Enantiomerically Pure Cyclopentadienyl- and Indenyl-Functionalized N-Heterocyclic Carbene Complexes of Iridium and Rhodium

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ABSTRACT: Novel enantiomerically pure cyclopentadienyl- and indenyl-functionalized N-heterocyclic carbene ligands have been prepared by reaction of a chiral imidazole tosylate derivative with the corresponding cyclopentadienyl and indenyl lithium salts. Coordination of the Cp-functionalized NHC ligand to iridium and rhodium allowed the preparation of enantiomerically pure chelating cyclopentadienyl-functionalized Ir(III) and Rh(III) metal complexes. In contrast, the indenyl-functionalized NHC coordinates to iridium in a monodentate fashion, giving an Ir(I)-NHC complex containing a dangling indene group.

INTRODUCTION

Due to their special chemical properties and their ubiquitous implications in homogeneous catalysis, half-sandwich transition metal complexes have attracted the attention of the organometallic chemistry community for a very long time.1–3 Chiral half-sandwich complexes were first studied in the late 1960s, and a renewed interest is evident from the most recent literature.2 Among half-sandwich complexes, those containing d6 transition metals have been extensively studied due to their applications in a wide variety of organic transformations. However, compared with the high number of ruthenium and rhodium chiral half-sandwich scaffolds, the iridium analogues have been investigated to a much lesser extent. On the other hand, “Cp*Ir(III)” complexes have delivered a great performance in a large number of transformations, implying Cz—H bond activations and all sorts of borrowing hydrogen processes. In the same context, during the past few years, the introduction of N-heterocyclic carbenes (NHCs) has undoubtedly boosted the use of “Cp*Ir(NHC)” complexes due to their improved catalytic applications, although the preparation of such chiral and enantiopure complexes is limited to only a few examples.

We now have access to a very large variety of procedures for the preparation of new NHC ligands with different topologies,4 and the incorporation of ancillary donor functionalities widens the scope for the preparation of new hemilabile chelating ligands.5 We recently reported a series of synthetic pathways for the preparation of cyclopentadienyl-functionalized NHC ligands that we coordinated to a variety of metal centers, such as Ir,6 Rh,7 Ru,8 Fe,9 and Mo10 (Scheme 1). The new complexes showed interesting catalytic properties, in reactions such as transfer hydrogenation,6,9 amination of alcohols with primary amines,6,7 β-alkylation of secondary alcohols,6,7 epoxidation of olefins,10 isomerization of allylic alcohols,8 and hydrodsylation of carbonyl groups.9 Most of these reactions are known to have their asymmetric version, for which the design of suitable chiral catalysts is a straightforward target. In the case of our mentioned Cp-NHC ligands, it may seem obvious that the introduction of a chiral center in the Cp-NHC tether should provide an easy access to chiral metal complexes, but all our efforts in this sense remained unsuccessful. However, we recently reported an example in which we were able to resolve enantiomerically pure chiral Cp-NHC-Ru complexes by separating the diastereomeric species resulting from the introduction of an auxiliary chiral amine. Although this protocol opened an access to chiral Cp-NHC-metal species, it lacked the simplicity required to be applied at a
large scale and also provided very low yields.8 The approach of controlling the metal configuration by using a chiral phosphine group tethered to a cyclopentadienyl ligand has been investigated for ruthenium half-sandwich complexes, although such complexes containing enantiopure chiral centers are limited to a few examples.11 The use of chiral tethered Cp-NHC ligands could offer some advantages due to the robustness of the NHC/Cp bond. Because we believe that there is an interest in the design of feasible methods for the preparation of this type of ligands, we now disclose a new synthetic pathway for the synthesis of Cp-NHC synthons for the preparation of enantiomerically pure metal complexes. This method has been extended to the synthesis of pure chiral indenyl-functionalized ligands. NHCs bearing indenyl ligands were disclosed in a seminal work reported by Danopoulos in 2006,12 and since then, its coordination chemistry has been explored for an array of transition metals, e.g., Ti, V, Cr, Rh, Ln, and Mo.12–17 However, chiral Ind-NHC systems have not been reported yet.

