<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Stereospecific synthesis and catalytic activity of L-histidylidene metal complexes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors(s)</strong></td>
<td>Monney, Angèle; Alberico, Elisabetta; Ortin, Yannick; Müller-Bunz, Helge; Gladiali, Serafino; Albrecht, Martin</td>
</tr>
<tr>
<td><strong>Publication date</strong></td>
<td>2012-05</td>
</tr>
<tr>
<td><strong>Publication information</strong></td>
<td>Dalton Transactions, 41 (29): 8813-8821</td>
</tr>
<tr>
<td><strong>Publisher</strong></td>
<td>Royal Society of Chemistry</td>
</tr>
<tr>
<td><strong>Item record/more information</strong></td>
<td><a href="http://hdl.handle.net/10197/6598">http://hdl.handle.net/10197/6598</a></td>
</tr>
<tr>
<td><strong>Publisher's version (DOI)</strong></td>
<td>10.1039/c2dt30799e</td>
</tr>
</tbody>
</table>
Stereospecific Synthesis and Catalytic Activity of L–Histidylidene Metal Complexes †‡

Angèle Monney, Elisabetta Alberico, Yannick Ortin, Helge Müller-Bunz, Serafino Gladiali and Martin Albrecht

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

We report on the synthesis, metal coordination, and catalytic impact of histidylidene, a histidine-derived N-heterocyclic carbene ligand. The histidinium salt 3, comprising methyl substituents at both heterocyclic nitrogens and protected at the C- and N-terminus of the amino acid, was rhodated and iridated by a transmetalation protocol using Ag₂O. Ambient temperature and short reaction times were pivotal for full retention of configuration at the α carbon. The stereospecificity of the reaction was conveniently probed by 31P NMR spectroscopy after transmetalation with rhodium(I) and coordination of enantiopure (S)-Ph-bipine. The histidylidene rhodium complexes are highly efficient catalysts for the hydrosilylation of ketones under mild reaction conditions. For the cationic complexes [Rh(cod)(histidylidene)(phosphine)]+, lowering the temperature shifted the rate-limiting step of the catalytic reaction to an earlier stage that is not enantioselective. Hence the asymmetric induction—which is governed by the chiral phosphine—did not improve at low temperature.

Introduction

Due to their abundance and chirality, biomolecules such as enzymes, carbohydrates, and nucleic acids provide a very attractive pool of ligand precursors for the synthesis of organometallic complexes. Slight modifications are generally required to introduce a metal-carbon bond and to access this area of bioorganometallic chemistry. Peptides are a particularly versatile class of precursors, since the chiral amino acid building blocks are readily available. In addition, the different side chain functionalities allow a variety of modifications and linkages to classical organometallic ligands to be introduced. Because of the imidazole side chain, histidine—ubiquitous as ligating amino acid in the active site of metalloenzymes—constitutes a particularly intriguing ligand precursor for bioorganometallic complexes, especially when considering the high and steadily growing popularity of imidazolium-derived N-heterocyclic carbenes (NHCs) as ligands for transition metals. Alkylation of both nitrogens of the imidazole side chain of naturally occurring L-histidine provides straightforward access to the synthesis of bio-inspired N-heterocyclic carbenes and to peptide-derived NHC complexes (Scheme 1). 9,10

Histidine alkylation has previously been reported to give functionalised ionic liquids.11 We have used a non-stereospecific protocol to prepare histidinium salts and the corresponding histidyldiene ruthenium complexes.12,13 Through a careful choice of protecting groups14 and metatllation conditions, we have now developed a protocol for the preparation of chiral L-histidylidene complexes. Here we report the stereospecific synthesis of rhodium and iridium complexes and their catalytic activity in the hydrosilylation of ketones. These investigations pertain to recent work directed towards using NHC ligands as mimics of histidine in metalloenzyme active sites.15

Results and discussion

Synthesis of the ligand precursor

The N₅-methylated histidine methyl ester 2 with a Boc-protected amino function was prepared according to a recently published procedure.16 A key step in this synthesis is the formation of the bicyclic urea 1, which is obtained in a solvent-free reaction of the histidine methyl ester and 1,1'-carbonyldiimidazole at 80 °C with a flow of nitrogen using a mechanical stirrer (Scheme 2). The neat reaction was equally successful in a ball mill without a nitrogen flow or external heating. Slightly heating of 2 and Mel in MeCN induced quaternisation at N₅ and afforded after column chromatography the histidinium salt 3 as a hygroscopic white solid (Scheme 2). Formation of an imidazolium unit was...
indicated by the diagnostic downfield shift of the \( \text{C}_2\text{H} \) and \( \text{C}_3\text{H} \) resonances in the \(^1\text{H}\) NMR spectrum from \( \delta_{\text{H}} = 6.64 \) to 7.44 and from 7.32 to 8.96 ppm respectively.

