Enantioselective hydroboration of olefins catalysed by cationic rhodium complexes of 2-phenylquinazolin-4-yl-2-(diphenylphosphino)naphthalene†

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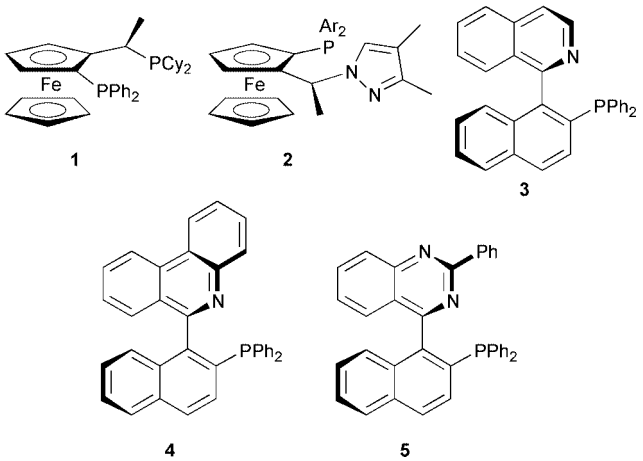
Cationic rhodium complexes of 2-phenylquinazolin-4-yl-2-(diphenylphosphino)naphthalene catalyse the hydroboration of indene, tetrahydronaphthalene and a range of styrenes in high yields, regioselectivities and with enantiomer excesses of up to 97%

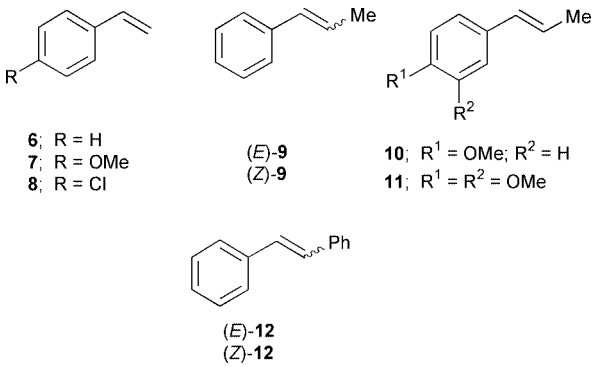
The report by Männig and Nöth[1] that Rh–phosphine complexes successfully catalysed the hydroboration of olefins added a new dimension to the hydroboration methodology developed by Brown.[2] With catecholborane as the borane source, the catalysed variant offered potential advantages in terms of chemo-, regio- and enantioselectivity.[3] Burgess[4] first reported catalytic enantioselective hydroboration and Hayashi subsequently used Rh–BINAP complexes for the hydroboration of styrene in ees of up to 96%.[5] Togni applied Rh complexes of the diphosphine Josiphos **1** (92% ee) and the related pyrazole-



1 **2** **3** **4** **5**

containing phosphinamine **2** (98% ee).[6,7] Brown used the axially chiral phosphinamine ligands QUINAP **3** (91% ee)[8] and PHENAP **4** (67% ee)[9] and also extended the standard hydroboration–oxidation sequence to include hydroboration–amination.[10] We have recently reported the synthesis and resolution of the related ligand, 2-phenylquinazolin-4-yl-2-(diphenylphosphino)naphthalene **5**, and, in view of the success of **3** and **4**, we wished to test its enantiodifferentiating ability in Rh-catalysed olefin hydroboration and we now report our preliminary results.[11]

The required cationic Rh catalyst was prepared in a standard manner from TMS triflate and (cycloocta-1,5-diene)(pentane-2,4-dionato)rhodium(I) and (*R*)-**5**.[12] Because of its susceptibility to oxidation, the catalyst was freshly made *in situ* and we also used freshly distilled catecholborane. We focused on vinylarene substrates, paying particular attention to those which would highlight the effect on reactivity and enantioselectivity of different aryl substituents and β-substitution, as exemplified by olefins **6**–**12**. In each of the reactions the catalysed hydroboration was followed by direct oxidation with H_2O_2 to afford the corresponding alcohol. The results of our investigations are given in Table 1.