RESULTS AND DISCUSSION

Starting from commercially available l-valinol, the imidazole tosylate (S)-A was synthesized following the procedure reported by Nagel and co-workers.18 The reaction of (S)-A with CpLi (Cp = η5-C5H5) followed by treatment with methyl iodide afforded the enantiomerically pure chiral cyclopentadienyl-functionalized imidazolium salt (R)-1 (Scheme 2). A similar synthetic strategy can be used for the preparation of the corresponding chiral indenyl-functionalized imidazolium (R)-2. Both imidazolium salts have been fully characterized by 1H and 13C NMR spectroscopy and by ESI-MS spectrometry ([M – I]+ = 217 m/z for 1 and 267 for 2). The 1H and 13C NMR spectra of (R)-1 showed the presence of two isomers resulting from the different position of the double bond in the cyclopentadienyl ring.

The Cp-NHC ligand precursor (R)-1 was coordinated to iridium and rhodium following the synthetic procedure depicted in Scheme 3. Treatment of (R)-1 with silver(I) oxide generated the corresponding silver-NHC, which was subsequently transmetalated to [M(μ-Cl)(cod)]2 (M = Ir, Rh). Further reflux in acetic acid was needed to promote C-H activation of the cyclopentadienyl ring, to afford the iridium(III) and rhodium(III) complexes (R)-3 and (R)-4, respectively (Scheme 3). Further treatment with KI in methanol prevents the formation of mixtures of coordinate halides. Compounds (R)-3 and (R)-4 were purified by column chromatography, yielding crystalline red solids in moderate yields (35% for (R)-3 and 30% for (R)-4). The relatively low yields obtained in these reactions are explained by the concomitant formation of bimetallic species, which in the case of iridium was isolated and characterized by ESI-MS spectrometry ([M – I]+ = 815 m/z) (complex 5, Scheme 3). Crystals of
were obtained from concentrated chloroform solutions. Although the X-ray resolution of the crystal structure of this complex was of not enough quality for the standards of publication, it allowed us to confirm the proposed structure. The crystallographic details can be found in the Supporting Information. The molecule contains two Ir(1) centers with different coordination spheres. One of the Ir atoms is coordinated to 1,5-cod, iodine, and an NHC, while the other Ir center is coordinated in a pentahapto fashion to the cyclopentadienyl ring, and one molecule of 1,5-cod completes its coordination sphere. A similar bimetallic rhodium species, in which two “Rh(cod)” fragments are linked through an indenyl-functionalized NHC ligand, was recently reported by Danopoulos, Cole-Hamilton, and co-workers. The methodology described above was also successfully applied by us in the preparation of tetramethylcyclopentadienyl-functionalized NHC complexes of iridium(III) and rhodium(III), to afford the corresponding chelating complexes as the only products, (Cp*-NHC)MI2 (Cp* = Cp*, Cp) have important consequences in the accessibility of their metal complexes.

We also investigated an alternative synthetic pathway for the synthesis of (R)-3. The reaction of the lithium salt 6 with [Ir(μ-Cl)(cod)]2 in THF, followed by oxidation with iodine, afforded (R)-3 as the sole compound in good yield (48%) (Scheme 4).

The 1H NMR spectrum of (R)-3 shows the characteristic signals due to the protons of the imidazole ring at 6.87 and 6.79 ppm. The resonances assigned to the protons at the cyclopentadienyl ring appear at 5.65, 5.37, and 5.27 ppm and confirm the asymmetry of the molecule. The methylene protons of the linker are diastereotopic, exhibiting two double doublets at 2.70 and 2.47 ppm. The 13C NMR spectrum of (R)-3 confirms the coordination of both the Cp and the NHC fragments of the ligand, with a signal at 137.9 ppm attributed to the Ir–Ccarbene bond distance is 2.041(7) Å, similar to the Ir–Ccarbene bond distances reported for related (Cp*-NHC)Ir2 complexes reported by us.

The coordination of indenyl-functionalized N-heterocyclic carbenes to rhodium was recently reported by Danopoulos and co-workers. They reported that reaction of the in situ generated Ag(Ind-NHC)Br with [Rh(μ-Cl)(cod)]2 in THF afforded the Rh(I)-NHC complex with the monodentate Ind-NHC ligand containing a dangling indene group. In an effort to synthesize the corresponding chelate (Ind-NHC)Ir2 complex, we attempted the synthetic pathways described above for the preparation of (Cp-NHC)Ir2, Treatment of (R)-2 with silver(I) oxide, subsequent addition of [Ir(μ-Cl)(cod)]2, and further reflux in acetic acid afforded the Ir(1) complex 7 in high yield. Compound 7 is formed as a mixture of two diastereotopic rotamers (7a and 7b, Scheme 5) in a 3:1 molar ratio, according to the integrals of the resonances due to the methyl groups in the 1H NMR spectrum. These two rotamers arise from the restricted rotation of the N-heterocycle about the Ir–C(carbene) bond. Compounds 7a and 7b could not be separated by conventional chromatographic means, and variable-temperature NMR experiments revealed that they do not interconvert on the 1H NMR time scale.

