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Rhodium-catalysed hydroboration employing new Quinazolinap ligands; an investigation into electronic effects

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Dedicated with respect and admiration to Professor Henri Kagan on the occasion of his 80th birthday

ABSTRACT

As part of an ongoing effort to improve the efficiency and substrate scope of our Quinazolinap ligand series in the rhodium-catalysed asymmetric hydroboration of vinyl arenes, 2-(*p*-trifluoromethylphenyl)-Quinazolinap and 2-(*p*-methoxyphenyl)-Quinazolinap have been synthesised and resolved in good yield. These, along with the previously reported 2-(2-pyridyl)-Quinazolinap and 2-(2-pyrazinyl)-Quinazolinap, form part of an electronic series of Quinazolinap ligands synthesised in order to explore electronic effects in this ligand class. The application of this series of ligands to the rhodium-catalysed asymmetric hydroboration of a range of vinylarenes is described. Good conversions and regioselectivities as well as excellent enantioselectivities up to 97% were obtained. 2-(*p*-Methoxyphenyl)-Quinazolinap demonstrated consistently high enantioselectivities in the hydroboration of sterically demanding vinylarenes.

1. Introduction

The use of atropisomeric ligands in transition metal-catalysed asymmetric transformations has been well documented.[1–3] We have developed a class of axially chiral ligands, which we term 'Quinazolinap', as they incorporate a quinazoline unit to the biaryl framework (Fig. 1).

Ligands **1a–f**, which constitute a steric series, have been applied in the rhodium-catalysed asymmetric hydroboration of vinylarenes where they achieved excellent conversions, regioselectivities and enantioselectivities as high as 99.5%.[4] We have focused on the rhodium-catalysed asymmetric hydroboration of vinylarenes due to the versatility of the organoboranes produced. They are important intermediates in many natural product and drug syntheses[5] and are often subjected to functionalisation of the carbon–boron bond,[6] which, importantly, occurs with the retention of stereochemistry.

While the majority of reports of ligand modification have been followed from systematic variation of the spatial demands of the catalyst, manipulation of ligand electronics is another important method of varying catalyst properties.[7] Examples include variations in the Salen-type ligands for asymmetric epoxidation,[8] an electronic series of H-MOP ligands[9] and BINAP-derived ligands.[10] Within the P,N ligand class, Brown has conducted a study of electronic effects in the QUINAP series by variation at the phosphorus donor atom.[11,12] We began our research into electronic effects in the Quinazolinap series with a small set of ligands varied at the phosphorus atom[13] and also through the addition of an electron-withdrawing group to the backbone of the ligand.[14] We aimed to expand this group of electronically varied Quinazolinap ligands through the synthesis of a further subset. It was postulated that by varying the electronic nature of the substituent in the 2-position, we could alter the basicity of the donor nitrogen. We wished to investigate whether this variation of electronics at the nitrogen could improve the results possible with more sterically demanding and traditionally challenging substrates for hydroboration.

The first members of this new series to be prepared were the 2-(2-pyridyl)- and 2-(2-pyrazinyl)-variants **2a–b**. The synthesis and resolution of these ligands and their application in palladium-catalysed allylic alkylation have already been reported.[15] Herein we report the extension of this new series to include the 2-(*p*-trifluoromethylphenyl)- and 2-(*p*-methoxyphenyl)-Quinazolinap **3a–b**. These were designed to preclude the possibility of an extra donor nitrogen and so be more directly comparable to the results obtained previously with ligands **1a–f**, and ligand **1c** in particular. We report in detail on the synthesis and resolution of ligands **3a–b** and the application of ligands **2–3** in the rhodium-catalysed asymmetric hydroboration of a range of vinylarenes.

2. Results and discussion

2.1. Ligand synthesis

The synthesis of 2-(*p*-trifluoromethylphenyl)- and 2-(*p*-methoxyphenyl)-Quinazolinap, ligands **3a–b**, has been achieved using methodology based on that developed for other members of the Quinazolinap family.[4,16] This synthesis involved two metal-catalysed couplings, the biaryl coupling and the formation of the

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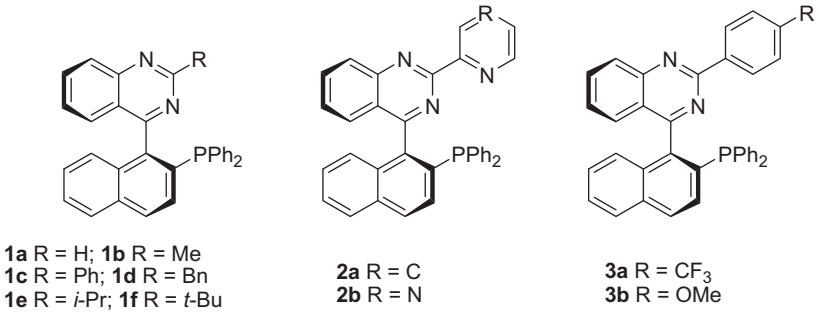


Figure 1. The Quinazolinap ligand series.

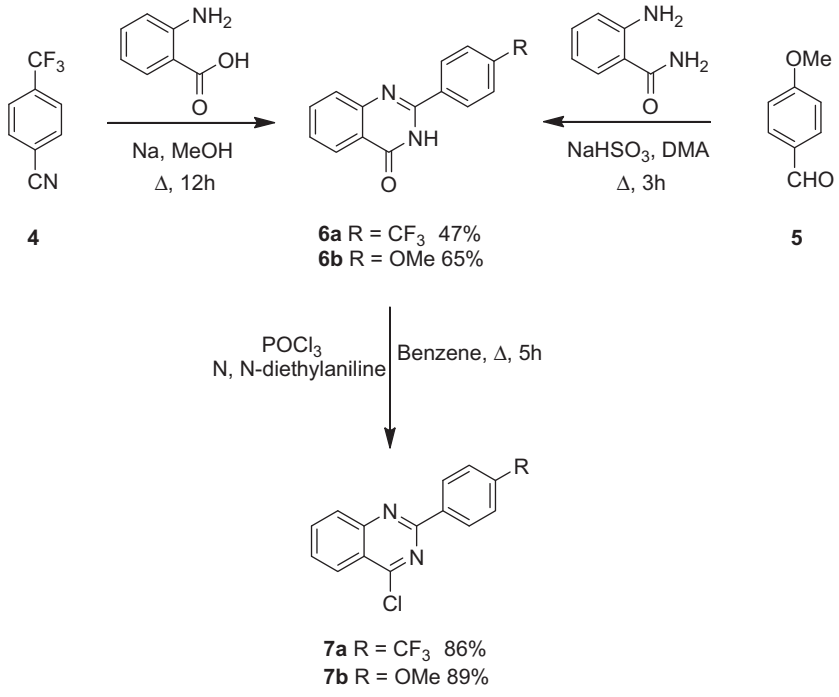
naphthyl-phosphorus bond, as the key steps. The weakness of this synthesis was a deprotection step involving BBr_3. This reagent was undesirable due to its toxicity and the step was characterised by relatively poor yields for a deprotection. The synthesis reported here for ligands **3a–b** avoids the use of this reagent through a change in the protecting group strategy.

The synthesis of substituted quinazolines has been the subject of considerable investigation[17] due to the diverse range of biological properties associated with this heterocycle.[18,19] 2-*p*-Trifluoromethylphenyl-4(3*H*)-quinazolinone **6a** was synthesised by the reaction of *p*-trifluorotolunitirile **4** with sodium methoxide and anthranilic acid to form the quinazolinone in a 47% yield (Scheme 1).[20] This approach was not suitable for the 2-*p*-methoxyphenyl analogue **6b** which was formed in a 65% yield by the reaction of *p*-anisaldehyde **5** with anthranilamide and sodium hydrogen sulfite.[21] Both of these ring-forming reactions could be easily performed on a medium to large scale (20–50 g). Phosphorus oxychloride was then used to convert the quinazolinones to 4-chloroquinazolines **7a–b** in good yield.

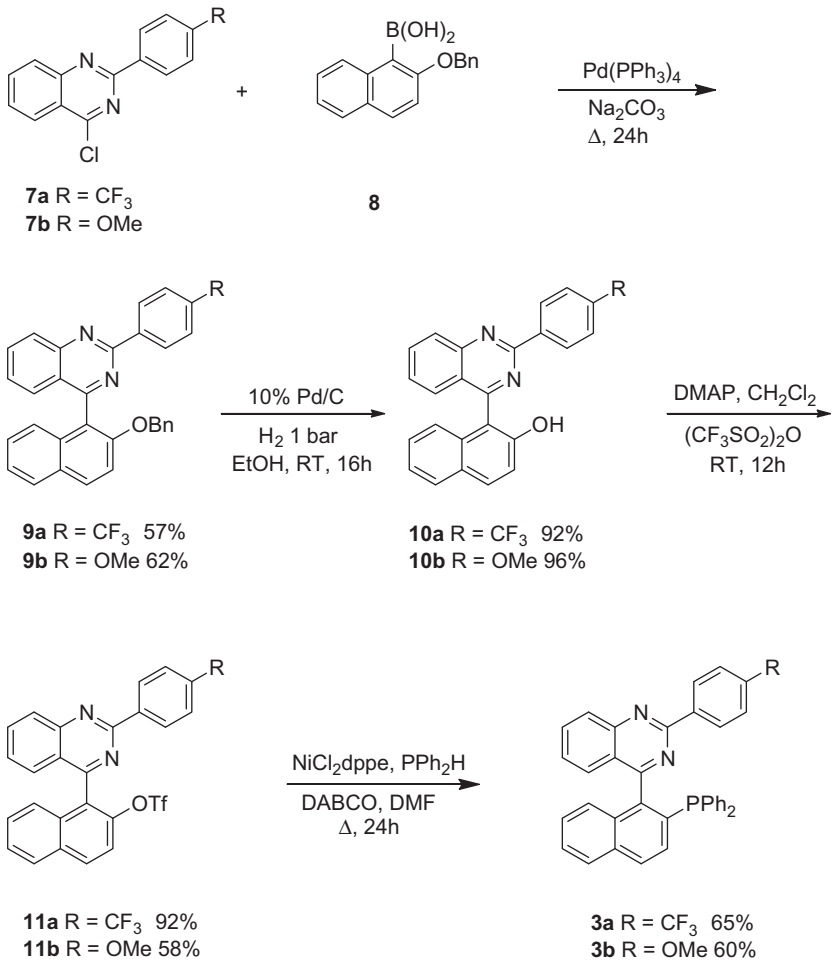
2-Benzyloxy-1-naphthylboronic acid **8** was chosen as the nucleophilic component of the Suzuki coupling as the benzyl ether can be removed cleanly in the presence of the methyl ether. This boronic acid was synthesised in three steps from 2-naphthol by the method of Spivey.[22] The Suzuki coupling was catalysed by 3 mol % tetrakis(triphenylphosphine)palladium and aqueous sodium carbonate was found to be the optimal base to afford the coupled biaryl in good yield (Scheme 2). Removal of the benzyl ether was achieved cleanly to form naphthols **10a–b** in excellent yields. The ease of removal of the benzyl group represents a significant improvement relative to the original Quinazolinap synthesis. Naphthols **10a–b** were then converted to trifluoromethanesulfonates **11a–b** by using the standard procedure of stirring with triflic anhydride and 4-dimethylaminopyridine in anhydrous dichloromethane.[23] The Ni-catalysed process developed by Cai was used to introduce the diphenylphosphino group in good yields (60–65%).[24] Hence, racemic 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a** and 2-(*p*-methoxyphenyl)-Quinazolinap **3b** were synthesised in good yield, from readily available starting materials, over six steps.

2.2. Ligand resolution

The formation of diastereomeric complexes with enantiopure palladium amine complexes is an important strategy in the resolu-



Scheme 1. Synthesis of 4-chloroquinazolines.



Scheme 2. Synthesis of racemic Quinazolinap ligands.

tion of phosphorus-containing ligands. The *ortho*-palladated derivative of (*R*)-dimethyl[1-(1-naphthyl)ethyl]amine has been used as the resolving agent for the resolution of QUINAP, PHENAP and previously synthesised members of the Quinazolinap ligand class.[23,25,4,15]

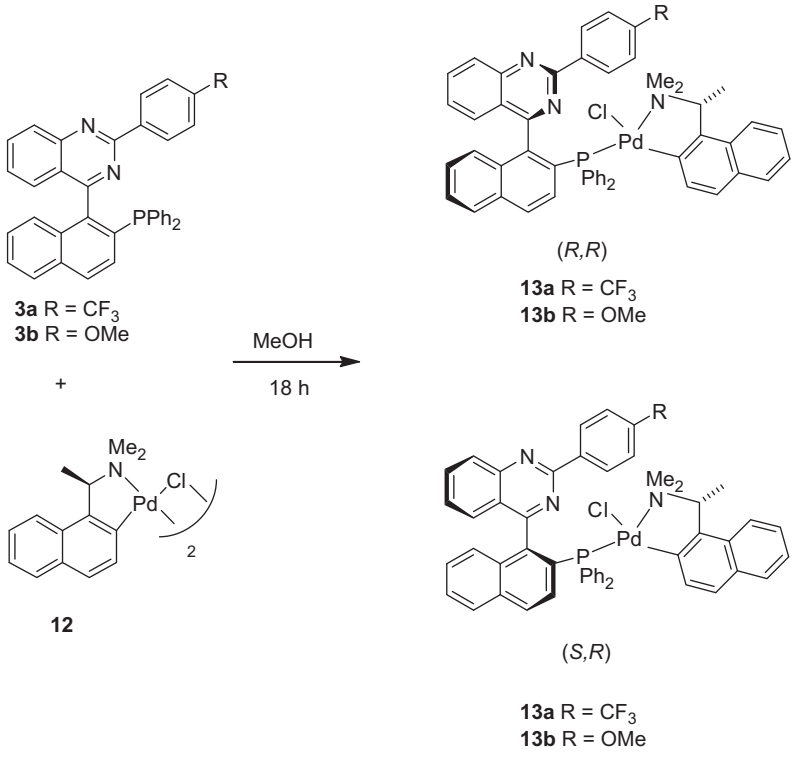
Therefore, racemic 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a** and (+)-di-μ-chlorobis((*R*)-dimethyl[1-(1-naphthyl)ethyl]aminato-C_2,N)dipalladium(II) **12** were stirred in a 2:1 ratio in methanol overnight (Scheme 3). The cream-coloured precipitate that formed was filtered and found by ^{1}H and ^{31}P NMR spectroscopy to be a single diastereomer. The benzylic methine of the isolated diastereomeric complex appeared as a multiplet at 4.18 ppm in the ^{1}H NMR spectrum and the phosphorus atom resonated at 42 ppm in the ^{31}P NMR spectrum. It was not possible to obtain crystals of this material suitable for X-ray crystallographic analysis. By redissolving the complex in methanol, however, and precipitating the cationic palladium complex **14** (Scheme 4) suitable crystals were obtained. By this method the diastereomerically pure material obtained was shown to be (*S*,*R*)-**13a**.

