Catalytic applications of Magnetic nanoparticles functionalized using iridium N-Heterocyclic carbene complexes

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Abstract

A synthetic modular methodology allows the preparation of catalytic materials based on magnetic nanoparticles with iridium-N-heterocyclic carbene (NHC) complexes. The preparation of imidazolium salts containing a ketone/aldehyde as pendant functional groups are the key species. The condensation reaction of the Cp*IrNHC-CHO compound with magnetic nanoparticles containing amine groups on the surface yields the covalent anchoring of the iridium complex to the surface of the magnetite. The catalytic properties have been evaluated in transfer hydrogenation. The iridium complexes and the material are active in the reduction of ketones using isopropanol as solvent and hydrogen donor. The catalytic results reveal that the catalytic activity of the material and the molecular complex is equivalent. We have not observed any change in activity due to the support. The recyclability properties of the magnetic material have been evaluated. The results show that the catalyst activity is maintained for two runs. This work describes a simple methodology for the anchoring of molecular complexes on the surface of magnetic nanoparticles.

Keywords. Magnetic nanoparticles, Transfer hydrogenation, Supported catalysis, Iridium catalysts, N-heterocyclic carbenes.

Electronic Supplementary Information (ESI) available: General procedures, Mass Spectroscopy, X-Ray diffraction studies, High resolution electron microscopy, Powder XRD and FTIR spectroscopy. See DOI: 10.1039/x0xx00000x

Introduction

The green chemistry definition proposed by Anastas and Warner[1] as "*the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products"* has encouraged the scientific community to look for efficient ways to separate homogenous catalysts from the reaction media and their subsequent recycling.[2] The use of magnetic nanoparticles (MNPs) as efficient supports for catalysts has become a subject of intense investigation.[3] The MNPs offer advantages in the development of clean and sustainable green processes as they are non-toxic, [4] easy-accessible, [5] retrievable and reusable.[6] In the last years, two seminal manuscripts describing the immobilization of ruthenium catalyst have been described (Chart 1). The Noyori type catalyst was immobilized over MNPs using a phosphoric acid-substituted BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl). The MNPs-Ru-BINAP chiral material catalyzed the asymmetric hydrogenation of aromatic ketones in quantitative yields and excellent enantioselectivities. The system could be recycled by magnetic decantation and reused for up 14 times without loss of activity and enantioselectivity.[7] The second generation Hoveyda-Gurbbs catalyst has been immobilized on surface modify magnetite nanoparticles by a divergent synthetic approach. The catalytic system is high effective for self- and cross-metathesis reactions of methyl oleate and could be easily separated by magnetic attraction.[8]

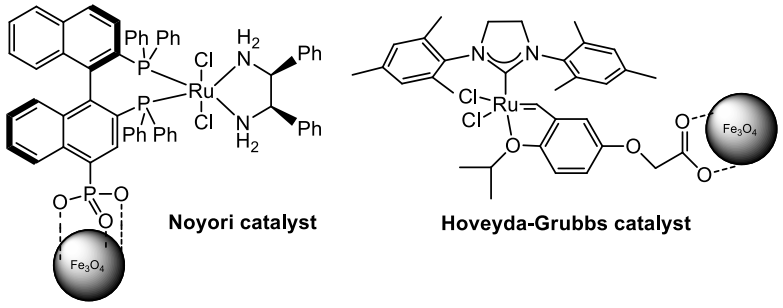


Chart 1 Noyori and Hoveyda-Grubbs catalysts immobilization strategies

The main advantages of homogeneous catalysis are selectivity and easy tuning of properties by ligand modification. In contrast, the main drawback is catalyst separation from the final reaction product.[9] Whilst for many processes small amount of metals is not a problem, just traces of metals become really important in the pharmaceutical industry. Using heterogeneous catalyst systems, separation is not a problem, as they

can be easily removed by simple filtration. The problem arises mostly from selectivity. Over the last decade the use of magnetic nanoparticles functionalized with transition metal for applications in catalysis has expanded considerably.[10] Most of the catalytic materials obtained lack of a general synthetic method for the preparation of different metal complexes. In this work we describe a modular approach method for development of catalytic materials based on magnetic nanoparticles decorated with metal-N-heterocyclic carbene (NHC) complexes.[11] The metal-NHC based complexes have demonstrated their wide scope application in catalysis, and their usefulness in the synthesis of complex natural products and valuable molecules.[12] The NHC ligands confer a high stability to the metal and act as spectator ligands.[13] These important characteristics make NHC ligands good candidates for the preparation of reusable magnetite based-catalysts.

In the course of our research we have developed efficient catalysts based on metal-NHC complexes for transfer hydrogenation.[14] On the basis of previous results we now described the synthesis of magnetic nanoparticles functionalized with iridium N-heterocyclic carbene complexes (NHCs) for the preparation of advanced catalytic materials that would be reusable and retrievable from the reaction mixture by simple decantation using an external magnet.

