CH_2Cl_2	>95	47 (*S*)
8	(S_a)-(–)-**5b**	NaOAc	CH_2Cl_2	>95	15 (*R*)
9	(S_a)-(–)-**5b**	KOAc	CH_2Cl_2	88	44 (*R*)
10	(S_a)-(–)-**5b**	Cs_2CO_3	CH_2Cl_2	>95	49 (*R*)
11	(S_a)-(–)-**5b**	LiOAc	THF	56	66 (*S*)
12	(S_a)-(–)-**5b**	LiOAc	PhMe	89	44 (*S*)
13	(S_a)-(–)-**5b**	LiOAc	MeCN	>95	21 (*R*)

[a] Isolated yield of **20**. [b] Determined by CSP HPLC (see Supporting Information). BSA: *N*,*O*-bis(trimethylsilyl)acetamide.

and 87% *ee*, respectively) that steadily decreases (entries 3 and 4) when smaller counterions (80% *ee* for Na^+ and 40% *ee* for Li^+) are present. For ligand **5b**, both the level and sense of enantioselection change as the size of the counterion decreases (entries 7–10). There is also a notable solvent effect (entries 7 and 11–13) with THF (entry 11) being optimal for enantiopurity of **20** (66% *ee*).

Our earlier studies demonstrated that varying a substitution pattern at the 2-position of Quinazolinap ligands is the most straightforward and effective way to modulate their catalytic properties.[10] Because no direct way to modify the previously prepared Quinazolinaps was developed, each new ligand could only be accessed through a relatively lengthy de novo synthesis and resolution along the lines similar to those described herein for the preparation of ligands **5a**,**b**. One potential strategy allowing for the synthesis of new ligands via modification of the known Quinazolinaps could take advantage of an increased acidity, due to the presence of the two activating azomethine groups, of benzylic-type protons attached to the quinazoline core. To test this hypothesis, deprotonation of cyclobutyl-Quinazolinap **5a** was investigated. Gratifyingly (Scheme 4, Table 2), when it was treated with a superbasic mixture comprising *i*Pr_2NH, KO*t*Bu, and BuLi (dubbed LIDAKOR)[24] in THF at –40 °C for 1 h, a dark blue solution of a presumed metalated species was formed.[25] Its subsequent treatment with D_2O resulted in an almost complete (>97%) incorporation of deuterium into the parent ligand **5a** to give its deuterated analogue **21a**. As summarized in Table 2, other electrophiles could also be used to quench the metalated species, thus providing access to a range of modified Quinazolinaps that themselves should also be amenable to further functionalization. This modification strategy should be suitable for the previously reported 2-alkyl-Quinazolinap ligands **3**[10] bearing benzylic-type protons at the 2-position.[26]



21a: R = D
21b: R = CHO
21c: R = CO_2Me
21d: R = CH(OH)Ph

Scheme 4. Metalation of phosphane (±)-**5a** with LIDAKOR and subsequent functionalization.

Table 2. Synthesis of modified 2-cyclobutyl-Quinazolinaps **21a**–**d**.[a]

Entry	Electrophile	R	Product	Yield (%)[b]
1	D_2O	D	**21a**	97[c]
2	HCO_2Et	CHO	**21b**	92
3	$(MeO)_2CO$	CO_2Me	**21c**	63
4	PhCHO	CH(OH)Ph	**21d**	94[d]

[a] For reaction conditions, see Scheme 4. [b] Isolated yield. [c] >97% deuterium incorporation by ^1H NMR and HRMS. [d] Ca. 6:4 mixture of diastereomers, analysed by ^1H NMR and HPLC.

Conclusions

In summary, we have developed short and operationally simple syntheses of homochiral bidentate Quinazolinap ligands bearing cyclobutyl and 1-adamantyl substituents. The ligands (especially **5a**) provide good levels of enantioselectivity (up to 89% *ee*) in the prototypical AAA reaction. We have also demonstrated that **5a** is a suitable substrate for the preparation of new Quinazolinap ligands via the metalation/functionalization strategy. Exploratory work is currently underway to test these new ligands in a wide range of asymmetric processes.

Experimental Section

General Methods: All reactions were performed under anhydrous conditions and an inert atmosphere of nitrogen in the oven-dried glassware with magnetic stirring. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise indicated. Reagents were used as obtained from commercial sources, or purified according to the guidelines of Perrin and Armarego.[27] Evaporation in vacuo refers to the removal of volatiles on a Büchi rotary evaporator attached to a water respirator (≈ 20 Torr). Flash chromatography was carried out using Merck Kiesegel 60 F_{254} (230–400 mesh) silica gel following the method of Still et al.[28] Only distilled solvents were used as eluents. Thin-layer chromatography (TLC) was performed on Merck DC-Alufolien plates pre-coated with silica gel 60 F_{254}. They were visualized either by quenching of ultraviolet fluorescence, or by charring with 5% w/v phosphomolybdic acid in 95% EtOH, 10% w/v ammonium molybdate in 1 M H_2SO_4, or 10% $KMnO_4$ in 1 M H_2SO_4. Observed retention factors (R_f) are quoted to the nearest 0.05, unless a higher accuracy was necessary to distinguish close-eluting compounds. All reaction solvents were distilled before use, unless otherwise indicated. Anhydrous CH_2Cl_2 and $CHCl_3$ were obtained by refluxing over CaH_2. Anhydrous DMF was obtained by distillation under reduced pressure from CaH_2, and stored over 4 Å molecular sieves. Anhydrous Et_2O was obtained by distillation, immediately before use, from sodium/benzophenone ketyl under an inert atmosphere of nitrogen. High-resolution mass spectrometry (HRMS) measurements are valid to ±5 ppm. Melting points (m.p.) are quoted to the nearest 0.5 °C.

2-(Cyclobutanecarbonylamino)benzamide (8a) and 2-Cyclobutylquinazolin-4-ol (9a): To a suspension of anthranilamide (**6**) (11.5 g, 84.4 mmol) in CH_2Cl_2 (250 mL) was added Et_3N (15 mL, 110 mmol) and the mixture was cooled in an ice bath. During vigorous stirring, cyclobutanecarbonyl chloride (**7a**) (10.0 g, 84.4 mmol) was added dropwise over 15 min. At the beginning of the addition, a clear solution resulted but later on a lot of precipitate formed. After the addition was complete, the reaction mixture was stirred at 0 °C for 15 min, and at room temperature for an additional 15 min. The volatiles were removed in vacuo to give an off-white solid (31.3 g) containing amide **8a** that was used in the next step without any further purification. An analytical sample of amide **8a** was obtained by chromatography of a small amount of the crude product (silica gel; EtOAc) followed by crystallization

(EtOAc/pentane). Amide **8a**: a white solid; R_f = 0.70 (EtOAc); m.p. 183.0–184.5 °C (EtOAc/pentane). ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.74–1.85 (m, 1 H), 1.88–2.01 (m, 1 H), 2.11–2.28 (m, 4 H), 3.21 (dquint, J = 8.6, 1.0 Hz, 1 H), 7.10 (ddd, J = 7.9, 7.4, 1.2 Hz, 1 H), 7.48 (ddd, J = 8.4, 7.4, 1.5 Hz, 1 H), 7.71 (br. s, 1 H), 7.80 (dd, J = 7.9, 1.4 Hz, 1 H), 8.26 (br. s, 1 H), 8.52 (dd, J = 8.4, 1.0 Hz, 1 H), and 11.9 (s, 1 H) ppm. ^{13}C{^{1}H} NMR (101 MHz, [D$_6$]DMSO): δ = 17.3, 24.7, 40.6, 119.1, 119.8, 122.0, 128.5, 132.1, 139.8, 170.7, and 172.8. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1664, 1608, 1579, 1518, 1448, 1377, and 1288 cm^{-1}. HRMS calcd. for $C_{12}H_{14}N_2NaO_2$ [MNa$^+$] 241.0953, found 241.0944. $C_{12}H_{14}N_2O_2$ (218.25): calcd. C 66.04, H 6.47, N 12.84; found C 66.06, H 6.47, N 12.79.

The foregoing solid was dissolved in EtOH (250 mL) and treated with 10 M NaOH (25 mL, 0.25 mol), and the reaction mixture was refluxed for 1 h. The resulting clear solution was subsequently re-cooled to 0 °C, neutralized with concd HCl and diluted with water (≈ 2 L). The precipitate formed was filtered, washed with a copious amount of water, and dried to give the title compound **9a** (15.8 g, 94% from **6**) as an off-white solid that was used in the next step without any further purification. An analytical sample of quinazolinol **9a** was obtained by chromatography of a small amount of the crude product (silica gel; EtOAc) followed by crystallization (EtOAc/pentane). Quinazolinol **9a**: a white solid; R_f = 0.70 (EtOAc); m.p. 238.5–239.5 °C (EtOAc/pentane). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.79–1.90 (m, 1 H), 1.93–2.06 (m, 1 H), 2.20–2.30 (m, 2 H), 2.35–2.48 (m, 2 H), 3.51 (dquint, J = 8.6, 0.9 Hz, 1 H), 7.46 (ddd, J = 8.1, 7.2, 1.2 Hz, 1 H), 7.65 (ddd, J = 8.3, 1.2, 0.5 Hz, 1 H), 7.78 (ddd, J = 8.3, 7.2, 1.6 Hz, 1 H), and 8.09 (ddd, J = 8.1, 1.6, 0.5 Hz, 1 H) ppm. ^{13}C{^{1}H} NMR (101 MHz, [D$_6$]DMSO): δ = 17.4, 25.7, 37.9, 120.7, 125.6, 125.8, 126.8, 134.1, 148.7, 159.0, and 161.8. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1676, 1610, and 1470 cm^{-1}. HRMS calcd. for $C_{12}H_{13}N_2O$ [MH$^+$] 201.1028, found 201.1028. $C_{12}H_{12}N_2O$ (200.24): calcd. C 71.98, H 6.04, N 13.99; found C 71.93, H 6.04, N 14.03.

