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Low-Valent Ene−Amido Iron Complexes for the Asymmetric Transfer Hydrogenation of Acetophenone without Base

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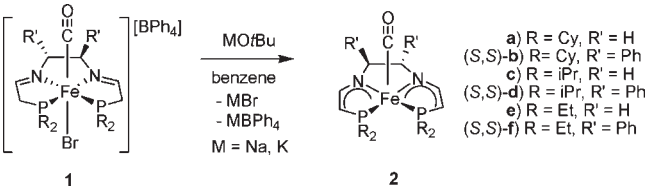
Supporting Information

ABSTRACT: Examination of the role of base in the activation of our previously reported iron(II) complexes having the general formula [Fe(CO)(Br)(PNNP)][BPh_4] revealed a five-coordinate iron(II) complex in which the tetradentate PNNP ligand had been doubly deprotonated. The new iron(II) complexes were used in the transfer hydrogenation of acetophenone in isopropanol in the absence of added base, and certain analogues showed catalytic activity.

The replacement of precious platinum metal-based complexes in catalysis with first-row transition metals, especially iron, is a growing phenomenon.[1] The impetus for this lies in the fact that these metals are more abundant and benign, thereby creating cost-effective and "green" catalysts. Our recent research has been focused on the development of iron(II) catalysts, and we have demonstrated complexes of the type *trans*-[Fe(CO)(Br)(PNNP)]$^+$ (PNNP = $PR_2CH_2CH{=}NCH(R){-}CH(R)N{=}CHCH_2PR_2$) form active and selective catalysts for the asymmetric transfer hydrogenation (ATH) of ketones in basic isopropanol.[2] However, the mechanism of this transformation is still elusive. As a starting point, we examined the role of base in the transfer hydrogenation reaction because these iron(II) complexes become active only upon the addition of a strong base (the use of 8 equiv of KO*t*Bu was found to be optimal). An observation indicating that base plays an important role in the activation of the catalyst was the immediate color change of the reaction mixture from yellow to green when base was added. Here we report that deprotonation of the tetradentate ligand backbone, specifically at the carbon α to the phosphorus, is an important part of the catalyst activation process. This allows the first iron-based catalytic ATH of acetophenone without the need for addition of base.[3]

We observed that the green color occurred even without the presence of the ketone substrate; thus, the iron(II) precatalysts, **1a**-**f**, (10 mg) were mixed with 8 equiv of KO*t*Bu to mimic the conditions for catalysis (Scheme 1). However, when this was done in isopropanol, the loss of the green color was evident within minutes or overnight, which implied that the green species was reactive toward that solvent. Hence, benzene was chosen instead. Both the base and the iron(II) precatalysts had limited solubility in benzene but reacted fully after 30 min to give a dark-green solution with disappearance of the yellow starting material. All of the solutions were filtered to remove an off-white precipitate, and evaporation in vacuo gave a green residue that was soluble in numerous solvents, such as alkanes. Solutions of the latter could be conveniently filtered to remove any residual excess base. The green compounds **2** were obtained as sticky residues despite extensive drying. They were air-sensitive and turned brown when exposed to air. Benzene solutions of compounds **2a**−**d** were stable for months in a glovebox under an inert atmosphere, while **2e** and (*S*,*S*)-**2f** were less stable, with a noticeable loss of color from green to brown after a couple of weeks.

Scheme 1. Synthesis of Doubly Deprotonated Iron(II) Complexes 2



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Compounds **2a**−**f** were analyzed by ^1H, $^{31}P\{^1H\}$, and ^{11}B NMR spectroscopy in C_6D_6. The ^{31}P NMR spectra in all cases revealed a downfield shift of up to 10 ppm for the phosphorus signal relative to that for the starting iron(II) complex.[2b] The absences of BPh_4^- aromatic protons and boron resonances in the ^1H and ^{11}B NMR spectra, respectively, are consistent with **2a**−**f** being neutral compounds. The ^1H NMR data (integrations, chemical shifts, and $^1H-^1H$ COSY results) revealed that while the carbons adjacent (i.e., α) to the phosphorus of the PNNP ligand backbone in **1a**−**f** had two inequivalent hydrogens, those in compounds **2a**−**f** had only one hydrogen (Figure 1). Hence, the base deprotonated the ligand at both α carbons. The diastereotopic nature of the $-CH_2-$ groups in the ethylene backbones of **2a**, **2c**, and **2e** was retained, with peaks appearing in a 1:1 ratio (Figure 1 bottom). In addition, the −CH(Ph) hydrogens were still present in the chiral compounds (*S*,*S*)-**2b**, (*S*,*S*)-**2d**, and (*S*,*S*)-**2f**.

