

Electronic Supplementary Information

Homogeneous Cobalt-Catalyzed Deoxygenative Hydrogenation of Amides to Amines

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1. GENERAL INFORMATION

All reagents were obtained commercially from various chemical companies and were used without further purification, unless otherwise mentioned. Phosphine ligands **L2**, **L3**, **L4**, **L5**, **L6** and **L7** were synthesized according to previously described methodology.¹ Dry and oxygen-free solvents (acetonitrile, DCM, toluene, THF, methanol and ethanol, heptane and hexane, ethyl ether) were collected from an Innovative Technology PS-MD-6 solvent purification system and stored over 3 Å molecular sieves, or they were bought from various suppliers in anhydrous grade. Deuterated organic solvents (CDCl₃) were purchased from euriso-top, degassed by freeze-pump-thaw techniques and subsequently dried over 3 Å molecular sieves. All manipulations involving air- and moisture-sensitive organometallic compounds were carried out in glovebox or using standard Schlenk techniques under an argon atmosphere. All hydrogenation experiments were carried out in 300 mL autoclave (PARR Instrument Company). In order to avoid unspecific reductions, all catalytic reactions were carried out in 4 mL glass vials, which were set in an alloy plate and placed inside the autoclave. GC conversion and yields were determined by GC-FID, HP 6890 with FID detector, column HP530 m x 250 mm x 0.25 µm and using *n*-hexadecane as an internal standard. Mass spectra were recorded on a GC-MS Agilent 5973 Network equipped with a mass selective detector. HRMS measurements were recorded on a MAT 95XP ThermoFisher Mass Spectrometer using Electrospray Ionization mode in UPLC (ultra-pressure) equipment. The products were isolated by silica gel column chromatography using (*n*-heptane / AcOEt) mixtures as eluent. ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra were recorded on a Bruker AV 300 or Bruker AV 400 spectrometer. All chemical shifts (δ) are reported in parts per million (ppm) downfield of tetramethylsilane and coupling constants (*J*) in hertz (Hz). The residual solvent signals were used as references for ¹H and ¹³C NMR spectra (CDCl₃: δH = 7.26 ppm, δC = 77.16 ppm). Abbreviations used in the reported NMR experiments: b, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. All measurements were carried out at room temperature unless otherwise stated. Diffraction data were collected on a Bruker Kappa APEX II Duo diffractometer. The structures were solved by direct methods² and refined by full-matrix least-squares procedures on *F*².³ XP (Bruker AXS) was used for graphical representations.

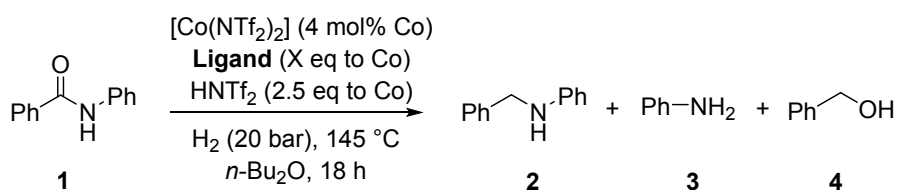
2. GENERAL EXPERIMENTAL PROCEDURES

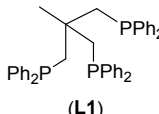



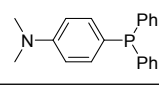
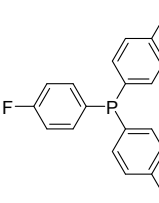
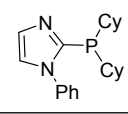
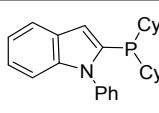
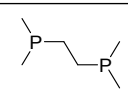
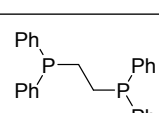
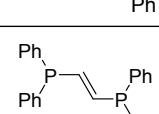
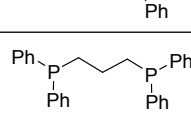
General procedure for the hydrogenation of amides: A 4 mL glass vial containing a stirring bar was sequentially charged with Co(N(Tf)₂)₂ (7.7 mg, 0.0125 mmol, 5 mol%), Ligand (**L3**) (12 mg, 0.015 mmol, 6 mol%), amide (0.25 mmol), SiMe₃OTf (10-12.5 mol%) as additive and *n*-heptane (2.0 mL) as solvent. Afterwards, the reaction vial was capped with a septum equipped with a syringe and set in the alloy plate, which was then placed into a 300 mL autoclave. Once sealed, the autoclave was purged three times with 10 bar of hydrogen, then pressurized to 5-10 bar and placed into an aluminium block, which was preheated at 125-135 °C. After 14/24 h, the autoclave was cooled in an ice bath and the remaining gas was carefully released. Finally, *n*-hexadecane (20 mg) was added as an external standard, and the reaction mixture was diluted with ethyl acetate and analysed by gas chromatography or it was purified directly by silica gel column chromatography to give the corresponding product as isolated yields.