4-Chloro-2-cyclobutylquinazoline (10a): A solution of quinazolinol **9a** (15.4 g, 77 mmol) in benzene (120 mL) was azeotropically dried under a Dean–Stark trap. The solution was cooled to room temperature and treated with $PhNEt_2$ (20 mL, 0.13 mol) followed by $POCl_3$ (4.7 mL, 51 mmol). The reaction mixture was then refluxed for 2 h, cooled to room temperature, and diluted with EtOAc (250 mL). The mixture was washed successively with water (3 × 250 mL), 1 M HCl (3 × 250 mL), water (250 mL), satd. $NaHCO_3$ (250 mL), water (250 mL), and brine (250 mL). The organic layer was dried ($MgSO_4$), and the solvents evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel; CH_2Cl_2/pentane, 1:1) gave the title compound **10a** (15.6 g, 96%) as a clear oil that solidified upon standing.[29] Quinazoline **10a**: a white solid; R_f = 0.40 (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92–2.20 (m, 2 H), 1.93–2.06 (m, 1 H), 2.38–2.67 (m, 4 H), 3.93 (quint, J = 8.6 Hz, 1 H), 7.56 (ddd, J = 8.2, 6.9, 1.1 Hz, 1 H), 7.84 (ddd, J = 8.3, 6.9, 1.3 Hz, 1 H), 7.95 (ddd, J = 8.3, 1.1, 0.6 Hz, 1 H), and 8.11 (ddd, J = 8.2, 1.3, 0.6 Hz, 1 H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 18.1, 27.4, 42.7, 121.6, 125.3, 127.5, 128.0, 134.2, 151.1, 162.0, and 168.2. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1618, 1568, 1555, 1480, 1461, 1335, 1310, and 1251 cm^{-1}. HRMS calcd. for $C_{12}H_{12}ClN_2$ [MH$^+$] 219.0689, found 219.0696.

2-Cyclobutyl-4-(2-methoxynaphthalen-1-yl)quinazoline (12a): To a solution of aryl chloride **10a** (4.36 g, 20.0 mmol) in 1,2-dimethoxyethane (DME, 25 mL) was added $Pd(PPh_3)_4$ (347 mg, 0.30 mmol) followed by 2 M Na_2CO_3 (20 mL, 40 mmol), arylboronic acid **11**[14] (4.24 g, 16.7 mmol), and EtOH (30 mL). The resulting thick suspension was refluxed for 18 h, cooled to room temperature, and partitioned between CH_2Cl_2 and water. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), and the solvents evaporated in vacuo. Purification by flash chromatography (silica gel; CH_2Cl_2/pentane, 1:1 → CH_2Cl_2) gave a pink solid that was triturated with pentane (100 mL), filtered, washed with pentane (100 mL), and dried to give the title compound **12a** (5.37 g, 79%) as a yellow solid: R_f = 0.55 (pentane/CH_2Cl_2, 15:1); m.p. 143.5–144.0 °C (EtOAc/pentane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.94–2.04 (m, 1 H), 2.05–2.20 (m, 1 H), 2.43–2.56 (m, 2 H), 2.62–2.76 (m, 2 H), 3.78 (s, 3 H), 4.10 (dquint, J = 8.5, 0.7 Hz, 1 H), 7.12 (≈ dd, J = 8.4, 1.1 Hz, 1 H), 7.29 (ddd, J = 8.4, 6.8, 1.5 Hz, 1 H), 7.32–7.38 (m, 2 H), 7.43 (d, J = 9.0 Hz, 1 H), 7.44 (ddd, J = 8.3, 1.5, 0.6 Hz, 1 H), 7.82 (ddd, J = 8.4, 6.8, 1.5 Hz, 1 H), 7.87 (≈ dd, J = 8.3, 1.2 Hz, 1 H), 8.02 (d, J = 9.0 Hz, 1 H), and 8.10 (≈ d, J = 8.4 Hz, 1 H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 18.3, 27.7, 27.8, 43.5, 56.6, 113.4, 120.0, 123.5, 123.8, 124.4, 126.5, 126.9, 127.0, 128.0, 128.3, 129.0, 131.0, 133.0, 133.5, 150.6, 154.6, 167.2, and 169.0. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1616, 1595, 1568, 1550, 1514, 1493, 1344, 1269, and 1252 cm^{-1}. HRMS calcd. for $C_{23}H_{21}N_2O$ [MH$^+$] 341.1654, found 341.1669. $C_{23}H_{20}N_2O$ (340.42): calcd. C 81.15, H 5.92, N 8.23; found C 81.16, H 5.95, N 8.17.

1-(2-Cyclobutylquinazolin-4-yl)naphthalen-2-ol (13a) and 1-(2-Cyclobutylquinazolin-4-yl)naphthalen-2-yl Trifluoromethanesulfonate (14a): A solution of biaryl **12a** (4.76 g, 14.0 mmol) in CH_2Cl_2 (55 mL) was cooled in an ice bath. During vigorous stirring, BBr_3 (1.0 M in CH_2Cl_2, 28 mL, 28 mmol) was added dropwise over 10 min to give a dark red solution. The reaction mixture was stirred at room temperature for 19 h, re-cooled to 0 °C, and quenched with 1 M HCl (50 mL) to give a yellow suspension. The precipitate was filtered, and washed successively with water (2 × 50 mL) and CH_2Cl_2 (50 mL). The organic phase from the filtrate was separated, and the extraction was completed with additional portions of CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and the solvents evaporated in vacuo to give a yellow residue that was combined with the previously isolated solid (4.82 g in total). An analytical sample of naphthol **13a** was obtained by chromatography of a small amount of the crude product (silica gel; CH_2Cl_2/EtOAc, 2:1) followed by crystallization (EtOAc/pentane). Naphthol **13a**: a yellow solid; R_f = 0.75 (CH_2Cl_2/EtOAc, 2:1); m.p. 197.0–198.0 °C (EtOAc/pentane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.91–2.02 (m, 1 H), 2.04–2.17 (m, 1 H), 2.40–2.64 (m, 4 H), 3.99 (dquint, J = 8.7, 0.8 Hz, 1 H), 7.21–7.25 (m, 2 H), 7.26–7.35 (m, 3 H), 7.55 (≈ ddd, J = 8.4, 1.2, 0.5 Hz, 1 H), 7.99 (ddd, J = 8.3, 6.8, 1.4 Hz, 1 H), 7.81 (d, J = 8.0 Hz, 1 H), 7.87 (d, J = 8.9 Hz, 1 H), 8.00 (≈ d, J = 8.5 Hz, 1 H), and 9.93 (br. s, 1 H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 18.4, 27.6, 27.8, 42.9, 114.8, 119.2, 122.2, 123.6, 124.9, 126.5, 126.7, 127.9, 128.3, 128.4, 128.7, 132.5, 132.6, 134.2, 151.5, 154.7, 166.3, and 168.0 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1620, 1597, 1562, 1549, 1489, 1462, 1406, 1392, 1348, 1286, 1269, 1232, and 1207 cm^{-1}. HRMS calcd. for $C_{22}H_{19}N_2O$ [MH$^+$] 327.1497, found 327.1491. $C_{22}H_{18}N_2O$ (326.39): calcd. C 80.96, H 5.56, N 8.58; found C 80.91, H 5.62, N 8.59.

The foregoing crude naphthol **13a** was dissolved in CH_2Cl_2 (70 mL) and treated with DMAP (5.12 g, 42.0 mmol). After the mixture had been cooled in an ice bath, Tf_2O (2.6 mL, 15 mmol) was added dropwise over 5 min, and the stirring was continued at room temperature for 4 h. The reaction mixture was re-cooled to 0 °C, 1 M HCl (50 mL) was added, and the mixture was stirred vigorously for 5 min. The phases were separated and the extraction was completed with additional portions of CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and the

solvents evaporated in vacuo to give an orange solid. Purification by flash chromatography (silica gel; CH_2Cl_2) gave the title compound **14a** (5.59 g, 87% from **12a**) as a white solid: R_f = 0.35 (CH_2Cl_2); m.p. 142.5–143.0 °C (EtOAc/pentane). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.93–2.05 (m, 1 H), 2.06–2.20 (m, 1 H), 2.42–2.55 (m, 2 H), 2.57–2.77 (m, 2 H), 4.10 (dquint, J = 8.7, 1.0 Hz, 1 H), 7.28 (≈ dd, J = 8.5, 0.8 Hz, 1 H), 7.35 (ddd, J = 8.3, 1.5, 0.6 Hz, 1 H), 7.41 (ddd, J = 7.9, 6.7, 1.1 Hz, 1 H), 7.43 (ddd, J = 8.4, 6.9, 1.2 Hz, 1 H), 7.59 (ddd, J = 8.2, 6.9, 1.1 Hz, 1 H), 7.61 (d, J = 9.0 Hz, 1 H), 7.88 (ddd, J = 8.5, 6.7, 1.6 Hz, 1 H), 8.00 (≈ d, J = 8.3 Hz, 1 H), 8.13 (d, J = 9.0 Hz, 1 H), and 8.14 (≈ d, J = 8.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 18.3, 27.4, 27.8, 43.4, 118.1 (q, J = 320 Hz), 119.5, 122.9, 126.1, 126.2, 127.1, 127.3, 127.4, 128.2, 128.3, 128.6, 131.8, 132.4, 134.1, 144.6, 150.9, 163.2, and 169.1 ppm (one-carbon signal, obscured). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1568, 1552, 1425, 1248, 1230, 1140, and 951 cm^{-1}. HRMS calcd. for $C_{23}H_{18}F_3N_2O_3S$ [MH^+] 459.0990, found 459.0970. $C_{23}H_{17}F_3N_2O_3S$ (458.45): calcd. C 60.26, H 3.74, N 6.11, S 6.99; found C 60.24, H 3.73, N 6.05, S 7.14.