Regardless whether 2 or 8 equiv of base was used in the synthesis of **2a**−**e**, the same ligand double deprotonation pattern was observed in the ^1H NMR spectra. However, the use of excess base in the synthesis of (*S*,*S*)-**2f** produced some side products according to the NMR spectra. The cleanest spectra obtained were from samples in which 2 equiv of base were used. Here a second, unidentified product was present in a ratio of 1:3 with (*S*,*S*)-**2f**. The $^{31}P\{^1H\}$ NMR spectra also showed the presence of two compounds by means of a doublet of doublets at 77.1 and

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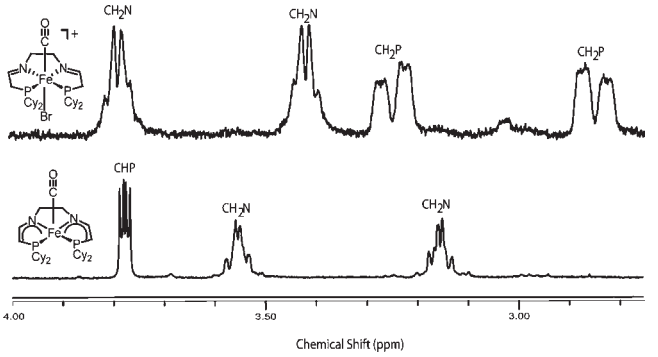
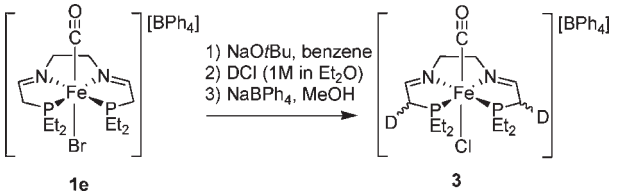


Figure 1. ^{1}H NMR spectra (400 MHz) of hydrogens of interest in the iron(II) complexes **1a** in CD_2Cl_2 (top) and **2a** in C_6D_6 (bottom).

Scheme 2. Synthesis of Deuterated Iron(II) Complex 3

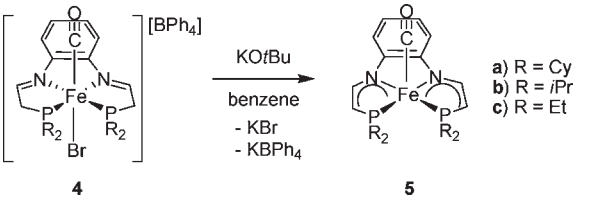


68.3 ppm and a broad signal at 67.7 ppm. The ^{31}P−^{1}H HMBC NMR spectrum showed that the doublet of doublets belonged to the minor product while the broad signal belonged to (*S*,*S*)-**2f**. A ^{31}P variable-temperature NMR (VT-NMR) experiment to as low as −80 °C resulted in the disappearance of the broad peak at 67.7 ppm to the baseline without the appearance of a new set of signals. Although the ^{31}P NMR spectrum of **2e** displayed a singlet, the resonance was rather broad in comparison with the sharp singlet resonances of **2a** and **2c**. Hence, we attribute the broad resonances in the ^{31}P NMR spectra of **2e** and (*S*,*S*)-**2f** to fluxional behavior of the Et groups on phosphorus.

To further support deprotonation at each carbon α to the phosphorus on the PNNP ligand backbone, DCl (1 M in Et_2O) was added to a filtered green solution of **2e** (Scheme 2). This gave an immediate change in the color of the reaction solution from green to yellow. The ^{1}H NMR spectrum showed that the carbon α to the phosphorus on the PNNP ligand was deuterated; a crystal of **3** suitable for X-ray diffraction was obtained (see the Supporting Information). This experiment implies a five-coordinate iron species upon deprotonation and also demonstrates the ease of deprotonation and protonation of the PNNP ligand.

To further support the inference that the carbon α to the phosphorus on the ligand backbone was deprotonated, iron(II) complexes **4a**−**c** with *o*-phenylene groups as NN linkers of the PNNP ligand (Scheme 3) were synthesized. The crystal structure of **4b** is shown in Figure 2. No protons exist on the NN linker backbone of the ligand, ruling out any possibility of deprotonation of that part of the ligand. The reaction of **4a**−**c** with KO*t*Bu followed by removal of KBr and $KBPh_4$ as well as excess base (Scheme 3) and subsequent NMR characterization of the isolated product again showed evidence of the double deprotonation at the same α carbon on the PNNP ligand. The doubly deprotonated compounds **5a**−**c** in these cases were not green but rather black unless diluted significantly to give purple (**5a**, **5b**) or blue (**5c**) solutions. The color is due to multiple absorbances at wavelengths

