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Asymmetric Catalytic Hydrogenolysis of Aryl–Halide Bonds in Fused Arene Chromium and Ruthenium Complexes

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Abstract: Access to highly enantioenriched planar chiral [Cr(5-bromonaphthalene)$(CO)_3$] (**6**), [Ru(η^5-C_5R_5)(5-bromonaphthalene)][PF_6] (**42**) and [Ru(η^5-C_5R_5)(4-bromoindene)] (**44**) was sought using asymmetric hydrogenolysis of [Cr(5,8-dibromonaphthalene)$(CO)_3$] (**5**), [Ru(η^5-C_5R_5)(5,8-dibromonaphthalene)] (**39**) and [Ru(η^5-C_5R_5)(4,7-dibromoindene)] (**40**), respectively. Initial efforts focused on the chromium complex **5**. Pd^0 catalysts with dimethoxyethane as the solvent and $LiBH_4$ or $NaBH_3CN$ as a hydride source worked best. Nineteen chiral bidentate phosphorus ligands were screened in this reaction. Asymmetric induction was low to modest with product *ee*'s in the range of 4 to 52% and yields of **6** of up to 70%. Chiral phosphoramidite ligands proved superior and a bulky ligand derived from a Whitesell amine and 3,3′-diphenyl-binaphtol afforded **6** with an *ee* of 97%. The high enantioselectivity is largely due to the initial desymmetrization reaction though kinetic resolution also plays an important role as shown by the determination of a selectivity factor $s = 8.5$ at $-10\,^{\circ}C$. Initially high ligand loadings (4 equiv/Pd) were necessary to achieve good asymmetric induction. This could be traced to the trapping of the chiral ligand by borane formed in the reaction. Addition of 1,4-diazabicyclo[2.2.2]octane (DABCO) suppressed this, and its addition led to the use of Pd and chiral ligand in a 1:1.2 ratio. Asymmetric hydrogenolysis of cationic dibromonaphthalene and neutral dibromoindenyl complexes of Ru cyclopentadienyl complexes was investigated and afforded the following results: [RuCp(5-bromonaphthalene)][PF_6] (**39a**; 75%, 90% *ee*), [RuCp*(5-bromonaphthalene)] [PF_6] (**39b**; 88%, 99% *ee*), [RuCp(4-bromoindenyl)] (**44a**; 72%, 96% *ee*), and [RuCp*(4-bromoindenyl)] (**44b**; 62%, 68% *ee*).

Keywords: asymmetric catalysis · chromium · enantioselectivity · hydrogenolysis · indenyl · naphthalene · ruthenium

Introduction

Highly enantioenriched (η^6-arene)tricarbonylchromium(0) complexes, the chirality of which originates from the 1,2-disubstitution pattern of the arene and the coordination of the metal to one enantiotopic face of the arene, are powerful chirons in asymmetric synthesis.[1] Robust planar chiral arene complexes are also finding increased application as chiral ligands in asymmetric catalysis.[2] In contrast to chromium–arene complexes, isoelectronic cationic (η^6-arene)(η^5-Cp)ruthenium complexes (Cp = cyclopentadiene) have received less attention.[3,4] They are more resistant to oxidative and thermal cleavage of the metal–arene bond, and, due to the higher electrophilicity of the $RuCp^+$ moiety, nucleophilic substitution reactions are facilitated.

The strategies to access enantiomerically enriched, planar chiral complexes are based either on asymmetric synthesis or on resolution of racemates. The asymmetric synthesis involves diastereoselective complexation,[2d–e,4,5] diastereo- or enantioselective nucleophilic addition/hydride abstraction,[2e,6] and lithiation/electrophile addition.[2d–e,7] Although these approaches are potent methods that often give the target complexes in high enantiomeric purity, they rely on the use of a stoichiometric amount of chiral reagents, and the diastereoselective methods often require additional steps for the introduction and the removal of chiral auxiliaries. A potentially very attractive catalytic route is the desymmetrization of prochiral complexes by a chiral catalyst

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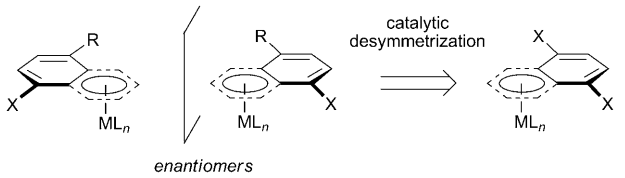
(Scheme 1). In this article we will present a full account of our investigations to carry out the title reaction using [Cr(5,8-dibromonaphthalene)(CO)$_3$] as a substrate, which



Scheme 1. Access to planar chiral complexes by catalytic desymmetrization (M = Cr, Ru).

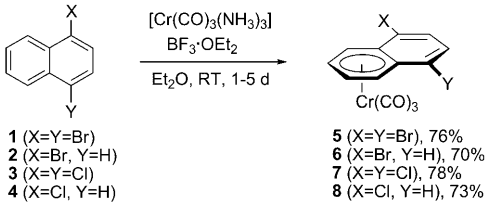
can be readily prepared from 1,4-dibromonaphthalene. In the second part, we will investigate the asymmetric hydrogenolysis of the more robust Cp and Cp* ruthenium complexes (Cp* = 1,2,3,4,5-pentamethylcyclopentadiene) of dibromonaphthalene and dibromoindene.

There were very few reports on Pd-catalyzed desymmetrization reactions of [Cr(CO$_3$)(dihaloarene)] complexes in the literature when we started this project, and to the best of our knowledge, an example of such reactions for ruthenium sandwich complexes has not yet been described. Uemura, Nishimura, and Hayashi reported Pd-catalyzed asymmetric cross-coupling reactions of alkenyl and aryl metal compounds with [Cr(CO)$_3$(1,2-dichlorobenzene)].[8] The best result was obtained using a Pd-catalyzed Suzuki–Miyaura aryl coupling reaction with a chiral bidentate ferrocene ligand (derived from Ugi's amine). This afforded the *ortho*-chloro biaryl complex in 55% yield and 69% *ee*. More recently, a very similar level of induction and yield was reported by Schmalz for a methoxycarbonylation of the same substrate (47% yield, 63% *ee*).[9a] In this particular reaction, the authors showed that kinetic resolution in the second step allows the isolation of the highly enantioenriched product (95% *ee*), although this lead to a drop in yield to 31%. Bidentate chiral ferrocenyl ligands were again the best performers in this transformation, as well as in analogous reactions of [Cr(CO)$_3$(2,6-dichlorotoluene)];[9b] however, the same ligand applied to a Pd-catalyzed vinyl/halide exchange of [Cr(CO)$_3$(1,2-dichlorobenzene)] using a divinyl aluminum reagent afforded poor asymmetric induction (16% *ee*).[9c] To complete the short list of precedents of asymmetric desymmetrizations in [Cr(arene)(CO)$_3$] complexes, a report by Kamikawa et al. appeared[10a] during the preparation of our preliminary communication of this study.[11] It described an asymmetric intramolecular Mizoroki–Heck reaction of [Cr(CO)$_3$(2,6-dibutenylchlorobenzene)] with the best result reaching 78% yield and 73% *ee*.[10a]

We decided to turn our attention first to naphthalene chromium complexes. Our choice was motivated by the potential of a highly enantiomerically enriched bromonaphthalene as a precursor for asymmetric synthesis,[5a,12] for the design of planar chiral ligands,[2] and as a chiral [Cr(CO)$_3$] transfer agent. In addition, enantioenriched naphthalene complexes such as those described in this paper are not accessible by the established methods. The desymmetrization reaction chosen for this study was the Pd-catalyzed asymmetric hydrogenolysis of [Cr(CO)$_3$(5,8-dibromonaphthalene)] (**5**). We also examined kinetic resolution of *rac*-[Cr(5-bromonaphthalene)(CO)$_3$] (**6**) and briefly checked [Cr(CO)$_3$(5,8-dichloronaphthalene)] (**7**) and [Cr(CO)$_3$(5-chloronaphthalene)] (**8**). The absence of literature precedent, the restrictions imposed by the lability of the substrate,[13] and the search for a chiral ligand capable of giving high asymmetric induction were all considered worthy challenges. Furthermore, enantioenriched planar chiral ruthenium complexes are of interest, not only to prove the applicability of the process, but also to access a less well studied, kinetically more inert family of planar chiral sandwich complexes. They represent valuable molecules which may find use in the synthesis of chiral ligands or in the chemistry of new materials.

Results and Discussion

Synthesis of the [Cr(CO)$_3$(naphthalene)] complexes: Naphthalene complexes **5**–**8** were obtained as single regioisomers by stirring a 1:1 mixture of [Cr(CO)$_3$(NH$_3$)$_3$] and the substituted naphthalene in diethylether at 25°C with $BF_3{\cdot}OEt_2$ (3.5 equiv, OEt_2 = diethylether, Scheme 2).[14] This mild and



1 (X=Y=Br)
2 (X=Br, Y=H)
3 (X=Y=Cl)
4 (X=Cl, Y=H)

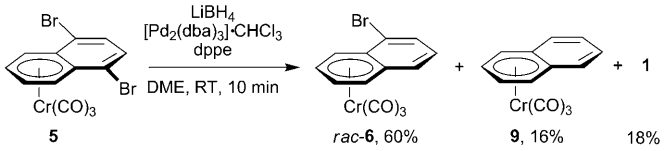
5 (X=Y=Br), 76%
6 (X=Br, Y=H), 70%
7 (X=Y=Cl), 78%
8 (X=Cl, Y=H), 73%

Scheme 2. Regioselective complexation of 1-substituted and 1,4-disubstituted halonaphthalenes.

high-yielding procedure avoids insertion of a zero-valent {Cr(CO)$_n$} fragment into the aryl–bromine bond, a process that occurs readily when using thermolysis of [Cr(CO)$_6$] in the presence of aryl bromides at high temperatures and which results in the decomposition of the starting materials. The regioisomers formed were those expected based on precedents of complexation of 1-substituted and 1,4-disubstituted naphthalenes.[12,15] Coordination occurred exclusively (>96%) on the unsubstituted aromatic ring.

