Supporting Information

Aqueous NMR Signal Enhancement by Reversible Exchange in a Single Step Using Water-Soluble Catalysts

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Experimental Methods

*Synthesis of the PEGylated catalyst (**7**).* General chemicals were purchased from Acros organics and Sigma-Aldrich. Acetone, methylene chloride, chloroform and ethyl acetate were reagent grade and used without further purification unless otherwise mentioned. THF was purified using an M-Braun solvent purification system. Analytical thin layer chromatography (TLC) was conducted on pre-coated silica gel TLC plates (layer thickness 0.25 mm, Sigma-Aldrich). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Mercury 400 MHz instrument using deuterated chloroform ($CDCl_3$). Chemical shifts are reported in (δ) parts per million (ppm). Splitting patterns are abbreviated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

The synthesis of **7** was inspired by the work of Grubbs and co-workers[1] and is summarized in Fig. S1. For the step resulting in the synthesis of **3**: To a solution containing 0.32 g of **1** dissolved in 15 mL of chloroform, 62 mg of DMAP, 0.37 g of 2, and 0.2 mL of pyridine were added in that order. The solution was allowed to stir for 4 hours before the solvent was removed under vacuum. The product was purified by eluting over SiO_2 with DCM then DCM:MeOH 10:1 and dried under vacuum to yield 330 mg of 3 (70%). R_F = 0.18 in DCM:MeOH 10:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 0.6 Hz, 2H), 6.97 (s, 1H), 4.61 (s, 2H), 3.83 – 3.58 (m, 44H), 3.57 – 3.45 (m, 4H), 3.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.33, 139.94, 133.98, 127.94, 127.16, 71.30, 69.96, 69.93, 69.90, 69.87, 69.85, 69.55, 69.22, 58.36, 44.92, 39.28.

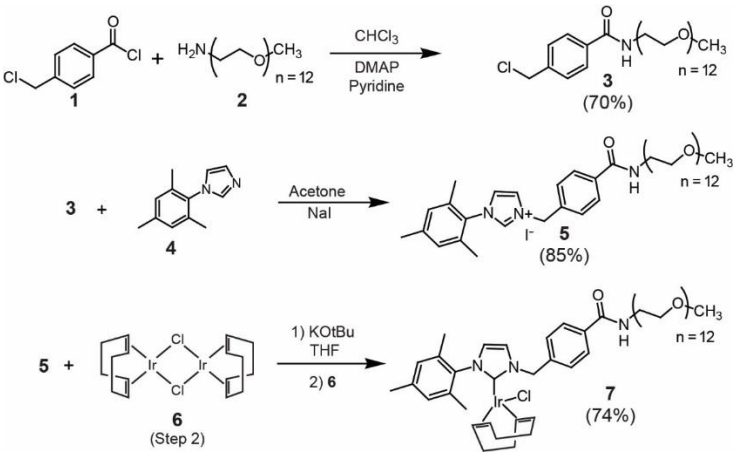

Fig. S1. Summary of synthetic steps for the preparation of the (pre-activated) water-soluble PEGylated heterocyclic aromatic carbene / Ir SABRE catalyst (**7**). 4-(chloromethyl)benzoyl chloride (**1**), is PEGylated (**2**) to produce intermediate product (**3**), which is further combined with 1-mesitylimidazole (**4**) to yield a PEGylated carbene precursor (**5**). In inert atmosphere, the carbene (**5**) is combined with the Ir source ($[Ir(cod)Cl]_2$) (**6**) to yield the new catalyst structure (**7**).

The synthesis of **4** was carried out according to procedures described in the literature (e.g. Ref. [2]), whereas synthesis of **5** proceeded as follows. In a 50 mL round bottom flask, equipped with a condenser, 0.2 g of **3** and 0.058 g of **4** were allowed to reflux with 25 mL of acetone and 0.075 g of NaI. Solvent was removed and the resulting product was dissolved in DCM, filtered through celite, and dried under vacuum. No further purification was necessary. Yield 236 mg (85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.10 (d, J = 8.3 Hz, 2H), 8.05 (s, 1H), 7.83 (d, J = 8.3 Hz, 2H), 7.18 (s, 1H), 6.98 (d, J = 0.6 Hz, 2H), 6.09 (s, 1H), 3.88 – 3.50 (m, 48H), 3.37 (s, 3H), 2.32 (s, 3H), 2.07 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$)) δ 167.32, 140.96, 136.74, 136.53, 134.69, 134.01, 130.41, 129.63, 129.10, 128.42, 123.85, 123.38, 71.11, 71.01, 69.70, 69.47, 69.41, 69.38, 69.36, 69.33, 69.31, 69.26, 69.24, 69.21, 69.18, 69.06, 69.03, 68.89, 68.82, 68.78, 68.62, 58.86, 52.08, 39.16, 20.97, 17.81. HRMS (ESI-TOF) m/z: [M - I]+ Calculated for $C_{45}H_{72}IN_3O_{13}$ is 862.5065; Found 862.5050.

