Supporting Information

Unprecedented Iron-Catalyzed Selective Hydrogenation of Activated Amides to Amines and Alcohols

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1. General Procedure:

All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glovebox equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques under argon atmosphere. All solvents were reagent grade or better. Non-deuterated solvents were dried over sodium/benzophenoneketyl (tetrahydrofuran, n-pentane, 1,4-dioxane, diethyl ether and toluene), magnesium (MeOH, EtOH and isopropanol) and distilled under argon atmosphere. All solvents were degassed with argon and kept in the glove box over activated 4Å molecular sieves. Deuterated solvents were purchased from Aldrich, purged with argon and stored over activated 4Å molecular sieves in the glove box. $^1$H, $^{13}$C, $^{31}$P and $^{19}$F NMR spectra were recorded using Bruker AMX-300 and AMX-400 NMR spectrometers. All spectra were recorded at 295 K, unless otherwise noted. NMR spectroscopy abbreviations: br, broad; s, singlet; d, doublet; m, multiplet. GCMS was carried out on HP 6890 (flame ionization detector and thermal conductivity detector) and HP 5973 (MS detector) instruments equipped with a 30 m column (Restek 5MS, 0.32 mm internal diameter) with a 5% phenylmethylsilicone coating (0.25 mm) and helium as carrier gas. GC analysis were carried out using a Carboxen 1000 column on a HP 690 series GC system or HP-5 cross linked 5% phenylmethylsilicone column (30m $\times$0.32mm $\times$ 0.25 µm film thickness, FID) on a HP 6890 series GC system. Commercially available reagents were used as received. All the products of the catalytic experiments are commercially available and were identified by comparison either with $^1$H NMR spectra or GC-MS analysis with those of the commercially available compounds. The following amides were obtained from commercial sources: 2,2,2-trifluoro-N-phenylacetamide and 2,2,2-trifluoro N-benzylacetamide. All other activated amides are also commercially available which were either purchased or prepared according to literature procedures.$^{[1-10]}$

Complexes 1, 2 and 3 were prepared as reported previously.$^{[11-13]}$
2. Experimental procedure for the catalytic reactions:

a) General procedure for the optimization experiments (Table S1):

In an inert atmosphere glove box (10-2 mol%) of complexes 1-3 (according to Table S1) were dissolved in 1.5 mL of 1,4-dioxane and an amount of base according to Table S1 was added to it and kept stirring for 5 min. Then 0.5 mmol of 2,2,2-trifluoro-N-phenylacetamide were added and the reaction mixture was placed in a high pressure autoclave and taken out of the glove box. The autoclave was pressurized with H₂ (see Table S1) and kept in an oil bath pre-heated at 140 °C with stirring for the specified time. The reaction mixture was then cooled down in an ice bath and H₂ was vented off. The conversions and yields of aniline were determined by GC-MS analysis.

b) General procedure for the catalytic hydrogenation reactions (Table 1):

Complex 3 (2-5 mol%) was dissolved in 1.5 mL of 1,4-dioxane in a glove box and 3 equivalents of KHMDS were added to it. The solution was stirred for 5 min. and the respective amide (0.5 mmol) (Table 1) was added to this solution. The reaction mixture was placed in a high pressure autoclave. The autoclave was taken out of the glovebox and pressurized with 60 bar H₂ and kept in a pre-heated oil bath at 140 °C with stirring for the specified time. The reaction mixture was then cooled down in an ice bath and H₂ was vented off. Mesitylene (0.5 mmol) was added to the reaction mixture as an internal standard. A sample of 50 microliter of the reaction mixture was placed in a NMR tube and 0.3 mL CDCl₃ was added to it, and $^{19}$F{$^1$H} NMR was measured in a 300 MHz spectrometer with (ns =1 and d1 = 1s). The yields of trifluoroethanol were determined by the integration ratio of the $^{19}$F{$^1$H} NMR resonances of the hydrogenated reaction mixtures. The conversion and yield of amines were determined by GC analysis using the mesitylene as an internal standard. All the product amines and trifluoroethanol were identified by $^{19}$F{$^1$H} NMR and GC-MS analysis in comparison with authentic commercially available samples.
3. Table S1. Optimization reactions for amide hydrogenation.

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*Conditions: amide (0.5 mmol), catalyst (10-2 mol%), base and dry 1,4-dioxane (1.5 mL), heated in an autoclave at 140 °C bath temperature under 60 bar H₂. *a* yields and conversions determined by GC-MS analysis and yield based on aniline. *b* 10 mol% (tBuPNPiFeBr₂) was used as catalyst and 10 mol% NaHBEt₃ as hydride source. *c* 10 mol% FeBr₂ and 10 mol% NaHBEt₃ was used. *d* 10 bar H₂; *e* 30 bar H₂. *f* RT °60 °C '100 °C '140°C. *g* THF used as solvent isoluene used as solvent. *h* The reaction was carried out in a pressure tube in the absence of H₂.

