Supplementary Information

Tunable iridium catalyst designs with bidentate N-heterocyclic carbene ligands for SABRE hyperpolarization of sterically hindered substrates

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Analytical methods

Supporting NMR spectra were measured using a Bruker 500 MHz NMR spectrometer (^{1}H at 500.13 MHz and ^{13}C{^{1}H} at 125.76 MHz) equipped with a TXI cryoprobe. Spectra were processed with Bruker Topspin software, version 4.0.6. Chemical shifts were referenced to solvent peaks including CD_2Cl_2 (^{1}H: 5.36 ppm and ^{13}C: 53.39 ppm) and $CDCl_3$ (^{1}H: 7.28 ppm and ^{13}C: 77.03 ppm). NMR abbreviations for peak patterns include s for singlet, d for doublet, t for triplet, dd for doublet of doublet, td for triplet of doublet, sep for septet, m for multiplets, and br for broad. Abbreviations for functional groups included Mes for 2,4,6-trimethylphenyl, Dipp for 2,6-diisopropylphenyl, pyd for pyridyl, pyz for pyrazolyl, and Im for imidazolyl.

High resolution mass spectra were measured by the Laboratory for Biological Mass Spectrometry at Texas A&M University, College Station, TX 77840. Electrospray ionization mass spectrometry (ESI-MS) experiments were performed using a Thermo Scientific Q Exactive Focus.

Elemental analysis for C, H, and N were performed in duplicate on a Carlo Erba Model 1108 Analyzers by Atlantic Microlab, Norcross, GA 30071.

X-ray diffraction data was collected at 110 K using Bruker D8-Quest, equipped with a CPAD – Photon II detector and graphite monochromated Mo radiation source (λ = 0.71073 Å). The crystal was coated with paraffin oil and mounted on a nylon loop. The structure of precatalyst 1 was solved by the intrinsic phasing method (SHELXT)[1] and refined by standard Fourier techniques against F squared with a full-matrix least squares algorithm using SHELXL.[2] Graphical representation was generated using Olex2 Crystallography software, version 1.4.[3] The crystal structure was deposited to the Cambridge Structural Database as CSD 2016119.

Synthesis and characterization

General

All solvents were dried by a MBraun Manual Solvent Purification System packed with Alcoa F200 and purged with nitrogen for 5 minutes before use. Purchased chemicals were used as received, without further purification. Glassware for synthesis was flame dried immediately before use.

Imidazolium chloride[4,5] was synthesized according to literature procedures as summarized below. [Ir(COD)(κC,N-NHC)]BPh_4 catalysts were synthesized using a common base method, described later.

Synthesis of 1-aryl-3-(1-pyrazolylmethyl)imidazolium chloride

A mixture of 0.68 g pyrazole (1 eq, TCI), 0.812 mL formaldehyde (1 eq, aqueous 37%), and 10 mL methanol was stirred overnight at room temperature, and subsequently the solvent was removed under reduced pressure. The 1-pyrazolylmethanol product was collected as white crystals and used without further purification. In a 5-mL round bottom flask equipped with a stirbar, 98 mg pyrazol-1-yl-methanol (1 eq), 146 µL thionyl chloride (2 eq, TCI), and 2 mL chloroform were added, stirred, and refluxed for 4 hours. The product mixture was dried under reduced pressure, followed by the addition of 186 mg 1-(2,4,6-trimethylphenyl)imidazole (1 eq) or 228 mg 1-(2,6-diisopropylphenyl)imidazole (1 eq), and 1 mL of acetonitrile. The mixture was refluxed with stirring for 24 hours, then cooled to room temperature, and finally mixed with 5 mL ethyl acetate. The product that formed as a precipitate was filtered and dried under vacuum. The imidazolium chloride product was obtained as a white solid.

Ligand precursor for precatalyst 1: 1-(2,4,6-trimethylphenyl)-3-(1-pyrazolylmethyl) imidazolium chloride

Yield: 235 mg or 77.6 %

^{1}H NMR δ [ppm] ($CDCl_3$): 10.95 (t, 1H, J = 1.4 Hz, Im), 8.62 (d, 1H, J = 2.5 Hz, pyz), 8.06 (t, 1H, J = 1.8 Hz, Im), 7.62 (d, 1H, J = 1.9 Hz, pyz), 7.32 (s, 2H, CH_2), 7.12 (t, 1H, J = 1.8 Hz, Im), 7.01 (s, 2H, Mes meta-H), 6.33 (dd, 2H, J = 2.5, 1.9 Hz, pyz), 2.35 (s, 3H, Mes para-CH_3), 2.02 (s, 6H, Mes ortho-CH_3)

^{13}C NMR [ppm] ($CDCl_3$): 142.2, 141.7, 138.8, 134.0, 132.6, 130.5, 130.0, 123.0, 122.7, 107.7, 61.7, 21.1, 17.5

Positive ESI-HRMS M/Z: found 267.1598, calc. 267.1604 for $[C_{16}H_{19}N_4]^+$ as $[M\text{-}Cl]^+$

