Chiral iridium(I) bis(NHC) complexes as catalysts for asymmetric transfer hydrogenation

Claus Diez and Ulrich Nagel*

The common use of NHC complexes in transition-metal mediated C–C coupling and metathesis reactions in recent decades has established N-heterocyclic carbene (NHCs) as a new class of ligand for catalysis. The field of asymmetric catalysis with complexes bearing NHC-containing chiral ligands is dominated by mixed carbene/oxazoline or carbene/phosphate chelating ligands. In contrast, applications of complexes with chiral, chelating bis(NHC) ligands are rare. In the present work new chiral iridium(I) bis(NHC) complexes and their application in the asymmetric transfer hydrogenation of ketones are described. A series of chiral bis(azolium) salts have been prepared following a synthetic pathway, starting from L-valinol and the modular buildup allows the structural variation of the ligand precursors. The iridium complexes were formed via a one-pot transmetallation procedure. The prepared complexes were applied as catalysts in the asymmetric transfer hydrogenation of various prochiral ketones, affording the corresponding chiral alcohols in high yields and moderate to good enantioselectivities of up to 68%. The enantioselectivities of the catalysts were strongly affected by the various, terminal N-substituents of the chelating bis(NHC) ligands. The results presented in this work indicate the potential of bis-carbenes as stereodirecting ligands for asymmetric catalysis and are offering a base for further developments. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: chiral iridium(I)-NHC complexes; asymmetric transfer hydrogenation; ketones

Introduction

Since their discovery, stable N-heterocyclic carbene (NHCs) have been the subject of intense interest, primarily as strong σ-donor ligands for transition metals. In comparison with phosphate complexes, NHC complexes display significant advantages, particularly their stability towards air, moisture and heat. Their common use in transition-metal mediated C–C coupling and metathesis reactions has established N-heterocyclic carbene as a new class of ligand in catalysis beside phosphate and oxazoline ligands.[1–5]

The field of asymmetric catalysis with complexes bearing chiral NHC-containing ligands is dominated by chelating ligands with a carbene unit and a second coordinating group, such as phosphate or oxazole.[6–9] Apart from the well-known bis(benzimidazolin-2-ylidine) palladium(II) and rhodium(III) complexes derived from BINAM, applications of chiral bis(NHC) complexes in asymmetric catalysis are notably rare.[10,11]

As recently demonstrated by Peris and Crabtree et al., rhodium(III) and iridium(III) complexes of achiral chelating bis(carbene) ligands are promising catalysts for the transfer hydrogenation of ketones using 2-propanol as hydrogen source and various amounts of KOH as cocatalyst.[12–14] Using benzophenone as the substrate and bis(imidazolin-2-ylidine) iridium(III) complexes as catalysts, Crabtree et al. observed turnover frequencies of up to 50 000 [h⁻¹].[12]

We recently reported the synthesis and structural characterization of Rh(I) and Ir(I) complexes bearing chiral bis(NHC) ligands derived from L-valinol.[15] In this article we wish to report the application of these iridium complexes as catalysts for the asymmetric transfer hydrogenation of prochiral ketones. For this purpose, chiral bis(NHC) ligands with various combinations of terminal N-substituents and their iridium(I) complexes were prepared.

Moreover the synthetic pathway allowed us to prepare a bis(NHC) ligand and its iridium(I) complex combining two different azolin-2-ylidenes. The influence of the ligand shape on the catalytic activity and selectivity of the corresponding iridium(I) bis(NHC) complexes was determined.

Results and Discussion

Ligand and Complex Synthesis

As previously reported, the bis-imidazolium salts 3a–f are accessible via a modular synthesis starting from L-valinol. The modular buildup of the ligand precursors makes it possible to introduce different substituents at the terminal nitrogen atoms in two steps using the chiral imidazolobromide 1 as a bifunctional synthon. The first reaction step was the alkylation of 1-R1-imidazoles (R1 = Me, iso-Pr and Ph) with 1 as alkylating agent. The resulting imidazolium salts 2a–c were then treated with an excess of various electrophiles R2Br (R2 = n-Pr and iso-Pr) in acetonitrile or methyl iodide in dichloromethane giving the bis-imidazolium salts 3a–f in good yields (Scheme 1).[13] In a similar manner the mixed bis-azolium salt 5, combining an imidazole and a benzimidazole unit, was obtained.

