Development of new thiazole-based iridium catalysts and their applications in the asymmetric hydrogenation of trisubstituted olefins†

Pradeep Cheruku,‡ Alexander Paptchikhine,‡ Muhammad Ali,‡ Jörg-M. Neudörfl and Pher G. Andersson*

Received 25th September 2007, Accepted 9th November 2007
First published as an Advance Article on the web 4th December 2007
DOI: 10.1039/b714744a

New thiazole-based chiral *N*,*P*-ligands that are open-chain analogues of known cyclic thiazole ligands have been synthesized and evaluated in the iridium-catalyzed asymmetric hydrogenation of trisubstituted olefins. Chirality was introduced into the ligands through a highly diastereoselective alkylation using Oppolzer's camphorsultam as chiral auxiliary. In general, the new catalysts are as reactive and selective as their cyclic counterparts for the asymmetric hydrogenation of various trisubstituted olefins.

Introduction

Asymmetric catalysis is a powerful tool for generating enantiomerically pure materials.[1] Asymmetric hydrogenation, the atom-economical addition of H_2 to a carbon–carbon or carbon–heteroatom double bond to obtain a single enantiomeric product, is the most versatile reaction in this family.[2]

Because of its simplicity, cost-effectiveness and environmental affability, transition-metal-catalyzed asymmetric hydrogenation has become a widely used method in organic synthesis. There are many examples of optically active compounds that contain a hydrogen atom at the stereocentre, and asymmetric hydrogenation is of particular importance to access these compounds in highly enantiomerically pure form.

There has been especially intense interest in the asymmetric hydrogenation of prochiral olefins. Since the first reports of Rh-diop[3] and Ru-binap[4] catalysts for this reaction, many phosphine ligands have been developed and evaluated for the hydrogenation of functionalized olefins.[5]

In preliminary studies with Ir complexes,[6] Crabtree's achiral version $[(COD)Ir(py)(PCy_3)]^+ [PF_6]^-$ served as a conceptual template for modifications. Replacing the monodentate pyridine and phosphine ligands provided the foundation for chiral bidentate *N*,*P*-ligands. The new Ir complexes emerged as powerful tools in asymmetric hydrogenations of mainly unfunctionalized olefins with good enantiofacial recognition, and are essentially complementary to Rh- and Ru-diphosphine catalysts.[7] Since then, development of new *N*,*P*-ligands[8] for Ir-catalysts has been an important and challenging area of research.

Lately, we have demonstrated that the substrate scope for these catalysts is not limited to unfunctionalized olefins; they can also selectively hydrogenate various functionalized olefinic substrates.[9] However, Ir-catalyzed asymmetric hydrogenation is still highly substrate-dependent, and the development of new efficient chiral ligands that can tolerate broader range of substrates is a requisite.

Recently, we reported a new class of iridium–phosphine-thiazole complexes **1–3**[10] (Fig. 1) that are highly enantioselective for a wide range of olefin substrates.

Department of Biochemistry and Organic Chemistry, Box 576, 75123, Uppsala University, Sweden. E-mail: Pher.Andersson@biorg.uu.se; Fax: +46-18-471 3820; Tel: +46-18-471 3816

† CCDC reference number 664206. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b714744a

‡ All authors have contributed equally to this work.

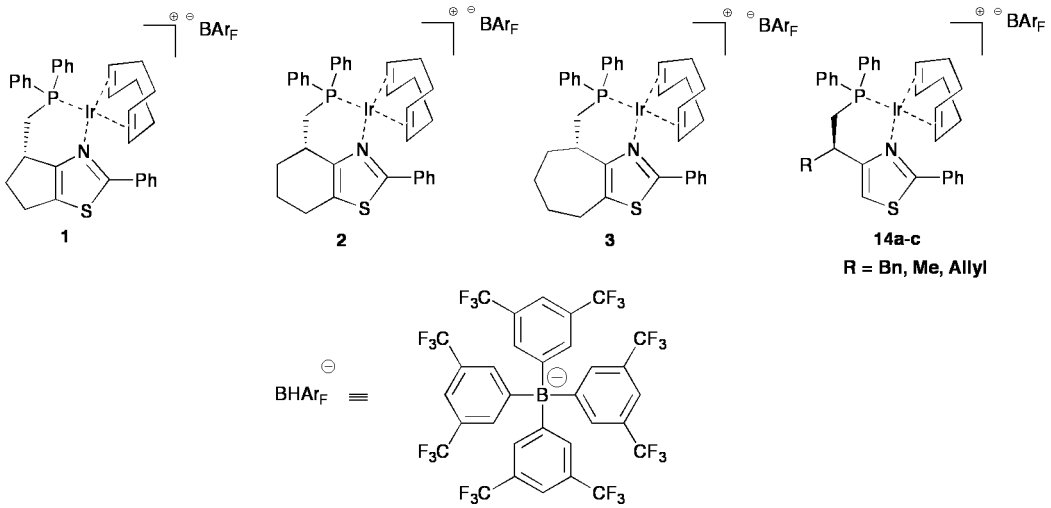


Fig. 1 Iridium complexes having thiazole-phosphine ligands with varying backbone structures.

We also investigated the effect of structural variations of the ligand on the stereochemical outcome of hydrogenation reactions. In our previous studies we evaluated the effect of the cyclic backbone by altering the size of the cycloalkane ring of the ligand, which significantly affected the stereochemical outcome of the hydrogenation of olefins.[10] Based on these findings, we decided to further alter the ligand structure by replacing the cycloalkane with an open-chain backbone having various substituents. We expected the open-chain ligands to be more flexible than the cyclic ones, and we hoped this would allow them to selectively reduce olefins that were challenging for catalysts with cycloalkane-based thiazole ligands.

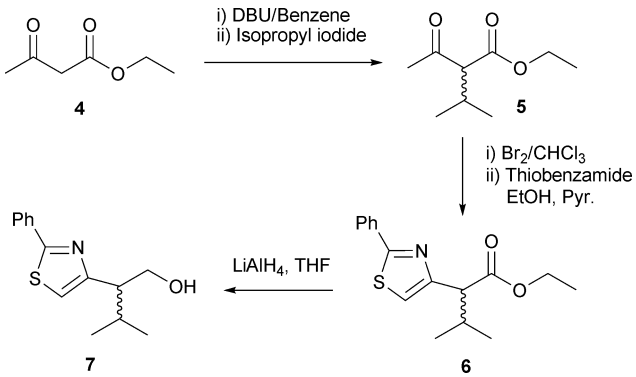
Here we report the synthesis of open-chain-backbone thiazole-phosphine ligands and their application in the asymmetric hydrogenation of olefins.

Results and discussion

The synthesis of new complexes (**14a–c**) starts with an inexpensive β-ketoester. Methyl acetoacetate **4a** was brominated in chloroform, and a stream of air was bubbled through the solution for 2 hours. This removed the HBr and introduced moisture to create the best conditions for the migration of bromine from the α-carbon to the γ-carbon.[11] Condensation of the resulting bromoketone with thiobenzamide gave ethyl 2-(2-phenylthiazol-4-yl)acetate **8a**.

Initially, we planned to introduce a bulky group, such as *tert*-butyl, into the backbone of the *N*,*P*-ligand by alkylation of β-ketoester **4**. All the efforts for this transformation proved to be futile, so an isopropyl group was introduced instead, using a much simpler route (Scheme 1).