Experimental

Materials and methods

All manipulations were carried out under aerobic conditions unless otherwise stated. The 4'-(Imidazol-1-yl)acetophenone and Fe_3O_4 magnetic nanoparticles were purchased from commercial suppliers. The imidazolium salt **1**[15], 4-(chloromethyl)benzaldehyde[16] and functionalized Fe_3O_4 magnetic nanoparticles[17] were prepared according to literature procedures. Anhydrous solvents were dried using a solvent purification system (SPS M BRAUN) or purchased from purchased from commercial suppliers and degassed prior to use by purging with dry nitrogen and kept over molecular sieves. NMR spectra were recorded on Varian Innova spectrometers operating at 300 or 500 MHz (^{1}H NMR) and 75 and 125 MHz (^{13}C NMR), respectively, using $CDCl_3$ as solvent at room temperature unless otherwise stated. Elemental analyses were carried out in an EA 1108 CHNS-O Carlo Erba analyzer. Electrospray mass spectra (ESI-MS) were recorded on a Micromass Quatro LC instrument, and nitrogen was employed as drying

and nebulizing gas. Infrared spectra (FTIR) were recorded on a JASCO FTIR-6200 spectrometer with aspectral window of 4000-500 cm-1. High resolution transmission electron microscopy images (HRTEM) and high-angle annular dark-field HAADF-STEM images of the samples were obtained using a Jem-2100 LaB6 (JEOL) transmission electron microscope coupled with an INCA Energy TEM 200 (Oxford) energy dispersive X-Ray spectrometer (EDX) operating at 200 kV. The crystallographic structure of the samples was analyzed by X-ray powder diffraction (XRD) using a Bruker D4-Endeavor diffractometer with a Cu-K radiation with a wavelength of 0.1542 nm. The determination of the metal loading was done by ICP–MS Agilent 7500 CX. The digestion of the samples was carried out under reflux of a mixture of concentrated nitric and hydrochloric acids (3:1) for 12 h. The digestion of the samples after the recycling experiments were carried out after several washes with milli-Q water (10 x 10 mL).

Crystallography

X-ray studies: Diffraction data was collected on a Agilent SuperNova diffractometer equipped with an Atlas CCD detector using Mo-Kα radiation (λ = 0.71073 Å). Single crystals were mounted on a polymer tip in a random orientation. Absorption corrections based on the multiscan method were applied.[18] The structures were solved by direct methods in SHELXS-97 and refined by the full-matrix method based on F^2 with the program SHELXL-97 using the OLEX software package.[19]

Synthetic procedures

Synthesis of 2. To a solution of 4'-(imidazol-1-yl)acetophenone (476 mg, 2.56 mmol) in methanol (5 mL) was added 1-Bromobutane (555 µL, 5.17 mmol) in a high pressure tube. The mixture was stirred at 100 ºC for 12h. After removal of the volatiles under reduced pressure the viscous precipitate was crystallized from dichloromethane/diethyl ether. The oily residue was filtered and washed with diethyl ether (3 x 5 mL) to afford the imidazolium salt 2 as a hygroscopic white solid. Yield 415 mg (50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.10 (s, 1H, NC*H*N), 8.16 (s, 1H, CH_{im}), 8.05 (s, 4H, CH_{Ph}), 7.81 (s, 1H, CH_{im}), 4.53 (t, J = 7.3 Hz, 2H, NCH_2), 2.56 (s, 3H, COCH_3), 2.03 – 1.88 (m, 2H, CH_2), 1.39 – 1.26 (m, 2H, CH_2), 0.91 (t, J = 7.3 Hz, 3H, CH_3). $^{13}C^{20}$ NMR (300 MHz, $CDCl_3$): δ 196.4 (*C*OCH_3), 137.9, 136.9, 136.0, 130.1, 124.9, 122.6, 120.9 (*C*H_{Ph}, *CH*$_{im}$), 51.7 (N*C*H_2), 33.5 (*C*H_2), 27.0 (CO*C*H_3), 21.2 (*C*H_2), 14.8 (*C*H_3). Not a proper elemental analysis could be obtained due to the oily character of the imidazolium salt. Electrospray MS (Cone 20V) (m/z, fragment): 243.0 $[M\text{-}Br]^+$. Electrospray Ms. (Cone

20V) (m/z, fragment): 243.14 $[M\text{-}Br]^+$. HRMS ESI-TOF-MS (positive mode): $[M\text{-}Br]^+$ monoisotopic peak 243.1494; calc. 243.1497, ε_r 1.2 ppm.

Synthesis of 3. In a high pressure tube Cesium Carbonate (246 mg, 0.75 mmol) was added to a solution of the imidazolium salt **1** (105 mg, 0.32 mmol) and $[Cp^*IrCl_2]_2$ (100 mg, 0.13 mmol) in acetonitrile (5 mL). The mixture was heated at 100 °C for 4 hours. After cooling, the mixture was filtered through a pad of celite and the solvent was removed under reduce pressure. The crude solid was purified by crystallization from a dichloromethane/hexane mixture giving a yellow powder. Yield 140 mg (95 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (s, 1H, C*H*$_{Ph}$), 7.57 (d, $^3J_{H\text{-}H}$ = 1.9 Hz, 1H, C*H*$_{Ph}$), 7.37 (s, 1H, C*H*$_{im}$), 7.16 (d, $^3J_{H\text{-}H}$ = 1.9 Hz, 2H, C*H*$_{Ph}$), 7.02 (s, 1H, C*H*$_{im}$), 3.90 (s, 3H, NC*H*$_3$), 2.62 (s, 3H, COC*H*$_3$), 1.93 (s, 15H, Cp*). ^{13}C {^{1}H} NMR (300 MHz, $CDCl_3$): δ 198.3 (*C*OCH$_3$), 167.2 (C$_{carbene}$), 150.8 (*C*$_{Ph}$-Ir), 142.1, 133.3, 134.8, 123.0, 122.8, 115.4, 110.3 (*C*H$_{Ph}$, *C*H$_{im}$), 91.3 (C$_{Cp^*}$), 36.9 (N*C*H$_3$), 26.8 (CO*C*H$_3$), 9.7 (CH$_{3,Cp^*}$). Anal. Calcd. For $C_{22}H_{26}N_2OClIr$ (562.1): C, 47.00; H, 4.66; N, 4.98. Found: C, 46.95; H, 4.54; N, 4.96. Electrospray MS (Cone 20V) (m/z, fragment): 568.1 $[M\text{-}Cl+MeCN]^+$. HRMS ESI-TOF-MS (positive mode): $[M\text{-}Cl]^+$ monoisotopic peak 527.1680; calc. 527.1675, ε_r 0.9 ppm.

