Supporting Information for

Base-Free Iridium-Catalyzed Hydrogenation of Esters and Lactones

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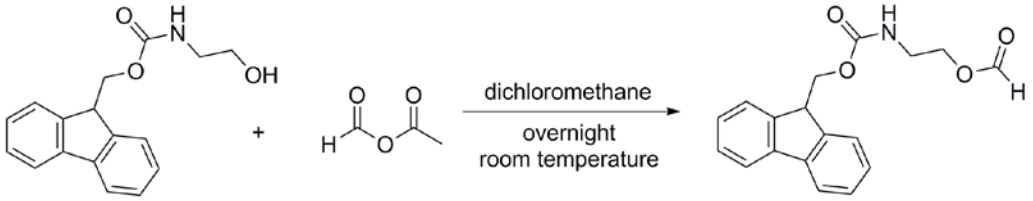
Experimental Details

Materials and Methods:

Procedures were performed using standard Schlenk techniques or in a nitrogen glovebox unless otherwise specified. Tetrahydrofuran was dried on a Grubbs-type solvent purification system.[1] All other liquid reagents and solvents were purchased from commercial sources and thoroughly degassed prior to use. $[Cp^*Ir(bpy\text{-}OMe)OH_2][OTf]_2$ (**1**),[2] $[Cp^*Ir(bpy)OH_2][OTf]_2$ (**2**),[3] and $[Cp^*Ir(bpy\text{-}COOMe)OH_2][OTf]_2$ (**3**)[4] were synthesized according to literature procedures. Authentic samples of the cyclic ethers tetrahydropyran,[5] 2-methyl tetrahydropyran[6] and oxepane[7] were synthesized by dehydration of the corresponding diol in the presence of Nafion-H.[8] Ethyl acetate, ethyl formate, methyl acetate, methyl benzoate, and methyl pivalate were obtained from commercial sources and dried according to literature procedures prior to use.[9] Products were verified by comparison with literature spectra. Other reagents were purchased from commercial sources and utilized without further purification. Deuterated solvents ($CDCl_3$, CD_2Cl_2, and CD_3CN) were obtained from Cambridge Isotope Laboratories and used as-received. ^1H NMR spectra were recorded on a 300 MHz Bruker, 500 MHz Bruker, or 500 MHz Varian spectrometer using a 90º pulse angle and a 35 s relaxation delay (unless otherwise specified) and referenced to the residual solvent peak.[10] ^{13}C NMR spectra were recorded on a 500 MHz Bruker spectrometer and referenced to the residual solvent peak.[10] Electrospray ionization mass spectrometry was performed by Loren Kruse at the University of Washington. Elemental analysis was obtained from the CENTC Elemental Analysis Facility at the University of Rochester, funded by NSF CHE-0650456.

Synthesis of 2-(N-fmoc-amino)ethyl formate (E12)



Acetic-formic anhydride[11] was synthesized by the addition of 2.7 mL formic acid (97%) to 5.9 mL of acetic anhydride under inert atmosphere. This material was stored in a Schlenk flask under N_2 and was used without further purification. 2-(N-Fmoc-amino)ethanol was synthesized as described in the literature.[12] In a round-bottom flask, 1.507 g (5.32 mmol) of 2-(N-fmoc-amino)ethanol was dissolved in 60 mL dichloromethane. Formic-acetic anhydride (3 mL, large excess) was added via syringe. The reaction was stirred under air overnight at room temperature. The resulting solution was then extracted with 3 x 60 mL saturated Na_2CO_3. The organic layer was dried over Na_2SO_4, and the volatiles were removed. The crude product was then purified by flash chromatography and isolated as a white powder (silica gel, 70:30 hexanes:ethyl acetate, R_f = 0.4). ^1H NMR (300 MHz, CD_2Cl_2) δ 8.06 (s, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.32 (td, *J* = 7.4, 1.3 Hz, 2H), 5.07 (s, 1H), 4.41 (d, *J* = 6.8 Hz, 2H), 4.22 (m, 3H), 3.46 (q, *J* = 5.7 Hz, 2H). 60 s relaxation delay employed to obtain proper integration of formate proton. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 161.13, 156.56, 144.40, 141.68, 128.04, 127.41, 125.38, 120.32, 66.98, 63.17, 47.65, 40.30. Elemental Analysis: Calculated C 69.44, H 5.50, N 4.50. Measured C 69.18 H 5.58 N 4.45. Yield: 874 mg (53.0%). Melting point: 111.7-113.0°C.