Crystals of (*S*,*R*)-**14** suitable for single-crystal X-ray structure determination were grown from $CDCl_3$/pentane (Fig. 2). In the crystal (*S*,*R*)-**14** adopts a conformation in which the 2-position of the 2-(*p*-trifluoromethylphenyl) substituent of the Quinazolinap ligand (C-10) closely approaches the Pd atom [Pd···C10 3.048(2) Å]. The Pd atom is not planar coordinated and the P1–Pd–N3 angle at 157.3(1)° is significantly smaller than the almost linear N-1–Pd–C-39 angle [173.6(1)°] indicating a weak C–H···Pd intramolecular interaction between the H atom on C-10 of the 2-(*p*-trifluoromethylphenyl) substituent on the quinazolinap ligand and the cationic metal centre, though steric effects cannot be ruled out.[15]

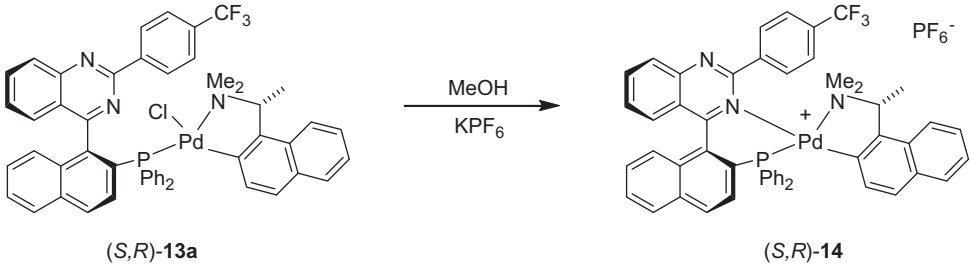
The cream-coloured precipitate which was formed when racemic ligand **3b** was employed was a 3:1 mixture of diastereomers. Fractional crystallisation using hot butanone/pentane afforded diastereomerically pure (*S*,*R*)-**13b**. The ^{1}H NMR spectrum shows the benzylic methine as a multiplet at 4.21 ppm while in ^{31}P NMR spectrum the phosphorus atom resonated at 44 ppm. To date no X-ray crystallographic analysis of this complex has been obtained; the configuration quoted has been deduced based on specific rotation values of decomplexed ligand and results obtained in catalysis and comparison with previously studied members of the Quinazolinap ligand class whose configurations have been unambiguously determined.[4]

It was also possible to isolate diastereomically pure (*R*,*R*)-**13b**, by recrystallisation of the filtrate using methanol. In this case, the ^{1}H NMR spectrum shows the benzylic methine as multiplet at 4.09 ppm while in ^{31}P NMR spectrum the phosphorus atom appears at 39 ppm.

Enantiomerically pure 2-(*p*-trifluoromethylphenyl)-Quinazolinap and 2-(*p*-methoxyphenyl)-Quinazolinap were readily obtained by decomplexation of the resolved diastereomers with 1,2-bis(diphenylphosphino)ethane in dichloromethane (Scheme 5). The specific rotation $[\alpha]_D$ was found to be +40.9 in $CHCl_3$ for (*S*)-2-(*p*-trifluoromethylphenyl)-Quinazolinap and +38.0 in $CHCl_3$ for (*S*)-2-(*p*-methoxyphenyl)-Quinazolinap, lending further weight to the assignment of diastereomer (*S*,*R*)-**13b**.



Scheme 3. Formation of diastereomeric monodentate ligand-palladium complexes.



Scheme 4. Formation of bidentate ligand-palladium complex.

2.3. Rhodium-catalysed hydroboration

Rhodium-catalysed enantioselective hydroboration of olefins is a valuable synthetic transformation, typically employing a chiral catalyst and an achiral borane source.[26,27] Diphosphine ligands were the first to be employed in this transformation; Burgess developed an enantioselective hydroboration process using BINAP- and DIOP-derived rhodium species with norbornene as the substrate.[28] Phosphinamine ligands have also been successfully employed in rhodium-catalysed asymmetric hydroboration. Brown has used the QUINAP and PHENAP ligands,[29,30] while Togni has applied ferrocenyl pyrazole ligands,[31] both with great success. Within our research group the Quinazolinap series of ligands (**1a–f**) have previously been applied in asymmetric rhodium-catalysed hydroboration. The Quinazolinap catalysts were found to be extremely active, giving excellent conversions, good to complete regioselectivities and the highest enantioselectivities obtained to date for several members of the vinylarene class, including *cis*-β-methylstyrene (97%), *cis*-stilbene (99%) and indene (99.5%).[4,32] Following the success of the application of this steric series of the Quinazolinaps, we now wish to report the application of the related electronic series of ligands **3a–b** to asymmetric rhodium-catalysed hydroboration, in order to study the potential electronic effects in this series.

The cationic rhodium catalysts were prepared in situ (Scheme 6). A range of vinylarenes and the cyclic olefins indene and 1,2-dihydronapathelene (Fig. 3) were screened as substrates in hydroborations using rhodium-Quinazolinap complexes **15a–d** as the active catalysts. Results obtained previously with 2-phenyl-Quinazolinap are included for comparative purposes as this has the same steric requirements as the 2-pyridyl and 2-(2-pyrazinyl)-Quinazolinap ligands. In addition, selected optimal results from our previous hydroboration work with 2-alkyl-substituted Quinazolinaps will be given to aid in determining whether the effects noted with ligands **2a–b** and **3a–b** can be attributed to size or electronics.

Catalysts **15a–d** were first applied in the rhodium-catalysed hydroboration of styrene **16** (Table 1). In this, and all subsequent catalytic reactions, 1 mol % of the active catalyst was used. The reactions were carried out at both room temperature and 0 °C and the reaction mixture was oxidised after the required reaction time. After work up the conversion and regioselectivity were determined by ^{1}H NMR spectroscopy and the enantiomeric excess was calculated using either chiral GC or HPLC.

Both the 2-(*p*-trifluoromethylphenyl)- and 2-(*p*-methoxyphenyl)-Quinazolinap ligands **3a–b** gave significantly better regioselectivities and enantioselectivities than 2-phenyl-Quinazolinap **1c** at

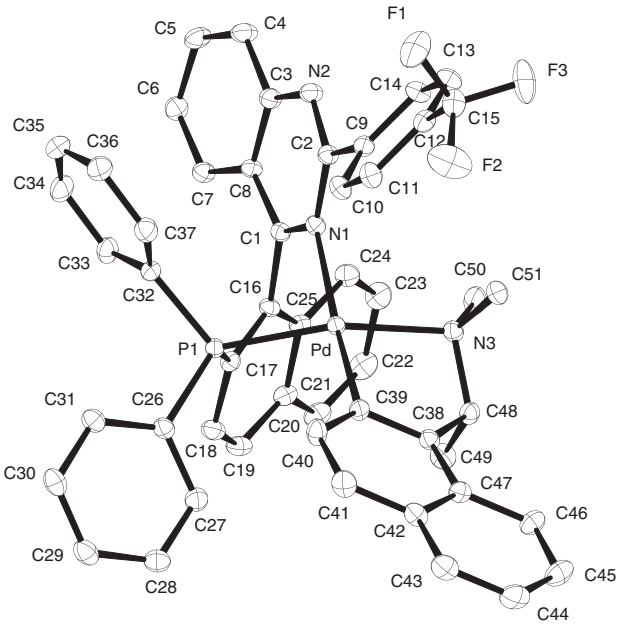


Figure 2. X-ray structure of (*S*,*R*)-**14** (H atoms and $CDCl_3$ solute have been removed for clarity). Selected distances (Å) and angles (°): Pd–P1 2.2608(5), Pd–N1 2.178(2), Pd–N3 2.140(2), Pd–C39 1.995(2), Pd···C10 3.048(2), P1–Pd–N1 84.0(1), P1–Pd–N3 157.3(1), N1–Pd–C39 173.6(1).

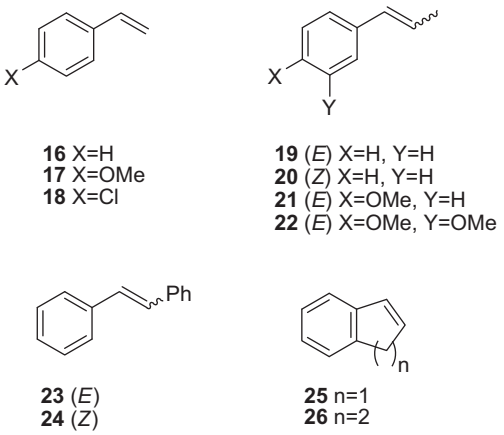
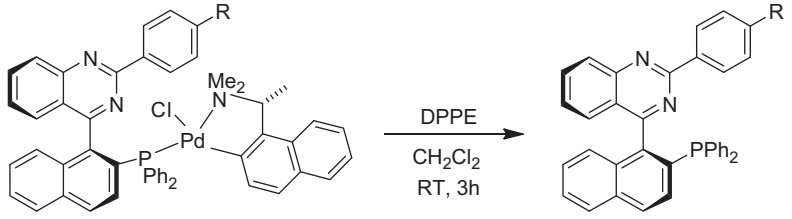


Figure 3. Substrates screened in rhodium-catalysed hydroboration.

room temperature (entries 1, 3 and 6). In particular the 2-(*p*-methoxyphenyl) analogue gave an excellent 90% ee, identical to the previously optimised ee using the 2-methyl-Quinazolinap ligand (entry 7).[4] At 0 °C the reactivity (and selectivity) of the 2-(*p*-trifluoromethylphenyl) ligand **3a** dropped dramatically (entry 2). The conversion was low (35%) and the regioselectivity showed that more of the β- than the α-product had been formed. A ligand-free reaction carried out at 0 °C gave a similar conversion of 30% and regioselectivity of 34:66.

In the hydroboration of *p*-methoxystyrene **17** using rhodium-Quinazolinap catalysts **1a–f**, it was observed that an electron-donating substituent on styrene had a favourable effect on the enantioselectivity, often accompanied by a negative effect on the regioselectivity.[4] The application of electronically varied Quinazolinap ligands **3a**–**b** in the hydroboration of this substrate showed a similar trend (Table 2).

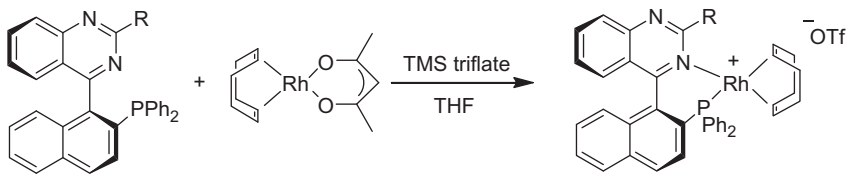
Catalysts derived from 2-(2-pyridyl)- and 2-(2-pyrazinyl)-Quinazolinap **2a–b** produced enantiomeric excesses of 77% and 80%, respectively (Table 2, entries 1 and 3). Although the regiochemistry observed was lower than the excellent results obtained for styrene, the use of these catalysts gave the highest regioselectivities (88:12) for the Quinazolinap series in the hydroboration of substrate **17**. Both 2-(*p*-trifluoromethylphenyl)- and 2-(*p*-methoxyphenyl)-Quinazolinap **3a–b** achieved excellent results at room temperature (entries 5 and 7). Enantioselectivities of 92% and 94%, respectively,



13a R = CF_3
13b R = OMe

(*S*)-**3a** R = CF_3
(*S*)-**3b** R = OMe

Scheme 5. Decomplexation of enantiopure ligands **3a**–**b**.

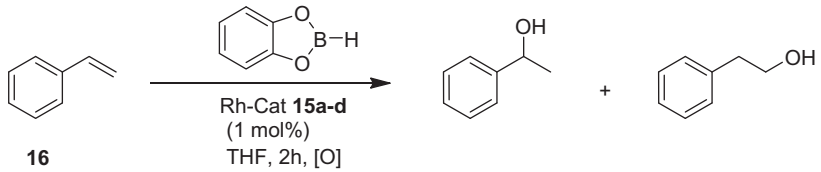


2a R = 2-(2-pyridyl)
2b R = 2-(2-pyrazinyl)
3a R = *p*-$CF_3C_6H_4$
3b R = *p*-$MeOC_6H_4$

15a R = 2-(2-pyridyl)
15b R = 2-(2-pyrazinyl)
15c R = *p*-$CF_3C_6H_4$
15d R = *p*-$MeOC_6H_4$

Scheme 6. Formation of Quinazolinap rhodium-catalysts.

