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Novel planar chiral diphosphines and their application in asymmetric hydrogenations and asymmetric Heck reactions

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Abstract—Nine planar chiral diphosphines **8a–i** have been synthesised by a versatile approach: The diphosphines have been assayed in an asymmetric hydrogenation reaction and an asymmetric Heck reaction and were found to give active catalysts that generated products of moderate to good enantiopurity.

1. Introduction

As a result of the success of planar chiral ligands such as the ferrocene 'Josiphos', **1**,[1] and the [2,2]paracyclophane 'Phanephos', **2**[2] (Fig. 1), in the arena of asymmetric catalysis, interest in other types of ligands possessing planar chirality has increased rapidly in recent years. Planar chiral ligands based on (arene)tricarbonylchromium(0) complexes are no exception,[3] and the increased activity in this area in the last few years[4] has led to the successful application of planar chiral (arene)tricarbonylchromium(0) complexes as catalyst ligands in several quite diverse reactions, including rhodium-catalysed hydrogenation of ketones,[5] palladium-catalysed hydrosilyations of styrene[6] and Lewis acid-catalysed Diels–Alder reactions.[7]

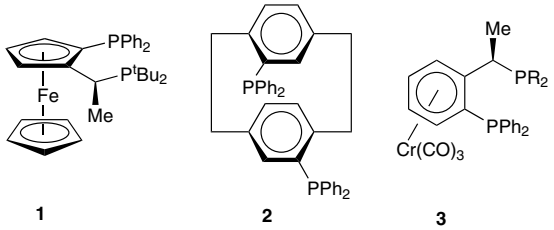
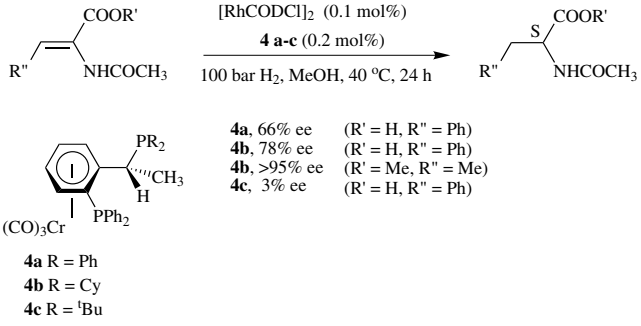


Figure 1.

Chelating diphosphines play an important role in transition metal catalysis, and it is thus of interest to combine the diphosphine motif with planar chirality and develop routes to diphosphine derivatives of (arene)tricarbonylchromium(0) complexes. Complexes of generalised structure **3** have been synthesised to date and tested in palladium-catalysed allylic alkylations,[8] palladium-catalysed allylic sulfonations,[9] rhodium-catalysed hydrogenations[9] and iridium-catalysed hydroaminations.[9] For example, complexes **4a–c** have been shown to give a very wide range of selectivities for the hydrogenation of dehydroamino acid derivatives (Scheme 1).[9] Complexes of general formula **3** are synthesised using α-methylbenzyl alchol[8] or α-methylbenzylamine[9] as the source of chirality. The benzylic phosphine substituent is introduced by nucleophilic displacement of either oxygen[8] or nitrogen[9] substituents either directly[8] or indirectly[9] via a chloro substituent.



Scheme 1.

Some time ago, we demonstrated that tricarbonylchromium(0) complexes of benzyl ethers could be asymmetrically functionalised in high yields and

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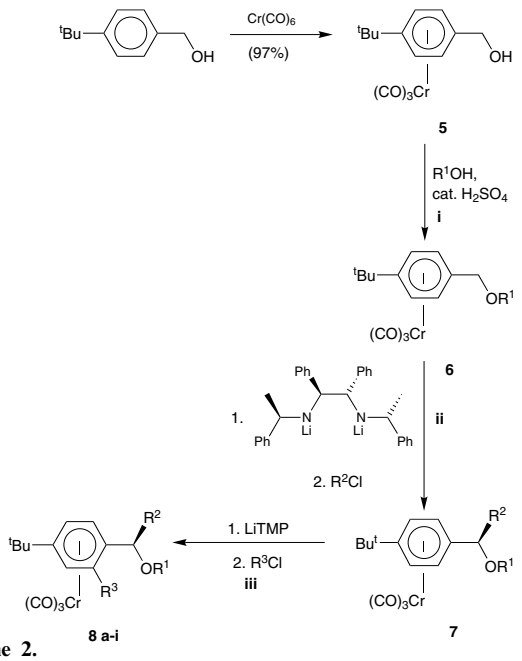
enantioselectivities by reaction with a chiral base followed by an electrophilic quench.[10] More recently, we reported that this reaction could be used to create a new approach to planar chiral (arene)tricarbonylchromium(0) complexes.[11,12] We report herein that this chemistry can be used to generate a range of novel planar chiral diphosphine ligands, and that we have started to probe the utility of these diphosphines in asymmetric catalysis with investigations of an asymmetric hydrogenation reaction and an asymmetric Heck reaction. The hydrogenation reaction was chosen for study because it was anticipated that it would give clean and high conversions to product, and thus provide direct insight into the effectiveness of a new ligand, whilst the Heck reaction was selected because to the best of our knowledge there have been no other reports to date of the application of (arene)tricarbonylchromium(0) based ligands in the Heck reaction. Some of the results described herein have been reported in communication form.[13]

2. Results and discussion

2.1. Synthesis of diphosphines

We planned to synthesise the planar chiral diphosphines based on the (arene)tricarbonylchromium(0) unit using the route shown in Scheme 2. The approach is based on complex **5**, which is readily formed in high yield from commercially available 4-*tert*-butylbenzyl alcohol and hexacarbonylchromium(0). In the first variable step (step i) we proposed to react tricarbonyl(4-*tert*-butylbenzyl alcohol)chromium(0) **5** with an alcohol R^1OH under acid catalysis to give an ether complex **6**. We then proposed to introduce asymmetry into complex **6** in a second flexible step (step ii) by its treatment with a chiral base [the diamine precursor of which is readily available from (*R*)- or (*S*)-α-methylbenzylamine in two steps[14] and an electrophilic quench with a chlorodiphosphine R^2Cl to give **7**. Finally it was proposed that a third variable step (step iii) involving a diastereoselective *ortho*-lithiation of **7** followed by an electrophilic quench with a second chlorodiphosphine R^3Cl would be used to give a range of planar chiral complexes **8**.