The alkylation of β-ketoester **4** using isopropyl iodide in the presence of freshly distilled DBU proceeded smoothly to yield

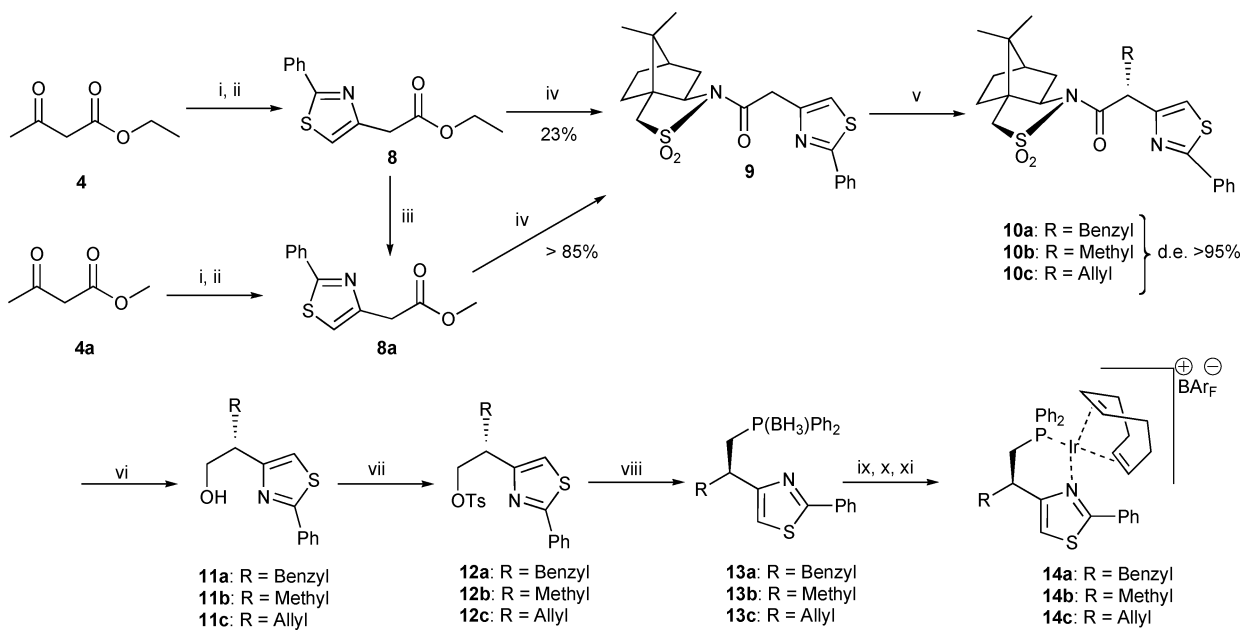


Scheme 1 Introduction of the isopropyl group.

the monoalkylated ethyl acetoacetate **5**.[12] Terminal bromination, followed by condensation with the thiobenzamide, afforded compound **6**, which was then reduced by $LiAlH_4$ to obtain a racemic primary alcohol **7** (Scheme 1). Unfortunately, we could not separate the enantiomers of the racemic ester **6** or of the corresponding alcohol **7** by any means.

As the separation of enantiomers of **6** or **7** was difficult to achieve, we envisaged an alternative strategy which involved a highly diastereoselective alkylation (initially isopropylation was studied) mediated by chiral auxiliaries. Preliminary screening of chiral auxiliaries revealed that the Oppolzer camphorsultam,[13] which is commonly used and demonstrates a great deal of versatility in asymmetric synthesis,[14] proved to be efficient.

In the alternative route (Scheme 2), ethyl acetoacetate **4** was brominated regioselectively at the γ-carbon in chloroform followed by the condensation of the resulting brominated ester with thiobenzamide, to give ethyl 2-(2-phenylthiazol-4-yl)acetate **8**. The coupling reaction of (2*R*)-(−)-bornane-2,10-sultam and ethyl



Scheme 2 Synthesis of the new iridium complexes. *Reagents and conditions*: i) Br_2, $CHCl_3$, 0 °C, 16 h; ii) thiobenzamide, ethanol, pyridine, reflux, 4 h; iii) $MeSO_3H$, methanol, reflux, 2 h; iv) Oppolzer sultam, Me_3Al, dichloromethane, reflux, 24 h; v) LiHMDS, THF, −78 °C, RBr, DMPU, 4 h; vi) $LiAlH_4$, THF, −10 °C to r.t., 4 h; vii) TsCl, pyridine, dichloromethane, 0 °C to r.t, 16 h; viii) $HP(BH_3)Ph_2$, *n*-BuLi, −78 °C to 0 °C, 40 min, then **12**, DMF, −78 °C to r.t, 16 h; ix) Et_2NH (excess), r.t, 16 h; x) $[Ir(COD)Cl]_2$, dichloromethane, reflux, 40 min; xi) H_2O, $NaBAr_F$, r.t, 2 h.

2-(2-phenylthiazol-4-yl)acetate was carried out by adding Me_3Al[15] to (2*R*)-(−)-bornane-2,10-sultam, then reacting the resulting aluminium amide with the ethyl ester **8**. Ethyl ester **8** was found to be a very resilient substrate under the coupling conditions, yielding only 23% of product even after 7 days of reflux. In contrast, methyl ester **8a** was smoothly converted to the desired acyl camphorsultam **9** after 24 hours of reflux, yielding more than 85% of the product. Ethyl ester **8** was converted to the methyl ester analogue **8a** by refluxing in an excess of methanol with a catalytic amount of methanesulfonic acid. Alternatively, **8a** could be obtained from methyl acetoacetate **4** in the same manner.

The coupling product, acyl camphorsultam **9**, was treated with lithium hexamethyldisilazide (LHMDS), the lithium enolate generated being quenched with an excess of isopropyl iodide in the presence of 10% DMPU in THF. The overall yield of the reaction was <10%, but the diastereomeric excess was >99%. However, the same method was then applied to introduce benzyl, methyl and allyl groups, which gave the best outcome in terms of reaction yield and also diastereoselectivity (>95%). Though only reactive alkyl halides could be used as electrophiles in this methodology, intermediate **9** was alkylated with several different electrophiles to obtain chiral ligand precursors with high diastereomeric purities.

The alkylated acyl sultams **10a–c** were reduced to corresponding enantiomerically pure alcohols with $LiAlH_4$. The enantiopurities of these alcohols **11a–c** were determined by chiral HPLC using Chiralcel OB-H in 10% isopropanol–hexane before being converted to the corresponding tosylates **12a–c** in good yields. Treatment of the tosylates with lithiated diphenylphosphine–borane adduct at −78 °C (then warming to room temperature) in THF–DMF yielded the borane-protected chiral phosphines in high yields.

Removal of the borane protecting group was achieved by treating it with an excess of freshly distilled diethylamine. The borane-free phosphines (**13a–c**) were eventually transformed into corresponding iridium complexes (**14a–c**) in moderate yields using the previously employed protocol.[10]

The absolute configuration of the alkylated compound **10a** was found by X-ray crystallography to be *R* (Fig. 2).

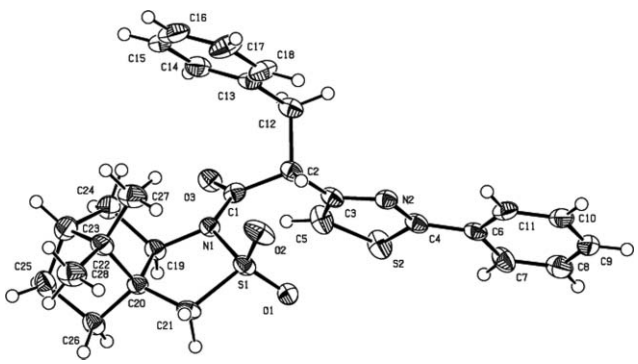


Fig. 2 The X-ray crystallographic structure of **10a** provides evidence for the *R* absolute configuration of the ligand.