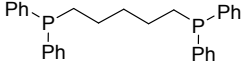
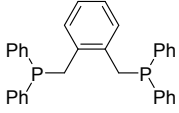
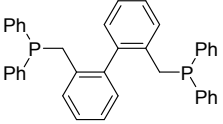
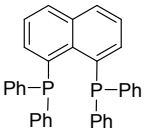
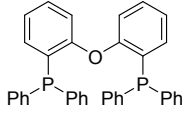
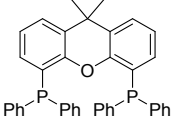
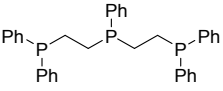
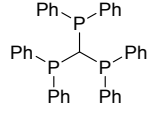
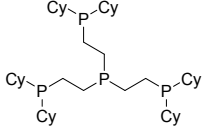
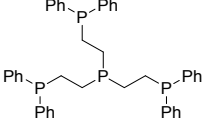
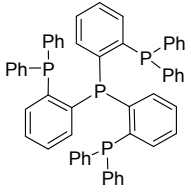
Note: the additive SiMe₃OTf was stored in the glove box and its addition to the catalytic reaction mixture took place inside the glove box.

3. ADDITIONAL TABLES

Table S1. Cobalt-catalyzed hydrogenation of benzanilide (**1**): Evaluation of the catalytic activity for mono- and multidentate phosphine ligands.



Entry ^[a]	Ligand	X eq	Conv. (%)	2 (%) ^[b]	3 (%) ^[b]	4 (%) ^[b]
1	 (L1)	2	95	46	49	49
2		6	-	-	-	-
3		6	-	-	-	-
4		6	-	-	-	-
5		6	-	-	-	-
6		6	-	-	-	-
7		6	<5	-	-	-
8		6	-	-	-	-
9		3	19	-	-	-
10		3	-	-	-	-
11		3	-	-	-	-
12		3	-	-	-	-

13		3	-	-	-	-
14		3	-	-	-	-
15		3	-	-	-	-
16		3	-	-	-	-
17		3	-	-	-	-
18		3	-	-	-	-
19		2	-	-	-	-
20		2	<5	-	-	-
21		2	-	-	-	-
22		2	-	-	-	-
23		2	-	-	-	-

[a] Standard reaction conditions: benzanilide **1** (49.3 mg, 0.25 mmol), $[\text{Co}(\text{NTf}_2)_2]$ (0.01 mmol, 4 mol%), Ligand (x equiv to Co), HNTf_2 (0.025 mmol, 10 mol%, 2.5 equiv to Co), $n\text{-Bu}_2\text{O}$ (2 mL) and H_2 (20 bar) at 145 °C. [b] Conversion of **1** and yield of products **2**, **3** and **4** were calculated by GC using $n\text{-hexadecane}$ as internal standard.