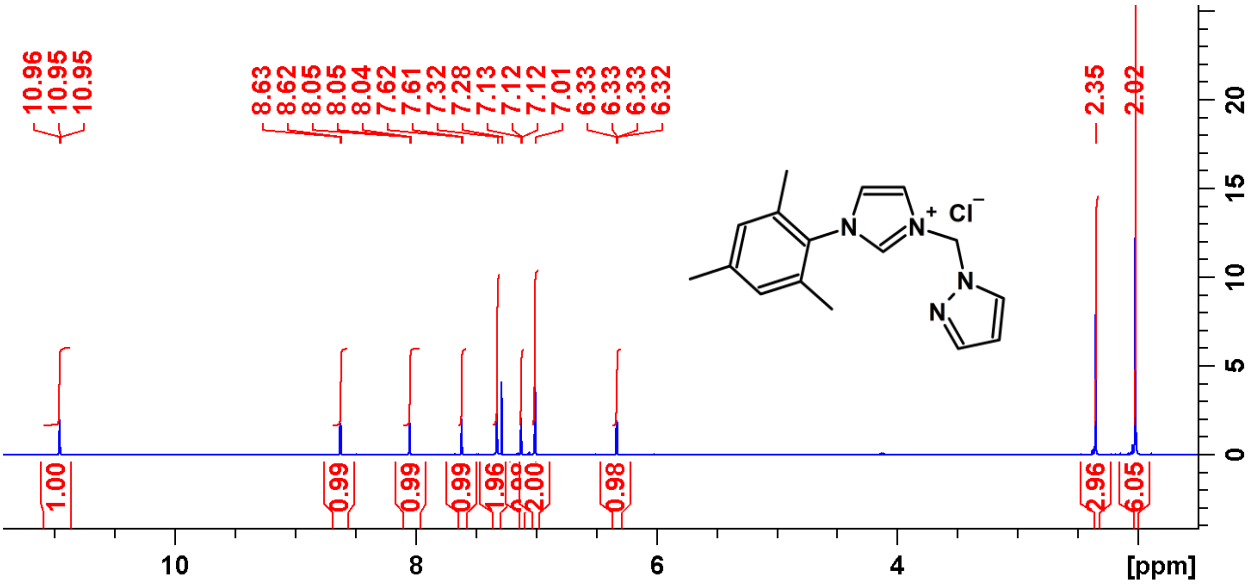


Figure S1a: ^{1}H NMR spectrum of 1-(2,4,6-trimethylphenyl)-3-(1-pyrazolylmethyl) imidazolium chloride

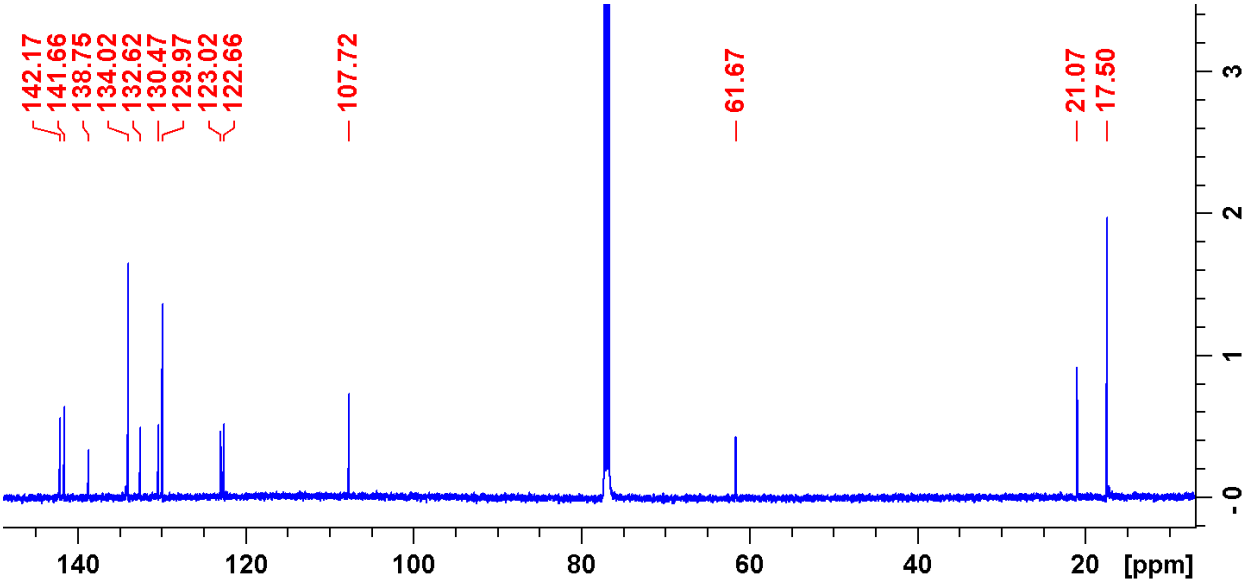


Figure S1b: ^{13}C NMR spectrum of 1-(2,4,6-trimethylphenyl)-3-(1-pyrazolylmethyl) imidazolium chloride

Ligand precursor for precatalyst 3: 1-(2,6-diisopropylphenyl)-3-(1-pyrazolyl methyl)imidazolium chloride

Yield: 260 mg or 75.5%

^{1}H NMR δ [ppm] ($CDCl_3$): 10.87 (t, 1H, J = 1.5 Hz, Im), 8.64 (d, 1H, J = 2.4 Hz, pyz), 8.20 (t, 1H, J = 1.6 Hz, Im), 7.60 (d, 1H, J = 1.8 Hz, pyz), 7.54 (t, 1H, J = 7.8 Hz, Dipp para-H), 7.39 (s, 2H, CH_2), 7.30 (d, 2H, J = 7.8 Hz, Dipp meta-H), 7.14 (t, 1H, J = 1.6 Hz, Im), 6.32