Complexes **14a** and **14b** were stable at ambient temperature for months, whereas complex **14c** decomposed after several days even at lower temperatures (−20 °C). The reason for the instability of complex **14c** is not known, but it might be due to the displacement of COD by an allyl group from another complex, which would result in polymerization of the complex. Upon decomposition, this complex changes colour from bright orange to dark brown. Due to its instability, complex **14c** was evaluated for hydrogenation activity immediately after it was synthesized.

Hydrogenation of various tri-substituted olefins (Entries 1–10, Table 1) using the newly synthesized complexes (**14a–c**) revealed that complexes **14a** and **14b** have equal reactivity and selectivity when compared to their cyclic analogue **2** (up to and above 99% ee). Complex **14c** is clearly less selective in general, although its activity is comparable with that of the other catalysts shown in Table 1. The lower selectivity of **14c** may be due to its instability.

An increase in ee was observed for substrates **22** (51%) and **24** (56%) (Entries 8 and 10, Table 1) with complex **14a**; the same substrates gave a product with 40% ee and racemic product, respectively, when complex **2** was used.

Complexes **14a** and **14b** also gave good enantioselectivities for imine substrate **25** (51% and 49%) (Entry 11, Table 1), whereas the closed-chain analogue **2** showed only 16% ee.

Conclusions

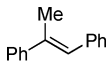
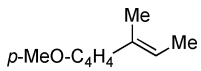
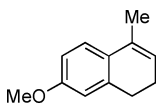
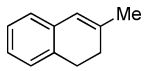
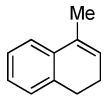
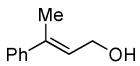
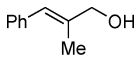
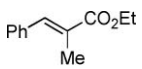
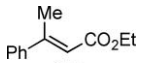
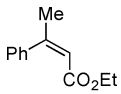
We have developed open-chain-backbone analogues of previously reported thiazole-phosphine ligands in order to study the effect of ligand backbone structure on the stereochemical outcome of iridium-catalyzed olefin hydrogenation. We have developed a route to synthesize these new ligands *via* diastereoselective alkylation. The new catalysts reduced several prochiral olefins in excellent yield and stereoselectivity, and reduced a prochiral imine in moderate ee. Comparing these catalysts to the closed-chain analogue **2**, we find that these new catalysts behaved similarly to the original catalysts in asymmetric hydrogenations for most of the substrates.

Experimental

General methods

All solvents were dried according to the reported procedures.[16] The chromatographic separations were performed on Kieselgel 60 H silica gel (particle size: 0.063–0.100 mm). Thin layer chromatography (TLC) was performed on aluminium-backed plates coated with Kieselgel 60 0.20 mm (UV254), and visualized under ultra-violet light (at 254 nm), or by staining with ethanolic phosphomolybdic acid followed by heating. ^{1}H-NMR spectra were recorded at 500, 400 or 300 MHz in $CDCl_3$, and referenced to the residual $CHCl_3$ peak (7.26 ppm). ^{13}C-NMR spectra were recorded with at 100 or 75 MHz in $CDCl_3$ and referenced to the central peak of $CDCl_3$ (77.0 ppm). ^{31}P-NMR spectra were recorded at 121.47 MHz in $CDCl_3$, using 85% phosphoric acid as an external standard. Chemical shifts are reported in ppm (δ scale). IR spectra were recorded on Perkin-Elmer 100 FT/IR spectrometer. Enantiomeric excesses were determined using chiral HPLC or GC. HPLC was performed at 254 nm UV detector, using a chiral column (Chiralcel OB-H), and GC analysis was performed using a chiral column (Chiral DexG-TA). Optical rotations were recorded on a thermostatted polarimeter using a 1.0 dm cell. Absolute configurations were determined by comparing the retention times of the products to the literature data.

Table 1 Iridium-catalyzed asymmetric hydrogenation of substrates **15–25**[a]

		14a		14b		14c		2[10]	
Entry	Substrate	Conv.[b] (%)	ee[c] (%)	Conv.[b] (%)	ee[c] (%)	Conv.[b] (%)	ee[c] (%)	Conv.[b] (%)	ee[c] (%)
1	 **15**	>99	96 (*R*)	>99	>99 (*R*)	>99	87(*R*)	>99	>99 (*S*)
2	 **16**	>99	94 (*R*)	>99	99 (*R*)	>99	85(*R*)	>99	99 (*S*)
3	 **17**	>99	80 (*S*)	>99	57 (*S*)	>99	88(*S*)	>99	93 (*R*)
4	 **18**	>99	98 (*R*)	>99	94 (*R*)	>99	87(*R*)	>99	>98 (*S*)
5	 **19**	>99	78 (*R*)	>99	78 (*R*)		—[d]	>99	98 (*R*)
6	 **20**	>99	90 (*R*)	>99	97 (*R*)		—[d]		—[d]
7	 **21**	>99	79 (*R*)	>99	91 (*R*)	90	70(*R*)	>99	99 (*S*)
8	 **22**	>99	51 (*R*)	>99	32 (*R*)	>99	40(*R*)	>99	40 (*S*)
9	 **23**	>99	97 (*R*)	>99	98 (*R*)	>99	90(*R*)	>99	98 (*S*)
10	 **24**	75	56 (*S*)	75	23 (*S*)		—[d]	>99	Racemic
11	 **25**	70[e]	51 (*S*)	27[e]	49 (*S*)		—[d]	65[e]	16 (*R*)

[a] *Reagents and conditions*: 50 bar H_2, rt, dichloromethane, 0.5 mol% catalyst. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC or chiral GC and compared to the literature data. Absolute configuration is given in parentheses. [d] Not attempted. [e] 1 mol% catalyst loading.

Methyl 4-bromo-3-oxobutanoate

A solution of bromine (14.8 g, 92.66 mmol) in 20 mL of chloroform was added to a stirred solution of methyl acetoacetate (10.76 g, 92.66 mmol) in 30 mL of chloroform at 0 °C under an inert atmosphere over a period of 1.5 hours. The reaction mixture was stirred for 16 hours at room temperature; air was blown in *via* a bubbler for the last 2 hours. This removed the HBr and introduced moisture to create the best conditions for the migration of bromine from the α-carbon to the γ-carbon. The reaction mixture was washed once with cold water, and then extracted with dichloromethane. The organic layer was dried over $MgSO_4$, filtered, and the solvent was removed *in vacuo* to obtain the crude bromoketoester as light yellow oil in a quantitative yield. The

crude product was utilized for the next step without further purification.

Synthesis of methyl 2-(2-phenylthiazol-4-yl)acetate (8a)

To a stirred solution of methyl 4-bromo-3-oxobutanoate (10.0 g, 51.3 mmol) in dry methanol was added thiobenzamide (7.03 g, 51.3 mmol), and then pyridine (4.14 mL, 51.3 mmol). The reaction mixture was stirred for one hour at room temperature and then refluxed for 4 hours. After the completion of reaction (TLC analysis), the reaction mixture was washed with water (2 × 20 mL) and the aqueous phase was extracted with dichloromethane (3 × 30 mL) followed by washing with brine. The combined organic phases were dried over $MgSO_4$ and the solvent was removed *in vacuo* to obtain the crude product. Flash chromatography eluting with dichloromethane–pentane (30 : 70) yielded **8a** as light yellow oil in 64% yield. Analytical data of compound **8a** was found to be consistent with earlier reported data.