Pd-catalyzed hydrogenolysis: We next tested the conditions for the Pd-catalyzed hydrogenolysis of one of the two C_{Ar}–Br (Ar = aryl) bonds in complex **5**. As anticipated, the lability of the naphthalene–chromium bond was a major hurdle in this project. Lewis bases readily cleave the naphthalene–metal bond and this excludes the use of Lewis basic solvents or polar additives. We investigated sodium formate[16] and

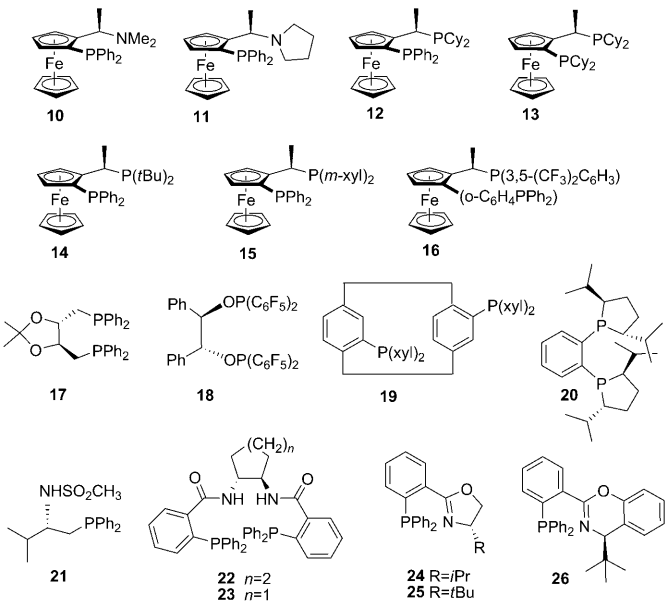
$NaBH_4$[17] as reducing agents in this reaction in combination with a number of Pd catalyst precursors ($Pd(OAc)_2/PPh_3$ or $Ph_2PCH_2CH_2PPh_2$ (dppe), $[Pd(PPh_3)_4]$ (OAc = acetate, PPh_3 = triphenylphosphine). We found that in most of the solvents tested (DMF, acetonitrile, CH_2Cl_2, methanol, toluene), decomplexation induced by either the solvent or the formate was faster than or competitive with arene–halide hydrogenolysis. Complex **5** is soluble and stable in toluene, but hydrogenolysis with $NaBH_4$ in the presence of $[Pd(PPh_3)_4]$ was hampered by the low solubility of the reducing agent and resulted in a slow reaction (2–3 days at 30 °C) even with 10–15 mol % catalyst. Worse, the yield of the sought-after monobromonaphthalene complex **6** never exceeded 20 % of the final mixture, in which 1,4-dibromonaphthalene (**1**) and the starting complex **5** were still present in quantities of 32 and 47 %, respectively, after 62 h. After much experimentation and after switching to more soluble $LiBH_4$ and using dimethoxyethane as the solvent and $[Pd_2(dba)_3]\cdot CHCl_3$/dppe (dba = dibenzylideneacetone) as the catalyst, conditions were found that afforded the monobromonaphthalene complex **6** in reasonable yield (Scheme 3).



Scheme 3. Pd-catalyzed hydrogenolysis of an aryl C–Br bond.

Chloroform slowly oxidizes the labile Cr^0 complex, accounting for some of the complex **1** isolated. Ligand dissociation could be reduced to < 10 % by using $[Pd(dba)_2]$ in place of the chloroform adduct. While overreduction to give **9** was a problem in this reaction, we hoped that with an efficient chiral catalyst the reaction would stop after one of the enantiotopic C_{Ar}–Br bonds had undergone hydrogenolysis.

Asymmetric hydrogenolysis using bidentate ligands: Following the optimization of the reaction conditions for the racemic hydrogenolysis, we probed chiral ligands for the asymmetric version. Because of literature precedents, we first turned our attention to bidentate ligands (Table 1). The ferrocenyl ligands **10** and **11** that were best for the desymmetrization of $[Cr(CO)_3$(1,2-dichlorobenzene)][8,9] and led to the formation of **6** in good yield, but in poor enantioselectivities. (Table 1, entries 1 and 2, respectively). Subsequently, chiral ferrocene ligands **12**–**16** (Solvias set) were screened followed by an array of bidentate (P,P) and (P,N) ligands (**17**–**26**) of varying steric bulk and donor strength. Reactions were run until the starting material **5** had been consumed. At 5 °C and with 5 mol % $[Pd(dba)_2]$, reaction times were in the range of 30–50 min. Overreduction to form $[Cr(CO)_3$(naphthalene)] (**9**) was found in all cases and was particularly important with ligands **13**, **17**, and **24** (Table 1, entries 4, 8, and 15). For the reaction detailed in entry 2



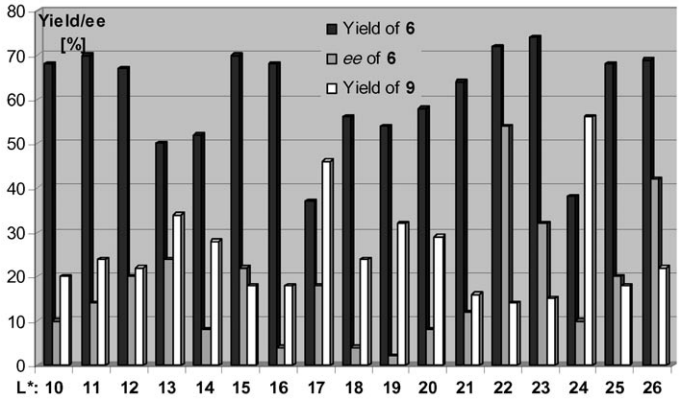
(Table 1), it was noted that the *ee* of **6** increased from 10 to 14 % during the time it took for **9** to increase from 14 to 24 %. This observation presumably arises from kinetic resolution connected to the formation of **9**. A more substantial indication of kinetic resolution was found for **22** (Table 1, entry 13). Here, the *ee* of **6** increased from 40 to 54 % when **9** rose from 10 to 14 %.

Incomplete dba dissociation in $[Pd(dba)_2]$ could be part of the problem and this was examined by using [Pd(allyl)Cp] (Cp = C_5H_5) as catalyst precursor. The results were not better, however, and the hypothesis of interference of dba could thus be ruled out. The absolute configuration was assigned based on the X-ray structure determination of (*S*)-**6** (Figure 1).[11]

In the crystal structure [Cr(5-bromonaphthalene)$(CO)_3$] (**6**) adopts an *anti*-staggered conformation of the $Cr(CO)_3$ tripoid with respect to the arene ring C atoms. The distance between Cr and the coordination plane of naphthalene is more accurately described with respect to the plane formed by C(1)–C(4). The slippage of the Cr atom from the center of the arene ring away from the naphthalene ring junction is a common feature in η^6-arene complexes of condensed arene ligands. This slippage in **6** is 0.08 Å. The asymmetric unit cell contains two [Cr(5-bromonaphthalene)$(CO)_3$] molecules. There is π-stacking between the two complexes with a mean stacking distance of 3.31(7) Å. Both molecules of the asymmetric unit show the same *S* configuration. Within the η^6-ring ligand, the C–C bond lengths vary in nonalternant fashion between 1.38(1) and 1.437(9) Å; the shorter bonds are C(1)–C(2) and C(2)–C(3), and the longer are the C(4)–C(10) and C(9)–C(1). This is consistent with the slight deformation of the naphthalene ring towards the η^4-coordination.

After screening the chiral ligands depicted in Table 1, we were faced with the fact that while catalytic hydrogenolysis

Table 1. Asymmetric hydrogenolysis of complex **5** using bidentate ligands. Top: ● **40a**; ■ **44a**, ▲ **45a**. Bottom: ● **40b**; ■ **44b**, ▲ **45b**. (For color figure see Supporting Information).[a]



Entry	Ligand	**6**[b] [%]	*ee*[c] of **6** [%]	**9**[b] [%]
1	**10**	68	10 (*S*)	20
2	**11**	70	14 (*S*)	24
3[d]	**12**	67	20 (*R*)	22
4[e]	**13**	50	24 (*R*)	34
5[e]	**14**	52	8 (*R*)	28
6[f]	**15**	70	22 (*R*)	18
7	**16**	68	4 (*R*)	18
8	**17**	37	18 (*R*)	46
9	**18**	56	4 (*R*)	24
10	**19**	54	2 (*S*)	32
11[f]	**20**	58	8 (*S*)	29
12[f]	**21**	64	12 (*S*)	16
13[e]	**22**	72	54 (*S*)	14
14[e]	**23**	74	32 (*S*)	15
15[d]	**24**	38	10 (*R*)	56
16	**25**	68	20 (*R*)	18
17[d]	**26**	69	42 (*S*)	22

[a] Reactions were carried out using 0.12 mmol of **5** in DME with [Pd(dba)$_2$] (5 mol%), L* (10 mol%), $LiBH_4$ (2.0 equiv), at 5°C for 40 min (unless otherwise noted). [b] HPLC yields (column: Daicel chiralcel OD-H, Calibration: phenanthrene). The product mixtures contained <10% decomplexed naphthalenes (mainly **1**). [c] Determined using a Daicel chiralcel OD-H column (95:5 hexane/*i*PrOH, 1.0 mL min^{-1}). The indicated absolute configuration is that of the major enantiomer and is based on the X-ray structure determination of (*S*)-**6**.[11] [d] Reaction time 45 min. [e] Reaction time 30 min. [f] Reaction time 50 min.

of the labile complex **5** works reasonably well, asymmetric induction with the bidentate ligands **10**–**26** reaches modest levels at best. For this reason we refrained from further optimizing conditions and/or quantification of the kinetic resolution of the second step and instead, turned to check the suitability of phosphoramidite ligands in this reaction (Table 2).

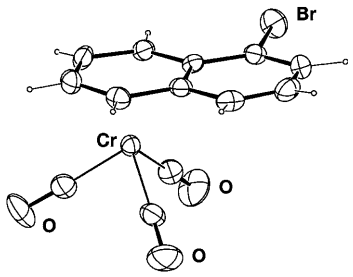


Figure 1. ORTEP view of compound (*S*)-[Ru(5-bromonaphthalene)(-CO)$_3$] [(*S*)-**6**] drawn using 40% probability ellipsoids (reproduced with the permission from ref. [11]).

Asymmetric hydrogenolysis using phosphoramidite ligands: Chiral phosphoramidite ligands have been widely and successfully used in the past ten years.[18] One of the salient features of these ligands is their fine-tuning capability through modification of either the amine moiety or the biaryl backbone. This high modularity allows access to a wide array of structures.[19] The first monodentate phosphoramidite ligand evaluated in the desymmetrization reaction was Feringa's ligand (S_a,*R*,*R*)-**27**.[20] Pleasingly, product **6** was obtained in high yield and the enantioselectivity rose up to 62% (Table 2, entry 1). The use of the diastereoisomer (S_a,*S*,*S*)-**28** led to a mismatch situation and this totally annihilated asymmetric induction (Table 2, entry 2). The use of MonoPhos (S_a)-**29** or tropos[21a] ligand (*R*,*R*)-**30** resulted in poor enantioselectivities, confirming the crucial roles of all chirality elements of the ligand (Table 2, entries 3 and 4). By modifying the amine component, the performance of the catalyst remained poor (Table 2, entry 5). However, changing the biaryl scaffold provided more efficient phosphoramidite ligands. For instance, substitution in the 3,3′- and 5,5′-positions of the biphenol by methyl, *tert*-butyl, and phenyl groups allowed for 64, 66, and 89% *ee*, respectively (Table 2, entries 6–8).[21b] Further improvement was made with the ligand (S_a,*R*,*R*)-**35** bearing phenyl substituents in the 3,3′-positions of the binaphtol core, affording **6** in 92% *ee* (Table 2, entry 9). The use of ligand (S_a,*R*,*R*)-**36** with phenyl substituents in 6,6′-positions resulted in lower *ee* (Table 2, entry 11).[22] Optimal reaction conditions using the new bulky ligand **35** were found by lowering the temperature to −10°C and by adding $LiBH_4$ dropwise as a solution in dimethyl ether (DME). Complex (*S*)-**6** could be obtained in 65% isolated yield and with an *ee* of 97%.