(dd, 1H, J = 2.6, 1.8 Hz, pyz), 2.17 (sep, 2H, J = 6.9 Hz, Dipp ^{i}Pr-CH), 1.19 (d, 6H, J = 6.9 Hz, Dipp ^{i}Pr-CH_3), 1.12 (d, 6H, J = 6.9 Hz, Dipp ^{i}Pr-CH_3)

^{13}C NMR [ppm] ($CDCl_3$): 145.2, 142.2, 139.0, 132.6, 132.1, 130.0, 124.8, 123.9, 122.8, 107.7, 61.8, 28.8, 24.3, 24.0

Positive ESI-HRMS M/Z: found 309.2068, calc. 309.2074 for $[C_{19}H_{25}N_4]^+$ as $[M\text{-}Cl]^+$

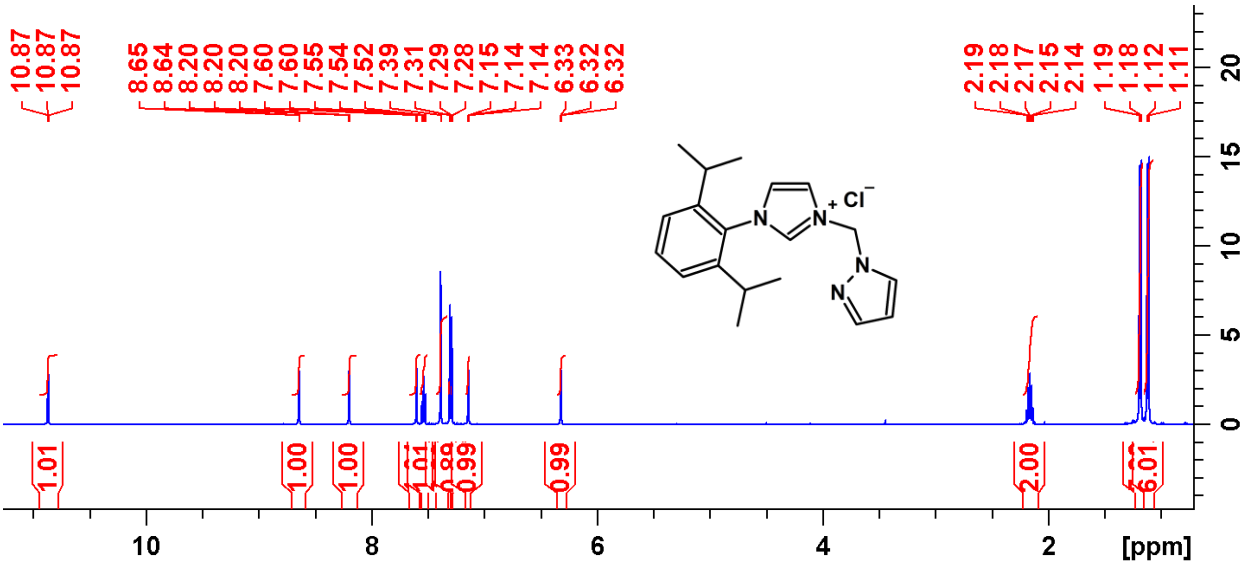


Figure S2a: ^{1}H NMR spectrum of 1-(2,6-diisopropylphenyl)-3-(1-pyrazolylmethyl) imidazolium chloride

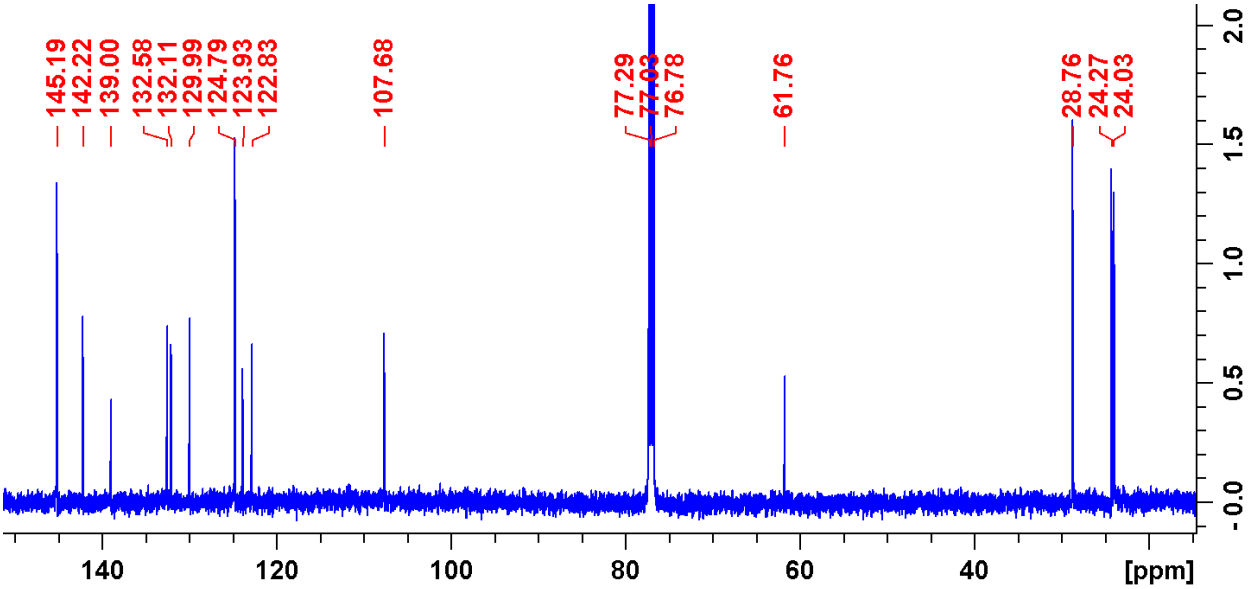


Figure S2b: ^{13}C NMR spectrum of 1-(2,6-diisopropylphenyl)-3-(1-pyrazolylmethyl) imidazolium chloride