General Procedures for Hydrogenation

High pressure hydrogenation reactions were carried out in 30 or 45 mL Parr Instruments 5000 Multiple Reactor system vessels fitted with a PTFE liners at the stated hydrogen pressure. Products were quantified by ^{1}H NMR spectroscopy against an internal standard (toluene, δ 2.36 in $CDCl_3$ or δ 2.34 in CD_2Cl_2) or by gas chromatography (GC-FID) against an internal standard of 1,4-dioxane. Product identities were confirmed by spiking the reaction mixture with commercial or independently prepared samples. GC-FID analysis was performed on an Agilent Technologies 7890A GC system using an Agilent Technologies DB-FFAP column. Samples were prepared by volumetrically diluting reaction aliquots to 5 mL with acetone. Substrates analyzed by GC-FID: hexyl formate (**E6**), isopropyl formate (**E7**), *tert*-butyl formate (**E8**), phenyl formate (**E9**), benzyl formate (**E10**), anisyl formate (**E11**), γ-butyrolactone (**L1**), γ-valerolactone (**L2**). Reaction mixtures containing 2-(N-fmoc-amino)ethyl formate were analyzed by ^{1}H NMR spectroscopy with a 60 s relaxation delay.

A) Neat Reactions

In a nitrogen-filled glovebox, 10.3 mg (0.012 mmol) of catalyst **1** was weighed into a glass vial and dissolved in 6 mL of substrate. 2 mL aliquots of the resulting yellow solution were dispensed into each of three PTFE-lined Parr reactors containing PTFE-covered stir bars. The reactors were then sealed, removed from the glovebox, briefly purged with H_2, and pressurized. The reaction vessels were heated to the specified temperature for the specified reaction time. Reactors were placed in a cold bath at either 0 °C or –84 °C to cool. Excess pressure was vented and the reactors were shaken and then opened in air. Products were then analyzed by either ^{1}H NMR spectroscopy or GC-FID.

Alternatively, 3.4 mg (0.0040 mmol) catalyst **1** was weighed directly into the PTFE liner, and 2 mL substrate was then added to the reaction vessel. The remaining procedure is as above.

B) Neat Reactions with Acid Additive

In a nitrogen-filled glovebox, $Sc(OTf)_3$ (19.7 mg, 0.0400 mmol) was weighted into each of three PTFE Parr reactor liners. Liners were equipped with stir bars and inserted into the reaction vessels. In a glass vial, catalyst **1** (10.3 mg, 0.0040 mmol) was weighed into a glass vial and dissolved in 6 mL of substrate. From the resulting yellow solution, 2 mL aliquots were dispensed into each of three PTFE-lined Parr reactors containing PTFE-covered stir bars. Reactors were then sealed, removed from the glovebox, briefly purged with H_2, and pressurized at room temperature. The reaction vessels were heated to the specified temperature for the specified reaction time. Reactors were placed in a cold bath at either 0 °C or –84 °C to cool. Excess pressure was vented, and the reactors were shaken and opened in air. Products were then analyzed by either ^{1}H NMR spectroscopy or GC-FID.

C) In Solvent with Acid Additive

In a nitrogen-filled glovebox, catalyst **1** (4.3 mg, 0.0050 mmol) and $Sc(OTf)_3$ (2.5 mg, 0.0050 mmol) were weighed into each of three PTFE Parr reactor liners. Liners were equipped with stir bars and inserted into the reaction vessels. Anhydrous dimethoxyethane (Acros, 1 mL) and substrate (1.0 mmol) was dispensed into each reactor. Reactors were then sealed, removed from the glovebox, briefly purged with H_2, and pressurized at room temperature. The reaction vessels were heated to the specified temperature for the specified reaction time. Reactors were placed in a cold bath at either 0 °C or –84 °C to cool. Excess pressure was vented, and the reactors were shaken and opened in air. Products were then analyzed by either ^{1}H NMR spectroscopy or GC-FID.