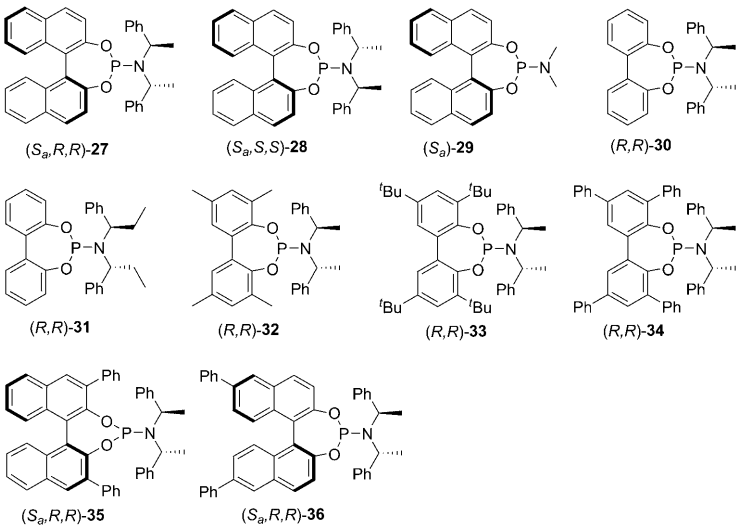
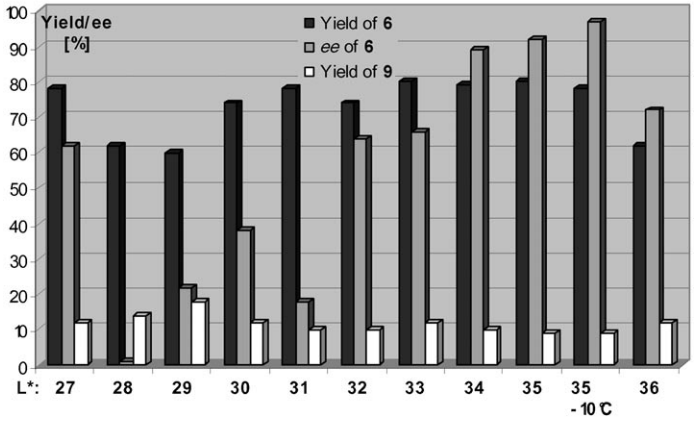


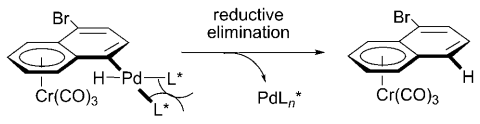
Table 2. Asymmetric hydrogenolysis of complex **5** using phosphoramidite ligands. (For color figure see Supporting Information).[a]



Entry	Ligand	**6**[b] [%]	*ee*[c] of **6** [%]	**9**[b] [%]
1	**27**	78	62 (*S*)	12
2	**28**	62	*rac*	14
3	**29**	60	22 (*S*)	18
4	**30**	74	38 (*S*)	12
5	**31**	78	18 (*S*)	10
6	**32**	78	64 (*S*)	10
7	**33**	80	66 (*S*)	12
8	**34**	79	89 (*S*)	10
9	**35**	80	92 (*S*)	9
10[d]	**35**	78, 65[e]	97 (*S*)	9
11	**36**	62	72 (*S*)	12

[a] Reactions were carried out using 0.12 mmol of **5** in DME with [Pd(dba)$_2$] (5 mol%), L* (20 mol%), $LiBH_4$ (2.0 equiv), at 5 °C for 15–60 min (unless otherwise noted). [b] HPLC yields (column: Daicel chiralcel OD-H, Calibration: phenanthrene). [c] Determined using a Daicel chiralcel OD-H column (95:5 hexane/*i*PrOH, 1.0 mL min^{-1}). The indicated absolute configuration is that of the major enantiomer and is based on the X-ray structure determination of (*S*)-**6**.[11] [d] Reaction carried out at −10 °C, in which $LiBH_4$ was added as a solution in DME. [e] Isolated yield.

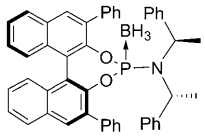
Although the process performed efficiently in terms of both activity and enantioselectivity, the use of 20 mol% of a high-molecular-weight ligand, which requires a five-step synthesis from BINOL (BINOL = 1,1′-bi-2-naphthol), remained a major limitation. Efforts to recycle the chiral ligand at the end of the reaction did not meet with success. Attempts to decrease the ligand loading resulted in lower enantioselectivity and diminished yield of complex **6**. This was difficult to rationalize at first. The product is formed in a reductive elimination step as depicted in Scheme 4. In a square-planar Pd^{II} complex, the aryl unit and the hydride must be coordinated in a *cis* fashion, implying that a maximum of two phophoramidite ligands could be coordinated to the metal. However, models clearly indicate that ligand **35** is too bulky



Scheme 4. Proposal for the reductive elimination step.

and that two ligands could not bind to Pd^{II} in a *cis* fashion. Thus, the necessity of an excess of four equivalents of the ligand was puzzling.

Careful analysis of the crude reaction mixture at the end of the reaction did not show any remaining free phosphoramidite. ^{1}H NMR analysis revealed the presence of a compound with both the 3,3′-diphenyl-BINOL and Whitesell amine fragments, but with different chemical shifts than those described for ligand **35**. At first, we suspected oxidation yielding a phosphoramidate (P=O), but the reductive conditions and ^{31}P shift (128 ppm) made this highly unlikely. An authentic sample of the phosphoramidate compound was prepared by treatment of the chiral ligand with aqueous hydrogen peroxide in acetone. ^{1}H and ^{31}P NMR analyses were not in agreement with this first hypothesis.[23] Instead, it turned out to be the phosphoramidite borane complex **37**.



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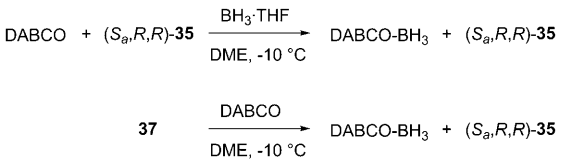
The presence of borane was confirmed by ^{11}B NMR analysis (−39.6 ppm), and the ^{31}P NMR signal at 128 ppm is in accordance with the few literature examples of isolated aminophosphane–borane adducts.[24] Now, it all became clear. On hydride transfer to Pd, $LiBH_4$ liberated borane and borane formed an adduct with ligand **35**, thus depleting the reaction of the essential chiral information. Hence, this explained the necessity of adding up to 20 mol% of chiral ligand for only 5 mol% of palladium source to attain a high degree of enantioselectivity.[25]

Borane has a high affinity for tertiary amines[26] and indeed, reacting the borane–phosphoramidite adduct **37** with DABCO (DABCO = 1,4-diazabicyclo[2.2.2]octane) in toluene for 2 h at RT provided an efficient recovery (>70%) of the free chiral ligand. The efficiency of DABCO as a borane trapping reagent was checked in two simple experiments carried out under the desymmetrization reaction conditions (Scheme 5). When BH_3, stabilized in THF, was

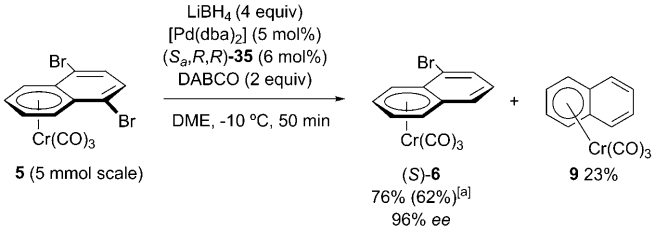


Scheme 5. Affinity of BH_3 for DABCO.

added to a mixture of ligand **35** and DABCO, the DABCO–borane adduct was formed, whereas ligand **35** remained intact. On the other hand, when DABCO was added to the phosphoramidite-borane complex **37**, borane was rapidly trapped by the diamine, delivering the free chiral ligand. The above experiments demonstrated the high affinity of BH_3 for DABCO and confirmed the potential of using

DABCO as additive in the asymmetric hydrogenolysis. Finally, given the known lability of the metal–arene bond, the stability of the naphthalene chromium complexes in the presence of the tertiary diamine was checked. Easy haptotropic slippage (change from η^6- to η^4- or η^2-coordination) of the naphthalene ligand facilitates arene dissociation and results in a dramatic increase in sensitivity towards air and Lewis basic solvents or reagents.[13] Decomplexation did not occur after leaving naphthalene complexes **5**, *rac*-**6** and **9** in the presence of DABCO in DME at −10 °C.

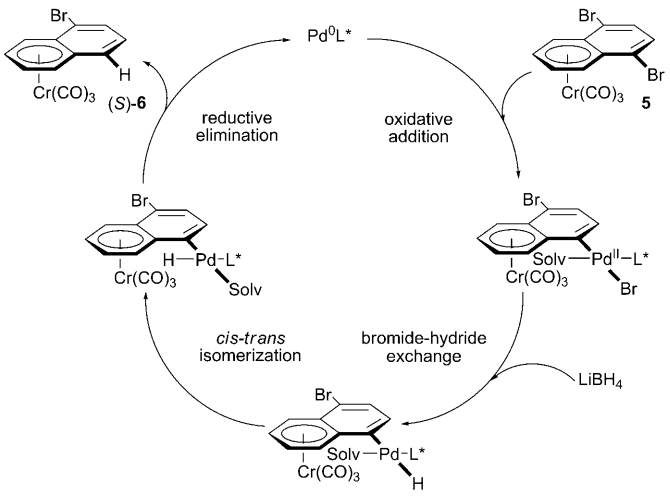
Satisfyingly, DABCO could be added to the catalytic hydrogenolysis reaction. The reaction was conducted under the standard conditions on a 5.0 mmol scale, using 5 mol% of $[Pd(dba)_2]$ and only 6 mol% of the chiral ligand, and in the presence of two equivalents of DABCO. Monobromonaphthalene chromium complex (*S*)-**6** was obtained in 76% HPLC yield (62% isolated yield) and high enantioselectivity (96% *ee*; Scheme 6).



Scheme 6. Asymmetric hydrogenolysis using DABCO as trapping agent of BH_3. [a] Yield after isolation.