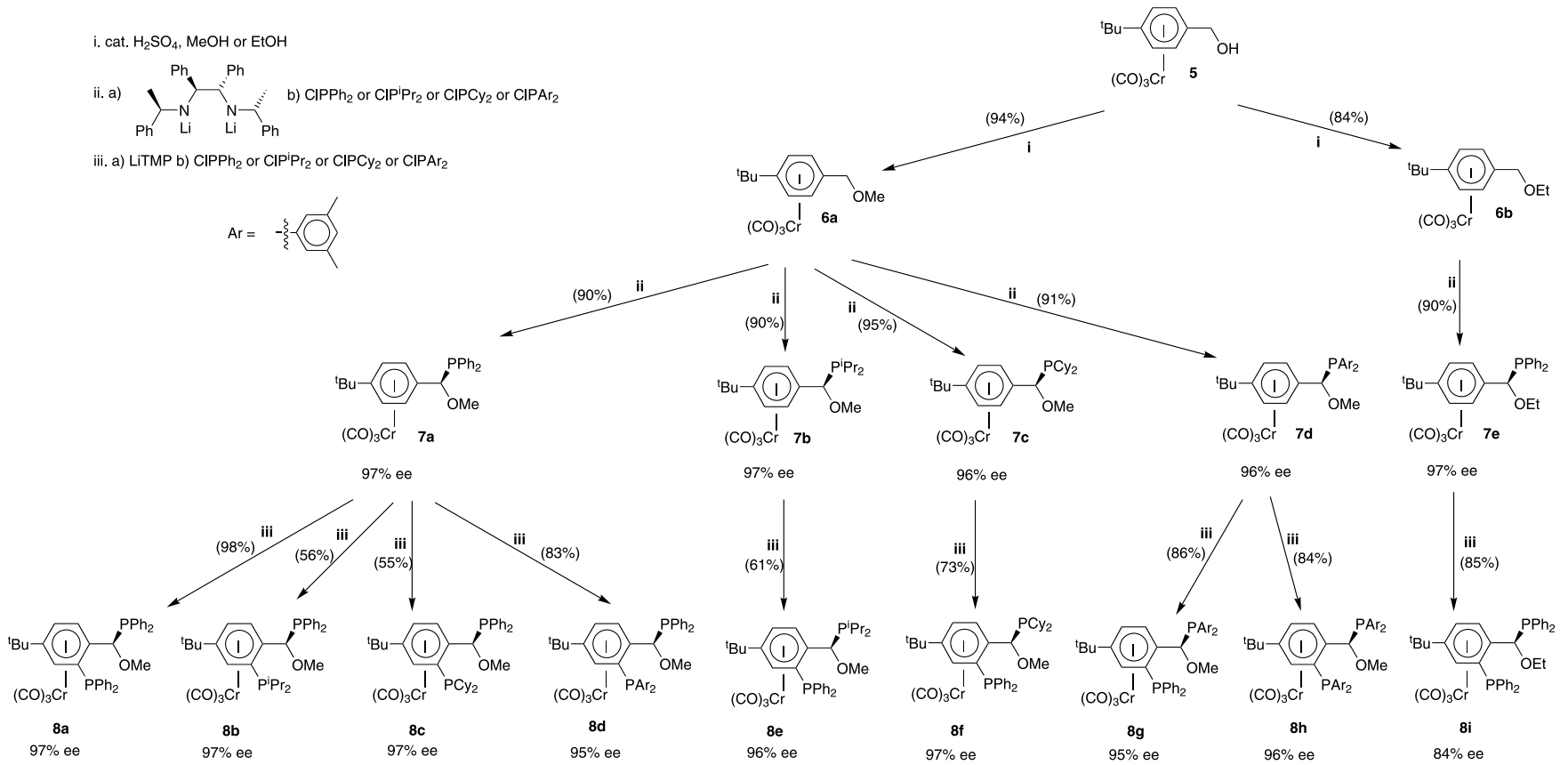
Scheme 2.

Preliminary studies in which complex **5** had been converted to diphosphine **8a** via methyl ether **6a** and monophosphine **7a** (Scheme 3) had demonstrated that the introduction of asymmetry in step ii and the diastereoselective installation of the second phosphine in step iii proceeded smoothly to generate the required diphosphine **8a** in high diastereo- and enantiopurity and good yield.[12] During the course of the hydrogenation and Heck studies reported below, one new ether complex **6b** was synthesised, together with four new monophosphines **7b–e** and eight new diphosphines **8b–i**. With one exception, the syntheses of these compounds proceeded in good to excellent yields providing monophosphines and diphosphines of very high enantiopurity. The exception to this is the low enantiopurity of **8i**. The origin of the loss of enantiopurity during the conversion of **7e–8i** was not investigated during the course of this study due to the inactivity of complex **8i** in both the hydrogenation and Heck assays (see below).

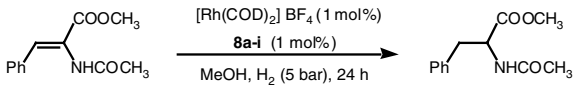
2.2. Asymmetric hydrogenations

The discovery of Wilkinson's hydrogenation catalyst in the late 1960s[15] stimulated much interest in the enantioselective hydrogenation of alkenes using optically active transition-metal complexes in order to generate stereogenic carbon centres. Many chiral ligands have been examined in the ensuing years and very high selectivities have been achieved.[16] In many cases the efficiency of the catalysts generated has been probed using (*Z*)-2-(acetamido)cinnamic acid, 2-(acetamido)acrylic acid, or their methyl or ethyl esters, with the reaction being performed in alcoholic solvents under 1–10 atm of hydrogen using cationic complexes of rhodium. As asymmetric hydrogenation is one of the key test reactions for chiral diphosphine ligands, we decided to determine how well planar chiral diphosphine ligands synthesised by our approach would perform in an asymmetric hydrogenation reaction. We decided to determine the effect of varying (i) the phosphine substituent on the aromatic ring, (ii) the phosphine substituent on the benzylic ring and (iii) the ether substituent R^1 that is to exploit the flexibility of our synthesis by changing all the possible variables introduced in steps i–iii. Thus ligands **8a–i** were synthesised and subjected to the standard hydrogenation reaction depicted in Scheme 4.

The diphosphines **8a–i** all cleanly hydrogenated methyl (*Z*)-2-(acetamido)cinnamate, apart from the ethyl ether complex **8i**, which did not form an active catalyst. Moderate to good enantioselectivities were observed, and, interestingly, the presence of a dialkyl phosphine unit on the aromatic ring, rather than a diaryl phosphine group, led to an inversion in product stereochemistry. Comparing our results with the results depicted in Scheme 1,[9] it can be seen that the highest selectivity obtained in this

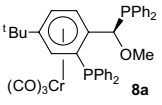
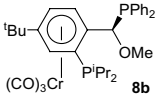
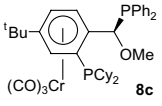
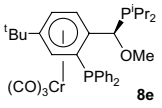
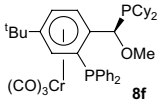
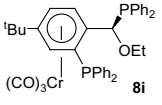
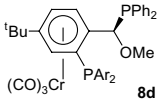
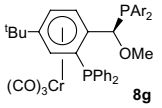
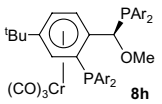

i. cat. H2SO4, MeOH or EtOH
ii. a)
b) ClPPh2 or ClPiPr2 or ClPCy2 or ClPAr2
iii. a) LiTMP b) ClPPh2 or ClPiPr2 or ClPCy2 or ClPAr2
Ar =
5
6a
6b
7a
7b
7c
7d
7e
8a
8b
8c
8d
8e
8f
8g
8h
8i
97% ee
96% ee
95% ee
84% ee

Scheme 3.