(±)-2-Cyclobutyl-4-(2-diphenylphosphanylnaphthalen-1-yl)quinazoline (±)-(5a): To a solution of $NiCl_2$(dppe) (549 mg, 1.04 mmol) in DMF (10 mL) was added Ph_2PH (0.7 mL, 4.0 mmol), and the mixture was stirred at 100 °C for 30 min. A solution of triflate **14a** (4.78 g, 10.4 mmol) and DABCO (4.66 g, 41.6 mmol) in DMF (10 mL) was added via cannula and the resulting dark brown mixture was stirred at 100 °C. Additional portions of Ph_2PH (0.7 mL, 4.0 mmol; and 0.8 mL, 4.6 mmol) were added after 25 min and 55 min, respectively. After 46 h at 100 °C, the volatiles were removed in vacuo, the residue was taken up in EtOAc, and washed successively with water and brine. The organic layer was dried ($MgSO_4$), and concentrated in vacuo to give a brown oil. Purification by flash chromatography (silica gel; CH_2Cl_2/pentane, 1:2→CH_2Cl_2) furnished a pale yellow foam. Re-crystallization (EtOAc/pentane) gave the title compound (±)-**5a** as a white solid (3.53 g, 69%). The mother liquor was concentrated and chromatographed (silica gel; CH_2Cl_2/pentane, 1:1) to give an additional portion of the product (±)-**5a** (0.43 g, 8%; 3.96 g, 77% overall). Biaryl (±)-**5a**: a white solid; R_f = 0.20 (CH_2Cl_2), 0.35 (hexane/EtOAc, 5:1); m.p. 164.0–164.5 °C (EtOAc/pentane). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.69–1.80 (m, 1 H), 1.88–2.04 (m, 1 H), 2.16–2.39 (m, 4 H), 3.87 (dquint, J = 8.7, 0.9 Hz, 1 H), 7.09 (≈ dd, J = 8.5, 0.7 Hz, 1 H), 7.12–7.18 (m, 2 H), 7.19–7.33 (m, 11 H), 7.37 (dd, J = 8.5, 3.2 Hz, 1 H), 7.48 (ddd, J = 8.1, 6.8, 1.1 Hz, 1 H), 7.79 (ddd, J = 8.4, 6.6, 1.7 Hz, 1 H), 7.88 (d, J = 8.2 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), and 8.07 (d, J = 8.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$):[30] δ = 18.3, 27.2, 27.5, 43.3, 123.5, 123.6, 126.2, 126.3, 126.6, 126.8, 126.9, 127.0, 128.0, 128.21, 128.25, 128.27, 128.29, 128.34, 128.35, 128.5, 129.1, 130.01, 130.02, 131.8, 131.9, 133.3, 133.5, 133.6, 133.7, 134.3, 134.5, 136.5, 136.6, 137.3, 137.4, 142.0, 142.3, 150.4, 168.7, 169.2, and 169.3 ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = –12.5. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1615, 1569, 1550, 1491, 1434, and 1338 cm^{-1}. HRMS calcd. for $C_{34}H_{28}N_2P$ [MH^+] 495.1990, found 495.1984. $C_{34}H_{27}N_2P$ (494.57): calcd. C 82.57, H 5.50, N 5.66; found C 82.43, H 5.50, N, 5.62. Crystals of phosphane (±)-**5a** suitable for X-ray diffraction analysis were grown by slow evaporation of a CH_2Cl_2/pentane solution. During the crystallization, phosphane (±)-**5a** underwent partial oxidation to the corresponding phosphane oxide (±)-**5a**-(O). For the crystallographic data of (±)-**5a/5a**-(O), see Supporting Information.

2-(Adamantane-1-carbonylamino)benzamide (8b) and 2-(Adamantan-1-yl)quinazolin-4-ol (9b): To a suspension of anthranilamide (**6**) (3.42 g, 25.1 mmol) in CH_2Cl_2 (50 mL) was added Et_3N (4.5 mL, 33 mmol) and the mixture was cooled in an ice bath. During vigorous stirring, a solution of 1-adamantoyl chloride (**7b**) (5.00 g, 25.1 mmol) in CH_2Cl_2 (30 mL) was added dropwise over 30 min. At the beginning of the addition, a clear solution resulted but later on a lot of precipitate formed. After the addition was complete, the reaction mixture was stirred at 0 °C for 2 h, and at room temperature for an additional 1 h. The reaction mixture was evaporated in vacuo to give an off-white solid (11.3 g) containing amide **8b** that was used in the next step without any further purification. An analytical sample of amide **8b** was obtained by chromatography of a small amount of the crude product (silica gel; CH_2Cl_2→CH_2Cl_2/EtOAc, 10:1) followed by crystallization (EtOAc/pentane). Amide **8b**: a white solid; R_f = 0.65 (CH_2Cl_2/EtOAc, 2:1); m.p. 228.0–229.0 °C (EtOAc/pentane). ^1H NMR (400 MHz, [D_6]DMSO): δ = 1.63–1.76 (m, 6 H), 1.88 (d, J = 2.7 Hz, 6 H), 2.03 (dt, J = 2.7 Hz, 3 H), 7.09 (ddd, J = 7.9, 7.5, 1.2 Hz, 1 H), 7.47 (ddd, J = 8.5, 7.5, 1.5 Hz, 1 H), 7.73 (br. s, 1 H), 7.80 (dd, J = 7.9, 1.4 Hz, 1 H), 8.29 (br. s, 1 H), 8.56 (dd, J = 8.5, 1.1 Hz, 1 H), and 11.9 (s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, [D_6]DMSO): δ = 27.5, 35.9, 38.6, 41.3, 119.0, 119.8, 121.9, 128.4, 132.2, 140.1, 170.9, and 175.8 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2914, 2854, 1664, 1606, 1577, 1523, 1448, 1377, 1298, and 1291 cm^{-1}. HRMS calcd. for $C_{18}H_{23}N_2O_2$ [MH^+] 299.1760, found 299.1744. $C_{18}H_{22}N_2O_2$ (298.38): calcd. C 72.46, H 7.43, N 9.39; found C 72.39, H 7.45, N 9.46.

The foregoing residue was suspended in EtOH (40 mL) and treated with 10 M NaOH (7.5 mL, 75 mmol). The reaction mixture was refluxed for 2 h, and the resulting clear solution was subsequently re-cooled to 0 °C, neutralized with concd HCl, and diluted with water (≈ 2 L). The precipitate formed was filtered, washed with a copious amount of water, and dried to give the title compound **9b** (6.20 g, 88% from **6**) as an off-white solid that was used in the next step without any further purification. An analytical sample of quinazolinol **9b** was obtained by chromatography of a small amount of the crude product (silica gel; CH_2Cl_2→CH_2Cl_2/EtOAc, 10:1) followed by crystallization (EtOAc/pentane). Quinazolinol **9b**: a white solid; R_f = 0.80 (CH_2Cl_2/EtOAc, 2:1); m.p. 213.5–215.0 °C (EtOAc/pentane). ^1H NMR (400 MHz, [D_6]DMSO): δ = 1.66–1.76 (m, 6 H), 1.99–2.09 (m, 9 H), 7.46 (ddd, J = 8.1, 7.2, 1.1 Hz, 1 H), 7.60 (ddd, J = 8.2, 1.1, 0.5 Hz, 1 H), 7.77 (ddd, J = 8.2, 7.2, 1.6 Hz, 1 H), and 8.08 (ddd, J = 8.1, 1.6, 0.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, [D_6]DMSO): δ = 27.6, 35.7, 38.65, 38.67, 120.7, 125.5, 126.0, 127.2, 134.1, 148.4, and 162.2 ppm (one carbon signal obscured). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2912, 1670, 1604, 1470 cm^{-1}. HRMS calcd. for $C_{18}H_{21}N_2O$ [MH^+] 281.1654, found 281.1646. $C_{18}H_{20}N_2O$ (280.36): calcd. C 77.11, H 7.19, N 9.99; found C 77.39, H 7.49, N 9.70.

2-(Adamantan-1-yl)-4-chloroquinazoline (10b): A solution of quinazolinol **9b** (5.97 g, 21.3 mmol) in benzene (40 mL) was azeotropically dried under a Dean–Stark trap. The solution was cooled to room temperature and treated with $PhNEt_2$ (5.1 mL, 32 mmol) followed by $POCl_3$ (1.2 mL, 13 mmol). The reaction mixture was then refluxed for 3 h, cooled to room temperature, and diluted with EtOAc (50 mL). The mixture was washed successively with water (3 × 50 mL), 1 M HCl (3 × 50 mL), water (50 mL), satd. $NaHCO_3$ (50 mL), water (50 mL), and brine (50 mL). The organic layer was dried ($MgSO_4$), and the solvents evaporated in vacuo to give an off-white solid.[29] Purification by flash chromatography (silica gel; CH_2Cl_2) gave the title compound **10b** (5.45 g, 86%) as a white solid: R_f = 0.60 (pentane/CH_2Cl_2, 3:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.76–1.87 (m, 6 H), 2.09–2.28 (m, 9 H), 7.60 (≈ dd, J = 8.3, 7.0 Hz, 1 H), 7.86 (ddd, J = 8.3, 7.0, 1.1 Hz, 1 H), 7.99 (d, J = 8.3 Hz, 1 H), and 8.18 (≈ d, J = 8.3 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 28.5, 36.7, 40.9, 41.1, 121.9, 125.5, 127.6,

128.5, 134.1, 151.4, 162.0, and 172.1 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2980, 2852, 1618, 1568, 1554, 1479, 1456, 1344, 1329, 1308, 1248, 987, and 976 cm^{-1}. HRMS calcd. for $C_{18}H_{20}ClN_2$ [MH^+] 299.1315, found 299.1323.