Synthesis of 4. In a round bottom flask, covered with aluminum foil, silver oxide (31.4 mg, 0.14 mmol) and the imidazolium salt of **2** (78.0 mg, 0.24 mmol) were dissolved in dichlorometane (20 mL). The mixture was stirred at room temperature for 6 hours. Then, $[Cp^*IrCl_2]_2$ (100 mg, 0.13 mmol) was added and the reaction was maintained at room temperature for 12 hours. The mixture was filtered through a pad of celite and the solvent was removed under reduce pressure. The crude solid was purified by crystallization from a dichloromethane/hexane mixture giving an orange powder. Yield 125 mg (86 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (s, 1H, C*H*$_{Ph}$), 7.63 (d, $^3J_{H\text{-}H}$ = 7.2 Hz, 1H, C*H*$_{Ph}$), 7.39 (s, 1H, C*H*$_{im}$), 7.17 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 1H, C*H*$_{Ph}$), 7.05 (s, 1H, C*H*$_{im}$), 4.42 – 4.39 (m, 1H, NC*H*$_2$), 4.19 – 4.15 (m, 1H, NC*H*$_2$), 2.63 (s, 3H, COC*H*$_3$), 1.79 (s, 15H, Cp*), 1.63 – 1.60 (m, 2H, C*H*$_2$), 1.46 – 1.42(m, 2H, C*H*$_2$), 0.99 (t, $^3J_{H\text{-}H}$ = 7.3 Hz, 3H, C*H*$_3$). ^{13}C {^{1}H} NMR (300 MHz, $CDCl_3$): δ 198.3 (*C*OCH$_3$), 166.2 (C$_{carbene}$), 150.6 (*C*$_{Ph}$-Ir), 142.1, 138.0, 134.7, 124.1, 121.1, 105.3, 109.9 (*C*$_{Ph}$, *C*H$_{im}$), 91.2, (C$_{Cp^*}$), 50.1 (N*C*H$_2$), 33.3 (*C*H$_2$),

27.2 (CO*C*H_3), 20.2 (*C*H_2), 13.9 (*C*H_3) 9.7 ($CH_{3.Cp*}$). Anal. Calcd. For $C_{25}H_{32}N_2OClIr$ (604.2): C, 49.70; H, 5.34; N, 4.64. Found: C, 49.31; H, 5.48; N, 4.76. Electrospray MS (Cone 20V) (m/z, fragment): 610.2, $[M - Cl+MeCN]^+$. HRMS ESI-TOF-MS (positive mode): $[M-Cl]^+$ monoisotopic peak 569.2145; calc. 569.2142, ε_r 0.5 ppm.

Synthesis of 5. To a solution of 4-(chloromethyl)benzaldehyde (480 mg, 3.10 mmol) in dry THF (8 mL) was added 1-methylimidazole (300 µL, 3.76 mmol). The mixture was stirred at 60 ºC for 72h. After removal of the volatiles under reduced pressure the viscous precipitate was extracted with dichloromethane (3 x 10 mL). The imidazolium salt 5 was obtained as colorless oil. Yield 305 mg (41%). ^{1}H NMR (300 MHz, CD_3CN): δ 10.02 (s, 1H, CHO), 9.87 (s, 1H, NC*H*N), 8.08 (d, $^3J_{H-H}$ = 8.0 Hz, 2H, C*H*$_{Ph}$), 7.70 (d, $^3J_{H-H}$ = 8.0 Hz, 2H, Ph), 7.67 (s, 1H, C*H*$_{im}$), 7.54 (s, 1H, C*H*$_{im}$), 5.64 (s, 2H, NC*H*$_2$), 3.89 (s, 3H, NC*H*$_3$). ^{13}C {^{1}H} NMR (75 MHz, CD_3CN): δ 192.4 (*C*HO), 140.7, 137.0, 136.7, 130.1, 129.2, 124.1, 122.3 (*C*H$_{Ph}$, *C*H$_{im}$, NCHN), 52.0 (N*C*H$_2$), 36.1 (N*C*H$_3$). Electrospray MS (Cone 20V) (m/z, fragment): 201.4. $[M-Cl]^+$. HRMS ESI-TOF-MS (positive mode): $[M-Cl]^+$ monoisotopic peak 201.1023; calc. 201.1028, ε_r 2.0 ppm.

Synthesis of 6. Following the same procedure as described for complex **3** using Cesium Carbonate (165 mg, 0.51 mmol), the imidazolium salt **5** (72 mg, 0.30 mmol) and $[Cp^*IrCl_2]_2$ (100 mg, 0.13 mmol). Complex **6** was obtained as an orange solid. Yield 101 mg (70 %). ^{1}H NMR (300 MHz, CD_3CN): δ 9.93 (s, 1H, C*H*O), 8.02(s, 1H, C*H*$_{Ph}$), 7.37 (d, $^3J_{H-H}$ = 7.6 Hz,*1H,* C*H*$_{Ph}$), 7.29 (m, *3H,* C*H*$_{Ph}$, C*H*$_{im}$), 4.96 – 4.79 (m, 2H, NC*H*$_2$), 3.89 (s, 3H, NC*H*$_3$), 2.01 (m, 15H, Cp*). ^{13}C {^{1}H} NMR (75 MHz, CD_3CN): δ 194.7 (*C*HO), 157.3 ($C_{carbene}$), 149.9 (C_{Ph}-Ir), 147.7, 144.8, 136.2, 125.7, 123.5, 122.8, 121.7 (*C*H$_{Ph}$, *C*H$_{im}$), 91.3 (C_{Cp*}), 57.4 (N*C*H$_2$), 37.3 (N*C*H$_3$), 9.6 (*C*H$_{3,Cp*}$). Anal. Calcd. For $C_{22}H_{26}N_2OClIr$ (562.1): C, 47.00; H, 4.66; N, 4.98. Found: C, 47.21; H, 4.73; N, 4.99. Electrospray MS (Cono 20V) (m/z, fragment): 527.4. $[M-Cl]^+$. HRMS ESI-TOF-MS (positive mode): $[M-Cl]^+$ monoisotopic peak 527.1680; calc. 527.1675, ε_r 1.0 ppm.

