# Application of three-legged piano-stool cyclopentadienyl-N-heterocyclic carbene iron(II) complexes as *in situ* catalysts for the transfer hydrogenation of ketones

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## ABSTRACT

A one pot system has been developed based on nine related 1,3-dialkylated imidazolium salts for the *in situ* generation of *N*-heterocyclic carbene iron(II) complexes in which the complexes were directly tested as catalysts for the transfer hydrogenation of ketones. This is a simplified reproducible process that aims to eliminate unnecessary purification steps for the isolation of such catalysts prior to application. Complexes **10**–**12** have been prepared under similar conditions, isolated and structurally characterized by spectroscopic and crystallographic methods. Solid state structures of the three complexes were similar and showed distorted octahedral three-legged piano stool geometry around each iron center similar to reported complexes bearing related ligands. As a basis for comparison with the *in situ* catalyzed systems, the isolated complexes were also tested as catalysts for the transfer hydrogenation of ketones. As a result, under optimized reaction conditions, all the *in situ* generated catalysts were found to provide excellent activities similar to those based on the isolated complexes with moderate to excellent conversions to the desired alcohol products. Turn over numbers up to 200 at a conversion of 100% was recorded for a wide range of aliphatic, aromatic and cyclic ketones.

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## 1. Introduction

The selective reduction of carbonyl groups for the production of alcohols is a vital process for the pharmaceutical and fine chemicals industries. Comparatively, it is best achieved by transfer hydrogenation (TH) instead of direct hydrogenation using molecular hydrogen since TH is cheaper and safer both because no free hydrogen is used and it does not require special reactor, stirring, or gas handling auxiliaries. Removal of the need for hydrogen storage, monitoring and dispensing equipment in principle means that ordinary glassware will suffice for most processes. It also implies that process scale up to industrial levels of production is easily achievable due to the elimination of mass transfer limitations associated with the poor solubility of hydrogen gas [1].

Thus far, because of their exceptional activities, the most studied catalysts for TH are based on platinum group metals (PGMs). However the PGMs suffer from limited availability, high cost and toxicity issues not particularly suited to pharmaceuticals and food processing applications [2]. Iron is a much suited metal for these

and related applications, thus it is not surprising that the chemistry of iron based N-heterocyclic carbene (NHC) complexes has been a very active topic in recent literature, especially in homogeneous catalysis [3] where catalyst recovery and contamination is a major concern. Ingleson and Layfield [4] have recently reviewed and contextualized the current state of iron-NHC chemistry which revealed that one of the reasons for the lesser development of iron-NHC complexes is the difficulty encountered in their synthesis and isolation [5]. However, three-legged piano-stool cyclopentadienyl (Cp)-Fe(II) complexes are well known to offer the advantage of ease of reaction monitoring by spectroscopy: infrared (carbonyl shifts are easily monitored) or NMR (shifts in Cp region) and can be prepared from a relatively inexpensive precursor [CpFe(CO)$_2$]$_2$ [6]. Recent interest in Fe-NHC chemistry includes a report on the direct activation of the NHC ligand in low coordinate Fe-NHC complexes to yield new complexes with unusual coordination [7]. It has been shown that iron-NHC complexes are usually prepared *via* the free carbene route which is a limited route due to well documented difficulties associated with the handling of reactive free carbenes [8]. To mitigate the handling of free carbenes, transmetallation of NHCs from a silver complex [9] is widely applied for the synthesis of NHC-metal complexes, but thus far no reported cases on adaptation for the preparation of iron based NHC complexes has been recorded. However, iron-NHC complexes can be prepared by the reaction of moisture sensitive and unstable basic

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metal acetates, alkoxides, or amides with imidazolium salts [10]. Hence, a few successful cases of iron-NHC complexes have been recorded as reviewed by Ingleson and Layfield [4]. More specifically, by combining the advantages of [CpFe(CO)$_2$]$_2$ as a precursor and the strong σ-donor properties of NHC ligands, Buchgraber et al. [11] and Mercs et al. [12] have studied the coordination chemistry of piano-stool Cp-iron-NHC complexes similar to those isolated in this study.