For the synthesis of **7**, in a N_2 filled glove box 80 mg of **5** was dissolved in 8 mL of THF inside a vial. To this solution, 60 μL of a 1 M tBuOK/THF (degassed) solution was added and the

mixture was allowed to stir for 30 minutes. During this time, the solution went from yellow, to clear (upon adding t-BuOK), then back to yellow. In a separate vial, 27 mg of 6 was dissolved in 4 mL of THF and then added dropwise to a solution containing **5**. After the addition, the color changed from dark orange to yellow over the course of 24 hours. The reaction mixture was removed from the glove box, care was taken to minimize long-term exposure to air, and the solvent was removed. The product was purified by eluting over SiO_2 with DCM then DCM:MeOH 20:1 and dried under vacuum to yield 78 mg of **7** (74%). R_F = 0.18 in DCM:MeOH 10:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 7.8 Hz, 2H), 6.96 (s, 1H), 6.89 (d, J = 2.0 Hz 2H), 6.76 (s, 1H), 5.82 (dd, J = 253.7, 15.4 Hz, 2H), 4.57 (m, 2H), 3.60 (m, 48H), 3.34 (s, 3H), 3.02 (m, 1H), 2.80 (m, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 1.87 (s, 3H), 1.79 – 1.47 (m, 3H), 1.45 – 1.05 (m, 4H), 0.97 – 0.81 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.15, 167.05, 139.88, 138.70, 136.49, 135.63, 134.61, 134.05, 129.56, 128.27, 128.11, 128.01, 124.01, 120.90, 81.83, 81.49, 71.70, 70.19, 70.15, 70.10, 70.06, 70.03, 70.00, 69.93, 69.89, 69.81, 58.96, 55.37, 55.26, 54.50, 39.48, 34.22, 31.35, 30.69, 29.04, 21.49, 21.05, 17.98ppm. HRMS (ESI-TOF) m/z: [M - Cl]+ Calculated for $C_{53}H_{84}ClIrN_3O_{13}$ is 1162.5555; Found 1162.5553.

*Synthesis of CODDA catalyst (**13**).* Chemicals and supplies were purchased and used as described above. ^{1}H NMR spectra were recorded on a Varian Mercury 400 MHz instrument or an Agilent DD2 400 MHz instrument using deuterated chloroform unless stated otherwise (deuterated solvents purchased from Cambridge Isotope Laboratories). Elemental analysis was performed by the Microanalysis Laboratory at UIUC. Iridium content of the catalyst was quantified via atomic absorption spectroscopy (AAS; Varian) with an Ir-specific bulb.

Synthesis of **13** is summarized in Fig. S2. For the step resulting in the synthesis of **9**: 0.52 g Nickel acetylacetone and 0.52 g triphenyl phosphine were added sequentially into a 50 mL Schlenk

tube filled with 25 mL dry/degassed toluene; the mixture was cooled to -10 ^{o}C by briefly exposing the container to liquid nitrogen. Then 0.52 g diethylaluminum ethoxide was added. After brief shaking, the resulting solution was left in the glove box to allow its temperature to increase to 20 ^{o}C over ~30 min, with its color changing from green to dark red; afterwards, ~7 mL (~5.6 g) 1-(trimethylsiloxy)-1,3-butadiene was injected into the Schlenk tube with a syringe. The resulting solution was sealed in the Schlenk tube under the glove box's nitrogen atmosphere, removed from the glovebox, and then set to be stirred constantly at a fixed temperature using an oil bath (80 ^{o}C), until the end of the 35th day to ensure completeness of the reaction,[3] by which time a dark red brown solution was produced. The raw liquid product was vacuumed for 18 h to remove solvent, until ~ 3 mL was left. ~30 mL n-hexane was transferred into the Schlenk tube, and a dark precipitate (the used catalyst) was observed to form slowly over time. After waiting ~1 h, this precipitate was removed with a syringe filter. This initial product was further purified by standard preparative liquid chromatography techniques (eluent: hexane:diethylether = 98:2). Portions of the resulting solution containing the desired product (yellow) were collected and dried via roto-evaporation at 21 ^{o}C for 17 h; the thick dark brown-red product 1,2-Bis(trimethylsiloxy) -3,7-cyclooctadiene, a soft, sticky solid (9) was collected. ^{1}H NMR (294 K) δ = 0.19 (s, 18 H), 2.30 (m, 4H), 4.60 (m, 2 H), 5.56 (m, 4 H), in good agreement with Ref. [3]. Elemental analysis: Expected: C, 60.14%; H, 10.13%; Found: C, 59.23%; H, 9.87%.