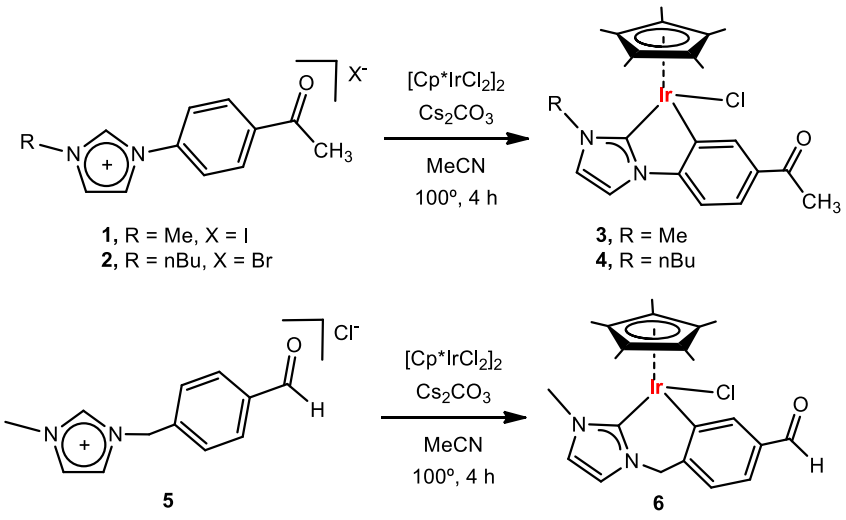
Synthesis of nano-Fe_3O_4-dopa@Cp*IrNHC (7). In a high pressure tube nano-Fe_3O_4-dopa (570 mg) was added to a solution of the iridium complex **6** (30 mg, 0.05 mmol) in toluene (5 mL). The mixture was heated at 100 °C for 20 hours. After cooling, the solid was separated using an external magnet, washed with toluene (3 x 5 mL) and dichlorometane (2 x 5 mL) and dried under reduced pressure. The nano-Fe_3O_4-dopa@Cp*IrNHC magnetic material (**7**) was obtained as a dark brown solid.

Catalytic studies. General procedure for transfer hydrogenation: In a high pressure tube were added the ketone (0.5 mmol), Cs_2CO_3 (1 equiv.), anisole as internal reference standard (0.5 equiv.), catalyst (0.5 mol%) and 3 mL of *i*PrOH used as solvent and hydrogen donor. The tube was closed and the mixture was heated at 100 ºC for 24 h. After cooling to room temperature the catalyst was separated using an external magnet and the solution was filtered using celite and analyzed. Yields were determined by GC analyses and products were identified according to spectroscopic data of commercially available compounds. The recycling experiments were carried out under identical reaction conditions. After completion of each run, the reaction mixture was allowed to reach room temperature and the solid catalyst was separated using an external magnet, washed with *i*PrOH (4 x 5 mL), dried and reused in the subsequent run.

Results and discussion

Synthesis and characterization: The imidazolium salts **1** and **2** were prepared by alkylation of 4'-(imidazol-1-yl)acetophenone using iodomethane or 1-bromobutane according to literature procedures.[15] The reaction of the imidazolium salts **1** or **2** under basic conditions (Cs_2CO_3) in the presence of $[Cp^*IrCl_2]_2$ afforded the orthometallated iridium complexes **3** and **4** in high yields, 95% and 86% respectively (Scheme 1). Cp*Ir complexes bearing an N-heterocyclic carbene ligand with phenyl or benzyl wingtip groups have a great tendency to orthometallate by C-H activation, most probably due to a chelate-assisted process.[21] The imidazolium salt **5** was obtained by alkylation of 1-methylimidazole using 4-(chloromethyl)benzaldehyde. The reaction of the imidazolium salt **5** under the reaction conditions previously described afforded the six-member

cyclometallated iridium complex **6** (Scheme 1). The iridium complexes obtained (**3** – **6**) are air stable in the solid state and solution. The characterization of the molecular complexes was performed by NMR, ESI/MS, HRMS and elemental analysis. The ^{1}H NMR confirms that the NHC ligand metallation has occurred by the disappearance of the C2-H acidic proton. The ^{13}C NMR confirms that metallation has occurred by the characteristic C-carbene signal at δ 167.2 (complex **3**), 166.2 (complex **4**) and 157.3 (complex **6**). The nature of the iridium complexes was further analyzed by means of electrospray mass spectrometry (ESI/MS) based on the mass/charge relation and the isotopic pattern distribution. Positive ion electrospray mass spectra analysis show base peaks for $[M\text{-}Cl+MeCN]^+$ at m/z = 568.2 for **3**, $[M\text{-}Cl+MeCN]^+$ at m/z = 610.2 for **4** and $[M\text{-}Cl]^+$ at m/z = 527.4 for **6**. High resolution mass spectrometry (HRMS) confirmed the exact mass with relative errors lower than 2 ppm.



Scheme 1. Synthesis of Cp*IrNHC complexes.