It is important to note that iron is not new to catalysis especially heterogeneously and as a component of biological systems. Prominent amongst its use are in Harber-Bosch ammonia synthesis [13] and Fischer-Tropsch process [14]. Examples of well-defined NHC or Cp containing homogeneous systems include work by Tatsumi and co-workers who utilized unsaturated half-sandwich NHC iron complexes to activate C—H bonds of thiophenes, furans and pyridine [15]. The application of organometallic and coordination complexes of iron as catalysts for the reduction of carbonyl groups has been explored by several groups. For example, the group of Morris and co-workers has developed very efficient systems for asymmetric TH of ketones based on tetradentate PNNP ligands [16]. Casey and co-workers, inspired by bifunctional, ionic hydrogenation catalysis established for ruthenium, have disclosed catalytic activity of related Cp-iron counterparts [17]. Their catalysts showed high activity in hydrogenation of several ketones, aldehydes, and imines using molecular H$_2$ as a reducing agent and also displayed activity in transfer hydrogenation reaction by use of 2-propanol as source of hydrogen. In addition, Kandepi and co-workers have developed new Fe(II) complexes containing functionalized-Cp NHC ligands that showed good catalytic activity in hydrosilylation of aldehydes and transfer hydrogenation of ketones [18].

The examples mentioned above reveal a reemergence in the last decade of interest in well-defined iron complexes as credible alternatives to PGMs in some homogeneous catalysis projects. Hence, in continuation with our interest in the study of imidazolium family of compounds as ionic liquids and ligands in organometallic chemistry [19], the current work was aimed at the evaluation of NHC-Fe systems as simple, active, *in situ* generated one pot catalysts. The study reports combination of the simplicity of TH, *in situ* one pot catalyst generation and use of abundant, cheap and environmentally friendlier iron catalyst in one process.

## 2. Experimental

### 2.1. General procedures

All manipulations were performed using standard Schlenk techniques under an atmosphere of dry nitrogen. All solvents were dried and purified by standard procedures prior to use. Glassware was oven dried at 110 °C. All NMR experiments were done using a 400 MHz Bruker Ultrashield spectrometer and samples were dissolved in deuterated chloroform. Infrared spectra for the ligands were recorded neat using a Perkin Elmer universal ATR Spectrum 100 FT-IR spectrophotometer, while the solution IR data for the complexes were recorded in CH$_2$Cl$_2$ on a Perkin Elmer FT-IR spectrophotometer; model RX 1. Low resolution MS samples were run on a Thermo Finnigan Linear ion trap mass spectrometer using electrospray ionization in positive mode. Accurate mass data was obtained on a Thermo Electron DFS Dual focusing magnetic sector instrument using ESI in positive mode; polyethylenimine was used as reference solution. Ligand 3 was purchased from Aldrich, while other ligands were synthesized according to a literature method [20]. Preparation of CpFe(CO)$_2$I was based on our published procedure [21]. Transfer hydrogenation reaction was monitored by gas chromatography (GC) with an Agilent capillary GC model 6820 fitted with a DB wax polyethylene column (0.25 mm in diameter, 30 m

in length), a flame ionization detector and nitrogen gas was used as carrier gas at a flow rate of 2 mL/min. Reagents were purchased from Aldrich or Merck and were used as received.

### 2.2. General procedure for the synthesis of ligands 1–9

The ligands (except 3) were all synthesized by adaptation of the methods of Starikova et al. [20]. A typical and generic procedure is described. Spectroscopic and analyses data are presented. *N*-monosubstituted azole (0.1 mmol) and dry toluene were placed in a two-neck flask and stirred until a homogeneous solution was formed; then alkyl halide (0.3 mmol) was added drop wise with continuous stirring. After addition of the alkyl halide, the mixture was stirred while heating at 40 °C for 24 h. The solvent was removed and the ligand was dried under vacuum.

#### 2.2.1. 1,3-Dimethylimidazolium iodide (1)
Brown solid. Yield (4.80 g, 98%) IR (ATR cm$^{-1}$): 3433, 3152, 3094, 2953, 1619, 1572, 1341, 1170, 1084, 1020, 826, 748, 617; $\delta_H$ (400 MHz, CDCl$_3$): 4.07 (6H, s, NCH$_3$), 7.35 (2H, s, NCH) and 9.97 ppm (1H, s, CH); $\delta_C$ (100 MHz, CDCl$_3$): 37.12 (NCH$_3$),123.36 (NCH) and 137.76 ppm.; *m/z* (ESI) 96.7 (M$^+$−I$^-$). HRMS (ESI) calcd for C$_5$H$_9$IN$_2$, 97.07657 (M$^+$−I$^-$); found, 97.07628 (M$^+$−I$^-$).