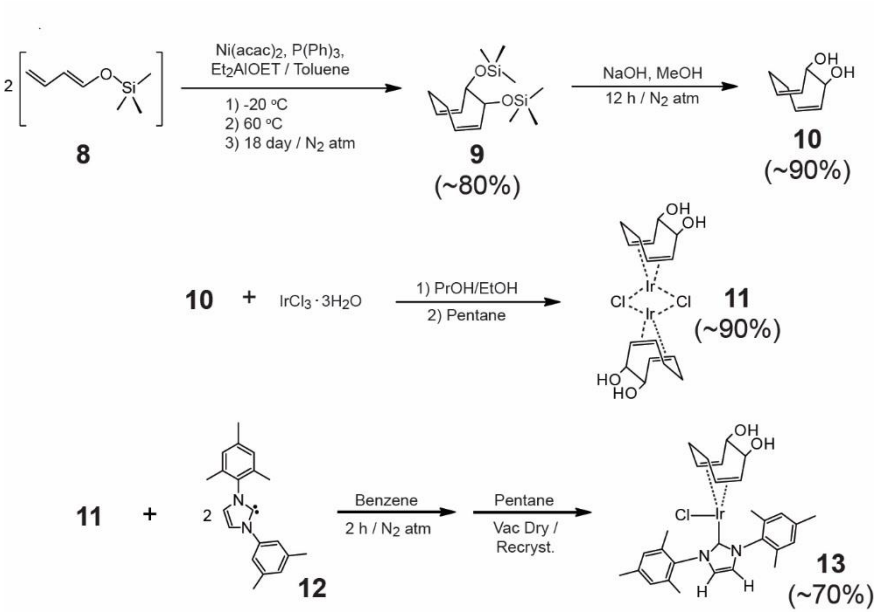

Fig. S2. Summary of synthetic steps for the preparation of the (pre-activated) water-soluble CODDA / Ir SABRE catalyst (**13**). 1-(Trimethylsiloxy)-1,3-butadiene (**8**), is catalyzed by the pre-made catalyst, made from nickel acetylacetone and triphenyl phosphine, to produce 1,2-Bis(trimethylsiloxy)-3,7-cyclooctadiene (**9**), which is hydrolyzed in an aqueous NaOH solution, generating 1,2-dihydroxy-3,7-cyclooctadiene solid (**10**). **10** is further reacted with iridium chloride trihydrate to produce Bis(3,7-cyclooctadiene-1,2-diol)diiridium(I) dichloride (**11**; with one possible isomer shown), which then is combined with IMes, 1,3-Bis(2,4,6-trimethylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene (**12**), to obtain the water soluble catalyst, [IrCl(CODDA)IMes] (**13**). Yields are estimated.

Next, ~4 g of **9** was dissolved in ~10 mL dry / degassed methanol. While stirring, ~ 1 mL NaOH solution (0.0996 g NaOH dissolved in ~10 mL dry / degassed methanol) was added drop-wise. A pale precipitate was generated gradually during the resulting hydrolysis. After ~12 h the suspension was transferred to a centrifuge tube; 3 min at 5000 rpm separated the white precipitate (to be discarded) from the supernatant. 1 mL 36% HCl aqueous solution was injected into the supernatant, and a white precipitate (NaCl) was formed after a few seconds. This precipitate was similarly separated via centrifugation. The white precipitate was washed with ~5 mL ethyl acetate to extract more product (**10**). The 5 mL ethyl acetate solution was mixed with the previously

obtained supernatant, which was then dried via roto-evaporation for ~20 min. at 21 ^{o}C to give the dark brown 1,2-dihydroxy-3,7-cyclooctadiene solid (**10**). ^{1}H NMR (294 K) δ = 2.30 (m, 4 H); 4.33 (m, 2 H); 4.55 (m, 2 H); 5.6 (m, 4H), in good agreement with Ref. [3]. Elemental analysis: Expected: C, 68.54%; H, 8.63%; Found: C, 67.31%; H, 8.14%.