4. ADDITIONAL FIGURES

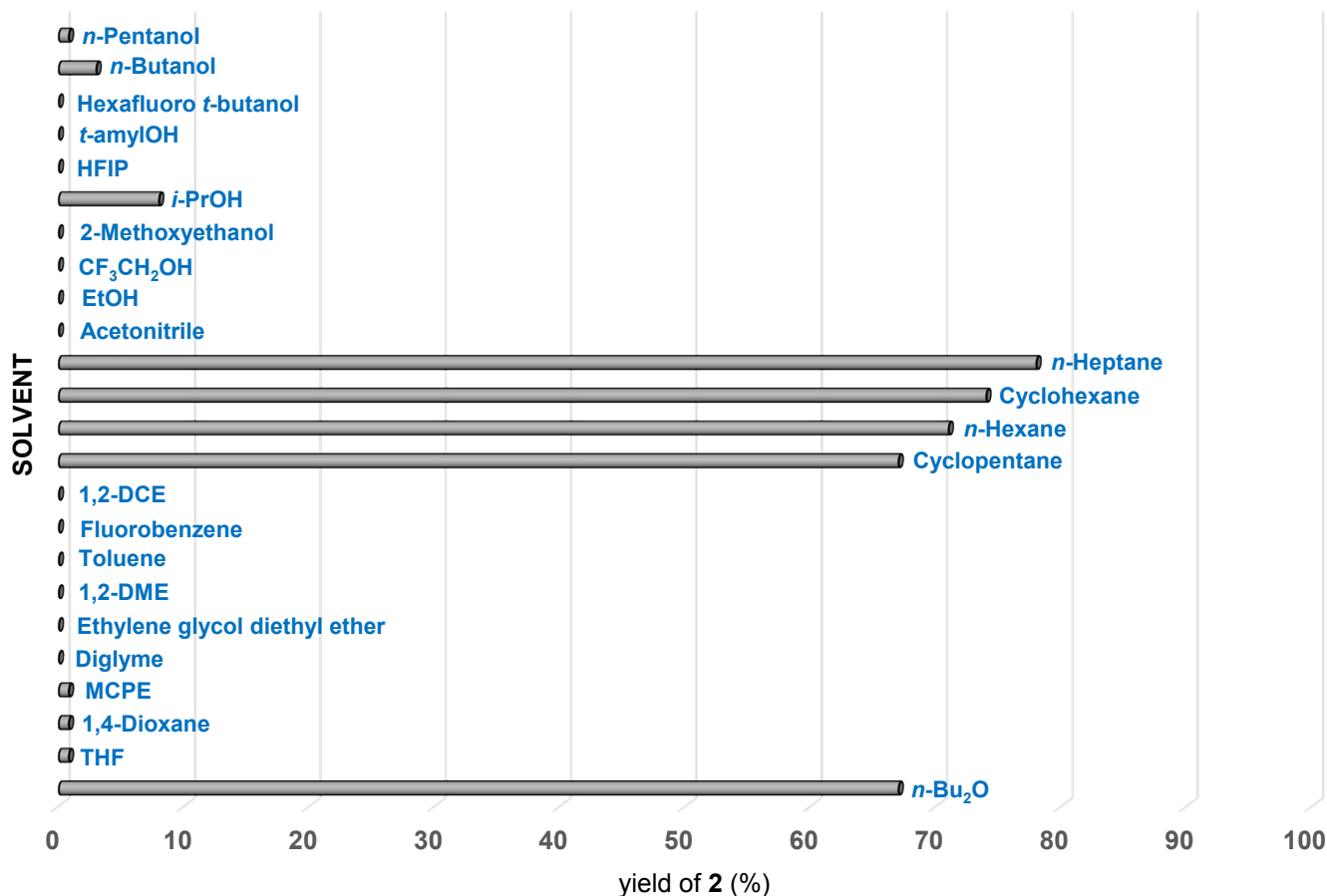
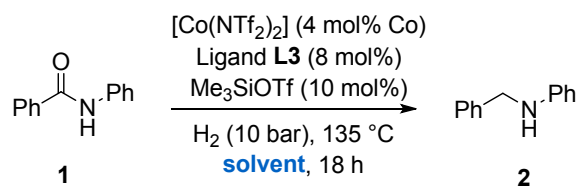


Figure S1. Deoxygenative hydrogenation of benzanilide (**1**) with [Co(NTf₂)₂]/**L3**/Me₃SiOTf system in the presence of different solvents. Standard reaction conditions: benzanilide **1** (50.3 mg, 0.25 mmol), [Co(NTf₂)₂] (0.01 mmol, 4 mol%), Ligand **L3** (0.02 mmol, 8 mol%, 2 equiv to Co), [Me₃SiOTf] (0.025 mmol, 10 mol%, 2.5 equiv to Co), solvent (2 mL) and H₂ (10 bar) at 135 °C. Conversion of **1** and yield of product **2** was calculated by GC using *n*-hexadecane as internal standard.