Synthesis of 1-aryl-3-(2-pyridylmethyl)imidazolium chloride

An amount of 196 mg 2-(chloromethyl)pyridine hydrochloride (1.2 eq, TCI) was

neutralized with 0.7 g K_2CO_3 (J.T. Baker) and 0.5 mL water. 2-(chloromethyl)pyridine was then extracted with 3 x 1 mL dichloromethane that was transferred in a 5 mL round bottom flask equipped with a stirbar. The dichloromethane was partially evaporated to ~0.2 mL under reduced pressure. To this mixture, 186 mg 1-(2,4,6-trimethyl)imidazole (1 eq) or 228 mg 1-(2,6-diisopropyl)imidazole (1 eq) and 1 mL of acetonitrile were added. The final mixture was refluxed with stirring for 24 hours, then cooled to room temperature, and finally mixed with 5 mL ethyl acetate. The product that formed as a precipitate was filtered and dried under vacuum. The imidazolium chloride product was obtained as yellowish solid.

Ligand precursor for precatalyst 2: 1-(2,4,6-trimethylphenyl)-3-(2-pyridylmethyl) imidazolium chloride

Yield: 235 mg or 77.6 %

^{1}H NMR δ [ppm] ($CDCl_3$): 10.69 (t, 1H, J = 1.5 Hz, Im), 8.55 (ddd, 1H, J = 5.0, 1.6, 0.8 Hz, pyd), 8.06 (t, 1H, J = 1.6 Hz, Im), 8.04 (d, 1 H, J = 7.8 Hz, pyd), 7.78 (td, 1H, J = 7.7, 1.7 Hz, pyd), 7.31 (ddd, 1H, J = 7.7, 5.0, 0.8 Hz, pyd), 7.11 (t, 1H, J = 1.6 Hz, Im), 7.00 (s, 2H, Mes meta-H), 6.20 (s, 2H, CH_2), 2.34 (s, 3H, Mes para-CH_3), 2.05 (s, 6H, Mes ortho-CH_3)

^{13}C NMR [ppm] ($CDCl_3$): 152.9, 149.4, 141.3, 138.9, 138.0, 134.2, 130.8, 129.9, 124.7, 124.0, 123.5, 122.5, 53.8, 21.1, 17.5

Positive ESI-HRMS M/Z: found 278.1647, calc. 278.1652 for $[C_{18}H_{20}N_3]^+$ as $[M\text{-}Cl]^+$

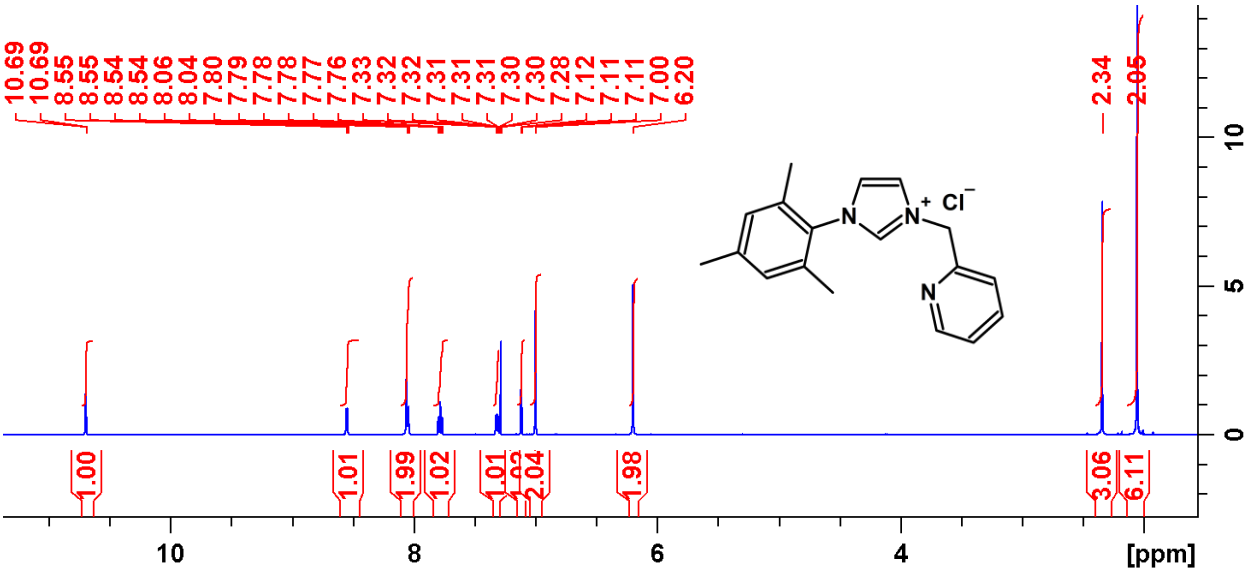


Figure S3a: ^{1}H NMR spectrum of 1-(2,4,6-trimethylphenyl)-3-(2-pyridylmethyl) imidazolium chloride