The iridium(I) complexes 6a–f and 7 were prepared from the corresponding bis-imidazolium salts 3a–f, silver(I) oxide

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and [Ir(cod)Cl]$_2$ according to a one-pot transmetallation procedure developed by Mata et al.$^{[12,16,17]}$ All complexes were purified by gradient column chromatography on SiO$_2$ using dichloromethane–acetone mixtures as eluent and KPF$_6$ for anion exchange. The iridium(I) compounds 6a–f were obtained as orange-red solids in 52–63% yield. Complex 7, bearing an imidazolin-2-ylidene–benzimidazolin-2-ylidene ligand, was obtained in a lower yield of 38% (Scheme 2). The iridium complexes were obtained as mixtures of exo and endo stereoisomers, referring to the position of the backbone iso-propyl group relative to the coordination plane. Hence, the iso-propyl group of the exo isomer lies outside the C–Ir–C plane, while in the endo form it is oriented to the metal. The transmetallation reactions always gave excess exo isomers, ranging from 55% for 6a to 94% for 6d. The isomers were not separable by column chromatography, but crystals containing the exo isomers exclusively were obtained by layering concentrated THF–DCM solutions of complexes 6b–f and 7 with cyclohexane.$^{[15]}$ Compound 6c was also prepared as a 65:35 exo/endo mixture by increasing the reaction temperature during the transmetallation in acetonitrile to 80 °C. Complex 6a did not crystallize and was obtained as a 55:45 exo/endo mixture after column chromatography.

All complexes were characterized by NMR spectroscopy, high-resolution mass spectrometry and elemental analysis. As previously reported, the structures of 6b and 6c were determined by single crystal X-ray crystallography (CCDC deposit numbers 696020 for 6b and 696021 for 6c). The $^{13}$C NMR spectra of the iridium compounds 6a–f show typical signals between 171 and 177 ppm for metallated carbene carbons.$^{[16,18]}$ In comparison, the signal of the metallated benzimidazolin-2-ylidene carbene carbon of complex 7 appears at 184 ppm. The amounts of exo and endo stereoisomers were determined by integration of their characteristic backbone proton signals in the $^1$H NMR spectra.$^{[15]}$

In addition to transfer hydrogenation, the prepared iridium(I) complexes were tested in further catalytic reactions and showed no activity in the hydrogenation of itaconic acid and 1-methylcyclohexene even at elevated hydrogen pressure. Only low activity with low to moderate enantioselection was observed in the hydrosilylation of prochiral ketones.

**Asymmetric Transfer Hydrogenation**

The iridium(I) complexes 6a–f and 7 were used as catalysts for the asymmetric transfer hydrogenation of various ketones.
with 2-propanol as solvent/hydrogen donor and 1 mol% KOH as cocatalyst (Scheme 3).[12,19] All reactions were heated for 15 h at 82 °C using ketone–catalyst–base ratios of 1000 : 1:10. It is well known that the catalyst–base ratio is essential to activate the catalysts for hydrogen transfer if no internal base is involved.[20,21]

While rhodium–NHC catalysts basically require higher amounts of cocatalyst, iridium complexes are activated at lower base concentrations.[13] In the present case a catalyst–base ratio of 1 : 10 has been proven to be optimal.

The results of the catalytic transfer hydrogenations of acetophenone, propiophenone and α-methylpropiophenone are listed in Table 1. Generally all ketones were hydrogenated to the corresponding alcohols with high yields. To investigate the effect of various combinations of terminal N-substituents at the ligands on the enantioselectivity, all complexes were tested in ATH with different phenylalkylketones as substrates.

Starting with acetophenone, the obtained enantiomeric excesses of (S)-1-phenylethanol were low for all complexes. The highest ee value of 14% (S)-1-phenylethanol was achieved with complex 7 (entry 6, Table 1). Higher ee values of up to 42% (entry 9, Table 1) were obtained using propiophenone as substrate, whereas the enantioselectivities of the catalysts were affected by the substitution patterns of the NHC-ligands. For α-methylpropiophenone as the substrate, the ee values of the corresponding product alcohol increased again for all catalysts.

Starting from the N-dimethyl substituted complex 6a, the enantioselectivity was enhanced using ligands with sterically more demanding R₂-N-substituents, like n-propyl and particularly iso-propyl. However complex 6d bearing the bulky diphenylmethyl group was generally less selective than complex 6c. Changing the R₁ group from methyl to iso-propyl (6e, R₂ = n-Pr) or phenyl (6f, R₂ = n-Pr) resulted in lower ee values in asymmetric transfer hydrogenations of the ketones 8a–c. The obtained ee values indicate that the combination of a small R₁ group with a branched R₂-alkyl group at the ligand, lead to enhanced catalyst selectivity. While most of the catalysts preferably generated the (S)-alcohols, the hydrogenation of α-methylpropiophenone with catalyst 6f gave an excess of 21% (R)-1-phenyl-2-methylpropanol (entry 21, Table 1).