The molecular structure of complex **3** was confirmed by single crystal X-ray diffraction. (Figure 1). Single crystals were obtained by slow diffusion of hexane into a high concentrated solution of **3** in dichloromethane. Complex **3** crystallizes in the achiral space group P-1 and contains a single molecule in the asymmetric unit. The geometry of the complex is the expected three-legged piano-stool with dihedral angles close to 90 degrees except the C(3) - Ir(1) - C(10) of 77.44(18)° due to the chelate coordination

of the NHC-phenyl ligand. The C-C orthometallated NHC-phenyl ligand forms a five-member ring in a planar conformation. The iridium distances are Ir(1)- C(3) 2.000(4) Å, Ir(1) - C(10) 2.055(4) Å and Ir(1) - C(12) 2.4583 (4) Å and lie in the expected range for Cp*Ir(NHC) complexes.

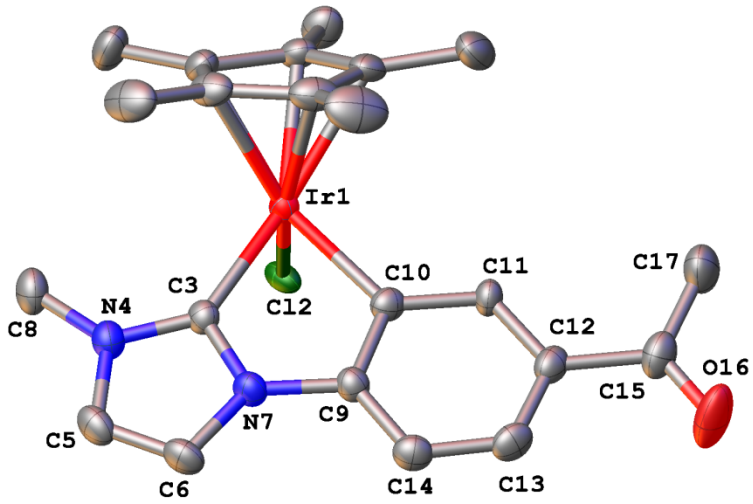
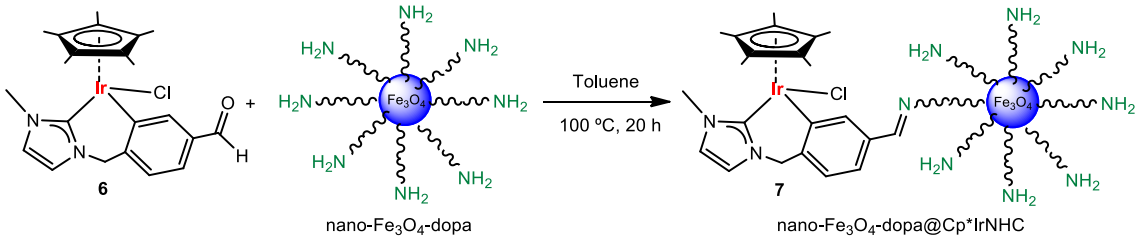


Figure 1. Molecular diagram of complex **3**. Ellipsoids are at 50% probability level. Hydrogen atoms omit for clarity. Selected bond lengths [Å] and angles [º]: Ir(1) - C(3) 2.000(4), Ir(1) - C(10) 2.055(4), Ir(1) - Cl(2) 2.4583(10), C(3) - Ir(1) - C(10) 77.44(18), C(3) - Ir(1) - Cl(2) 91.17(12), C(10) - Ir(1) - Cl(2) 91.98(12).



Scheme 2. Condensation reaction of Cp*IrNHC-CHO (**6**) with the nano-Fe_3O_4-dopa

The magnetite nano-Fe_3O_4 functionalized with dopamine (nano-Fe_3O_4-dopa) was synthesized according to Varma's method.[17] The Cp*Ir molecular complex (**6**) was covalently anchored on the surface of the magnetic nanoparticles by condensation (Scheme 2). The reaction of the orthometalated iridium complex bearing an NHC-CHO functionalized ligand (**6**) with the amine groups of the nano-Fe_3O_4-dopa afforded the

nano-Fe_3O_4-dopa@Cp*IrNHC magnetic material (**7**). After 20 h reaction the material was washed thoroughly with toluene and dichlorometane. The exact iridium content on **7** was determined by ICP-MS analysis. The results obtained accounted for a 2.7 wt% of the molecular complex **6** in the material **7**. The characterization of the materials was performed using XRD, FTIR and HRTEM (See supplementary data for details). The HRTEM analysis of **7** shows the presence of Fe_3O_4 spherical nanoparticles of a size range 20 – 30 nm (Figure 2). The HRTEM analysis before and after the functionalization with the iridium complex reveals that shape and size of the Fe_3O_4 nanoparticles are preserved after the condensation reaction (Compare Figure 2 and Figures S1 – S3).