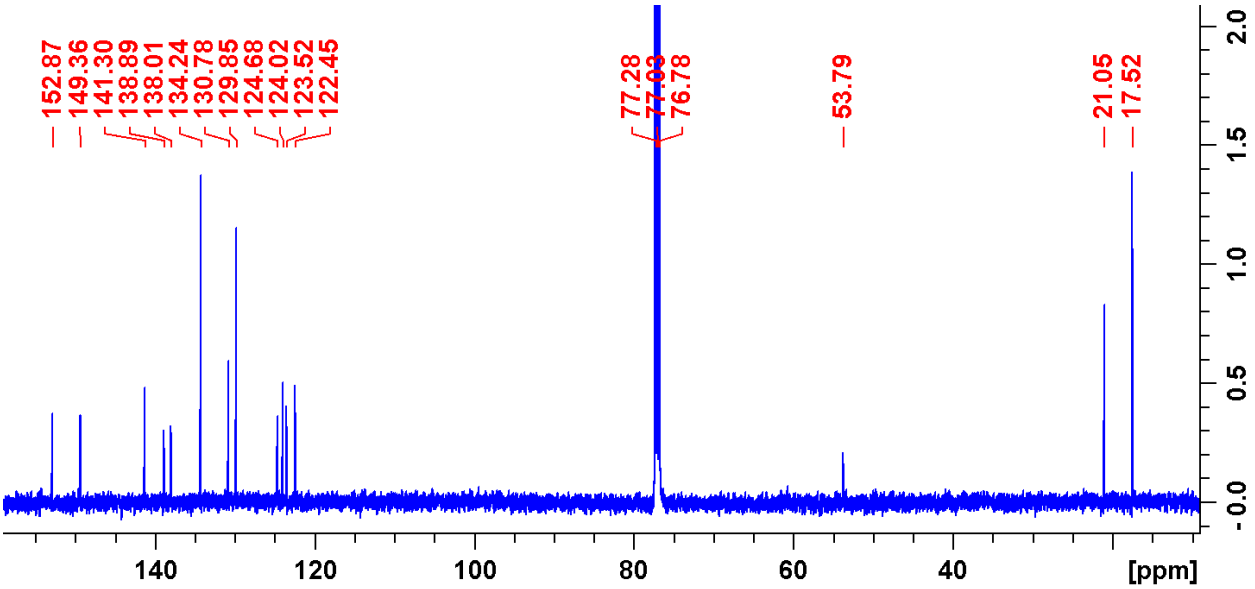


Figure S3b: ^{13}C NMR spectrum of 1-(2,4,6-trimethylphenyl)-3-(2-pyridylmethyl) imidazolium chloride

Ligand precursor for precatalyst 4: 1-(2,6-diisopropylphenyl)-3-(2-pyridylmethyl)imidazolium chloride

Yield: 260 mg or 75.5%

^{1}***H NMR δ [ppm] ($CDCl_3$)***: 10.37 (t, 1H, 1.5 Hz, Im), 8.52 (ddd, 1H, J = 4.9, 1.6, 0.8 Hz, pyd), 8.29 (t, 1H, J = 1.6 Hz, Im), 8.04 (d, 1H, J = 7.8 Hz, pyd), 7.78 (td, 1H, J = 7.7, 1.8 Hz, pyd), 7.53 (t, 1H, J = 7.8 Hz, Dipp para-H), 7.31 (m, 1H, pyd), 7.30 (d, 2H, J = 7.8 Hz, Dipp meta-H), 7.13 (t, 1H, J = 1.6 Hz, Im), 6.27 (s, 2H, CH_2), 2.32 (sep, 2H, J = 6.8 Hz, Dipp ^{i}Pr-CH), 1.21, (d, 6H, J = 6.8, Dipp ^{i}Pr-CH_3), 1.14 (d, 6H, J = 6.8, Dipp ^{i}Pr-CH_3)

^{13}C NMR [ppm] ($CDCl_3$): 149.3, 145.5, 139.0, 137.9, 131.9, 130.3, 124.7, 124.5, 124.5, 124.0, 123.9, 123.4, 53.9, 28.6, 24.3, 24.2

Positive ESI-HRMS M/Z: found 320.2116, calc. 320.2121 for $[C_{21}H_{26}N_3]^+$ as $[M\text{-}Cl]^+$