Scheme 4.

Table 1

Entry	Ligand	Ee (%)[a,b]	Configuration of the major enantiomer
1	 **8a**	45	*R*
2	 **8b**	69	*R*
3	 **8c**	41	*R*
4	 **8e**	48	*S*
5	 **8f**	60	*S*
6	 **8i**	No reaction	
7	 **8d**	48	*R*
8	 **8g**	36	*R*
9	 **8h**	31	*R*

[a] Ees were determined by HPLC using a Chiracel OD-H column and 95:5 hexane isopropanol as eluent with a flow rate of 900 μL/min.
[b] All reactions proceeded with 100% conversion.

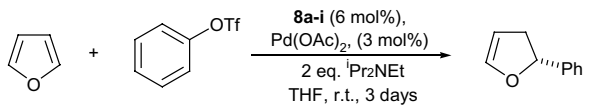
study (69% with complex **8b**, Table 1, entry 2) is broadly comparable with the selectivities recorded for the hydrogenation of (*Z*)-2-(acetamido)cinnamic acid with diphosphines **4a** and **4b** (66% and 78% ee, respectively).

2.3. Asymmetric Heck reactions

Transition metal catalysed carbon–carbon bond forming reactions have become an invaluable tool for synthetic chemists. Among the most successful and widely applied of such transformations is the Heck reaction, which has been known since the late 1960s. Many new and exciting developments concerning the Heck coupling reaction have appeared in recent years, such as the utilisation of aryl bromides and chlorides as coupling partners.[17] One of the most significant developments has been the discovery that the Heck reaction could be carried out in an asymmetric manner.[18] This reaction, which utilises chiral palladium catalysts, can be carried out in an intramolecular or intermolecular fashion.

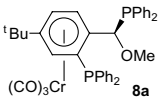
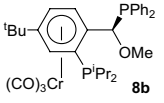
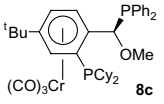
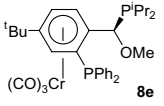
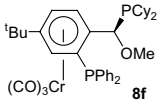
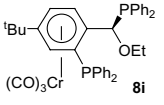
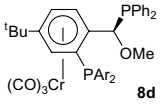
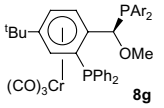
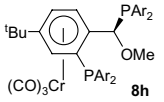
Hayashi reported the first example of an intermolecular asymmetric Heck reaction in 1991.[19] It involved the phenylation of 2,3-dihydrofuran with phenyl triflate catalysed by a $Pd(OAc)_2$/(*R*)-BINAP combination. Although several other substrates were examined, much of the investigation into the mechanism and reaction parameters focused around the phenylation of 2,3-dihydrofuran, and thus this has become one of the benchmark reactions for the intermolecular Heck reaction. We thus decided to conduct a second assay of ligands **8a**–**i** using this reaction (Scheme 5). Standard conditions were employed to perform the catalyst, perform the coupling reaction and assess the yield and enantiopurity of the product.[20]

The reaction was initially performed using the bis diphenylphosphine complex **8a**. This gave (*R*)-2-phenyl-2,3-dihydrofuran in 60% yield and 60% ee (Table 2, entry 1). Encouraged by this result, given that this was the first asymmetric Heck reaction conducted using a planar chiral (arene)tricarbonylchromium(0) complex, we decided to assay the other diphosphines synthesised. Changing the diphenylphosphine aromatic substituent to a dialkylphosphine substituent resulted in no reaction taking place (Table 2, entries 2 and 3), while, in contrast, changing the benzylic diphenylphosphine substituent to a dialkylphosphine substituent maintained catalyst activity, but gave no significant improvement in selectivity (Table 2, entries 4 and 5). Attempts to examine the effect of placing *tert*-butyl phosphine or methyl phosphine substituents at the benzylic position were thwarted by problems encountered in the introduction of the aromatic substituent in the former case (presumably due to steric effects), and the highly unstable nature of chlorodimethylphosphine in the latter case. Changing the methyl ether to an ethyl ether resulted in no reaction (Table 2, entry 6). This effect was also observed in the hydrogenation assay (see above). It is possible that this inactivity is caused by poor co-ordination of the two phosphines to the transition metal (rhodium or palladium). Co-ordination of both phosphines leads to the alkoxy substituent being forced towards the tricarbonylchromium(0) rotor, a situation, which may be acceptable for the methoxy substituent but not for the more bulky ethoxy substituent. Finally, the diphenylphosphine substituents of **8a** were replaced with di(3,5-dimethylphenyl)phsophine groups, but this lead to



Scheme 5.

Table 2

Entry	Ligand	Yield (%)	Ee (%)[a]
1	 **8a**	60	60
2	 **8b**	No reaction	
3	 **8c**	No reaction	
4	 **8e**	55	42
5	 **8f**	58	62
6	 **8i**	No reaction	
7	 **8d**	52	48
8	 **8g**	54	50
9	 **8h**	20	62

[a] Ees were determined by HPLC using a Chiracel OD-H column and 99.6:0.4 hexane isopropanol as eluent with a flow rate of 900 μL/min.

reduced selectivity (Table 2, entries 7 and 8) or reduced activity (Table 2, entry 9).

3. Conclusions

We have synthesised a series of planar chiral diphosphines using an efficient and versatile approach, thus providing a new set of planar chiral diphosphines for use in asymmetric catalysis. The diphosphines have been assayed to date in two asymmetric catalytic reactions: an asymmetric hydrogenation, a reaction that is used widely to test the efficiency of new chiral diphosphines, and an asymmetric Heck reaction, a reaction that to date has not been investigated using (arene)tricarbonylchromium(0) based ligands. Almost all of the diphosphines synthesised in this study formed active catalysts that proved stable under the catalytic conditions employed. Although the enantioselectivities measured were only moderate to good, and much lower than some of the best results obtained with some planar chiral ferrocene complexes in asymmetric catalysis, it is anticipated that future investigations using different catalyst systems and substrates will identify highly enantioselective processes mediated by these ligands.

4. Experimental

All reactions and manipulations involving organometallic compounds were performed under an inert atmosphere of dry nitrogen, using standard vacuum line and Schlenk tube techniques.[21] Reactions and operations involving (arene)tricarbonylchromium(0) complexes were protected from light. THF was distilled from sodium benzophenone ketyl. The concentration of alkyllithums was determined by titration against diphenylacetic acid in THF.[22] Tetramethylpiperidine was purchased from Aldrich and stored without further purification over potassium hydroxide, or alternatively it was distilled over CaH_2 and stored over potassium hydroxide. Chlorodiphenylphosphine was distilled prior to use. Flash column chromatography was performed using Merck silica gel 60 (230–400 mesh). All other reagents were used as obtained from commercial sources. Melting points were recorded in open capillaries on a Büchi 510 melting point apparatus, and are uncorrected. IR spectra were recorded on a Perkin Elmer 1600 FT-IR spectrometer. NMR spectra were recorded at room temperature on Brüker AM 360, DRX 400 and DRX 500 instruments and J values are reported in Hz. Mass spectra were recorded at the mass spectroscopy facility at King's College London on JEOL AX 505W and Kratos MS890MS spectrometers and the EPSRC mass spectral facility, Swansea. Elemental analyses were performed by the London Metropolitan University microanalytical service.