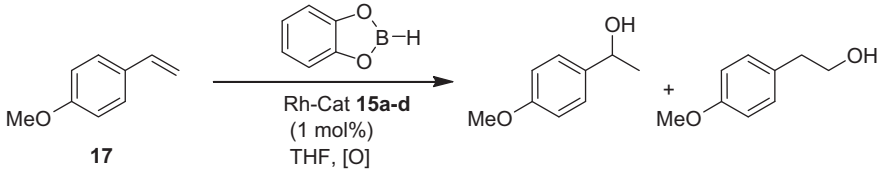
Table 1
Hydroboration of styrene



16

Entry	2-Substituent	Temp (°C)	Conv. (%)	α:β	ee (%)
1	*p*-Trifluoromethylphenyl	20	93	85:15	82 (*S*)
2	*p*-Trifluoromethylphenyl	0	35	45:55	14 (*S*)
3	*p*-Methoxyphenyl	20	97	89:11	90 (*S*)
4	*p*-Methoxyphenyl	0	80	85:15	84 (*S*)
5[32]	Phenyl	20	100	68:32	63 (*S*)
6[32]	Phenyl	0	100	80:20	89 (*S*)
7[4]	Methyl	20	100	88:12	90 (*S*)

Table 2
Hydroboration of *p*-methoxystyrene



17

Entry	2-Substituent	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyridyl	20	83	87:13	77 (*S*)
2	2-Pyridyl	0	33	74:26	66 (*S*)
3	2-Pyrazinyl	20	99	88:12	80 (*R*)
4	2-Pyrazinyl	0	81	86:14	52 (*R*)
5	*p*-Trifluoromethylphenyl	20	92	79:21	92 (*S*)
6	*p*-Trifluoromethylphenyl	0	15	52:48	20 (*S*)
7	*p*-Methoxyphenyl	20	91	82:18	94 (*S*)
8	*p*-Methoxyphenyl	0	48	65:35	74 (*S*)
9[32]	Phenyl	20	100	75:25	77 (*S*)
10[32]	Phenyl	0	100	77:23	81 (*S*)
11[4]	Methyl	20	99	88:12	95 (*S*)

were significantly higher than the comparable result for the 22-phenyl ligand **1c** (entry 9), but slightly lower than the previously optimised ee of 95% using the 2-methyl-Quinazolinap ligand (entry 11).[4] The regioselectivity was also higher for both these ligands in comparison with that of the 2-phenyl ligand. As with the results obtained for styrene, 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a** showed a dramatic drop in activity at 0 °C.

The hydroboration of *p*-chlorostyrene **18** using catalysts **15a,b,c** gave relatively low conversions, regioselectivities and enantioselectivities at room temperature. The use of 2-(2-pyridyl)- and 2-(2-pyrazinyl)-Quinazolinap **2a–b** as ligands was found to decrease the enantioselectivity of styrene from 74% and 83% to 28% and 59% (Table 3, entries 1 and 3), respectively. The other electron-deficient ligand system 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a** also showed a drop in the enantioselectivity to 54% (entry 5). In comparison, the 2-(*p*-methoxyphenyl) analogue **3b** gave one of the best results obtained for the Quinazolinap ligand series in the hydroboration of this substrate. An enantioselectivity of 80% was accompanied by an excellent regiochemistry of 92:8 with a moderate conversion of 75% (entry 7). This compares to the previous 81% ee value obtained using the unsubstituted Quinazolinap ligand (entry 11).[4] As 2-phenyl-Quinazolinap **1c** itself achieved poor enantioselectivity in this reaction (entries 9 and 10), the addition of the *p*-methoxy group to the ligand has an important effect on the ee. As seen previously, 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a** showed a drop in the activity at 0 °C, mainly manifested as a large drop in enantioselectivity.

Substitution of the vinylarene double bond resulted in a marked reduction in the enantioselectivity obtained with BINAP and other diphosphines.[26,27] In contrast, the application of P,N-ligand systems to more sterically demanding substrates leads to an overall increase in enantioselection. The Quinazolinap ligands have been successful in the hydroboration of this type of substrate, giving ees up to 95% in the hydroboration of *trans*-β-methylstyrene **19**. The 2-phenyl analogue gave one of the best results at room temperature; enantioselectivity of 94% combined with full conversion and a regioselectivity of 91:9 (Table 4, entry 9). In comparison with this result, our electronic series of catalysts **15a–d** show significantly reduced activity. Catalyst **15a**, derived from 2-(2-pyridyl)-Quinazolinap **2a**, showed no activity at all in this reaction (entries 1 and 2). Although the regioselectivity using catalyst **15b**, based on 2-(2-pyrazinyl)-Quinazolinap **2b**, was the highest obtained with any of the Quinazolinap ligands, it was combined with low conversion and a maximum ee of 90% at 0 °C (entries 2 and 3). Catalyst **15c**, based on 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a**, gave a comparable ee and regioselectivity to those obtained using 2-phenyl-Quinazolinap **1c** but with a conversion of 71% (entry 5). Catalyst **15d**, based on 2-(*p*-methoxyphenyl)-Quinazolinap **3b**, also gave an enantioselectivity of 94% at both room temperature and 0 °C (entries 7 and 8), though with lower conversion and regiose-

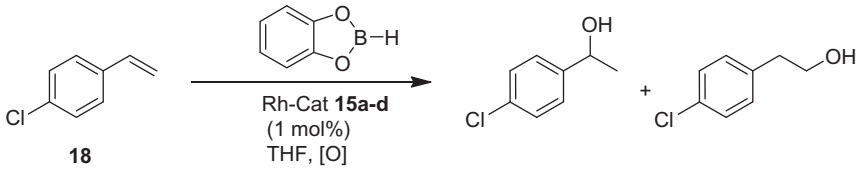
lectivity than the parent 2-phenyl-Quinazolinap and slightly lower than our optimised ee value of 95% using the 2-methyl-Quinazolinap ligand (entry 11).[4]

Quinazolinap catalysts have previously given excellent results in the hydroboration of *cis*-β-methylstyrene **20**, for example 2-phenyl-Quinazolinap **1c** gave full conversion and excellent regio- and enantioselectivity after 2 h at both room temperature and 0 °C (Table 5, entries 8 and 9) and the 2-methyl-Quinazolinap ligand gave an ee value of 97% (entry 10).[4] In contrast the results obtained for our series of electronically modified ligands are characterised by low conversion to the hydroborated products accompanied by a relatively high degree of isomerisation to *trans*-β-methylstyrene. Catalyst **15a** showed only a trace amount of the product alcohol and a high level of isomeristation (entry 1). In all catalyst systems **15a–d**, the degree of isomerisation was higher than the conversion to alcohol product. A potential explanation for these results may be that, following olefin association and migratory insertion, instead of reductive elimination to generate the organoborane product, the reaction proceeds via rotation about the carbon–carbon bond (likely as a response to steric demand); subsequent β-hydride elimination and dissociation would produce *trans*-β-methylstyrene. As minimal hydroboration product was obtained, it could be inferred that the reductive elimination route followed during the reaction of simpler styrenes proceeds at a much slower rate when bulkier substrates are employed.

The stereochemistry of the alkene in *trans*-anethole **21** seems to have a significant effect on the conversion, similar to that observed for the hydroboration of *trans*-β-methylstyrene **19**, when rhodium-Quinazolinap complexes are used as catalysts. Even the usually very active 2-phenyl-Quinazolinap catalyst showed decreased conversion. Despite the poor conversion, complex **15b**, based on 2-(2-pyrazinyl)-Quinazolinap, gave the best regioselectivity observed with any of the Quinazolinap catalysts and also an excellent ee of 93% (Table 6, entry 1). 2-(*p*-Trifluoromethylphenyl)- and 2-(*p*-methoxyphenyl)-Quinazolinap **3a–b** gave consistently high enantioselectivity though the regioselectivity was modest (entries 3–5) and still below the optimal ee value of 975 obtained with the 2-methyl-Quinazolinap ligand (entry 8).[4] All conversions for these electronically modified ligands are lower than that obtained for the comparable 2-phenyl-Quinazolinap **1c**, though the ee has been improved in all cases at room temperature.

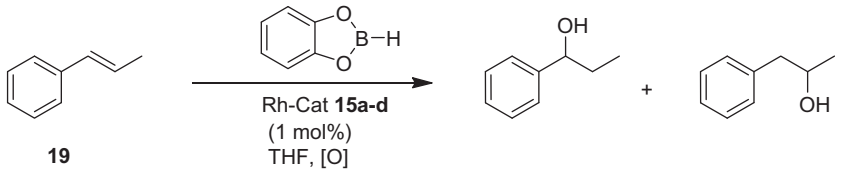
As expected, the stereochemistry of the alkene in *trans*-3,4-dimethoxy-β-methylstyrene **22** also had a detrimental effect on the conversion. 2-(2-Pyrazinyl)-Quinazolinap **3b** was the exception

Table 3
Hydroboration of *p*-chlorostyrene



Entry	2-Substituent	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyridyl	20	73	71:29	28 (*S*)
2	2-Pyridyl	0	62	70:30	18 (*S*)
3	2-Pyrazinyl	20	99	85:15	59 (*S*)
4	2-Pyrazinyl	0	81	87:13	52 (*S*)
5	*p*-Trifluoromethylphenyl	20	97	74:26	54 (*S*)
6	*p*-Trifluoromethylphenyl	0	46	75:25	4 (*S*)
7	*p*-Methoxyphenyl	20	75	92:8	80 (*S*)
8	*p*-Methoxyphenyl	0	76	67:33	50 (*S*)
9[32]	Phenyl	20	100	78:22	46 (*S*)
10[32]	Phenyl	0	100	83:17	49 (*S*)
11[4]	H	20	100	83:17	81 (*S*)

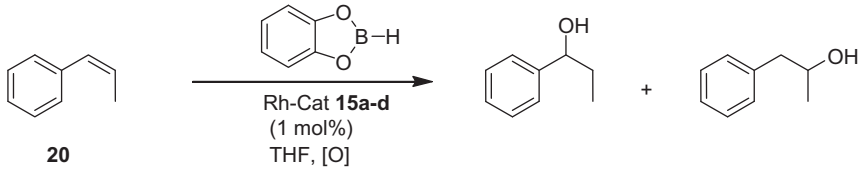
Table 4
Hydroboration of *trans*-β-methylstyrene



Entry	2-Substituent	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyridyl	20	0	—	—
2	2-Pyridyl	0	0	—	—
3	2-Pyrazinyl	20	23	99:1	77 (*S*)
4	2-Pyrazinyl	0	50	99:1	90 (*S*)
5	*p*-Trifluoromethylphenyl	20	71	89:12	94 (*S*)
6	*p*-Trifluoromethylphenyl	0	22	22:78	48 (*S*)
7	*p*-Methoxyphenyl	20	89	84:16	94 (*S*)
8	*p*-Methoxyphenyl	0	49	44:56	94 (*S*)
9[32]	Phenyl	20	100	91:9	94 (*S*)
10[32]	Phenyl	0	100	96:4	85 (*S*)
11[4]	Methyl	0	96	94:6	95 (*S*)

to this observation; it gave excellent conversion after 2 h at both room temperature and 0 °C (Table 7, entries 1 and 2). In comparison with the results obtained for *trans*-anethole **21**, regioselectivity also improved generally; perhaps has a result of the substitution pattern on the phenyl ring of the substrate. The enantioselectivities obtained with 2-(*p*-trifluoromethylphenyl)- and 2-(*p*-methoxy-

Table 5
Hydroboration of *cis*-β-methylstyrene

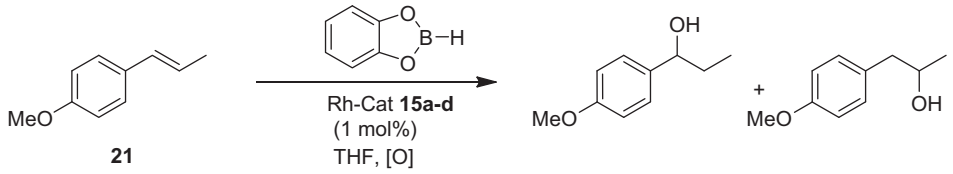


20

Entry	2-Substituent	Temp (°C)	Conv. (%)	*cis:trans*[a]	α:β	ee (%)
1	2-Pyridyl	20	<1	34:66	—	—
2	2-Pyrazinyl	20	18	46:54	68:32	64 (*S*)
3	2-Pyrazinyl	0	5	79:21	86:14	40 (*S*)
4	*p*-Trifluoromethylphenyl	20	11	53:47	85:15	60 (*S*)
5	*p*-Trifluoromethylphenyl	0	3	92:8	55:45	0
6	*p*-Methoxyphenyl	20	12	75:25	55:45	94 (*S*)
7	*p*-Methoxyphenyl	0	6	81:19	62:38	48 (*S*)
8[32]	Phenyl	20	100	—	92:8	91 (*S*)
9[32]	Phenyl	0	100	—	94:6	88 (*S*)
10[4]	Methyl	0	100	—	99:1	97 (*S*)

[a] Ratio of *cis:trans* β-methylstyrene after 2 h reaction.