With this modification, the reaction could now be carried out on a multigram scale without wasting large amounts of the chiral ligand (L*). The reduction of the L*/Pd ratio to 1.2:1 indicates that the active catalytic species involves only one bulky phosphoramidite, either by P-monodentate or P,C-bidentate coordination (involving π-interaction of an aryl substituent at the nitrogen atom rather than C−H activation).[27] On the basis of the above consideration, the proposed mechanism is illustrated in Scheme 7. Oxidative addition of complex **5** to Pd^0 is followed by a bromide–hydride exchange. The resulting complex undergoes a *cis–trans* isomerization bringing the aryl unit and the hydride into a *cis* relationship. Subsequent reductive elimination produces complex **6** and regenerates the active catalytic species to complete the catalytic cycle.

By reducing the amount of $LiBH_4$, the formation of naphthalene chromium complex **9** could be reduced and compound **6** was obtained in higher yield (up to 90%), albeit with lower enantioselectivity (88% *ee*).[28] HPLC traces of the two experiments clearly shows the difference in enantioselectivities (Figure 2). In the first case, 88% *ee* is obtained, while consumption of the starting material is not complete (Figure 2, top). On the other hand, when complete conversion was attained, the enantioselectivity reached 97% and the amount of **9** was slightly higher (Figure 2, bottom). Con-



Scheme 7. Proposed mechanism of the asymmetric hydrogenolysis.

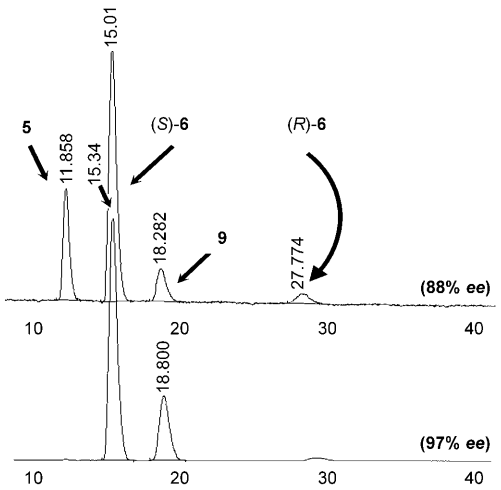
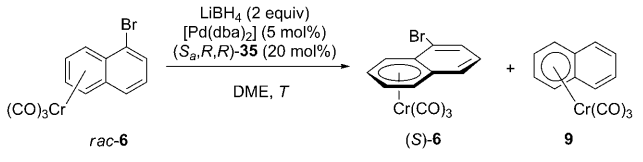


Figure 2. HPLC traces of the asymmetric hydrogenolysis.

trary to what we previously reported,[11] these observations show that the kinetic resolution connected to the formation of **9** takes place in the process. Similarly, Schmalz reported that the initial enantioselectivity in the asymmetric methoxycarbonylation of $[Cr(CO)_3$(1,2-dichlorobenzene)] was enhanced by a subsequent kinetic resolution, in which the minor enantiomer reacts faster to give the bis-methoxycarbonylated product.[9c] This is also the case here.

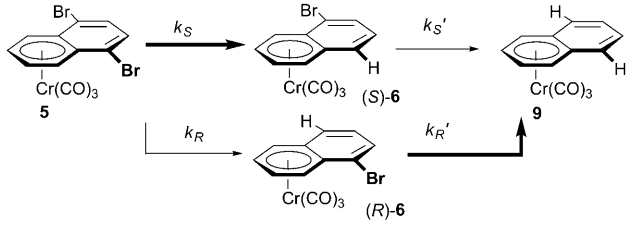
Kinetic resolution experiments: The kinetic resolution[29] was studied with the monobromonaphthalene complex **6** (Table 3, Scheme 8). Racemic complex **6** was reacted under the standard conditions. After 50% conversion, the recovered starting material **6** exhibited an enantiomeric excess of 64% in favor of the (*S*)-enantiomer ($k_R' > k_S'$). This corresponds to a selectivity factor s (k_R'/k_S') of 8.5 (Table 3, entry 4).[30] Higher temperatures afforded lower values of s (Table 3, entries 1–3). Further decrease of the temperature

Table 3. Kinetic resolution experiments.[a]



Entry	T [°C]	Conv.[b] [%]	ee[c] of **6** [%]	s[d]
1	RT	55	42	3.0
2	+10	60	73	6.1
3	0	65	83	6.3
4	−10	50	64	8.5
5	−30	45	41	4.4

[a] Reactions were carried out using 0.1 mmol of *rac*-**6** (0.033 M). [b] Determined by HPLC (column: Daicel chiralcel OD-H, Calibration: anthracene). [c] Determined using a Daicel chiralcel OD-H column (95:5 hexane/*i*PrOH, 1.0 mL min^{-1}). [d] $s = \ln[(1-c)(1-ee)]/\ln[(1-c)(1+ee)]$, average of three runs.



Scheme 8. Kinetic resolution connected to the formation of **9**.

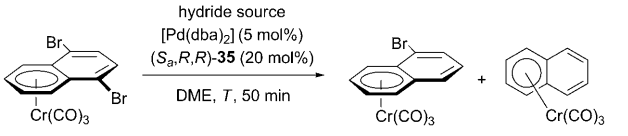
also affected the selectivity factor negatively (Table 3, entry 5). In the desymmetrization of prochiral complex **5**, the minor (*R*)-**6** enantiomer ($k_R < k_S$) is converted faster into naphthalene chromium complex **9** ($k_R' > k_S'$), resulting in further enrichement in (*S*)-**6** (Scheme 8).

To determine whether the halide plays an important role in the desymmetrization, other racemic monohalonaphthalene chromium complexes were prepared. [Cr(5-trifluoromethanesulfonylnaphthalene)(CO)$_3$][31] was very reactive and the selectivity factor was around 1.3–2.0 in the temperature range from −20 °C to RT. Almost no conversion (<5%) was obtained for [Cr(5-chloronaphthalene)(CO)$_3$] (**8**), due to its reluctance to undergo oxidative addition. This situation also prevailed for the desymmetrization of the [Cr(5,8-dichloronaphthalene)(CO)$_3$] (**7**), hence this was not investigated further.

Alternative hydride sources: LiBH$_4$ solutions are quite tedious to prepare[32a] and retain satisfactory activity for only a few weeks when stored in the refrigerator. Prior to each use, the hydride molarity has to be determined by titration.[32b] For all these reasons, the use of alternative hydride sources was investigated. The results are summarized in Table 4.

Strong hydride sources such as L-selectride, DIBAL-H (DIBAL-H = diisobutylaluminium hydride) and Red-Al (Red-Al = sodium bis(2-methoxyethoxy)aluminumhydride; Table 4, entries 1–3) led to either decomplexation of the

Table 4. Alternative hydride sources for the asymmetric hydrogenolysis.[a]

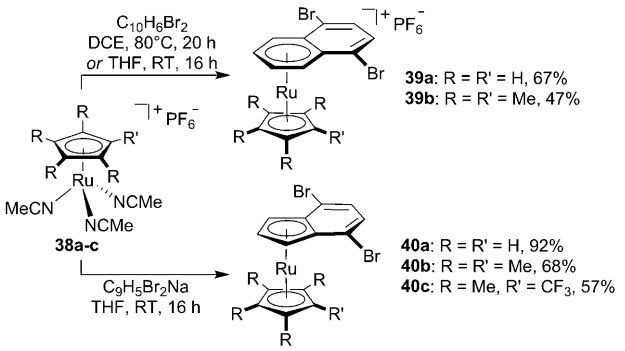


Entry	Hydride [equiv]	T [°C]	Conv.[b] [%]	**6**[b] [%]	ee[c] of **6** [%]	**9**[b] [%]
1	L-Selectride (2.0)	0	–[d]	–	–	–
2	DIBAL-H (2.0)	RT	0	0	–	0
3	Red-Al (2.0)	−10	90	60	<5	30
4	TBAC (2.0)	RT	–[d]	–	–	–
5	PMHS (2.0)	RT	0	0	–	0
6[e]	NaBH(OMe)$_3$ (2.3)	RT	48	48	47	0
7[e]	NaBH(OAc)$_3$ (2.3)	RT	55	46	56	9
8	NaBH$_3$CN (1.3)	RT	98	61	91	37
9	NaBH$_3$CN (1.3)	0	98	68	92	30
10	NaBH$_3$CN (1.3)	−10	75	68	84	7

[a] Reactions were carried out using 0.1 mmol of **5** (0.033 M). [b] Determined by HPLC (column: Daicel chiralcel OD-H, Calibration: anthracene). [c] Determined using a Daicel chiralcel OD-H column (95:5 hexane/*i*PrOH, 1.0 mL min^{-1}). [d] Decomplexation. [e] 4 h reaction time.

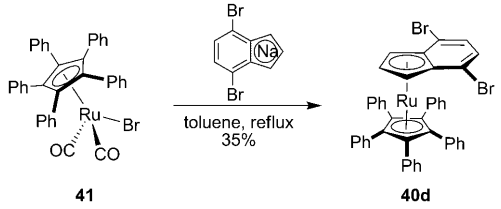
starting material, low conversion, or poor enantioselectivity. Milder reducing agents were then considered. NaBH(OMe)$_3$[33] (Table 4, entry 6) and NaBH(OAc)$_3$[34] (Table 4, entry 7) showed similar behaviors. Significant conversions and moderate enantioselectivities, along with some decomplexation, were obtained after long reaction times at RT. Although tetrabutylammonium cyanoborohydride (TBAC)[35] and polymethylhydrosiloxane (PHMS)[36] failed (Table 4, entries 4 and 5, respectively), NaBH$_3$CN[37] proved promising (Table 4, entries 8–10). There is literature precedent for the use of NaBH$_3$CN in reductions of allylic acetates[38a] or allylic amines[38b] through catalytic activation with Pd^0 complexes. Similar levels of reactivity and asymmetric induction to those obtained with LiBH$_4$ were reached (Table 4, entry 8). Kinetic resolutions studies using *rac*-**6** also showed a similar selectivity factor s.[39] Nevertheless, performing the reaction below 0 °C significantly slowed down the process (Table 4, entry 9) and the use of DABCO as an additive had no effect due to the inertness of complex BH$_2$CN-**35** towards DABCO. Reduction with NaBH$_3$CN gave good results, but this comes at the price of having to use four equivalents of the chiral ligand.

Synthesis of ruthenium complexes: With conditions for naphthalene chromium complexes established, we next explored the scope of this desymmetrization. Ligand exchange from the pivotal precursor [Ru(η^5-C$_5$R$_5$)(CH$_3$CN)$_3$][PF$_6$] (**38**)[40] (Scheme 10)[41] afforded the cationic complexes [Ru(η^5-C$_5$R$_5$)(η^6-5,8-dibromonaphthalene)][PF$_6$] (**39a**,**b**), which are isoelectronic with **5**, and the neutral analogues [Ru(η^5-C$_5$R$_5$)(η^5-4,7-dibromoindene)] (**40a**–**c**, Scheme 9). Similarly, the corresponding racemic monobromo ruthenium complexes were also prepared (see Experimental Section).