![Scheme 2](image)

**Scheme 2** Synthesis of histidylidene iridium and rhodium complexes.

All compounds 1–3 were optically active at the sodium D-line and the enantiomeric purity of 2 was previously assessed by chiral HPLC.\(^{11}\) We applied an amino acid coupling protocol to confirm the full retention of chirality throughout the synthesis. Therefore, the histidinium salt 3 was deprotected at the N-terminus using methanolic HCl and subsequently coupled with Boc-L-methionine using HATU as coupling agent.\(^{12}\) Only one set of signals was recorded by \(^1\text{H}\) NMR spectroscopy, consistent with the presence of one diastereomer. In comparison, the corresponding dipeptide revealed two sets of resonances in the \(^1\text{H}\) NMR spectrum when 3 was synthesised following a non-stereospecific protocol.\(^{13}\) These sets are clearly distinguishable by two resonances around \( \delta_{\text{H}} = 7.2 \) and 4.8 ppm, attributed to the \( \text{C}_\beta \)- and \( \text{C}_\alpha\)-bound protons, respectively. Integration of these signals suggests a diastereomeric excess of about 25%.

**Synthesis of the metal complexes**

Metallation of the optically pure histidinium salt 3 was performed using a standard transmetallation procedure,\(^{17}\) involving the *in situ* formation of a silver carbene intermediate by refluxing 3 with Ag\(\text{O}\) in \( \text{CH}_2\text{Cl}_2 \) in the dark. Subsequent transmetallation with Ir(\(\text{Cp}^*\))Cl\(_2\) or [Rh(\(\text{cod}\))Cl]\(_2\) afforded the corresponding histidylidene iridium(III) and rhodium(I) complexes 4 and 5 in good yields (Scheme 2). Both complexes are air- and moisture-stable as solids and were purified by flash chromatography on SiO\(_2\). Formation of the complexes was evidenced by the disappearance of the signal for the \( \text{C}_\alpha \)-bound proton in the \(^1\text{H}\) NMR spectrum and by the downfield shift of the carbene signal in the \(^{13}\text{C}\) NMR spectrum to \( \delta_{\text{C}} = 155.2 \) and 183.3 ppm for 4 and 5, respectively.\(^{18,19}\) In the case of 5, the latter resonance appeared as a doublet due to coupling with \(^{103}\text{Rh}(I)\) (\( J_{\text{RhC}} = 51 \) Hz). Two full sets of signals were observed for complex 5 both by \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectroscopy, indicating the presence of two rotamers in approximate 0.8:1 ratio as a consequence of hindered rotation about the Rh–\( \text{C}_\alpha \) bond.\(^{20,21}\) For example, four distinct singlets appeared in the 3.9–4.0 ppm range for the \( \text{N} \)-bound methyl protons. In the \(^{13}\text{C}\) NMR spectrum, the largest shift was observed for the stereogenic \( \text{C}_\alpha \) nucleus, which resonates in one rotamer at 52.6 ppm and at 52.1 ppm in the other rotamer. No coalescence was observed upon moderate heating to 50 °C (CDCl\(_3\) solution).

![Fig. 1](image)

**Fig. 1** ORTEP plot of complex 4 (50 % probability, hydrogen atoms omitted for clarity). Selected bond lengths (Å) and angles (°): Ir–Cl 2.041(3), Ir–Cl1 2.152 (3), Ir–Cl2 2.146 (3), Ir–C\(\text{ cen}\) 1.809(3), C11–Ir–C11 90.21(8), C11–Ir–Cl2 94.36(8), C11–Ir–Cl2 85.30(2).