Similar yields and slightly lower enantiomeric excesses of the (S) product alcohols were obtained if a 65 : 35 exo/endo mixture of catalyst 6c was used instead of enantiomerically pure 6c (entries 9/10 and 17/18, Table 1). If the exo/endo mixture was applied, for example, to α-methylpropiophenone the ee value decreased from 55 to 49%. These results are indicating either a slightly different, but aligned stereoselectivity of both isomers or an opposite selectivity, associated with a lower activity of the endo isomer.

The most selective catalyst 6c was then applied to other ketones with long or branched alkyl chains and bulky phenyl substituents. Additionally some catalytic runs were carried out at lower temperatures (entries 1 and 5, Table 2) or with an alternative cocatalyst (entry 2, Table 2).

The highest enantiomeric excess of 58% of the (S)-alcohol was obtained for the substrate n-butyrophonone (entry 3, Table 2). The reduction of 2′,4′,6′-trimethylacetophenone (8h) bearing a very bulky phenylring with catalyst 6c gave a marginally lower ee value of 57% of the (R)-enantiotomer (entry 8, Table 2). Alkylphenylketones with sterically demanding alkylgroups like tert-butyl in 8e or isobutyl in 8f were hydrogenated to the corresponding alcohols with ee values of 54 and 28% (entries 4 and 6, Table 2). Alkylketones

**Scheme 3.** ATH of ketones.

**Table 1.** ATH of ketones catalyzed by 6a–f and 7

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>R₁/R₂</th>
<th>Conversion (%)</th>
<th>ee (%) (config.)</th>
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<td>6 (R)</td>
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<td>2</td>
<td>6b</td>
<td>Me/n-Pr</td>
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<tr>
<td>3</td>
<td>6c</td>
<td>Me/iso-Pr</td>
<td>&gt;99</td>
<td>11 (S)</td>
</tr>
<tr>
<td>4</td>
<td>6d</td>
<td>Me/CHPh₂</td>
<td>&gt;99</td>
<td>7 (S)</td>
</tr>
<tr>
<td>5</td>
<td>6d</td>
<td>Ph/n-Pr</td>
<td>&gt;99</td>
<td>7 (R)</td>
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<tr>
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<td>98</td>
<td>14 (S)</td>
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<tr>
<td>7</td>
<td>6a</td>
<td>Me/Me</td>
<td>&gt;99</td>
<td>20 (S)</td>
</tr>
<tr>
<td>8</td>
<td>6b</td>
<td>Me/n-Pr</td>
<td>&gt;99</td>
<td>12 (S)</td>
</tr>
<tr>
<td>9</td>
<td>6c</td>
<td>Me/iso-Pr</td>
<td>97</td>
<td>42 (S)</td>
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<tr>
<td>10</td>
<td>6c</td>
<td>Me/iso-Pr</td>
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<td>Me/CHPh₂</td>
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<td>12</td>
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<td>n-Pr/iso-Pr</td>
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<td>13</td>
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<td>17</td>
<td>6c</td>
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<td>&gt;99</td>
<td>55 (S)</td>
</tr>
<tr>
<td>18</td>
<td>6c</td>
<td>Me/iso-Pr</td>
<td>&gt;99</td>
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<td>22</td>
<td>7</td>
<td>Me/n-Pr</td>
<td>91</td>
<td>25 (S)</td>
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a Reaction conditions: 10 ml 2-propanol, 2.0 mmol ketone, temperature = 82 °C, time 15 h, ketone–catalyst–KOH = 1000 : 1:10, catalysts were applied in pure exo form, unless otherwise stated. b Conversion was determined by GC. c Measured by GC using chiral columns. d Determined by comparison of the sign of optical rotation to literature values. e Applied as 55 : 45 mixture of exo/endo isomers. f Applied as 65 : 35 mixture of exo/endo isomers.
Table 2. ATH of various ketones catalyzed by 6c