Scheme 9. Synthesis of cationic and neutral ruthenium complexes.

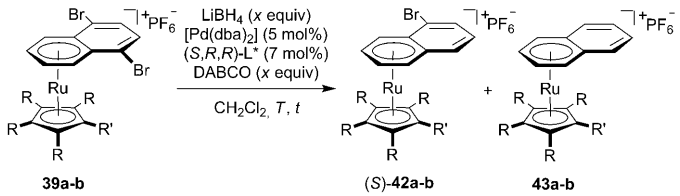
The synthesis of **40d** (R = R′ = phenyl), incorporating a pentaphenylcyclopentadienyl moiety, requires a different approach. The only method described for the synthesis of ruthenocenes that bear a η^5-C_5Ph_5 group involves treatment of $[Ru(\eta^5\text{-}C_5Ph_5)(CO)_2X]$ (X = halide; for complex **41** X = Br)[42] with a cyclopentadienyl anion.[43a] This strategy was applied to the synthesis of **40d** (Scheme 10).



Scheme 10. Synthesis of **40d**.

Asymmetric hydrogenolysis of cationic Ru complexes: Cationic $[Ru(\eta^5\text{-Cp})(\eta^6\text{-5,8-dibromonaphthalene})][PF_6]$ (**39a**) was subjected to the optimal reaction conditions established for the desymmetrization of **5**. This resulted in only moderate conversion and enantioselectivity (Table 5, entry 1). Replacing DME by dichloromethane and adjusting the temperature to −50 °C and the amount of $LiBH_4$ to one equivalent allowed **42a** to be obtained with 90 % *ee* with a good selectivity between **42a** and the overreduced complex **43a** (Table 5, entry 2). Similar levels of asymmetric induction but higher **42**/**43** selectivity were reached when **39b**, incorporating the bulky and electron-rich Cp* moiety, was used as the substrate (Table 5, entry 3). The optimal temperature was found to be −40 °C (Table 5, entries 4-5). After 3 h, full conversion was attained and **42b** was produced in 96 % *ee*, together with only 8 % of **43b** (Table 5, entry 4). Longer reaction times furnished **42b** in 99 % *ee*, albeit with a larger amount of overreduced complex **43b** (12 %; Table 5, entry 5). Kinetic resolution accounts for this result (see below). The catalyst loading could be lowered to 2 mol % of Pd and 4 mol % of the chiral ligand, without adverse effects on the reaction rate and outcome (Table 5, entry 6). However, when only 1 mol % of Pd and 2 mol % of the chiral ligand were used, significant amounts of the overreduced complex **43b** and erosion of the enantioselectivity were observed (Table 5, entry 7).[44] A control experiment, in which the chiral ligand was not added, showed that $[\{Pd(allyl)Cl\}_2]$ alone could catalyze the reaction (Table 5, entry 8). The presence of this background reaction might account for the moderate results obtained in entry 7 (Table 5). The process was successfully scaled up to 3 mmol using as low as 1 mol % of Pd and 4 mol % of the chiral ligand (Table 5, entry 9).

Table 5. Asymmetric hydrogenolysis of cationic complexes **39**.[a]



Entry	39	T [°C]	$LiBH_4$ [equiv]	t [h]	Ratio[b] [%] **42**:**43**:**39**	Yield [%] **42**+**43**	*ee*[c] of **42** [%]
1[d,e]	**39a**	−20	2.0	1.7	56:17:27	73	74
2[d,f]	**39a**	−50	1.0	1.7	75:19:2	94	90
3[e]	**39b**	−50	1.0	1.7	90: 3:7	93	92
4[g]	**39b**	−40	1.5	3.0	92: 8:0	>95	96
5[g]	**39b**	−40	1.5	4.0	88:12:0	>95	99
6[h]	**39b**	−40	1.5	3.0	87:13:0	>95	98
7[i]	**39b**	−40	1.5	3.0	79:21:0	>95	94
8[j]	**39b**	−40	1.5	3.0	48:28:24	76	–
9[k]	**39b**	−40	1.5	2.5	90:10:0	92	97
10	**39b**	−50	1.0[l]	2.5	84:16:0	90	96

[a] Unless otherwise stated, the reactions were carried out using 0.2 mmol of **39** (0.025 M in CH_2Cl_2). $LiBH_4$ was added dropwise as a DME solution. [b] Determined by ^{1}H NMR analysis. [c] Determined by ^{1}H NMR analysis in the presence of an excess of $[n\text{Bu}_4\text{N}][\Delta\text{-TRISPHAT}]$. [d] Reaction carried out in DME. [e] 20 mol % L*, without DABCO. [f] 3 % of decomplexation product. [g] 2.5 mol % $[\{Pd(allyl)Cl\}_2]$, 7 mol % L*. [h] **39b**: 0.4 mmol; 1 mol % $[\{Pd(allyl)Cl\}_2]$, 4 mol % L*. [i] **39b**: 1.0 mmol; 0.5 mol % $[\{Pd(allyl)Cl\}_2]$, 2 mol % L*. [j] 5 mol % $[\{Pd(allyl)Cl\}_2]$, without L*. [k] **39b**: 3.0 mmol; 0.5 mol % $[\{Pd(allyl)Cl\}_2]$, 4 mol % L*; 92 % isolated yield of a 9:1 mixture of **42**/**43**. [l] Use of 1 equiv of 2,6-lutidine in place of DABCO.

One limitation of the reaction, however, lies in the formation of DABCO-$(BH_3)_2$, which could not be hydrolyzed under the workup conditions (quenched with 1 M HCl)[45] and the separation of which from complexes **42** and **43** was tedious. Alternative borane scavengers were therefore investigated. The bulky 2,6-lutidine drew our attention given the easy cleavage of its borane–amine complex under acidic conditions.[45] After slight modifications of the previously used reaction conditions, 2,6-lutidine proved to be as efficient as DABCO (Table 5, entry 10).

The absolute configuration was assigned by an X-ray crystal structural analysis of a derivative of **42b** (Figure 3),[46] which confirmed the predicted configuration made in analogy with the chromium complex (*S*)-**6**.[11] Under the conditions used for the C_{Ar}–Br hydrogenolysis in the ruthenium complexes, the reaction does not take place with free 1,4-dibromonaphthalene. The cationic $Ru(\eta^5\text{-}C_5R_5)^+$ moiety thus exerts an activating effect on the reaction.

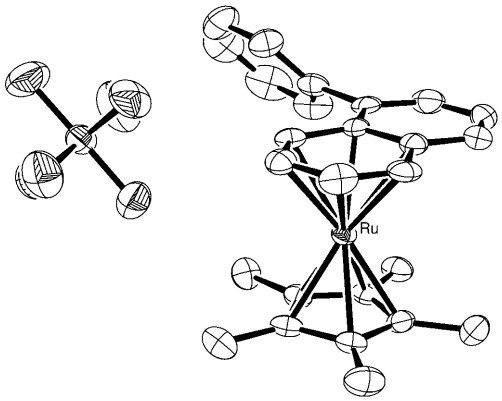


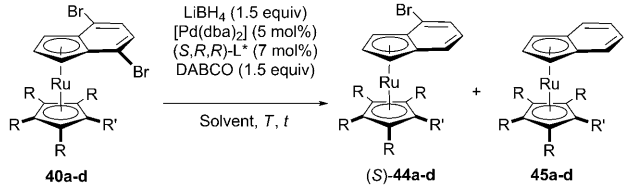
Figure 3. ORTEP view of (*S*)-[Ru(η^5-Cp*)(η^6-5-phenylnaphthalene)][PF_6] drawn using 50% probability ellipsoids (reproduced with the permission from reference [40a]).

The functionalized complex (*S*)-**42b** has a η^5/η^6-sandwich structure. The two ligand planes are almost parallel (1.63°). The distance between the ruthenium and the plane of the naphthalene (1.736 Å) is slightly shorter than the distance between the ruthenium and the Cp* plane (1.813 Å).

Asymmetric hydrogenolysis of neutral Ru complexes: Extension of the reaction scope was pursued with the neutral [Ru(η^5-C_5R_5)(η^5-4,7-dibromoindene)] (**40**). These complexes show higher stability and ease of handling compared to their cationic analogues (Table 6). In our initial experiments, we found that the use of [{Pd(allyl)Cl}$_2$] gave sluggish reactions and that [Pd(dba)$_2$] was the precursor of choice. Almost no reaction occurred in dichloromethane, whereas the reaction of **40a** in DME gave substantial overreduction (Table 6, entry 1). The reaction in toluene displayed the best **44**/**45** selectivity (Table 6, entries 2 and 3). The reaction rate was strongly dependent on the solvent. The highest enantiomeric excess (96% *ee*) was reached at −20°C (Table 6, entry 4). Similar levels of reactivity and enantioselectivity were obtained upon scale up (Table 6, entry 5). When the sterically more hindered and electron richer complex **40b** was employed, the hydrogenolysis product **44b** was produced in only 68% *ee* (Table 6, entry 6). Reaction of complex **40c** (R = Me, R′ = CF_3) was then examined to clarify whether steric or electronic parameters are responsible for this low asymmetric induction. The 1,2,3,4-tetramethyl-5-(trifluoromethyl)cyclopentadiene ligand (Cp*^{CF_3}) developed by Gassman[47] exhibits the electronic properties of a Cp and the steric bulk of a Cp*, which makes **40c** isoelectronic with **40a** and isosteric with **40b**. The reaction furnished **44c** with an intermediate enantiomeric excess of 78% (Table 6, entry 7), suggesting that both electronic and steric properties influence the enantioselection of the reaction. To further confirm these observations, complex **40d**, bearing a pentaphenylcyclopentadienyl ligand, was evaluated. Given its poor solubility in toluene, it was reacted in DME at −20°C to give the corresponding complex **44d** in 77% *ee*, albeit in poor yield (Table 6, entry 8). Complete conversion was achieved at RT, affording **44d** in 69% *ee*. (Table 6, entry 9). This result confirmed that increased steric hindrance has a detrimental impact on both reactivity and catalyst selectivity.[48]

Further ligand screening: Faced with the modest asymmetric induction in the desymmetrization of complexes **40b–d**, variations of the ligand structure to further optimize these results were undertaken (Table 7). Inspired by the fact that ligands **33** and **34** have shown interesting results in terms of enantioselectivity in the desymmetrization of chromium

Table 6. Asymmetric hydrogenolysis of complexes **40**.[a]



Entry	40	Solvent	T [°C]	t [h]	**40**[b] [%]	**44**[b] [%] (*ee*)[c]	**45**[b] [%]
1	**40a**	DME	10	1.5	0	30 (96)	70
2	**40a**	tol	10	1.5	0	65 (89)	35
3	**40a**	tol	−10	2.5	2	72 (91)	26
4	**40a**	tol	−20	18.0	0	72, 72[d] (96)	28
5[e]	**40a**	tol	−20	8.5	0	67, 66[d] (95)	33
6	**40b**	tol	−20	22.5	0	69, 62[d] (68)	31
7	**40c**	tol	−20	24.0	3	77, 71[d] (78)	21
8	**40d**	DME	−20	18.0	>80	n.d. (77)	n.d.
9	**40d**	DME	RT	16.0	7	72, 65[d] (69)	21

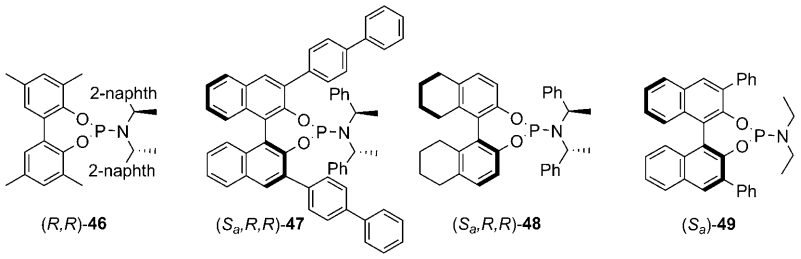
[a] Unless otherwise stated, the reactions were carried out using 0.1 mmol of **40** (0.025 M). $LiBH_4$ was added dropwise as a DME solution. [b] Determined by ^{1}H NMR analysis. [c] Determined by HPLC analysis. [d] Isolated yield after flash chromatography. [e] **40a**: 2.0 mmol; 4 mol% [Pd(dba)$_2$], 5 mol% L*. n.d. = non-determined.

Table 7. Asymmetric hydrogenolysis of complex **40b**: ligand screening.[a]

Entry	Ligand	t [h]	**40b**[b] [%]	**44b**[b] [%] (*ee*[c])	**45b**[b] [%]
1	**35**	20.0	0	69 (68, *S*)	31
2	**33**	19.0	>70	n.d. (64, *S*)	n.d.
3[d]	**34**	23.0	16	70 (54, *S*)	14
4	**46**	24.0	83	17 (n.d)	0
5	**30**	24.0	>99	–	n.d.
6	**27**	24.0	>99	–	n.d.
7	**47**	17.0	6	69 (44, *S*)	25
8	**48**	48.0	>99	–	n.d.
9	**49**	16.0	>99	–	n.d.
10	**50**	23.0	17	65 (57, *R*)	18
11	**51**	20.0	38	58 (56, *R*)	6
12	**52**	20.0	53	43 (29, *R*)	4
13	**53**	30.0	26	46 (0)	28
14[e]	**54**	15.0	54	36 (7, *R*)	10

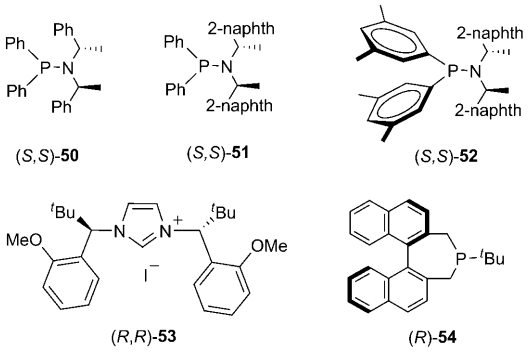
[a] Reactions were carried out using 0.1 mmol of **40b** in toluene (0.025 M) with Pd(dba)$_2$ (5 mol%), L* (10 mol%), $LiBH_4$ (1.5 equiv), at −20°C for the time indicated (unless otherwise noted). [b] Determined by ^{1}H NMR analysis. [c] Determined by HPLC analysis using a Pirkle Covalent column (100:0 hexane/*i*PrOH, 0.5 mL min^{-1}). The indicated absolute configuration is that of the major enantiomer and is based on the X-ray structure determination.[46] [d] Run at −10°C. [e] Run at RT. n.d = non-determined.

complex **5** (66% and 68% *ee*, respectively), their effectiveness was evaluated. In both cases, moderate *ee*'s were obtained (Table 7, entries 2 and 3). No reaction occurred when **46**, **30**, and **27** were used (Table 7, entries 4–6). Substitution



in the 3,3′-positions of the binaphtol by a biphenyl group allowed for a high reactivity, albeit with a poor enantioselectivity (44% *ee*; Table 7, entry 7). The use of Feringa's ligand with a partially hydrogenated BINOL backbone **48**[49] and **49**, possessing an achiral amine, did not give a reaction (Table 7, entries 8 and 9). This last result in particular highlights the important role of the chiral amine side chain in the enantioselection of the reaction. Although phosphoramidite ligands are generally considered to be monodentate chiral ligands, Mezzetti recently found that they are capable of secondary interactions with d^6 and d^8 metals when they contain substituents at the nitrogen atom.[27a]

Some SimplePhos ligands developed by Alexakis and coworkers[50,51] were also examined in the asymmetric hydrogenolysis. The use of SimplePhos **50** and **51** in the desymmetri-



zation of complex **40b** resulted in similar enantioselectivities (56 and 57% *ee*), with 83 and 62% conversion, respectively (Table 7, entries 10 and 11).[52a] The bulkier **52** was less efficient, affording poor conversion and enantioselectivity (Table 7, entry 12).[52b] We then turned our attention to N-heterocyclic carbenes (NHCs) given their propensity to facilitate oxidative addition. The chiral carbene ligand **53**, developed in our group and successfully applied to asymmetric intramolecular arylation of amides,[53] produced **44b** as a racemate (Table 7, entry 13). Finally, phosphepine[54,55] ligand **54** was tested but it was found to perform poorly (Table 7, entry 14).

Monitoring experiments: To obtain more detailed information about the reaction course, standard experiments using **40a–b** as substrates were monitored by means of ^{1}H NMR analysis and HPLC. The results are depicted in Figure 4. Once most starting material has been consumed, the enantioenriched complex **44** starts to be converted into the overreduced com-

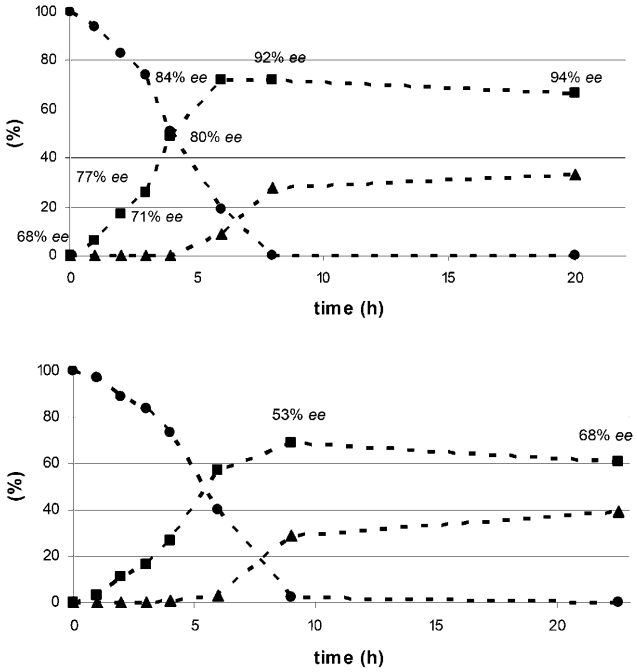
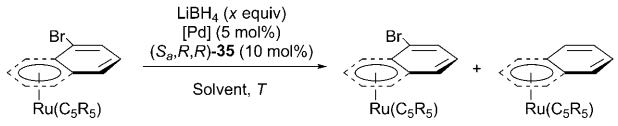


Figure 4. Relative composition of the reaction mixture during the reaction course. Reaction conditions: [Pd(dba)$_2$] (5 mol%), (S_a,*R*,*R*)-**35** (7 mol%), $LiBH_4$ (1.5 equiv), DABCO (1.5 equiv), toluene, −20°C. Top: Reaction of **40a**. Bottom: Reaction of **40b**.

pound **45**. The, albeit small, increase of the enantiomeric purity of **44** in the second part of the reaction confirms a kinetic resolution process connected to the formation of the overreduced complex **45**.[56] At present, it remains unclear why the enantioselectivity increases during the initial period of the reaction, at a time when formation of **45** is below detection level (Figure 4, top).

Kinetic resolution studies: Samples of racemic monohalide Ru complexes **42b** and **44a** were treated under standard conditions at different temperatures to determine the corresponding *s* factor values (Table 8). The racemic [RuCp*(5-bromonaphthalene)][PF_6] (**42b**) was very reactive under the hydrogenolysis conditions at −20°C (Table 8, entry 1). By

Table 8. Kinetic resolution experiments.



rac-**42b** *rac*-**44a** (*S*)-**42b** (*S*)-**44a** **43b** **45a**

Entry[a]	*rac* SM	*T* [°C]	Conv.[b] [%]	*ee* of SM [%]	*s*[c]
1[f]	**42b**	−20	83	56[c]	2.0
2[f]	**42b**	−40	38	28[c]	3.5
3[g]	**44a**	10	71	71[d]	3.7
4[g]	**44a**	0	47	42[d]	4.2
5[g]	**44a**	−20	60	70[d]	5.0

[a] Reactions were carried out using 0.1 mmol of racemic samples (0.025 M). [b] Conversions were determined by ^{1}H NMR analysis using an internal standard. [c] Determined by ^{1}H NMR analysis in the presence of an excess of [*n*Bu$_4$N][Δ-TRISPHAT]. [d] Determined using a Daicel chiralcel OD-H column (99:1: hexane/*i*PrOH, 0.5 mL min^{-1}). [e] $s = \ln[(1-c)(1-ee)]/\ln[(1-c)(1+ee)]$, average of three runs. [f] Reaction was run in CH_2Cl_2 with $LiBH_4$ (1.2 equiv) and DABCO (1.2 equiv). [g] Reaction was run in toluene with $LiBH_4$ (2 equiv) and DABCO (2 equiv).

performing the reaction at −40 °C, the starting material was recovered with an enantiomeric excess of 28 %, corresponding to a selectivity factor *s* of 3.5 (Table 8, entry 2). Unlike in the corresponding chromium complexes, kinetic resolution plays only a very minor role. Hence, for complexes **39**, the initial enantiodiscrimination is sufficient for obtaining **42** in high enantiomeric purity. As for the reaction of racemic [RuCp(4-bromoindene)] (**44a**), the best *s* factor (5.0) was reached at −20 °C (Table 8, entry 5).[57]

Conclusion

In conclusion, we have demonstrated that the Pd-catalyzed asymmetric hydrogenolysis can be carried out on multigram scale. The reaction gives access to highly enantioenriched, planar, chiral, fused arene complexes. It was shown that the presence of DABCO was essential to prevent ligand sequestration through the formation of the BH_3 ligand adduct. This finding has allowed for the reduction of the chiral ligand loading from 20 to 6 mol %. The 1.2:1 L*/Pd ratio indicates that the active catalytic species involves one chiral ligand. We have also highlighted the kinetic resolution at play in this process, which contributes to enhance the outcome of the reaction. The potential utility of this reaction has already been illustrated with the synthesis of a wide range of planar chiral arene complexes from the highly enantioenriched [Cr(5-bromonaphthalene)(CO)$_3$] ((*S*)-**6**) either by simple metallation/electrophile trapping sequences or by palladium catalyzed coupling reactions.[58] Extension to naphthalene and indenyl complexes incorporating cyclopentadienyl ruthenium fragments were highly successful in several cases though they leave room for improvement for indenyl complexes incorporating the RuCp* fragment. Access to diverse enantiomerically enriched planar chiral ruthenium complexes is in progress in our laboratory.