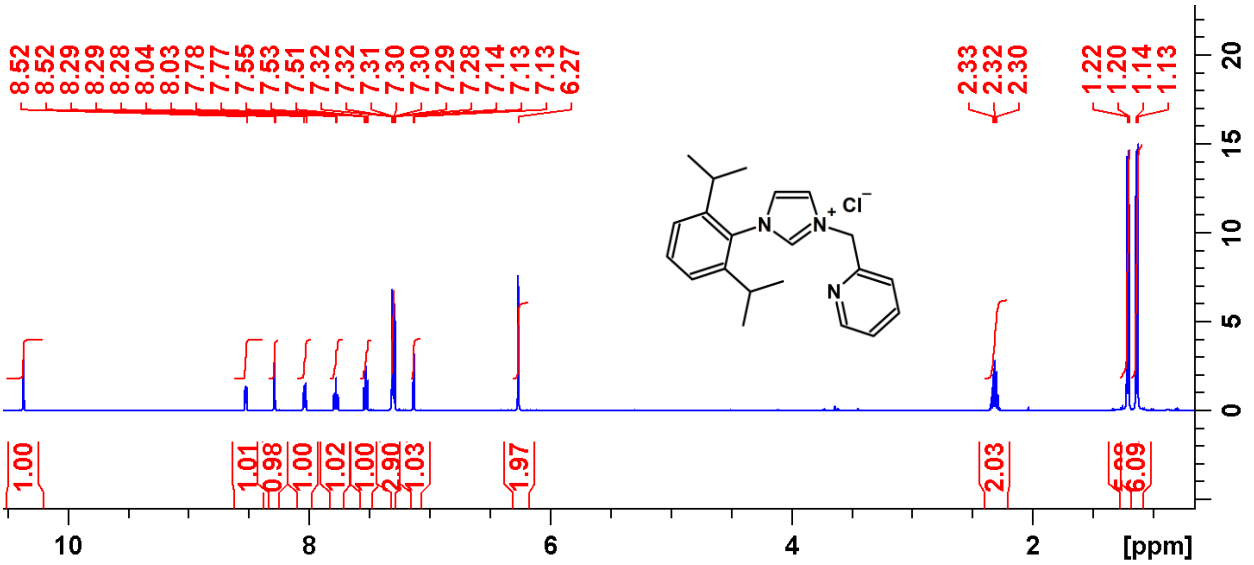


Figure S4a: ^{1}H NMR spectrum of 1-(2,6-diisopropylphenyl)-3-(2-pyridylmethyl) imidazolium chloride

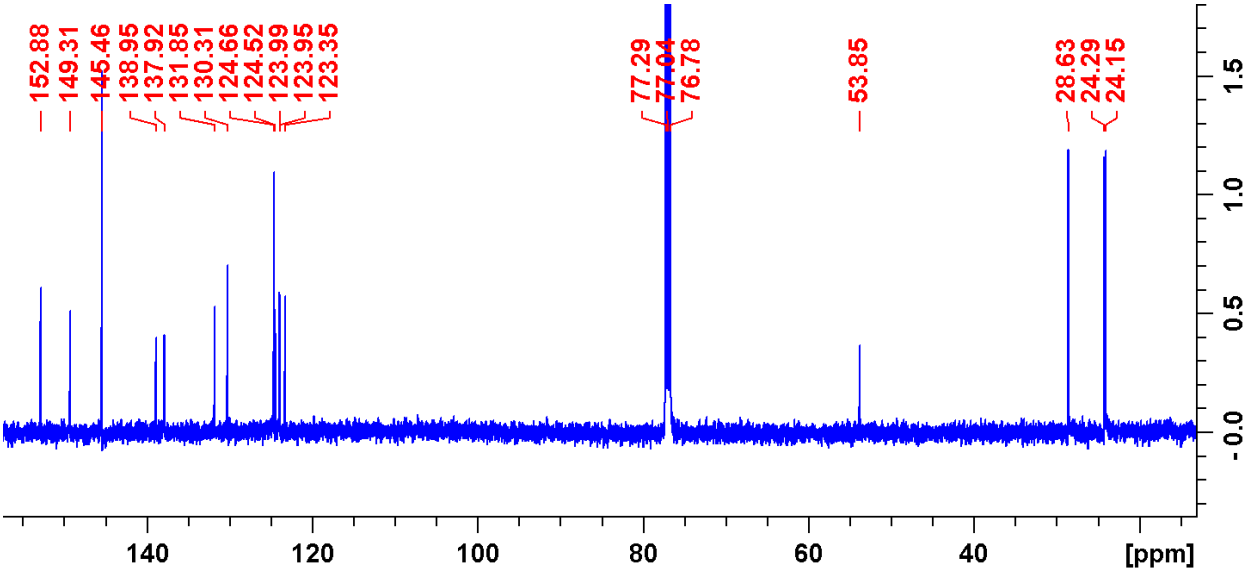


Figure S4b: ^{13}C NMR spectrum of 1-(2,6-diisopropylphenyl)-3-(2-pyridylmethyl) imidazolium chloride

Synthesis of [Ir(COD)(κC,N-NHC)]BPh$_4$

The [Ir(COD)(κC,N-NHC)]BPh$_4$ catalysts with different κC,N-NHC ligands were synthesized using a general base method comprising the following steps. Under argon atmosphere, 0.05 mmol (0.5 eq) [Ir(COD)Cl]$_2$, 1 eq respective imidazolium chloride, and 1 eq sodium tetraphenylborate in 4 ml tetrahydrofuran were successively added. The mixture was stirred for 30 minutes, followed by the addition of 3 eq sodium methoxide (TCI, Portland, OR). The mixture was stirred at room temperature for 3 days, during which

the color of the mixture turned to orange/red. A white precipitate was filtered off through a 0.45 µm PES membrane filter (P/N 28145, VWR, Radnor, PA). From the remaining solution, the solvent was removed under vacuum. The orange solid was recrystallized by dissolving in dichloromethane and layering with pentane. The crystalline solid was collected, washed with ~2 mL methanol, and dried under vacuum.