Initially, we observed that better conversion (67%) was obtained upon increasing the amount of KOrBu (30 mol%) with respect to the catalyst (10 mol%) (Table S1, entry 4). Also, the stronger base KHMDS (potassium hexamethyldisilazane) was found to be superior to KOrBu. After 18 h, with 5.0 mol% of I and 15 mol% of KHMDS under the same conditions of pressure and temperature (60 bar H₂ and 140 ºC.), 46% of the amide was hydrogenated to aniline and trifluoroethanol, whereas use of tBuOK as base under
the same condition gave only 21% conversion (Table S1, entries 5 and 6). Decreasing either the pressure (Table S1, entries 7 and 8) or temperature (Table S1, entries 9-12) led to a drop in the efficiency of the catalysis. Dioxane was a better reaction solvent than THF or toluene (Table S1, entries 13 and 14).

A control experiment in the absence of H₂ with a loading of 2 mol% catalyst 3, 6 mol% KHMDS at 140 °C using dioxane as solvent did not show any conversion of 2,2,2-trifluor-N-phenylacetamide after 7 h, as revealed by the GC-MS analysis, indicating that base attack on the amide to generate aniline does not occur under the reaction conditions (Table S1, entry 22). For the rest of the entries, see the main text.
4. Selected $^{19}\text{F}\{^{1}\text{H}\}$ NMR spectra of the reaction mixtures of the hydrogenated amides:

**Figure S1.** $^{19}\text{F}\{^{1}\text{H}\}$ NMR spectrum of the catalytic reaction of (4-$N,N$-dimethylphenyl)-2,2,2-trifluoroacetamide described in Table 2, entry 3 (ns = 1, d1 = 1 sec, CDCl$_3$, 23 °C).
Figure S2. $^{19}$F-$^1$H NMR spectrum of the catalytic reaction of 2,2,2-trifluoro-N-cyclohexylacetamide described in Table 2, entry 5 (ns = 1, d1 = 1 sec, CDCl$_3$, 23 °C).

Figure S3. $^{19}$F-$^1$H NMR spectrum of the catalytic reaction of 2,2,2-trifluoro-N-hexyl acetamide described in Table 2, entry 6 (ns = 1, d1 = 1 sec, 282.4 MHz, CDCl$_3$, 23 °C).

Figure S4. $^{19}$F-$^1$H NMR spectrum of the catalytic reaction of 2,2,2-trifluoro-N-methylacetamide described in Table 2, entry 7 (ns = 1, d1 = 1 sec, CDCl$_3$, 23 °C).
**Figure S5.** $^{19}\text{F}\{^1\text{H}\}$ NMR spectrum of the catalytic reaction of 2,2,2-trifluoro $N$-benzylacetamide described in Table 2, entry 8 (ns = 1, d1 = 1 sec, CDCl$_3$, 23 °C).
Figure S6. $^{19}$F{$_1$H} NMR spectrum of the catalytic reaction of 2,2,2-trifluoro N-(4-fluorobenzyl)acetamide described in Table 2, entry 9 (ns = 1, d1 = 1 sec, CDCl$_3$, 23 °C).

Figure S7. $^{19}$F{$_1$H} NMR spectrum of the catalytic reaction of 2,2,2-trifluoro N-(4-methylbenzyl) acetamide described in Table 2, entry 10 (ns = 1, d1 = 1 sec, CDCl$_3$, 23 °C).

5. Stoichiometric experiments:
While no reaction of complex 1 with 3 equiv. 2,2,2-trifluoro-N-phenylacetamide at room temperature in 1, 4-dioxane was observed, complex 2 reacts with 3 equiv. 2,2,2-trifluoro-N-phenylacetamide at room temperature giving a new species of type C (Scheme 2) as revealed by $^1$H NMR and $^{31}$P NMR spectroscopy.

Reaction of [(iPr-PNP)Fe(H)(BH$_4$)(CO)] (2) with 2,2,2- trifluoro-N-phenylacetamide (3 equiv.) in 1,4-dioxane.
Complex 2 (7 mg) was dissolved in 0.5 mL of 1,4-dioxane and the solution was transferred to a Young NMR tube. The recorded $^1$H and $^{31}$P{$_1$H} NMR spectra were according to a literature report.$^{[11]}$
2,2,2-trifluoro-N-phenylacetamide (3 equiv.) was added and \(^1\)H, and \(^{31}\)P\{\(^1\)H\}\(\)NMR spectra were recorded over time. Monitoring the reaction mixture by \(^1\)H and \(^{31}\)P NMR at room temperature, after 30 min of mixing a new triplet hydride signal at -18.4 ppm was observed, which is shifted up field compared to complex 2, and \(^{31}\)P NMR revealed a new singlet at 88 ppm (Figure S8 and S9). Complete conversion of 2 to this new species took place after 3 h. This new species is very likely the monohydride with a \textit{trans} anionic ligand of type C in Scheme 2. The \(^1\)H and \(^{31}\)P NMR spectra recorded are shown in Figure S8 and S9. A broad borohydride signal at -5.7 ppm might indicate BH\(_3\) coordinated to solvent or to excess substrate. The above mentioned observations are in accord with our proposed mechanism shown in Scheme 2.

![Figure S8](image)

**Figure S8.** \(^1\)H NMR spectrum of the reaction of 2,2,2-trifluoro N-phenylacetamide with complex 2 in dioxane over time at RT.
Figure S9. $^{31}\text{P}^{1\text{H}}$ NMR spectra of the reaction of 2,2,2-trifluoro N-phenylacetamide with complex 2 in dioxane over time at RT.

6. REFERENCES:


