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The preparation and resolution of 2-(2-pyridyl)- and 2-(2-pyrazinyl)-Quinazolinap and their application in palladium-catalysed allylic substitution

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Abstract—The preparation and resolution of two new axially chiral quinazoline-containing phosphinamine ligands, 2-(2-pyridyl)-Quinazolinap and 2-(2-pyrazinyl)-Quinazolinap, is described. The ligands were synthesised in good yield over eight steps and included two Pd-catalysed reactions, a Suzuki coupling to form the biaryl linkage and the introduction of the diphenylphosphino group, as the key transformations. The racemic ligands were resolved via the fractional crystallisation of diastereomeric palladacycles derived from (+)-di-μ-chlorobis{(*R*)-dimethyl[1-(1-naphthyl)ethyl]aminato-C_2,N}dipalladium (II) X-ray crystal structures of the (*S*,*R*)-2-pyridyl- and (*S*,*R*)-2-pyrazinyl-palladacycles are included. Displacement of the resolving agent by reaction with 1,2-bis(diphenylphosphino)ethane gave enantiopure 2-(2-pyridyl)-Quinazolinap and 2-(2-pyrazinyl)-Quinazolinap, new atropisomeric phosphinamine ligands for asymmetric catalysis. These ligands were applied in the palladium-catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate resulting in moderate conversions and enantioselectivities of up to 81%.

1. Introduction

To date, atropisomeric ligands have been applied in a wide range of transition metal catalysed asymmetric transformations.[1] One of the most successful and widely applicable of these ligands is Noyori's diphosphine BINAP.[2] The principle of inducing enantioselectivity through the influence of electronic as well as steric factors led to the design of axially chiral heterobidentate ligands such as Brown's Quinap (**1**), the first example of this class successfully applied in asymmetric catalysis.[3] During solid state and solution ^{1}H NMR investigations into the mechanism of allylic substitution catalysed by Pd–Quinap complexes, it had been determined that the 3H of the isoquinoline unit occupies a position of crucial steric influence over ligand–reactant interactions and hence over the stereochemical outcome of the reaction.[4] This led to the preparation of the vaulted analogue Phenap, also developed by Brown, which was applied in the rhodium-catalysed hydroboration of olefins and palladium-catalysed allylic alkylation resulting in enantioselectivities of up to 84 and 95%, respectively.[5,6]

Within our research group, attention has focused on the development of a new class of atropisomeric ligands with a quinazoline unit incorporated into the biaryl framework. We call this ligand series 'Quinazolinaps' and their preparation involves a synthetic route similar to that of Quinap and Phenap. The first of these synthesised and resolved was 2-phenyl-Quinazolinap (**2a**), which was successfully applied in Pd-catalysed allylic substitution providing good conversions but moderate enantioselectivities.[7,8] Following on from the aforementioned mechanistic insight into allylic substitution provided by Brown's study, we were prompted to vary the size of the substituent at the corresponding 2-position of the quinazoline moiety and hence the series of ligands **2b–f** were prepared and resolved.[9] Improved conversions and enantioselectivities up to 91% were obtained in the Pd-catalysed allylic alkylation of 1,3-diphenyl-propenyl acetate[10] and dimethyl malonate and up to 99% in the Rh-catalysed hydroboration of vinylarenes.[9]

Due to the success of this ligand series we wished to examine the effect of altering the electronic nature of the 2-substituent. Herein we report the extension of the Quinazolinap ligand class to include the 2-(2-pyridyl)- and 2-(2-pyrazinyl)-variants (**3a–b**). It was intended that the presence of the nitrogen atom(s) of the pyridyl and

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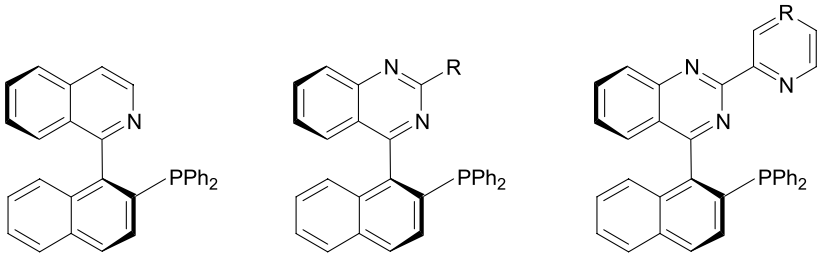
pyrazinyl rings would alter the basicity of the donor nitrogen of the quinazoline unit. There is also the added possibility of hemi-labile coordination of the extra nitrogen atom (**3** vs **2**) with potentially beneficial effects in transition metal catalysed asymmetric transformations.



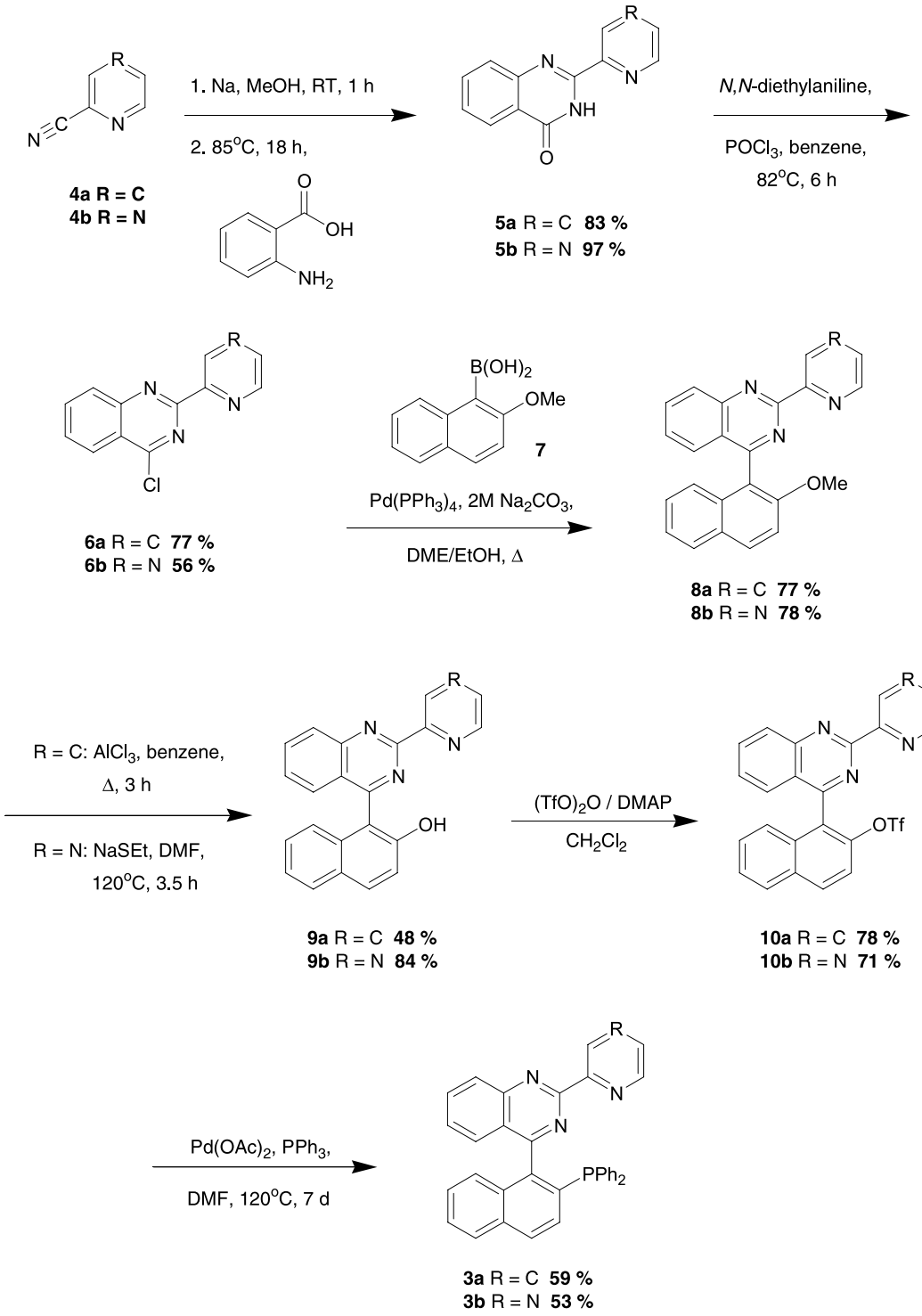
1 **2a,** R = Ph; **2b**, R = Me; **2c**, R = ^{i}Pr; **2d**, R = ^{t}Bu; **2e**, R = H; **2f**, R = Bn. **3a,** R = C **3b,** R = N

2. Ligand preparation

The synthetic approach chosen to prepare ligands **3a–b** is analogous to that used to obtain Quinazolinaps **2a–f**. The two key steps in the synthesis are the Pd-catalysed reactions to effect the biaryl coupling, and the formation of the naphthyl–phosphorus bond. The introduction of the phosphine in the final step is preferred as it allows facile handling of the intermediate compounds. The coupling partners of the palladium catalysed Suzuki reaction were the appropriate 4-chloroquinazoline (**6a–b**) and 2-methoxy-1-naphthylboronic acid (**7**), Scheme 1. The boronic acid was easily prepared from 1-bromo-2-methoxynaphthalene via a Grignard reaction, while the 4-chloroquinazolines were derived from the corresponding 2-substituted 4(3*H*)-quinazolinones (**5a–b**). These quinazolinones were readily obtained in yields of 83 and 97%, respectively, using a highly versatile methodology developed within our research group involving a sodium methoxide-mediated cyclisation between anthranilic acid and the appropriately substituted nitrile (**4a–b**).[11] The Suzuki coupling was catalysed by 3 mol% of tetrakis(triphenylphosphine)palladium (0) in dimethoxyethane at reflux in the presence of 2 M aqueous sodium carbonate and gave the methyl ethers (**8a–b**) as white solids in good yield (77 and 78%) after column chromatography. In order to introduce the diphenylphosphino group, it is first necessary to convert the methoxy group to a trifluoromethanesulfonate. For the earlier ligands of the Quinazolinap series, treatment with boron tribromide in dichloromethane provided the desired naphthol in all cases in high yields. However, the presence of the extra nitrogen atom(s) of the 2-pyridyl and 2-pyrazinyl analogues altered the process sufficiently that none of the required naphthol was obtained when boron tribromide was employed. The problem was solved through the use of aluminium chloride for the demethylation of 2-(2-pyridyl)-4-(2-methoxynaphthalen-1-yl)-quinazoline,[12] whereas heating at 120 °C with sodium ethanethiolate in dimethyl formamide removed the methyl group of the pyrazinyl analogue.[13] Both naphthols (**9a–b**) were then converted to their trifluoromethanesulfonate analogues (**10a–b**) by reaction with trifluoromethanesulfonic anhydride in the presence of 4-dimethylaminopyridine. The trifluoromethanesulfonates were formed in good yield (71–78%) although a longer reaction time of 48 h was necessary in the case of the 2-pyrazinyl variant. The Ni-catalysed process developed by Cai et al. had been successfully employed for the incorporation of the diphenylphosphino group into Quinazolinaps (**2a–f**) but it proved unsuitable for the transformation of the 2-pyridyl and 2-pyrazinyl triflates with a substantial amount of unreacted triflate remaining after 6 days at reflux.[14] Conversion of **10a** to the aryldiphenylphosphine oxide followed by subsequent reduction using trichlorosilane and triethylamine also resulted in low yields.[15] Direct formation of the desired products was achieved through the use of palladium acetate as catalyst and triphenylphosphine as the phosphinylating agent in dimethyl formamide, as reported by Chan and co-workers.[16] Thus 2-(2-pyridyl)-Quinazolinap (**3a**) and 2-(2-pyrazinyl)-Quinazolinap (**3b**) were obtained in racemic form over eight steps in good yields.