Experimental Section

General: Reactions and manipulations involving organometallic or moisture sensitive compounds were carried out under an atmosphere of anhydrous nitrogen in glassware heated under vacuum prior to use. Solvents were purified over Al_2O_3 drying columns using a Solvtek© system or by following standard procedures.[59] Thin-layer chromatography (TLC): precoated aluminum plates (Merck silica 60F$_{254}$). Flash column chromatography (f.c): in air using silica gel (60 Å, Fluka) or neutral alumina (50–200 μ, Acros).

^{1}H, ^{13}C, ^{31}P, ^{19}F, and ^{11}B NMR spectroscopy: Bruker AMX-300, 400 or 500 spectrometers. ^{1}H and ^{13}C NMR chemical shifts (δ) are quoted in parts per million (ppm) relative to TMS ($CDCl_3$: $\delta_C \equiv 77.05$ ppm; residual $CHCl_3$: $\delta_H \equiv 7.26$ ppm; CD_2Cl_2: $\delta_C \equiv 53.9$ ppm; residual $CHDCl_2$: $\delta_H \equiv 5.32$ ppm; [D$_6$]acetone: $\delta_C \equiv 28.8$ ppm; residual [D$_5$]acetone: $\delta_H \equiv 2.05$; C_6D_6: $\delta_C \equiv 128.0$ ppm; residual C_6HD_5: $\delta_H \equiv 7.15$ ppm). ^{31}P NMR chemical shifts are referenced to H_3PO_4 as an external standard. ^{19}F NMR chemical shifts are referenced to $CFCl_3$ as an external standard. Coupling constants *J* are quoted in Hz. Infrared spectra: Perkin–Elmer Spectrum One spectrophotometer using diamond ATR Golden Gate accessory. Electron impact (EI) HR-MS mass spectra: Finningan MAT 95 operating at 70 eV. Electrospray ionization (ESI) high-resolution mass spectroscopic (HR-MS) analyses: VG analytical 7070E. Optical rotations: Perkin–Elmer 241 Polarimeter, 20 °C, quartz cell ($l = 10$ cm), Na high-pressure lamp ($\lambda = 589$ nm). Analytical HPLC: Agilent 1100 series. Melting points: Büchi 540, uncorrected. Elemental analyses ; H. Eder, Service de Microanalyse, Section de Pharmacie, Université de Genève. Commercial chemicals were used as received unless otherwise stated.

General procedure for the synthesis of [Cr(CO)$_3$(naphthalene)] complexes 5–8: [Cr(CO)$_3$(NH$_3$)$_3$] (1 equiv) and substituted naphthalene (1 equiv) were combined in a Schlenk tube. Degassed diethyl ether was added followed by borontrifluoride etherate (3.6 equiv). The resulting mixture was subjected to three freeze-pump-thaw cycles, and then stirred for one to five days at RT. The red heterogeneous reaction mixture was filtered through a pad of celite, which was washed with small portions of degassed toluene until the washings became colorless. The solvent was removed under reduced pressure. The residue was recrystallized from a hexane/toluene mixture to yield deep red crystals.

[Cr(CO)$_3$(η^6-5,8-dibromonaphthalene)] (5): Prepared from [Cr(CO)$_3$(NH$_3$)$_3$] (1.5 g, 8.0 mmol), **1** (2.1 g, 8.0 mmol), and $BF_3{\cdot}OEt_2$ (3.6 mL, 28.5 mmol) in degassed diethyl ether (30 mL) after 5 days of reaction time. Yield: 2.28 g (76 %), red solid; $R_f = 0.70$ (cyclohexane/toluene 1:1); m.p. 130–132 °C (decomp); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 6.68$ (s, 2H; ArH), 5.91–5.88 (dd, $^3J(H,H) = 5.1$ Hz, $^4J(H,H) = 2.8$ Hz, 2H; ArH), 4.58–4.55 ppm (dd, $^3J(H,H) = 5.1$ Hz, $^4J(H,H) = 2.8$ Hz, 2H; ArH); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 230.2$ (C≡O), 130.7, 122.3, 104.7, 91.7, 88.4 ppm; IR (CH_2Cl_2): $\tilde{\nu} = 1969$, 1898 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} (ε) = 358, 295, 234 nm; HR-MS (EI): *m*/*z* calcd for $C_{13}H_6CrO_3{}^{81}Br_2$ $[M]^+$: 423.8048; found: 423.8049; HPLC (Daicel Chiralcel OD-H, hexane/*i*PrOH 95:5, 1 mL min^{-1}, $\lambda = 355$ nm): $t = 12$ min.

Chiral phosphoramidite ligand (*S*$_a$,*R*,*R*)-35: Distilled PCl_3 (90 μL, 1.0 mmol) was added to a solution of freshly distilled triethylamine (Et_3N, 840.0 μL, 6.0 mmol) in CH_2Cl_2 (7.5 mL) at 0 °C and was stirred for 0.5 h at this temperature. Then, the HCl salt of the (*R*,*R*)-Whitesell's amine[60] (262.0 mg, 1.0 mmol) was added at 0 °C and stirred for 4 h at RT. The mixture was cooled to 0 °C, then (*S*)-3,3′-biphenyl-1,1′-binaphthalenyl-2,2′-diol[61] (440.0 mg, 1.0 mmol) was added and the reaction was stirred overnight at RT. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with H_2O. The organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography on silica gel (cyclohexane/toluene 1:1) to afford the air stable ligand (*S*$_a$,*R*,*R*)-**35** (586.0 mg, 85 %) as a white foamy solid. $R_f = 0.64$ (cyclohexane/toluene 1:1); m.p. 147–149 °C; $[\alpha]_D = +446$ ($c = 1.0$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.14$ (s, 1H; ArH), 8.00–7.93 (m, 5H; ArH), 7.56–7.48 (m, 4H; ArH), 7.47–7.37 (m, 5H; ArH), 7.35–7.24 (m, 5H; ArH), 7.01–6.96 (m, 2H; ArH), 6.93–6.89 (m, 4H; ArH), 6.71 (br s, 4H, ArH), 4.31 (br s, 2H, NCH), 1.04 ppm (d, $^3J(H,H) = 6.8$ Hz, 6H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.5$, 147.3 (d, $J(C,P) = 5.5$ Hz),

143.1 (br), 138.1, 137.8, 135.2 (d, J(C,P) = 2.8 Hz), 134.2, 132.6 (d, J-(C,P) = 12.0 Hz), 131.1, 130.7, 130.5, 130.4, 130.1, 130.0, 128.3 (d, J(C,P) = 3.7 Hz), 128.2, 128.0, 127.6 (br), 127.4, 127.2, 127.0 (d, J(C,P) = 1.8 Hz), 126.1, 126.0 (d, J(C,P) = 3.7 Hz), 125.1, 124.9 (d, J(C,P) = 5.5 Hz), 124.8, 123.7 (d, J(C,P) = 2.8 Hz), 51.8, 51.7, 20.6 ppm (br); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 145.4 ppm; IR (neat): $\tilde{\nu}$ = 3060, 3330, 2968, 1601, 1495, 1452, 1406, 1248, 1218, 1198, 1182, 1133, 1051, 962, 839, 751, 697 cm^{-1}; HR-MS (ESI): m/z calcd for $C_{48}H_{39}O_2NP$ $[M+H]^+$: 692.2712; found: 692.2658.

General procedure for the desymmetrization of [Cr(CO)$_3$(η^6-5,8-dibromonaphthalene)] (5) using LiBH$_4$ as hydride source: [Pd(dba)$_2$] (144.0 mg, 0.25 mmol, 5 mol %) and the phosphoramidite ligand (S_a,R,R)-**35** (208.0 mg, 0.3 mmol, 6 mol %) were charged in a Schlenk tube and purged with N_2. Freshly distilled DME (150 mL) was added and the solution was stirred for 30 min at RT before being cooled to −10 °C. Complex **5** (2.1 g, 5 mmol) followed by DABCO (sublimed, 1.1 g, 9.9 mmol) were added at −10 °C. The mixture was stirred for 15 min at this temperature before the LiBH$_4$ solution (4.4 mL of a freshly prepared and titrated 4.5 M solution in DME, 4 mmol) was added dropwise over 10 min. After stirring for 1 h at −10 °C, the solution was filtered through silica gel under a N_2 atmosphere and washed with a 1:1 toluene/n-hexane mixture until colorless. After concentration of the solution in vacuo to about 20 mL, the crude mixture was quickly purified by flash chromatography on silica gel (cyclohexane/toluene 1:1) to yield 1.51 g of a red powder, consisting of a 9:1 mixture of (*S*)-**6** (88 % *ee*)/**9**. Crystallization at 45 °C from a 4:1 solution of toluene/n-hexane gave (*S*)-**6** (98 % *ee*) as red crystals (1.0 g, 60 %). $[\alpha]_D$ = +401 (c = 0.12 in $CHCl_3$).

General procedure for the kinetic resolution of [Cr(CO)$_3$(η^6-5-bromonaphthalene)] (*rac*-6) without DABCO: [Pd(dba)$_2$] (5 mol %) and the phosphoramidite ligand (S_a,R,R)-**35** (20 mol %) were charged in a Schlenk tube and purged with N_2. Freshly distilled DME was added and the solution was stirred for 30 min at RT before being cooled to the desired temperature. Racemic **6** (1 equiv) was added at this temperature. The mixture was stirred for 10 min before LiBH$_4$ solution (2 equiv) was added dropwise over 5 min. After stirring for the time required at the indicated temperature, the solution was filtered through silica gel under a N_2 atmosphere and washed with 1:1 toluene/n-hexane mixture until colorless. After concentration of the solution in vacuo to about 10 mL, the crude mixture was quickly purified by flash chromatography on silica gel (cyclohexane/toluene 1:1). The residue was subsequently analyzed using HPLC.