HPLC analysis was performed using a Unicam Crystal 200 pump, Unicam Spectra 100 UV–vis detector (set at 330 nm) and Chiracel OD-H or AD columns. Racemic monophosphines **7c–e** and diphosphines **8b–i**, used as standards for the HPLC analysis, were synthesised using *t*-BuLi as the base instead of the chiral diamide in step ii.

The chiral diamine[14] and bis(3,5-dimethylphenyl) chlorophosphine[23] were prepared according to literature methods. Complexes **6a**, **7a**, **7b** and **8a** were prepared following our reported literature procedures.[12]

4.1. Tricarbonyl(1-ethoxymethyl-4-*tert*-butylbenzene)-chromium(0) 6b

Concentrated sulfuric acid (2.2 mL) was added dropwise to a solution of complex **5** (1.0 g, 3.33 mmol) in nitrogen-saturated methanol (10 mL). The mixture was heated at 50 °C for 3 h and stirred for a further 2 h at room temperature. To neutralise the reaction mixture, saturated aqueous Na_2CO_3 (10 mL) was added carefully followed by the addition of diethyl ether (50 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3×50 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to give a yellow oil. Column chromatography (SiO_2; hexane/diethyl ether, 1:1) of this material gave 1.01 g (95%) of *title complex* **6b** as a yellow oil; ν_{max} (CH_2Cl_2), cm^{-1} 1950s (C≡O), 1880s (C≡O); δ_H (360 MHz, $CDCl_3$) 1.27–129 [12H, m, $(CH_3)_3C$ and CH_3CH_2O], 3.46 (2H, q, *J* 6.2, OCH_2CH_3), 4.14 (2H, s, CH_2OEt), 5.20 [2H, d, *J* 6.8, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$], 5.49 [2H, d, *J* 6.8, $C_{Cr}(t\text{-Bu})C_{Cr}H_{Cr}H$]; $\delta_C\{^1H\}$ (100 MHz, $CDCl_3$) 15.5 (CH_3CH_2), 31.5 [$(CH_3)_3C$], 34.3 [$(CH_3)_3C$], 67.5 (OCH_2CH_3), 71.2 ($C_{Cr}CH_2O$), 91.0 ($C_{Cr}H$), 93.0 ($C_{Cr}H$), 108.6 ($C_{Cr}CH_2OMe$), 122.2 [$C_{Cr}(t\text{-Bu})$], 233.0 (C≡O); *m*/*z* (EI, %) 328 (M^+, 68), 244 (M−3CO, 51), 52 (Cr, 100); HRMS (ESI) found 351.0642, $C_{16}H_{20}CrO_4Na$ requires 351.0660.

4.2. General procedure for the synthesis of complexes 7c–e (step ii)

n-Butyllithium (2*n* mmol) was added dropwise to a stirred solution of the chiral diamine (1*n* mmol) in THF (8*n* mL) at −78 °C and the solution was allowed to reach room temperature over 30 min. The resulting deep pink solution was then re-cooled to −78 °C and a solution of heat gun-dried lithium chloride (1*n* mmol) in THF (4*n* mL) was added via a cannula. Stirring was continued for a further 5 min before a pre-cooled solution (−78 °C) of the complex **6a**–**b** (1*n* mmol) in THF (4*n* mL) was added dropwise (ca. 2 min) via a short cannula. After stirring the orange solution at −78 °C for 30 min, chlorodialkyl or chlorodiarylphosphine (2*n* mmol) was added in one portion, which resulted in a colour change of the solution from orange to yellow. Stirring was continued at −78 °C for 1.5 h before methanol (1*n* mL) was added. The reaction mixture was warmed to room temperature and the solvent was removed in vacuo to give the crude complex, which was purified by flash column chromatography. All the reactions were performed on 1.0 mmol or 1.5 mmol scale.

4.3. (+)-(*R*)-Tricarbonyl[1-(1-dicyclohexylphosphine-1-methoxymethyl)-4-*tert*-butylbenzene]chromium(0) (+)-7c

Flash column chromatography (SiO_2; hexane/dichloromethane, 10:0–7:3) of the crude product gave a 95% yield of the *title complex* (+)-**7c** as a yellow solid; mp 140–142 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.8:0.2, 0.4 mL/min, 330 nm); (*S*)-enantiomer t_R = 14.2 min (minor); (*R*)-enantiomer t_R = 16.5 min (major): 96% ee; $[\alpha]_D^{24}$ = +83.4 (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1959s (C≡O), 1880s (C≡O); δ_H (360 MHz, $CDCl_3$) 1.05–1.30 (10H, m, Cy), 1.27 [9H, s, $(CH_3)_3C$], 1.62–1.84 (12H, m, Cy), 3.58 (3H, s, OCH_3), 4.51 (1H, d, *J* 5.0, $CHPCy_2$), 5.17 (1H, dd, *J* 8.7, 1.8, $C_{Cr}H$), 5.49–5.57 (3H, m, $C_{Cr}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 28.9 (PCy_2); $\delta_C\{^1H\}$ (125 MHz, $CDCl_3$) 25.7 (d, *J* 2.9, CH_2), 26.4–26.8 (m, CH_2), 29.5 (t, *J* 12.6, CH_2), 30.3 [$(CH_3)_3C$], 32.2 [$(CH_3)_3C$], 33.2 ($C_{cy}HP$), 59.6 (OCH_3), 78.8 [d, *J* 26.7 Hz, CHP(OMe)], 88.1 [d, *J* 1.9, $C_{Cr}HC_{Cr}CH(PCy_2)$ OMe], 88.3 [d, *J* 12.0, C_{Cr} $HC_{Cr}CH(PCy_2)OMe$], 90.2 [$C_{Cr}(t\text{-Bu})C_{Cr}H$], 90.7 [$C_{Cr}(t\text{-Bu})C_{Cr}H$], 109.4 (d, *J* 17.4, $C_{Cr}CHPCy_2OMe$), 122.3 [$C_{Cr}(t\text{-Bu})$], 233.2 (C≡O); *m*/*z* (EI, %) 510 (M^+, 1), 482 (M−CO, 68), 454 (M−2CO, 100), 426 (M−3CO, 100), 396 (M−3CO−H_2CO, 9), 177 [M−Cr(CO)$_3$−PCy_2, 45]; HRMS (ESI) found 555.1755, $C_{31}H_{35}O_4CrP$+H requires 555.1751.