3. Ligand resolution

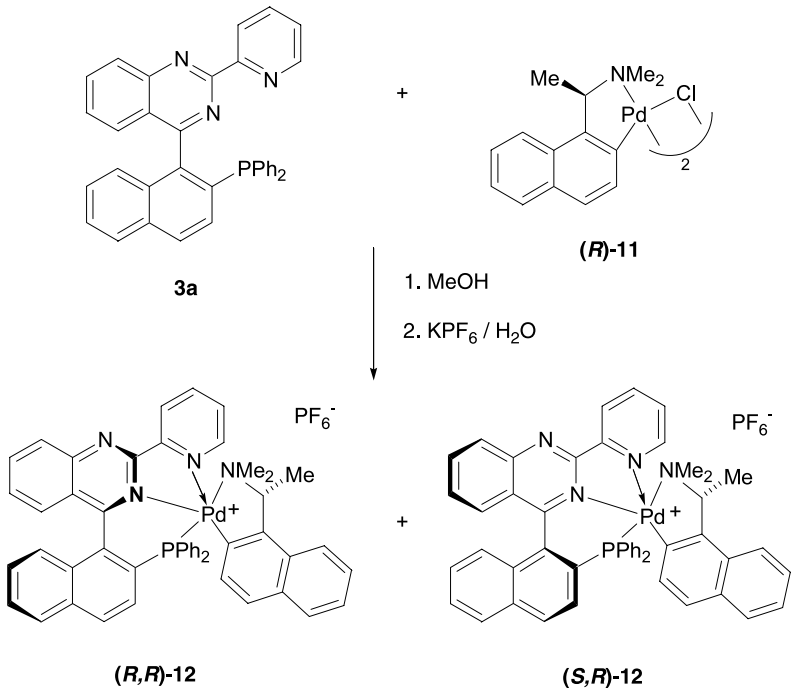
The resolution of many racemic phosphorus-containing ligand systems has been accomplished by the formation of diastereomeric complexes with enantiopure palladium amine complexes, followed by fractional crystallisation to obtain diastereomerically pure material.[17] As the *ortho*-palladated derivative of (*R*)-dimethyl[1-(1-naphthyl)ethyl] amine (**11**) had been successfully employed as the resolving agent for the resolution of Quinap and the earlier members of the Quinazolinap series, it was also applied in the attempts to resolve 2-(2-pyridyl)- and 2-(2-pyrazinyl)-Quinazolinap. Therefore, 2-(2-pyridyl)-Quinazolinap (**3a**) and (+)-di-μ-chlorobis{(*R*)-dimethyl[1-(1-naphthyl)ethyl] aminato-C_2,N}dipalladium (II) (**11**) were stirred in a 2:1 ratio in methanol for 18 h at room temperature, Scheme 2. An aqueous solution of KPF_6 was added to precipitate a yellow solid, which was shown by ^{1}H NMR to consist of a 2:1 mixture of diastereomers. The benzylic methines appeared as quintets, at 4.10 ppm for the major diastereomer and at 4.46 ppm for the minor. In the ^{31}P NMR spectrum the resonances associated with the two species appear at 27.61 and 22.16 ppm, respectively. A range of solvent systems was investigated to separate the diastereomeric pair before a mixture of hot butanone and diethyl ether proved successful. The precipitate that had formed was found to be a mixture of the two diastereomers but the mother liquor was proven to contain only the major one with a single peak in the ^{31}P



Scheme 1.

NMR at 27.61 ppm. A sample of this diastereomer was recrystallised from a dichloromethane–diethyl ether mixture to obtain crystals suitable for X-ray analysis. The crystal structure indicated that the (*S*,*R*)-diastereomer had been isolated, Figure 1. It also shows that, interestingly, the Pd atom adopts an almost ideal trigonal-bipyramidal coordination geometry in which the equatorial ligand and the metal are almost coplanar (rms deviation 0.04 Å).

Resolution of 2-(2-pyrazinyl)-Quinazolinap (**3b**) followed a similar approach, Scheme 3, although the mixture containing the ligand and resolving agent had to be stirred at 60 °C for 18 h to ensure complete complexation. By this time a pale yellow precipitate had formed and was removed by filtration. ^{1}H NMR spectroscopy confirmed the presence of a single diastereomer with the benzylic methine quintet at 4.11 ppm and only one peak appeared in the ^{31}P NMR at 39.50 ppm. The filtrate was found to contain both diastereomers but attempts to separate the two failed and so the residue was re-dissolved in methanol and the counter-ion



Scheme 2.

changed to PF_6^-. Both diastereomers were apparent in the ^1H NMR spectrum, this time in a 1:1 ratio with the benzylic methine quintets appearing at 4.37 and 4.12 ppm and the phosphorus resonances at 28.97 and 24.50 ppm. Again, isolation of diastereomerically pure material was effected by fractional crystallisation from hot butanone–diethyl ether and crystals for X-ray analysis were obtained through recystallisation from chloroform–diethyl ether. The X-ray structure showed this to be the (*S*,*R*)-2-(2-pyrazinyl) diastereomer, which adopts a similar trigonal–bipyramidal geometry as had been found for the (*S*,*R*)-2-(2-pyridyl) diastereomer, Figure 2. The geometries of the two palladium cations in both crystal structures are markedly similar in spite of their different crystal environments. The most significant difference between the two structures is a shortening of the Pd–N3 bond by 0.062(4) Å and an

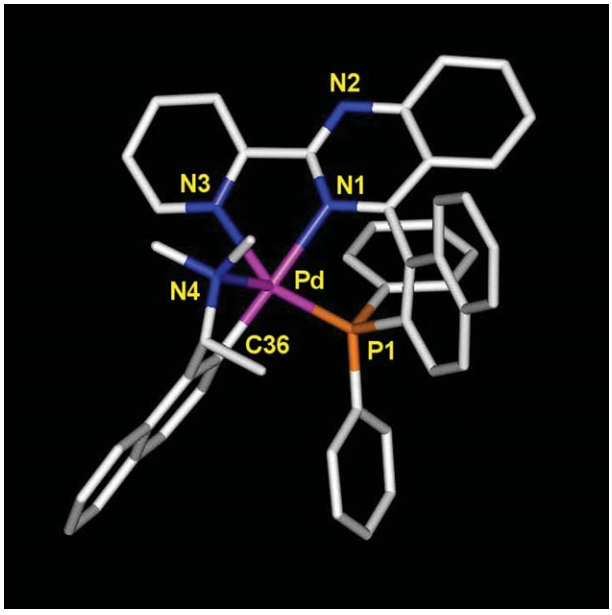


Figure 1. Structure of the cation in (*S*,*R*)-**12**·1.5(CH_2Cl_2), showing the approximate trigonal–bipyramidal coordination geometry of the Pd atom. Selected distances (Å) and angles (°): Pd–P1 2.223(1), Pd–N1 2.182(3), Pd–N3 2.408(3), Pd–N4 2.216(3), Pd–C36 1.982(3), P1–Pd–N1 83.7(1), P1–Pd–N3 120.7(1), P1–Pd–N4 145.8(1), P1–Pd–C36 96.2(1), N1–Pd–N3 72.9(1), N1–Pd–N4 102.5(1), N1–Pd–C36 176.2(1), N3–Pd–N4 93.0(1), N3–Pd–C36 104.1(1), N4–Pd–C36 79.8(1).

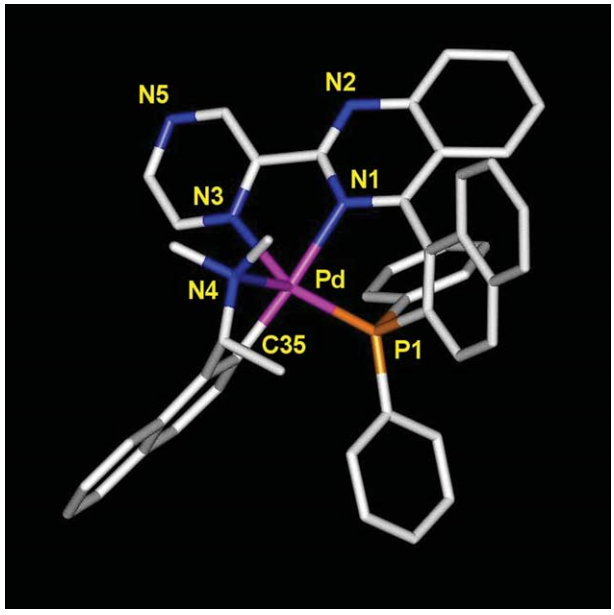
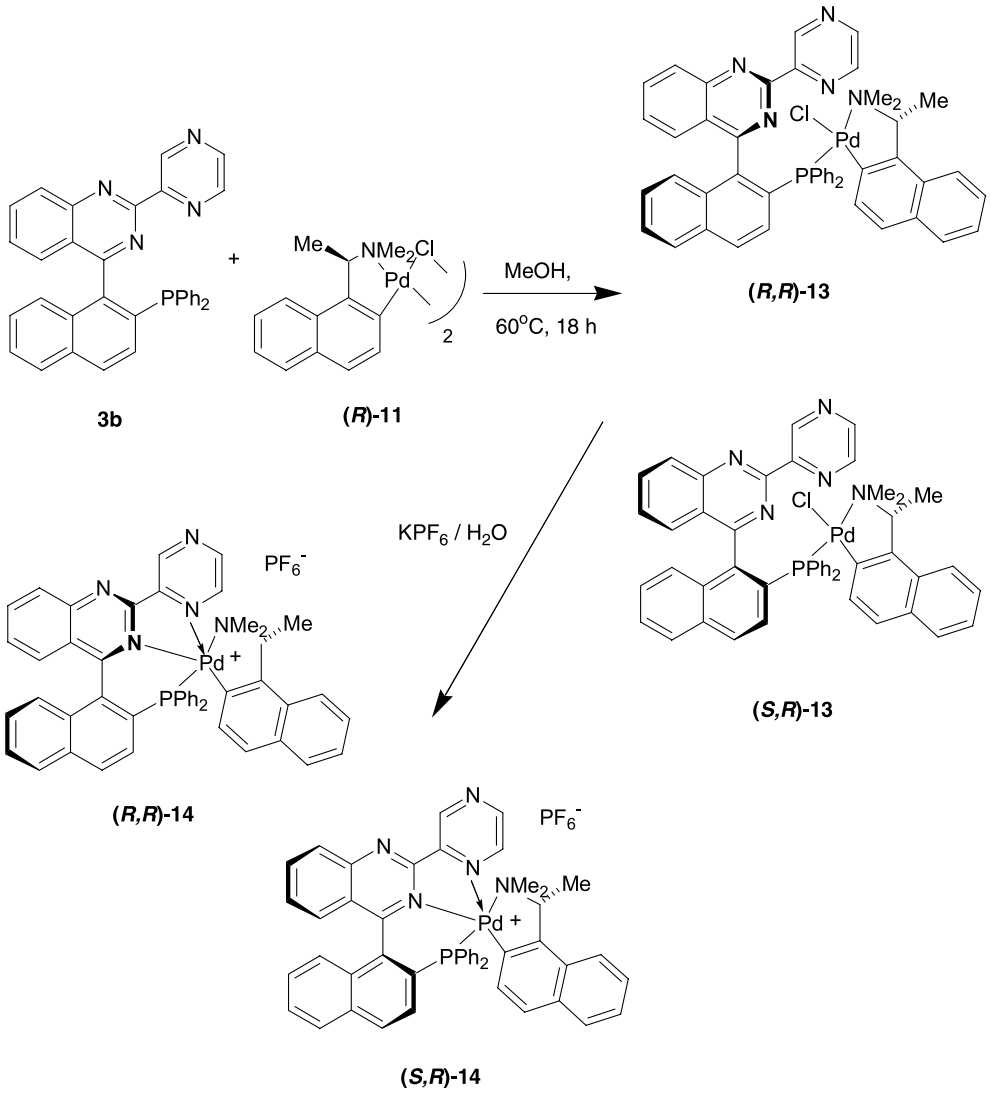