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ketone</th>
<th>Conversionb (%)</th>
<th>ee c (%) (configuration)d</th>
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<td>8b</td>
<td>92</td>
<td>42 (S)</td>
<td>920</td>
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<td>3</td>
<td>8d</td>
<td>82</td>
<td>58 (S)</td>
<td>820</td>
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<tr>
<td>4</td>
<td>8e</td>
<td>83</td>
<td>54 (S)</td>
<td>830</td>
</tr>
<tr>
<td>5a</td>
<td>8e</td>
<td>15</td>
<td>53 (S)</td>
<td>150</td>
</tr>
<tr>
<td>6</td>
<td>8f</td>
<td>&gt;99</td>
<td>28 (S)</td>
<td>1000</td>
</tr>
<tr>
<td>7</td>
<td>8g</td>
<td>92</td>
<td>30 (S)</td>
<td>920</td>
</tr>
<tr>
<td>8</td>
<td>8h</td>
<td>93</td>
<td>57 (R)</td>
<td>930</td>
</tr>
<tr>
<td>10</td>
<td>8i</td>
<td>46</td>
<td>21 (S)</td>
<td>460</td>
</tr>
</tbody>
</table>

a Reaction conditions: 10 ml 2-propanol, 2.0 mmol ketone, temperature = 82 °C, time 15 h, ketone–catalyst–KOH = 1000 : 1 : 10, unless otherwise stated, catalyst 6c was applied as pure exo isomer.
b Conversion was determined by GC. c Measured by GC using chiral columns. d Determined by comparison of the sign of optical rotation to literature values. e Reaction temperature 60 °C. f Base: t-BuOK.

Table 3. ATH of various ketones catalyzed by 6f

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ketone</th>
<th>Conversionb (%)</th>
<th>ee c (%) (configuration)d</th>
<th>TON</th>
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<td>1</td>
<td>8d</td>
<td>98</td>
<td>22 (S)</td>
<td>980</td>
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<tr>
<td>4</td>
<td>8h</td>
<td>82</td>
<td>68 (R)</td>
<td>820</td>
</tr>
<tr>
<td>5a</td>
<td>8h</td>
<td>79</td>
<td>64 (R)</td>
<td>790</td>
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<tr>
<td>6f</td>
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<td>75</td>
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<td>750</td>
</tr>
<tr>
<td>7</td>
<td>8i</td>
<td>97</td>
<td>31 (S)</td>
<td>970</td>
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</table>

a Reaction conditions: 10 ml 2-propanol, 2.0 mmol ketone, temperature = 82 °C, time 15 h, ketone–catalyst–KOH = 1000 : 1 : 10, unless otherwise stated, catalyst 6f was applied as pure exo isomer.
b Conversion was determined by GC. c Measured by GC using chiral columns. d Determined by comparison of the sign of optical rotation to literature values. e Base: K2CO3. f Base: Cs2CO3.

In conclusion we have synthesized a series of new chiral iridium(I)–bis(NHC) complexes. The versatile synthetic pathway makes it possible to vary the terminal N-substituents at both imidazole rings separately. In this way, the chiral environment of the iridium center can be formed specifically. Furthermore we described the synthesis of a mixed imidazolin-2-ylidene–benzimidazolin-2-ylidene chelating ligand and its iridium complex.

The obtained iridium(I) complexes were then used as catalysts for asymmetric transfer hydrogenations of prochiral ketones and showed high activities under the described reaction conditions. Lower yields and ee values were observed if the reaction temperature was decreased. To determine how the enantioselectivity is affected by the substrates and different combinations of terminal N-substituents at the imidazolin-2-ylidene units, various catalyst/ketone pairs have been tested in ATH. The highest enantioselectivities, within this work, of 58 and 68% ee were obtained by catalysts, bearing methyl-/iso-propyl and methyl-/phenyl-N-substituents. These results were obtained using alkylphenylketones with long alkyl chains or methylated phenyl rings as substrates. Currently efforts are in progress to improve the activity of the complexes for other catalytic reactions as well as the enantioselectivity.

Experimental

General Remarks

NMR spectra were recorded on a Bruker DRX-400 spectrometer, with CDCl3, CD3OD and D2O as solvents. Elemental analyses were carried out in a Vario EL analyzer. Electron impact (EI+) and Fast Atom Bombardment (FAB+) mass spectra were recorded on a Finnigan MAT, TSQ 70 instrument, using 3-nitrobenzyl alcohol as matrix. Electrospray mass spectra were recorded on a Bruker Daltonics APEX II FT-ICR instrument using CH3OH as solvent and nitrogen as drying and nebulizing gas. Melting points are uncorrected and were determined on a Mel-Temp Z15 apparatus. Chiral GC was performed on a Chrompack 438A with chiral columns from Macherey-Nagel (FS-Lipodex E, 50 mm, 0.25 mm diameter) and Chrompack (FS-Cyclodex beta-L/P, 60 mm, 0.25 mm diameter). Optical rotations of chiral alcohols were determined on a Knauer, Polar-M polarimeter. Imidazolebromide 1 was prepared from L-valinol (97% ee, Sigma-Aldrich) according to our previously reported procedure.[15] All other reagents are commercially available and were used as received.