4.4. (+)-(*R*)-Tricarbonyl[1-(1-di-3,5-dimethylphenylphosphine-1-methoxymethyl)-4-*tert*-butylbenzene]chromium(0) (+)-7d

Flash column chromatography (SiO_2; hexane/ether, 10:0–95:5) of the crude product gave a 91% yield of the *title complex* (+)-**7d** as a yellow solid; mp 128–129 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel AD, *n*-hexane/*i*-PrOH, 98:2, 0.6 mL/min, 330 nm); (*S*)-enantiomer t_R = 8.5 min (minor); (*R*)-enantiomer t_R = 10.3 min (major): 97% ee; $[\alpha]_D^{24}$ = +36.4 (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1955s (C≡O), 1880s (C≡O); δ_H (360 MHz, $CDCl_3$) 1.18 [9H, s, $(CH_3)_3C$], 2.18 (6H, s, $C_{ar}CH_3$), 2.22 (6H, s, $C_{ar}CH_3$), 3.23 (3H, s, OCH_3), 4.60–4.64 (2H, m, $C_{Cr}H$ and $CHPAr_2$), 5.08 (1H, dd, *J* 7.4, 1.4, $C_{Cr}H$), 5.24–5.29 (m, 2H, $C_{Cr}H$), 6.86 (1H, s, $C_{ar}H$), 6.88 (1H, s, $C_{ar}H$), 6.91 (1H, s, $C_{ar}H$), 6.94 (1H, s, $C_{ar}H$), 7.01 (1H, s, $C_{ar}H$), 7.03 (1H, s, $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 10.7 ($CHPAr_2$); $\delta_C\{^1H\}$ (90 MHz, $CDCl_3$) 21.8 ($C_{ar}CH_3$), 21.9 ($C_{ar}CH_3$), 31.6 [$C(CH_3)_3$], 34.4 [$C(CH_3)_3$], 60.5 (d, *J* 4.9, OCH_3), 83.6 (d, *J* 13.4, $CHPAr_2OCH_3$), 89.9 [$C_{Cr}HC_{Cr}C(CH_3)_3$], 90.5 [$C_{Cr}HC_{Cr}C(CH_3)_3$], 91.1 (d, *J* 4.0, $C_{Cr}HC_{Cr}CHPAr_2OMe$), 91.4 (d, *J* 5.4, $C_{Cr}HC_{Cr}CHPAr_2OMe$), 110.8 (d, *J* 17.4, $C_{Cr}CHPAr_2$-OMe), 124.5 [$C_{Cr}C(CH_3)_3$], 131.6 (d, *J* 3.9, $C_{ar}H$), 132.1 (d, *J* 18.5, $C_{ar}H$), 132.4 (d, *J* 19.3, $C_{ar}H$), 138.1 (d, *J* 18.2, $C_{ar}P$), 138.2 (d, *J* 7.18, $C_{ar}CH_3$), 234.38 (Cr*C*≡O); *m*/*z* (EI, %) 555 (M^++H, 20), 419 [M+H−Cr(CO)$_3$, 100], 313 [M−P(C_8H_9)$_2$, 11], 177 [M−P(C_8H_9)$_2$−Cr(CO)$_3$, 13]; HRMS (ESI) found 555.1755, $C_{31}H_{35}O_4$ CrP+H requires 555.1751.

4.5. (+)-(*R*)-Tricarbonyl[1-(1-diphenylphosphine-1-ethoxymethyl)-4-*tert*-butylbenzene]chromium(0) (+)-7e

Flash column chromatography (SiO_2; hexane/diethyl-ether, 100:0–95:5) of the crude product gave (90%) of the *title complex* (+)-**7e** as a yellow solid; mp 113–114 °C; found C = 65.41 H = 5.86, $C_{28}H_{29}CrO_4P$ requires C = 65.62 H = 5.70; enantiomeric excess was determined by HPLC analysis (Chiralcel AD, *n*-hexane/

i-PrOH, 98:2, 0.6 mL/min, 330 nm); (*S*)-enantiomer $t_R = 13.5$ min (minor); (*R*)-enantiomer $t_R = 18.0$ min (major): 97% ee; $[\alpha]_D^{24} = +133.4$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1960s (C≡O), 1882s (C≡O). δ_H (360 MHz, $CDCl_3$) 1.08 (3H, t, *J* 7.2, CH_3CH_2), 1.16 [9H, s, $(CH_3)_3C$], 3.43–3.42 (1H, m, CH_3CHH), 3.90 (1H, m, CH_3CHH), 5.07 (2H, m, $CHPPh_2$ and $C_{Cr}H$), 5.07 (1H, dd, *J* 8.0, 1.6, $C_{Cr}H$), 5.19 (1H, dd, *J* 8.6, 1.6, $C_{Cr}H$), 5.28 (1H, d, *J* 6.9, $C_{Cr}H$), 7.18–7.31 (8H, m, $C_{ar}H$), 7.45–7.50 (2H, t, *J* 7.4 $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 11.4 ($CPPh_2$); $\delta_C\{^1H\}$ (90 MHz, $CDCl_3$) 14.2 (CH_3CH_2) 29.8 [$(CH_3)_3C$], 32.8 [$(CH_3)_3C$], 53.9 (d, *J* 4.2, OCH_2), 64.6 (d, *J* 14.3, $CHPPh_2$), 80.6 [$C_{Cr}(t\text{-Bu})C_{Cr}H$], 88.4 [$C_{Cr}(t\text{-Bu})C_{Cr}H$], 88.7 [d, *J* 3.6, $C_{Cr}HC_{Cr}CH(PPh_2)OMe$], 89.4 [d, *J* 4.0, $C_{Cr}HC_{Cr}CH(PPh_2)OMe$], 108.5 [d, *J* 16.5, $C_{Cr}CH(PPh_2)OMe$], 122.9 [$C_{Cr}(t\text{-Bu})$], 125.6 ($C_{ar}H$), 126.8 (d, *J* 16.5, $C_{ar}H$), 127.1 ($C_{ar}H$), 127.2 (d, *J* 6.6, $C_{ar}H$), 132.4 (C_{ar}), 132.9 (d, *J* 19.0, $C_{ar}H$), 133.2 (d, *J* 20.4, $C_{ar}H$), 133.6 (C_{ar}), 140.5 (C_{ar}), 144.2 (C_{ar}), 233.7 (Cr-C≡O); *m*/*z* (%) 512 (M^+,1), 428 (M−3CO, 100), 384 (MH−3CO−C_2H_5O, 38), 332 [MH−$Cr(CO)_3$−C_2H_5O, 3], 191 [M−$Cr(CO)_3$−PPh_2, 57], 52 (Cr, 21); HRMS (ESI) found 533.1878, $C_{27}H_{39}O_4$ CrP+Na requires 533.1888.