Figure 2. Structure of the cation in (*S*,*R*)-**14**·$C_4H_{10}O$, with the (*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato ligand in the same orientation as for Figure 1. Selected distances (Å) angles (°): Pd–P1 2.2211(4), Pd–N1 2.185(1), Pd–N3 2.346(2), Pd–N4 2.245(2), Pd–C35 1.981(2), P1–Pd–N1 85.06(4), P1–Pd–N3 124.49(4), P1–Pd–N4 139.66(4), P1–Pd–C35 97.5(1), N1–Pd–N3 74.3(1), N1–Pd–N4 102.7(1), N1–Pd–C35 173.3(1), N3–Pd–N4 95.5(1), N3–Pd–C35 99.2(1), N4–Pd–C35 79.4(1).



Scheme 3.

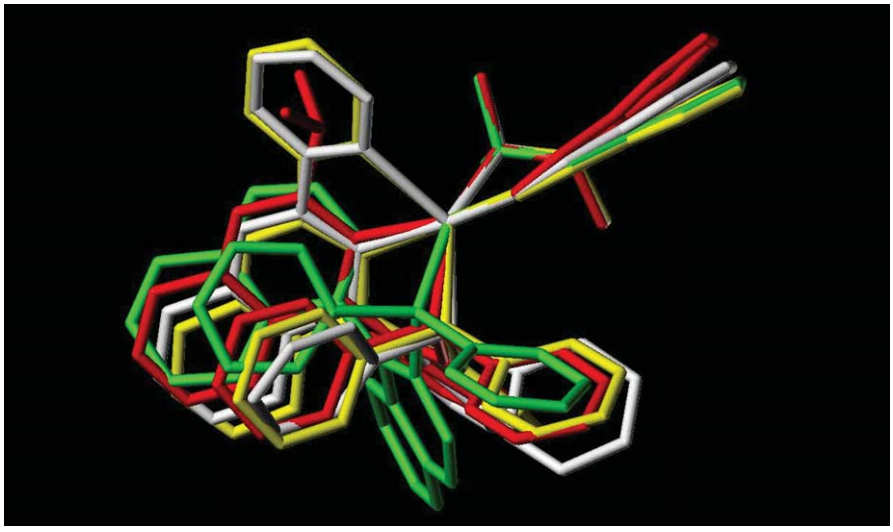


Figure 3. Structures of the palladium cations of variously substituted 2-Quinazolinaps (H=green; isopropyl=red; pyridyl=yellow; pyrazinyl=white) with the (*R*)-dimethyl[1-(1-naphthyl)ethyl]aminato ligand in the same orientation as for Figures 1 and 2.

Table 1. A comparison of the geometries of cationic substituted (*S*,*R*)-Quinazolinap Pd complexes

Quinazolinap ligand								
Ligand	R	P1–Pd–N1 angle (deg)	N1–Pd–N3 angle (deg)	Plane (naphthyl)/ plane (quinazolinyl) dihedral angle (deg)	Plane (quinazolinyl)/ plane (pyr/pyraz) dihedral angle (deg)	Pd–P1 distance (Å)	Pd–N1 distance (Å)	Pd–N3 distance (Å)
2a[a]	H	84.7(1)	—	112(2)	—	2.256(2)	2.189(5)	—
2b[a]	Me	82.34(6)	—	119(1)	—	2.2423(5)	2.187(2)	—
2e[a]	^{i}Pr	84.6(2)	—	113(2)	—	2.238(2)	2.192(5)	—
3a[b]	Pyr	83.7(1)	72.9(1)	115(1)	159(1)	2.223(1)	2.182(3)	2.408(3)
3b[b]	Pyraz	85.06(4)	74.3(1)	118(1)	154(1)	2.2211(4)	2.185(1)	2.346(2)

Aminato ligand				Inter-ligand geometry		
C[c]–Pd–N4 angle (deg)	Pd–N3[a]/N4[b] distance (Å)	Pd–C[c] distance (Å)	Trans-N1-Pd-C[c] angle (deg)	N3[b]–Pd–N4[b] angle (deg)	P1–Pd–N3[a]/N4[b] angle (deg)	Plane(P1,Pd,N1)/plane (N3[a]/N4[b],Pd,C[c]) dihedral angle (deg)
80.4(2)	2.132(5)	2.002(6)	171.2(2)	—	165.9(2)	17(2)
80.2(1)	2.147(2)	1.978(3)	171.0(1)	—	155.3(1)	28(1)
80.9(2)	2.164(6)	1.993(6)	166.7(2)	—	152.9(2)	32(2)
79.8(1)	2.216(3)	1.982(3)	176.2(1)	93.0(1)	145.8(1)	35(1)
79.4(1)	2.245(2)	1.981(2)	173.3(1)	95.5(1)	139.7(1)	42(1)

[a] Ref. 9.
[b] This publication.
[c] Carbon atom attached to Pd.

associated increase in the N3–Pd–N4 angle of 2.5(2)° on substitution of the 2-pyridyl group by the 2-pyrazinyl group on the Quinazolinap ligand. Since both the pyridyl and pyrazinyl groups are sterically similar, the difference is presumably due to the increased electron donor ability of the pyrazinyl substituent compared with the pyridyl group.

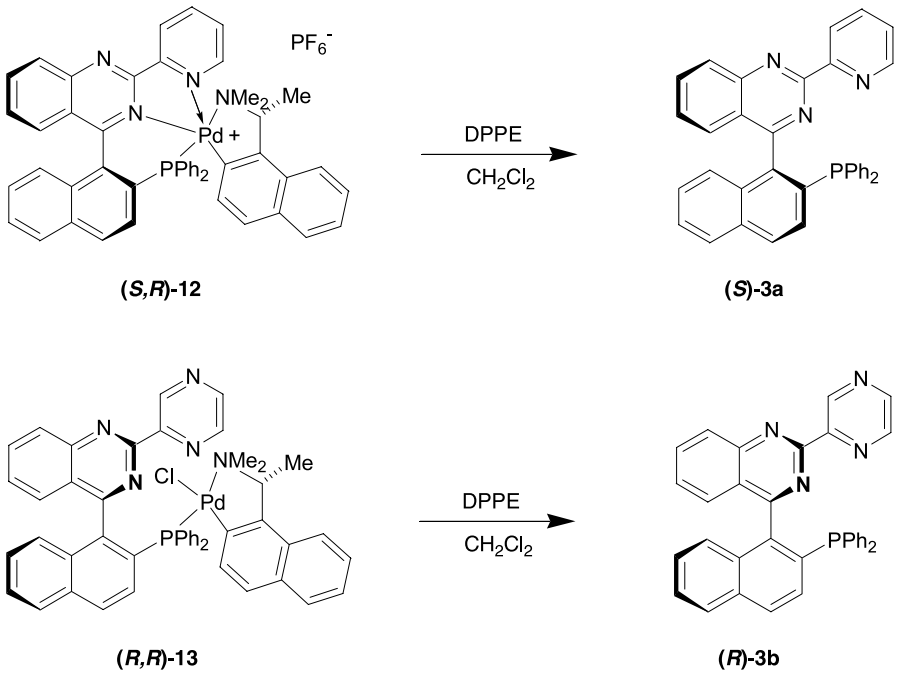
If one compares the structures of various 2-substituted Quinazolinap Pd cations containing the same (*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato ligand, there is a clear rearrangement of the ligands with respect to one another depending on the nature of the 2-substituent, Figure 3. Thus, in going from H→Me→isopropyl→2-pyridyl→2-pyrazinyl, the P1–Pd–N angle between the P atom of the Quinazolinap ligand and the N atom of the amidato ligand decreases steadily from 166 to 140° whereas the dihedral angle between the planes defined by P1, Pd and N1 of the Quinazolinap ligand and N, Pd and C of the amidato ligand increases by 25° (Table 1). Although the most significant change takes place in the equatorial plane of the metal, increase in steric bulk of the ligand along the series is likely to be the most dominant cause, though donor ability of the substituent must be a contributing factor since steric bulk alone does not explain the difference resulting from substitution of the 2-pyridyl substituent by the more electron-donating 2-pyrazinyl group.

Enantiomerically pure 2-(2-pyridyl)- and 2-(2-pyrazinyl)-Quinazolinap derived from the resolved diastereomers were readily obtained following decomplexation by stirring in dichloromethane in the presence of 1,2-bis(diphenylphosphino)ethane and purification by column chromatography, Scheme 4.

4. Pd-catalysed allylic alkylation

The formation of asymmetric carbon–carbon linkages catalysed by palladium complexes of chiral ligands is a useful way of assessing the ability of the ligand to induce enantioselectivity.[18] One of the most typically used systems involves nucleophilic attack of the dimethyl malonate anion on 1,3-diphenylprop-2-enyl acetate. Palladium complexes of homobidentate ligands have proven to be successful in this transformation by creating a chiral environment, which influences the orientation of the reactants sufficiently to cause one enantiomer of product to predominate.[19] Heterobidentate ligands such as the phosphinamines developed by Pfaltz,[20] Williams,[21] Helmchen[22] and Brown[3] affect the stereochemical outcome of the bond-forming process by the desymmetrisation of the substrate allyl through electronic effects. The incoming nucleophile then reacts preferentially at the more electrophilic end of the substrate, giving rise to the enantioselectivity observed. This is referred to as the trans effect as nucleophilic attack tends to occur trans to the phosphorus atom of the ligand–Pd complex.[23] The two standard methods employed for the reaction between dimethyl malonate and 1,3-diphenylprop-2-enyl acetate are the malonate procedure (method A), in which the nucleophile is preformed as its sodium salt, and the BSA procedure (method B), in which it is generated in situ upon addition of a base (typically a bis(trimethylsilyl)acetamide–KOAc mixture). Both methods were applied in the alkylation of 1,3-diphenylprop-2-enyl acetate catalysed by palladium complexes of Quinazolinaps **3a** and **3b**. In some cases, 15-crown-5 was added to aid the dissolution of the preformed sodium malonate.