Introduction of (2*R*)-(−)-bornane-2,10-sultam to the ester 8a (9)

To a stirred solution of (2*R*)-(−)-bornane-2,10-sultam (2.76 g, 12.9 mmol) in 20 mL of dry dichloromethane was added Me_3Al (2 M in heptane, 8.35 mL, 16.7 mmol, 1.3 eq.) dropwise at room temperature under N_2. The reaction mixture was stirred at room temperature for 30 min. Methyl 2-(2-phenylthiazol-4-yl)acetate (**8a**) (3.0 g, 12.9 mmol) in 5 mL dichloromethane was added to the reaction mixture and refluxed for 24 hours. HCl (1 M, 20 mL) was added slowly (addition of HCl causes methane gas to evolve) and the reaction mixture was then extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with brine and dried over $MgSO_4$. Purification by flash chromatography (1% methanol in toluene) yielded compound **9** as a white solid. The purified product was recrystallized from diethyl ether to obtain white crystals. Yield = 4.24 g (86%); $[\alpha]_D^{24.5} = -143.0$ (*c* 1, $CHCl_3$); $R_f = 0.26$ (1% methanol in toluene); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.97–7.92 (m, 2H, ArH), 7.46–7.40 (m, 3H, ArH), 7.22 (s, 1H, het.), 4.39 (d, $J = 17.7$ Hz, 1H), 4.28 (d, $J = 17.7$ Hz, 1H), 3.95 (dd, $J = 7.71$, 4.72 Hz, 1H), 3.56 (d, $J = 13.91$ Hz, 1H), 3.50 (d, $J = 13.91$ Hz, 1H), 2.24–2.05 (m, 2H), 2.0–1.85 (m, 3H), 1.48–1.32 (m, 2H), 1.20 (s, 3H), 0.98 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 168.8, 168.0, 149.2, 134.0, 130.0, 129.0, 127.0, 117.0, 65.8, 53.2, 49.0, 48.2, 45.0, 38.8, 38.3, 33.2, 26.8, 21.2, 20.2; IR ($CHCl_3$): 3013, 2961, 2884, 1698, 1327, 1213 cm^{-1}; MS (GC) *m*/*z*: 416.48 (M^+, 1%), 352 (3), 203 (10), 164 (13), 151 (38), 138 (81), 125 (100).

General procedure for diastereoselective alkylation of acyl sultam 9

Lithium hexamethyldisilazide (LiHMDS, 1 M in THF, 5.04 mmol, 1.2 eq.) was added dropwise over a period of 10 min to a stirred solution of (2*R*)-(−)-acyl sultam **9** (4.2 mmol) in 15 mL of dry THF at −78 °C under inert atmosphere. The reaction mixture was stirred at this temperature for an additional 45 min. The lithium enolate of **9** was then quenched with an excess of freshly distilled alkyl halide (37 mmol) in 5 mL of THF, after which 2 mL of freshly distilled DMPU was added. The reaction mixture was brought up to room temperature and stirred for 4 hours until all the starting materials disappeared (TLC). The reaction mixture was quenched with 10% $NaHCO_3$ solution, extracted with dichloromethane (4 × 20 mL) and washed with brine. The combined organic extracts were dried over $MgSO_4$ and evaporated to dryness.

(2*R*)-(−)-Benzylated acyl sultam (10a). The crude product was subjected to column chromatography using 10% ethyl acetate in pentane as eluent. The purified product was then recrystallized from diethyl ether to afford **10a** as white needle-shaped crystals. The crystals had >99% diastereomeric purity by ^{1}H-NMR. Yield = 85%; $[\alpha]_D^{24.5} = -95.0$ (*c* 1, $CHCl_3$); $R_f = 0.48$ (20% ethyl acetate in pentane); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.03–7.97 (m, 2H, ArH), 7.48–7.38 (m, 3H, ArH), 7.35–7.30 (m, 2H, ArH), 7.27–7.22 (m, 3H, ArH), 7.19 (s, 1H, het.), 4.99 (t, $J = 7.58$ Hz, 1H), 3.82 (dd, $J = 7.71$, 4.73 Hz, 1H), 3.49 (d, $J = 7.58$ Hz, 2H), 3.42 (d, $J = 14.4$ Hz, 1H), 3.36 (d, $J = 14.4$ Hz, 1H), 2.05–1.95 (m, 2H), 1.91–1.72 (m, 3H), 1.36–1.20 (m, 2H), 0.89 (s, 3H), 0.65 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.5, 167.7, 153.4, 139.0, 138.8, 130.0, 129.82, 129.0, 128.5, 126.92, 126.85, 65.6, 53.4, 49.95, 48.4, 48.0, 45.0, 41.0, 38.8, 33.2, 26.7, 20.8, 20.2; IR ($CHCl_3$): 3019, 2961, 2885, 1690, 1333, 1215 cm^{-1}; MS (GC) *m*/*z*: 506 (M^+, 1%), 476 (1), 448 (1), 334 (5), 264 (8), 202 (12), 138 (11), 125 (21), 91 (3).

(2*R*)-(−)-Methylated acyl sultam (10b). The crude product was dissolved in toluene and washed with water to remove DMPU. Flash chromatography using toluene–methanol (99 : 1 gradient to 75 : 25) afforded **10b** as a colourless oil. ^{1}H-NMR showed 95% diastereomeric excess. Yield = 91%; $[\alpha]_D^{23.8} = -58.3$ (*c* 1, $CHCl_3$); $R_f = 0.3$ (dichloromethane); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.98–7.92 (m, 2H, ArH), 7.43–7.34 (m, 3H, ArH), 7.21 (d, $J = 0.8$ Hz, 1H, ArH), 4.72 (dq, $J = 7.1$, 0.8 Hz, 1H), 3.94 (dd, $J = 7.8$, 4.9 Hz, 1H), 3,53 (d, $J = 13.8$ Hz, 1H), 3,45 (d, $J = 13.8$ Hz, 1H), 2.16 (m, 1H), 2.07 (dd, $J = 13.9$, 7.8 Hz, 1H), 1.95–1.82 (m, 3H), 1,71 (d, $J = 7.0$ Hz, 3H, Me), 1.45–1.26 (m, 2H), 1.21 (s, 3H, Me), δ 0.98 (s, 3H, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 19.2, 20.1, 21.1, 26.7, 33.1, 38.7, 42.9, 45.0, 48.0, 48.7, 53.4, 65.6, 115.3, 126.9, 128.9, 129.9, 134.2, 155.2, 167.5, 173.1; IR ($CDCl_3$): 2960, 1693, 1329, 1209, 908, 725 cm^{-1}; MS (GC) *m*/*z*: 431 (M^+, 12%), 251 (100), 188 (47), 150 (10), 86 (34), 84 (46).

(2*R*)-(−)-Allylated acyl sultam (10c). Flash chromatography eluting with toluene–methanol (99 : 1 gradient to 75 : 25) afforded **10c** as a pale yellow solid. ^{1}H-NMR showed 93% diastereomeric excess. Yield = 87%; $[\alpha]_D^{24.5} = -33.4$ (*c* 0.8, $CHCl_3$); $R_f = 0.3$ (dichloromethane); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.97–7.94 (m, 2H, ArH), 7.43–7.35 (m, 3H, ArH), 7.24 (s, 1H, het.), 5.89 (m, 1H), 5.16 (dq, $J = 17.0$, 3.24, 1.62 Hz, 1H), 5.03 (dm, 1H) 4.76 (dd, $J = 8.5$, 5.7 Hz, 1H), 3.93 (dd, $J = 7.7$, 5.2 Hz, 1H), 3.57 (d, $J = 13.9$ Hz, 1H) 3.48 (d, $J = 13.9$ Hz, 1H), 3.0–2.86 (m, 2H), 2.16–2.04 (m, 3H), 1.95–1.85 (m, 4H), 1.42–1.25 (m, 3H), 1.21 (s, 3H), 0.98 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.5, 167.3, 153.1, 134.6, 133.7, 129.7, 128.7, 126.6, 117.9,115.8, 65.5, 53.2, 48.3, 47.7, 47.3, 44.7, 40.95, 38.8, 38.4, 32.9, 26.4, 20.9, 19.9; IR ($CHCl_3$): 3076, 2960, 2883, 1693, 1641, 1363, 1208 cm^{-1}; MS (GC) *m*/*z*: 457.25 (M^+, 1, 18%), 456.26 (M^+, 40), 455.28 (100), 241.11 (17), 239.27 (12), 214.23 (18), 213.21 (12), 121.16 (14), 91.1 (4), 77.14 (11).