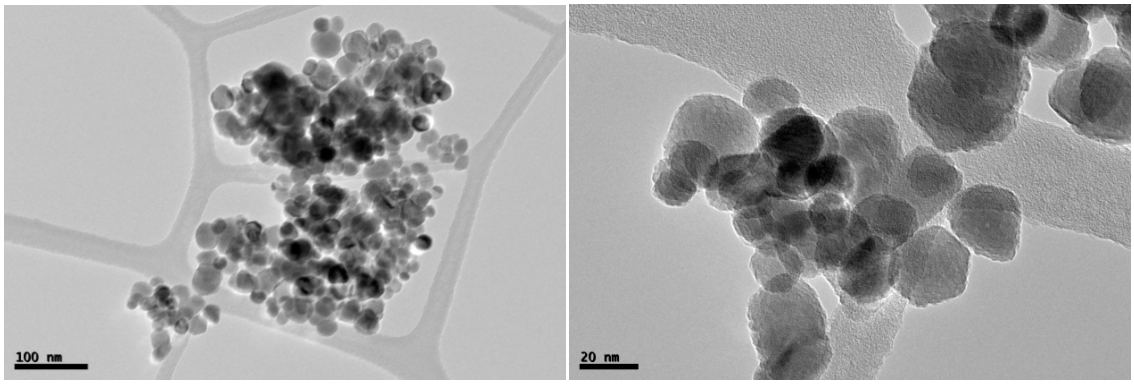
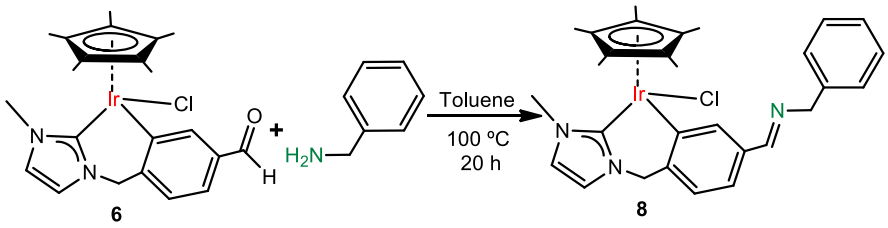


Figure 2. HRTEM images at different magnification showing the spherical morphology of the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**).



Scheme 3. Condensation reaction of Cp*IrNHC-CHO (**6**) with benzylamine.

In order to confirm that the condensation reaction is the responsible for the anchoring of the iridium complex on the surface of the nano-Fe_3O_4-dopa, we performed a control experiment (Scheme 3). In this experiment the Cp*IrNHC-CHO complex (**6**) was condensed with benzylamine under exactly the same reactions conditions. The characterization of the condensed iridium complex (**8**) was performed by means of ESI/MS and HRMS. Positive ion electrospray mass spectra analysis after the condensation reaction reveals the presence of two intense peaks for $[M\text{-}Cl]^+$ at m/z = 527.2 and 617.2. These two peaks correspond to the presence of complexes **6** and **8** respectively, just confirming that the condensation reaction is not quantitative. High

resolution mass spectrometry (HRMS) confirmed the exact mass of complex **8** with relative errors inferior to 1 ppm. When the same experiment was carried out using the Cp*IrNHC-$COCH_3$ complexes (**3**) and (**4**), we observed that no condensation reaction occurred.

The catalytic activity of the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) was evaluated in transfer hydrogenation.[22] The Cp*Ir type complexes have extensively been evaluated as homogeneous catalysts in the reduction of ketones and imines under transfer hydrogenation conditions.[23] The reactions were carried out using *i*PrOH as solvent and hydrogen donor in the presence of stoichiometric amounts Cs_2CO_3 and using a catalyst loading of 0.5 mol%, under aerobic conditions and using regular solvents. (Table 1). The catalytic activity of the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) was compared with the molecular iridium complex (**6**). In both catalytic systems the addition of base is required for the formation of the catalytic active species, as has previously been described.[24] In the development of this work, we wanted to use complex **8** as an analogue for the magnetite-immobilized complex and all our efforts persuade the isolation and purification of the complex. Unfortunately complex **8** was not obtained pure enough for catalyst testing and complex (**6**) was used instead. For comparative purposes, a table in the supplementary information shows the catalytic activity of different Cp*Ir complexes in the reduction of acetophenone by transfer hydrogenation (Table S7).

In a first experiment the catalytic activity of the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) and the molecular iridium complex (**6**) was compared in the transfer hydrogenation of acetophenone (Figure 3). The comparative reaction profile shows that there is not any significant difference in activity between the molecular complex and the supported counterpart.

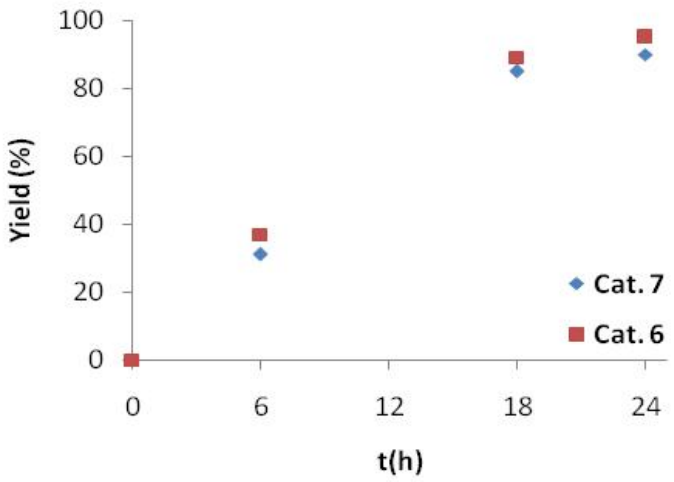
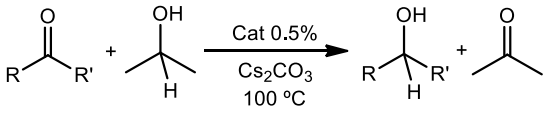
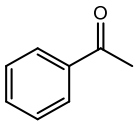
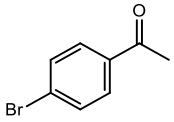
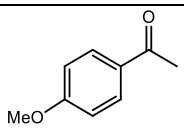
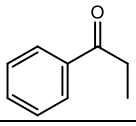
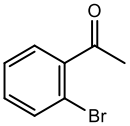
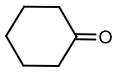


Figure 3. Comparative reaction profile in the transfer hydrogenation of acetophenone using the molecular catalyst (6) and the nano-Fe_3O_4-dopa@Cp*IrNHC (7). Reaction conditions: 0.5 mmol of acetophenone, Cs_2CO_3 (1 Eq), catalyst (0.5 mol %), 3 mL of *i*PrOH for 24 hours at 100 ºC. Yields determined by GC analyses using anisole as internal standard.