2-(Adamantan-1-yl)-4-(2-methoxynaphthalen-1-yl)quinazoline (12b): To a solution of aryl chloride **10b** (4.73 g, 15.9 mmol) in DME (40 mL) was added $Pd(PPh_3)_4$ (276 mg, 0.24 mmol) followed by 2 M Na_2CO_3 (17.5 mL, 35 mmol), arylboronic acid **11**[14] (3.37 g, 16.7 mmol), and EtOH (45 mL). The resulting thick suspension was refluxed for 25 h, cooled to room temperature, and partitioned between $CHCl_3$ (due to poor solubility of **12b** in common organic solvent, a large amount of $CHCl_3$ was required) and water. The phases were separated, and the extraction was completed with additional portions of $CHCl_3$. The combined organic extracts were dried ($MgSO_4$), and the solvents evaporated in vacuo. The residue was loaded on top of a column filled with silica gel, and the column was eluted with CH_2Cl_2/pentane (1:1) and, after the fractions containing the desired product **12b** began to elute, with pure CH_2Cl_2. Fractions containing **12b** were combined and the solvents evaporated in vacuo. The resulting pink solid was triturated with Et_2O (50 mL), filtered, washed with Et_2O (50 mL), and dried to give the title compound **12b** (6.48 g, 97%) as a white solid: R_f = 0.75 (CH_2Cl_2); m.p. 275.5–276.5 °C (EtOAc). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.76–1.87 (m, 6 H), 2.10–2.17 (m, 3 H), 2.28 (d, J = 2.8 Hz, 6 H), 3.77 (s, 3 H), 7.12–7.17 (m, 1 H), 7.30 (ddd, J = 8.2, 6.8, 1.4 Hz, 1 H), 7.34 (ddd, J = 7.9, 6.8, 1.4 Hz, 1 H), 7.36 (ddd, J = 8.2, 6.8, 1.2 Hz, 1 H), 7.41 (ddd, J = 8.2, 1.6, 0.6 Hz, 1 H), 7.44 (d, J = 9.1 Hz, 1 H), 7.80 (ddd, J = 8.5, 6.8, 1.6 Hz, 1 H), 7.88 (≈ d, J = 7.9 Hz, 1 H), 8.03 (d, J = 9.1 Hz, 1 H), and 8.09 (d, J = 8.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 28.8, 36.9, 41.2, 41.3, 56.9, 113.9, 123.3, 123.9, 124.6, 126.3, 126.7, 127.0, 128.0, 128.6, 129.2, 130.9, 133.0, 133.2, 150.7, 154.7, 166.5, and 172.6 ppm (one carbon signal obscured). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2929, 2913, 1850, 1616, 1597, 1568, 1347, 1514, 1454, 1346, 1304, 1269, 1250, and 1223 cm^{-1}. HRMS calcd. for $C_{29}H_{29}N_2O$ [MH^+] 421.2280, found 421.2274. $C_{29}H_{28}N_2O$ (420.55): calcd. C 82.82, H 6.71, N 6.66; found C 82.47, H 6.74, N 6.66.

1-(2-Adamantan-1-yl-quinazolin-4-yl)naphthalen-2-ol (13b) and 1-(2-Adamantan-1-yl-quinazolin-4-yl)naphthalen-2-yl Trifluoroethanesulfonate (14b): A suspension of biaryl **12b** (6.68 g, 15.9 mmol) in CH_2Cl_2 (70 mL) was cooled in an ice bath. During vigorous stirring, BBr_3 (1.0 M in CH_2Cl_2, 32 mL, 32 mmol) was added dropwise over 10 min to give a red solution. The reaction mixture was stirred at room temperature for 20 h, re-cooled to 0 °C, and quenched with 1 M HCl (50 mL) to give a yellow solution. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and the solvents evaporated in vacuo to give the crude naphthol **13b** as a bright-yellow solid (6.28 g). An analytical sample of naphthol **13b** was obtained by chromatography of a small amount of the crude product (silica gel; CH_2Cl_2) followed by crystallization (EtOAc/pentane). Naphthol **13b**: a yellow solid; R_f = 0.75 (CH_2Cl_2); m.p. 230.0–231.5 °C (EtOAc/pentane). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.80–1.90 (m, 6 H), 2.14–2.22 (m, 3 H), 2.24–2.30 (m, 6 H), 7.26 (≈ ddd, J = 7.9, 7.9, 1.2 Hz, 1 H), 7.30–7.37 (m, 3 H), 7.38 (d, J = 8.9 Hz, 1 H), 7.59 (d, J = 8.3 Hz, 1 H), 7.80–7.89 (m, 2 H), 7.95 (d, J = 8.9 Hz, 1 H), 8.10 (d, J = 8.5 Hz, 1 H), and 10.4 (br. s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 28.7, 36.8, 41.1, 41.3, 114.3, 119.2, 121.7, 123.6, 125.3, 126.3, 126.5, 128.0, 128.4, 128.7, 129.0, 132.4, 132.7, 133.9, 152.1, 155.5, 165.2, and 171.2. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2908, 2852, 1620, 1599, 1560, 1545, 1487, 1462, 1454, 1406, 1396, 1302, and 1213 cm^{-1}. HRMS calcd. for $C_{28}H_{27}N_2O$ [MH^+] 407.2123, found 407.2136. $C_{28}H_{26}N_2O$ (406.52): calcd. C 82.73, H 6.45, N 6.89; found C 82.43, H 6.47, N 6.83.

The foregoing crude naphthol **13b** was dissolved in CH_2Cl_2 (100 mL) and treated with DMAP (5.64 g, 46.2 mmol). After the mixture had been cooled in an ice bath, Tf_2O (2.9 mL, 17 mmol) was added dropwise over 5 min, and the stirring was continued at room temperature for 4 h. The reaction mixture was re-cooled to 0 °C, 1 M HCl (50 mL) was added, and the mixture was stirred vigorously for 5 min. The phases were separated and the extraction was completed with additional portions of CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and the solvents evaporated in vacuo to give an orange solid. Purification by flash chromatography (silica gel; pentane/CH_2Cl_2, 1:1) gave the title compound **14b** (8.10 g, 97% from **12b**) as a white solid: R_f = 0.40 (CH_2Cl_2/pentane, 2:1); m.p. 217.5–218.5 °C (EtOAc/pentane). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.77–1.89 (m, 6 H), 2.11–2.18 (m, 3 H), 2.27 (≈ d, J = 2.6 Hz, 6 H), 7.31 (≈ dd, J = 8.5, 0.8 Hz, 1 H), 7.34 (ddd, J = 8.3, 1.5, 0.5 Hz, 1 H), 7.40 (ddd, J = 7.9, 6.7, 1.1 Hz, 1 H), 7.44 (ddd, J = 8.4, 6.9, 1.2 Hz, 1 H), 7.59 (ddd, J = 8.1, 6.8, 1.1 Hz, 1 H), 7.61 (d, J = 9.1 Hz, 1 H), 7.86 (ddd, J = 8.4, 6.7, 1.6 Hz, 1 H), 8.01 (d, J = 8.3 Hz, 1 H), and 8.10–8.17 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 28.7, 36.9, 41.0, 41.4, 118.1 (q, J = 320 Hz), 119.5, 122.7, 125.9, 126.2, 127.0, 127.3, 127.7, 128.1, 128.3, 128.9, 131.6, 132.5, 132.6, 133.7, 144.5, 150.9, 162.5, and 172.6 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2908, 2852, 1570, 1549, 1425, 1306, 1248, 1230, 1213, 1140, and 949 cm^{-1}. HRMS calcd. for $C_{29}H_{26}F_3N_2O_3S$ [MH^+] 539.1616, found 539.1594. $C_{29}H_{25}F_3N_2O_3S$ (538.58): calcd. C 64.67, H 4.68, N 5.20, S 5.95; found C 64.53, H 4.65, N 5.11, S 6.30.

(±)-2-(Adamantan-1-yl)-4-(2-diphenylphosphanylnaphthalen-1-yl)-quinazoline (±)-(5b): To a solution of $NiCl_2$(dppe) (686 mg, 1.30 mmol) in DMF (25 mL) was added Ph_2PH (0.8 mL, 4.6 mmol), and the mixture was stirred at 100 °C for 30 min. A solution of triflate **14b** (7.00 g, 13.0 mmol) and DABCO (5.82 g, 52 mmol) in DMF (10 mL) was added via cannula and the resulting dark brown mixture was stirred at 100 °C. Additional portions of Ph_2PH (0.9 mL, 5.2 mmol; and 1.0 mL, 5.8 mmol) were added after 1 h and 3 h, respectively. After 65 h at 100 °C, the volatiles were removed in vacuo, the residue was taken up in EtOAc, and washed successively with water and brine. The organic layer was dried ($MgSO_4$), and concentrated in vacuo to give a brown oil. Purification by flash chromatography (silica gel; CH_2Cl_2/pentane, 1:2) gave a yellow foam, and its re-crystallization (EtOAc/pentane) provided the title compound (±)-**5b** as a white solid (4.7 g, 63%). The mother liquor was concentrated and chromatographed (silica gel; pentane/CH_2Cl_2, 4:1→2:1) to give an additional portion of the product (±)-**5b** (0.85 g, 11%; 5.55 g, 74% overall). Biaryl (±)-**5b**: a white solid; R_f = 0.15 (CH_2Cl_2/pentane, 2:1); m.p. 235.5–236.5 °C (EtOAc/pentane).[31] ^1H NMR (400 MHz, $CDCl_3$): δ = 1.63–1.75 (m, 6 H), 1.87–2.03 (m, 9 H), 7.09 (dd, J = 8.5, 0.7 Hz, 1 H), 7.15–7.39 (m, 14 H), 7.51 (ddd, J = 8.1, 6.9, 1.1 Hz, 1 H), 7.81 (ddd, J = 8.4, 6.5, 1.9 Hz, 1 H), 7.91 (≈ d, J = 8.4 Hz, 2 H), and 8.12 (d, J = 8.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$):[30] δ = 28.7, 36.8, 40.7, 41.1, 123.32, 123.34, 126.3, 126.4, 126.5, 126.8, 126.9, 128.05, 128.09, 128.2, 128.29, 128.35, 128.43, 128.7, 129.0, 130.13, 130.14, 131.8, 131.9, 133.1, 133.3, 133.4 (two signals overlapped), 133.5, 133.6, 134.0, 134.1, 136.6, 136.7, 137.7, 137.8, 142.6, 142.9, 150.5, 168.35, 168.42, and 172.3 ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = –12.5 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2908, 2850, 1614, 1572, 1547, 1489, 1452, 1435, 1333, 1304, 1223, and 1213 cm^{-1}. HRMS calcd. for $C_{40}H_{36}N_2P$ [MH^+] 575.2616, found 575.2633. $C_{40}H_{35}N_2P$ (574.69): calcd. C 83.60, H 6.14, N 4.87; found C 83.43, H 6.09, N 4.82.