The application of the palladium complex derived from (*S*)-(2-pyridyl)-Quinazolinap resulted in good conversions to product **15** when dichloromethane was used as solvent, reaching an optimum of 92% when the BSA method was employed (Table 2, entry 3). However, the enantioselectivities were low in all cases (13–19% (*S*)). When acetonitrile was used, conversions were poor for both the malonate and BSA procedures but showed a substantial improvement when 15-crown-5 was added (entry 5 vs entry 4). Again, the enantioselectivities were quite poor with the

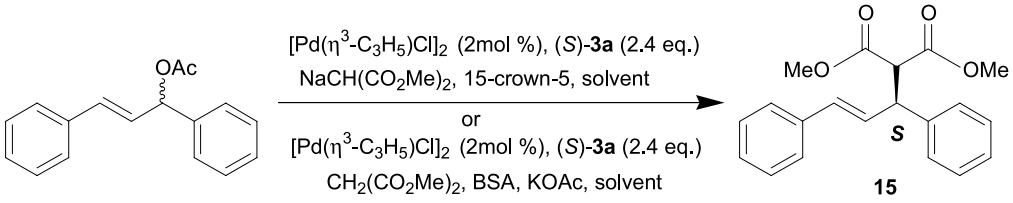


Scheme 4.

(*R*)-product predominating when the conversions were low (entries 4 and 6). When the reactions were carried out in THF, the malonate procedure resulted in a yield of 59% and an ee of 12% (entry 7). The conversion showed an increase to 84% when 15-crown-5 was added but the opposite enantiomer of product was obtained (entry 8). When the BSA method was applied the reaction proceeded much more slowly, with only an 11% conversion being recorded (entry 9). Poor, if any, enantio-differentiation was also achieved in DMF (entries 10–12). Again, the conversion was lowest for the BSA method (11%) but contrary to the results obtained when dichloromethane, acetonitrile and THF were used, the addition of 15-crown-5 actually lead to a decrease in the conversion from 63 to 20% (entries 10 vs 11).

Improved enantioselectivities were obtained when (*R*)-2-(2-pyrazinyl)-Quinazolinap was applied, Table 3. When dichloromethane was employed an increase in conversion from 15 to 38% was apparent with the addition of 15-crown-5 (entry 1 vs 2). The conversion was further improved to 72% with the BSA method (entry 3). When acetonitrile or dimethylformamide were used as solvent, the inclusion of the additive to increase the solubility of the malonate nucleophile had a slightly detrimental effect on the yield and

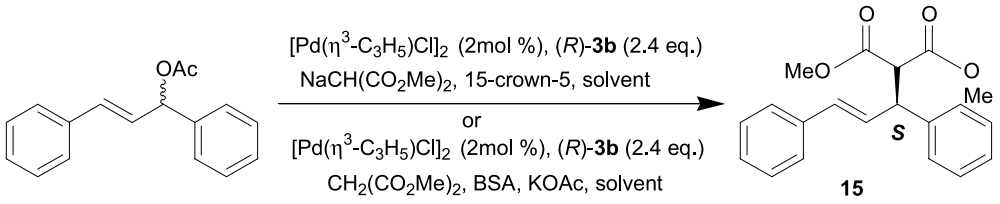
Table 2. Palladium-catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate with 2-(2-pyridyl)-Quinazolinap **3a**



Entry	Method[a]	Solvent	Conv. (%)[b]	Ee (%)[c]
1	A	CH_2Cl_2	79	16 (*S*)
2	A[d]	CH_2Cl_2	89	19 (*S*)
3	B	CH_2Cl_2	92	13 (*S*)
4	A	MeCN	27	6 (*R*)
5	A[d]	MeCN	82	12 (*S*)
6	B	MeCN	25	8 (*R*)
7	A	THF	59	12 (*S*)
8	A[d]	THF	84	23 (*R*)
9	B	THF	11	3 (*R*)
10	A	DMF	63	10 (*S*)
11	A[d]	DMF	20	5 (*S*)
12	B	DMF	11	Racemic

[a] Reactions performed at room temperature for 3 days.
[b] Conversions detemined by ^{1}H NMR.
[c] Enantiomeric excesses of **15** determined by chiral HPLC.
[d] 15-crown-5 added.

Table 3. Palladium-catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate with 2-(2-pyrazinyl)-Quinazolinap **3b**



Entry	Method[a]	Solvent	Conv. (%)[b]	Ee (%)[c]
1	A	CH_2Cl_2	15	14 (*S*)
2	A[d]	CH_2Cl_2	38	24 (*S*)
3	B	CH_2Cl_2	72	26 (*S*)
4	A	MeCN	25	60 (*S*)
5	A[d]	MeCN	13	19 (*S*)
6	B	MeCN	52	45 (*S*)
7	A	THF	20	22 (*S*)
8	A[d]	THF	22	20 (*S*)
9	B	THF	8	6 (*S*)
10	A	DMF	18	68 (*S*)
11	A[d]	DMF	15	6 (*S*)
12	B	DMF	79	38 (*S*)

[a] Reactions performed at room temperature for 3 days.
[b] Conversions determined by ^{1}H NMR.
[c] Enantiomeric excesses of **15** determined by chiral HPLC.
[d] 15-crown-5 added.

also led to a dramatic decrease in the enantioselectivity from 60 to 19% in the case of acetonitrile (entries 4 and 5), and from 68 to 6% for DMF (entries 10 and 11). On changing to the BSA method, the conversions obtained in both these solvents increased, however, the enantioselectivities were lower with respect to those seen for the malonate procedure (entries 6 vs 4 and 12 vs 10). The reaction was also carried out in THF but in all instances the conversions and enantioselectivities were poor (entries 7–9).

When the reaction temperature was lowered to 0 °C the yields decreased sharply, although enhanced ees were achieved with an optimum result for (*R*)-2-(2-pyrazinyl)-Quinazolinap of 81% being obtained in acetonitrile (Table 4, entry 2). Improvements were also seen for the reaction in DMF, wherein the enantioselectivity rose from 38 to 61% (Table 3, entry 12 vs Table 4, entry 5). In an effort to increase the conversion, reactions were then carried out at 40 °C (entries 6–8). When acetonitrile was used as solvent the conversion was greatly enhanced, reaching completion when the BSA-promoted procedure was employed although the enantioselectivity remained unchanged. On changing solvent to DMF, an improved conversion was again seen at the higher reaction temperature but a slight decrease in enantioselectivity was apparent (entry 6).

The fact that low enantioselectivities were obtained using palladium complexes derived from Quinazolinaps **3a** and **3b** is consistent with the presence of a bulky substituent in the 2-position of the quinazoline ring. Low to moderate enantio-differentiation had been observed in the case of the similarly sized 2-(phenyl)-Quinazolinap **2e**, although the rate of reaction was not as slow for **2e**, with some reactions reaching completion after a couple of hours.[8] Similar reaction times were recorded for the other members of the Quinazolinap ligand series, **2a–f**, all of which possess alkyl groups as the 2-substituent.[10] Hence, the retardation of reaction rate seen when ligands **3a** and **3b** were employed could possibly be attributed to electronic alterations to the catalytic complex due to the presence of the electron-withdrawing 2-pyridyl and 2-pyrazinyl substituents. The possible hemi-labile nature of these substituents, evident in the crystal structures obtained in the present study, Figures 1 and 2, may also be a factor in hindering the progress and stereochemical outcome of the reaction.

Table 4. Palladium-catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate with 2-(2-pyrazinyl)-Quinazolinap **3b**

Entry	Method	Solvent	Time (d)	Temperature (°C)	Conv. (%)[a]	Ee (%)[b]
1	A[c]	CH_2Cl_2	5	0	29	37 (*S*)
2	A	MeCN	5	0	25	81 (*S*)
3	B	MeCN	5	0	36	42 (*S*)
4	A	DMF	5	0	0	n/a
5	B	DMF	5	0	18	61 (*S*)
6	A	DMF	3	40	60	61 (*S*)
7	A	MeCN	3	40	85	75 (*S*)
8	B	MeCN	3	40	100	45 (*S*)

[a] Conversions determined by ^{1}H NMR.
[b] Enantiomeric excesses of **15** determined by chiral HPLC.
[c] 15-crown-5 added.

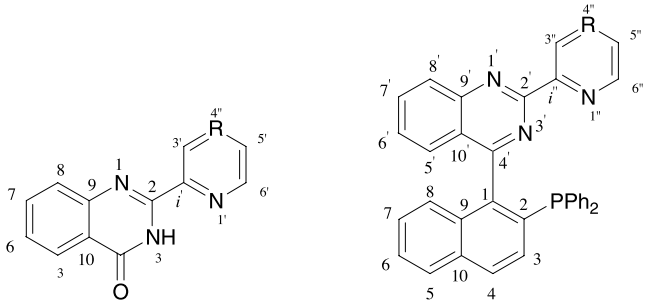
Also noteworthy in the reactions catalysed by (*S*)-2-(2-pyridyl)-Quinazolinap (Table 3), is that, in some instances the (*S*)-enantiomer was formed preferentially. This is the opposite sense of asymmetry to that obtained by Pd-complexes of the less sterically demanding members of the Quinazolinap ligand series (**2a–c**) but was observed in reactions involving the bulky 2-phenyl and 2-*tert*-butyl analogues (**2d–e**).

In conclusion, two new atropisomeric phosphinamine ligands, 2-(2-pyridyl)-Quinazolinap and 2-(2-pyrazinyl)-Quinazolinap were synthesised and resolved via fractional crystallisation of their diastereomeric palladacycles. These ligands were applied in the palladium-catalysed asymmetric allylic alkylation of 1,3-diphenylprop-2-enyl acetate by dimethyl malonate. Low conversions and enantioselectivities were obtained with both ligands, possibly due to the hemi-labile nature of the nitrogen atom of the 2-substituent as revealed in the X-ray crystal structures of the Pd-bound diastereomers. Mechanistic studies are currently underway to further investigate both the steric and electronic influences of 2-(2-pyridyl)- and 2-(2-pyrazinyl)-Quinazolinap on the outcome of the allylic alkylation reaction.

5. Experimental

5.1. General

Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Paragon 1000 Infrared FT spectrometer. The Microanalytical Laboratory, University College Dublin, performed elemental analyses. Electron impact mass spectra were determined on a VG Analytical 770 mass spectrometer with attached INCOS 2400 data system in the EI mode unless otherwise stated. Electrospray mass spectra were recorded on a Micromass Quattro with electrospray probe. 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 MHz Varian-Unity spectrometer and a 500 MHz Varian-Unity spectrometer. ^{1}H–^{1}H COSY spectra were recorded on a 300 MHz Varian-Unity spectrometer and a 500 MHz Varian-Unity 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 Varian-Unity 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 Varian-Unity 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 aluminium oxide 90, standardized (activity II–III). Merck precoated Kieselgel $60F_{254}$ and alumina (neutral, type E) were used for thin layer chromatography. HPLC analysis was carried out using a Chiralcel OD column (0.46 cm 1.d.×25 cm). Optical rotation values were measured on a Perkin Elmer 241 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 (purchased from Aldrich Chemical Co.) used were purified according to the procedures in 'Purification of Laboratory Chemicals'. Pd salts were obtained on loan from Johnson Matthey. Solvents were degassed using three freeze–thaw cycles. Oxygen-free nitrogen was obtained from BOC gases. The following compounds, 2-methoxy-1-naphthylboronic acid,[3] (+)-di-μ-chlorobis{(*R*)-dimethyl[1-(1-naphthyl)ethyl]aminato-C_2,N}dipalladium (II),[24] 1,3-diphenylprop-2-enyl acetate[25] and di-μ-chloro-bis(π-allyl)dipalladium[26] were prepared according to literature procedures. For ease of interpretation of NMR data the following numbering schemes were used for compounds **5** and **3** and related compounds are numbered similarly.