A single crystal of the iridium complex 4 was analysed by X-ray diffraction. The molecular structure (Fig. 1) features an iridium centre in a piano-stool-type arrangement. The Ir–\( \text{C}_{\text{carbene}} \) bond length is 2.041(3) Å and hence within the typical range observed for NHC iridium(III) species.\(^{19,20}\) The complex crystallised in the triclinic non-centrosymmetric space group \( P\overline{1} \), implying the co-crystallisation of both the \( L\)- and \( D\)-histidylidene complexes as a racemate. In agreement with racemisation, amorphous samples of the iridium and the rhodium complex did not display any optical rotation at the sodium D-line. Since the ligand precursor 3 was enantiopure (see above), racemisation at \( \text{C}_\alpha \) must have occurred under the reaction conditions used for (trans)metallation. Most likely, proton exchange at the \( \alpha\)-carbon of the amino acid is induced by the strong basicity of Ag\(\text{O}\) or of intermediate hydroxides, leading to partial or full loss of enantiomeric purity. The lability of acidic protons e.g. \( \alpha \) to the heterocyclic nitrogen, in the presence of a base has been documented.\(^{21}\) This lability is obviously closely associated with the racemisation of various chiral NHC ligand precursors upon metallation via base-mediated proton abstraction (free carbene route) or via transmetallation involving Ag\(\text{O}\),\(^{22}\) and it may also account for the low performance of many NHC complexes in enantioselective catalysis.\(^{23}\) Such racemisation processes also have direct implications for catalytic reactions involving strong bases, such as KOH-assisted transfer hydrogenation.\(^{24}\)

Due to the observed racemisation, we investigated the transmetallation reaction in more detail. For this purpose, the chiral phosphine (S)-Ph-binepine\(^{25}\) was coordinated to the histidylidene-bound rhodium centre, thus providing a diagnostic spectroscopic probe for the presence of diastereoisomers due to racemisation at the \( \text{C}_\alpha \) centre. Hence, treatment of complex 5 with (S)-Ph-binepine in the presence of KPF\(_6\) afforded the cationic complex 6 (Scheme 3). Displacement of cod under a CO atmosphere yielded the corresponding di(carbene) complex 7. Both complexes rac-6 and rac-7 feature a seemingly similar resonance pattern in the \(^{13}\text{C}\) NMR spectrum (Fig. 2), consisting of a low-field doublet and two partially overlapping doublets at higher field. Four distinct resonances would be expected in rac-6 and rac-7 due to the presence of two diastereoisomers (originating from \( L\)- and \( D\)-histidylidene), both existing as two rotamers in almost equimolar ratio (cf. NMR discussion of 5).

Integration of the signals of rac-6 revealed a 1:1 ratio between the low-field and the two high-field signals at \( \delta_p = 39.95 \) and 39.73
silver that would release bicarbonate as a significantly less basic potential basicity of the intermediate AgOH released in reactions 31 carbene intermediate were then evaluated by using the diagnostic in Table 1 of the signal sets indicates diasteromERICally pure corresponding to the rotamer ratio observed for c) the measure for the stereospecificity of the (trans)metallation reaction. The two rotamers of L-7 thus each display a doublet (δ 42.03 and 42.08 ppm; J_{\text{HH}} 123 Hz), while the resonance for D-7 appears as a single doublet at lower field, δ 42.47 (J_{\text{HH}} 122 Hz; rotamers unresolved). Hence, the carbonyl complex 7 provides a direct probe for the Cα configuration and thus offers an indirect measure for the stereospecificity of the (trans)metallation reaction.

**Scheme 3 Synthesis of complexes 6 and 7.**

![Scheme 3 Synthesis of complexes 6 and 7.](image)