When the reaction is carried out between theimidazolium proligand (R)-2, previously treated with 2 equiv of nBuLi, and [Ir(μ-Cl)(cod)]2, again, a mixture of 7a and 7b was obtained (Scheme 5). C–H activation of the indene group did not occur.
under these conditions, in contrast to the results obtained for the
cyclopentadienyl system (Scheme 4). Further addition of I2 to 7
did not provide any transformation into any expected Ir(III)
species. The 13C NMR spectrum of 7 displays the characteristic
Ir(I)-carbene signal at 178.4 ppm. Attempts to coordinate the
dangling indene by reluxing complex 7 in different solvents
such as toluene, methanol, or acetic acid/dichloromethane were
unsuccessful.

In conclusion, we have presented here a new synthetic
pathway for the synthesis of enantiomerically pure cyclopenta-
dietyl- and indenyl-functionalized ligands that have been co-
ordinated to iridium and rhodium. We have demonstrated the
preferred chelate coordination mode for cyclopentadienyl-NHC
ligands compared to the indenyl systems. We are currently
exploring the catalytic efficiency of our systems in enantioselective
processes and investigating the coordination chemistry to
other transition metal centers.

**EXPERIMENTAL SECTION**

**General Procedures.** All experiments were performed using
standard Schlenk techniques. The starting materials [(S)-A]18  
[Ir(μ-Cl)(cod)]219 and [Rh(μ-Cl)(cod)]220 were prepared following litera-
ture procedures. All other reagents were used as received from
commercial suppliers and used without further purification. Elemental
analyses were performed in our laboratories at ITQB.

1H and 13C NMR spectra were recorded on Bruker Avance III
400 MHz. Infrared (IR) spectra were recorded on samples as KBr pellets
and Rh) was added, and the mixture was refluxed for 30 min, followed by
addition of brine (100 mL). The reaction mixture was stirred for 1 h at low temperature and
then allowed to warm to 4°C. After being stirred for 16 h the solution
was evaporated to dryness and the product was extracted with diethyl ether,
afforded a yellow oil. This oil (140 mg, 5.4 mmol) was dissolved
in 10 mL of acetone, and iodomethane (1.7 mL, 27.0 mmol) was added
at once. After being stirred overnight at room temperature, the reaction
mixture was evaporated to dryness and the remaining solid was washed
several times with diethyl ether. Compound 2 was isolated as a hygro-
scopic light yellow solid (200 mg, 5.1 mmol, 57%). 1H NMR (400 MHz, 
CDCl3): δ 10.24 (s, 1H, CHImid), 7.42–7.70 (2m, 4H, CHInd), 7.05
(s, 1H, CHImid), 6.94 (s, 1H, CHImid), 6.34 (s, 1H, CHInd), 4.53–4.50 (m, 1H, 
CHlinker), 4.0 (1s, 3H, NCH3), 3.40–3.25 (2m, 4H, CH2Ind + CH2linker),
2.34 (m, 1H, CHPr), 1.15 (d, 3H, CH3Pr), 0.77 (d, 3H, CH3Pr). 13C [H]
NMR (100 MHz, CDCl3): δ 144.1 (CImid), 143.8 (CImid), 138.2
(1H, CHInd), 136.7 (CHInd), 132.2 (CHInd), 126.3 (CHInd), 125.2 (CHInd), 124.2
(CHInd), 123.0 (CHInd), 121.5 (CHInd), 118.4 (CHInd), 67.4 (CHInd),
38.2 (CHInd), 37.1 (NCH3), 33.2 (CH2Ind), 30.8 (CH2Ind), 19.8
(CH3Pr), 19.2 (CH3Pr). MS-ESI: m/z 267 [M – 1]–.