Preparation of 2a

A mixture of 1 (495 mg, 2.28 mmol) and 1-methylimidazole (936 mg, 11.4 mmol) was stirred at 50 °C for 72 h. After cooling to ambient temperature, diethyl ether (20 ml) was added, while stirring to dissolve excess 1-methylimidazole. The ether was removed via syringe and the colorless, oily precipitate was washed...
two more times with diethyl ether and dried in vacuo. The oil was then dissolved in CHCl₃ (10 ml) and extracted in water (2 × 8 ml). After removal of the water under reduced pressure, the resulting solid was washed with diethyl ether (2 × 15 ml) and dried in vacuo, giving 2a as a hygroscopic, white solid. Yield: 556 mg (82%). MS (FAB): m/z 219 (100%). MS (HRESI+) calcld for C₁₅H₁₄N₄, 219.16042; found, 219.16042. ¹H NMR (CDCl₃, 400 MHz): δ 8.93 (s, 1H, NCH₃), 7.77 (s, 1H, NCH₃), 7.54 (t, JHH = 1.6 Hz, 1H, CH(CH₂)₂), 7.47 (brs, 1H, CH₃mid), 7.42 (t, JHH = 1.7 Hz, 1H, CH₃mid), 7.08 (brs, 1H, CH₃mid), 4.98–4.81 (m, 2H, NCH₂CH₃), 4.60 (qd, JHH = 3.4 Hz, 1H, CH₂CH₃), 3.90 (s, 3H, NCH₃), 2.35 [m, 1H, CH(CH₂)₂], 1.20 [d, JHH = 6.7 Hz, 3H, CH(CH₃)₃], 0.86 [d, JHH = 6.7 Hz, 3H, CH(CH₃)₃]. ¹³C NMR (CDCl₃, 100 MHz): δ 139.06, 138.40 (CH₃mid), 124.89, 124.99, 123.88, 119.21 (CH₃mid), 65.41 (CH₂CH₃), 52.93 (NCH₂CH₃), 36.83 (NCH₃), 32.79 [CH(CH₃)₂], 20.03, 19.43 [CH(CH₃)₂].

Preparation of 2b

The same procedure as for 2a was carried out by stirring imidazole-bromide 1 (230 mg, 1.1 mmol) and 1-iso-propylimidazole (473 mg, 4.5 mmol) at 60 °C for 48 h. Compound 2b was obtained as a hygroscopic white solid. Yield: 267 mg (74%). MS (FAB): 247 (100%). MS (HRESI+): calcld for C₁₄H₂₃N₄, 247.19172; found, 247.19171. ¹H NMR (CDCl₃, 400 MHz): δ 9.06 (s, 1H, NCHN(CH₂)₃), 7.75 (bs, 2H, NCH₃), 7.57 (s, 1H, CH₃mid), 7.51 (bs, 1H, CH₃mid), 7.07 (s, 1H, CH₃mid), 4.95–4.80 (m, 2H, NCH₂CH₃), 4.64–4.55 (m, 1H, CH₂CH₃), 4.38 [m, 1H, NCH(CH₂)₃], 2.44–2.33 [m, 1H, CH(CH₂)₂], 1.51 [d, JHH = 6.7 Hz, 6H, NCH₂CH₃], 1.21 [d, JHH = 6.7 Hz, 3H, CH(CH₃)₂], 0.87 [d, JHH = 6.7 Hz, 3H, CH₃(CH₂)₂]. ¹³C NMR (CDCl₃, 100 MHz): δ 136.38 [NCHNC(CH₂)₃], 129.10 (NCH₃), 123.98, 122.14, 121.97, 119.40 (CH₃mid), 65.88 (CH₂CH₃), 54.78 [NCH₂CH₃], 52.96 (NCH₂CH₃), 32.67 [CH(CH₂)₃], 23.14, 22.91 [NCH₃(CH₂)₃], 19.85, 19.50 [CH(CH₃)₂].