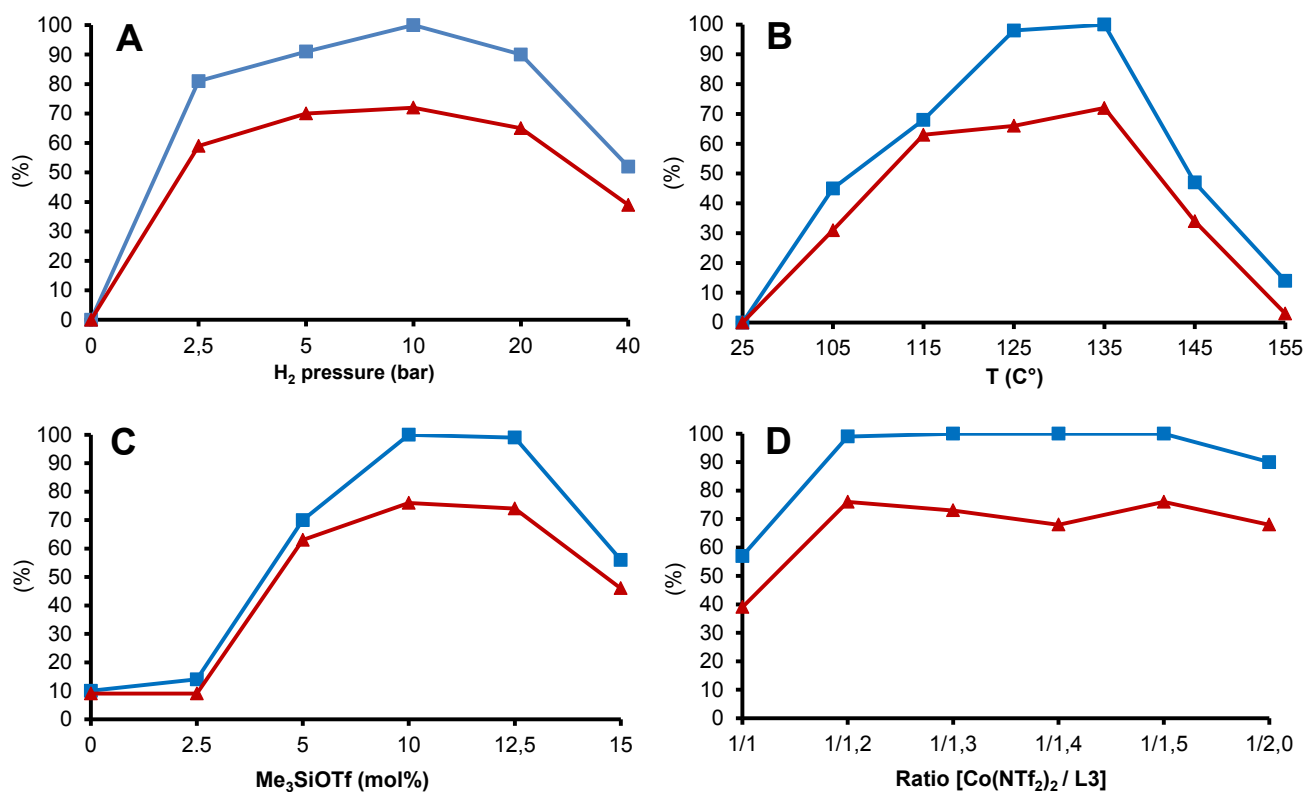
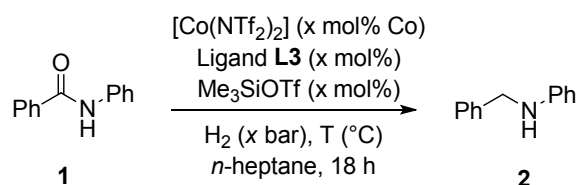


Figure S2. Deoxygenative hydrogenation of benzanilide (**1**) with [Co(NTf₂)₂]/L3/Me₃SiOTf system using *n*-heptane as solvent: further optimization of additional reaction conditions. The graphics show the conversion of amide **1** (% , blue line) and the yield of higher amine **2** (% , red line) obtained *versus* A) molecular hydrogen pressure, B) reaction temperature C) amount of Me₃SiOTf additive (keeping constant cobalt precursor and 2 equiv of ligand **L3** respect to cobalt), and D) [Co(NTf₂)₂]/L3 molar ratio (keeping constant 2.5 equiv of Me₃SiOTf additive respect to cobalt). Standard reaction conditions: benzanilide (**1**) (50.3 mg, 0.25 mmol), [Co(NTf₂)₂] (2-5 mol%), Ligand **L3** (4-12 mol%), [Me₃SiOTf] (2.5-15 mol%), *n*-heptane (2 mL) and H₂ (2.5-40 bar) from 25 to 155 °C. Conversion of **1** and yield of product **2** was calculated by GC using *n*-hexadecane as internal standard.