Synthesis of Imidazolium Proligand Ind-NHC (R)-2. The
imidazole tosylate (S)-A (280 mg, 9.0 mmol) in THF (10 mL) was
added to a solution of IndLi (550 mg, 45.0 mmol) in THF (20 mL) at
–78°C. The reaction mixture was stirred for 1 h at low temperature and
then allowed to warm to 4°C. After being stirred for 16 h the solution
was evaporated to dryness and the product was extracted with diethyl ether,
affording a yellow oil. This oil (140 mg, 5.4 mmol) was dissolved
in 10 mL of acetone, and iodomethane (1.7 mL, 27.0 mmol) was added
at once. After being stirred overnight at room temperature, the reaction
mixture was evaporated to dryness and the remaining solid was washed
several times with diethyl ether. Compound 2 was isolated as a hygro-
scopic light yellow solid (200 mg, 5.1 mmol, 57%). 1H NMR (400 MHz, 
CDCl3): δ 10.24 (s, 1H, CHImid), 7.42–7.70 (2m, 4H, CHInd), 7.05
(s, 1H, CHImid), 6.94 (s, 1H, CHImid), 6.34 (s, 1H, CHInd), 4.53–4.50 (m, 1H, 
CHlinker), 4.0 (1s, 3H, NCH3), 3.40–3.25 (2m, 4H, CH2Ind + CH2linker),
2.34 (m, 1H, CHPr), 1.15 (d, 3H, CH3Pr), 0.77 (d, 3H, CH3Pr). 13C [H]
NMR (100 MHz, CDCl3): δ 144.1 (CImid), 143.8 (CImid), 138.2
(1H, CHInd), 136.7 (CHInd), 132.2 (CHInd), 126.3 (CHInd), 125.2 (CHInd), 124.2
(CHInd), 123.0 (CHInd), 121.5 (CHInd), 118.4 (CHInd), 67.4 (CHInd),
38.2 (CHInd), 37.1 (NCH3), 33.2 (CH2Ind), 30.8 (CH2Ind), 19.8
(CH3Pr), 19.2 (CH3Pr). MS-ESI: m/z 267 [M – 1]–.

Synthesis of (Cp-NHCl)Ir(M = Ir, Rh) Complexes (R)-3 and
(R)-4: General Procedure. The proligand (R)-1 (1 equiv) was
reacted with Ag2O (1.2 equiv), and the mixture was heated under reflux
in 1,2-dichloroethane for 1 h. Then, [M(μ-Cl)(cod)]2 (0.5 equiv, M = Ir
and Rh) was added, and the mixture was refluxed for 30 min, followed by
addition of glacial acetic acid. After being refluxed overnight, the
solution was filtered through Celite, the filtrate was evaporated to
dryness, and KI (5 equiv) and methanol were added to the remaining
residue. The mixture was then refluxed for a further 1 h. After cooling,
the solvent was removed in a vacuum and the crude solid was purified by
flash chromatography with silica (CH2Cl2/acetone).