Optical Resolution of Racemic Phosphane (5a): To a solution of the racemic phosphane **5a** (1.00 g, 2.02 mmol) in CH_2Cl_2 (70 mL) was added the resolving agent (*R*,*R*)-*cis*-**15**·CH_2Cl_2[32] (771 mg, 1.01 mmol) and the reaction mixture was stirred at room temperature for 28 h. The solvent was evaporated in vacuo to give a light green foam that was dissolved in $CHCl_3$ (5 mL) and brought to reflux. Et_2O (70 mL) was added dropwise over 5 min, the reflux was continued for an additional 5 min, and the resulting yellow solution was cooled to room temperature. The mixture was stirred for 45 h (after ca. 30 min a precipitate began to form). The precipitate was filtered, washed with Et_2O (18 mL), and dried to give the Pd^{II} complex (S_a,*R*)-(–)-**16a** (SOLID 1A, 762 mg, 45%) as a pale yellow solid. The mother liquor was evaporated to give the Pd^{II} complex (R_a,*R*)-(+)-**17a** as a yellow solid (SOLID 2A, 946 mg, 56%). SOLID 1A (ca. 4 mg) was suspended in CH_2Cl_2 (0.5 mL) and treated with dppe (2.3 mg, 5.7 μmol). The mixture was stirred at room temperature for 2 h and chromatographed directly (silica gel; CH_2Cl_2/pentane, 1:1) to give a small sample of the enantioenriched phosphane (S_a)-(–)-**5a**. The CSP HPLC analysis [Daicel's Chiralcel® OD, 4.6 mm × 25 cm; hexanes/2-propanol, 99:1; 0.7 mL min^{-1}; 10 °C; 254 nm; t_{R1} = 9.8 min for (S_a)-(–)-**5a** and t_{R2} = 11.2 min for (R_a)-(+)-**5a**], revealed the sample to be of 96.0% *ee*. SOLID 2A was analyzed as described for SOLID 1A and the corresponding phosphane (R_a)-(+)-**5a** was shown to be of 82.7% *ee*. The remainder of SOLID 1A was suspended in Et_2O (40 mL), refluxed for 30 min, cooled to room temperature, and stirred for 46 h. The precipitate was filtered, washed with Et_2O (18 mL), and dried to give the re-purified Pd^{II} complex (S_a,*R*)-(–)-**16a** (SOLID 1B, 731 mg, 43%) as a pale yellow solid. The remainder of SOLID 2A was dissolved in Et_2O (20 mL) and stirred at room temperature for 49 h. The precipitate formed was filtered, washed with Et_2O (5 mL), and dried to give the re-purified Pd^{II} complex (R_a,*R*)-(+)-**17a** as a pale yellow solid (SOLID 2B, 620 mg, 37%). SOLID 1B and SOLID 2B were analyzed as described for SOLID 1A, and the corresponding enantiomeric phosphanes (S_a)-(–)-**5a** and (R_a)-(+)-**5a** were shown to be of >99.9% *ee* and 98.6% *ee*, respectively (Figure S1, Supporting Information). The remainder of SOLID 1B was treated with dppe (383 mg, 0.96 mmol) in CH_2Cl_2 (5 mL) for 1 h. Direct purification by column chromatography (silica gel; pentane/CH_2Cl_2, 4:1→CH_2Cl_2) gave the free phosphane (S_a)-(–)-**5a** (406 mg, 41%) as a white foam. Similarly, the remainder of SOLID 2B was treated with dppe (325 mg, 0.82 mmol) in CH_2Cl_2 (5 mL) for 1 h to give, after chromatographic purification, the free phosphane (R_a)-(+)-**5a** (349 mg, 35%) as a white foam. (*sp*,*cis*)-Chloro{1-[(1*R*)-1-(dimethylamino-κN)ethyl]-2-naphthalenyl-κC}-{(S_a)-4-[2-(diphenylphosphanyl-κP)-1-naphthalenyl]-2-cyclobutylquinazoline}palladium (S_a,*R*)-(–)-**16a**: a yellow solid; m.p. 214.0–215.5 °C (dec., $CHCl_3$/Et_2O); $[\alpha]_D^{20}$ = –104 (*c* = 0.68, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.73–1.83 (m, 1 H), 1.77 (d, *J* = 6.3 Hz, 3 H), 1.88–2.03 (m, 1 H), 2.10–2.25 (m, 3 H), 2.36–2.54 (m, 4 H), 2.86 (d, *J* = 3.0 Hz, 3 H), 3.66 (quint, *J* = 8.6 Hz, 1 H), 4.21 (quint, *J* = 6.1 Hz, 1 H), 6.41–6.53 (m, 1 H), 6.66 (d, *J* = 8.6 Hz, 1 H), 6.71 (≈ t, *J* = 6.3 Hz, 2 H), 6.81 (d, *J* = 8.6 Hz, 1 H), 6.94 (t, *J* = 7.1 Hz, 1 H), 7.19 (ddd, *J* = 8.4, 7.0, 1.1 Hz, 1 H), 7.23–7.41 (m, 6 H), 7.35 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1 H), 7.39–7.45 (m, 1 H), 7.49 (≈ dt, *J* = 7.9, 0.8 Hz, 1 H), 7.56 (≈ d, *J* = 8.2 Hz, 1 H), 7.63 (d, *J* = 8.4 Hz, 1 H), 7.67 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1 H), 7.71–7.87 (m, 4 H), 7.92 (d, *J* = 8.1 Hz, 1 H), 8.00 (d, *J* = 8.7 Hz, 1 H), and 8.23 (t, *J* = 8.6 Hz, 1 H) ppm. $^{13}C\{^1H\}$/^{13}C DEPT 135 NMR (101 MHz, $CDCl_3$):[30] δ = 18.3 (*C*H_2), 23.3 (*C*H_3), 27.3 (*C*H_2), 27.7 (*C*H_2), 43.2 (*C*H), 48.43 (*C*H), 48.44 (*C*H), 50.69 (*C*H_3), 50.72 (*C*H_3), 73.02 (*C*H_3), 73.05 (*C*H_3), 123.2 (*C*H), 123.75 (*ipso C*), 123.87 (*C*H), 123.92 (*C*H), 125.5 (*C*H), 126.1 (*C*H), 126.5 (*C*H), 126.6 (*C*H), 126.7 (*C*H), 126.9 (*C*H), 127.4 (*C*H), 127.6 (*C*H), 127.7 (*C*H), 127.9 (*C*H), 128.0 (*C*H), 128.1 (*C*H), 128.2 (*ipso C*), 128.5 (*C*H), 128.7 (*ipso C*), 128.8 (*C*H), 129.57 (*C*H), 129.59 (*C*H), 130.0 (*ipso C*), 130.4 (*ipso C*), 130.68 (*C*H), 130.71 (*C*H), 130.9 (*ipso C*), 132.4 (*ipso C*), 132.5 (*ipso C*), 133.4 (*C*H), 133.99 (*ipso C*), 134.01 (*ipso C*), 135.6 (*C*H), 135.7 (*C*H), 135.7 (*C*H), 136.0 (*C*H), 136.1 (*C*H), 137.1 (*C*H), 137.2 (*C*H), 139.5 (*ipso C*), 148.84 (*ipso C*), 148.86 (*ipso C*), 150.1 (*ipso C*), 150.3 (*ipso C*), 167.2 (*ipso C*), 168.0 (*ipso C*) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 45.19 (br. s) ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1614, 1572, 1550, 1502, 1491, and 1473 cm^{-1}. HRMS calcd. for $C_{48}H_{43}N_3PPd$ (M – Cl^-) 798.2229, found 798.2232. Crystals of (S_a,*R*)-(–)-**16a** suitable for X-ray diffraction analysis were grown by slow evaporation of a $CHCl_3$/pentane solution. For the crystallographic data, see Supporting Information. (*sp*,*cis*)-Chloro{1-[(1*R*)-1-(dimethylamino-κN)ethyl]-2-naphthalenyl-κC}{(R_a)-4-[2-(diphenylphosphanyl-κP)-1-naphthalenyl]-2-cyclobutylquinazoline}palladium (R_a,*R*)-(+)-**17a**: A yellow solid; m.p. 227.0–228.0 °C (dec., $CHCl_3$/Et_2O); $[\alpha]_D^{20}$ = +241 (*c* = 0.66, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.92–1.99 (m, 1 H), 2.08 (d, *J* = 6.3 Hz, 3 H), 2.08–2.21 (m, 1 H), 2.26 (s, 3 H), 2.38–2.50 (m, 2 H), 2.53–2.66 (m, 2 H), 2.94 (d, *J* = 3.2 Hz, 3 H), 3.96 (dquint, *J* = 8.4, 0.8 Hz, 1 H), 4.22 (quint, *J* = 6.1 Hz, 1 H), 5.95 (dd, *J* = 8.2, 6.5 Hz, 1 H), 6.64 (d, *J* = 8.6 Hz, 1 H), 6.81 (d, *J* = 8.6 Hz, 1 H), 6.87 (≈ t, *J* = 6.9 Hz, 2 H), 7.11 (t, *J* = 7.2 Hz, 1 H), 7.19 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1 H), 7.22–7.34 (m, 4 H), 7.36 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1 H), 7.43 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1 H), 7.46 (ddd, *J* = 7.9, 6.9, 0.9 Hz, 1 H), 7.59 (dd, *J* = 8.1, 0.9 Hz, 1 H), 7.60–7.65 (m, 2 H), 7.66 (d, *J* = 8.5 Hz, 1 H), 7.69 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1 H), 7.77 (≈ d, *J* = 8.2 Hz, 1 H), 7.86 (d, *J* = 8.2 Hz, 1 H), 7.88–7.93 (m, 2 H), 7.95 (≈ d, *J* = 8.2 Hz, 1 H), and 8.12–8.21 (m, 1 H) ppm. $^{13}C\{^1H\}$/^{13}C DEPT-135 NMR (101 MHz, $CDCl_3$):[30] δ = 18.4 (*C*H_2), 23.4 (*C*H_3), 27.3 (*C*H_2), 27.9 (*C*H_2), 43.4 (*C*H), 48.41 (*C*H), 48.43 (*C*H), 50.59 (*C*H_3), 50.61 (*C*H_3), 72.78 (*C*H_3), 72.81 (*C*H_3), 123.0 (*C*H), 123.81 (*C*H), 123.89 (*C*H), 123.95 (*C*H), 124.02 (*ipso C*), 125.3 (*C*H), 126.0 (*C*H), 126.62 (*C*H), 126.69 (*C*H), 126.73 (*C*H), 127.0 (*C*H), 127.4 (*C*H), 127.8 (*C*H), 127.9 (*C*H), 128.1 (*C*H), 128.4 (*ipso C*), 128.5 (*C*H), 128.8 (*ipso C*), 129.3 (*ipso C*), 129.4 (*C*H), 129.96 (*C*H), 129.99 (*C*H), 130.2 (*ipso C*), 130.3 (*C*H), 130.4 (*C*H), 130.7 (*ipso C*), 131.1 (*ipso C*), 131.4 (*C*H), 131.6 (*C*H), 132.2 (*ipso C*), 132.3 (*ipso C*), 133.2 (*ipso C*), 133.3 (*ipso C*), 133.6 (*C*H), 135.1 (*C*H), 135.2 (*C*H), 135.4 (*C*H), 137.7 (*C*H), 137.9 (*C*H), 148.6 (*ipso C*), 148.69 (*ipso C*), 148.71 (*ipso C*), 150.3 (*ipso C*), 167.78 (*ipso C*), 167.83 (*ipso C*), and 167.9 (*ipso C*) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ = 42.12 (br. s) ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1614, 1522, 1549, 1502, 1491, and 1437 cm^{-1}. HRMS calcd. for $C_{48}H_{43}N_3PPd$ (M – Cl^-) 798.2229, found 798.2216. Phosphane (S_a)-(–)-**5a**:[33] a white foam; $[\alpha]_D^{20}$ = –102 (*c* = 0.71, $CHCl_3$). Phosphane (R_a)-(+)-**5a**:[33] a white foam; $[\alpha]_D^{20}$ +100 (*c* = 0.66, $CHCl_3$).