The molecular complex **6** is active in the reduction of ketones yielding the corresponding alcohols in quantitative yields after 24 hours reaction at 100 ºC. The same catalytic activity was obtained when using the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) material under the same reaction conditions and metal amount. This is an indication that the support does not have any influence in the catalytic process. When the reaction was carried out without catalyst or using nano-Fe_3O_4-dopa as catalyst the yields were less than 5% (entries 1, 2 and 5). These experiments reveal that the Cp*IrNHC fragment is the responsible of catalytic process. Acetophenone was converted into 1-phenyl ethanol in 90% yield by using catalyst **6**. When the same reaction was carried out using nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) the yield of 1-phenyl ethanol was 93% (entries 3 – 4). Introduction of different electron withdrawing/donating groups does not have much influence in the catalytic outcomes (entries 6 – 9). When increasing the sterics of substrates the molecular complex **6** gave slightly better results than the catalytic material (entries 10 – 13). Both catalytic systems are moderately active in the reduction of aliphatic ketones (entries 14 – 15). A list of comparative Cp*Ir catalysts activity in transfer hydrogenation of acetophenone can be found in table S7.

Table 1 Transfer Hydrogenation using the molecular complex **6** and the NHC-Ir-MNP (**7**).[a]



Entry	Catalyst	Substrate	Yield [b]
1	-		< 5%
2	Fe_3O_4dopa		< 5%
3	**6**		90
4	**7**		93
5	-		< 5%
6	**6**		98
7	**7**		75
8	**6**		75
9	**7**		72
10	**6**		96
11	**7**		85
12	**6**		99
13	**7**		90
14	**6**		99
15	**7**		99

[a] Reactions were carried out with 0.5 mmol of substrate, Cs_2CO_3 (1 Eq), catalyst (0.5 mol %), 3 mL of *i*PrOH for 24 hours at 100 ºC. [b] Yields determined by GC analyses using anisole as internal standard.

In view of the results obtained in the transfer hydrogenation, we decided to explore the catalyst stability by exploring the catalyst recovery and reuse. Recycling experiments of nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) were carried out using acetophenone, cyclohexanone, *p*-bromoacetophenone and *p*-methoxyacetophenone (Figure 4). The reaction conditions were the same as those described in the transfer hydrogenation process described in Table 1. After completion of each run (24 h.), the reaction mixture

was allowed to reach room temperature, and the solid catalyst was separated using and external magnet (Figure S8), washed with *i*PrOH (4 x 5 mL), dried and reused in the subsequent run. Following this methodology the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) was reused for two times without any decrease of activity in the case of acetophenone. Then, the catalytic activity decrease to 50% yield and is maintained up to the fifth run. In the case of the other substrates, the catalyst activity is maintained for two runs, and then a dramatic decrease in activity was observed, except in the case of the *p*-methoxyacetophenone were after the first catalytic run the catalyst activity is completely lost. These results suggest a deactivation of the molecular iridium complex anchored on the surface of the nano-Fe_3O_4-dopa. The deactivation process is substrate dependent. In order to increase the recyclability of the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) we performed a recycling experiment using acetophenone under inert conditions. The results were the same as using aerobic conditions and the catalyst activity drops to 50% after the second catalytic run. Then we analyze the catalytic material by means of HRTEM analysis (Figure 5). The results show that after three catalytic runs the size and morphology of the nano-Fe_3O_4 are preserved and no degradation of the material is observed.

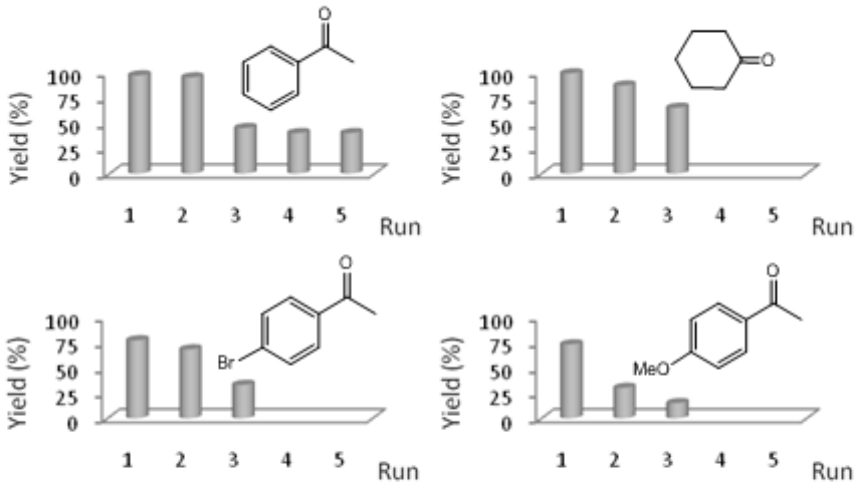


Figure 4. Recycling experiments in transfer hydrogenation using Cp*IrNHC@NPsFe_3O_4 (**7**) as catalyst. Reaction conditions: 0.5 mmol of substrate, Cs_2CO_3 (1 Eq), catalyst (0.5 mol %), 3 mL of *i*PrOH for 24 hours at 100 ºC for each run. Yields of the corresponding alcohols obtained were determined by GC analyses using anisole as internal standard.