Preparation of 2c

The same procedure as for 2a was used by stirring imidazole-bromide 1 (173 mg, 0.8 mmol) and 1-phenylimidazole (473 mg, 4.5 mmol) at 65 °C for 72 h. The title compound 2c was obtained as hygroscopic white solid. Yield: 198 mg (69%). MS (FAB): 281 (100%).MS (HRESI+): calcld for C₁₆H₂₄N₄, 281.17607; found, 281.17630. ¹H NMR (CDCl₃, 400 MHz): δ 8.91 (s, 1H, NCHNC(Phenyl)), 7.72 (s, 1H, NCH₃), 7.52 (s, 1H, CH₃mid), 7.48 (m, 4H, C₆H₅CH₃), 7.36 (m, 6H, C₆H₅CH₃), 7.12 (br s, 1H, CH₃mid), 4.96–4.80 (m, 2H, NCH₂CH₃), 4.44 (m, 1H, NCH₂CH₃), 2.23 [m, 1H, CH(CH₂)₂], 1.09 [d, JHH = 6.6 Hz, 3H, CH₃(CH₂)₂], 0.74 [d, JHH = 6.6 Hz, 3H, CH₃(CH₂)₂]. ¹³C NMR (CDCl₃, 100 MHz): δ 136.91 (NCHNC(Phenyl), 136.05 (NPhenyl), 131.60 (C₆H₅CH₃), 128.99 (NCH₃), 128.96, 124.75 (CH₃mid), 123.36 (CH₃CH₃), 122.95 (CH₃mid), 122.37 (C₆H₅CH₃), 119.23 (CH₃mid), 65.44 (CH₂CH₃), 53.46 (NCH₂CH₃), 32.81 [CH(CH₃)₂], 19.95, 19.56 [CH₃(CH₂)₂].

Preparation of 3a

To a solution of 2a (132 mg, 0.44 mmol) in dichloromethane (3 ml), methyliodide (0.5 ml) was added in one portion. The clear solution was then stirred for 18 h at ambient temperature. After all volatiles were removed under reduced pressure, the resulting white solid was redissolved in dichloromethane and added dropwise to diethylether while stirring. The resulting white precipitate was washed several times with ether and dried in vacuo to give the title compound 3a as very hygroscopic, white powder. Yield: 172 mg (89%). MS (FAB): m/z 313 [M – Br]⁺ (40%). ¹H NMR (CDCl₃, 400 MHz): δ 9.17, 9.03 (s, 2H, NCH₃N), 7.83, 7.61 (s, 2H, C₆H₅CH₃), 7.48 (m, 2H, C₆H₅CH₃), 4.98–4.87 (m, 3H, 3H, CH₃CH₂N), 3.89, 3.85 (s, 6H, NCH₃), 2.39–2.31 (m, 1H, CH(CH₂)₂), 1.12 [d, JHH = 6.7 Hz, 3H, CH₃(CH₂)₂], 0.83 [d, JHH = 6.7 Hz, 3H, CH₃(CH₂)₂], 1.3(C¹H) NMR (CDCl₃, 100 MHz): δ 138.73 (NCH₃), 138.18 (NCH₃), 126.33, 125.71, 123.77, 122.51 (CH₃mid), 67.86 (CH₂CH₃), 51.89 (NCH₂CH₃), 37.71, 37.52 (NCH₃), 32.44 [CH(CH₂)₂], 19.77, 19.04 [CH₃(CH₂)₂].

Preparation of 3b

Hygroscopic white solid; Yield: 200 mg (86%) MS (FAB), m/z 341 (40%). ¹H NMR (CDCl₃, 400 MHz): δ 9.32 (s, 1H, NCH₃), 9.08 (s, 1H, NCH₃), 7.91 (d, JHH = 1.8 Hz, 1H, CH₃mid), 7.75 (d, JHH = 1.7 Hz, 1H, CH₃mid), 7.52 (d, JHH = 1.7 Hz, 1H, CH₃mid), 7.50 (d, JHH = 1.8 Hz, 1H, CH₃mid), 5.00–4.85 (m, 3H, CH₃CH₂N), 4.18 (t, JHH = 7.1 Hz, 2H, NCH₂CH₃), 3.88 (s, 3H, NCH₃), 2.38 [m, 1H, CH(CH₂)₂], 1.87 (sext, JHH = 3.6 Hz, 2H, NCH₂CH₃), 1.17 [d, JHH = 6.7 Hz, 3H, CH₃CH₂N]. ¹³C NMR (CDCl₃, 100 MHz): δ 138.91, 137.82 (NCH₃), 125.76, 125.29, 123.91, 122.70 (CH₃mid), 68.27 (CH₂CH₃), 52.96 (NCH₂CH₃), 51.96 (NCH₂CH₃), 37.19 (NCH₃), 32.53 [CH(CH₂)₂], 24.45 (NCH₂CH₃), 19.75, 19.11 [CH₃(CH₂)₂], 11.00 (CH₃CH₂).
Preparation of 3e