5.1.1. 2-(2-Pyridyl)-4(3*H*)quinazolinone 5a. 2-Cyanopyridine (7.18 g, 6.64 mL, 68.97 mmol) was added to anhydrous methanol (20 mL) under an atmosphere of nitrogen. A solution of sodium metal (0.40 g, 17.40 mmol) in anhydrous methanol (100 mL) was added via cannula. This was stirred at room temperature for 1 h. A solution of anthranilic acid (12.00 g, 87.51 mmol) in dry methanol (125 mL) was added via cannula and the resulting yellow solution stirred at room temperature for a further 45 min. The reaction mixture was then refluxed for 18 h at 85 °C. After cooling to room temperature and then in an ice bath for 1 h a yellow precipitate of 2-(2-pyridyl)-4(3*H*)quinazolinone (11.14 g, 72%) was removed by filtration. On standing overnight, the mother liquor yielded a yellow needle-like precipitate (1.73 g, 11%), which was also collected by filtration, mp 169–171 °C (lit.[27], mp 168.3–168.4 °C); ν_{max} (KBr) 3339 (N–H), 1682 (C=O), 1616 (C=C), 1471 (Ar-H), 1329 (C=N) and 737 (Ar-H) cm^{-1}; ^{1}H NMR (300 MHz): δ ($CDCl_3$) 10.94 (br s, 1H, NH), 8.67 (d, 1H, J=4.8 Hz, $H_{6'}$), 8.59 (d, 1H, J=8.1 Hz, $H_{3'}$), 8.36 (dd, 1H, J_1=7.2 Hz, J_2=1.6 Hz, H_5), 7.92 (dt, J_1=8.1 Hz, J_2=1.6 Hz, H_7), 7.80 (m, 2H, $H_{4'}$, H_8) and 7.50 (m, 2H, H_7, $H_{5'}$); Found: C, 69.64; H, 3.96; N, 19.05. $C_{13}H_9N_3O$ requires C, 69.94; H, 4.06; N, 18.82%.

2-(2-Pyrazinyl)-4(3*H*)quinazolinone **5b** was prepared from pyrazinecarbonitrile on a similar scale and in a similar manner and was obtained in 97% yield as a yellow solid, mp 218–220 °C; ν_{max} (KBr) 3040 (N–H), 1697 (C=O), 1603 (C=C), 1472 (Ar-H) and 766 (Ar-H) cm^{-1}; ^{1}H NMR (300 MHz): δ ($CDCl_3$) 10.63 (br s, 1H, NH), 9.82 (d, 1H, J=1.3 Hz, $H_{3'}$), 8.79 (d, 1H, J=2.5 Hz, $H_{5'}$), 8.65 (d, 1H, J=1.9 Hz, $H_{6'}$), 8.36 (d, 1H, J=7.9 Hz, H_5), 7.85 (m, 2H,

H_7, H_8) and 7.56 (dt, 1H, $J_1=8.1$ Hz, $J_2=1.8$ Hz, H_6); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 161.1, 148.7, 147.3, 146.9, 144.3, 143.8, 142.9, 134.9, 128.3, 128.0, 126.8, 122.6; Found: C, 63.95; H, 3.44; N, 24.85. $C_{12}H_8N_4O$ requires C, 64.28; H, 3.60; N, 24.99%.

5.1.2. 2-(2-Pyridyl)-4-chloroquinazolinone 6a. *N*,*N*-Diethylaniline (4.09 g, 4.39 mL, 27.61 mmol) was added via syringe to 2-(2-pyridyl)-4(3*H*)quinazolinone (4.11 g, 18.41 mmol) in anhydrous benzene (85 mL). This was heated for 5 min at 100 °C to remove water. Phosphorus oxychloride (2.22 g, 1.33 mL, 14.53 mmol) was added via syringe and the resulting deep red solution was refluxed for 4 h at 90 °C after, which time additional phosphorus oxychloride (0.44 g, 0.27 mL, 3.20 mmol) was added. The solution was refluxed for a further 2 h, allowed to cool then washed with iced water (40 mL). The organic layer was then washed sequentially with 20% NaOH (2×30 mL), iced water (30 mL) and brine (30 mL) and dried over anhydrous sodium sulfate. The organic solvent was removed in vacuo and the residue was purified by column chromatography (aluminium oxide, cyclohexane until the *N*,*N*-diethylaniline eluted, then 2:1 cyclohexane–ethyl acetate) to give 2-(2-pyridyl)-4-chloroquinazoline (4.45 g, 68%) as a pale yellow powder. The aqueous layers were combined and extracted with dichloromethane. The organic layer was reduced in vacuo to yield a yellow oil, which was purified by column chromatography as above, providing further product to give a total yield of 3.33 g (77%). Mp 120–121 °C (lit.[28], mp 119.7–122.4 °C); ν_{max} (KBr) 3068 (Ar-H), 2922 (Ar-H), 1546 (C=C), 1483 (Ar-H), 1342 (C–N) and 779 (C–Cl) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.92 (d, 1H, $J=4.7$ Hz, $H_{6'}$), 8.68 (d, 1H, $J=7.8$ Hz, $H_{3'}$), 8.31 (m, 2H, H_8, H_5), 7.99 (dt, 1H, $J_1=8.5$ Hz, $J_2=1.5$ Hz, H_7), 7.91 (dt, 1H, $J_1=7.9$ Hz, $J_2=1.8$ Hz, $H_{4'}$), 7.75 (t, 1H, $J=8.1$ Hz, H_6) and 7.45 (m, 1H, $H_{5'}$); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 163.1, 158.8, 153.9, 151.8, 150.4, 137.1, 135.1, 129.6, 129.1, 125.8, 125.2, 124.4 and 123.0.

2-(2-Pyrazinyl)-4-chloroquinazoline **6b** was similarly prepared in 56% yield as a yellow solid, mp 178–180 °C; ν_{max} (KBr) 2928 (Ar-H), 1549 (C=C), 1486 (Ar-H), 1342 (C=N) and 758 (C–Cl) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 9.87 (s, 1H, $H_{3'}$), 8.86 (dd, $J_1=2.5$ Hz, $J_2=1.5$ Hz, 1H, $H_{5'}$), 8.74 (d, $J=2.5$ Hz, 1H, $H_{6'}$), 8.35 (d, 1H, $J=7.6$ Hz, H_5), 8.29 (d, 1H, $J=8.1$ Hz, H_8), 8.03 (dt, 1H, $J_1=6.9$ Hz, $J_2=1.5$ Hz, H_7) and 7.80 (dt, 1H, $J_1=8.3$ Hz, $J_2=1.2$ Hz, H_6); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 163.5, 157.8, 151.6, 149.3, 145.9, 145.8, 144.7, 135.5, 129.7, 129.6, 126.0 and 122.7; Found: C, 59.71; H, 2.72; N, 14.66, Cl, 22.89. $C_{12}H_7N_4Cl$ requires C, 59.39; H, 2.91; N, 14.61, Cl, 23.09%.

5.1.3. 2-(2-Pyridyl)-4-(2-methoxynaphthalen-1-yl)-quinazoline 8a. 2-(2-Pyridyl)-4-chloroquinazoline (6.68 g, 27.64 mmol) and tetrakis(triphenylphosphine)palladium (0) (1.10 g, 0.96 mmol) were dissolved in anhydrous, degassed DME (65 mL) in a Schlenk tube under nitrogen and stirred for 1 h to give a yellow solution. 2-Methoxy-1-naphthylboronic acid (5.75 g, 28.46 mmol), in the minimum amount of degassed ethanol (18 mL) was added via syringe resulting in a dark purple solution. Sodium carbonate solution (28.4 mL, 2 M) was added causing the solution to turn green followed by the formation of a white precipitate. The mixture was refluxed at 95 °C for 4 days. The solution was cooled to room temperature and filtered. The solid was washed with dichloromethane and the filtrate reduced in vacuo to give a purple residue, which was redissolved in dichloromethane (100 mL), washed with brine (3×50 mL), dried over magnesium sulfate and the solvent removed in vacuo yielding a dark orange solid. 2-(2-Pyridyl)-4-(2-methoxynaphthalen-1-yl)-quinazoline (7.81 g, 77%) was isolated via column chromatography (aluminium oxide, 2:1 petrol ether–ethyl acetate), mp 204–206 °C; ν_{max} (KBr) 3056 (Ar-H), 1622 (C=N), 1582 (C=C), 1511 (Ar-H), 1341 (C–O), 1249 (C–O) and 789 (Ar-H) cm^{-1}; ^1H NMR (500 MHz): δ ($CDCl_3$) 8.92 (d, 1H, $J=4.5$ Hz, $H_{6''}$), 8.68 (d, 1H, $J=8.1$ Hz, $H_{3''}$), 8.40 (d, 1H, $J=8.4$ Hz, $H_{5'}$), 8.05 (d, 1H, $J=9.1$ Hz, H_4), 7.89 (m, 2H, $H_{7'}$, H_5), 7.81 (dt, 1H, $J_1=7.4$ Hz, $J_2=1.6$ Hz, $H_{4''}$), 7.52 (d, 1H, $J=8.4$ Hz, H_7), 7.44 (m, 2H, H_3, $H_{8'}$), 7.36 (m, 2H, $H_{5''}$, $H_{6'}$), 7.28 (dt, 1H, $J_1=8.7$ Hz, $J_2=1.6$ Hz, H_6), 7.18 (d, 1H, $J=8.4$ Hz, H_8) and 3.77 (s, 3H, OCH_3); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 168.1, 160.1, 155.9, 155.0, 151.5, 150.5, 137.0, 134.1, 133.4, 131.5, 129.9, 129.3, 128.3, 128.0, 127.4, 127.2, 124.9, 124.9, 124.7, 124.7, 124.2, 120.2, 113.6, 56.8; Found: C, 79.06; H, 4.77; N, 11.49. $C_{24}H_{17}N_3O$ requires C, 79.32; H, 4.72; N, 11.56%.