Optical Resolution of Racemic Phosphane (5b): To a solution of the racemic phosphane **5b** (3.73 g, 6.49 mmol) in CH_2Cl_2 (100 mL) was added the resolving agent (*R*,*R*)-*cis*-**15**·CH_2Cl_2[32] (2.47 g, 3.24 mmol) and the reaction mixture was stirred at room temperature for 28 h. The solvent was evaporated in vacuo to give a yellow foam that was suspended in $CHCl_3$ (22 mL) and brought to reflux. After 10 min, Et_2O (52 mL) was added dropwise over 5 min, and the reflux was continued for an additional 5 min. The resulting yellow suspension was stirred at room temperature for 22 h, the precipitate was filtered, washed with Et_2O/$CHCl_3$ (8:1, 75 mL), and dried to give the Pd^{II} complex (R_a,*R*)-(+)-**17b** a pale yellow solid (SOLID 1, 3.11 g). The mother liquor was evaporated to give the Pd^{II} complex (S_a,*R*)-(–)-**16b** as a yellow solid (SOLID 2, 3.28 g). SOLID 1 (ca. 8 mg) was suspended in CH_2Cl_2 (0.5 mL) and treated

with dppe (4 mg, 10 μmol). The mixture was stirred at room temperature for 2 h and chromatographed directly (silica gel; CH_2Cl_2/pentane, 1:1) to give a small sample of an enantioenriched phosphane (R_a)-(+)-**5b**. The CSP HPLC analysis (Daicel's Chiralcel® OD-H, hexanes/2-propanol, 99.6:0.4; 1 mL min^{-1}; 40 °C; t_{R1} = 10.4 min, t_{R2} = 13.3 min) revealed the sample to be of 97.8% *ee* (Figure S2, Supporting Information). SOLID 2 was analyzed as described for SOLID 1 and the corresponding phosphane (S_a)-(–)-**5b** was shown to be of 98.2% *ee*. The remainder of SOLID 1 was treated with dppe (1.49 g, 3.74 mmol) in CH_2Cl_2 (20 mL) for 1 h. The volatiles were removed in vacuo and the residue was purified by column chromatography (silica gel; pentane/CH_2Cl_2, 4:1→2:1) to give the free phosphane (R_a)-(+)-**5b** (1.72 g, 46%) as a white solid. Similarly, the remainder of SOLID 2 was treated with dppe (1.57 g, 3.94 mmol) in CH_2Cl_2 (20 mL) for 1 h to give, after chromatographic purification, the free phosphane (S_a)-(–)-**5b** (1.67 g, 45%) as a white solid. (*sp*,*cis*)-Chloro{1-[(1*R*)-1-(dimethylamino-κN)ethyl]-2-naphthalenyl-κC}{(R_a)-4-[2-(diphenylphosphanyl-κP)-1-naphthalenyl]-2-(1-adamantyl)quinazoline}palladium (R_a,*R*)-(+)-**17b** (SOLID 1): a yellow solid; m.p. 224.0–225.5 °C (dec., $CHCl_3$/Et_2O); $[\alpha]_D^{20}$ = +215 (*c* = 0.54, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (t, *J* = 3.0 Hz, 6 H), 2.13 (d, *J* = 6.3 Hz, 3 H), 2.12–2.20 (m, 3 H), 2.24 (≈ s, 6 H), 2.46 (s, 3 H), 3.00 (d, *J* = 3.1 Hz, 3 H), 4.28 (quint, *J* = 8.4, 0.8 Hz, 1 H), 6.03 (≈ t, *J* ≈ 7.0 Hz, 1 H), 6.52 (d, *J* = 8.6 Hz, 1 H), 6.71–6.79 (m, 2 H), 6.79 (d, *J* = 8.6 Hz, 1 H), 6.99 (t, *J* = 7.0 Hz, 1 H), 7.14–7.23 (m, 3 H), 7.26–7.33 (m, 3 H), 7.35–7.48 (m, 3 H), 7.58 (d, *J* = 7.9 Hz, 1 H), 7.64–7.74 (m, 3 H), 7.77 (d, *J* = 8.4 Hz, 1 H), 7.84 (d, *J* = 8.1 Hz, 1 H), 7.86–7.94 (m, 2 H), 8.00 (t, *J* ≈ 7.0 Hz, 1 H), and 8.09–8.20 (m, 2 H) ppm. ^{13}C{^{1}H}/^{13}C DEPT 135 NMR (101 MHz, $CDCl_3$):[30] δ = 23.5 (*C*H$_3$), 28.8 (*C*H), 36.9 (*C*H$_2$), 41.24 (*ipso C*), 41.27 (*C*H$_2$), 48.5 (*C*H), 50.80 (*C*H), 50.82 (*C*H), 72.92 (*C*H$_3$), 72.95 (*C*H$_3$), 123.1 (*C*H), 123.9 (*C*H), 124.0 (*ipso C*), 124.1 (*C*H), 124.2 (*C*H), 125.5 (*C*H), 126.0 (*C*H), 126.6 (*C*H), 126.70 (*C*H), 126.73 (*C*H), 126.8 (*C*H), 127.0 (*C*H), 127.5 (*C*H), 127.7 (*C*H), 127.8 (*C*H), 127.93 (*C*H), 127.97 (*C*H), 128.1 (*C*H), 128.6 (*C*H), 128.9 (*C*H), 129.84 (*C*H), 129.87 (*C*H), 130.30 (*C*H), 130.32 (*C*H), 131.1 (*ipso C*), 132.2 (br., *C*H), 132.4 (br., *C*H), 132.5 (*ipso C*), 132.6 (*ipso C*), 133.19 (*C*H), 133.25 (*ipso C*), 133.27 (*ipso C*), 135.1 (*C*H), 135.2 (*C*H), 137.6 (*C*H), 137.8 (*C*H), 148.6 (*ipso C*), 148.86 (*ipso C*), 148.87 (*ipso C*), 150.4 (*ipso C*), 167.21 (*ipso C*), 167.25 (*ipso C*), and 171.2 (*ipso C*) ppm. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ = 42.75 (br. s) ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3020, 2906, 2851, 1547, 1436, and 1305 cm^{-1}. IR (KBr): $\tilde{\nu}_{max}$ = 2900, 1554, 1502, 1489, 1454, and 1435 cm^{-1}. HRMS calcd. for $C_{54}H_{51}N_3PPd$ (M – Cl$^-$) 878.2855, found 878.2820. Crystals of (R_a,*R*)-(+)-**17b** suitable for X-ray diffraction analysis were grown by slow evaporation of a $CHCl_3$/pentane solution. For the crystallographic data, see Supporting Information. (*sp*,*cis*)-Chloro{1-[(1*R*)-1-(dimethylamino-κN)ethyl]-2-naphthalenyl-κC}{(S_a)-4-[2-(diphenylphosphanyl-κP)-1-naphthalenyl]-2-(1-adamantyl)quinazoline}palladium (S_a,*R*)-(–)-**16b** (SOLID 2): a yellow solid; $[\alpha]_D^{20}$ = –130 (*c* = 1.06, $CHCl_3$). ^{1}H NMR (400 MHz, [D$_6$]Me_2CO): δ = 1.68–1.79 (m, 6 H), 1.88 (d, *J* = 6.2 Hz, 3 H), 1.88–2.03 (m, 9 H), 2.43 (br. s, 3 H), 2.87 (s, 3 H), 4.43 (quint, *J* = 6.2 Hz, 1 H), 6.56 (d, *J* = 8.5 Hz, 1 H), 6.66 (br. s, 3 H), 6.82–6.98 (m, 2 H), 7.14–7.33 (m, 6 H), 7.37 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1 H), 7.41–7.54 (m, 4 H), 7.58 (ddd, *J* = 8.1, 7.0, 1.0 Hz, 1 H), 7.59–7.67 (m, 2 H), 7.70 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 2 H), 7.77 (d, *J* = 8.4 Hz, 2 H), 8.05 (d, *J* = 8.2 Hz, 1 H), and 8.08–8.16 (m, 1 H) ppm. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69–1.79 (m, 6 H), 1.85–1.96 (m, 6 H), 1.96–2.06 (m, 6 H), 2.55 (br. s, 3 H), 2.92 (s, 3 H), 4.25 (quint, *J* = 6.1 Hz, 1 H), 6.50–6.70 (br. s, 3 H), 6.59 (d, *J* = 8.6 Hz, 1 H), 6.80 (br. s, 1 H), 6.91 (d, *J* = 8.5 Hz, 1 H), 7.10–7.26 (m, 4 H), 7.28–7.57 (m, 9 H), 7.60 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1 H), 7.62 (d, *J* = 7.4 Hz, 2 H), 7.68 (d, *J* = 8.3 Hz, 1 H), 7.73–7.83 (m, 1 H), 7.95 (d, *J* = 8.1 Hz, 1 H), and 8.11 (br. s, 1 H) ppm. ^{13}C{^{1}H}/^{13}C DEPT-135 NMR (101 MHz, $CDCl_3$):[30] δ = 23.2 (*C*H$_3$), 28.6 (*C*H), 36.7 (*C*H$_2$), 40.8 (*C*H$_2$), 40.9 (*ipso C*), 48.4 (*C*H), 50.63 (*C*H), 50.65 (*C*H), 73.00 (*C*H$_3$), 73.03 (*C*H$_3$), 123.1 (*C*H), 123.4 (*ipso C*), 123.84 (*C*H), 123.87 (*C*H), 123.92 (*C*H), 125.4 (*C*H), 126.1 (sh, *C*H), 126.4 (*C*H), 126.5 (*C*H), 126.8 (*C*H), 127.0 (*ipso C*), 127.38 (*C*H), 127.41 (*ipso C*), 127.5 (*C*H), 127.6 (*C*H), 127.8 (br., *C*H), 127.9 (br., *C*H), 128.0 (*C*H), 128.1 (*C*H), 128.2 (*C*H), 128.37 (*ipso C*), 128.42 (*C*H), 129.19 (*C*H), 129.21 (*C*H), 130.13 (*C*H), 130.15 (*C*H), 130.8 (*ipso C*), 132.57 (*ipso C*), 132.65 (*ipso C*), 132.73 (*C*H), 134.0 (*ipso C*), 135.3 (br., *C*H), 135.4 (br., *C*H), 135.7 (*C*H), 135.8 (*C*H), 136.5 (br., *C*H), 148.73 (*ipso C*), 148.74 (*ipso C*), 149.9 (*ipso C*), 166.49 (*ipso C*), 166.53 (*ipso C*), and 171.1 (*ipso C*) ppm. ^{31}P{^{1}H} NMR (162 MHz, [D$_6$]Me_2CO): δ = 44.44 (br. s) ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2981, 2905, 2851, 1547, 1436, and 1305 cm^{-1}. HRMS calcd. for $C_{54}H_{51}N_3PPd$ (M – Cl$^-$) 878.2855, found 878.2816. Phosphane (S_a)-(–)-**5b**:[34] a white solid; $[\alpha]_D^{20}$ = –84.0 (*c* = 0.87, $CHCl_3$). Phosphane (R_a)-(+)-**5b**:[34] a white solid; $[\alpha]_D^{20}$ = +83.2 (*c* = 0.75, $CHCl_3$). It was attempted to grow crystals of phosphane (S_a)-(–)-**5b** suitable for X-ray diffraction analysis by slow evaporation of a CH_2Cl_2/pentane solution. During the crystallization, phosphane (S_a)-(–)-**5b** underwent oxidation to the corresponding phosphane oxide (S_a)-**5b**-(O). For the crystallographic data of (S_a)-**5b**-(O), see Supporting Information.