Scheme 3. Synthesis of Doubly Deprotonated Iron(II) Complexes 5



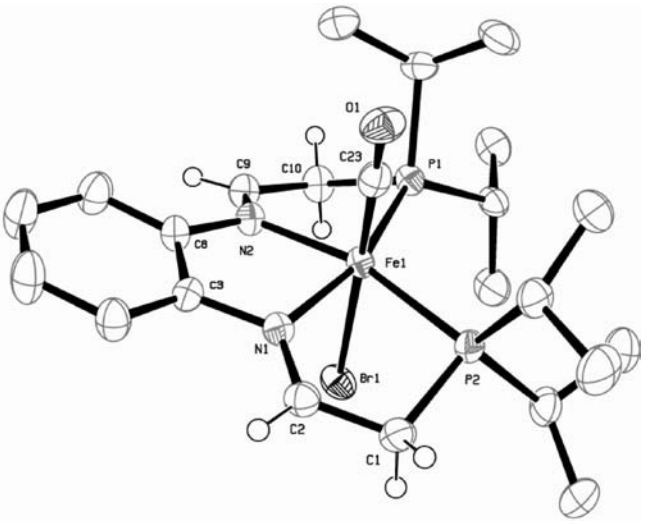


Figure 2. ORTEP plot (thermal ellipsoids at 50% probability) of the X-ray crystal structure of **4b**. The BPh_4 anion and most of the H atoms have been removed for clarity.

across the visible spectrum, as determined from UV−vis spectroscopic measurements (see the Supporting Information).

The proposed structure of the neutral, five-coordinate iron complexes was confirmed by a single-crystal X-ray diffraction study of **5b** (Figure 3). The structure has a pseudo-square-pyramidal geometry. There is no anion present. The CO ligand is apical; there is no spectroscopic or crystallographic evidence of a hydride trans to CO. On going from **4b** to **5b**, the PCH_x−CHN distance contracts from 1.481(4) to 1.342(4) Å. All of the other distances in the five-membered Fe−P−C−C−N rings also contract upon deprotonation except for the distances corresponding to N1−C2, which lengthen from 1.277(5) to 1.385(3) Å. All of these changes suggest that there is extensive delocalization of bonding in **5b**. Square-pyramidal, five-coordinate iron compounds are not prevalent.[4] Of all of the examples, two were found that contain a tetradentate ligand and an apical CO ligand analogous to the compounds presented in this report. The $\nu_{C\equiv O}$ of the reported compounds $[Fe(CO)(C_{21}H_{22}N_4)]$[5a] and $[Fe(CO)(C_{36}H_{44}N_4)]$[5b] containing macrocyclic ligands were found at 1921 or 1948 cm^{-1}, respectively. These are higher than those for compounds **2a**−**f** and **5a**−**c**, which were found to be in the 1880−1898 cm^{-1} range. The $\nu_{C\equiv O}$ of the parent compounds **1a**−**f** and **4a**-**c** range between 1945 and 1958 cm^{-1}.[2b] Hence, the lower wavenumbers of **2a**−**f** and **5a**−**c** are believed to be due to not only extensive delocalization of the negative charge across the ligand but delocalization into the metal as well.

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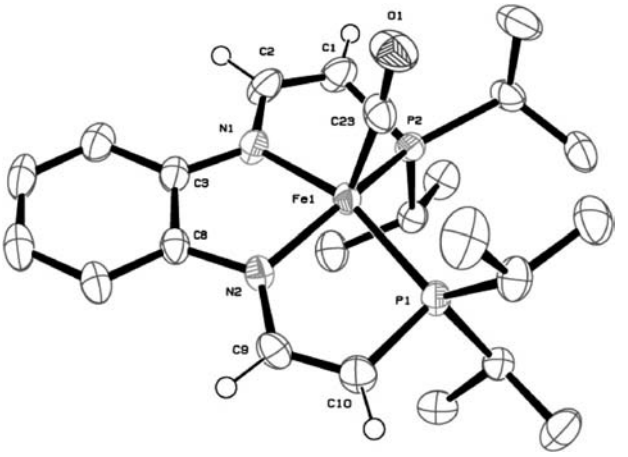

Figure 3. ORTEP plot (thermal ellipsoids at 50% probability) of the X-ray crystal structure of **5b**. Most of the H atoms have been removed for clarity.