D) In Solvent, No Acid

In a nitrogen-filled glovebox, catalyst **1** (4.3 mg, 0.0050 mmol) was weighed into each of three PTFE Parr reactor liners. Liners were equipped with stir bars and inserted into the reaction vessels. Anhydrous dimethoxyethane (Acros, 1 mL) and substrate (1.0 mmol) was dispensed into each reactor. Reactors were then sealed, removed from the glovebox, briefly purged with H_2, and pressurized at room temperature. The reaction vessels were heated to the specified temperature for the specified reaction time. Reactors were placed in a cold bath at either 0 °C or –84 °C to cool. Excess pressure was vented and the reactors were shaken and opened in air. Products were then analyzed by either ^{1}H NMR spectroscopy or GC-FID.

ESI-MS analysis of oligomeric Products: Electrospray ionization mass spectrometry was performed by Loren Kruse at the University of Washington. All samples prepared for ESI-MS were obtained from reactions containing 2 mM catalyst in 2 mL substrate heated at 100 °C for 65 hours (Procedure A).

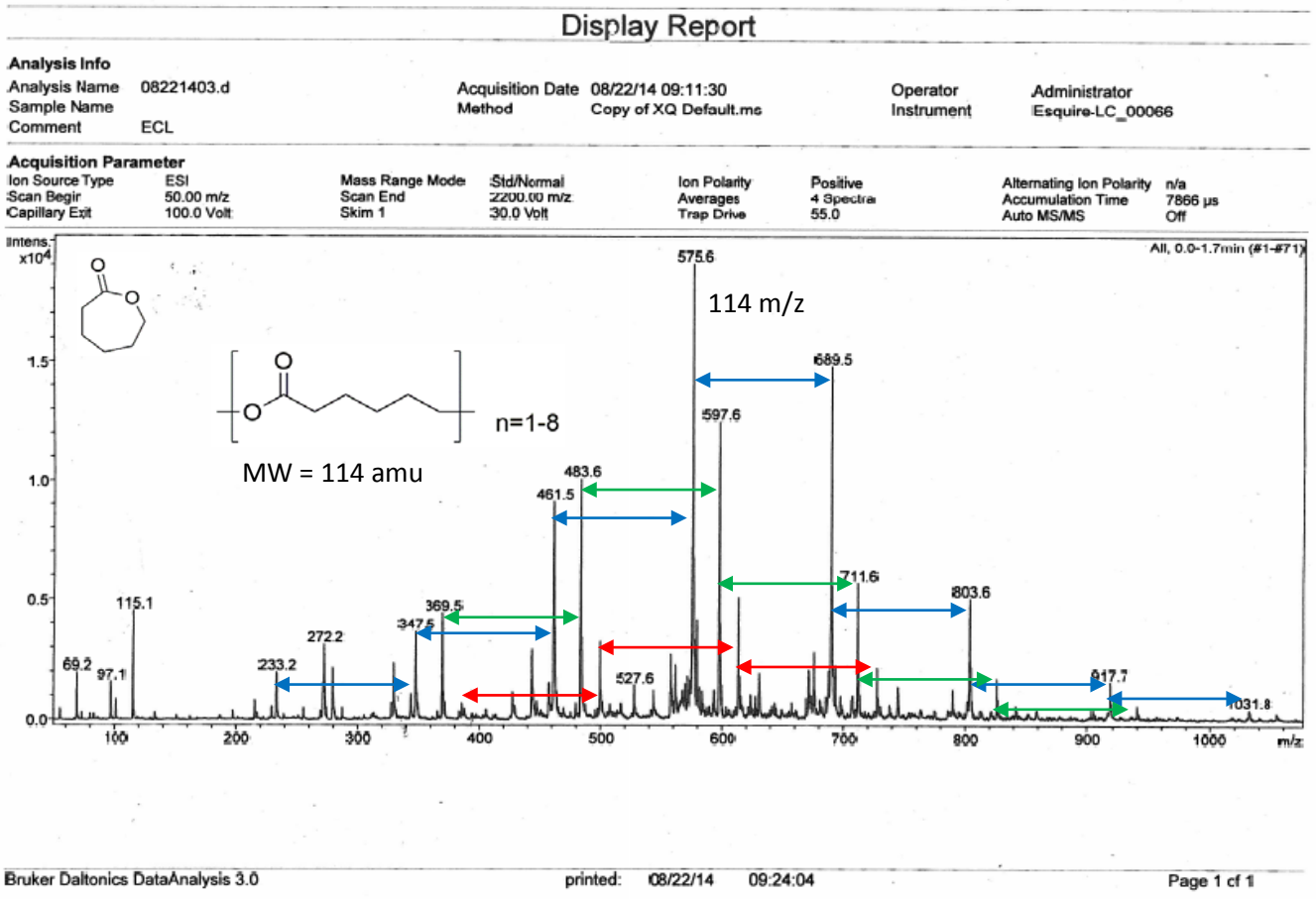


Figure S1. Oligomeric products from hydrogenation of ε-caprolactone.