Asymmetric Allylic Alkylation (AAA) Studies. General Procedure: See Table 1, entry 1. A solution of [(η^3-C_3H_5)PdCl]$_2$ (1.4 mg, 3.8 μmol, 1.8 mol-%) and ligand (S_a)-(–)-**5a** (4.5 mg, 9.1 μmol, 4.3 mol-%) in CH_2Cl_2 (0.9 mL) was stirred at room temperature for 30 min. The resulting pale yellow solution was added to (±)-(*E*)-1,3-diphenyl-2-propenyl acetate (**19**)[35] (53.7 mg, 0.21 mmol) and stirred for an additional 5 min. Dimethyl malonate (**18**) (51 μL, 0.45 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 111 μL, 0.45 mmol), and a pinch of KOAc (≈ 1 mg) were added. The resulting yellow mixture was stirred at room temperature for 24 h, quenched with satd. NH_4Cl, and extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), and the solvents evaporated in vacuo to give a yellow oil (91 mg). The level of conversion of (±)-(**19**) and the yield of **20** were estimated by ^{1}H NMR (300 MHz, $CDCl_3$) analysis. Alternatively, purification by flash chromatography (silica gel; hexane/EtOAc, 9:1) gave the title compound **20** (67 mg, 97%) as a clear oil: R_f = 0.25 (hexane/EtOAc, 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.49 (s, 3 H), 3.68 (s, 3 H), 3.93 (d, *J* = 10.9 Hz, 1 H), 4.24 (dd, *J* = 10.9, 8.3 Hz, 1 H), 6.30 (dd, *J* = 15.7, 8.3 Hz, 1 H), 6.45 (d, *J* = 15.8 Hz, 1 H), and 7.15–7.33 (m, 10 H). Its enantiomeric composition (89.2% *ee*) was established by CSP HPLC [Figure S3; Daicel's Chiralpak® AD, 4.6 mm × 25 cm; hexanes/2-propanol, 95:5; 1.0 mL min^{-1}; 10 °C; 250 nm; t_{R1} = 16.1 min for (*R*)-**20** and t_{R2} = 24.2 min for (*S*)-**20**], and its optical rotation was compared with the literature data[36] to assign the absolute configuration of the major (dextrorotatory) enantiomer as *R*.

General Procedure for Metalation of Phosphane (±)-(5a): A solution of *i*Pr$_2$NH (63 μL, 0.45 mmol) and KO*t*Bu (50 mg, 0.45 mmol) in THF (5 mL) was cooled to –78 °C. BuLi (2.5 M in hexanes, 180 μL, 0.45 mmol) was added dropwise, and the resulting yellow solution was warmed to –50 °C over 35 min. A solution of phosphane (±)-(**5a**) (149 mg, 0.30 mmol) in THF (2 mL) was added dropwise, and the mixture was stirred between –50 and –40 °C for 1 h to give a dark blue solution. The reaction mixture was re-cooled to –78 °C, treated with an appropriate electrophile (3–30 equiv.), and stirred at a specified temperature for a specified period of time. After hy-

drolysis with H_2O (3 mL), the reaction mixture was warmed to room temperature, and then extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and the solvents evaporated in vacuo. Purification by flash chromatography furnished the desired product.

Deuterium Incorporation into Phosphane (±)-(5a): Preparation of (±)-2-(1-Deuteriocyclobutyl)-4-(2-diphenylphosphanylnaphthalen-1-yl)quinazoline (21a): Phosphane (±)-(**5a**) (149 mg, 0.30 mmol) was metalated as described in the general procedure and treated with D_2O (99.9% D, 540 μL, 30 mmol). The reaction mixture was then stirred at –78 °C for 10 min. The standard workup provided a crude product as a pale yellow oil. Purification by chromatography (silica gel; hexanes/EtOAc, 10:1) gave the title compound **21a** (145 mg, 97%, 98% D) as a clear oil: R_f = 0.35 (hexane/EtOAc, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64–1.82 (m, 1 H), 1.88–2.02 (m, 1 H), 2.16–2.40 (m, 4 H), 3.88 (quint, J = 8.8 Hz, 0.02 H), 7.09 (d, J = 8.5 Hz, 1 H), 7.12–7.18 (m, 2 H), 7.13–7.33 (m, 11 H), 7.37 (dd, J = 8.5, 3.2 Hz, 1 H), 7.47 (dd, J = 8.1, 6.8 Hz, 1 H), 7.78 (dd, J = 8.4, 6.6 Hz, 1 H), 7.88 (d, J = 8.2 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), and 8.07 (d, J = 8.5 Hz, 1 H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$):[30,37] δ = 18.3, 27.0, 27.2, 27.3, 27.5, 42.9 (t, J = 20.7 Hz), 43.3, 123.5, 123.6, 126.2, 126.3, 126.6, 126.7, 126.9, 127.0, 128.0, 128.19, 128.24, 128.26, 128.27, 128.34, 128.5, 129.1, 130.00, 130.01, 131.8, 131.9, 133.3, 133.4, 133.5, 133.6, 134.3, 134.5, 136.5, 136.6, 137.3, 137.4, 142.0, 142.4, 150.4, 168.7, 169.16, and 169.22 ppm. ^{31}P{^{1}H} NMR (101 MHz, $CDCl_3$): δ = –13.5 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1615, 1569, 1548, 1491, 1435, and 1334 cm^{-1}. HRMS calcd. for $C_{34}H_{27}DN_2P$ [MH$^+$] 496.2053, found 496.2037.