Similarly, 2-(2-pyrazinyl)-4-(2-methoxynaphthalen-1-yl)-quinazoline **8b** was prepared by the coupling of 2-(2-pyrazinyl)-4-chloroquinazoline with 2-methoxy-1-naphthylboronic acid in a 78% yield, mp 202–204 °C; ν_{max} (KBr) 3080 (Ar-H), 2936 (Ar-H), 1620 (C=N), 1541 (C=C), 1512 (Ar-H), 1272 (C–O) and 758 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 9.90 (s, 1H, $H_{3''}$), 8.85 (deform. T., 1H, $J=1.5$ Hz, $H_{5''}$), 8.69 (d, 1H, $J=2.3$ Hz, $H_{6''}$), 8.39 (d, 1H, $J=8.5$ Hz, $H_{8'}$), 8.08 (d, 1H, $J=9.1$ Hz, H_4), 7.93 (m, 2H, $H_{7'}$, H_6), 7.57 (d, 1H, $J=7.6$ Hz, $H_{5'}$), 7.51 (d, 1H, $J=6.6$ Hz, $H_{6'}$), 7.46 (d, 1H, $J=8.9$ Hz, H_3), 7.33 (m, 2H, H_5, H_7), 7.16 (d, 1H, $J=8.3$ Hz, H_8) and 3.80 (s, 3H, OCH_3); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 186.4, 158.7, 154.8, 151.2, 151.0, 146.3, 145.2, 144.6, 134.4, 133.1, 131.5, 129.6, 129.0, 128.4, 128.2, 127.4, 127.2, 125.0, 124.3, 124.0, 119.5, 113.3, 56.6; Found: C, 75.51; H, 4.49; N, 15.19. $C_{23}H_{16}N_4O$ requires C, 75.81; H, 4.43; N, 15.38%.

5.1.4. 1-[2-(2-Pyridyl)-quinazolin-4-yl]-2-hydroxynaphthalene 9a. 2-(2-Pyridyl)-4-(2-methoxynaphthalen-1-yl)-quinazoline (1.02 g, 2.81 mmol) and aluminium chloride (2.24 g, 16.80 mmol) were refluxed in anhydrous benzene (110 mL) under a nitrogen atmosphere for 3 h. The dark purple mixture was allowed to cool and the pH was adjusted to 4 using 10% HCl. The resulting fine orange precipitate formed was filtered through sintered glass to yield 1-[2-(2-pyridyl)-quinazolin-4-yl]-2-hydroxynaphthalene (0.48 g, 48%). T_{dec} 226 °C; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.92 (d, 1H, $J=4.7$ Hz, $H_{6''}$), 8.72 (d, 1H, $J=8.2$ Hz, $H_{5''}$), 8.33 (d, 1H, $J=8.2$ Hz, $H_{4''}$), 8.00–7.91 (m, 3H), 7.86 (d, 1H, $J=7.8$ Hz), 7.66 (d, 1H, $J=7.8$ Hz), 7.51–7.43 (m, 2H), 7.41 (d, 1H, $J=8.9$ Hz and 7.38–7.32) (m, 3H); *m*/*z* (HRMS, ES) found: 350.1306; $C_{23}H_{16}N_3O$ requires 350.1293.

5.1.5. 1-[2-(2-Pyrazinyl)-quinazolin-4-yl]-2-hydroxynaphthalene 9b. Sodium ethanethiolate (2.41 g, 28.6 mmol)

was added to a solution of 2-(2-pyrazinyl)-4-(2-methoxynaphthalen-1-yl)-quinazoline (4.70 g, 12.90 mmol) in degassed DMF (80 mL) and the red solution refluxed at 120 °C for 3.5 h. After cooling to room temperature, the pH was adjusted to 5 using 10% HCl (3 mL), which caused the solution to turn orange in colour. The solution was allowed to stir for 10 min and a yellow precipitate formed. This was filtered through sintered glass to yield 1-[2-(2-pyrazinyl)-quinazolin-4-yl]-2-hydroxynaphthalene (3.01 g, 66%) as a bright yellow powder. The filtrate was extracted into dichloromethane (100 mL). The organic layer was washed with water (4×100 mL), dried over sodium sulfate and the solvent removed in vacuo giving a dull yellow solid. Recrystallisation of this solid from hot dichloromethane furnished a further 0.80 g of the desired naphthol resulting in a combined yield of 84%. T_{dec} 250 °C; ν_{max} (KBr), 3732 (OH), 3060 (Ar-H), 1563 (Ar-H), 1494 (OH), 1341 (C=N), 1210 (C–O), 763 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 9.84 (s, 1H, $H_{3''}$), 9.31 (br s, 1H, OH), 8.66 (m, 2H, $H_{5''}$, $H_{6''}$), 8.26 (d, 1H, $J=8.5$ Hz, $H_{8'}$), 7.93 (dt, 1H, $J_1=6.8$ Hz, $J_2=1.5$ Hz, $H_{7'}$), 7.85 (d, 2H, $J=9.0$ Hz, H_4, H_5), 7.68 (d, 1H, $J=8.2$ Hz, $H_{5'}$), 7.48 (dt, 1H, $J_1=6.8$ Hz, $J_2=1.2$ Hz, $H_{6'}$), 7.36 (dt, 1H, $J_1=6.6$ Hz, $J_2=1.5$ Hz, H_6) and 7.25 (m, 3H, H_3, H_7, H_8); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 167.7, 157.2, 154.1, 151.6, 150.0, 145.6, 145.5, 144.2, 134.8, 132.8, 132.1, 129.6, 128.7, 128.4, 128.3, 128.0, 127.4, 126.9, 124.4, 124.2, 123.6, 119.4 and 115.3; Found: C, 74.93; H, 4.13; N, 15.51. $C_{22}H_{14}N_4O$ requires C, 75.41; H, 4.03; N, 15.99%.

5.1.6. 1-[2-(2-Pyridyl)quinazolin-4-yl]-2-naphthyltrifluoromethylsulfonate 10a. 1-[2-(2-Pyridyl)-quinazolin-4-yl]-2-hydroxynaphthalene (0.38 g, 1.10 mmol) and 4-dimethylaminopyridine (0.34 g, 2.75 mmol) were dissolved in dry dichloromethane (20 mL). Trifluoromethanesulfonic anhydride (0.66 g, 0.4 mL, 2.37 mmol) was added and the solution stirred for 20 h under nitrogen. A white precipitate formed, which was removed by filtration. The solid was washed with dichloromethane and the combined filtrates were reduced in vacuo to give a yellow solid. This was purified by column chromatography (aluminium oxide, 2:1 petrol ether–ethyl acetate) to yield 1-[2-(2-pridyl)-quinazolin-4-yl]-2-naphthyltrifluoromethylsulfonate (0.47 g, 78%) as a white solid, mp 176–177 °C; ν_{max} (KBr) 2929 (Ar-H), 1544 (Ar-H), 1405 (–SO_3–), 1219 (–SO_3–), 1135 (C–O) and 828 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.94 (d, 1H, $J=3.8$ Hz, $H_{6''}$), 8.70 (d, 1H, $J=7.9$ Hz, $H_{3''}$), 8.46 (d, 1H, $J=8.6$ Hz, $H_{8'}$), 8.17 (d, 1H, $J=9.1$ Hz, H_4), 8.03 (d, 1H, $J=8.3$ Hz, H_5), 7.97 (dt, 1H, $J_1=6.7$ Hz, $J_2=1.6$ Hz, $H_{7'}$), 7.86 (dt, 1H, $J_1=7.5$ Hz, $J_2=1.8$ Hz, $H_{4''}$), 7.64 (d, 1H, $J=9.1$ Hz, H_3), 7.60 (dt, 1H, $J_1=6.8$ Hz, $J_2=1.3$ Hz, H_6), 7.47 (m, 4H, $H_{6'}$, $H_{5'}$, H_7, $H_{5''}$) and 7.31 (d, 1H, $J=7.5$ Hz, H_8); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 163.8, 159.7, 155.0, 151.6, 150.4, 144.8, 137.1, 134.7, 132.5, 132.4, 132.1, 130.1, 128.5, 128.5, 128.4, 127.5, 127.3, 126.3, 126.2, 124.9, 124.8, 124.0, 119.6; Found: C, 59.58; H, 2.83; N, 8.54; S, 6.76; F, 11.39. $C_{24}H_{14}N_3SF_3O_3$ requires C, 59.87; H, 2.93; N, 8.73; S, 6.66; F, 11.84%.

5.1.7. 1-[2-(2-Pyrazinyl)quinazolin-4-yl]-2-naphthyltrifluoromethylsulfonate 10b. 1-[2-(2-Pyrazinyl)-quinazolin-4-yl]-2-hydroxynaphthalene (1.28 g, 3.64 mmol) and 4-dimethylaminopyridine (1.30 g, 10.81 mmol) were dissolved in dry dichloromethane (40 mL) to give a bright yellow solution. Trifluoromethanesulfonic anhydride (1.53 g, 0.91 mL, 7.28 mmol) was added and the orange solution stirred at room temperature for 48 h under nitrogen. A white precipitate formed, which was removed by filtration. The solid was washed with dichloromethane and the combined filtrates were reduced in vacuo to give a yellow solid. This was purified by column chromatography (aluminium oxide, 2:1 pentane–ethyl acetate) to yield 1-[2-(2-pyrazinyl)-quinazolin-4-yl]-2-naphthyltrifluoromethylsulfonate (1.24 g, 71%) as a white solid, mp 160–162 °C; ν_{max} (KBr) 3070 (Ar-H), 1512 (C=C), 1427 (–SO_3–), 1343 (C=N), 1218 (–SO_3–), 1142 (C–O) and 831 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 9.91 (s, 1H, $H_{3''}$), 8.87 (app t, 1H, $J=1.6$ Hz, $H_{5''}$), 8.72 (d, 1H, $J=2.3$ Hz, $H_{6''}$), 8.45 (d, 1H, $J=8.5$ Hz, $H_{8'}$), 8.19 (d, 1H, $J=9.1$ Hz, H_4), 8.05 (d, 1H, $J=7.6$ Hz, H_5), 8.00 (dt, 1H, $J_1=7.0$ Hz, $J_2=1.5$ Hz, $H_{7'}$), 7.65 (d, 1H, $J=9.1$ Hz, H_3), 7.54 (m, 4H, $H_{5'}$, $H_{6'}$, H_6, H_7) and 7.31 (d, 1H, $J=8.3$ Hz, H_8); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 164.2, 158.1, 151.4, 150.3, 146.3, 145.6, 144.8, 144.7, 135.1, 132.4, 132.3, 123.0, 129.1, 128.5, 128.5, 127.6, 126.6, 126.1, 124.3 and 119.6; Found: C, 57.05; H, 2.91; N, 11.32; S, 6.95; F, 11.72. $C_{23}H_{13}N_4SF_3O_3$ requires C, 57.26; H, 2.72; N, 11.61; S 6.65; F, 11.81%.