6; R = H
7; R = OMe
8; R = Cl

(*E*)-**9**
(*Z*)-**9**

10; R^1 = OMe; R^2 = H
11; R^1 = R^2 = OMe

(*E*)-**12**
(*Z*)-**12**

The α:β regioselectivity obtained using phenylethene **6** was found to increase using lowered reaction temperatures and the optimised values obtained were 80:20 with an ee value of 79% after a reaction time of 2 h. This ee value compares favourably with PHENAP **4** (67%) but is lower than that obtained with QUINAP **3** (88%) and our regioselectivity was poorer than both **3** and **4** (97:3 and 90:10, respectively).[8a,9] The sense of

Table 1 Catalytic hydroboration of stilbenes[a]

Entry	Olefin	*T*/°C	α:β[b]	Conversion (%)[b]	Ee (%) (*R*)[c]
1	**6**	25	68:32	100	63[d]
2	**6**	0	80:20	100	79[d]
3	**7**	25	75:25	100	77[d]
4	**7**	0	77:23	91	81[d]
5	**8**	25	78:22	100	46[d]
6	**8**	0	83:17	100	49[d]
7	(*E*)-**9**	25	91:9	100	94[d]
8	(*Z*)-**9**	25	92:8	100	91[d]
9	**10**	25	88:12	87	88[d]
10	**10**	0	89:11	72	92[d]
11	**11**	25	93:7	75	97[d]
12	**11**	0	91:9	65	93[d]
13	(*E*)-**12**	25	—	—	—
14	(*Z*)-**12**	25	—	100	59[e]
15	(*Z*)-**12**	0	—	100	62[e]

[a] *Typical procedure*: Freshly distilled catecholborane (0.5 mmol) in THF (1 ml) was added dropwise to a solution of olefin (0.5 mmol) and [(*R*)-diphenyl[1-(2-phenylquinazolin-4-yl)(2-naphthyl)]phosphine]rhodium(cycloocta-1,5-diene)trifluoromethanesulfonate (5 μmol) in THF (1 ml). The solution turned brown and was stirred at room temp. for 2 h. The reaction was placed in an ice bath and quenched with EtOH (1 ml). 30% H_2O_2 (aq.) (3 ml) and 1 M NaOH (aq.) (3 ml) were added and the mixture was allowed to warm and stirred for 1 h at room temp. The mixture was transferred to a separating funnel and Et_2O was added (10 ml). The organic extracts were washed with 1 M NaOH (aq.), brine and then dried over $MgSO_4$. The solvent was removed *in vacuo* to give the product as an oil. ^{1}H NMR obtained gave % conversion and regioselectivity. Enantioselectivities were determined by either GC or HPLC. [b] Regioselectivities and conversions by ^{1}H NMR. [c] Absolute configuration assigned by similarity in order of elution in the GC analysis and from the sign of the optical rotation.[8] [d] Enantiomeric excesses were determined by GC (β-Dex®120 column, 30 m × 0.25 mm, 0.25 μm film thickness). [e] Enantiomeric excesses were determined by HPLC (Chiralcel OD column 99.5:0.5 Hex–*i*PrOH.

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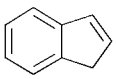
asymmetry was identical to **3** and **4**, *i.e*. the (*R*)-ligand affords the (*R*)-product alcohol. The more electron-rich 4-methoxyphenylethene **7** gave similar regioselectivities and an increased ee of 81%, but again lower than the 94% ee value observed with QUINAP **3**.[8a] The electron-deficient substrate, 4-chlorophenylethene **8**, afforded similar regioselectivities but significantly lowered ees of 46–49%, which is in agreement with trends observed employing QUINAP **3** and analogues.[8b] More promising results in terms of regio- and stereoselectivity were obtained using β-substituted arylethenes. Both the (*E*)- and (*Z*)-isomers of propenylbenzene **9** demonstrated a preference for reaction at the benzylic position and similarly in high ees of 94 and 91%, respectively. Similar values were obtained with QUINAP **3** and PHENAP **4**[9] whereas BINAP afforded an ee of 42% for (*E*)-**9** and 18% for (*Z*)-**9**.[5] (*Z*)-Propenyl-4-methoxybenzene **10** was a similarly successful substrate giving up to 92% ee in 72% yield after reaction for 6 days at 0 °C. The combination of an even more electron-rich arene and β-substituted olefin **11** gave the best ee of 97% using ligand **5**. Again it was noted that increasing the electron richness of the arene was beneficial in terms of enantioselectivity but led to a retardation of the reaction as seen by the poorer yields obtained. In order to determine the effect of increasing the bulk at the β-position we tested (*E*)- and (*Z*)-stilbene **12** and found that (*E*)-**12** was an unreactive substrate whereas (*Z*)-**12** afforded up to 62% ee in excellent yield. This result is similar to that obtained with QUINAP **3** where high ees (85–91%) were obtained with both isomers, although it was noted that (*E*)-**12** reacted at a significantly lower rate (45 turnovers after 20 h).[8b] The best ee reported for (*Z*)-**12** using BINAP was significantly lower at 16%.[5]