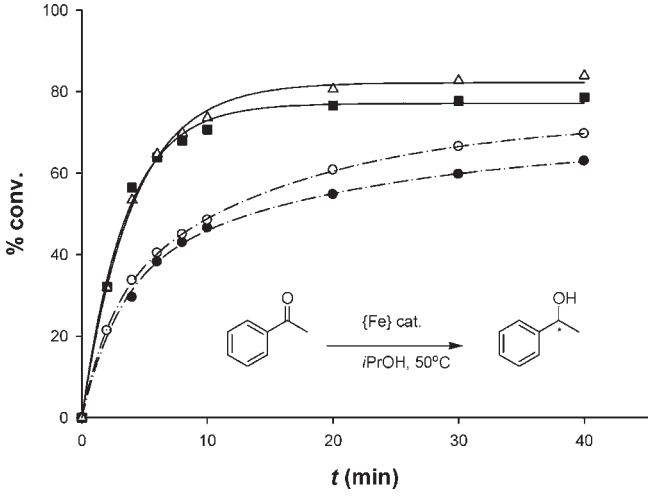

Figure 4. Catalytic transfer hydrogenation of acetophenone to 1-phenylethanol in isopropanol at 50 °C in the presence of (■) (*S*,*S*)-**1f**, KO*t*Bu (catalyst/base/substrate = 1/8/500) (see ref 9); (△) (*S*,*S*)-**2f** (catalyst/substrate = 1/500); (●) **1e**, KO*t*Bu (catalyst/base/substrate = 1/8/200) (see ref 9); (○) **2e** (catalyst/substrate = 1/200).

Ligands chelating via phosphine and ene−amido are rare. Complexes with bidentate $R_2P-CR{=}CH-NAr$ ligands are of interest for their possible use in the Shell higher olefin process.[6] Platinum group metal complexes with tridentate pincer ligands[7] such as $iPr_2P-CH{=}CH-N-CH_2CH_2-PiPr_2$[8] and $iPr_2P-C_6H_3Me-N-C_6H_3Me-PiPr_2$[9] are active toward small-molecule activation. Milstein and co-workers have shown that PNP- and PNN-type ligands [where PNN is 2-(di-*tert*-butylphosphinomethyl)-6-(diethylaminomethyl)pyridine] are reversibly converted into ene−amido forms during catalysis in the ruthenium-catalyzed direct synthesis of amides from alcohols and amines and other dehydrogenative processes.[10] Compounds **2a**−**f** and **5a**−**c** in this report are the first examples of tetradentate ene−amido phosphine ligands.

Complexes **2a**−**f** were tested as catalysts for the transfer hydrogenation of acetophenone to 1-phenylethanol in isopropanol at 50 °C without the addition of base. Complexes **2a**−**d** were inactive while complexes **2e** and (*S*,*S*)-**2f** were active for transfer hydrogenation. The fact that **2a**−**d** were not active was not surprising because we previously ascribed the inactivity of their parent compounds under transfer hydrogenation to the steric crowding of the Cy or *i*Pr substituents on phosphorus.[2b] The catalytic activities of **2e** and (*S*,*S*)-**2f** were similar to those of their parent compounds **1e** and (*S*,*S*)-**1f**, respectively, upon activation with base (Figure 4). However, in the case of (*S*,*S*)-**2f**, the order of addition of substrate caused a significant change in the activity. When isopropanol was added first and then the acetophenone substrate, the activity profile was identical to that for (*S*,*S*)-**1f** and base (Figure 4). However, when acetophenone was added first and then isopropanol, the catalysis was slower (see the Supporting Information). The observed difference signifies that for productive catalyst activation, interaction with isopropanol must occur first, before interaction with the substrate.

A similar enantiomeric excess of (*R*)-1-phenylethanol was obtained after transfer hydrogenation using (*S*,*S*)-**2f** (52%) in comparison to its parent compound (*S*,*S*)-**1f** (52%) at 50% conversion.[10] This observation also implies that, in situ, the activated precatalyst and compounds **2e** and **2f** both lead to similar active species and that base does not play any further role in the catalysis.

The base-sensitive substrate 4-acetylbenzoate ethyl ester[3a] was tested for transfer hydrogenation using (*S*,*S*)-**2f**. The compound was reduced, but both the ethyl ester and the isopropanol ester of the alcohol were produced. Therefore, base must be generated when (*S*,*S*)-**2f** reacts with isopropanol, and this catalyzes the transesterification reaction.

In conclusion, we have isolated a series of five-coordinate iron(II) complexes formed from the deprotonation of the ligand by base, specifically at the carbon α to the phosphorus on the PNNP ligand backbone. The complexes that were active for the transfer hydrogenation of acetophenone in isopropanol had catalytic behavior similar to that for catalysts generated from precursor complexes by reaction with excess base. Hence, we have identified intermediates that are close to, or within, the catalytic cycle. These compounds may be of use in the activation of other small molecules and are currently under investigation in our group.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, spectroscopic data for new compounds, and complete crystallographic data (CIF) for complexes **3**, **4a**, **4b**, and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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