5.1.8. (*R*,*S*)-2-Diphenylphosphino-1-[2-(2-pyridylquinazolin-4)-yl]naphthalene 3a. 1-[2-(2-Pyridyl)quinazolin-4-yl]-2-naphthyltrifluoromethylsulfonate (2.66 g, 5.54 mmol), palladium acetate (0.12 g, 0.55 mmol) and triphenylphosphine (3.34 g, 12.74 mmol) were dissolved under a nitrogen atmosphere in degassed DMF (24 mL). The yellow solution was heated at 115 °C causing it to turn red in colour. The solution was maintained at this temperature, under an atmosphere of nitrogen, for 6 days. The solvent was removed in vacuo. The residue was purified by column chromatography (aluminium oxide, 2:1 petroleum ether–ethyl acetate) to furnish (*R*,*S*)-2-diphenylphosphino-1-[2-(2-pyridylquinazolin-4)-yl]naphthalene (1.68 g, 59%) as a white solid, mp 216–218 °C; ν_{max} (KBr) 3053 (Ar-H), 2921 (Ar-H), 1613 (Ar-H), 1542 (Ph), 1491 (Ph), 1340 (C=N) and 744 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.86 (d, 1H, $J=4.6$ Hz, $H_{6''}$), 8.44 (d, 1H, $J=8.6$ Hz, $H_{3''}$), 7.97–7.87 (m, 3H), 7.75 (d, 1H, $J=7.7$ Hz), 7.56–7.48 (m, 2H), 7.43–7.37 (m, 3H) and 7.34–7.10 (m, 14H); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 169.4, 161.2, 155.2, 151.3, 150.1, 141.8, 141.5, 136.7, 134.6, 134.0, 133.9, 133.7, 133.6, 133.4, 131.8, 129.9, 129.3, 128.5, 128.4, 128.3, 128.1, 127.9, 127.0, 126.8, 126.2, 124.7 and 124.4; ^{31}P NMR (121 MHz): δ ($CDCl_3$) −12.23 ppm. *m/z* (HRMS, ES) 518.1808 $C_{35}H_{25}N_3P$ cation.

(*R*,*S*)-2-Diphenylphosphino-1-[2-(2-pyrazinylquinazolin-4)-yl]naphthalene **3b** was prepared in an analogous fashion via phosphinylation of 1-[2-(2-pyrazinyl)quinazolin-4-yl]-2-naphthyltrifluoromethylsulfonate in a 53% yield after column chromatography on aluminium oxide. Mp 220–222 °C; ν_{max} (KBr) 3050 (Ar-H), 2904 (Ar-H), 1612 (Ar-H), 1564 (Ph), 1546 (Ph), 1340 (C=N) and 744 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 9.02 (d, $J=1.4$ Hz, 1H, $H_{3''}$), 8.79 (d, $J=2.3$ Hz, 1H, $H_{5''}$), 8.61 (d, $J=2.5$ Hz, 1H, $H_{6''}$), 8.42 (d, $J=8.1$ Hz, 1H, $H_{8'}$), 7.99–7.91 (m, 3H, Ar-H) and 7.55–7.10 (m, 16H, Ar-H); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 170.0, 157.7, 151.2, 150.5, 146.2, 145.2, 144.4,

141.4, 141.0, 136.9, 136.3, 134.8, 134.4, 133.8, 133.5, 132.2–131.9, 130.0, 129.4, 128.7–128.2, 127.1, 127.0, 126.0, 125.5, and 124.7; ^{31}P NMR (121 MHz): δ ($CDCl_3$) −13.20 ppm; *m/z* (HRMS, ES) 519.1754 $C_{34}H_{24}N_4P$ cation.

5.1.9. Resolution of (*R*,*S*)-2-diphenylphosphino-1-[2-(2-pyridylquinazolin-4)-yl]naphthalene. (*R*,*S*)-2-Diphenylphosphino-1-[2-(2-pyridylquinazolin-4)-yl]naphthalene (1.67 g, 3.2 mmol) and (+)-di-μ-chlorobis{(*R*)-dimethyl[1-(1-naphthyl)ethyl]aminato-C_2,N}dipalladium (II) (1.10 g, 1.62 mmol) were dissolved in dry, degassed methanol (110 mL) under an atmosphere of nitrogen and stirred for 18 h. Aqueous potassium hexafluorophosphate (0.65 g, 110 mL water) was added causing a yellow suspension to form. This was stirred for 1 h and water was added (100 mL) and stirring continued for a further 3 h. The mixture was filtered to give an orange solid (2.61 g, 84%). The solid was dissolved in hot butanone and diethyl ethyl until a light suspension had formed. After standing overnight the mixture was filtered and the mother liquor was concentrated in vacuo to yield (*S*,*R*)-**12** as a bright orange solid, (1.86 g, 60%). T_{dec} 200 °C; ν_{max} (KBr) 3060 (Ar-H), 1569 (C=C), 1438 (P-Ph), 1098 (Ar-H) and 841 (P-F) cm^{-1}; ^{1}H NMR (300 MHz): δ ($CDCl_3$) 8.89 (d, 1H, J=8.0 Hz, $H_{6''}$), 8.44 (d, 1H, J=4.3 Hz, $H_{3''}$), 8.25 (dt, 1H, J_1=8.0 Hz, J_2=1.8 Hz, $H_{5''}$), 8.07–7.93 (m, 3H), 7.74 (d, 1H, J=7.6 Hz), 7.66 (t, 1H, J=7.3 Hz), 7.59–6.82 (m, 22H), 4.10 (q, 1H, J=6.0 Hz, C*H*(Me)), 2.06 (s, 3H, NMe), 1.90 (s, 3H, NMe) and 1.26 (d, 1H, J=6.5 Hz, CH(*Me*)); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 165.8, 156.6, 153.9, 152.0, 150.1, 148.8, 147.8, 138.9, 136.7, 135.2, 135.0, 133.1, 132.7, 132.6, 132.6, 131.7, 131.2, 130.1, 129.2, 129.1, 128.9, 128.8, 128.6, 128.4, 128.1, 126.6, 126.5, 126.3, 125.9, 125.1, 124.6, 124.3, 122.9, 71.7 (*C*H(Me)), 51.2 (NMe), 47.3 (NMe) and 20.5 (CH(*Me*)); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 27.61 ppm; −324 (*c* 0.58, $CHCl_3$), *m/z* (HRMS, ES) found: 822.2116; $C_{49}H_{40}N_4PPd$ requires 822.2104.

5.1.10. Resolution of (*R*,*S*)-2-diphenylphosphino-1-[2-(2-pyrazinylquinazolin-4)-yl]naphthalene. (*R*,*S*)-2-Diphenylphosphino-1-[2-(2-pyrazinylquinazolin-4)-yl]naphthalene (0.94 g, 1.8 mmol) and (+)-di-μ-chlorobis{(*R*)-dimethyl[1-(1-naphthyl)ethyl]aminato-C_2,N}dipalladium (II) (0.61 g, 0.9 mmol) were dissolved in dry, degassed methanol (42 mL) under an atmosphere of nitrogen and stirred at 60 °C for 20 h. A white precipitate had formed by this time, which was removed by filtration and washed with a small amount of cold methanol to give (*R*,*R*)-**13** (0.49 g, 28%). T_{dec} 240 °C; ν_{max} (KBr) 3057 (Ar-H), 2919, (Ar-H), 1569 (C=C), 1545 (C=C), 1434 (P-Ph), 1098 (Ar-H) and 747 (Ar-H) cm^{-1}; ^{1}H NMR (300 MHz): δ ($CDCl_3$) 9.65 (s, 1H, $H_{3''}$), 8.82 (d, 1H, J=2.3 Hz, $H_{6''}$), 8.71 (d, 1H, J=2.3 Hz, $H_{5''}$), 8.18–8.08 (m, 3H), 7.97–7.79 (m, 5H), 7.57–7.40 (m, 6H), 7.31–7.16 (m, 8H), 6.95 (appt, 2H), 6.70 (d, 1H, J=8.7 Hz), 6.19 (d, 1H, J=8.2 Hz), 5.93 (t, 1H, J=6.1 Hz) 4.12 (q, 1H, J=5.6 Hz, C*H*(Me)), 2.83 (s, 3H, NMe), 1.93 (d, 3H, J=6.1 Hz, CH(*Me*)) and 1.63 (s, 1H, NMe); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 168.9, 164.5, 157.4, 150.9, 150.7, 148.8, 148.1, 146.0, 145.2, 144.6, 138.2, 138.1, 135.7, 135.6, 153.4, 134.4, 133.4, 132.3, 132.3, 131.1, 130.6, 130.4, 130.3, 128.9, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 127.3, 127.2, 127.0, 126.2, 125.4, 125.2, 123.9, 123.5, 123.0, 72.8 (*C*H(Me)), 50.6 (NMe), 48.6 (NMe) and 23.5 (CH(*Me*)); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 27.61 ppm; +89 (*c* 0.69, $CHCl_3$), *m/z* (HRMS, ES) found: 823.2048; $C_{48}H_{40}N_5PPd$ requires 823.2056.

To the orange filtrate, was added aqueous potassium hexafluorophosphate and the yellow suspension was stirred at room temperature for 18 h. Water (50 mL) was added and stirring continued for 1 h. The orange solid was filtered off, dissolved in hot butanone and diethyl ether was added until a light suspension formed. The suspension was left to stand overnight, then filtered. The mother liquor was reduced in vacuo to yield (*S*,*R*)-**14** as a bright orange solid, (0.97 g, 56%), mp 230–232 °C; ν_{max} (KBr) 3056 (Ar-H), 2868 (Ar-H), 1562 (C=C), 1437 (P-Ph), 1098 (Ar-H) and 842 (P–F) cm^{-1}; ^{1}H NMR (300 MHz): δ ($CDCl_3$) 10.06 (d, 1H, J=2.0 Hz, $H_{3''}$), 8.87 (s, 1H, $H_{6''}$), 8.45 (s, 1H, $H_{5''}$), 8.17 (d, 1H, J=8.4 Hz), 8.09–7.97 (m, 3H), 7.75–7.63 (m, 3H), 7.52–6.83 (m, 19H), 4.12 (q, 1H, J=6.0 Hz, C*H*(Me)), 2.13 (s, 3H, NMe), 1.97 (s, 3H, NMe) and 1.26 (d, 3H, J=3.7 Hz, CH(*Me*)); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 166.4, 154.9, 151.4, 150.0, 149.1, 148.2, 149.1, 148.2, 147.6, 147.0, 142.1, 137.0, 135.1, 133.2, 132.7, 132.3, 132.3, 132.0, 131.4, 130.7, 129.4, 129.1, 128.9, 128.8, 128.7, 128.1, 126.7, 126.5, 126.4, 126.0, 125.3, 124.8, 124.5, 123.2, 123.0, 122.3, 72.2 (*C*H(Me)), 51.3 (NMe), 47.4 (NMe) and 20.8 CH(*Me*)); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 28.97 ppm; −249 (*c* 0.74, $CHCl_3$), *m/z* (HRMS, ES) found: 822.2018; $C_{48}H_{39}N_5PPd$ requires 822.1978.

5.1.11. (*S*)-2-Diphenylphosphino-1-[2-(2-pyridylquinazolin-4)-yl]naphthalene. *Compound* (*S*,*R*)-**12** (0.62 g, 0.65 mmol) and 1,2-bis(diphenylphosphino)ethane (0.257 g, 0.65 mmol) were dissolved in dichloromethane under an atmosphere of nitrogen and stirred at room temperature for 2 h. The solvent was almost all reduced in vacuo to a yellow oil, which was purified using a short aluminium oxide column (pentane–ethyl acetate 2:1) to give (*S*)-diphenylphosphino-1-[2-(2-pyridylquinazolin-4)-yl] naphthalene as a white solid (0.29 g, 85%), +319 (*c* 0.3, $CHCl_3$), and identical in all other respects to the racemic diphenyl phosphine.

(*R*)-diphenylphosphino-1-[2-(2-pyrazinylquinazolin-4)-yl] naphthalene was similarly isolated from (*R*,*R*)-**13**as a white solid in a 95% yield, +8.0 (*c* 0.55, $CHCl_3$), and identical in all other respects to the previously prepared racemic sample.