4.6. General procedure for the synthesis of complexes 8b–c (step iii)

Methyllithium (1.1*n* mmol) was added dropwise to a stirred solution of tetramethylpiperidine (1.1*n* mmol) in THF (10*n* mL) at −78 °C. The solution was allowed to reach room temperature and re-cooled to −78 °C. Diphosphine complex **7a**–**e** (1*n* mmol) in THF (4*n* mL) was added via a cannula and the resulting orange solution was stirred for 1 h, Chlorodialkyl or chlorodiaryl phosphine (2*n* mmol) was added in one portion and stirring was continued for a further 1 h at −78 °C. The reaction mixture was warmed to room temperature and stirred for 1 h before methanol (0.5 mL) was added. Removal of solvent in vacuo gave the crude product, which was purified by flash column chromatography. All the reactions were performed on 0.35–0.50 mmol scale.

4.7. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-diisopropylphosphine-2-(1′-diphenylphosphine-1′-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8b

Flash column chromatography (SiO_2; hexane/dichloromethane, 10:0–7:3) of the crude compound gave a 56% yield of the *title complex* (−)-**8b**; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.6:0.4, 0.3 mL/min, 330 nm); ($_pRR$) enantiomer $t_R = 18.0$ min (major); ($_pSS$) enantiomer $t_R = 20.3$ min (minor): 97% ee; $[\alpha]_D^{24} = -48.2$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1962s (C≡O), 1889s (C≡O); δ_H (360 MHz, $CDCl_3$) 1.01–1.08 (6H, m, 2×$CHCH_3$), 1.18–1.25 (12H, m, $(CH_3)_3C$ and $CHCH_3$), 1.34 (3H, dd, *J* 16.0, 7.0, $CHCH_3$), 1.98–2.05 [m, 1H, $CH(CH_3)_2$], 2.12–2.20 [1H, m, $CH(CH_3)_2$], 3.11 (3H, s, OCH_3), 5.06 [1H, ddd, *J* 6.5, 2.8, 1.6, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$], 5.33 [1H, d, *J* 6.5, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$], 5.59 [1H, s, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}HPi\text{-}Pr_2$], 5.74 (1H, dd, *J* 7.3, 4.0, $CHPPh_2$), 7.25–7.31 (3H, m, $C_{ar}H$), 7.41–7.47 (5H, m, $C_{ar}H$), 7.91–7.96 (2H, m, $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 0.3 (d, *J* 16.2, $CHPPh_2$), 0.6 [d, *J* 16.2, $C_{Cr}P(i\text{-}Pr_2)$]; *m*/*z* (EI, %) 586 (M^+−CO, 2), 558 (M−2CO, 4), 530 (M−3CO, 100), 293 [M−$Cr(CO)_3$− PPh_2, 52]; HRMS (ESI) found 637.1690, $C_{33}H_{40}CrO_4P_2Na$ requires 637.1704.

4.8. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-dicyclohexylphosphine-2-(1-diphenylphosphine-1-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8c

Flash column chromatography (SiO_2; hexane/dichloromethane, 10:0–7:3) of the crude compound gave a 54% yield of the *title complex* (−)-**8c** as a yellow solid; mp 121–122 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.8:0.2, 0.15 mL/min, 330 nm); ($_pRR$) enantiomer $t_R = 40.2$ min (major); ($_pSS$) enantiomer $t_R = 44.2$ min (minor): 97% ee; $[\alpha]_D^{24} = -111.2$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1962s (C≡O), 1889s (C≡O); δ_H (360 MHz, $CDCl_3$) 0.84 (2H, t, $J = 7.0$ Hz, Cy), 1.17 [9H, s, $(CH_3)_3C$], 1.13–1.95 (17H, m, Cy), 3.09–3.14 (3H, m, Cy), 3.40 (3H, s, OCH_3), 4.88 [1H, ddd, *J* 7.0, 3.0, 1.2, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$], 5.25 [1H, d, *J* 7.0, $CHPPh_2$], 5.58 (1H, s, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$), 5.63 [1H, dd, *J* 7.5, 4.0 Hz, $(t\text{-Bu})C_{Cr}CHC_{Cr}PCy_2$], 7.16–7.22 (6H, m, $C_{ar}H$), 7.35 (2H, dt, *J* 7.1, 1.7, $C_{ar}H$), 7.84–7.88 (2H, m, $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 0.8 (d, *J* 55.5 Hz, $CHPPh_2$), −6.9 (d, *J* 55.5 Hz, $C_{Cr}PCy_2$); *m*/*z* (EI, %) 695 (2%, MH^+), 612 (100, M−2CO−CH_3+H), 369 [33, M−PCy_2−$Cr(CO)_3$], 197 (9, PCy_2); HRMS (ESI) found 695.2496 $C_{39}H_{48}CrO_4P_2$+H, requires 695.2506.

4.9. (−)(1*pR*,1′*R*b)-Tricarbonyl[1-di-3,5-dimethylphenylphosphine-2-(1′-diphenylphosphine-1′-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8d

Flash column chromatography (SiO_2; hexane/diethyl ether, 10:0–95:5) of the crude compound gave a 83% yield of *title complex* (−)-**8d** as a crystalline yellow solid; mp 98–100 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.6:0.4, 0.5 mL/min, 330 nm); ($_pSS$)-enantiomer $t_R = 10.8$ min (minor); ($_pRR$)-enantiomer $t_R = 2.6$ min (major): 97% ee; $[\alpha]_D^{24} = -171$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1962s (C≡O), 1885s (C≡O); δ_H (360 MHz, $CDCl_3$) 0.98, [9H, s, $(CH_3)_3C$], 2.20 (6H, s, 2×$PC_{ar}CH_3$), 2.25 (6H, s, 2×$PC_{ar}CH_3$) 3.02 (3H, s, OCH_3), 4.75 [1H, t, *J* 1.1 $(t\text{-Bu})C_{Cr}C_{Cr}HC_{Cr}PAr_2$], 5.16 [1H, ddd, *J* 6.8, 3.6, 1.7, $(t\text{-Bu})C_{Cr}C_{Cr}HC_{Cr}H$], 5.25 [1H, dd, *J* 6.8, 1.1, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$], 5.47 (1H, dd, *J* 6.3, 4.3, $CHPPh_2$), 6.82 (1H, s, $C_{ar}H$), 6.98 (1H, s, $C_{ar}H$), 7.00 (1H, s, $C_{ar}H$), 7.02 (1H, s, $C_{ar}H$), 7.31–7.47 (12H, m, $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) −0.7 (d, *J* 10.3, $CHPPh_2$), −13.9 (d, *J* 10.3, $C_{Cr}PAr_2$); *m*/*z* (EI, %) 738 (M^+, 25), 710 (M−CO, 14), 682 [MH−$C(CH)_3$], 15), 654 (M−3CO, 100), 571 (M−$Cr(CO)_3$−OCH_3, 32), 377 [MH−$P(C_8H_9)_2$−3CO−OCH_3, 35]; HRMS (ESI) found 739.2186, $C_{43}H_{44}CrO_4P_2$+H requires 739.2194.