Following the procedure described for 3d, reaction between 2b (165 mg, 0.50 mmol) and 1-bromopropane (0.4 ml) gave the title compound 3e as hygroscopic white solid. Yield: 187 mg (84%).

Preparation of 3f

Following the procedure described for 3d, reaction between 2c (120 mg, 0.34 mmol) and 1-bromopropane (0.3 ml) gave the title compound 3f as hygroscopic white solid. Yield: 147 mg (91%).

Preparation of 4

Following the procedure described for 2a, reaction between 1 (120 mg, 0.34 mmol) and 1-methylbenzimidazol-2-yl (462 mg, 3.5 mmol), the title compound 4 was obtained as a hygroscopic white solid. Yield: 195 mg (52%).

Complex Synthesis: General Procedure

Silver(I) oxide (0.70 mmol) was added to a dichloromethane (15 ml) solution of bis imidazolium salts (0.35 mmol) and stirred in the dark at room temperature for 2.5 h under argon. Then [Ir(COD)Cl2] (0.17 mmol) was added to the gray suspension in one portion, under formation of a white precipitate. To complete the reaction, the mixture was stirred in the dark at room temperature for 14 h. To remove insoluble silver salts, the suspension was filtered through celite and the resulting orange-red solution was concentrated under reduced pressure. The crude solid was then purified by gradient column chromatography (SiO2, first CH2Cl2; CH2Cl2- acetone 2:1; then CH2Cl2- acetone 1:1 with 2 equiv. KPF6). Analytically pure material was obtained by a second flash column chromatography, with CH2Cl2- acetone 4:1 as eluant. The title compounds were obtained as orange-red solids.

Preparation of 6a

Complex 6a was obtained as 55:45 mixture of exo and endo stereoisomers. Yield: 120 mg (52%). MS (FAB): m/z 269 (M-Br)+ (70%). 1H NMR (CD2OD, 400 MHz): δ 9.73, 9.35 (s, 2 H, NCH=CH); 7.67 (m, 2 H, O=CH); 7.59–7.48 (m, 3 H, C6H5); 5.08–4.92 (m, 3 H, NCH=NCH2); 4.13 (t, 13JH=H = 7.1 Hz, 2 H, NCH2CH2); 2.38 (m, 1 H, CHCH2(N)); 1.79 (m, 2 H, NCH2CH2); 1.16 [d, 13JH=H = 6.6 Hz, 3 H, CHCH2(N)]; 1.04 (m, 2 H, CH2CH2(N)); 0.84 (d, 3H, 3JH=H = 6.6 Hz, 3 H, CHCH2(N)); 0.76 [t, 3JH=H = 7.4 Hz, 3 H, CH2CH3]; 13C{1H} NMR (CD2OD, 100 MHz): δ 137.78, 137.33 (NCHN), 131.56 (C6H5), 125.13, 124.70, 123.52 (NOCH, CH2, C6H5), 122.05, 121.55 (NOCH2, CH2); 67.94 (CH2CH3), 52.80 (NCH2), 52.52 (NCH2CH2), 24.30 (CH2CH3), 19.64, 18.97 [CH2CH3], 10.85 (CH2CH3).

Preparation of 5

Following the procedure described for 3d, reaction between 4 (95 mg, 0.27 mmol) and 1-bromopropane (0.5 ml) gave the title compound 5 as a hygroscopic white solid. Yield: 107 mg (85%).

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Chiral iridium(I) bis(NHC) complexes

24.46 (NCH₂CH₂), 20.82, 19.88 [CH(CH₂)₃], 10.58 (CH₂CH₃). Anal. calcd for C₂₅H₄₀F₆IrN₄P (783.79), C, 40.87; H, 5.45; N, 7.63; found, C, 40.87; H, 5.49; N, 7.63.

**Compound 6c**

Diastereomerically pure (100% exo), crystalline material was obtained by layering a THF–CH₂Cl₂ (1:1) solution of 6c with cyclohexane. Yield: 143 mg (56%).