General procedure for reduction of alkylated acyl sultam to the corresponding primary alcohols

$LiAlH_4$ (2.0 mmol) was added to a stirred solution of (2*R*)-(−)-alkylated acyl sultam (**10a–c**) (1.5 g, 1.0 mmol) in 10 mL of dry THF at −10 °C. The reaction mixture was brought up to room temperature and stirred for 4 hours. The reaction was then quenched by adding a mixture of H_2O (0.22 mL), NaOH (2 M, 0.44 mL) and H_2O (0.22 mL). The cake formed was filtered through a pad of Celite and washed several times with ethyl acetate. The filtrate was dried over Na_2SO_4 and the solvent was evaporated to obtain crude alcohol (**11a–c**).

(*R*)-(−)-3-Phenyl-2-(2-phenylthiazol-4-yl)propan-1-ol (11a). The crude product was purified by silica gel column chromatography using 1% methanol in toluene as eluent to afford the pure alcohol as a colourless oil. Yield = 75%; $[\alpha]_D^{24.5} = -17.8$ (*c* 1, $CHCl_3$); $R_f = 0.61$ (5% methanol in toluene); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.03–7.95 (m, 2H, ArH), 7.53–7.44 (m, 3H, ArH), 7.35–7.29 (m, 2H, ArH), 7.27–7.19 (m, 3H, ArH), 6.81 (s, 1H, het.), 4.05–3.88 (m, 2H), 3.84 (br, 1H), 3.35–3.26 (m, 1H), 3.16 (d, $J = 7.0$ Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 168.4, 159.2, 140.2, 133.6, 130.4, 129.4, 129.3, 128.6, 126.8, 126.4, 114.5, 65.2, 45.8, 38.0; IR ($CHCl_3$): 3386, 3024, 2924, 2864, 1514, 1495, 1454 cm^{-1}; MS (GC) *m*/*z*: 296 (M + 1, 23%), 295 (M$^+$, 19), 266 (18), 265 (75), 264 (100), 176 (24), 128 (32), 92 (6), 66 (4).

(*R*)-2-(2-Phenylthiazol-4-yl) propan-1-ol (11b). The crude product was purified by column chromatography using dichloromethane–methanol (100 : 0 gradient to 95 : 5) to afford the alcohol as a colourless oil. Yield = 69%; $[\alpha]_D^{24.5} = -19.1$ (*c* 1.6, $CHCl_3$); $R_f = 0.57$ (5% methanol in dichloromethane); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.95–7.88 (m, ArH), 7.46–7.36 (m, 3H, ArH), 6.96 (d, $J = 1.0$ Hz, 1H, ArH), 3.90–3.75 (m, 2H), 3.60 (br, 1H), 3.19 (m, 1H), δ 1.36 (d, $J = 7.1$ Hz, 3H, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 16.2, 38.1, 67.7, 112.7, 126.5, 128.9, 130.0, 133.5, 161.1, 168.1; IR ($CDCl_3$): 3353 (br.), 2965, 2928, 2872, 1513, 1455, 1435, 1240, 1027, 987, 918, 761 cm^{-1}; MS (GC) *m*/*z*: 220 (M + 1, 100%), 189 (13), 188 (12), 104 (2), 85 (4).

(*R*)-2-(2-Phenylthiazol-4-yl) pent-4-en-1-ol (11c). The crude product was purified by column chromatography using dichloromethane–methanol (100 : 0 gradient to 95 : 3) to afford the alcohol as a colourless oil. Yield = 72%; $[\alpha]_D^{24.5} = -18.3$ (*c* 1, $CHCl_3$); $R_f = 0.4$ (20% ethyl acetate in pentane); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.94–7.90 (m, 2H, ArH), 7.45–7.38 (m, 3H, ArH), 6.98 (s, 1H, het.), 5.82 (m, 1H), 5.09 (dq, $J = 17.1$, 3.4, 1.6 Hz, 1H), 5.04 (dm, 1H), 3.92 (ddd, $J = 14.6$, 10.7, 3.9 Hz, 2H), 3.63 (br, 1H), 3.09 (m, 2H), 2.54 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 168.1, 159.0, 144.8, 136.1, 133.3, 130.0, 128.9, 126.4, 116.7, 113.7, 65.3, 43.2, 35.5; IR ($CHCl_3$): 3389, 3021, 2920, 2859, 1514, 1495, 1454 cm^{-1}; MS (GC) *m*/*z*: 246.03 (M + 1, 14%), 245.06 (M$^+$, 23), 244.16 (100), 228.3 (22), 215.2 (14), 176 (21), 121.2 (15), 104.4 (10), 77.0 (8).

General procedure for tosylation of alcohols

To a solution of alcohol (0.35 g, 1.18 mmol) in 10 mL of dry dichloromethane was added *p*-toluenesulfonyl chloride (0.45 g, 2.36 mmol) and pyridine (0.24 mL, 2.36 mmol) at 0 °C. The reaction mixture was allowed to stir at room temperature overnight. After completion of the reaction (TLC), the reaction mixture was diluted with dichloromethane, and then washed with cold 10% $NaHCO_3$ (aq.) and brine. The organic phase was dried over $MgSO_4$ and the solvent was removed *in vacuo* to yield the tosylates **12a–c**.

(*R*)-3-Phenyl-2-(2-phenylthiazol-4-yl)propyl 4-methylbenzenesulfonate (12a). The crude reaction mixture was purified by chromatography (5% ethyl acetate in pentane) to afford **12a**. Yield = 90%; $[\alpha]_D^{24.5} = -2.45$ (*c* 1, $CHCl_3$); $R_f = 0.56$ (20% ethyl acetate in pentane); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.87–80 (m, 2H, ArH), 7.60 (d, 2H, $J = 8.3$ Hz, ArH), 7.47–7.41 m, 3H, ArH), 7.26–7.17(m, 3H, ArH), 7.15 (d, 2H, $J = 8.3$ Hz, ArH), 7.05 (d, 2H, $J = 7.93$ Hz, ArH), 6.82 (s, 1H, het.), 4.25 (m, 2H, SO_3-CH_2), 3.50–3.40 (m, 1H, CH), 3.07 (d, 2H, $J = 7.43$ Hz, Ph-CH_2), 2.22 (s, 1H, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 167.9 (het.), 156.0 (het.), 144.9, 138.8, 133.9, 132.7, 130.2, 129.9, 129.3, 129.1, 128.7, 128.0, 126.7, 126.6 (arom.), 115.7 (het.), 71.8, 43.8, 37.1, 21.7; IR ($CHCl_3$): 3028, 1598, 1516, 1496, 1456, 1359, 1216, 1189, 1175 cm^{-1}; MS (GC) *m*/*z*: 450 (M + 1, 2), 449 (M$^+$, 5), 419 (2), 388 (14), 295 (5), 264 (39), 202 (62), 92 (100), 91 (93).