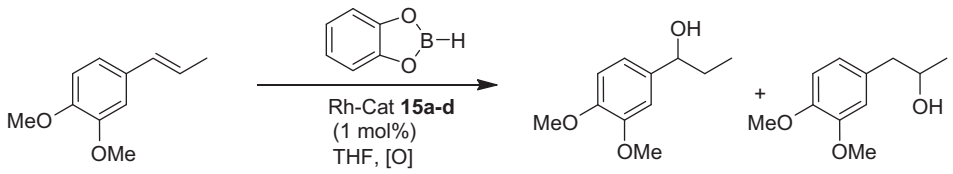
Table 6
Hydroboration of *trans*-anethole



21

Entry	2-Substituent	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyrazinyl	20	52	96:4	93 (*S*)
2	2-Pyrazinyl	0	68	97:3	86 (*S*)
3	*p*-Trifluoromethylphenyl	20	66	79:21	94 (*S*)
4	*p*-Methoxyphenyl	20	63	80:20	93 (*S*)
5	*p*-Methoxyphenyl	0	52	79:21	94 (*S*)
6[32]	Phenyl	20	87	88:12	88 (*S*)
7[32]	Phenyl	0	72	89:11	92 (*S*)
8[4]	Methyl	0	100	99:1	97 (*S*)

Table 7
Hydroboration of *trans*-3,4-dimethoxy-β-methylstyrene



22

Entry	2-Substituent	Time	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyrazinyl	2	20	94	97:3	85 (*S*)
2	2-Pyrazinyl	2	0	88	98:2	85 (*S*)
3	*p*-Trifluoromethylphenyl	2	20	58	74:26	94 (*S*)
4	*p*-Methoxyphenyl	2	20	64	83:17	96 (*S*)
5	*p*-Methoxyphenyl	2	0	37	43:57	94 (*S*)
6[32]	Phenyl	2	20	62	93:7	94 (*S*)
7[32]	Phenyl	24	0	65	92:8	93 (*S*)
8[4]	Methyl	2	0	75	92:8	98 (*S*)

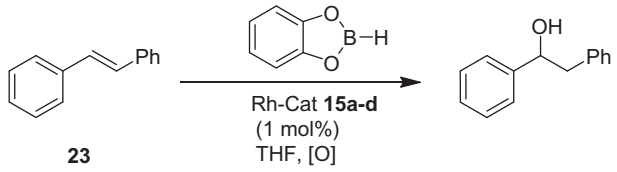
phenyl)-Quinazolinap **3a–b** (entries 3–5) were consistently very high (94–96%) and comparable with 2-phenyl-Quinazolinap **1c** and slightly lower than the 98% ee obtained with the 2-methyl-Quinazolinap ligand (entry 8).[4]

The hydroboration of *trans*-stilbene **23** is significantly hindered by its steric bulk. In previous studies with Quinazolinap ligands reaction times of 24 h were needed to obtain conversions over 10%. In the present study, the 2-(*p*-methoxyphenyl)-Quinazolinap-based catalyst **15d** gave an excellent ee of 92% and a conversion of 34% after 24 h at room temperature (Table 8, entry 5). Using 2-(*p*-trifluoromethylphenyl)-Quinazolinap **3a** as the ligand also gave a similar conversion and a slightly lower ee of 88% after 24 h (entry 3). In comparison the 2-phenyl-Quinazolinap ligand system **1c** showed no conversion after 24 h at room temperature (entry 6) and the less sterically encumbered 2-methyl-Quinazolinap afforded 87% ee (entry 7).[4] 2-(2-Pyrazinyl)-Quinazolinap **2b** was also not active in this reaction.

In comparison with the *trans* isomer, the hydroboration of *cis*-stilbene **24** usually occurs rapidly at room temperature in the presence of rhodium-Quinazolinap catalysts. In the present study it was found that the electronically modified ligands **2b** and **3a–b** gave significantly lower conversions than those obtained with the steric series **1a–f**, although the ees ranged from very good to excellent. In particular, the use of the 2-(*p*-methoxyphenyl)-Quinazolinap-based rhodium-catalyst **15d** resulted in 97% ee after 2 h at room temperature (Table 9, entry 5), still lower than the optimal value of 99% ee obtained using the 2-isopropyl-Quinazolinap ligand (entry 9).[4] The conversion obtained was low (23%), however, and a large proportion of the unreacted starting material had been isomerised to the *trans*-isomer. The enantioselectivities obtained with all electronically varied ligands **2–3** (entries 1–6) were significantly higher than that obtained with 2-phenyl-Quinazolinap **1c** (57% ee), although in that case full conversion was obtained (entry 7). The rhodium-Quinazolinap catalysts **15a**,**c**,**d** applied in this reaction showed a degree of isomerisation to the *trans*-isomer of the starting material. The same mechanism as that postulated for the isomerisation of *cis*-β-methylstyrene is proposed.

The final part of this study looked at the hydroboration of the cyclic olefins indene **25** and 1,2-dihydronaphthalene **26**. It is with this type of substrate that Quinazolinap ligands have previously proved very successful. From previous investigations it has been shown that the size of the group in the 2-position of the ligand is particularly important when indene **25** is tested. The size of 2-phenyl-Quinazolinap means that it gave an enantioselectivity of 84% at room temperature in this reaction (Table 10, entry 9); this is a significant decrease from the 2-methyl analogue **1b** which gave an ee

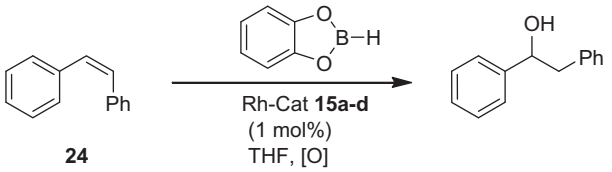
Table 8
Hydroboration of *trans*-stilbene



23

Entry	2-Substituent	Time	Temp (°C)	Conv (%)	ee (%)
1	2-Pyrazinyl	24	20	0	—
2	*p*-Trifluoromethylphenyl	2	20	7	81 (*S*)
3	*p*-Trifluoromethylphenyl	24	20	33	88 (*S*)
4	*p*-Methoxyphenyl	2	20	<5	—
5	*p*-Methoxyphenyl	24	20	34	92 (*S*)
6[32]	Phenyl	24	20	0	—
7[4]	Methyl	21	20	50	87 (*S*)

Table 9
Hydroboration of *cis*-stilbene

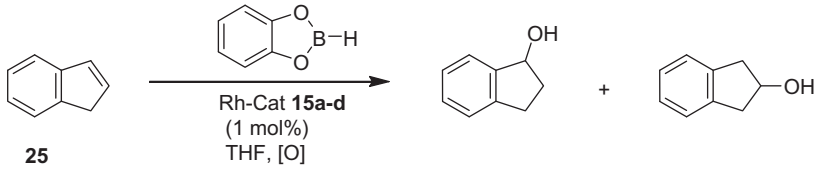


24

Entry	2-Substituent	Time	Temp (°C)	Conv. (%)	*cis:trans*[a]	ee (%)
1	2-Pyrazinyl	2	20	40	44:56	87 (*S*)
2	2-Pyrazinyl	2	0	35	63:37	92 (*S*)
3	*p*-Trifluoromethylphenyl	2	20	12	59:41	92 (*S*)
4	*p*-Trifluoromethylphenyl	24	20	61	0:100	83 (*S*)
5	*p*-Methoxyphenyl	2	20	23	32:68	97 (*S*)
6	*p*-Methoxyphenyl	2	0	6	84:16	97 (*S*)
7[32]	Phenyl	2	20	100	—	59 (*S*)
8[32]	Phenyl	2	0	100	—	62 (*S*)
9[4]	*i*-Propyl	2	20	84	—	99 (*S*)

[a] Ratio of *cis:trans* β-methylstyrene after reaction time.

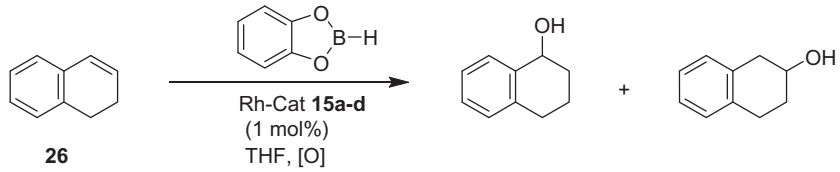
Table 10
Hydroboration of indene



25

Entry	2-Substituent	Time	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyridyl	20	20	81	96:4	84 (*S*)
2	2-Pyridyl	20	0	38	95:5	80 (*S*)
3	2-Pyrazinyl	2	20	81	>99:1	70 (*S*)
4	2-Pyrazinyl	2	0	25	>99:1	73 (*S*)
5	*p*-Trifluoromethylphenyl	2	20	83	99:1	87 (*S*)
6	*p*-Trifluoromethylphenyl	24	0	9	100:0	—
7	*p*-Methoxyphenyl	2	20	60	99:1	82 (*S*)
8	*p*-Methoxyphenyl	24	0	81	59:41	54 (*S*)
9[32]	Phenyl	2	20	98	98:2	84 (*S*)
10[32]	Phenyl	2	0	99	98:2	81 (*S*)
11[4]	Methyl	2	20	100	>99:1	99.5 (*S*)

Table 11
Hydroboration of 1, 2-dihydronaphthalene



26

Entry	2-Substituent	Time	Temp (°C)	Conv. (%)	α:β	ee (%)
1	2-Pyrazinyl	2	20	77	>99:1	90 (*S*)
2	2-Pyrazinyl	2	0	76	>99:1	91 (*S*)
3	*p*-Trifluoromethylphenyl	2	20	56	>99:1	87 (*S*)
4	*p*-Trifluoromethylphenyl	24	0	<5	>99:1	—
5	*p*-Methoxyphenyl	2	20	76	>99:1	91 (*S*)
6	*p*-Methoxyphenyl	2	0	8	>99:1	78 (*S*)
7[32]	Phenyl	2	20	100	>99:1	89 (*S*)
8[32]	Phenyl	2	0	>99	>99:1	88 (*S*)
9[4]	Methyl	2	20	90	>99:1	93 (*S*)

of 99.5% (entry 11).[4] The enantioselectivities and regioselectivities obtained for electronically varied catalysts **15a–d** at room temperature are quite similar to those obtained for the 2-phenyl-ligand **1c** and show the importance of the size of the ligand rather than electronic effects for the hydroboration of this substrate. The major differences are the activity of the catalyst systems. The 2-(2-pyridyl)-Quinazolinap rhodium-catalyst **15a** showed no reaction after 2 h and only after 20 h were comparable results obtained (entries 1 and 2). A significant decrease in the conversion was seen for catalysts **15a–c** at 0 °C (entries 2, 4 and 6) though the enantioselectivities were not affected. Like all members of the Quinazolinap ligand class these new ligands gave excellent regioselectivities in the hydroboration of this substrate at room temperature.

In the hydroboration of 1,2-dihydronaphthalene **26**, excellent regioselectivities have been generated by all members of the Quinazolinap family. The highest enantioselectivity (93%) was obtained previously using 2-methyl analogue **1b** (entry 9).[4] In the present study this was closely followed by 2-(2-pyrazinyl)-Quinazolinap and 2-(*p*-methoxyphenyl)-Quinazolinap at 91% (Table 11, entries 2 and 5). Lowering the reaction temperature led to an unexpected reduction in conversion when using the 2-(*p*-methoxyphenyl)-Quinazolinap rhodium-catalyst **15b** (entry 6), though this was not seen for 2-(2-pyrazinyl)-Quinazolinap **2b** or 2-phenyl-Quinazolinap **1c** (entries 2 and 8).

3. Conclusion

In conclusion, new Quinazolinap ligands have been synthesised as part of an electronic series of ligands. These ligands have been applied in the enantioselective hydroboration of substituted styrenes with the aim of studying electronic effects in this reaction. Conversions with the electronically varied ligands tended to be lower than that achieved with the comparable 2-phenyl ligand. 2-(2-Pyridyl)-Quinazolinap proved capable of hydroborating simple styrene derivatives only. In contrast 2-(2-pyrazinyl)-Quinazolinap was successful in hydroborating all but one of the substrates tested, with regioselectivities which were almost always superior to those obtained using the earlier members of the Quinazolinap series. The optimum enantioselectivity obtained for this ligand was 93%, in the hydroboration of *trans*-anethole. The strong electron-withdrawing effect of the 2-(*p*-trifluoromethylphenyl) ligand seemed to affect the activity of the catalyst system at 0 °C, with decreases observed in conversion, regioselectivity and enantioselectivity. The similarity of these results with those obtained when no ligand is used in the reaction seems to suggest that the electron-poor nitrogen donor atom is not binding properly to the metal at 0 °C. The use of 2-(*p*-methoxyphenyl)-Quinazolinap as the ligand gave one of the best results obtained for the Quinazolinap ligand series in the hydroboration of *p*-chlorostyrene (80% ee), which was also accompanied by excellent regioselectivity (92:8). In comparison the other ligands tested in this study produced a maximum of 59% ee. The relatively electron-rich nitrogen donor atom of ligand **3b** seems to have a positive effect on the reaction of what is often seen as a challenging substrate for hydroboration. 2-(*p*-Methoxyphenyl)-Quinazolinap also gave consistently high enantioselectivities, mainly between 90% and 97% ee.

From this study of the electronically varied Quinazolinap ligands it does seem that the introduction of an electron-withdrawing substituent can result in an improvement in regioselection. The size of the substituent in the 2-position of the Quinazolinap ligand seems to have more of an impact on certain types of substrate, particularly cyclic olefins. The introduction of an electron-donating group in the 2-position resulted in a Quinazolinap ligand that gave some of the most consistently high enantioselectivities seen in this series, although still consistently lower than those obtained with the 2-methyl-Quinazolinap ligand. Further investigation into the Quinazolinap ligand series continues and the results of this research will be reported in due course.

4. Experimental

4.1. General remarks

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. ^{1}H NMR spectra and ^{1}H–^{1}H COSY spectra were recorded on a 300 MHz Varian-Unity spectrometer, a 400 MHz Varian-Unity spectrometer. Chemical shifts are quoted in parts per million (ppm) relative to tetramethylsilane and coupling constants (*J*) are quoted in hertz and are uncorrected. 75.4 MHz ^{13}C spectra were recorded on a 300 MHz Varian-Unity spectrometer and 100 MHz ^{13}C spectra on a 400 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 162 MHz ^{31}P spectra on a 400 MHz Varian-Unity spectrometer. ^{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). Merck precoated Kieselgel 60F_{254} was used for thin layer chromatography. GC and HPLC analysis was carried out using a Supelco 2-4304 beta-Dex® 120 (30 × 0.25 mm, 0.25 mm film) and a Chiralcel OD column (0.46 cm I.D. × 25 cm), respectively. Optical rotation values were measured on a 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 used were purified according to the procedures in 'Purification of Laboratory Chemicals'.[33] 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.