Precatalyst 1: (1,5-cyclooctadiene)[1-(2,4,6-trimethylphenyl)-3-(1-pyrazolylmethyl) imidazol-2-ylidene]iridium(I) tetraphenylborate

Yield: 74 mg or 78% as orange needle-like crystals

^{1}H NMR [ppm] (CD_2Cl_2): 7.53 (dd, 1H, J = 2.4, 0.5 Hz, pyz), 7.49 (m, 8H, BPh_4), 7.28 (dd, 1H, J = 2.5, 0.5 Hz, pyz), 7.09 (t, 8H, J = 7.4 Hz, BPh_4), 7.05 (s, 2H, Mes meta-H), 6.96 (tt, 4H, J = 7.2, 1.3 Hz, BPh_4), 6.74 (d, 1H, J = 2.0 Hz, Im), 6.72 (d, 1H, J = 2.0 Hz, Im), 6.40 (t, 1H, J = 2.5 Hz, pyz), 5.1 (br, 2H, CH_2), 4.37 (br, 2H, COD sp^2), 3.45 (br, 2H, COD sp^2), 2.39 (br, 3H, Mes para-CH_3), 2.15 (br m, 2H, COD sp^3), 1.99 (s, 6H, Mes ortho-CH_3), 1.97 (br, 2H, COD sp^3), 1.84 (br, 2H, COD sp^3), 1.75 (br, 2H, COD sp^3)

^{13}C NMR [ppm] (CD_2Cl_2): 172.4, 164.1 (q, $^{1}J_{CB}$ = 49.2 Hz, BPh_4), 141.5, 140.0, 136.0 (BPh_4), 135.0, 134.8, 133.4, 129.1, 125.9 (q, $^{3}J_{CB}$ = 2.7 Hz, BPh_4), 123.2, 122.1 (BPh_4), 121.1, 108.0, 83.8, 64.2, 62.5, 33.0, 29.4, 20.8, 18.0

Positive ESI-HRMS M/Z: found 567.2084, calc. 567.2094 for $[C_{24}H_{30}N_4Ir]^+$ as $[M\text{-}BPh_4]^+$

Elemental Analysis: found 62.24% C, 5.51% H, 6.11% N; calculated 62.01% C, 5.49% H, 5.94% N for $C_{48}H_{50}N_4IrB \cdot 0.67\ CH_2Cl_2$

Crystals for X-ray diffraction were grown by slow vapor diffusion of pentane to tetrahydrofuran.