4.10. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-diphenylphosphine-2-(1′-diisopropylphosphine-1′-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8e

Flash column chromatography (SiO_2; hexane/dichloromethane, 10:0–7:3) of the crude compound gave a 61% yield of the *title complex* (−)-**8e**; mp 95–97 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.9:0.1, 0.4 mL/min, 330 nm); ($_pSS$)-enantiomer $t_R = 15.9$ min (minor); ($_pRR$)-enantiomer $t_R = 20.6$ min (major): 96% ee; $[\alpha]_D^{24} = -104.6$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1959s (C≡O), 1889s (C≡O); δ_H (360 MHz, $CDCl_3$) 1.09 [9H, s, $(CH_3)_3C$], 1.06–1.34 [12H, m, $2CH(CH_3)_2$], 2.17–2.25 [1H, m, $CH(CH_3)_2$], 2.28–2.35 [1H, m, $CH(CH_3)_2$], 2.73 (3H, s, OCH_3), 4.74 [1H, t, *J* 1.4, C_{Cr}(*t*-Bu) $C_{Cr}HC_{Cr}PPh_2$], 4.84 [1H, t, *J* 3.4 CHP(*i*-Pr_2)], 5.45 [1H, dd, *J* 6.8, 1.5, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}$H], 5.65 [1H, dt, *J* 6.8, 2.6, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}H$], 7.36–7.45 (10H, m, C_{ar}H); $\delta_P\{^1H\}$ (146 MHz) 22.2 [d, *J* 28.2, CHP(*i*-Pr_2)], −13.8 (d, *J* 28.2, $C_{Cr}PPh_2$); HRMS (ESI) found 637.1699 $C_{33}H_{40}CrO_4P_2Na$, requires 637.1704.

4.11. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-diphenylphosphine-2-(1′-dicyclohexylphosphine-1′-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8f

Flash column chromatography (SiO_2; hexane/dichloromethane, 10:0–7:3) of the crude compound gave a 73% yield of the *title complex* (−)-**8f**; mp 85–87 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.8:0.2, 0.15 mL/min, 330 nm); ($_pRR$)-enantiomer $t_R = 41.8$ min (major); ($_pSS$)-enantiomer $t_R = 49.8$ min (minor): 97% ee; $[\alpha]_D^{24} = -82.9$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1962s (C≡O), 1889s (C≡O); δ_H (360 MHz, $CDCl_3$) 0.84–0.90 (3H, m, Cy), 1.08 [9H, s, $(CH_3)_3C$], 1.13–2.10 (19H, m, Cy), 2.68 (3H, s, OCH_3), 4.73 (1H, t, *J* 1.2, C_{Cr}(*t*-Bu) $C_{Cr}HC_{Cr}PPh_2$), 4.87 (1H, t, *J* 3.4, $CHPCy_2$), 5.45 [1H, dd, *J* 6.8, 1.2, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}$H], 5.61 [1H, dt, *J* 6.8, 2.4, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}H$], 7.35–7.44 (10H, m, C_{ar}H); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 14.9 (d, *J* 31.0, $CHPCy_2$), −14.1 (d, *J* 30.7, $C_{Cr}PPh_2$); *m*/*z* (EI, %) 638 (M^+−2CO, 5), 610 (M−3CO, 100), 361 [M−$Cr(CO)_3$− PCy_2, 28]; HRMS (FAB): found 610.2592, $C_{39}H_{48}CrO_4$ P_2–3CO requires 610.2586.

4.12. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-diphenylphoshine-2-(1′-di-3,5-dimethylphenylphosphine-1′-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8g

Flash column chromatography (SiO_2; hexane/diethyl ether, 10:0–95:5) of the crude compound gave a 84% yield of *title complex* (−)-**8g** as a crystalline yellow solid; found C = 69.52% H = 5.62%, $C_{43}H_{44}CrO_4P_2$ requires C = 69.91% H = 6.00%; mp 80–81 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.6:0.4, 0.5 mL/min, 330 nm); ($_pRR$)-enantiomer $t_R = 10.8$ min (major); ($_pSS$)-enantiomer $t_R = 12.6$ min (minor): 97% ee; $[\alpha]_D^{24} = -132.0$ (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1960s (C≡O), 1882s (C≡O); δ_H (360 MHz, $CDCl_3$) 0.98 [9H, s, $(CH_3)_3C$], 2.20 (6H, s, $2\times C_{ar}CH_3$), 2.28 (6H, s, $2\times C_{ar}CH_3$), 2.55 (s, 3H, OCH_3), 4.70 [1H, t, *J* 1.4, C_{Cr}(*t*-Bu) $C_{Cr}HC_{Cr}PPh_2$)], 5.04–5.08 [1H, dt, *J* 6.5, 1.9, C_{Cr}(*t*-Bu) $C_{Cr}HC_{Cr}H$)] 5.25 [1H, dd, *J* 6.5, 1.4, C_{Cr}(*t*-Bu) $C_{Cr}HC_{Cr}$H] 5.57 (1H, dd, *J* 6.7, 4.7, $CHPAr_2$), 6.91 (1H, s, C_{ar}H), 6.93 (1H, s, C_{ar}H), 6.95 (1H, s, C_{ar}H), 6.97 (1H, s, C_{ar}H), 6.99 (1H, s, C_{ar}H), 7.20–7.24 (4H, m, C_{ar}H), 7.35–7.40 (4H, m, C_{ar}H), 7.86 (2H, t, *J* 6.8, $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) −1.5 (d, *J* 10.4, $CHPAr_2$), −12.7 (d, *J* 10.4, $C_{Cr}PPh_2$); *m*/*z* (EI, %) 682 [15, MH^+-(*t*-Bu)], 654 [100, M−$(CO)_3$], 571 [32, MH− $Cr(CO)_3$−OMe], 377 [48, MH−$P(C_8H_9)_2$−3CO−OMe].

4.13. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-(di-3,5-dimethylphenylphosphine)-2-(1′-di-3,5-dimethylphenylphosphine-1′-methoxymethyl)-5-*tert*-butylbenzene]chromium(0) (−)-8h

Flash column chromatography (SiO_2; hexane/diethyl ether, 10:0–95:5) of the crude compound gave a 84% yield of *title complex* (−)-**8h** as a crystalline yellow solid; mp 117–118 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, *n*-hexane/*i*-PrOH, 99.6:0.4, 0.5 mL/min, 330 nm); ($_pSS$)-enantiomer $t_R = 16.0$ min (minor); ($_pRR$)-enantiomer $t_R = 17.6$ min (major): 97% ee; $[\alpha]_D^{24} = -27.6$ (*c* 0.75, CH_2Cl_2); ν_{max} (CH_2Cl_2), cm^{-1} 1958s (C≡O), 1880s (C≡O); δ_H (360 MHz, $CDCl_3$) 1.05 [9H, s, $(CH_3)_3C$], 2.14 (12H, s, $4\times PC_{ar}CH_3$), 2.31 (6H, s, $2\times PC_{ar}CH_3$), 2.36 (6H, s, $2\times PC_{ar}CH_3$), 3.04 (3H, s, OCH_3), 4.87 (1H, t, *J* 2.0, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}PAr_2$), 5.06 (1H, ddd, *J* 6.0, 3.0, 2.0, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}H$), 5.22 [1H, dd, *J* 6.0, 2.0, C_{Cr}(*t*-Bu)$C_{Cr}HC_{Cr}$H] 5.47 (1H, dd, *J* 6.0, 4.0, $CHPAr_2$), 6.76 (1 H, s, C_{ar}H), 6.81 (1H, s, C_{ar}H), 6.92 (1H, s, C_{ar}H), 6.94 (1H, s, C_{ar}H), 6.96–7.04 (6H, m, C_{ar}H), 7.42 (1H, s, C_{ar}H), 7.44 (1H, s, C_{ar}H); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) 0.3 (d, *J* 10.4, $CHPAr_2$), −13.4 (d, *J* 10.4, $C_{Cr}PAr_2$); *m*/*z* (EI, %) 710 (M^+−3CO, 100), 627 [M−$Cr(CO)_3$−OCH_3, 18], 417 [M^+−$Cr(CO)_3$−$P(C_8H_9)_2$, 52], 242 [$P(C_8H_9)_2$+H, 17]; HRMS (ESI) found 795.2831, $C_{47}H_{52}CrO_4P_2$+H requires 795.2818.