4.1.1. 2-*p*-Trifluoromethylphenyl-4(3*H*)quinazolinone 6a

α,α,α-Trifluoro-*p*-tolunitrile (50.00 g, 292 mmol) was dissolved in dry methanol (285 mL) under nitrogen. To this solution sodium metal (1.22 g, 53 mmol) was added carefully in several portions. Once addition was complete, the solution was stirred for 1 h. Anthranilic acid (36.43 g, 265 mmol) in dry methanol (285 mL) was added via cannula. The solution was then refluxed overnight. The cream-coloured precipitate that formed was filtered, washed with cold methanol and dried under vacuum to afford 2-*p*-trifluoromethylphenyl-4(3*H*)quinazolinone (40.96 g, 45%) as a cream solid. For analysis, a sample was recrystallised from ethanol to yield white needles, mp 310–312 °C (lit. mp 306–308 °C); ν_{max} (KBr) 3311 (N–H), 1687 (C=O), 1608 (C=C), 1452 (Ar-H), 1303 (CF_3) and 758 (Ar-H) cm^{-1}; ^1H NMR (400 MHz): δ (DMSO) 12.79 (1H, br s, NH), 8.36 (2H, d, J = 8.2 Hz, *o*-H), 8.16 (1H, dd, J = 7.9, 1.02 Hz, H_5), 7.91 (2H, d, J = 8.2 Hz, *m*-H), 7.85 (1H, dt, J = 7.6, 1.02 Hz, H_7), 7.76 (1H, app. d, J = 7.6, H_8), 7.55 (1H, dt, J = 7.9, 1.3, H_6); ^{13}C NMR (100 MHz): δ (DMSO) 162.4 (C4), 152.0 (C2), 148.8 (C9), 136.8 (*i*-C), 135.4 (C7), 131.9 (*p*-C), 129.4 (2*o*-C), 127.8 (C5), 126.6 (2*m*-C), 126.2 (C6), 126.1 (C8), 122.5 (C10), 121.9 (CF_3); Anal. Calcd for $C_{15}H_9F_3N_2O$: C, 62.07; H, 3.13; F, 19.64; N, 9.65. Found: C, 62.05; H, 3.16; F, 19.90; N, 9.61.

4.1.2. 2-*p*-Methoxyphenyl-4(3*H*)quinazolinone 6b

Sodium hydrogen sulfite (11.20 g, 107.63 mmol) was added to a solution of anthranilamide (14.00 g, 102.82 mmol) and *p*-anisaldehyde (14.00 g, 102.82 mmol) in *N*,*N*-dimethylacetamide (280 mL). The mixture was refluxed overnight and then poured onto ice water (500 mL). The white solid that precipitated was collected by filtration and stirred in diethyl ether for 1 h to yield 2-*p*-methoxyphenyl-4(3*H*)quinazolinone (11.55 g, 65%) as a cream solid. For analysis, a sample was recrystallised from ethanol to give cream needles, mp 250–252 °C (lit. mp 252 °C); ν_{max} (KBr) 3158 (N–H), 1678 (C=O), 1600 (C=C), 1458 (Ar-H), 1322 (C=N), 1249 (C–O) and 767 (Ar-H) cm^{-1}; ^1H NMR (400 MHz): δ (DMSO) 12.41 (1H, br s, NH), 8.18 (2H, d, J = 8.9, *o*-H) 8.12, (1H, dd, J = 7.9, 1.0 Hz, H_5), 7.80 (1H, dt, J = 7.6, 1.0 Hz, H_7), 7.69 (1H, app. d, J = 7.6 Hz, H_8), 7.47 (1H, dt, J = 7.6, 1.0 Hz, H_6), 7.07 (2H, d, J = 8.9, *m*-H), 3.83 (3H, s, OCH_3); ^{13}C NMR (100 MHz): δ (DMSO) 163.0 (*p*-C), 162.6 (C4), 152.6 (C2), 149.7 (C9), 135.2 (C7), 130.1 (2*o*-C), 127.8 (C5), 126.8 (C6), 126.5 (C8), 125.5 (C10), 121.4 (i-C), 114.7 (2*m*-C), 56.1 (OMe); Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.19; H, 4.78; N, 10.93.

4.1.3. 2-*p*-Trifluoromethylphenyl-4-chloroquinazoline 7a

2-*p*-Trifluoromethylphenyl-4(3*H*)quinazolinone (20.00 g, 64.78 mmol) and *N*,*N*-diethylanaline (15.5 mL, 97.18 mmol) were refluxed in benzene (300 mL) for 15 min. Phosphorus oxychloride (4.5 mL, 48.58 mmol) was added carefully to this white suspension, which was refluxed for 2 h. Phosphorus oxychloride (1.5 mL, 16.20 mmol) was added and the suspension was refluxed overnight or until a pale yellow solution was formed. The solvent was removed in vacuo to yield a dark orange solid. After column chromatography (silica, dichloromethane/pentane 1:1), 2-*p*-trifluoromethylphenyl-4-chloroquinazoline (18.16 g, 86%) was obtained as a white solid, R_f 0.64; mp 102–104 °C; ν_{max} (KBr) 1562 (C=C), 1483 (Ar-H), 1320 (CF_3) and 767 (C–Cl) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.65 (2H, d, J = 8.5 Hz, *o*-H), 8.22 (1H, dd, J = 8.3, 0.44 Hz, H_5), 8.07 (1H, d, J = 8.3 Hz, H_8), 7.93 (1H, dt, J = 8.3, 1.3 Hz, H_7), 7.74 (2H, d, J = 8.5 Hz, *m*-H), 7.67 (1H, dt, J = 7.0, 1.1 Hz, H_6); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 162.7 (C4), 158.5 (C2), 151.6 (C9), 139.8 (*i*-C), 135.0 (C7), 132.8 (*p*-C), 132.3 (C10), 129.0 (2*o*-C), 128.8 (2*m*-C), 125.8 (C5), 125.5 (C6), 125.4 (C8), 122.7 (CF_3); Anal. Calcd for $C_{15}H_8F_3ClN_2$: C, 58.36; H, 2.61; F, 18.46; Cl, 11.49; N, 9.08. Found: C, 58.30; H, 2.61; F, 18.25; Cl, 11.57; N, 8.88.

4.1.4. 2-*p*-Methoxyphenyl-4-chloroquinazoline 7b

2-*p*-Methoxyphenyl-4(3*H*)quinazolinone (10.84 g, 42.98 mmol) and *N*,*N*-diethylanaline (9.74 mL, 64.47 mmol) were refluxed in benzene (200 mL) for 15 min. Phosphorus oxychloride (4.0 mL, 42.98 mmol) was added carefully to this white suspension, which was then refluxed overnight or until all the solid was in solution. The solvent was removed in vacuo to yield a pale yellow solid. After column chromatography (silica, dichloromethane/pentane 3:1) 2-*p*-methoxyphenyl-4-chloroquinazoline (10.35 g, 89%) was obtained as a white solid, R_f 0.29; mp 123–125 °C (lit. mp 123–124 °C); ν_{max} (KBr) 1534 (C=C), 1509 (Ar-H), 1337 (C–N), 1176 (C–O) and 769 (C–Cl) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.54 (2H, d, J = 8.8, *o*-H), 8.20 (1H, app. d, J = 8.3 Hz, H_5), 8.02 (1H, app. d, J = 8.5 Hz, H_8), 7.88 (1H, app. t, J = 7.7 Hz, H_7), 7.60 (1H, app. t, J = 7.6 Hz, H_6), 7.02 (2H, d, J = 8.8, *m*-H), 3.89 (3H, s, OCH_3); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 162.3 (*p*-C), 162.2 (C4), 159.9 (C2), 152.0 (C9), 134.7 (C7), 130.4 (2*o*-C), 129.3 (*i*-C), 128.6 (C5), 127.7 (C6), 125.8 (C8), 122.1 (C10), 114.0 (2*m*-C), 55.4 (OMe); Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.55; H, 4.10; Cl, 13.10; N, 10.35. Found: C, 66.52; H, 4.11; Cl, 13.36; N, 10.30.

4.1.5. 2-*p*-Trifluoromethylphenyl-4-(2-benzyloxy-naphthalen-1-yl)-quinazoline 9a

2-*p*-Trifluoromethylphenyl-4-chloroquinazoline (0.506 g, 1.64 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.057 g, 0.049 mmol) were stirred in DME (15 mL) at ambient temperature for 20 min. 2-Benzyloxy-1-naphthylboronic acid (0.500 g, 1.80 mmol) and Na_2CO_3 (7 mL, 2 M) were added and the reaction was heated to reflux overnight. After cooling, the reaction mixture was filtered and the filtrate was washed three times with brine (30 mL) and once with deionised water (30 mL). The organic layer was dried over magnesium sulfate and the solvent removed in vacuo. The brown oil obtained was stirred in pentane to yield a white precipitate of 2-*p*-trifluoromethylphenyl-4-(2-benzyloxy-naphthalen-1-yl)-quinazoline (0.470 g, 57%), mp 128–130 °C; ν_{max} (KBr) 3062 (Ar-H), 1617 (C–C), 1538 (Ar-H), 1300 (CF_3), 1267 (C–O) and 755 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.81 (2H, d, J = 8.2 Hz, *o*-H), 8.22 (1H, d, J = 8.5 Hz, $H_{8'}$), 8.04 (1H, d, J = 9.1 Hz, H_4), 7.91 (2H, m, $H_{7'}$, $H_{6'}$), 7.76 (2H, d, J = 8.2 Hz, *m*-H), 7.57 (1H, d, J = 7.6 Hz, H_5), 7.48 (1H, app. d, J = 9.1, H_3), 7.43 (1H, app. d, J = 6.6, $H_{5'}$), 7.36 (1H, dd, J = 6.8, 1.4 H_6), 7.31 (1H, dd, J = 6.7, 1.2, H_7), 7.25 (1H, d, J = 8.2, H_8), 7.13 (3H, m, Ph), 7.01 (2H, m, Ph), 5.14 (2H, s, CH_2); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 168.4 (4 °C), 154.4 (4 °C), 151.4 (4 °C), 141.9 (4 °C), 137.1 (4 °C), 134.7 (CH), 134.6 (4 °C), 133.5 (4 °C), 131.8 (CH), 131.7 (4 °C), 129.7 (CH), 129.6 (4 °C), 129.4 (CH), 128.8 (CH), 128.7 (4 °C), 128.6 (CH), 128.2 (CH), 128.1 (CH), 127.8 (4 °C), 127.3 (CH), 127.2 (4 °C), 126.0 (CH), 125.1 (CH), 125.0 (CH), 124.8 (CH), 115.6 (CH), 71.8

(CH_2); Anal. Calcd for $C_{32}H_{21}F_3N_2O$: C, 75.88; H, 4.18; F, 11.25; N, 5.53. Found: C, 75.76; H, 4.47; F, 11.34; N, 5.28.

4.1.6. 2-*p*-Methoxyphenyl-4-(2-benzyloxy-naphthalen-1-yl)-quinazoline 9b

2-*p*-Methoxyphenyl-4-chloroquinazoline (5.70 g, 21.00 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.73 g, 0.63 mmol) were dissolved in degassed toluene (85 mL). 2-Benzyloxy-1-naphthylboronic acid (7.57 g, 27.30 mmol), sodium carbonate (85 mL, 2 M) and ethanol (5 mL) were added and the reaction was heated to reflux overnight. After cooling, the layers were separated and the aqueous layer was extracted twice with dichloromethane (200 mL). The organic layers were combined, dried over magnesium sulphate and the solvent was removed in vacuo. The brown oil obtained was stirred in diethyl ether to yield a white precipitate of 2-*p*-methoxyphenyl-4-(2-benzyloxy-naphthalen-1-yl)-quinazoline (6.09 g, 62%), mp 168–169 °C; ν_{max} (KBr) 1523 (C=C), 1513 (Ar-H), 1334 (C–N), 1244 (C–O), 1214 (C–O), 1025 (C–O) and 1005 (C–O) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.63 (2H, d, J = 7.3, *o*-H) 8.15 (1H, d, J = 8.5 Hz, $H_{8'}$), 8.00 (1H, d, J = 8.5 Hz, $H_{6'}$), 7.86 (2H, app. t, J = 9.2 Hz, $H_{7'}$, H_5), 7.47 (2H, app. t, J = 8.9 Hz, $H_{5'}$, H_4), 7.36–7.25 (4H, m, H_3, H_8, H_7, H_6), 7.12 (3H, s Ph), 7.01 (4H, m, *o*-H, Ph), 5.12 (2H, s, CH_2), 3.87 (3H, s, OCH_3); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 167.7 (4 °C), 162.1 (4 °C), 161.3 (4 °C), 160.9 (4 °C), 154.2 (4 °C), 151.5 (4 °C), 144.2 (4 °C), 137.1 (4 °C), 134.1 (CH), 133.5 (4 °C), 131.4 (CH), 130.9 (CH), 129.6 (4 °C), 129.0 (CH), 128.7 (CH), 128.4 (CH), 128.0 (CH), 127.5 (CH), 127.3 (CH), 126.9 (CH), 125.1 (CH), 124.5 (CH), 124.2 (4 °C), 121.7 (4 °C), 115.6 (CH), 114.2 (CH), 71.7 (CH_2), 55.4 (OMe); Anal. Calcd for $C_{32}H_{24}N_2O_2$: C, 82.03; H, 5.16; N, 5.98. Found: C, 81.73; H, 5.18; N, 5.91.

4.1.7. 1-(2-*p*-Trifluoromethylphenyl-quinazolin-4-yl)-naphthalen-2-ol 10a

2-*p*-Trifluoromethylphenyl-4-(2-benzyloxy-naphthalen-1-yl)-quinazoline (0.257 g, 0.507 mmol) was dissolved in ethanol (40 mL) in a 500 mL flask and 10% Pd/C (0.960 g) was added. The reaction vessel was filled with hydrogen gas (1 atm) and the mixture was stirred extremely vigorously overnight. The black mixture was filtered over Celite and the yellow filtrate was evaporated to obtain 1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)-naphthalen-2-ol (0.195 g, 92%) as a yellow solid, mp 164–166 °C; ν_{max} (KBr) 3200 (OH), 3060 (Ar-H), 1619 (Ar-H), 1536 (Ar-H), 1300 (CF_3), 1280 (C–O) and 1014 (C–O) cm^{-1}; ^1H NMR (400 MHz): δ ($CDCl_3$) 8.97 (1H, br s, OH), 8.65 (2H, d, J = 8.2 Hz, *o*-H), 8.09 (1H, d, J = 8.3 Hz, $H_{8'}$), 7.94 (1H, d, J = 9.0 Hz, H_4), 7.87 (1H, d, J = 8.0 Hz, H_5), 7.82 (1H, dt, J = 8.3, 1.4 Hz, $H_{7'}$), 7.71 (2H, d, J = 8.3 Hz, *m*-H), 7.54 (1H, dt, J = 9.3, 0.8 Hz, $H_{5'}$), 7.38–7.28 (3H, m, $H_{6'}$, H_3, H_6), 7.27–7.21 (2H, m, H_7, H_8); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 166.8 (4 °C), 158.6 (4 °C), 154.1 (4 °C), 152.0 (4 °C), 140.7 (4 °C), 140.6 (4 °C), 135.0 (CH), 132.8 (CH), 132.7 (4 °C), 132.6 (4 °C), 129.4 (CH), 129.1 (4 °C), 129.0 (CH), 128.7 (CH), 128.1 (CH), 127.9 (CH), 127.2 (CH), 125.8 (CH), 124.9 (CH), 124.1 (CH), 123.3 (4 °C), 119.4 (CH), 115.3 (4 °C); Anal. Calcd for $C_{25}H_{15}F_3N_2O$: C, 72.11; H, 3.63; F, 13.69; N, 6.73. Found: C, 71.85; H, 3.72; F, 13.38; N, 6.43.