(*R*)-2-(2-Phenylthiazol-4-yl)propyl 4-methylbenzenesulfonate (12b). The crude tosylate was precipitated twice from hot methanol–water (8 : 1) to afford **12b** as white powder. Yield = 71%; $[\alpha]_D^{24.5} = -0.72$ (*c* 1.38, $CHCl_3$); $R_f = 0.42$ (dichloromethane); HPLC on OD-H (heptane–isopropanol 97 : 3, 0.4 mL min^{-1}) 42.5 min (major) and 49.0 min (minor), >99% ee; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.85–7.80 (m, 2H, ArH), 7.67–7.62 (m, 2H, ArH), 7.43–7.37 (m, 3H, ArH), 7.20–7.14 (m, 2H, ArH), 6.94 (d, $J = 0.7$ Hz, 1H, ArH), 4.36 (dd, $J = 9.4$, 6.4 Hz), 4.26 (dd, $J = 9.4$, 6.0 Hz), 3.34 (m, 1H), 2.26 (s, 3H, Me), δ 1.37 (d, $J = 7.1$ Hz, 3H, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 16.3, 21.4, 36.1, 73.6, 114.0, 126.4, 127.7, 128.8, 129.6, 129.9, 133.0, 133.7, 144.4, 157.8, 167.7; IR (solid): 2972, 1598, 1518, 1461, 1352, 1172, 949, 844, 765, 667 cm^{-1}; MS (GC) *m*/*z*: 374 (M + 1, 22%), 201 (100), 188 (15), 121 (15), 98 (11), 97 (17).

(*R*)-2-(2-Phenylthiazol-4-yl)pent-4-enyl 4-methylbenzenesulfonate (12c). The crude mixture was purified by silica gel column chromatography using dichloromethane–methanol (100 : 0 gradient to 99.5 : 0.5) to afford **12c** as a white crystalline solid. Yield = 80%; $[\alpha]_D^{23.5} = -4.8$ (*c* 1, $CHCl_3$); $R_f = 0.52$ (0.5% methanol in dichloromethane); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.83–7.78 (m, 2H, ArH), 7.62–7.58 (m, 2H, ArH), 7.43–7.39 (m, 3H, ArH), 7.14 (dm, 2H, ArH), 6.94 (s, 1H, het.), 5.73–5.64 (m, 1H), 5.05-4.98 (m, 2H) 4.33 (ddd, $J = 14.5$, 9.5, 5.4 Hz, 2H), 3.26 (dddd, $J = 12.8$. 7.0, 5.4 Hz, 1H), 2.57–2.46 (m, 2H), 2.2 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 167.9, 156.2, 144.8, 135.1, 133.8, 132.8, 130.1, 129.9, 129.1, 128.0, 126.7, 117.8, 115.3, 72.1, 41.5, 35.1, 21.6.; IR ($CHCl_3$): 3115.25, 2976.63, 1641.80, 1597.24, 1457.00, 1354.79, 1190.07, 1175.36, 1097.69, 973.08, 927.06, 830.00, 814.56, 701.21, 691.24, 650.00 cm^{-1}; MS (GC) *m*/*z*: 400.17 (M + 1, 19%), 399.16 (M$^+$, 36), 398.20 (100), 244.19 (36), 226.24 (35), 222.21 (12), 121.13 (15), 91.13 (20).

General procedure for the preparation of borane-protected phosphines (13a–c)

n-BuLi (1.6 M, 1.2 eq.) was added dropwise to a solution of diphenylphosphine–borane adduct (1.16 mmol) in 5 mL of dry THF at −78 °C under inert atmosphere. The reaction mixture

was warmed to 0 °C and stirred for 40 min. The lithiated diphenylphosphine–borane adduct was transferred dropwise *via* a cannula to a pre-stirred solution of tosylate (0.77 mmol) in 1 mL of dry DMF at −78 °C. The reaction mixture was then warmed to room temperature and stirred for 16 hours. After completion (NMR), the reaction mixture was poured into 10% ice-cold $NaHCO_3$ solution and extracted with dichloromethane (15 mL × 3). The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by column chromatography to obtain **13a–c**.

(*R*)-4-(1-(Diphenylphosphino)-3-phenylpropan-2-yl)-2-phenylthiazole–borane adduct (13a). Chromatography on silica gel using toluene as an eluent afforded **13a** as colourless oil. Yield = 92%; $[a]_D^{24.5} = -194.0$ (*c* 1, $CHCl_3$); $R_f = 0.66$ (toluene); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.90–7.83 (m, 2H, ArH), 7.67–7.58 (m, 2H, ArH), 7.55–7.34 (m, 8H, ArH), 7.26–7.08 (m, 6H, ArH), 7.05 (d, $J = 7.71$ Hz, 2H, ArH), 6.54 (s, 1H, het.), 3.78–3.65 (m, 1H), 3.28–3.04 (m, 3H), 2.60–2.48 (m, 1H), 1.62–0.60 (br, 3H, BH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 167.8, 157.6, 139.7, 134.2, 132.6 (d, $J_{C,P} = 9.64$ Hz), 131.9 (d, $J_{C,P} = 9.6$ Hz), 131.1 (d, $J_{C,P} = 2.7$ Hz), 130.8 (d, $J_{C,P} = 2.7$ Hz), 130.0, 129.4, 129.3, 129.0, 128.9, 128.5, 128.4, 128.3, 126.8, 126.4, 116.3, 43.8 (d, $J_{C,P} = 11.4$ Hz), 39.8 (d, $J_{C,P} = 1.6$ Hz), 30.4 (d, $J_{C,P} = 37.2$ Hz); ^{31}P-NMR (121 MHz, $CDCl_3$): δ 15.8 (br); IR ($CHCl_3$): 3726, 3060, 3007, 2382, 1518, 1494, 1461, 1436, 1216 cm^{-1}; MS (GC) *m*/*z*: 477 (M^+, 1%), 386 (15), 264 (16), 219 (45), 214 (100), 202 (49), 183 (16), 91 (7).

(*R*)-4-(1-(Diphenylphosphino)propan-2-yl)-2-phenylthiazole–borane adduct (13b). Chromatography on silica gel with pentane–dichloromethane (90 : 10 gradient to 40 : 60) afforded **13b** as a colourless oil. Yield = 91%; $[a]_D^{24.6} = +94.9$ (*c* 1, $CHCl_3$); $R_f = 0.52$ (dichloromethane); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.54–1.60 (m, 3H, BH_3), 1.44 (dd, J = 6.7, 1.1 Hz, 3H), 2.40 (ddd, $J = 14.0$, 8.4, 5.5 Hz, 1H), 3.15 (td, $J = 14.1$, 7.9 Hz, 1H), 3.59 (m, 1H), 6.78 (m, 1H, ArH), 7.16–7.27 (m, 3H, ArH), 7.35–7.45 (m, 6H, ArH), 7.54–7.62 (m, 2H, ArH), 7.63–7.70 (m, 2H, ArH), 7.81–7.86 (m, 2H, ArH); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 23.0 (d, 9.9 Hz), 32.1 (d, $J = 4.2$ Hz), 32.3 (d, $J = 41.6$ Hz), 113.9, 126.4, 127.9, 128.2 (d, $J = 9.9$ Hz), 128.6–128.8 (m), 129.7, 130.6–130.9 (m), 131.5–131.8 (m), 132.3–132.6 (m), 133.8, 160.3 (d, $J = 5.5$ Hz), 167.7; ^{31}P-NMR (121 MHz, $CDCl_3$): 15.1 (br. d, 15.4 Hz); IR ($CHCl_3$): 3057, 2966, 2375, 1960, 1888, 1812, 1436, 1106, 1061, 909, 764, 730 cm^{-1}; MS (GC) *m*/*z*: 401 (M^+, 44%), 400 (100), 387 (21), 386 (26), 359 (9), 310 (25), 297 (11), 265 (16), 264 (11), 200 (11), 183 (14), 121 (6).