5.1.12. Allylic alkylation procedures. *Method A*. (*S*)-2-(2-pyridyl)- or (*R*)-2-(2-pyrazinyl)-Quinazolinap (0.006 mmol) and di-μ-chloro-bis(π-allyl)dipalladium (0.0025 mmol) were placed in a Schlenk tube under an atmosphere of nitrogen. Dry, degassed solvent was added (0.3 mL) and the mixture stirred for 10 min. To this was added a solution of 1,3-diphenylprop-2-enyl acetate (0.063 g, 0.250 mmol) in dry, degassed solvent (0.2 mL). The suspension was stirred for 10 min and then sodium dimethyl malonate (0.042 g, 0.275 mmol) was added and also, if required, 15-crown-5 (55 μL, 0.275 mmol). Reaction progress was monitored by TLC (pentane–diethyl ether 2:1). The reactions were stirred at room temperature for 3 days, or at 0 °C for 5 days, before being quenched by the addition of acetic acid (0.1 mL). The solvent was reduced in vacuo and water (25 mL) was added.

The reaction mixture was extracted into diethyl ether (25 mL), washed with water (25 mL) then brine (25 mL), dried over $MgSO_4$, filtered and the solvent removed in vacuo to give a yellow oil. The % conversion was calculated using ^1H NMR of the crude product. The product was purified on preparative silica plates (pentane–diethyl ether 2:1) to afford (*R*)- or (*S*)-methyl-2-carbomethoxy-3,5-diphenylpent-4-enoate **15** as a colourless oil.[20] ^1H NMR (300 MHz): δ ($CDCl_3$) 7.34–7.20 (10H, m, Ar-H), 6.47 (1H, d, $J=15.82$ Hz, H_3), 6.34 (1H, dd, $J=15.82$, 8.35, H_2), 4.27 (1H, dd, $J=10.84$, 8.49 Hz, H_1), 3.95 (1H, d, $J=10.84$ Hz, C*H*(CO_2Me)$_2$), 3.70 (3H, s, OMe) and 3.52 (3H, s, OMe). The enantiomeric excess was determined by chiral HPLC [Daicel (Chiracel OD) column, 0.46 cm I.D.×25 cm], pentane–isopropanol 99:1, 0.3 mL/min, $R_t=(R)-42$ min, $(S)-45$ min.

Method B. (*S*)-2-(2-pyridyl)- or (*R*)-2-(2-pyrazinyl)-Quinazolinap (0.006 mmol) and di-μ-chloro-bis(π-allyl)dipalladium (0.0025 mmol) were placed in a Schlenk tube under an atmosphere of nitrogen. Dry, degassed solvent was added (0.3 mL) and the mixture stirred for 10 min. To this was added a solution of 1,3-diphenylprop-2-enyl acetate (0.063 g, 0.250 mmol) in dry, degassed solvent (0.2 mL). Potassium acetate (0.005 mmol) was added and the suspension was stirred for 10 min. Dimethyl malonate (31.5 μL, 0.275 mmol) and *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (68 μL, 0.275 mmol) were added and the reactions stirred at room temperature for 3 days, or 0 °C for 5 days. The work-up and determination of conversion and enantioselectivity were the same as described for method A.

5.2. X-ray analysis of (*S*,*R*)-12

Crystal data for (*S*,*R*)-**12**·1.5(CH_2Cl_2): $[C_{49}H_{40}N_4PPd]^+[PF_6]^-\cdot 1.5(CH_2Cl_2)$, from dichloromethane/diethylether, $M_r=1094.58$, orange prism, crystal size: 0.04×0.09×0.16 mm^3; $a=32.1529(6)$ Å, $b=12.7212(3)$ Å, $c=11.7891(3)$ Å, $\beta=104.120(1)°$, $V=4676.3(2)$ $Å^3$, $T=100$ K, monoclinic, space group *C* 2 (No. 5), $Z=4$, $\rho_{calcd}=1.555$ g cm^{-3}, $F(000)=2220$, Nonius Kappa CCD diffractometer, λ(Mo K_α)=0.71073 Å, $\mu=0.702$ mm^{-1}, 39,890 measured and 17,396 independent reflections ($R_{int}=0.068$), 14,603 with $I>2\sigma(I)$, $\theta_{max}=33.14°$, $T_{min}=0.933$, $T_{max}=0.979$, direct methods (SHELXS-97) and least-squares refinement (SHELXL-97) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 302 parameters, Flack parameter 0.00(2), one of the dichloromethane solute molecules is disordered about a two-fold axis, H atoms riding, Chebyshev type weights, $R_1=0.0533$ ($I>2\sigma(I)$), $wR_2=0.1200$ (all data), $\Delta\rho_{max/min}=0.816/-0.850$ e $Å^{-3}$. CCDC 265942.[1]

5.3. X-ray analysis of (*S*,*R*)-14

Crystal data for (*S*,*R*)-**14**·$C_4H_{10}O$: $[C_{48}H_{39}N_5PPd]^+[PF_6]^-\cdot C_4H_{10}O$, from chloroform/diethylether, $M_r=1042.3$, orange-red prism, crystal size: 0.02×0.06×0.11 mm^2; $a=8.9132(1)$ Å, $b=22.5067(3)$ Å, $c=12.0303(1)$ Å, $\beta=103.079(1)°$, $V=2350.75(5)$ $Å^3$, $T=100$ K, monoclinic, space group $P2_1$ (No. 4), $Z=2$, $\rho_{calcd}=1.473$ g cm^{-3}, $F(000)=1068$, Nonius KappaCCD diffractometer, λ(Mo K_α)=0.71073 Å, $\mu=0.532$ mm^{-1}, 64011 measured and 14940 independent reflections ($R_{int}=0.038$), 14207 with $I>2\sigma(I)$, $\theta_{max}=30.99°$, $T_{min}=0.956$, $T_{max}=0.989$, direct methods (*SHELXS*−97) and least-squares refinement (*SHELXL*-97) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 631 parameters, Flack parameter −0.03(1), the diethylether solute is disordered over two positions, H atoms riding except for the solute where they are absent, Chebyshev type weights, $R_1=0.0259$ ($I>2\sigma(I)$), $wR_2=0.0615$ (all data), $\Delta\rho_{max/min}=0.440/-0.376$ e $Å^{-3}$. CCDC 265943.[1]

Data for the crystal structures of (*S*,*R*)-**12**·1.5(CH_2Cl_2) and (*S*,*R*)-**14**·$C_4H_{10}O$ can be obtained free of charge on quotation of the CCDC deposition numbers 265942 and 265943 via www.ccdc.cam.ac.uk/conts/retrieving.html (or) from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223-336-033; or e-mail: deposit@ccdc.cam.ax.uk.

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References and notes

1. McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809–3844. Terry, T.-L.; Au-Yeung, T. T.-L.; Chan, A. S. C. *Coord. Chem. Rev.* **2004**, *248*, 2151–2164. Ila, H.; Bell, H. P.; Tietze, L. F. *Chem. Rev.* **2004**, *104*, 3453–3516.
2. Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932–7934.
3. Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743–756. Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Chem. Commun.* **1995**, 395–397. Brown, J. M.; Hulmes, D. I.; Layzell, T. P. *Chem. Commun.* **1993**, 1673–1674.
4. Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493–4506.
5. Valk, J.-M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2593–2596.
6. Valk, J.-M.; Claridge, T. D. W.; Brown, J. M.; Hibbs, D.; Hursthouse, M. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2597–2610.
7. McCarthy, M.; Goddard, R.; Guiry, P. J. *Tetrahedron: Asymmetry* **1999**, *10*, 2797–2807.
8. McCarthy, M.; Guiry, P. J. *Polyhedron* **2000**, *19*, 541–543.
9. Connolly, D. J.; Lacey, P. M.; McCarthy, M.; Saunders, C. P.; Carroll, A.-M.; Goddard, R.; Guiry, P. J. *J. Org. Chem.* **2004**, *69*, 6572–6589.
10. Connolly, D. J. PhD Thesis, National University of Ireland, 2004.
11. Connolly, D. J.; Guiry, P. J. *Synlett* **2001**, *11*, 1707–1710.
12. Liao, Y.; Boettcher, H.; Bartoszyk, G. D.; Greiner, H. E.; Harting, J.; de Boer, P.; Wikstroem, H. V.; Mensonides-Harsema, M. M. *J. Med. Chem.* **2000**, *43*, 432–439.
13. Stocksdale, M. G.; Fahey, K. J.; Jones, C. D.; Dodge, J. A. *J. Org. Chem.* **1995**, *60*, 739–741.

14. Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180–7181.
15. Vyskocil, S.; Smrcina, M.; Hanus, V.; Polasek, M.; Kocovsky, P. *J. Org. Chem.* **1998**, *63*, 7738–7748.
16. Kwong, F. Y.; Chan, K. S. *Organometallics* **2000**, *19*, 2058–2060.
17. Leung, P. H.; Loh, S.; Mok, K. F.; White, A. J. P.; Williams, D. *J. Chem. Soc., Chem. Commun.* **1996**, 591–592. Kerr, P. G.; Leung, P. H.; Wild, S. B. *J. Am. Chem. Soc.* **1987**, *109*, 4321–4328. Otsuka, S.; Nakamura, A.; Kano, T.; Tani, K. *J. Am. Chem. Soc.* **1971**, *93*, 4301–4303.
18. Pfaltz, A.; Lautens, M.; Comprehensive Asymmetric Catalysis; Springer: New York, 1999; Vol. I. Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422. Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336–345. Ojima, I. *Catalytic Asymmetric Synthesis* 2nd ed.; VCH: Weinheim, 2000. Johannsen, M.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689–1708.
19. van Vranken, D.L; Binge, C.; Trost, B. M. *J. Am. Chem. Soc.* **1992**, *114*, 9327–9343. van Vranken, D. L.; Trost, B. M. *Chem. Rev.* **1996**, *96*, 395–422.
20. von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566–568.
21. Dawson, G. J.; Frost, C. G.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1993**, *34*, 3149–3150.
22. Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769–1772.
23. Kollmar, M.; Goldfuss, B.; Reggelin, M.; Rominger, F.; Helmchen, G. *Chem. Eur. J.* **2001**, *7*, 4913–4927.
24. Martin, J. W. L.; Palmer, J. A. L.; Wild, S. B. *Inorg. Chem.* **1984**, *23*, 2664–2668. Martin, J. W. L. *J. Am. Chem. Soc.* **1988**, *110*, 4346–4356.
25. Gotov, B.; Toma, S.; Solcaniova, E.; Cvengos, J. *Tetrahedron* **2000**, *56*, 671–675.
26. Leung, W.; Cosway, S.; Jones, R. H. V.; McCann, H.; Wills, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2588–2594.
27. Linschoten, M. R.; Gaisser, H.-D.; van der Goot, H.; Timmerman, H. *Eur. J. Med. Chem. Chim. Ther.* **1984**, *19*, 137–142.
28. Scheiner, P.; Frank, L.; Giusti, I.; Arwin, S.; Pearson, S. A.; Excellent, F.; Harper, A. P. *J. Heterocycl. Chem.* **1984**, *21*, 1817–1824.