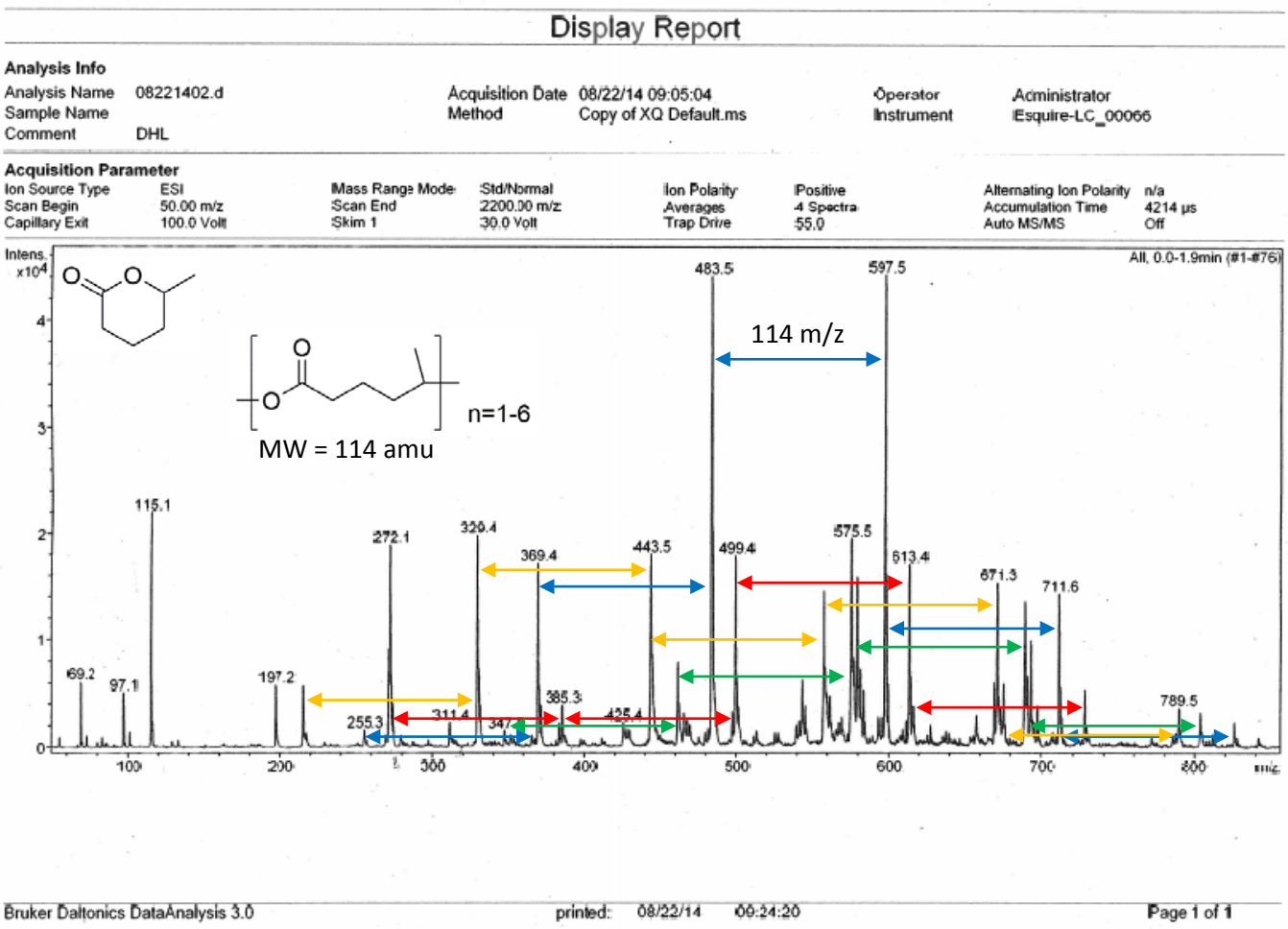


Figure S2. Oligomeric products from hydrogenation of δ-caprolactone.