4.14. (−)-(1*pR*,1′*R*)-Tricarbonyl[1-diphenylphosphine-2-(1′-diphenylphosphine-1′-ethoxymethyl)-5-*tert*-butylbenzene]chromium(0)(−)-8i

Flash column chromatography (SiO_2; hexane/diethyl ether, 10:0–96:4) of the crude compound gave a 85% yield of the *title complex* (−)-**8i** as a crystalline yellow solid; mp 74–76 °C; enantiomeric excess was determined by HPLC analysis (Chiralcel AD, *n*-hexane/*i*-PrOH, 99:1, 0.6 mL/min, 330 nm); ($_pSS$)-enantiomer $t_R = 11.2$ min (minor); ($_pRR$)-enantiomer $t_R = 14.0$ min (major): 84% ee; $[\alpha]_D^{24} = -162$ (*c* 0.25, CH_2Cl_2); (CH_2Cl_2), cm^{-1} 1964s (C≡O), 1893s (C≡O); δ_H (500 MHz, $CDCl_3$) 0.23 (3H, t, *J* 6.9, CH_3CH_2O), 0.90 [9H, s, $(CH_3)_3C$], 2.45–2.65 (2H, m OCH_2CH_3), 4.76 (1H, s, C_{Cr}(*t*-Bu)

$C_{Cr}HC_{Cr}PPh_2$), 5.22–5.24 (1H, ddd, *J* 6.0, 3.2, 2.3, $C_{Cr}(t\text{-Bu})C_{Cr}HC_{Cr}H$), 5.31 [1H, d, *J* 6.0, $C_{Cr}(t\text{-Bu})_{Cr}HC_{Cr}H$], 5.74 [1H, dd, *J* 7.0, 4.6, $CHPPh_2$], 7.21–7.47 (18H, m, $C_{ar}H$), 7.84 (2H, dt, *J* 7.7, 1.7, $C_{ar}H$); $\delta_P\{^1H\}$ (146 MHz, $CDCl_3$) −1.4 (d, *J* 10.1, $CHPPh_2$), −13.0 (d, *J* 10.1, $C_{Cr}PPh_2$); *m/z* (EI, %) 640 (M^+−2CO, 16), 612 (M−3CO, 100), 375 [M−$Cr(CO)_3$−PPh_2, 23]; HRMS (ESI) found 719.1516, $C_{40}H_{38}CrO_4P_2$+Na, requires 719.1548.

4.15. Procedure for asymmetric hydrogenation reaction

To a mixture of the ligand (0.01 mmol) and $[Rh(COD)_2]BF_4$ (11 μmol) in a Schlenk tube was added degassed methanol (5 mL) and the reaction mixture was stirred at room temperature for 15 min under nitrogen. The hydrogenation autoclave was charged with 1.0 mmol of the substrate and a magnetic stirrer bar. The methanolic solution of the rhodium catalyst was added very quickly to the substrate and the autoclave was assembled and flushed 10 times with hydrogen. The reaction mixture was stirred in the autoclave at room temperature for 24 h under 5 bar pressure of hydrogen. The reaction was filtered through a pad of Celite and concentrated in vacuo to give the crude product, which was purified by column chromatography (SiO_2; 3:1, toluene/ethyl acetate). Enantiomeric excess was determined by HPLC using a Chiracel OD-H column with *n*-hexane/isopropanol (95:5) as the eluent with a flow rate of 0.9 mL/min: $t_R = 23.5$ (*R*)-enantiomer, $t_R = 33.6$ (*S*)-enantiomer. The configuration of the major enantiomer was identified as *R* by comparison of the optical rotation of the product with literature data.[24] δ_H (360 MHz, $CDCl_3$) 1.81 (s, 3H, $NHCOCH_3$), 2.95 (dd, 1H, *J* 14.0, 5.5, C*H*HPh), 3.04 (dd, 1H, *J* 14.0, 6.2, C*H*HPh), 3.60 (s, 3H, $COOCH_3$), 4.77 (dd, *J* 6.2, 5.5, 1H, $CHCH_2Ph$), 6.34 (br s, 1H, NH), 7.02 (d, 2H, *J* 6.1, $C_{ar}H$), 7.24–7.04 (m, 3H, $C_{ar}H$).

4.16. Procedure for asymmetric Heck reaction

A mixture of the phosphine (6 mol%), $Pd(OAc)_2$ (3 mol%) and THF (5 mL) was stirred at room temperature under a nitrogen atmosphere for 30 min. 2,3-Dihydrofuran (3 mmol), phenyl triflate (1 mmol) and *N*,*N*-diisopropylethylamine (2 mmol) were added and the reaction was stirred at room temperature for 3 days. Diethyl ether (10 cm^3) was added and the resulting mixture filtered through a pad of Celite. The filtrate was carefully concentrated in vacuo to give the crude product, which was purified by column chromatography (SiO_2; hexane/diethyl ether, 4:1) to give 2-phenyl-2,3-dihydrofuran as a colourless oil. Enantiomeric excess was determined by HPLC using a Chiracel OD-H column with *n*-hexane/isopropanol (99.6:0.4) as the eluent with a flow rate of 0.6 mL/min; $t_R = 12.0$ min (major), $t_R = 13.8$ (minor). The configuration of the major enantiomer was identified as *R* by comparison of the specific rotation of the product with literature data.[8] δ_H (360 MHz, $CDCl_3$) 2.57 (ddt, *J* 15.0, 8.4, 2.5, 1H, C*H*HPh), 3.08 (ddt, *J* 15.0, 10.0, 2.5, 1H, C*H*HPh), 4.97 (dd, *J* 4.5, 2.5, 1H, OCHC*H*), 5.52 (dd, *J* 10.0, 8.4, 1H, OCHPh), 6.46 (dd, *J* 4.5, 2.5, 1H, OC*H*CH), 7.27–7.37 (m, 5H, Ph).

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