(*R*)-4-(1-(Diphenylphosphino)pent-4-en-2-yl)-2-phenylthiazole–borane adduct (13c). Chromatography using toluene as an eluent afforded **13c** as a colourless oil. Yield = 89%; $[a]_D^{24.5} = -94.5$ (*c* 1.1, $CHCl_3$); $R_f = 0.5$ (0.5% methanol in dichloromethane); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.83–7.78 (m, 2H, ArH), 7.65–7.59 (m, 2H, ArH), 7.51–7.35 (m, 8H, ArH), 7.20–7.06 (m, 3H, ArH), 6.74 (s, 1H, ArH), 5.75–5.64 (m, 1H), 5.04 (dd, $J = 3.4$, 1.46 Hz, 1H), 5.02–4.98 (m, 1H) 3.57–3.48 (m, 1H), 3.12 (ddd, $J = 15.1$, 10.2 Hz, 1H), 2.68–2.52 (m, 2H), 2.46 (dddd, $J = 14.5$, 8.16, 3.5 Hz, 1H), 1.6–0.7 (br, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 167.6, 157.8 (d, $J = 3.4$ Hz), 135.7, 133.8, 132.4, 132.3, 131.6, 131.5, 131.4, 131.0, 130.7 (d, $J = 2.5$ Hz), 130.5 (d, $J = 2.5$ Hz), 129.6, 129.0, 128.7, 128.6, 128.1, 128.0, 127.9, 127.6, 126.4, 117.2, 115.6, 41.4 (d, $J = 11.6$ Hz), 37.1, (d, $J = 1.4$ Hz), 30.0, 29.7; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 14.7 (m); IR ($CHCl_3$): 3058.80, 2911.34, 2379.17, 1970.73, 1889.38, 1824.91, 1640.13, 1436.98, 1106.71, 1061.17, 985.29, 917.05, 838.63, 765.27, 736.22 cm^{-1}; MS (GC) *m*/*z*: 428.38 (M + 1, 3%), 427.29 (M^+, 5), 426.32 (17), 387.31 (28), 386.25 (100), 385.28 (28), 296.24 (15), 225.30 (16), 198.22 (13), 185.24 (14), 183.26 (26), 121.16 (8), 77.13 (4).

General procedure for preparation of Ir complexes 14a–c

Borane adduct **13a–c** (0.6 mmol) was stirred with an excess of freshly distilled diethylamine under N_2 overnight. Excess diethylamine was then removed *in vacuo* and the product was filtered through a short pad of silica using toluene as the eluent. The borane-free *N*,*P*-ligand was employed in the next step without further characterization.

To the solution of borane-free *N*,*P*-ligand (0.6 mmol) in 15 mL of dry dichloromethane was added $[Ir(COD)Cl]_2$ (0.3 mmol), and the mixture was refluxed under an inert atmosphere for 40 min. The reaction mixture was cooled to room temperature and the replacement of chloride ion with BAr_F^- anion was carried out by adding first 20 mL of distilled water, then $NaBAr_F$ (1.5 eq.), to the reaction mixture. The resultant mixture was stirred vigorously at room temperature for 2 hours and extracted with dichloromethane (20 mL × 3). Combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo* to obtain crude complex **14a–c**.

Complex 14a. The iridium complex was purified by column chromatography using pentane–dichloromethane 50 : 50 as the eluent to afford **14a** as an orange solid. Yield = 54%; $[a]_D^{24.5} = -124.0$ (*c* 1, $CHCl_3$); $R_f = 0.66$ (dichloromethane); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.04–7.98 (m, 2H), 7.78–7.76 (m, 2H), 7.73–7.68 (m, 8H, BAr_F), 7.67–7.65 (m, 2H), 7.63–7.59 (m, 2H), 7.53-7.49 (m, 4H, BAr_F), 7.48–7.43 (m, 6H), 7.31–7.27 (m, 2H), 7.19–7.15 (m, 2H), 7.02 (s, 1H), 6.64 (dd, $J = 7.79$, 3.65 Hz, 2H), 4.53–4.49 (m, 1H, COD), 4.34–4.30 (m, 1H, COD), 3.62 (dt, $J = 13.06$, 4.13 Hz, 1H), 3.33–3.20 (m, 1H, COD), 3.10-2.98 (m, 2H), 2.72–2.62 (m, 1H, COD), 2.56–2.40 (m, 2H, COD-H), 2.36–2.22 (m, 2H), 2.20–2.10 (m, 1H, COD-H), 1.80–1.75 (m, 1H, COD-H), 1.42–1.20 (m, 4H, COD-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.0, 162.7, 162.2, 161.7, 161.2 (4C, BAr_F), 160.1, 137.6, 135.0 (m, 8C, BAr_F), 133.7, 133.6, 133.3, 132.6 (d, $J_{C,P} = 2.9$ Hz), 131.8, 131.3 (d, $J_{C,P} = 2.9$ Hz), 131.0, 130.5 (d, $J_{C,P} = 9.6$ Hz), 129.8 (d, $J_{C,P} = 9.6$ Hz), 129.7, 129.5, 129.3, 129.2, 129.0, 128.0, 126.1, 118.0 (m, 4C, BAr_F), 115.5, 67.7, 64.6, 39.6 (d, $J_{C,P} = 14.6$ Hz), 37.3 (d, $J_{C,P} = 4.3$ Hz), 34.0 (4C, COD), 30.1 (d, $J_{C,P} = 35.4$ Hz), 28.4 (4C, COD-C); ^{31}P-NMR (121 MHz, $CDCl_3$): δ 10.0 (s); ^{19}F-NMR (282 MHz, $CDCl_3$): δ −62.4 (s); IR ($CHCl_3$): 3065, 3031, 2997, 1610, 1353, 1273 cm^{-1}.

Complex 14b. The iridium complex was purified by column chromatography using pentane–dichloromethane (75 : 25 gradient to 20 : 80), affording **14b** as an orange solid. Yield = 60%; $[a]_D^{23.8} = -35.2$ (*c* 1.21, $CHCl_3$); $R_f = 0.29$ (dichloromethane–pentane 50 : 50); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.51–1.27 (m, 3H), 1.73 (br.

dd, $J = 6.8$, 1.6 Hz, 3H), 1.93 (m, 1H), 2.10 (dd, $J = 14.9$, 7.6 Hz, 1H), 2.35–2.22 (m, 2H), 2.55-2.39 (m, 2H), 2.98 (ddd, $J = 14.8$, 10.6, 3.2 Hz, 1H), 3.08 (m, 1H), 3.32 (m, 1H), 4.48–4.34 (m, 2H), 4.60 (m, 1H), 7.32–7.19 (m, 3H, ArH), 7.61–7.38 (m, 14H, ArH), 7.83–7.64 (m, 9H, ArH), 8.07–7.99 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 19.8 (d, $J = 15.6$ Hz), 25.6, 28.3, 33.3, 33.6 (d, $J =$ 34.3 Hz), 37.0 (m), 65.8 (d, $J = 179.8$ Hz), 88.3 (d, $J = 15.0$ Hz), 96.0 (d, $J = 8.7$ Hz), 115.3, 117.5 (m), 120.6, 123.3, 126.0, 128.3–129.7 (m), 130.8, 130.9, 131.4 (m), 132.1, 132.8, 132.9, 134.9 (m), 160.8 (m), 161.1, 161.5, 162.0, 162.5, 172.4; ^{31}P-NMR (121 MHz, $CDCl_3$): δ 10.9; IR (solid): 1610, 1353, 1274, 1163, 1126, 887, 716, 682, 669 cm^{-1}.