4.1.8. 1-(2-*p*-Methoxyphenyl-quinazolin-4-yl)-naphthalen-2-ol 10b

2-*p*-Methoxyphenyl-4-(2-benzyloxy-naphthalen-1-yl)-quinazoline (4.00 g, 9.45 mmol) was dissolved in EtOH (300 mL) in a 1 L flask and 10% Pd/C (1.79 g) was added. The reaction vessel was filled with hydrogen gas (1 atm) and the mixture was stirred vigorously overnight. The black mixture was filtered over Celite and the yellow filtrate removed in vacuo to obtain 1-(2-*p*-methoxyphenyl-quinazolin-4-yl)-naphthalen-2-ol (3.43 g, 96%) as a yellow solid, mp 112–114 °C; ν_{max} (KBr) 3306 (OH), 1614 (Ar-H), 1536 (Ar-H), 1485 (OH), 1290 (C–O) and 1027 (C–O) cm^{-1}; ^1H NMR (400 MHz): δ ($CDCl_3$) 8.63 (2H, d, J = 8.4 Hz, *o*-H), 8.17 (1H, d, J = 8.5 Hz, $H_{8'}$), 8.13 (1H, d, J = 9.1 Hz, H_4), 8.00 (1H, d, J = 8.3 Hz, H_5), 7.87 (1H, dt, J = 7.5, 2.0 Hz, $H_{7'}$), 7.63 (1H, d, J = 9.2 Hz, H_3), 7.57 (1H, dt, J = 7.5, 1.3 Hz, H_6), 7.41 (1H, dt, J = 7.8, 1.2 Hz, $H_{6'}$), 7.36 (3H, m, $H_{5'}$, H_7, H_8), 7.02 (2H, d, J = 8.2 Hz, *m*-H), 7.36 (3H, s, OCH_3); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 163.4 (4 °C), 162.2 (4 °C), 160.8 (4 °C), 151.7 (4 °C), 144.9 (4 °C), 134.9 (CH), 132.7 (4 °C), 132.6 (4 °C), 132.1 (CH), 130.8 (CH), 130.7 (4 °C), 129.3 (CH), 128.6 (CH), 128.4 (CH), 127.8 (4 °C), 127.6 (CH), 127.3 (CH), 126.6 (CH), 126.5 (CH), 123.3 (4 °C), 119.8 (CH), 114.2 (CH), 55.61 (CH_3); Anal. Calcd for $C_{25}H_{18}N_2O_2$: C, 79.35; H, 4.79; N, 7.40. Found: C, 79.09; H, 4.93; N, 7.29.

4.1.9. 1-(2-*p*-Trifluoromethylphenyl-quinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate 11a

Trifluoromethylsulfonic anhydride (2.24 g, 7.92 mmol) was added dropwise to a yellow solution of 1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)-naphthalen-2-ol (3.00 g, 7.20 mmol) and 4-dimethylaminopyridine (2.63 g, 21.60 mmol) in dry dichloromethane (150 mL). The colour of the solution gradually faded during the addition. The pale yellow solution was allowed to stir overnight under nitrogen. The solution was then washed with 1 M HCl (3 × 50 mL), water (2 × 60 mL), brine (1 × 60 mL) and dried over magnesium sulfate. The solvent was reduced in vacuo and the concentrated solution was passed through a short column of silica to give 1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)-2-naphthyl-(trifluoromethyl)sulfonate as a white solid (3.51 g, 92%), mp 144–146 °C; ν_{max} (KBr) 3068 (Ar-H), 1619 (Ar-H), 1542 (Ar-H), 1423 (–SO_3–), 1340 (CF_3), 1211 (–SO_3–), 1124 (C–O), 1064 (C–O) and 819 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.82 (2H, d, J = 8.2 Hz, *o*-H), 8.27 (1H, d, J = 8.5 Hz, $H_{8'}$), 8.19 (1H, d, J = 9.1 Hz, H_4), 8.05 (1H, d, J = 8.2 Hz, H_5), 7.96 (1H, dt, J = 7.6, 1.6 Hz, $H_{7'}$), 7.85 (2H, d, J = 8.2 Hz, *m*-H), 7.66 (1H, d, J = 9.1, H_3), 7.60 (1H, d, J = 7.7, H_6), 7.47 (3H, m, $H_{6'}$, $H_{5'}$, H_7), 7.34 (1H, d, J = 8.5, H_8); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 163.8 (4 °C), 159.9 (4 °C), 151.5 (4 °C), 145.0 (4 °C), 141.6 (4 °C), 134.9 (CH), 132.6 (4 °C), 132.3 (CH), 129.6 (CH), 129.3 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 127.7 (CH), 127.4 (4 °C), 126.7 (CH), 126.6 (CH), 125.7 (CH), 125.6 (4 °C), 123.9 (4 °C), 122.8 (4 °C), 119.8 (CH), 119.6 (4 °C), 117.6 (4 °C); Anal. Calcd for $C_{26}H_{14}F_6N_2O_3S$: C, 56.94; H, 2.57; F, 20.78; N, 5.11; S, 5.85. Found: C, 56.68; H, 2.61; F, 20.48; N, 5.30; S, 6.20.

4.1.10. 1-(2-*p*-Methoxyphenyl-quinazolin-4-yl)-2-naphthyl (trifluoromethyl)sulfonate 11b

Trifluoromethylsulfonic anhydride (2.25 g, 7.97 mmol) was added dropwise to a yellow solution of 1-(2-*p*-methoxyphenyl-quinazolin-4-yl)-naphthalen-2-ol (2.74 g, 7.24 mmol) and 4-dimethylaminopyridine (2.65 g, 21.73 mmol) in dry dichloromethane (100 mL). The pale yellow solution was allowed to stir overnight. The solvent was removed in vacuo and the reaction mixture purified by column chromatography (silica, dichloromethane) to yield 1-(2-*p*-methoxyphenyl-quinazolin-4-yl)-2-naphthyl(trifluoromethyl)-sulfonate (1.92 g, 52%) as a white solid, R_f 0.40, mp 151–153 °C; ν_{max} (KBr) 3077 (Ar-H), 1604 (Ar-H), 1540 (Ar-H), 1434 (–SO3–), 1229 (–SO3–), 1137 (C–O), 1047 (C–O) and 819 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.64 (2H, d, J = 8.9, *o*-H), 8.17 (2H, m, H_4, $H_{8'}$), 8.03 (1H, d, J = 8.2 Hz, H_5), 7.89 (1H, dt, J = 7.4, 1.9, $H_{7'}$), 7.65 (1H, d, J = 9.2 Hz, H_3), 7.59 (1H, d, J = 7.0, H_6), 7.36 (4H, m, H_8, H_7, $H_{5'}$, $H_{6'}$), 7.03 (2H, d, J = 8.9, *m*-H), 3.88 (3H, s, OCH_3); ^{13}C NMR (75 MHz): δ ($CDCl_3$) 163.1 (4 °C), 162.0 (4 °C), 160.5 (4 °C), 151.5 (4 °C), 144.7 (4 °C), 134.3 (CH), 132.5 (4 °C), 132.4 (4 °C), 131.8 (CH), 130.6 (2*o*-C), 130.5 (4 °C), 129.1 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 127.5 (4 °C), 127.4 (CH), 127.1 (CH), 126.3 (CH), 123.1 (4 °C), 119.5 (CH), 114.0 (2*m*-C), 55.4 (CH_3); Anal. Calcd for: $C_{26}H_{17}F_3N_2O_4S$: C,

61.17; H, 3.56; F, 11.16; N, 5.49; S, 6.28. Found: C, 60.96; H, 3.42; F, 11.27; N, 5.26; S, 6.57.

4.1.11. (*R,S*)-Diphenyl(1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)phosphine 3a

Diphenylphosphine (0.53 g, 2.83 mmol) was added to a solution of nickel dichloride diphenylphosphinoethane (0.28 g, 0.53 mmol) in anhydrous DMF (4 mL) and the reaction mixture was heated to 100 °C under nitrogen. After 30 min a solution of 1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate (2.50 g, 4.72 mmol) and diazobicyclooctane (1.27 g, 11.32 mmol) in anhydrous DMF (7 mL) was added to the reaction mixture and heating was continued at 100 °C for a further hour. After this time an additional portion of diphenylphosphine (0.53 g, 2.83 mmol) was added. The reaction mixture was stirred at 100 °C under nitrogen for three days. The solvent was removed in vacuo and the reaction mixture purified by column chromatography (silica, pentane/dichloromethane, 3:1) to yield (*R,S*)-diphenyl(1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)phosphine as a white solid (1.79 g, 65%), R_f 0.11, mp 209–211 °C; ν_{max} (KBr) 3066 (Ar-H), 1540 (Ar-H), 1490 (P-Ph), 1300 (CF_3), 1118 (Ph) and 694 (Ar-H) cm^{-1}; ^1H NMR (400 MHz): δ ($CDCl_3$) 8.25 (2H, d, J = 8.2 Hz, *o*-H), 8.21 (1H, d, J = 8.6 Hz, $H_{8'}$), 7.94 (2H, m, $H_{7'}$, H_5), 7.87 (1H, d, J = 7.6 Hz, H_4), 7.55 (2H, d, J = 8.2 Hz, *m*-H), 7.49 (1H, d, J = 7.6 Hz, H_3), 7.41 (3H, m, H_6, $H_{6'}$, H_7), 7.35–7.21 (9H, m, $H_{5'}$, Ar-H), 7.18–7.11 (3H, m, H_8, Ar-H); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 169.8 (4 °C), 159.3 (4 °C), 151.4 (4 °C), 142.1 (4 °C), 141.8 (4 °C), 137.6 (4 °C), 137.0 (4 °C), 135.1 (4 °C), 134.5 (CH), 134.2 (CH), 134.1 (CH), 134.0 (CH), 133.8 (CH), 132.6 (4 °C), 132.2 (4 °C), 131.8 (4 °C), 130.5 (CH), 129.7 (CH), 129.6 (CH), 129.4 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 127.4 (CH), 126.6 (CH), 125.5 (CH), 124.5 (CH), 124.5 (4 °C); ^{31}P NMR (162 MHz): δ ($CDCl_3$) −13.2 ppm; Anal. Calcd for $C_{37}H_{24}F_3N_2P$: C, 76.02; H, 4.14; F, 9.75; N, 4.79; P, 5.30. Found: C, 75.58; H, 4.09; F, 9.87; N, 4.63; P, 5.51.

4.1.12. (*R,S*)-Diphenyl(1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)phosphine 3b

Diphenylphosphine (0.397 g, 2.13 mmol) was added to a solution of nickel dichloride diphenylphosphinoethane (0.247 g, 0.46 mmol) in anhydrous DMF (4 mL) and the reaction mixture was heated to 100 °C under nitrogen. After 30 min, a solution of 1-(2-*p*-methoxyphenyl-quinazolin-4-yl)-2-naphthyl(trifluoromethyl)sulfonate (2.170 g, 4.26 mmol) and diazobicyclooctane (1.194 g, 10.65 mmol) in anhydrous DMF (7 mL) was added to the reaction mixture and heating was continued at 100 °C for a further hour. After this time an additional portion of diphenylphosphine (0.397 g, 2.13 mmol) was added. The reaction mixture was stirred at 100 °C under nitrogen for three days. The solvent was removed in vacuo and the reaction mixture purified by column chromatography (silica, pentane/ethyl acetate, 6:1) to yield (*R,S*)-diphenyl(1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)phosphine as a white solid, R_f 0.17, mp 109–111 °C; ν_{max} (KBr) 3066 (Ar-H), 1530 (Ar-H), 1486 (P-Ph), 1255 (C–O), 1027 (Ph) and 696 (Ar-H) cm^{-1}; ^1H NMR (400 MHz): δ ($CDCl_3$) 8.13 (3H, d, J = 8.6, *o*-H, $H_{8'}$), 7.91 (2H, app. t, J = 7.9 Hz, H_4, H_5), 7.81 (1H, t, J = 6.9 Hz, $H_{7'}$), 7.49 (1H, t, J = 7.4 Hz, H_6), 7.40 (1H, dd, J = 8.5, 3.1 Hz, H_3), 7.35–7.17 (14H, m, $H_{6'}$, $H_{5'}$, H_7, H_8, Ar-H), 6.83 (2H, d, J = 8.8 Hz, *m*-H), 3.83 (3H, s, OCH_3); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 169.3 (4 °C), 161.8 (4 °C), 160.4 (4 °C), 151.3 (4 °C), 142.5 (4 °C), 137.8 (4 °C), 137.1 (4 °C), 134.0 (4 °C), 134.8 (4 °C), 134.0 (CH), 133.9 (CH), 133.7 (CH), 132.1 (4 °C), 131.1 (4 °C), 130.7 (2*o*-C), 130.3 (CH), 129.4 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.2 (CH), 127.1 (CH), 126.9 (CH), 126.7 (CH), 123.9 (4 °C), 113.8 (2*m*-C), 55.6 (CH_3); ^{31}P NMR (162 MHz): δ ($CDCl_3$) −12.3 ppm; Anal. Calcd for $C_{37}H_{27}N_2OP$: C, 81.30; H, 4.98; N, 5.13; P, 5.67. Found: C, 81.12; H, 4.99; N, 5.00; P, 5.51.