**Compound (R)-3.** Yield: 35%. Crystals of 3 suitable for X-ray
crystallography were obtained by slow diffusion of Et3O in a THF
solution of 3. 1H NMR (400 MHz, CDCl3): δ 6.87 (s, 1H, CHImid), 6.79
(s, 1H, CHImid), 5.65 + 5.37 + 5.27 (3s, 4H, CH2Cy), 4.05 (s, 3H, NCH3),
3.80 (m, 1H, CHlinker), 2.70 (dd, 1H, J = 15.4 Hz, JH1–H1 = 5.2 Hz, 
CHlinker), 2.47 (dd, 1H, J = 15.4 Hz, JH1–H1 = 3.3 Hz, CHlinker), 2.20
(m, 1H, CHPr), 1.06 (d, 3H, J = 6.9 Hz, CH3Pr), 0.82 (d, 3H, J = 6.6 Hz, 
CH3Pr). 13C [H] NMR (100 MHz, CDCl3): δ 137.9 (CImid), 121.5
(CHInd), 120.9 (CHInd), 92.2 (CHCy), 90.1 (CHCy), 87.5 (CCy),
73.3 (CCy), 72.8 (CHPr), 68.9 (CHlinker), 43.4 (NCH3), 29.8 (CH2Cy),
23.2 (CH2linker), 20.1 (CH2Pr), 17.5 (CH2Pr). Anal. Calcd for C18H19F4N4Ir:
C, 25.42; H, 2.90; N, 4.24. Found: C, 25.30; H, 2.64; N, 4.46. MS-ESI:
m/z 535 [M – 1]+.
Compound (R)-4. Yield: 30%. 1H NMR (400 MHz, CDCl3): δ 6.99 (s, 1H, CH$_{\text{Imid}}$), 6.85 (s, 1H, CH$_{\text{Ind}}$), 5.82 + 5.74 + 5.3 + 5.21 (4s, 4H, CH$_2$Cod), 3.99 (m, 4H, NCH$_2$ + CH$_{\text{linker}}$), 2.75 (dd, 1H, $^3$J$_{IH}$ = 15.4 Hz, $^2$J$_{IH}$ = 5.1 Hz, CH$_{\text{linker}}$), 2.48 (dd, 1H, $^3$J$_{IH}$ = 15.4 Hz, $^2$J$_{IH}$ = 5.1 Hz, CH$_{\text{linker}}$), 2.25 (m, 1H, CH$_{\text{Py}}$), 1.07 (d, 3H, $^3$J$_{IH}$ = 7.4 Hz, CH$_{3}$), 0.81 (d, 3H, $^3$J$_{IH}$ = 6.0 Hz, CH$_{3}$)$_2$. Anal. Calcd for C$_{26}$H$_{34}$IN$_2$Ir: C, 45.02; H, 4.94; N, 4.04. Found: C, 61.8 (CH$_{\text{linker}}$), 4.20 CH$_2$linker + 4.63 (CHCOD), 19.3 (CH$_3$), 7.4 Hz, CH$_{3}$), 8.01 (d, 3H, $^3$J$_{IH}$ = 6.0 Hz, CH$_{3}$)$_2$. 13C NMR (100 MHz, CDCl3): δ 156.1 (d, $^3$J$_{IH}$ = 5.4 Hz, C$_{\text{NH}}$), 122.1 (CH$_{\text{linker}}$), 121.8 (CH$_{\text{linker}}$), 96.1 (C$_{\text{Py}}$), 94.0 (CH$_{\text{Py}}$), 81.4 (d, $^3$J$_{IH}$ = 6.6 Hz, CH$_{3}$), 80.8 (d, $^3$J$_{IH}$ = 6.4 Hz, CH$_{3}$), 69.0 (CH$_{\text{linker}}$), 44.23 (NCH$_3$), 30.1 (CH$_{\text{linker}}$), 23.8 (CH$_{\text{linker}}$), 20.1 (CH$_{3}$), 17.8 (CH$_{3}$)$_2$. Anal. Calcd for C$_{14}$H$_{19}$I$_2$N$_2$Rh: C, 29.39; H, 3.47; N, 4.68. MS-ESI: $m/z$ 445 [M – 1$^-$].

Synthesis of (CP-NHC)IrI(cod) (7). Then, [Ir($\mu$-Cl)(COD)$_2$]$_2$ (70 mg, 0.21 mmol, 41%) as a red solid. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): δ 6.77 (s, 1H, CH$_{\text{Imid}}$), 5.46, 5.21 (s, 4H, CH$_{\text{Py}}$), 3.69 (m, 1H, CH$_{\text{linker}}$), 3.47 (m, 4H, OC$_4$H$_8$), 3.37 (s, 3H, NCH$_3$), 2.87, 2.34 (dd, CH$_{\text{linker}}$), 2.34 (m, 1H, CH$_{\text{Py}}$), 1.62 (d, 3H, $^3$J$_{IH}$ = 6.9 Hz, CH$_{3}$), 0.54 (d, 3H, $^3$J$_{IH}$ = 6.6 Hz, CH$_{3}$)$_2$. Anal. Calcd for C$_{14}$H$_{19}$I$_2$N$_2$Rh: C, 29.42; H, 3.47; N, 4.68. MS-ESI: $m/z$ 445 [M – 1$^-$].

Supporting Information. ESI-MS spectra of compounds 3 – 5 and 7, molecular diagram of 5, details concerning 3, and CIF files giving the crystal structure of 3 are available free of charge via the Internet at http://pubs.acs.org.

Acknowledgment

We gratefully acknowledge financial support from FCT of Portugal, POCI 2010, and FEDER through project PTDC/QUI/QUI/110349/2009 and the MEC of Spain (CTQ2008-04460). A.P.C. and J.M.S.C. thank FCT of Portugal for grants SFRH/BDE/28490/2006 and SFRH/BDE/66386/2009, respectively. We thank FCT for REDE/1504/REM/2005. The Bruker Avance III 400 MHz spectrometer is part of the National NMR Network and was purchased in the framework of the National Program for Scientific Re-equipment, contract REDE/1517/RMN/2005, with funds from POCI 2010 (FEDER) and Fundação para a Ciência e a Tecnologia (FCT).

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