The cyclic olefins, indene **13** and 1,2-dihydronaphthalene **14**, are two of the most challenging substrates in Rh-catalysed



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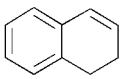

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hydroboration. We tested Rh complexes of **5** with these substrates and the results are shown in Table 2. Excellent conversions and regioselectivities were obtained and optimised ees of 84% and 89% were obtained with **13** and **14**, respectively. The result for **13** is slightly lower than that reported for QUINAP **3** (86%),[8b] but compares favourably to PHENAP **4** (64%)[9] and even more so when compared to BINAP (19%).[5] A similar trend is observed for substrate **14** as our result of 89% is again lower than that reported for QUINAP **3** (96%),[8b] but is higher than the value obtained with PHENAP **4** (84%)[9] and in this case no result has been quoted for BINAP.

All the reactions noted in Table 1 were run on a 0.5 mmol scale with 1 mol% catalyst. In a further study, the hydroboration of (*E*)-propenylbenzene **9** was carried out using 0.5 mol% catalyst and our results are given in Table 3. Using 0.5 mol% catalyst, the ee obtained after 15 min was slightly lower than the values obtained after 1 h (94% ee), 4 h (96% ee), and 16 h (95% ee) which were not lowered in comparison with the value obtained with 1 mol% catalyst (Table 1, entry 7).

In conclusion, our results demonstrate that **5**, applied in Rh catalysed hydroboration of substituted arylethenes, β-substituted arylethenes and cyclic olefins, gives excellent conversions, good regioselectivities and ees of up to 97%. For substituted arylethenes our ligand, 2-phenylquinazolin-4-yl-2-(diphenylphosphino)naphthalene **5**, as with QUINAP **3** and PHENAP **4**, afforded lower ees than both BINAP and Josiphos **1**. However, for β-substituted arylethenes and cyclic olefins these axially chiral phosphinamine ligands are far superior. This can be explained by inferring that the increased steric demand of the olefin is more easily accommodated by these less sterically demanding ligands. Further hydroboration studies employing structurally related quinazoline-containing ligands[13] are in progress and will be reported in due course from these laboratories.[14]

Table 2 Catalytic hydroboration of cyclic olefins

Entry	Olefin	*T*/°C	α:β[a]	Conversion (%)[a]	Ee (%) (*R*)[b]
1	**13**	25	98:2	98	84[c]
2	**13**	0	98:2	99	81[c]
3	**14**	25	>99:1	100	89[d]
4	**14**	0	>99:1	>99	88[d]

[a] Regioselectivities and conversions by ^{1}H NMR. [b] Absolute configuration assigned by similarity in order of elution in the GC analysis and from the sign of the optical rotation.[8] [c] Enantiomeric excesses were determined by GC (Supelco 2-4310 α-Dex®120 column, 30 m × 0.25 mm, 0.25 μm film thickness). [d] Enantiomeric excesses were determined by GC (β-Dex®120 column, 30 m × 0.25 mm, 0.25 μm film thickness).

Table 3 Variation of catalyst concentration in the hydroboration of (*E*)-**9**

Entry	Mol % Catalyst	Time/h	Conversion (%)	Ee (%) (*R*)
1	0.5	0.25	17	92
2	0.5	1	31	94
3	0.5	4	75	96
4	0.5	16	100	95

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Notes and references

† This compound has previously been published under the name 2-phenylquinazolinap.

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