4.1.13. (*S,R*)-*cis*-[Dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl) diphenylphosphine]palladium(II) chloride (*S,R*)-13a

A solution of (*R,S*)-diphenyl(1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)phosphine (1.0 g, 1.71 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]dipalladium(II) (0.58 g, 0.86 mmol) in dry, degassed methanol (70 mL) was stirred for 18 h under an atmosphere of nitrogen. After 4 h a cream-coloured precipitate was observed. The precipitate was filtered to yield (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)-diphenylphosphine]palladium(II) chloride as a cream solid (0.592 g, 75%), mp 190–192 °C; $[\alpha]_D^{20} = -48.7$ (*c* 1.18, $CHCl_3$); ν_{max} (KBr) 3054 (Ar-H), 2867 (Ar-H), 1569 (C=C), 1435 (P-Ph), 1320 (CF_3) and 1124 (Ar-H) cm^{-1}; ^1H NMR (300 MHz): δ ($CDCl_3$) 8.22 (3H, app. d, J = 8.4 Hz), 8.08 (1H, d, J = 8.5 Hz), 7.96 (2H, d, J = 9.2 Hz), 7.75 (4H, m), 7.65–7.40 (6H, m), 7.40–7.27 (7H, m), 7.19 (1H, t, J = 7.3 Hz), 6.82 (2H, d, J = 8.5 Hz), 6.70 (3H, m), 6.50 (1H, app t, J = 7.6 Hz), 4.18 (1H, m, C*H*(Me)), 2.82 (3H, s, NMe), 2.39 (3H, s, NMe), 1.74 (3H, d, J = 6.2 Hz, CH*Me*); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 167.9 (4 °C), 159.2 (4 °C), 150.8 (4 °C), 150.2 (4 °C), 149.3 (4 °C), 141.7 (4 °C), 139.4 (4 °C), 137.5 (CH), 137.3 (CH), 136.1 (CH), 136.0 (CH), 134.3 (4 °C), 134.1 (CH), 134.0 (CH), 132.8 (4 °C), 132.7 (4 °C), 131.9 (4 °C), 131.5 (4 °C), 131.3 (4 °C), 131.0 (CH), 130.6 (4 °C), 130.2 (CH), 130.0 (CH), 129.4 (CH), 129.2 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.9 (CH), 127.7 (CH), 127.3 (CH), 127.2 (CH), 127.0 (CH), 126.5 (CH), 125.8 (CH), 125.2 (CH), 125.1 (CH), 124.6 (4 °C), 124.3 (CH), 73.3 (*C*HMe), 50.9 (NMe), 48.7 (NMe), 23.5 (CH*Me*); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 42.8. The filtrate was reduced in vacuo to yield a 4:1 mixture of diastereomers (*R,R*)- and (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)diphenyl phosphine]palladium(II)chloride (0.988 g) as a light yellow solid. The major diastereomer was the (*R,R*) diastereomer. Further crystallisation from methanol yielded additional (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride (0.091 g) from this mixture of diastereomers.

4.1.14. (*S,R*)-*cis*-[Dimethyl(1-(1-naphthyl) ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl) diphenylphosphine]palladium (II)hexafluorophosphate (*S,R*)-14

(*S,R*)-*cis*-[Dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride (0.689 g, 0.746 mmol) was dissolved in methanol (100 mL). Potassium hexafluorophosphate (0.137 g, 0.746 mmol) in distilled water (60 mL) was added to this solution. A creamy precipitate was seen and this was stirred overnight. The cationic palladium complex that precipitated was filtered and recrystallised from deuterated chloroform and pentane to give yellow crystals of (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)-diphenylphosphine]palladium(II)hexafluorophosphate (0.703 g, 89%); ^1H NMR (300 MHz): δ ($CDCl_3$) 9.12 (2H, d, J = 7.5 Hz), 8.16 (1H, d, J = 9.4 Hz), 8.07–7.95 (3H, m), 7.84 (2H, d, J = 8.2 Hz), 7.72 (2H, 7, J = 7.02 Hz), 7.61–7.09 (15H, m), 6.85 (3H, app. d, J = 9.7 Hz), 6.76 (2H, br s), 3.96 (1H, m, C*H*(Me)), 2.12 (3H, s, NMe), 1.29 (3H, s, NMe), 1.14 (3H, d, J = J = 4.99 Hz, CH*Me*); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 31.0, -144.7 (sept., J = 712.2 Hz) ppm.

4.1.15. Crystal data for (*S,R*)-14

$[C_{51}H_{40}F_3N_3PPd]^+$ $[PF_6]^-\cdot 2[CCl_3D]$, from deuterochloroform/pentane, M_r = 1274.94, yellow plate, crystal size: 0.30 × 0.14 × 0.08 mm^3; a = 10.7119(1), b = 21.3500(2), c = 12.5470(1) Å, β = 113.353(1)°, V = 2634.42(4) $Å^3$, T = 100 K, monoclinic, space group

$P2_1$ (No. 4), $Z = 2$, $\rho_{calcd} = 1.61$ g cm^{-3}, $F(0\,0\,0) = 1280$, Nonius KappaCCD diffractometer, λ(Mo Kα) = 0.71073 Å, $\mu = 0.79$ mm^{-1}, 72841 measured and 19998 independent reflections ($R_{int} = 0.043$), 19049 with $I > 2\sigma(I)$, $\theta_{max} = 33.1°$, $T_{min} = 0.878$, $T_{max} = 0.967$, direct methods (SHELXS-97) and least-squares refinement (SHELXL-97) on F_o^2, both programs from G. Sheldrick, University of Göttingen, 1997; 667 parameters, H atoms riding, absolute configuration established (Flack parameter −0.01(1)), Chebyshev type weights, $R_1 = 0.0346$ ($I > 2\sigma(I)$), $wR_2 = 0.0866$ (all data), $\Delta\rho_{max/min} = 1.313$ (0.85 Å from Pd)/−1.286 (0.68 Å from Cl6) e Å^{-3}, CCDC 630664.[34]

4.1.16. (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride (*S,R*)-13b

A solution of (*RS*)-diphenyl(1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)phosphine (0.33 g, 0.59 mmol) and (+)-di-μ-chlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-C_2,N]dipalladium(II) (0.20 g, 0.29 mmol) in dry, degassed methanol (40 mL) was stirred for 18 h under an atmosphere of nitrogen. After 2 h a cream-coloured precipitate was observed. The precipitate was filtered to yield (*R,R*) and (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl) ethyl)-aminato-C^2,N]-[1-(2-*p*-methoxy-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride as a cream solid. This mixture was dissolved in hot butanone and pentane was added slowly until a cream precipitate was just seen. Further hot butanone was added and the solution was allowed to stand overnight. By this time a cream-coloured precipitate had formed. Filtration of this precipitate gave diastereomerically pure (*S,R*)-*cis*-[dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride (0.148 g, 56%), mp 203–205 °C; $[\alpha]_D^{20} = -44.2$ (*c* 0.65, $CHCl_3$); ν_{max} (KBr) 3052 (Ar-H), 2913 (Ar-H), 1540 (C=C), 1435 (P-Ph), 1250 (C–O) and 1168 (Ar-H) cm^{-1}; ^{1}H NMR (400 MHz): δ ($CDCl_3$) 8.33 (1H, t, $J = 3.9$ Hz), 8.14 (2H, d, $J = 9.0$ Hz, *o*-H), 8.03 (1H, d, $J = 8.7$ Hz), 7.92 (1H, d, $J = 8.0$ Hz), 7.84 (3H, m), 7.76 (1H, d, $J = 8.1$ Hz), 7.73 (1H, m), 7.63 (1H, d, $J = 8.4$ Hz), 7.55 (1H, d, $J = 8.3$ Hz), 7.46 (2H, m), 7.37–7.26 (7H, m), 7.17 (1H, m), 6.86 (2H, d, $J = 9.0$ Hz, *m*-H), 6.81 (1H, d, $J = 8.6$ Hz), 6.74 (2H, m), 6.59 (2H, t, $J = 6.5$ Hz), 6.48 (1H, t, $J = 6.0$ Hz), 4.21 (1H, m, C*H*(Me)), 3.85 (3H, s, OMe), 2.88 (3H, d, $J = 3.4$ Hz, NMe), 2.56 (3H, s, NMe), 1.76 (3H, d, $J = 6.3$ Hz, CH*Me*); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 167.5 (4 °C), 161.7 (4 °C), 160.0 (4 °C), 150.9 (4 °C), 150.7 (4 °C), 149.2 (4 °C), 139.7 (4 °C), 137.3 (CH), 137.2 (CH), 136.5 (CH), 136.4 (CH), 136.1 (CH), 136.0 (CH), 134.2 (4 °C), 133.8 (CH), 133.3 (CH), 132.7 (4 °C), 131.1 (4 °C), 130.9 (CH), 130.8 (4 °C), 130.7 (CH), 130.6 (CH), 130.1 (4 °C), 130.0 (CH), 129.1 (CH), 128.8 (CH), 128.7 (4 °C), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 127.1 (CH), 127.0 (CH), 126.8 (CH), 126.6 (CH), 125.7 (CH), 124.3 (CH), 124.2 (4 °C), 124.12 (CH), 124.10 (4 °C), 123.4 (CH), 113.7 (CH), 73.3 (*C*HMe), 55.6 (OMe), 51.1 (NMe), 48.7 (NMe), 23.6 (CH*Me*); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 45.2 ppm. The filtrate contained a mixture of diastereomers; two subsequent recrystallisations with hot butanone/pentane realised further quantities of the (*S,R*) diastereomer (0.053 g and 0.024 g). By recrystallisation of the remaining filtrate from methanol the isolation of a small quantity of (*R,R*)-*cis*-[dimethyl(1-(1-naphthyl)-ethyl)aminato-C^2,N] -[1-(2-*p*-methoxy-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride (0.048 g, 18%) was possible, mp 200–202 °C; $[\alpha]_D^{20} = +43.3$ (*c* 0.91, $CHCl_3$); ν_{max} (KBr) 3050 (Ar-H), 2892 (Ar-H), 1538 (C=C), 1435 (P-Ph), 1250 (C–O) and 1166 (Ar-H) cm^{-1}; ^{1}H NMR (300 MHz): δ ($CDCl_3$) 8.41 (2H, d, $J = 8.8$ Hz), 8.18 (2H, t, $J = 8.9$ Hz), 7.99–7.80 (5H, m), 7.71 (1H, t, $J = 7.7$ Hz), 7.59 (1H, d, $J = 8.2$ Hz), 7.52–7.38 (5H, m), 7.32–7.19 (7H, m), 6.99 (4H, d, $J = 8.8$ Hz), 6.80 (1H, d, $J = 8.6$ Hz), 6.21 (1H, d, $J = 8.5$ Hz), 6.03 (1H, t, $J = 6.2$ Hz), 4.12 (1H, m, C*H*(Me)), 3.95 (3H, s, OMe), 2.85 (3H, d, $J = 2.4$ Hz, NMe), 2.00 (3H, s, NMe), 1.97 (3H, s, CH*Me*); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 168.2 (4 °C), 162.0 (4 °C), 160.1 (4 °C), 152.8 (4 °C), 148.6 (4 °C), 138.5 (CH), 138.4 (CH), 136.3 (4 °C), 135.9 (4 °C), 133.9 (CH), 131.8 (4°°C), 131.7 (4 °C), 130.8 (CH), 130.7 (CH), 130.6 (CH), 130.2 (CH), 130.1 (4 °C), 128.9 (CH), 128.7 (4 °C), 128.6 (4 °C), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.4 (CH), 127.3 (CH), 127.2 (CH), 127.1 (CH), 126.7 (CH), 126.6 (CH), 125.4 (CH), 124.3 (4 °C), 124.1 (4 °C), 124.0 (CH), 123.9 (4 °C), 123.3 (4 °C), 123.0 (CH), 123.3 (CH), 113.8 (CH), 73.0 (*C*HMe), 55.7 (OMe), 50.6 (NMe), 48.8 (NMe), 23.7 (CH*Me*); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 39.9 ppm.

4.1.17. (*S*)-Diphenyl(1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)phosphine (*S*)-3a

(*S,R*)-*cis*-[Dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]palladium(II)chloride (0.20 g, 0.22 mmol) and 1,2-bis (diphenylphosphino)ethane (0.09 g, 0.22 mmol) were dissolved in dry, degassed dichloromethane (15 mL). The pale yellow solution was stirred for 3 h at room temperature under an atmosphere of nitrogen. The dichloromethane was removed in vacuo and purified by column chromatography (silica, dichloromethane) to give (*S*)-diphenyl(1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)phosphine as a white solid (0.12 g, 97%), R_f 0.66, $[\alpha]_D^{20} = +40.9$ (*c* 0.70, $CHCl_3$), identical in all other respects to the previously prepared racemic sample.

4.1.18. (*S*)-Diphenyl(1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)phosphine (*S*)-3b

(*S,R*)-*cis*-[Dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)diphenylphosphine]-palladium(II)chloride (0.45 g, 0.50 mmol) and 1,2-bis (diphenylphosphino)ethane (0.20 g, 0.50 mmol) were dissolved in dry, degassed dichloromethane (30 mL). The pale yellow solution was stirred for 3 h at room temperature under an atmosphere of nitrogen. The dichloromethane was removed in vacuo and purified by column chromatography (silica, pentane/ethyl acetate, 6:1) to give (*S*)-diphenyl(1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)-phosphine as a white solid (0.21 g, 77%), R_f 0.17, $[\alpha]_D^{20} = +38.0$ (*c* 0.65, $CHCl_3$), identical in all other respects to the previously prepared racemic sample.