#### 2.2.2. 1-Methyl-3-ethylimidazolium bromide (2)
White solid. Yield (4.70 g, 98%). IR (ATR cm$^{-1}$): 3065, 2975, 1670, 1571, 1467, 1172, 1101, 856, 789, 649, 789, 621, 417; $\delta_H$ (400 MHz, CDCl$_3$): 1.47 (3H, t, *J* 7.3 Hz, CH$_3$), 3.97 (3H, s, NCH$_3$), 4.32 (2H, q, NCH$_2$), 7.54 (2H, s, NCH) and 10.07 ppm (1H, s, CH); $\delta_C$ (100 MHz, CDCl$_3$): 15.64 (CH$_3$), 36.63 (NCH$_3$), 45.18 (NCH$_2$), 122.01 (NCH), 123.71 (NCH) and 136.73 ppm.; *m/z* (ESI) 111.5 (M$^+$−Br$^-$). HRMS (ESI) calcd for C$_6$H$_{11}$BrN$_2$, 111.09222 (M$^+$−Br$^-$); found, 111.09196 (M$^+$−Br$^-$).

#### 2.2.3. 1-Methyl-3-butylimidazolium bromide (4)
Colorless oil. Yield (1.98 g, 91%). IR (ATR cm$^{-1}$): 3077, 2959, 1626, 1570, 1463, 1166, 1109, 752, 619, 460; $\delta_H$ (400 MHz, CDCl$_3$): 0.74 (3H, t, *J* 7.4 Hz, CH$_3$), 1.18 (2H, m, CH$_2$), 1.70 (2H, m, CH$_2$), 3.92 (3H, s, NCH$_3$), 4.14 (2H, t, *J* 6.7 Hz, NCH$_2$), 7.42 (1H, s, NCH), 7.53 (1H, s, NCH) and 10.03 ppm (1H, s, CH), $\delta_C$ (100 MHz, CDCl$_3$): 13.41 (CH$_3$), 19.37 (CH$_2$), 32.11 (CH$_2$), 36.65 (NCH$_3$), 49.72 (NCH$_2$), 122.29, 123.83, 136.99 ppm; *m/z* (ESI) 139.4 (M$^+$−Br$^-$) HRMS (ESI) calcd for C$_6$H$_{11}$BrN$_2$, 139.12352 (M$^+$−Br$^-$); found, 139.12327 (M$^+$−Br$^-$).

#### 2.2.4. 1-Methyl-3-pentylimidazolium chloride (5)
Light yellowish oil. Yield (1.62 g, 86%). IR (ATR cm$^{-1}$): 2929, 2859, 1520, 1466, 1123, 1108, 731, 662; $\delta_H$ (400 MHz, CDCl$_3$): 0.82 (3H, t, *J* 7.4 Hz, CH$_3$), 1.24 (4H, m, CH$_2$), 1.48 (2H, q, CH$_2$), 3.52 (2H, t, *J* 6.7 Hz, NCH$_2$), 3.58 (3H, s, NCH$_3$), 6.78 (1H, s, NCH), 6.93 (1H, s, NCH) and 7.33 ppm (1H, s, CH), $\delta_C$ (100 MHz, CDCl$_3$): 14.05 (CH$_3$), 22.52 (CH$_2$), 28.04, 32.51, 33.29, 62.36, 125.29, 128.21, 137.73 ppm; *m/z* (ESI) 153.0 (M$^+$−Cl$^-$) HRMS (ESI) calcd for C$_9$H$_{17}$ClN$_2$, 153.13917 (M$^+$−Cl$^-$); found, 153.13877 (M$^+$−Cl$^-$).

#### 2.2.5. 1,3-Diethylimidazolium bromide (6)
Colorless oil. Yield (1.34 g, 94%). IR (ATR cm$^{-1}$): 3426, 3066, 2977, 1562, 1448, 1350, 1229, 1164, 1083, 1032, 956, 908, 803, 753, 643; $\delta_H$ (400 MHz, CDCl$_3$): 1.40 (6H, t, *J* 7.4 Hz, CH$_3$), 4.38 (4H, q, NCH$_2$), 7.45 (2H, s, NCH) and 10.38 ppm (1H, s, CH), $\delta_C$ (100 MHz, CDCl$_3$): 16.48 (CH$_3$), 41.96 (NCH$_2$), 129.46 (NCH), 136.72 ppm; *m/z* (ESI) 124 (M$^+$−Br$^-$) HRMS (ESI) calcd for C$_7$H$_{13}$BrN$_2$, 125.10787 (M$^+$−Br$^-$), found, 125.10700 (M$^+$−Br$^-$).

#### 2.2.6. 1,3-Dibutylimidazolium bromide (7)
Colorless oil. Yield (1.45 g, 80%). IR (ATR cm$^{-1}$): 3401, 2959, 2874, 1649, 1510, 1462, 1280, 1107, 1080, 1025, 951, 734, 664; $\delta_H$