5. SYNTHESIS AND CHARACTERIZATION OF COMPLEX $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$

Under an argon atmosphere, a 25 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with $[\text{Co}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}]$ (170.3 mg, 0.5 mmol) and ligand **L3** (442.6 mg, 0.55 mmol, 1.1 equiv); they were dissolved in 15 mL of dry THF and the brown mixture was stirred overnight at 70 °C. Afterwards the resulting brown mixture was cooled to room temperature allowing the deposition of the brown powder. After filtration, the brownish solid was washed several times with diethyl ether and then dried under reduced pressure. 690 mg of $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$ could be isolated (71% yield). The complex is paramagnetic. Crystals suitable for X-ray analysis were grown by vapor diffusion of pentane into a concentrated solution of $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$ in dichloromethane. ESI-LCMS [m/z pos, calculated for $\text{C}_{47}\text{H}_{51}\text{CoFO}_6\text{P}_3$: 882.22] found m/z 882.

Crystal structure analysis of $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$:

Data were collected on a Bruker Kappa APEX II Duo diffractometer. The structure was solved by direct methods² and refined by full-matrix least-squares procedures on F^2 .³ XP (Bruker AXS) and Diamond (Diamond - Crystal and Molecular Structure Visualization, Crystal Impact - Dr. H. Putz & Dr. K. Brandenburg GbR, Kreuzherrenstr. 102, 53227 Bonn, Germany, <http://www.crystalimpact.com/diamond>) were used for graphical representations. Crystals of $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$ contain co-crystallized solvent (see Figure S3). Contributions of further solvent molecules were removed from the diffraction data with PLATON/SQUEEZE.⁴

Crystal data of $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$: $\text{C}_{95}\text{H}_{104}\text{B}_2\text{Cl}_2\text{Co}_2\text{F}_{10}\text{O}_{12}\text{P}_6$, $M = 2023.98$, orthorhombic, space group $Pbca$, $a = 26.2086(8)$, $b = 27.5599(8)$, $c = 28.9629(8)$ Å, $V = 20920.1(11)$ Å³, $T = 150(2)$ K, $Z = 8$, 140227 reflections measured, 18493 independent reflections ($R_{\text{int}} = 0.0419$), final R values ($I > 2\sigma(I)$): $R_1 = 0.0509$, $wR_2 = 0.1304$, final R values (all data): $R_1 = 0.0560$, $wR_2 = 0.1345$, 1105 parameters.

CCDC 1972329 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

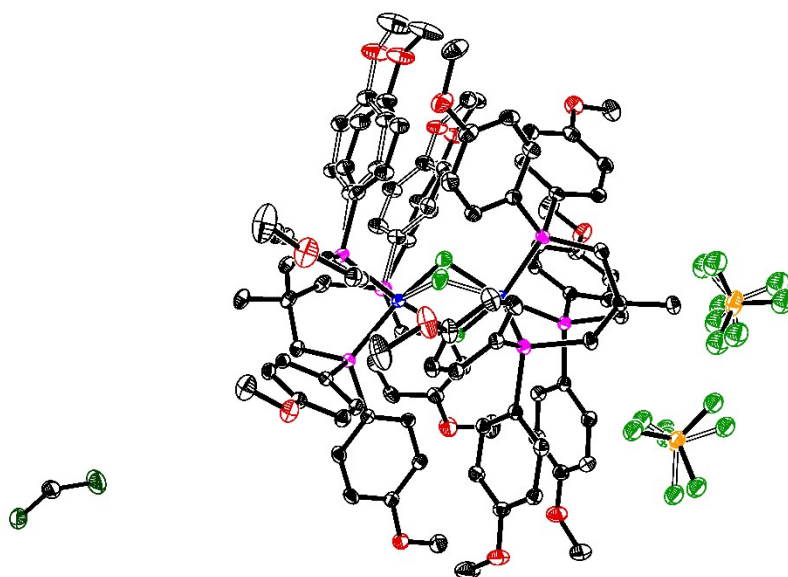


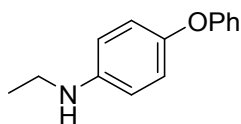
Figure S3. Molecular structure of $[\text{Co}(\text{L3})\text{F}_2](\text{BF}_4)_2$. Hydrogen atoms are omitted for clarity. Displacement ellipsoids correspond to 30% probability. The anions are disordered and the cation is also partly disordered; minor occupancy components are depicted with white coloured bonds.