**Table 1 Impact of metallation conditions on the configurational stability at Cα.**

<table>
<thead>
<tr>
<th>entry</th>
<th>silver salt</th>
<th>molequiv.</th>
<th>solvent</th>
<th>temperature</th>
<th>time (h)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ag₂O</td>
<td>0.7</td>
<td>CH₂Cl₂</td>
<td>reflux</td>
<td>16</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>Ag₂CO₃</td>
<td>0.7</td>
<td>CH₂Cl₂</td>
<td>reflux</td>
<td>16</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>Ag₂O</td>
<td>0.7</td>
<td>MeOH</td>
<td>50 °C</td>
<td>13</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>Ag₂CO₃</td>
<td>0.7</td>
<td>MeOH</td>
<td>50 °C</td>
<td>13</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>Ag₂O</td>
<td>0.5</td>
<td>CH₂Cl₂</td>
<td>20 °C</td>
<td>1</td>
<td>96%</td>
</tr>
<tr>
<td>6</td>
<td>Ag₂O</td>
<td>1.1</td>
<td>CH₂Cl₂</td>
<td>20 °C</td>
<td>3</td>
<td>0%</td>
</tr>
<tr>
<td>7</td>
<td>Ag₂O</td>
<td>0.5</td>
<td>CH₂Cl₂</td>
<td>20 °C</td>
<td>21</td>
<td>74%</td>
</tr>
</tbody>
</table>

*ee determined by 31P NMR spectroscopy from the diastereomERIC excess in 7.

**Fig. 2 Relevant section of the 31P NMR spectrum of a) rac-6 and b) rac-7; c) the 31P NMR spectrum of L-6 displays only two doublets in 0.8:1 ratio, corresponding to the rotamer ratio observed for 5; d) disappearance of one of the signal sets indicates diasteromERICally pure L-7.**

Alternative rhodation procedures met little success. Reaction of the enantiopure histidinium salt 3 with in situ prepared [Rh(cod)(OEt)]₂ yielded, after ligand exchange, the complex 7 as a 1:1 diastereomERIC mixture. Metallation of 3 with [Rh(cod)Cl]₂ in the presence of a mild base such as NaOAc, NEt₃ or Cs₂CO₃ failed in our hands, as did attempts to thermally induce cleavage of the in situ formed CHCl₃ adduct. Catalytic hydrosilylation

The histidylidene rhodium complexes 5 and 6 were tested as catalyst precursors for the asymmetric hydrosilylation of ketones. Their performance was compared with the analogous NHC rhodium complexes 8 and 9 which lack the amino acid backbone. Para-fluorinated acetophenone was chosen since its consumption as well as product formation can be readily monitored by 31P NMR spectroscopy without the need for any work-up. In a typical reaction, 4'-fluoracetophenone 1 and diphenylsilane were stirred...
in the presence of 1 mol% rhodium catalyst, producing the silyl ether II together with minor quantities of the silylated enol ether III (Table 2).31,32 Release of gaseous H₂ was generally observed.

Table 2 Hydroisilylation of fluoroacetophenone with rhodium complexes

<table>
<thead>
<tr>
<th>entry</th>
<th>[Rh]</th>
<th>conversion (selectivity)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5 min</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>77 (90.0)</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>57 (98.7)</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>89 (99.4)</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>82 (98.7)</td>
</tr>
</tbody>
</table>

General conditions: ketone (1 mmol), silane (2 mmol), catalyst (10 µmol, 1 mol%) in CD₂Cl₂ (1 mL) at rt.

Conversion (selectivity towards II in parentheses) determined by ³¹H and ¹²C NMR spectroscopy.

With all four catalysts high conversions were accomplished within 5 minutes (Table 2).§ This performance corresponds to a turnover frequency at 50% conversion (TOF₅₀) around 1000 h⁻¹ and places these complexes amongst the most active NHC-based hydrosilylation catalysts known to date.25e,27 The amount of silylenolether (III) formed during the reaction was consistently lower in runs catalysed by the cationic complexes 6 or 9 (entries 2, 4), than in reactions with the neutral complexes 5 and 8 (entries 1, 3). This higher selectivity is in agreement with recent mechanistic studies which propose the bonding of the substrate ketone to a silylene-rhodium dihydride species as a critical step.32 According to such a model, keto-enol tautomerisation and ensuing formation of the silylenolether side product strongly depends on the Lewis acidity of the silicon atom and thus indirectly on the electronic properties of the rhodium centre. Electron-rich neutral rhodium centres as in 5 and 8 increase the electron density at the silylene and hence facilitate substrate bonding in its tautomeric enol form. In contrast, the cationic nature of the rhodium centre in 6 and 9 enhances the Lewis acidity of the silicon nucleus and thus favours substrate bonding in the keto form, reflected in the almost exclusive formation of II. It is interesting to note that the product selectivity eroded at the later stages of the reaction when using the neutral complexes 5 and 8. This lower selectivity may be compensated for to some degree by extending the reaction time beyond full conversion. For example, the product selectivity obtained with the histidyldiene complex 5 raised to 92.7% after 5 h, presumably due to slow tautomerisation of the enol ether.

Lowering the catalyst loading to 0.1 mol% decelerated the reaction and allowed the activity of the different complexes to be evaluated (Fig. 4). The cationic complexes 6 and 9 displayed 3-5 times higher initial activity than their corresponding neutral complexes 5 and 8, respectively. After 30 min, approximately 60% conversion was reached with the cationic species, corresponding to an estimated turnover frequency TOF₅₀ = 1300 h⁻¹. This value is closely related to the TOF₅₀ deduced at higher catalyst loading and suggests a molecularly based process. The phosphine-free neutral complexes required substantially longer reaction times to reach 50% conversion (ca. 2 h), corresponding to a TOF₅₀ around 250 h⁻¹ (for 5) and even less for 8. With all complexes, the product selectivity was significantly lower, yet again higher when the cationic analogues 6 and 9 were used (around 80%) than with the neutral complexes (ca. 60%). Of note, both 6 and 9 displayed identical activity within errors, indicating that the amino acid backbone of the histidyldiene ligand does not have any substantial influence on the catalytic performance under these conditions.

Experiments performed at low temperature revealed a different behaviour. In contrast to the catalytic runs at room temperature, conversions at –18 °C were substantially slower with the cationic complexes 6 and 9 than with their corresponding neutral analogues 5 and 8 (Fig. 5). This change of relative activity may be a consequence of a different rate-limiting step in the cationic complexes. Dissociation of a weakly bound ligand, for example, may become increasingly difficult at low temperature, in particular with electron-deficient metal centres.34 Possibly,
catalyst pre-activation may thus be the rate-determining process in catalytic hydrosilylation using 6 or 9.

At these low temperatures, the histidylidene ligand induced consistently lower activity than the simple imidazolylidene homologue, both with the cationic and the neutral catalyst precursors. This result corroborates previous observations with related ruthenium complexes, which demonstrated a direct impact of the remote amino acid functionality on the properties of the metal centre. It is interesting to note that a decreased catalyst loading had a much stronger impact on the performance of the neutral complex 5 than on the cationic phosphine carbene complex 6, while a decrease in reaction temperature had an inverse effect and reduced the activity of 6 more substantially than that of 5. Irrespective of the catalyst precursor, however, the product selectivity was considerably higher in hydrosilylation reactions performed at −18 °C and only traces of silylenoether were detected (selectivity > 99%).

Table 3 Enantioselectivity of hydrosilylation with complexes 5, 6, and 9

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst precursor</th>
<th>temperature (°C)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>rac-6</td>
<td>rt</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>rt</td>
<td>26 (S)</td>
</tr>
<tr>
<td>3</td>
<td>L-5</td>
<td>−18</td>
<td>31 (S)</td>
</tr>
<tr>
<td>4</td>
<td>rac-6</td>
<td>−18</td>
<td>34 (S)</td>
</tr>
<tr>
<td>5</td>
<td>L-5</td>
<td>−18</td>
<td>37 (S)</td>
</tr>
</tbody>
</table>

* See Table 2 for general conditions; ee determined by chiral HPLC after hydrosylation of the silyl ether II with methanolic TFA.

Since complexes L-5, rac-6 and 9 are comprised of at least one chiral ligand, the potential for asymmetric hydrosilylation was investigated. To this end, the formed silyl ether II was hydrolysed with methanolic TFA and the corresponding alcohol was analysed by chiral HPLC (Table 3). As expected from the remote position of the stereocentre, the histidylidene ligand did not induce any enantioselectivity, neither at room temperature nor at −18 °C (entries 1, 4). In contrast, complexes 6 and 9 containing (S)-Ph-binap as an enantipure phosphine ligand generated a moderate 30% enantiomeric excess (ee) in the product alcohol (entries 2, 3). The enantioselectivity did not improve significantly when lowering the temperature to −18 °C (entries 5, 6). The independence of the ee on temperature is in agreement with a rate-limiting step that is stereoselectively not relevant. This result corroborates the conclusions from NMR analyses, which suggest a shift of the rate-limiting step to an early stage upon lowering the temperature (see above).

Conclusions

We have developed a synthetic protocol towards chiral histidylidene iridium and rhodium complexes starting from L-histidine. The full retention of configuration at the stereogenic amino acid carbon is strongly dependent on the conditions used for the mettallation, in particular for the instalment of the silver(I) centre for subsequent transmetallation. Coordination of a chiral phosphine has double advantage, firstly in serving as a diagnostic and straightforward probe for the stereospecific course of the mettallation, and secondly as stereo-discriminating ligand in the asymmetric hydrosilylation of ketones catalysed by the histidylidene rhodium complexes. Although the chiral amino acid functionality of the histidylidene ligand did not induce any enantiomeric excess, vast opportunities emerge from modification of the complex by classic concepts of peptide synthesis to induce, e.g., chelation. Moreover, the versatility of the transmetallation route will also allow transition metals of direct biological relevance to be coordinated to the histidylidene ligand.

Experimental section

We thank S. L. James (Queen’s University Belfast) and F. O’Meara (University College Dublin) for technical assistance. The authors gratefully acknowledge financial support from the Swiss National Science Foundation and the European Research Council.

Acknowledgment

We thank S. L. James (Queen’s University Belfast) and F. O’Meara (University College Dublin) for technical assistance. The authors gratefully acknowledge financial support from the Swiss National Science Foundation and the European Research Council.

Notes and references

1 School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland. Fax: +353-17162501; Tel: +353-17162504; E-mail: martin.albrecht@acd.ie

2 Istituto di Chimica Biomolecolare, CNR, tr. La Crucca n. 3, 07040 Sassari, Italy

3 Department of Chemistry and Pharmacy, University of Sassari, Via Vienna 2, 07100 Sassari, Italy.

‡ Electronic Supplementary Information (ESI) available: Experimental details for all new compounds and crystallographic data for rac-4 (CCDC No. 870836). See DOI: 10.1039/b000000x/

† Dedicated to Professor David Cole-Hamilton on the occasion of his retirement and for his outstanding contribution to transition metal catalysis § In a typical catalytic procedure, the catalyst (10 µmol) and 4'-fluoroacetophenone (0.12 mL, 1.0 mmol) were dissolved in CDCl3 (1 mL). Diphenyldisilane (0.37 mL, 2.0 mmol) was added and the mixture was placed in an NMR tube. Conversions were determined by 1H and 13C NMR spectroscopy. Hydrolysis was performed by addition of TFA in MeOH (1%, 0.5 mL). The solution was stirred for 10 min and then filtered through a small pad of SiO2, sluting with pentane/EtO (3:1). The enantiomeric excess was determined by chiral HPLC (IA or OHB column, heptane/ETOH 99:1, 1 mL min−1).


In a different approach, the amino functionality of amino acids was used as building block to prepare the imidaizolium heterocycle, see: A. Meyer, M. A. Taige and T. Leonhard and M. Meldal, Angew. Chem. Int. Ed., 2008, 1309-1314.

In our hands, this procedure induced significant racemisation at the α-carbon and was thus not further pursued.


In addition, the temperature-dependence of the relative permittivity of the solvent may further affect ligand dissociation and the stabilisation of polarised intermediates. These data are in agreement with previous studies (ref. 33). Chelation is generally required for achieving high enantioselectivity. For examples, see: (a) W.-L. Duan, M. Shi and G.-B. Rong, Chem. Commun., 2003, 2916-2917; (b) L. H. Gade, V. Cesar and S. Bellemin-Laonnaz, Angew. Chem. Int. Ed., 2004, 43, 1014-1017; (c) V. Cesar, S. Bellemin-Laonnaz, H. Wadepohl and L. H. Gade, Chem. Eur. J., 2005, 11, 2862-2873.

Histidine-derived NHC rhodium and iridium complexes were synthesized and used as catalyst precursor in (asymmetric) hydrosilylation reaction. The stereospecific course of the reaction was assessed by using the enantiopure phosphine (S)-Ph-binepine as chiral reporter group.