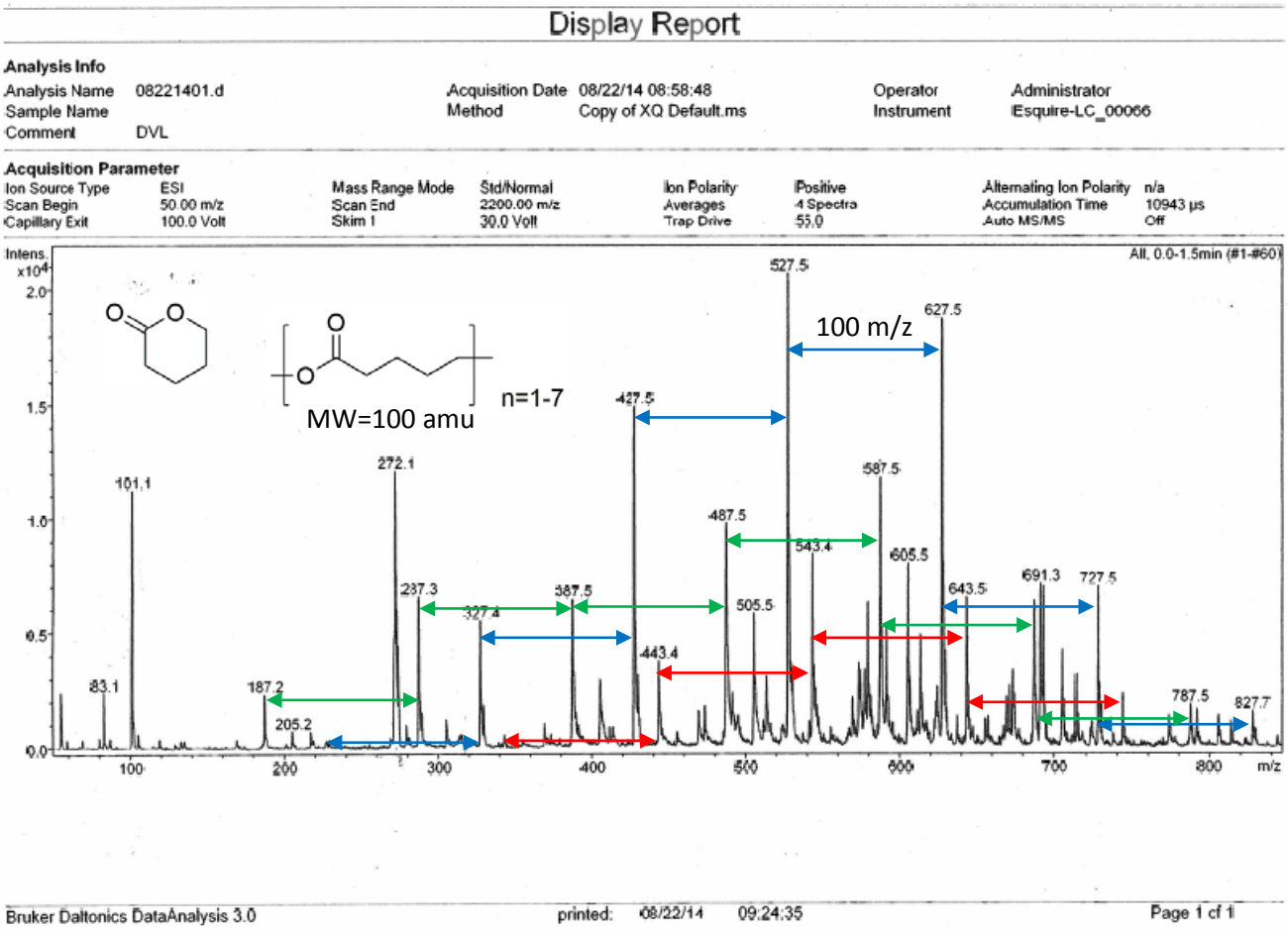


Figure S3. Oligomeric products from hydrogenation of *δ*-valerolactone.