6. SYNTHESIS AND CHARACTERIZATION OF COMPLEX [Co/(L3)/OTf]OTf

Under an argon atmosphere, a 25 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with [Co(L3)F]₂(BF₄)₂ (387.8 mg, 0.2 mmol) and [SiMe₃OTf] (177.8 mg, 0.144 mL, 0.8 mmol, 4 equiv); they were dissolved in 15 mL dry THF and the light brown solution was stirred overnight at 70 °C. Afterwards the solution was cooled to room temperature and the solvent removed by evaporation under reduced pressure. The gold-colored powder was washed several times with pentane and then with diethyl ether; in the end the solid was dried under reduced pressure. The complex is paramagnetic; the cobalt complex could be assigned to [Co/(L3)/OTf]OTf according to HR-MS.

ESI-HRMS [m/z pos; calculated for C₄₈H₅₁CoF₃O₉P₃S: 1012,1751] found m/z 1012,1781. [m/z neg; found m/z 148,9525]

7. CHARACTERIZATION DATA OF THE ISOLATED PRODUCTS



N-ethyl-4-phenoxyaniline Isolated yield: 82%. (The NMR spectrum is consistent with the reported data). ¹H NMR (400MHz, CDCl₃): ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.26 (m, 2H), 7.03-6.99 (t, 1H), 6.95-6.91 (m, 4H), 6.62-6.60 (m, 2H), 3.18-3.13 (q, 2H), 1.29-1.26 (q, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.28, 147.58, 145.27, 129.59, 121.98, 121.39, 117.14, 113.81, 39.14, 15.06.

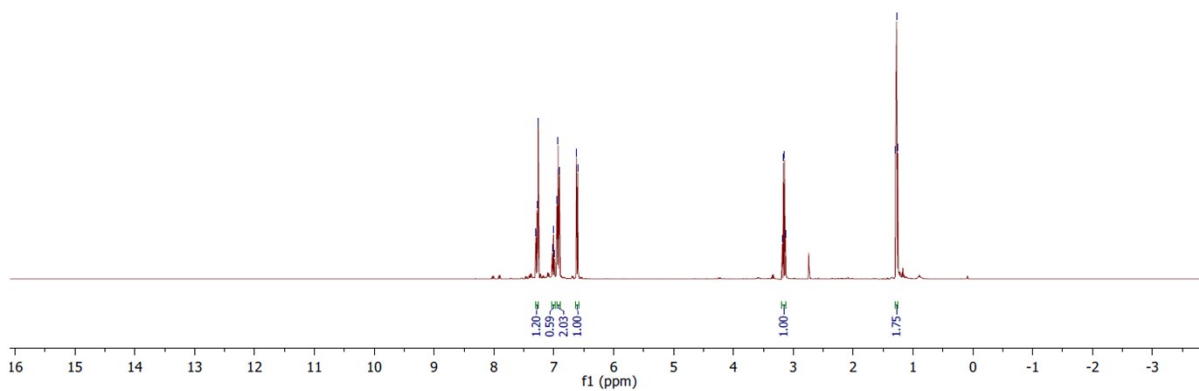
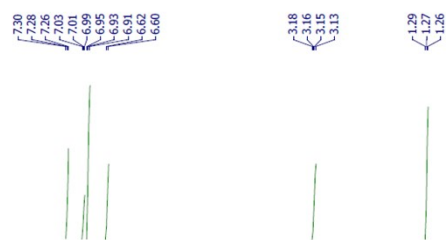
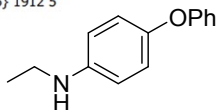
8. REFERENCES

1. Liu, W.; Sahoo, B.; Spannenberg, A.; Junge, K.; Beller, M., Tailored Cobalt-Catalysts for Reductive Alkylation of Amines with Carboxylic Acids under Mild Conditions. *Angew.Chem., Int.Ed.* **2018**, *57* (36), 11673-11677.
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4. Spek, A. L.. PLATON SQUEEZE: a tool for the calculation of the disordered solvent contribution to the calculated structure factors. *Acta Cryst.* **2015**, *C71*, 9-18.

9. NMR SPECTRA OF THE ISOLATED PRODUCTS

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¹H NMR



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¹³C NMR