[Ru(η^5-Cp)(η^6-5,8-dibromonaphthalene)][PF$_6$] (39a): Complex **38a** (3.3 g, 7.7 mmol) and 1,4-dibromonaphthalene (3.3 g, 11.6 mmol) were charged in a Carrius tube, distilled and degassed dichloroethane was added. The reaction mixture was heated to 80 °C and stirred for 20 h. After cooling to RT, the reaction mixture was filtered over celite under a N_2 atmosphere and washed with degassed dichloroethane (3 × 10 mL). The resulting solution was evaporated in vacuo and the residue was recrystallized from dichloroethane/hexane (30:10 mL) to afford a yellow solid (3.1 g, 67 %). M.p. 205–207 °C (decomp); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.79 (s, 2H; ArH), 7.32 (dd, ^3J(H,H) = 4.4 Hz, ^4J(H,H) = 2.4 Hz, 2H; ArH), 6.51 (dd, ^3J(H,H) = 4.4 Hz, ^4J(H,H) = 2.4 Hz, 2H; ArH), 5.14 ppm (s, 5H; Cp-H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 135.0, 123.7, 97.9, 87.9, 84.5, 81.3 ppm; ^{31}P NMR (162 MHz, CD_2Cl_2): δ = −144.3 ppm (sept, ^1J(P,F) = 708 Hz); IR (neat): $\tilde{\nu}$ = 3121, 3089, 1603, 1523, 1471, 1415, 1345, 1237, 1171, 1109, 961, 870, 825, 780, 666 cm^{-1}; HR-MS (ESI): m/z calcd for $C_{15}H_{11}Br_2Ru$ $[M-PF_6]^+$: 452.8252; found: 452.8242.

[Ru(η^5-Cp*)(η^6-5,8-dibromonaphthalene)][PF$_6$] (39b): Complex **38b** (7.5 g, 14.9 mmol) and 1,4-dibromonaphthalene (**1**) (6.4 g, 22.4 mmol) were stirred in anhydrous, degassed THF (140 mL) at RT for 16 h. Then, anhydrous, degassed hexane (110 mL) was added and stirred for a few minutes. The precipitate was filtered and washed with a 1:1 mixture of THF/hexane (100 mL). The crude product was passed through a short pad of neutral alumina initially with dichloromethane, then 1:1 dichloromethane/acetone as eluent. Crystallization from dichloromethane/pentane gave orange crystals (4.6 g, 47 %). M.p. 251–253 °C (decomp); ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.86 (s, 2H; ArH), 6.87 (dd, ^3J(H,H) = 4.6 Hz, ^4J(H,H) = 2.5 Hz, 2H; ArH), 6.20 (dd, ^3J(H,H) = 4.6 Hz, ^4J(H,H) = 2.5 Hz, 2H; ArH), 1.77 pm (s, 15H; Cp*-CH$_3$); ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 134.0, 122.6, 97.4, 96.5, 89.9, 85.4, 10.1 ppm; ^{31}P NMR (162 MHz, CD_2Cl_2): δ = −144.1 ppm (sept, ^1J(P,F) = 711 Hz); IR (neat): $\tilde{\nu}$ = 3090, 2918, 1607, 1521, 1471, 1453, 1389, 1347, 1238, 1177, 1109, 1076, 1028, 985, 958, 869, 823, 740, 666 cm^{-1}; HR-MS (ESI): m/z calcd for $C_{20}H_{21}Br_2Ru$ $[M-PF_6]^+$: 519.9054; found: 519.9031; elemental analysis calcd (%) for $C_{20}H_{21}Br_2PF_6Ru$ (667.22): C 36.00, H 3.17; found: C 35.99, H 3.06.

General procedure for the desymmetrization of [Ru(η^5-Cp*)(η^6-5,8-dibromonaphthalene)][PF$_6$] (39b): [Pd(allyl)Cl]$_2$ (5.5 mg, 0.015 mmol, 1 mol %) and the phosphoramidite ligand (S_a,R,R)-**35** (83 mg, 0.12 mmol, 4 mol %) were charged in a Schlenk tube and purged with N_2. Anhydrous, degassed dichloromethane (60 mL) was added and the solution was stirred for 30 min at RT before being cooled to −40 °C. Complex **39b** followed by DABCO (sublimed, 504.8 mg, 4.5 mmol) and then anhydrous, degassed dichloromethane (60 mL) were added to the mixture. The mixture was stirred for 10 min before the LiBH$_4$ solution (4.5 mmol) was added dropwise over 10 min. After stirring for 2.5 h at −40 °C, 1 M HCl (80 mL) was added and stirred for 10 min at −40 °C before being warmed to RT. The organic layer was separated and washed with 1 M HCl, water and dried over $MgSO_4$. The solvents were evaporated and the solid was dried under vacuum before being analyzed by ^{1}H NMR first without [Δ-TRISPHAT][NBu$_4$][62] (CD_2Cl_2 as solvent), then with two equivalents of [Δ-TRISPHAT][NBu$_4$] ($CDCl_3$ as solvent). The crude product was dissolved in a minimum amount of $CHCl_3$ and filtered through celite (to remove some of the colorless DABCO-bis(BH_3) adduct) and washed with a small amount of $CHCl_3$/diethyl ether. This process was repeated before recrystallization was performed with CH_2Cl_2/diethyl ether to give yellow crystals (92 % isolated yield as a combined mixture of **42b** (87, 97 % *ee*) and **43b** (13 %)).

General procedure for the synthesis of complexes 40a–c and *rac*-44a–c: To a cooled (0 °C) solution of the corresponding indene ligand (1 equiv) in anhydrous, degassed THF, NaHMDS (1 M in THF solution, 1 equiv) was slowly added. The resulting solution was stirred at 0 °C for 30 min. before being added to a cooled (0 °C) Schlenk flask containing **38** (1 equiv). The mixture was stirred overnight, filtered through a short pad of silica and concentrated in vacuo. The residue was purified by flash chromatography (pentane) and crystallized.

[Ru(η^5-Cp)(η^5-4,7-dibromoindene)] (40a): Complex **40a** was prepared from **38a** (2,8 g, 6.4 mmol), NaHMDS (6.4 mL, 6.4 mmol), and 4,7-dibromoindene (1.8 g, 6.4 mmol) in THF (20 mL) and was crystallized from dichloromethane/pentane. Yield: 4.0 g (92 %), orange crystals. R_f = 0.53 (pentane); m.p. 152–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2H; ArH), 5.39 (d, ^3J(H,H) = 2.3 Hz, 2H; ArH), 4.69 (t, ^3J(H,H) = 2.3 Hz, 1H; ArH), 4.33 ppm (s, 5H, Cp-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 124.6, 121.0, 93.9, 73.5, 70.7, 67.9 ppm; IR (neat): $\tilde{\nu}$ = 3090, 1798, 1740, 1600, 1466, 1427, 1404, 1375, 1309, 1291, 1240, 1133, 1097, 1028, 996, 890, 833, 816, 800 cm^{-1}; HR-MS (EI): m/z calcd for $C_{14}H_{10}Br_2Ru$ $[M,^{96}Ru]^+$: 431.8225; found: 431.8220; elemental analysis calcd (%) for $C_{14}H_{10}Br_2Ru$ (439.11): C 38.29, H 2.30; found: C 38.35, H 2.27; HPLC (Daicel Chiralcel OD-H, hexane/iPrOH 99:1, 0.5 mL min^{-1}, λ = 254 nm): t = 10.2 min.

[Ru(η^5-Cp*)(η^5-4,7-dibromoindene)] (40b): Complex **40b** was prepared from **38b** (3.5 g, 13.0 mmol), NaHMDS (13.0 mL, 13.0 mmol), and 4,7-dibromoindene (6.40 g, 13.0 mmol) in THF (30 mL) and was crystallized from dichloromethane/pentane. Yield: 4.5 g (68 %), orange crystals. R_f = 0.75 (pentane); m.p. 170–172 °C; ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 6.85 (s, 2H; ArH), 4.96 (d, ^3J(H,H) = 2.5 Hz, 2H; ArH), 4.52 (t, ^3J(H,H) = 2.5 Hz, 1H; ArH), 1.67 ppm (s, 15H; Cp*-CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 122.4, 119.2, 93.9, 83.7, 77.7, 70.3, 10.4 ppm; IR (neat): $\tilde{\nu}$ = 3078, 3040, 2965, 2897, 2852, 1737, 1592, 1498, 1471, 1441, 1377, 1372, 1328, 1297, 1127, 1029, 891, 870, 801, 783, 752, 706 cm^{-1}; HR-MS (EI): m/z calcd for $C_{19}H_{20}Br_2Ru$ $[M,^{96}Ru]^+$: 501.9007; found: 501.9000; elemental analysis calcd (%) for $C_{19}H_{20}Br_2Ru$ (509.24): C 44.81, H 3.96; found: C 44.72, H 3.89; HPLC (Pirkle Covalent, hexane/iPrOH 100:0, 0.5 mL min^{-1}, λ = 254 nm): t = 16.1 min.

General procedure for the desymmetrization of [Ru(η^5-Cp)(η^6-4,7-dibromoindene)] (40a): [Pd(dba)$_2$] (46.0 mg, 0.008 mmol, 4 mol %) and ligand (S_a,R,R)-**35** (69.2 mg, 0.010 mol, 5 mol %) were placed in a Schlenk tube

and purged with N_2. Anhydrous, degassed toluene (40 mL) was added and the solution was stirred for 30 min at RT before cooling to −20 °C. Complex **40** (878.2 mg, 2.0 mmol) followed by DABCO (336.5 mg, 3.0 mmol) and then anhydrous, degassed toluene (40 mL) were added to the mixture. The mixture was stirred for 10 min before the $LiBH_4$ solution (3.0 mmol) was added dropwise over 10 min. After stirring for 8.5 h at −20 °C, the solution was filtered through silica gel. The silica gel was washed with pentane until colorless. After concentration in vacuo, the residue was analyzed using HPLC and ^1H NMR. Separation and isolation of the different compounds could be achieved by flash chromatography over silica gel (pentane) to yield (*S*)-**44a** (95 % *ee*) as a yellow solid (474 mg, 66 %). $[\alpha]_D = +746$ ($c = 0.61$ in $CHCl_3$).

General procedure for the kinetic resolution of [Ru(η⁵-Cp)(η⁶-4-bromoindene)] (*rac*-44a): $[Pd(dba)_2]$ (5 mol %) and the phosphoramidite ligand (S_a,*R*,*R*)-**35** (10 mol %) were charged in a Schlenk tube and purged with N_2. Anhydrous, degassed toluene was added and the solution was stirred for 30 min at RT before being cooled to the desired temperature. Racemic **44a** (1 equiv) followed by DABCO (2 equiv) were added at this temperature. The mixture was stirred for 10 min before the $LiBH_4$ solution (2 equiv) was added dropwise over 5 min. After stirring for the time required at the indicated temperature, the solution was filtered through silica gel and washed with pentane until colorless. After concentration in vacuo, the residue was analyzed using HPLC and ^1H NMR spectroscopy.

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