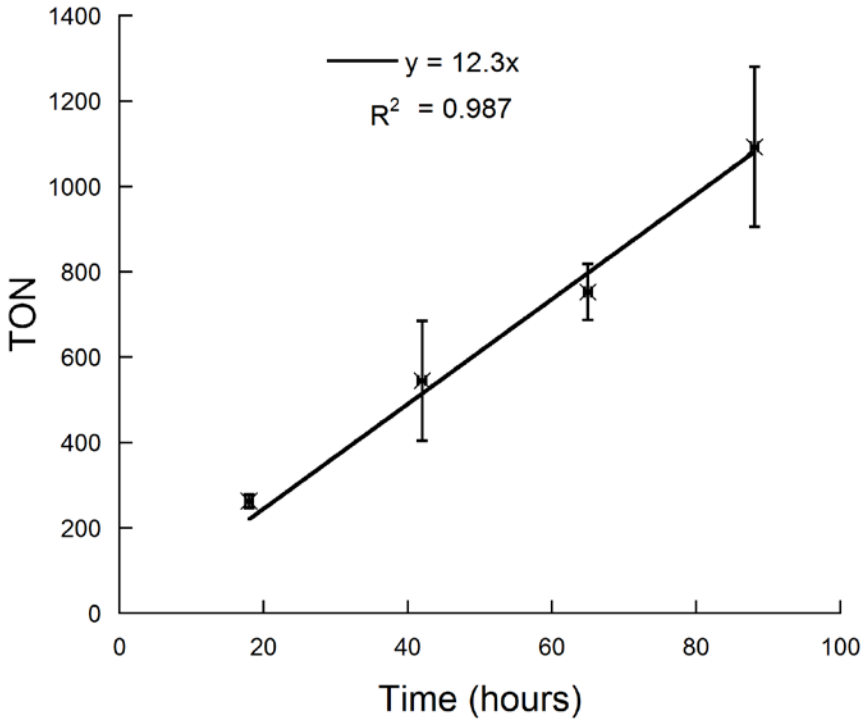


Figure S4. Time course for ethyl acetate hydrogenation. Reactions conducted using 2 mM catalyst **1** in neat ethyl acetate at 30 bar H_2 and 120 °C. Catalyst order experiments run for 18 h to be within this initial rate regime.

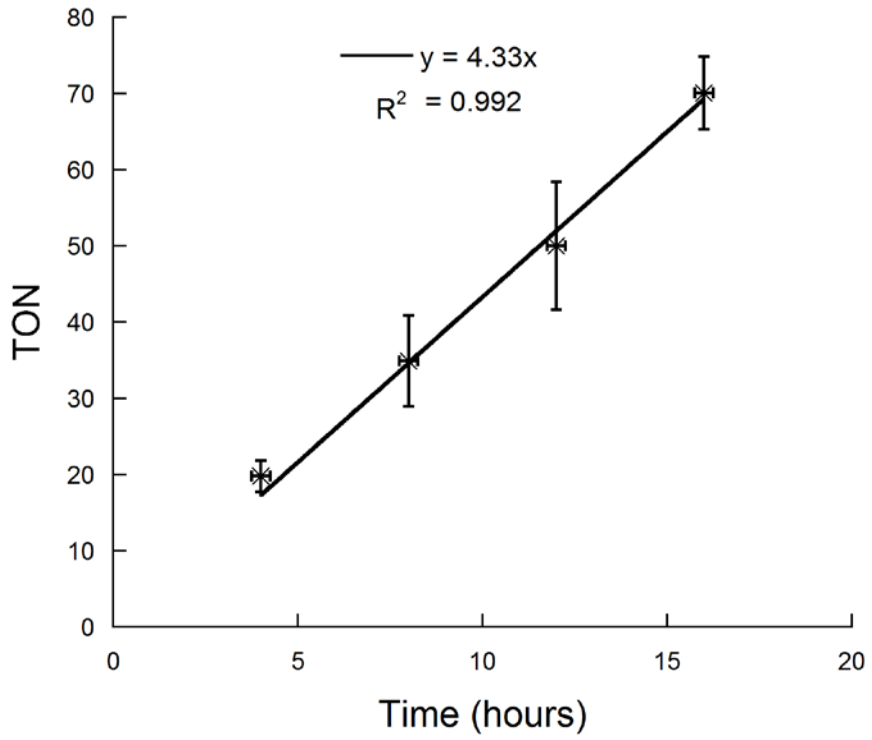


Figure S5. Time course of hexyl formate hydrogenation in DME solution. Reactions conducted using 0.321 M hexyl formate and 2 mM catalyst **1** in DME at 60 bar H_2 and 100 °C. Substrate order experiments run for 4 h to be within this initial rate regime.

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