To create **11**, within a glovebox (N_2 atmosphere) 0.448 g iridium chloride trihydrate was first dissolved in ~5 mL dry / degassed 2-propanol to give a dark purple solution. Separately, 0.421 g of **10** (a.k.a. 3,7-cyclooctadiene-1,2-diol) was then dissolved in a composite solvent (comprising ~10 mL dry / degassed propanol and ~25 mL dry / degassed ethanol) to give a dark red solution. The contents of the two vials were combined together in a 100 mL round-bottom flask, which was capped with a rubber septum and then quickly removed from the glovebox and connected to a Schlenk line; the solution was stirred under refluxing conditions. After 1 h reaction, a black solution was generated and was transferred to a 50 mL Schlenk tube. ~9/10 of the solvent was removed via vacuum, then ~5 mL dry / degassed pentane was added to generate the precipitate. The black precipitate (i.e., bis(3,7-cyclooctadiene-1,2-diol)iridium(I) dichloride, **11**) was separated by 3 min. centrifugation at 5000 rpm, followed by 3 washing cycles using 5 mL pentane. ^{1}H NMR (294 K) δ = 2.33 (m, 8 H), 3.46 (m, 4H), 5.39 (m, 4H), 7.51 (m, 8H); Elemental analysis: Expected: C, 26.12%; H, 3.29%; Found: C, 25.94%; H, 3.01%.

Finally, the synthesis of the [IrCl(CODDA)IMes] catalyst (**13**) followed a procedure similar to that used to create the standard SABRE catalyst (**16**, see Refs. [4-7]). Here, 0.034 g IMes (1,3-Bis(2,4,6-trimethylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene; **12**, Aldrich) and 0.029 g Bis(3,7-cyclooctadiene-1,2-diol)diiridium(I) dichloride (**11**) were added to a small Schlenk tube (Kontes). Then 1 ml dried / degassed benzene was transferred into the Schlenk tube with a syringe. After 2 h stirring, excess solvent was removed from the Schlenk tube via evacuation until only ~20% of

the solution volume remained. 0.5 ml dried / degassed pentane was added into the Schlenk tube and the supernatant from the Schlenk tube was transferred into a small beaker. This process was repeated twice, after which brown precipitate was left on the bottom of the Schlenk tube. The Schlenk tube was left to evacuate for 12 h to give the final product [IrCl(CODDA)IMes] (**13**). ^{1}H NMR (D_2O, 294 K) δ = 1.12 (s, 4H), 2.14 (s, 4H), 2.36 (s, 2 H), 3.56 (m, 6 H), 3.64 (m, 6 H), 3.76 (m, 6 H), 7.20 (s, 2 H), 7.46 (m, 2 H), 7,86 (m, 2 H), 8.51 (d, 2 H); Elemental analysis: Expected: C, 51.81%; H, 5.4%; Found: C, 51.57%; H, 5.26%. AAS was performed on **13** to measure Ir content and compared to **16**. Estimated equimolar amounts (0.003 mmol) of **13** and **16** were each separately dissolved in vials containing ~0.5 mL methanol, and then diluted with ~19.5 mL Milli-Q water. Each vial was shaken a few times to yield a solution and a fine suspension (respectively) that were subjected to AAS (three measurements each). Average values of 27.6±0.6 ppm and 27.5±0.8 ppm were obtained for **13** and **16**, respectively; given an expected value of 28.83 ppm for 0.003 mmol of Ir, these results are consistent with similar, high (>95%) purity levels for these catalysts. AAS was also used to estimate the solubility of the CODDA catalyst in water. 10 mg was added to 20 mL of milli-Q water; after ~20 min sonication, the resulting suspension was filtered with a syringe filter; the resulting solution yielded ~0.2 mg/mL solubility. Using the same approach, solubility for the standard SABRE catalyst in methanol was >4 mg/mL but no signal was obtained for that catalyst in water.

SABRE experiments. Samples of pH_2 were created using a home-built pH_2 generator.[8] ^{1}H SABRE experiments were performed using two different setups: At Vanderbilt, a previously described pH_2 delivery setup[7] allowed pH_2 bubbling into the sample at pressures up to ~5.1 atm. NMR experiments were conducted using a 9.4 T (400 MHz) Bruker Avance III spectrometer. At SIUC, pH_2 gas bubbling was regulated by a manual flow meter and delivered to and from the NMR

sample via Teflon tubing at constant (near-ambient) overpressure. NMR experiments were conducted using a 9.4 T (400 MHz) Agilent DD2 spectrometer.

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