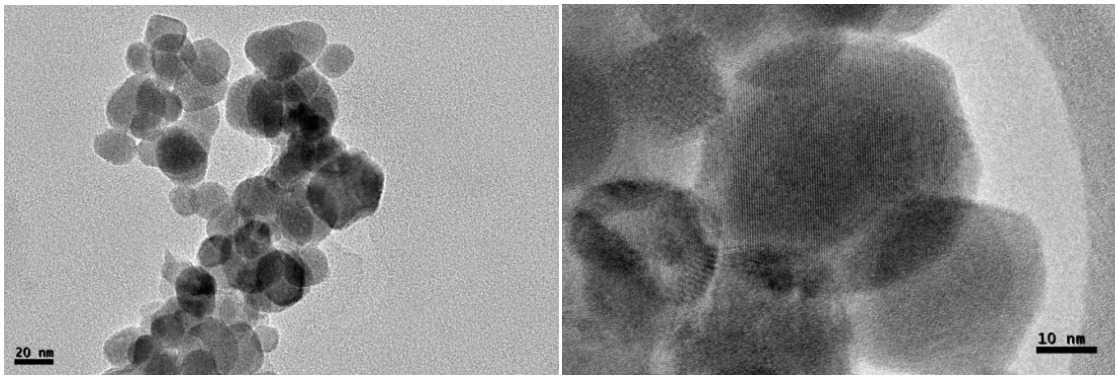


Figure 5. HRTEM images at different magnification of nano-Fe_3O_4-dopa@Cp*IrNHC (7) after three catalytic runs using acetophenone as substrate.

The poor recyclability of the nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) could be attributed to the attachment of the molecular complex **6** by an imine formation. In principle, the imine functionality is hydrolytically unstable and liable to break under basic conditions. In order the check this hypothesis the amount of iridium leaching was analyzed by ICP/MS analysis in the recycling experiment using acetophenone as substrate. The results reveal that the amount of iridium is negligible in five consecutive runs, just indicating that decoordination of the molecular complex **6** by imine hydrolysis is not occurring. These results are supported by other examples previously developed by our group [14f] and others[23h, 25] where imines are not hydrolyzed under transfer hydrogenation conditions using strong bases.[14b, 14d, 26] The transfer hydrogenation of imines using *i*PrOH as solvent and hydrogen donor in the presence of stoichiometric amounts Cs_2CO_3 has been successfully achieve with iridium and rhodium N-heterocyclic carbene complexes without any detectable hydrolysis product formation.[25f]

Other important factor related to supported catalysis is the so called "boomerang effect" or "release and catch" catalytic systems.[27] This effect consists in a release-and-return of the molecular complex form the support, therefore implying that the catalytic process is carried out homogeneously and then the catalytic active species are "caugh" at the end of the reaction by the support. The imine hydrolysis of the material nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) could yield the corresponding aldehyde (molecular complex **6**) and the amine (nano-Fe_3O_4-dopa). Note that this process is an equilibrium reaction and could go back to the condensation product (nano-Fe_3O_4-dopa@Cp*IrNHC (**7**)). A hot filtration experiment was realized in order to determine if the boomerang effect is governing the catalytic process. The hot filtration experiment was carried out using the general conditions described in table 1 using acetophenone

as substrate and nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) as catalyst. After 6h reaction, the catalyst was separated from the solution by using an external magnet at 100 ºC. At this point, an aliquot was analyzed by GC and the yield of 1-phenyl ethanol was 38%. The filtrate was further heated at 100 ºC for 18 h and then analyzed. The results reveal that no further alcohol is formed (GC final yield is maintained in 38%). This experiment suggests the absence of catalytic active species in solution due to imine hydrolysis.

Cp*Ir type complexes have been used as homogeneous catalysts in the reduction imines under transfer hydrogenation conditions.[28] The presence of an imine in the supported catalyst nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) could lead to the hydrogenation of the imine producing the modification of the parent catalyst. The formation of the corresponding amine should not modify the catalytic properties of the system. To check the possibility of imine hydrogenation a control experiment was carried out using N-benzylideneaniline as model substrate. The reaction was carried out using *i*PrOH as solvent in the presence of stoichiometric amounts Cs_2CO_3 and a catalyst loading of 0.5 mol%. The results reveal that the N-benzylideneaniline is not hydrogenated to the corresponding amine just indicating that the iridium catalyst is not active in the hydrogenation of imines under this reaction conditions. We have also observed that the N-benzylideneaniline is recovered quantitatively, indicating that no hydrolysis has occurred.

Based on the previous experiments the most plausible mechanism for the poor recyclability of the supported nano-Fe_3O_4-dopa@Cp*IrNHC (**7**) catalyst in transfer hydrogenation could be attributed to the formation of inactive iridium species that are not catalytically active. The nature of this species is unknown but they are attached to the magnetite and no release to solution has been observed. The situation is similar to the catalyst activity/deactivation procedure observed for the molecular complexes. Development of highly active and stable molecular catalysts should increase the possibility of recycling and reuse of catalytic systems based on supported magnetite catalysts.

Conclusions

We have described a synthetic modular methodology that allowed us to obtain catalytic materials based on magnetic nanoparticles with iridium-N-heterocyclic carbene (NHC) complexes. Imidazolium salts containing a ketone/aldehyde as pendant functional group have been synthesized. Metallation of the imidazolium salts leads to

molecular Cp*iridium complexes. The condensation reaction of the Cp*IrNHC-CHO with magnetic nanoparticles containing amine groups on the surface yields the covalent anchoring of the iridium complex to the surface of the magnetite. The iridium complexes and the material are active in the reduction of ketones under transfer hydrogenation conditions. The catalytic results reveal that the catalytic activity of the material and the molecular complex is equivalent. We have not observed any change in activity due to the support. The recyclability properties of the magnetic material have been evaluated. The results show that the catalyst activity is maintained for two runs. This work describes a simple methodology for the anchoring of molecular complexes on the surface of magnetic nanoparticles by the formation of an imine. Further research into the preparation of new catalytic materials following the same methodology but with the formation of an amine or amide to improve the attachment with the support is currently underway in our laboratory.

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