1-{4-[2-(Diphenylphosphanyl)naphthalen-1-yl]quinazolin-2-yl}cyclobutanecarbaldehyde (21b): Phosphane (±)-(**5a**) (149 mg, 0.30 mmol) was metalated as described in the general procedure and treated with ethyl formate (72 μL, 0.90 mmol). The reaction mixture was stirred at –78 °C for 30 min. The standard workup provided a crude product as a yellow oil. Purification by flash chromatography (silica gel; hexanes/EtOAc, 10:1 → 5:1) gave the title compound **21b** (145 mg, 92%) as a white foam: R_f = 0.35 (hexane/EtOAc, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62–1.87 (m, 2 H), 2.28–2.50 (m, 4 H), 6.93–7.34 (m, 15 H), 7.41 (≈ t, J = 7.5 Hz, 1 H), 7.58–7.84 (m, 3 H), 8.01 (dd, J = 8.4, 0.4 Hz, 1 H), and 9.73 (s 1 H) ppm. ^{13}C{^{1}H}/^{13}C DEPT-135 NMR (101 MHz, $CDCl_3$):[30] δ = 15.4 (*C*H$_2$), 27.2 (*C*H$_2$), 27.7 (*C*H$_2$), 59.5 (*ipso C*), 123.61 (*ipso C*), 123.63 (*ipso C*), 126.04 (*C*H), 126.06 (*C*H), 126.8 (*C*H), 127.0 (*C*H), 127.1 (*C*H), 127.4 (*C*H), 128.1 (*C*H), 128.2 (*C*H), 128.31 (*C*H), 128.34 (*C*H), 128.35 (*C*H), 128.41 (*C*H), 128.6 (*C*H), 129.3 (*C*H), 129.98 (*C*H), 129.98 (*C*H), 131.7 (*ipso C*), 131.8 (*ipso C*), 133.1 (*C*H), 133.3 (*C*H), 133.37 (*ipso C*), 133.43 (*C*H), 133.6 (*C*H), 133.9 (*C*H), 134.2 (*ipso C*), 134.3 (*ipso C*), 136.3 (*ipso C*), 136.4 (*ipso C*), 137.0 (*ipso C*), 137.2 (*ipso C*), 141.6 (*ipso C*), 141.9 (*ipso C*), 150.4 (*ipso C*), 165.4 (*ipso C*), 169.7 (*ipso C*), 169.8 (*ipso C*), 200.3 (*ipso C*) ppm. ^{31}P{^{1}H} NMR (101 MHz, $CDCl_3$): δ = –13.5 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1717, 1615, 1548, 1490, 1435, and 1335 cm^{-1}. HRMS calcd. for $C_{35}H_{28}N_2OP$ [MH$^+$] 523.1939, found 523.1919.

Methyl 1-{4-[2-(Diphenylphosphanyl)naphthalen-1-yl]quinazolin-2-yl}cyclobutanecarboxylate (21c): Phosphane (±)-(**5a**) (149 mg, 0.30 mmol) was metalated as described in the general procedure and treated with dimethyl carbonate (76 μL, 0.90 mmol). The reaction mixture was stirred at –45 °C for 3 h and then warmed to room temperature. The standard workup provided a crude product as a yellow oil. Purification by flash chromatography (silica gel; hexanes/EtOAc, 10:1 → 5:1) gave the title compound **21c** (105 mg, 63%) as a clear oil: R_f = 0.30 (hexane/EtOAc, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81–1.92 (m, 1 H), 1.98–2.09 (m, 1 H), 2.55–2.71 (m, 2 H), 2.73–2.88 (m, 2 H), 3.61 (s, 3 H), 7.12 (d, J = 8.4 Hz, 1 H), 7.17–7.37 (m, 13 H), 7.40 (dd, J = 8.5, 3.1 Hz, 1 H), 7.53 (ddd, J = 8.2, 6.9, 1.0 Hz, 1 H), 7.86 (ddd, J = 8.4, 5.8, 2.5 Hz, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 7.94 (d, J = 8.5 Hz, 1 H), and 8.15 (d, J = 8.5 Hz, 1 H) ppm. ^{13}C{^{1}H}/^{13}C DEPT-135 NMR (101 MHz, $CDCl_3$):[30] δ = 16.2 (*C*H$_2$), 30.38 (*C*H$_2$), 30.4 (*C*H$_2$), 52.1 (*C*H$_3$), 55.5 (*ipso C*), 123.68 (*ipso C*), 123.71 (*ipso C*), 126.21 (*C*H), 126.23 (*C*H), 126.7 (*C*H), 126.8 (*C*H), 127.0 (*C*H), 127.1 (*C*H), 128.06 (*C*H), 128.12 (*ipso C*), 128.19 (*C*H), 128.21 (*C*H), 128.28 (*C*H), 128.33 (*C*H), 128.4 (*C*H), 128.6 (*C*H), 128.8 (*C*H), 129.2 (*C*H), 129.99 (*C*H), 130.00 (*C*H), 131.9 (*ipso C*), 132.0 (*ipso C*), 133.0 (*C*H), 133.2 (*C*H), 133.5 (*C*H), 133.6 (*C*H), 133.7 (*C*H), 133.8 (*ipso C*), 134.1 (*ipso C*), 134.3 (*ipso C*), 136.6 (*ipso C*), 136.7 (*ipso C*), 137.2 (*ipso C*), 137.3 (*ipso C*), 142.0 (*ipso C*), 142.3 (*ipso C*), 150.2 (*ipso C*), 166.3 (*ipso C*), 169.6 (*ipso C*), 169.7 (*ipso C*), and 175.2 (*ipso C*) ppm. ^{31}P{^{1}H} NMR (101 MHz, $CDCl_3$): δ = –13.9 ppm. IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1731, 1552, 1435, 1334, and 1280 cm^{-1}. HRMS calcd. for $C_{36}H_{30}N_2O_2P$ [MH$^+$] 553.2045, found 553.2018.

Phenyl(1-{4-[2-(Diphenylphosphanyl)naphthalen-1-yl]quinazolin-2-yl}-cyclobutyl)methanol (21d): Phosphane (±)-(**5a**) (149 mg, 0.30 mmol) was metalated as described in the general procedure and treated with benzaldehyde (91 μL, 0.90 mmol). The reaction mixture was stirred at –78 °C for 1 h. The standard workup provided a crude product as a yellow oil. Purification by flash chromatography (silica gel; hexanes/EtOAc, 10:1 → 5:1) gave the title compound **21d** (173 mg, 96%)[38] as a white foam: R_f = 0.25 (hexane/EtOAc, 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.59–1.83 (m, 0.9 H, *minor* 2 H), 1.83–1.98 (m, 1.2 H, *major* 2 H), 1.98–2.11 (m, 0.6 H, *major* 1 H), 2.15–2.26 (m, 0.4 H, *minor* 1 H), 2.30–2.40 (m, 0.6 H, *major* 1 H), 2.40–2.50 (m, 1.0 H, *major* 1 H and *minor* 1 H), 2.65–21.83 (m, 0.7 H, *minor* 2 H), 3.10–3.22 (m, 0.5 H, *major* 1 H), 5.15 (br. d, J ≈ 5.5 Hz, 0.6 H, *major* 1 H), 5.19 (br. s, 0.4 H, *minor* 1 H), 5.79 (br. d, J ≈ 5.5 Hz, 0.6 H, *major* 1 H), 5.91 (br. s, 0.4 H, *minor* 1 H), 6.90 (≈ d, J = 8.4 Hz, 1 H), 7.10–7.45 (m, 19 H), 7.51–7.61 (m, 1 H), 7.81–7.90 (m, 1 H), 7.92–8.03 (m, 3 H), and 8.05–8.14 (m, 1 H) ppm. ^{13}C{^{1}H}/^{13}C DEPT-135 NMR (101 MHz, $CDCl_3$):[30] δ = 15.30 (*C*H$_2$), 15.34 (*C*H$_2$), 27.1 (*C*H$_2$), 27.6 (*C*H$_2$), 31.4 (*C*H$_2$), 31.9 (*C*H$_2$), 53.06 (*ipso C*), 53.12 (*ipso C*), 79.3 (*C*H), 79.4 (*C*H), 126.05 (*C*H), 126.07 (*C*H), 126.07 (*C*H), 126.6 (*C*H), 126.7 (*C*H), 126.8 (*C*H), 126.91 (*C*H), 126.96 (*C*H), 127.03 (*C*H), 127.05 (*C*H), 127.11 (*C*H), 127.13 (*C*H), 127.5 (*C*H), 127.6 (*C*H), 128.0 (*C*H), 128.17 (*C*H), 128.27 (*C*H), 128.30 (*C*H), 128.31 (*C*H), 128.34 (*C*H), 128.36 (*C*H), 128.40 (*C*H), 128.41 (*C*H), 128.42 (*C*H), 128.46 (*C*H), 128.60 (*C*H), 128.64 (*C*H), 128.66 (*C*H), 129.2 (*C*H), 129.4 (*C*H), 129.86 (*C*H), 129.86 (*C*H), 129.90 (*C*H), 129.91 (*C*H), 131.56 (*ipso C*), 131.64 (*ipso C*), 131.74 (*ipso C*), 131.82 (*ipso C*), 132.94 (*C*H), 133.00 (*C*H), 133.1 (*C*H), 133.2 (*C*H), 133.38 (*ipso C*), 133.42 (*C*H), 133.5 (*C*H), 133.6 (*C*H), 133.7 (*C*H), 133.89 (*C*H), 133.92 (*C*H), 133.94 (*C*H), 134.03 (*ipso C*), 134.06 (*ipso C*), 134.2 (*ipso C*), 136.1 (*ipso C*), 136.2 (*ipso C*), 136.4 (*ipso C*), 136.5 (*ipso C*), 136.8 (*ipso C*), 136.9 (*ipso C*), 137.1 (*ipso C*), 137.2 (*ipso C*), 141.4 (*ipso C*), 141.67 (*ipso C*), 141.68 (*ipso C*), 142.0 (*ipso C*), 142.1 (*ipso C*), 142.5 (*ipso C*), 149.7 (*ipso C*), 149.9 (*ipso C*), 168.56 (*ipso C*), 168.58 (*ipso C*), 168.62 (*ipso C*), 169.0 (*ipso C*), 169.1 (*ipso C*), and 169.3 (*ipso C*) ppm. ^{31}P{^{1}H} NMR (101 MHz, $CDCl_3$): δ = –14.2 and –13.9 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = ν_{max} 3352 (br), 1558, 1491, 1435, (and 1335) cm^{-1}. HRMS calcd. for $C_{41}H_{34}N_2OP$ [MH$^+$] 601.2409, found 601.2394.

Supporting Information (see also the footnote on the first page of this article): CSP HPLC profiles for **5a**,**b**, ^{1}H/^{13}C/^{31}P NMR spectra

for all new compounds, and additional views of X-ray single-crystal structures of (±)-**5a/5a**-(O), and (S_a)-**5b**-(O), (S_a,*R*)-(–)-**16a**, and (R_a,*R*)-(+)-**17b**.

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