A 65:35 exo/endo mixture of complex 6c was obtained by heating the transmetallation reaction in acetonitrile to 80 °C for 5 h. Then the general purification procedure was used. M.p.: 151–152 °C dec.; MS (HRESI+): calcd for C₂₅H₃₆F₆IrN₄P (829.88), C, 47.92; H, 4.86; N, 7.63; found, C, 47.87; H, 4.88; N, 7.65; C, 48.14; H, 4.73; N, 6.90.

**Compound 6d**

Diastereomerically pure (100% exo), crystalline material was obtained by layering a THF–CH₂Cl₂ (1:1) solution of 6d with cyclohexane. Yield: 43 mg (66%). M.p.: 169–171 °C (Zers.).

**Compound 6f**

Yield: 105 mg (64%). M.p.: 146–147 °C. MS (HRESI+): calcd for C₂₈H₃₈F₆IrN₄P (767.81), C, 43.80; H, 4.99; N, 7.30; found, C, 44.08; H, 4.97; N, 7.39.

**Compound 6g**

Yield: 49 mg (38%). M.p.: 157–159 °C. MS (HRESI+): calcd for C₂₉H₃₄IrN₄ (699.2696), 699.2696. M.p.: 185 °C. MS (HRESI+): calcd for C₂₉H₃₄IrN₄ (699.2696), 699.2696. 1H NMR (CDCl₃, 400 MHz): δ 7.71 (m, 2H, CH₂), 7.43 (m, 3H, CH₃), 7.14 (d, J₃H₃ = 2.1 Hz, 1H, CH₃), 7.12 (d, J₃H₃ = 2.1 Hz, 1H, CH₃), 6.57 (d, J₃H₃ = 2.1 Hz, 1H, CH₃), 6.92 (d, J₃H₃ = 2.1 Hz, 1H, CH₃), 6.65 (td, J₃H₃ = 4.0 Hz, 1H, CH₃), 4.48–4.29 (m, 2H, CH₂CH₂N), 4.24 (m, 1H, CH₂CO), 4.13–3.93 (m, 3H, NCH₂CH₂CO), 2.80 (m, 1H, CH₂CO), 2.41 (m, 1H, CH₂CO), 2.06–1.91 (m, 4H, CH₂CO), 1.78–1.67 (m, 4H, CH₂CO), 1.19 (d, J₃H₃ = 6.5 Hz, 1H, CH₃), 1.01 (d, J₃H₃ = 6.4 Hz, 3H, CH₂), 1.05 (d, J₃H₃ = 6.4 Hz, 3H, CH₂), 1.3 (d, J₃H₃ = 6.4 Hz, 3H, CH₂). 13C NMR (CDCl₃, 100 MHz): δ 171.14, 171.14, 140.24 (CH), 132.76, 132.76, 129.27, 129.27, 128.81, 128.81, 127.76, 127.76, 126.73, 126.73, 120.27, 120.27, 115.98, 115.98, 114.88, 114.88, 111.71 (CH₃), 78.00, 78.00, 73.22, 73.22, 73.01 (CH₂CO), 65.67 (NCH₂CH₂CO), 63.73 (CH₂CH₂N), 51.60 (CH₂CH₃), 37.09 (NCH₂CH₃), 31.48, 31.38, 29.41, 29.07 (CH₂CO), 28.19 [CH(CH₂)₃], 19.93, 18.84 [CH(CH₂)₃]. Anal. calcd for C₃₀H₃₀F₆IrN₄P (787.88), C, 47.76; H, 4.86; N, 6.75; found, C, 47.87; H, 4.86; N, 6.75.

**General Procedure for Transfer Hydrogenations**

A solution of the catalyst (0.002 mmol), KOH (0.02 mmol) and the ketone (2.0 mmol) in 2-propanol (10 ml) was heated under
argon in a Schlenktube at 82 °C for 15 h. After cooling to ambient temperature, water was added to the reaction mixture and extracted with ether (2 × 10 ml). The organic phase was dried over MgSO4 and filtered through celite. After removing all volatiles under reduced pressure, the product alcohols were obtained as oils. Turnovers and enantiomeric excesses were determined by GC with chiral columns (see General Remarks). Absolute configurations of the product alcohols were determined by comparing the retention times of the products with enantiomerically pure samples (1-phenylethanol, 1-phenylpropanol) or by comparing the sense of optical rotations of the product samples with literature values.

References