Complex 14c. The iridium complex was purified by column chromatography using pentane–dichloromethane (50 : 50) as eluent to afford **14c** as an orange solid. Yield = 70%; $[\alpha]_D^{23.8} = -23.7$ (c 0.7, $CHCl_3$); $R_f = 0.38$ (dichloromethane–pentane 50 : 50); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.03–7.99 (m, 2H), 7.80–7.71 (m, 8H), 7.60–7.45 (m, 14H, BAr_F), 7.30–7.21 (m, 3H), 7.25–7.22 (m, 2H), 6.20–5.90 (m, 1H), 5.20–5.09 (m, 1H), 5.06–5.02 (m, 1H), 4.51–4.20 (m, 2H), 4.53–4.49 (m, 1H, COD), 4.34–4.30 (m, 1H, COD), 3.62 (dt, $J = 13.06$, 4.13 Hz, 1H), 3.33–3.20 (m, 1H, COD), 3.10–2.98 (m, 2H), 2.72–2.62 (m, 1H, COD), 2.56–2.40 (m, 2H, COD-H), 2.36–2.22 (m, 2H), 2.20–2.10 (m, 1H, COD-H), 1.80–1.75 (m, 1H, COD-H), 1.42–1.20 (m, 4H, COD-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.0, 162.7, 162.2, 161.7, 161.2 (4C, BAr_F), 160.1, 137.6, 135.0 (m, 8C, BAr_F), 133.7, 133.6, 133.3, 132.6 (d, $J_{C,P} = 2.9$ Hz), 131.8, 131.3 (d, $J_{C,P} = 2.9$ Hz), 131.0, 130.5 (d, $J_{C,P} = 9.6$ Hz), 129.8 (d, $J_{C,P} = 9.6$ Hz), 129.7, 129.5, 129.3, 129.2, 129.0, 128.0, 126.1, 118.0 (m, 4C, BAr_F), 115.5, 67.7, 64.6, 39.6 (d, $J_{C,P} = 14.6$ Hz), 37.3 (d, $J_{C,P} = 4.3$ Hz), 34.0 (4C, COD), 30.1 (d, $J_{C,P} = 35.4$ Hz), 28.4 (4C, COD-C); ^{31}P-NMR (121 MHz, $CDCl_3$): δ 10.0 (s); ^{19}F-NMR (282 MHz, $CDCl_3$): δ −62.4 (s); IR ($CHCl_3$): 3065, 3031, 2997, 1610, 1353, 1273 cm^{-1}

General procedure for hydrogenation reactions

The substrate (0.5 mmol) and catalyst (0.5–1 mol%) were weighed into a glass vial and 2.0 mL of anhydrous dichloromethane was added. The vial was placed in high-pressure hydrogenation equipment, which was purged three times with nitrogen before being pressurized to 50 bar with hydrogen gas. The pressure was held overnight, then vented. The solvent was removed *in vacuo*. The crude product was redissolved in ether, filtered through a short plug of silica and the solvent was evaporated. Enantiomeric excesses were determined by HPLC and GC analysis and comparison of the retention times with previously reported data.[10]

Acknowledgements

This work was supported by grants from AstraZeneca, the Swedish Research Council (VR) and Ligbank, and M.A. gratefully acknowledges the financial support from the Pakistan Higher Education Commission. We are also grateful to Mr Tobias Robert and Dr Jörg-M. Neudörfl for helping with X-ray crystal structure determination.

References

1 (*a*) J. M. Brown, in *Comprehensive Asymmetric Catalysis*, ed. E. N. Jacobsen, A. Pfaltz and H. Yamamoto, Springer-Verlag, Berlin, 1999; (*b*) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, VCH, New York, 1994; *Catalytic asymmetric synthesis*, ed. I. Ojima, Wiley-VCH, New York, 2000.

2 (*a*) W. S. Knowles, *Angew. Chem., Int. Ed.*, 2002, **41**, 1998; (*b*) R. Noyori, *Angew. Chem., Int. Ed.*, 2002, **41**, 1998.

3 T. P. Dang and H. B. Kagan, *J. Am. Chem. Soc.*, 1972, **94**, 6429.

4 T. Ikariya, Y. Ishii, H. Kawano, T. Arai, M. Saburi, S. Yoshikawa and S. Akutagawa, *J. Chem. Soc., Chem. Commun.*, 1985, 922.

5 (*a*) Y. Chi, W. Tang and X. Zhang, *Modern Rhodium-Catalyzed Organic Reactions*, Wiley-VCH, Weinheim, 2005; (*b*) M. Kitamura and Y. Noyori, *Ruthenium in Organic Synthesis*, Wiley-VCH, Weinheim, 2004.

6 R. H. Crabtree, *Acc. Chem. Res.*, 1979, **12**, 331.

7 (*a*) A. Lightfoot, P. Schnider and A. Pfaltz, *Angew. Chem., Int. Ed.*, 1998, **37**, 2897; (*b*) A. Pfaltz, *Synlett*, 1999, 835; (*c*) T. Bunlaksananusorn, K. Polborn and P. Knochel, *Angew. Chem.*, 2003, **115**, 4071; (*d*) T. Bunlaksananusorn, K. Polborn and P. Knochel, *Angew. Chem., Int. Ed.*, 2003, **42**, 3941; (*e*) G. Helmchen and A. Pfaltz, *Acc. Chem. Res.*, 2000, **33**, 336.

8 (*a*) A. Pfaltz, J. Blankenstein, E. Hcrmann, S. McIntyre, F. Menges, M. Schcnleber, S. P. Smit, B. Wustenberg and N. Zimmermann, *Adv. Synth. Catal.*, 2003, **345**, 33; (*b*) K. Källström, I. Munslow and P. G. Andersson, *Chem. Eur. J.*, 2006, **12**, 3194; (*c*) X. Cui and K. Burgess, *Chem. Rev.*, 2005, **105**, 3272.

9 (*a*) M. Engman, J. S. Diesen, A. Paptchikhine and P. G. Andersson, *J. Am. Chem. Soc.*, 2007, **129**, 4536; (*b*) P. Cheruku, S. Gohil and P. G. Andersson, *Org. Lett.*, 2007, **9**, 1659; (*c*) K. Källström, I. J. Munslow, C. Hedberg and P. G. Andersson, *Adv. Synth. Catal.*, 2006, **348**, 2575; (*d*) T. L. Church and P. G. Andersson, *Coord. Chem. Rev.*, DOI: 10.1016/j.ccr.2007.09.015.

10 C. Hedberg, K. Källstörm, P. Brandt, L. K. Hansen and P. G. Andersson, *J. Am. Chem. Soc.*, 2006, **128**, 2995.

11 (*a*) A. Svendsen and P. M. Boll, *Tetrahedron*, 1973, **29**, 4251; (*b*) R. O. Duthaler, *Helv. Chim. Acta*, 1983, **66**, 1475.

12 N. Ono, T. Yoshimura, T. Saito, R. Tamura, R. Tanikaga and A. Kaji, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 1716.

13 (*a*) W. Oppolzer and G. Poli, *Tetrahedron Lett.*, 1986, **27**, 4717–4720; (*b*) W. Oppolzer, *Pure Appl. Chem.*, 1990, **62**, 1241.

14 (*a*) A. Bierstedt, J. Stölting, R. Fröhlich and P. Metz, *Tetrahedron: Asymmetry*, 2001, **12**, 3399; (*b*) J. Liu, Y. Yang and R. Ji, *Helv. Chim. Acta*, 2004, **87**, 1935.

15 A. Basha, M. Lipton and S. M. Weinreb, *Tetrahedron Lett.*, 1977, **18**, 4171.

16 D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, 1985.