4.1.19. (*S*)-Diphenyl[1-(2-(2-pyridyl)-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium(1,5-cyclooctadiene) methanesulfonate 15a

(1,5-Cyclooctadiene)(2,4-pentanedionato)rhodium (3.1 mg, 0.01 mmol) and (*S*)-2-(2-pyridyl)-Quinazolinap (5.1 mg, 0.01 mmol) were dissolved in dry THF (2 mL) under an atmosphere of nitrogen to give a clear yellow solution. Trimethylsilyltrifluoromethanesulfonate (2 μL, 1.11 equiv) was added via syringe producing a light brown solution. The solution was stirred for 20 min and the volume reduced in vacuo to approx. 0.5 mL. Pentane (15 mL) was added via syringe, resulting in the formation of a pale brown precipitate. This was stirred for 10 min and the pentane was removed via syringe. The precipitate was washed once more with pentane (15 mL), which was again removed using a syringe to leave (*S*)-diphenyl{1-[2-(2-pyridyl)-quinazolin-4-yl][2-naphthyl]}phosphine rhodium(1,5-cyclooctadiene)methanesulfonate as a light yellow powder. ^{1}H NMR (300 MHz): δ ($CDCl_3$) 9.87 (d, 1H, $J = 5.1$ Hz), 8.78 (d, 1H, $J = 8.0$ Hz), 8.24 (d, 1H, $J = 7.6$ Hz), 8.23–6.35 (m, 21H), 5.59 (br s, 1H CH=CH), 4.09 (br s, 1H CH=CH), 3.47 (br s, 1H CH=CH), 2.37 (br s, 1H CH=CH), 1.85 (m, 2H, CH_2), 1.74–1.60 (m, 4H, CH_2, CH_2), 1.26 (m, 2H, CH_2); ^{31}P NMR (121 MHz): δ ($CDCl_3$) 25.84 ppm (d, $J = 123$ Hz). The product was dried under vacuum for 45 min before use in Rh-catalysed hydroboration. Dry THF (4 mL) was added to the Schlenk tube and 2 mL portions of the catalyst

precursor (1 mol %) were transferred to two oven-dried Schlenk tubes under nitrogen.

4.1.20. (*S*)-Diphenyl[1-(2-(2-pyrazinyl)-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium(1,5-cyclooctadiene) methanesulfonate 15b

(1,5-Cyclooctadiene)(2,4-pentanedionato)rhodium **32** (3.1 mg, 0.01 mmol) and (*S*)-2-(2-pyrazinyl)-Quinazolinap (5.1 mg, 0.01 mmol) were dissolved in dry THF (2 mL) under an atmosphere of nitrogen to give a clear yellow solution. Trimethylsilyltrifluoromethanesulfonate (2 μL, 1.11 equiv) was added via syringe, producing a light brown solution. The solution was stirred for 20 min and the volume reduced in vacuo to approx. 0.5 mL. Pentane (15 mL) was added via syringe, resulting in the formation of a pale brown precipitate. This was stirred for 10 min and the pentane was removed via syringe. The precipitate was washed once more with pentane (15 mL), which was again removed using a syringe to leave (*S*)-diphenyl[1-(2-(2-pyrazinyl)-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium(1,5-cyclooctadiene)methanesulfonate as a light brown powder. The product was dried under vacuum for 45 min before use in Rh-catalysed hydroboration. Dry THF (4 mL) was added to the Schlenk tube and 2 mL portions of the catalyst precursor (1 mol %) were transferred to two oven-dried Schlenk tubes under nitrogen.

4.1.21. (*S*)-Diphenyl[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium(1,5-cyclooctadiene) methanesulfonate 15c

(1,5-Cyclooctadiene)(2,4-pentanedionato)rhodium (3.2 mg, 0.01 mmol) and (*S*)-diphenyl[1-(2-*p*-trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)]phosphine (5.8 mg, 0.01 mmol) were dissolved in dry THF (2 mL) under an atmosphere of nitrogen to give a clear yellow solution. Trimethylsilylmethanesulfonate (2 μL, 1.11 equiv) was added via syringe and a dark orange/red colour developed. The reaction mixture was stirred for 20 min and the volume was then reduced in vacuo to 0.5 mL. Pentane (10 mL) was added via syringe to produce a light orange precipitate. This was allowed to stir for 5 min before the pentane was removed. The precipitate was washed with fresh pentane (2 × 10 mL), which was syringed from the Schlenk tube to leave (*S*)-diphenyl[1-(2-*p*trifluoromethylphenyl-quinazolin-4-yl)(2-naphthyl)]phosphinerhodium-(1,5-cyclooctadiene)trifluoromethanesulfonate as a light orange powder. ^{1}H NMR (400 MHz): δ ($CDCl_3$) = 9.10 (2H, s), 8.34 (1H, d, *J* = 8.6 Hz), 8.09 (3H, d, *J* = 8.3 Hz), 7.90 (2H, m), 7.77 (1H, s), 7.63 (1H, t, *J* = 7.2 Hz), 7.48 (7H, m), 7.26 (3H, t, *J* = 8.3 Hz), 7.16 (1H, s), 6.76 (1H, s), 6.64 (2H, s), 4.18 (1H, br s, C*H*═CH), 3.95 (1H, br s, C*H*═CH), 2.65 (1H, br s, C*H*═CH), 2.20 (1H, br s, C*H*═CH), 1.78 (2H, m, CH_2), 1.39 (2H, m, CH_2), 1.33 (2H, m, CH_2), 0.80 (2H, m, CH_2); ^{13}P NMR (162 MHz): δ ($CDCl_3$) 19.42 (d, *J* = 126.0 Hz) ppm. The product was dried under vacuum for 45 min before use in Rh-catalysed hydroboration. Dry THF (4 mL) was added to the Schlenk tube and 2 mL portions of the catalyst precursor (1 mol %) were transferred to two oven-dried Schlenk tubes under nitrogen.

4.1.22. (*S*)-Diphenyl[1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium(1,5-cyclooctadiene) methanesulfonate 15d

(1,5-Cyclooctadiene)(2,4-pentanedionato)rhodium (3.2 mg, 0.01 mmol) and (*S*)-diphenyl[1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)]phosphine (5.6 mg, 0.01 mmol) were dissolved in dry THF (2 mL) under an atmosphere of nitrogen to give a clear yellow solution. Trimethylsilyltrifluoromethanesulfonate (2 μL, 1.11 equiv) was added via syringe and a bright yellow colour developed. The reaction mixture was allowed to stir for 20 min and the volume was then reduced in vacuo to 0.5 mL. Pentane (10 mL) was added via syringe and to produce a bright yellow precipitate. This was allowed stir for 5 min before the pentane was removed via syringe. The precipitate was washed twice more with pentane (2 × 10 mL), which was syringed from the Schlenk tube to leave (*S*)-diphenyl[1-(2-*p*-methoxyphenyl-quinazolin-4-yl)(2-naphthyl)]phosphine rhodium(1,5-cyclooctadiene)trifluoromethanesulfonate as a light yellow powder. ^{1}H NMR (400 MHz): δ ($CDCl_3$) = 8.99 (2H, d, *J* = 8.4 Hz), 8.33 (1H, d, *J* = 8.7 Hz), 8.10 (1H, d, *J* = 8.2 Hz), 7.88–7.81 (2H, m), 7.74 (1H, t, *J* = 8.1 Hz), 7.63–7.57 (3H, m), 7.50 (3H, m), 7.47–7.39 (5H, m), 7.25 (3H, m), 7.09 (1H, d, *J* = 8.8 Hz), 6.71 (1H, t, *J* = 7.0 Hz), 6.59 (1H, t, *J* = 6.9 Hz), 5.60 (1H, br s, C*H*═CH), 4.22 (1H, br s, C*H*═CH), 3.99 (3H, s, OMe), 3.79 (1H, br s, C*H*═CH), 3.28 (1H, br s, C*H*═CH), 1.55 (2H, m, CH_2), 1.28 (2H, m, CH_2), 1.15 (2H, m, CH_2), 0.81 (2H, m, CH_2); ^{13}P NMR (162 MHz): δ ($CDCl_3$) 19.25 (d, *J* = *J* = 133.5 Hz) ppm. The product was dried under vacuum for 45 min before use in Rh-catalysed hydroboration. Dry THF (4 mL) was added to the Schlenk tube and 2 mL portions of the catalyst precursor (1 mol %) were transferred to two oven-dried Schlenk tubes under nitrogen.

4.2. Asymmetric hydroboration general procedure

The required Quinazolinap-rhodium(1,5-cyclooctadiene)trifluoromethanesulfonate catalyst (5 μmol) in THF (2 mL) was placed under nitrogen in a Schlenk tube. Freshly distilled catecholborane (53 μL, 0.5 mmol) was added via microlitre syringe and the light brown solution was allowed to stir for 5 min at the required temperature. The substrate olefin (0.5 mmol) was injected and the reaction mixture was stirred for either 2 h or 24 h at room temperature or at 0 °C. The reaction was then cooled to 0 °C; ethanol (1 mL) was added; followed by 1 M NaOH (3 mL) and H_2O_2 (3 mL). The ice bath was removed and the solution was stirred for 1 h at room temperature. The reaction mixture was transferred to a separatory funnel and diethyl ether (10 mL) was added. The organic layer was washed with 1 M NaOH (10 mL), brine (10 mL) and dried with $MgSO_4$. The solution was filtered and the solvent was removed in vacuo to give the hydroborated product as an oil. Conversion and regioselectivity were determined by ^{1}H NMR. The ee was calculated by chiral GC or HPLC analysis. Conditions for chiral GC and HPLC analysis as previously reported.[4]

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References

1. McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809–3844.
2. Au-Leung, T. T.-L.; Chan, A. S. C. *Coord. Chem. Rev.* **2004**, *248*, 2151–2164.
3. Ila, H.; Bell, H. P.; Tietze, L. F. *Chem. Rev.* **2004**, *104*, 3453–3516.
4. 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.
5. Fu, G. C. In *Transition Metals for Organic Synthesis*; Wiley-VCH: Weinheim, 1998; Vol. II.
6. (a) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695–4712; (b) Guiry, P. J. *ChemCatChem* **2009**, *1*, 233–235.
7. Flanagan, S. P.; Guiry, P. J. *J. Organomet. Chem.* **2006**, *691*, 2125–2154.
8. Jacobsen, E. N.; Zhang, W.; Guler, M. L. *J. Am. Chem. Soc.* **1991**, *113*, 6703–6704.
9. Hayashi, T.; Hirate, S.; Kitayama, K.; Tsuji, H.; Uozumi, Y. *Chem. Lett.* **2000**, 1272–1273.

10. Mashima, K.; Kusano, K.; Sato, N.; Matsumura, Y.; Nozaki, K.; Kumobayashi, H.; Sayo, N.; Hori, Y.; Ishizaki, T.; Akutagawa, S.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 3064–3076.
11. Doucet, H.; Brown, J. M. *Tetrahedron: Asymmetry* **1997**, *8*, 3775–3784.
12. Doucet, H.; Fernandez, E.; Layzell, T. P.; Brown, J. M. *Chem. Eur. J.* **1999**, *5*, 1320–1330.
13. Maxwell, A. C.; Franc, C.; Pouchain, L.; Müller-Bunz, H.; Guiry, P. J. *Org. Biomol. Chem.* **2008**, *6*, 3848–3853.
14. Fleming, W. J.; Muller-Bunz, H.; Lillo, V.; Fernandez, E.; Guiry, P. J. *Org. Biomol. Chem.* **2009**, *12*, 2520–2524.
15. Flanagan, S. P.; Guiry, P. J.; Goddard, R. *Tetrahedron* **2005**, *61*, 9808–9821.
16. McCarthy, M.; Goddard, R.; Guiry, P. J. *Tetrahedron: Asymmetry* **1999**, *10*, 2797–2807.
17. Connolly, D. J.; Cusack, D.; O'Sullivan, T. P.; Guiry, P. J. *Tetrahedron* **2005**, *61*, 10153–10202.
18. Chan, J. H.; Hong, J. S.; Kuyper, L. F.; Jones, M. L.; Baccanari, D. P.; Tansik, R. L.; Boytos, C. M.; Rudolph, S. K.; Brown, A. D. *Heterocycl. Chem.* **1997**, *34*, 145–151.
19. Dempcy, R. O.; Skibo, E. B. *Biochemistry* **1991**, *30*, 8480–8487.
20. Connolly, D. J.; Guiry, P. J. *Synlett* **2001**, 1707–1710.
21. Imai, Y.; Sato, S.; Takasawa, R.; Ueda, M. *Synthesis* **1981**, 35–36.
22. Spivey, A. C.; Fekner, T.; Spey, S. E.; Adams, H. *J. Org. Chem.* **1999**, *64*, 9430–9443.
23. Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743–756.
24. Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180–7181.
25. Valk, J.-M.; Claridge, T. D. W.; Brown, J. M.; Hibbs, D.; Hursthouse, M. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2597–2610.
26. Guiry, P. J.; Carroll, A. M.; O'Sullivan, T. P. *Adv. Synth. Catal.* **2005**, *347*, 609–631.
27. Guiry, P. J.; Carroll, A.-M.; Coyne, A. G. *In: R.H. Crabtree, D.M.P. Mingos (Eds.)*; Comprehensive Organometallic Chemistry III: Elsevier, 2006. pp. 839–869.
28. Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1988**, *53*, 5178–5179.
29. Brown, J. M.; Hulmes, D. I.; Layzell, T. P. *J. Chem. Soc., Chem. Commun.* **1993**, 1673–1674.
30. Black, A.; Brown, J. M.; Pichon, C. *Chem. Commun.* **2005**, 5284–5286.
31. Schnyder, A.; Hintermann, L.; Togni, A. *Angew. Chem., Int. Ed.* **1995**, *34*, 931–933.
32. Guiry, P. J.; Hooper, M. W.; McCarthy, M. *Chem. Commun.* **2000**, 1333–1334.
33. Perrin, D.; Armarego, W. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon: Oxford, 1988.
34. A CIF file containing the X-ray crystallographic data for (*S*,*R*)-**14** has been deposited. Data may be obtained from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK or deposit@ccdc.cam.ac.uk by quoting the number CCDC 630664 and the literature reference.