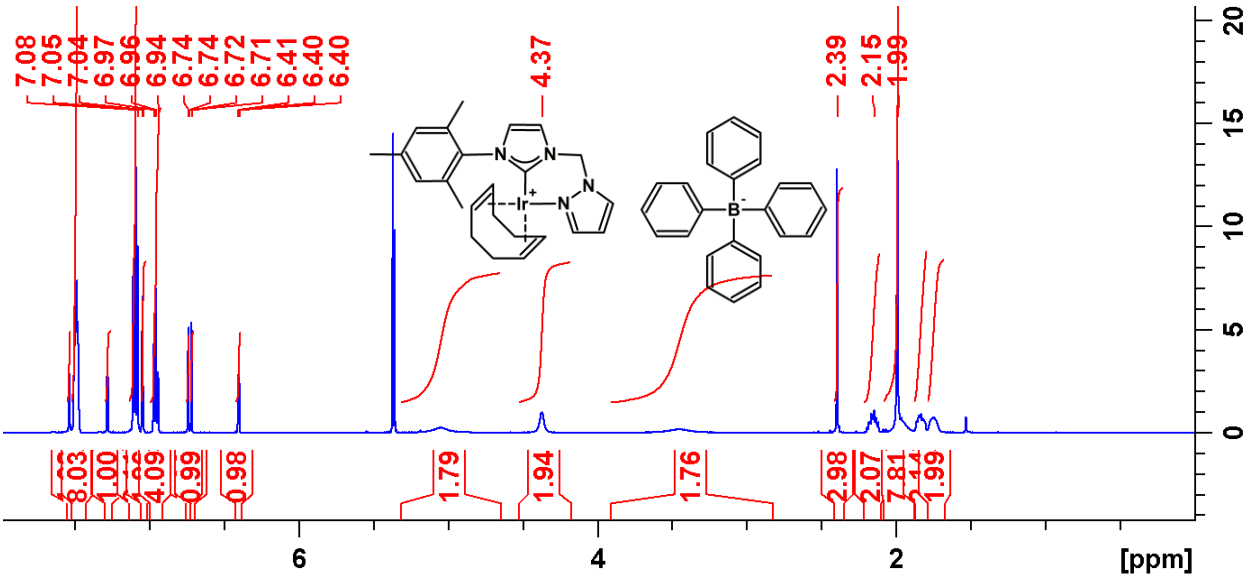


Figure S5a: ^{1}H NMR spectrum of precatalyst 1

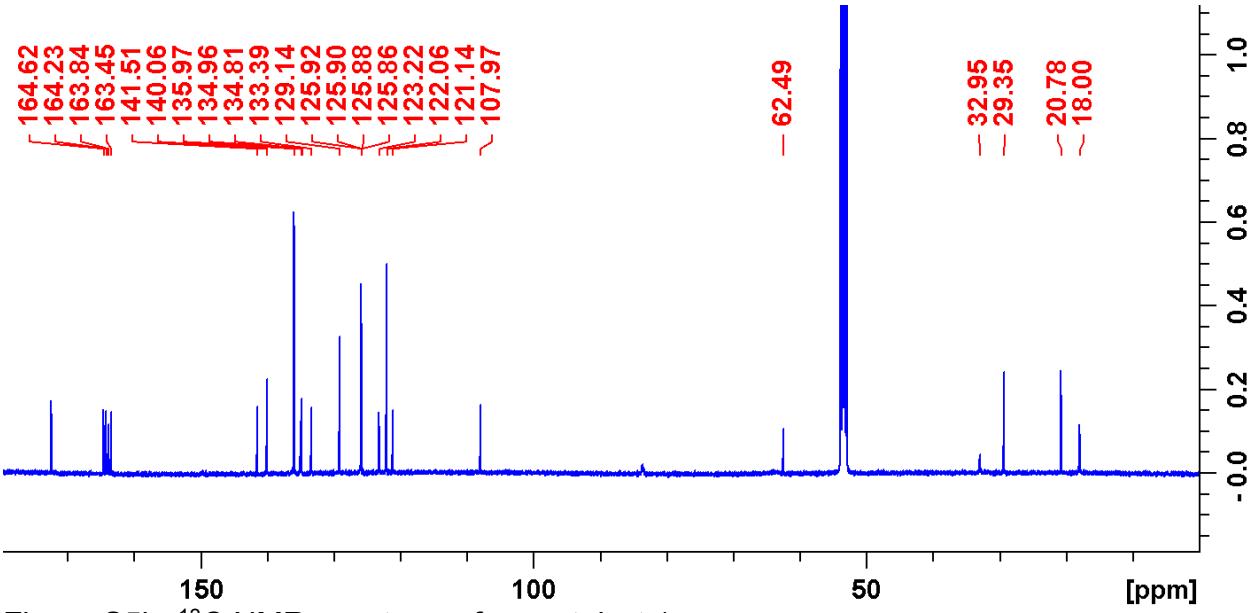


Figure S5b: ^{13}C NMR spectrum of precatalyst 1

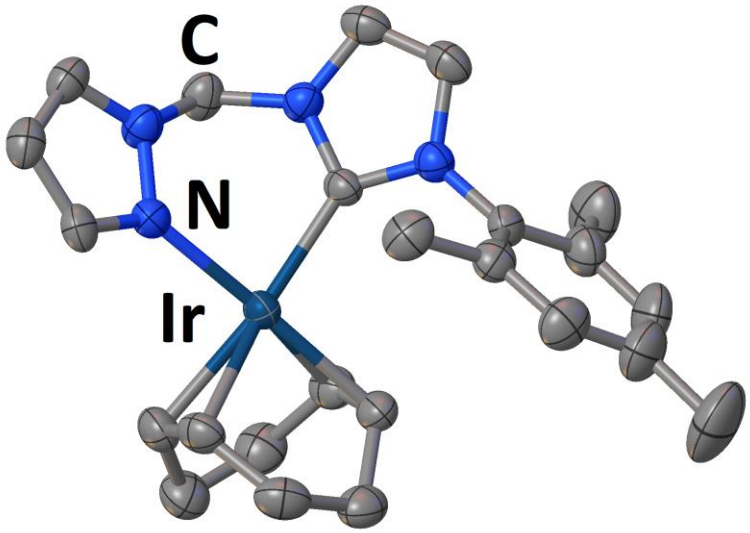


Figure S5c. X-ray crystal structure of precatalyst 1 represented with thermal ellipsoids at 50% probability. Protons and counter anion are omitted.

Table S1. Crystal data and structure refinement parameters for precatalyst 1

Identification code	precatalyst1_0ma
Empirical formula	$C_{53}H_{47}BIrN_3O_{0.25}$
Formula weight	932.94
Temperature/K	110.0

Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	22.2922(15)
b/Å	13.8681(9)
c/Å	14.6786(9)
α/°	90
β/°	107.043(2)
γ/°	90
Volume/Å^3	4338.6(5)
Z	4
ρ_{calc}g/cm^3	1.428
μ/mm^{-1}	3.117
F(000)	1880.0
Crystal size/mm^3	0.2 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.178 to 60.124
Index ranges	-31 ≤ h ≤ 31, -19 ≤ k ≤ 19, -20 ≤ l ≤ 20
Reflections collected	245032
Independent reflections	12719 [R_{int} = 0.0646, R_{sigma} = 0.0235]
Data/restraints/parameters	12719/0/535
Goodness-of-fit on F^2	1.088
Final R indexes [I>=2σ (I)]	R_1 = 0.0271, wR_2 = 0.0579
Final R indexes [all data]	R_1 = 0.0376, wR_2 = 0.0629
Largest diff. peak/hole / e Å^{-3}	0.90/-1.70

Precatalyst 2: (1,5-cyclooctadiene)[1-(2,4,6-trimethylphenyl)-3-(2-pyridylmethyl) imidazol-2-ylidene]iridium(I) tetraphenylborate

Yield: 75 mg or 80% as orange/red needle-like crystals

^{1}H NMR [ppm] (CD_2Cl_2): 8.41 (dd, 1H, J = 6.0, 1.6 Hz, pyr), 7.83 (td, 1H, J = 7.7, 1.6 Hz, pyr), 7.39 (br m, 1H, pyr, 8H, BPh_4), 7.38 (m, 1H, pyr), 7.06 (s, 2H, Mes meta-H), 7.06 (t, 8H, J = 7.4 Hz, BPh_4) 6.96 (d, 1H, J = 2.0 Hz, Im), 6.92 (tt, 4H, J = 7.4, 1.3 Hz, BPh_4), 6.81 (d, 1H, J = 2.0 Hz, Im), 5.4 (br, 1H, CH_2), 4.6 (br, 1H, CH_2), 4.15 (s, 1H, COD sp^2), 4.08 (s, 1H, COD sp^2), 3.95 (s, 1H, COD sp^2), 3.23 (s, 1H, COD sp^2), 2.41 (s, 3H, Mes

para-H), 2.09 (s, 3H, Mes ortho-H), 1.90 (s, 3H, Mes ortho-H), 2.3 - 1.8 (br, 6H, COD sp^3), 1.68 (s, 1H, COD sp^3), 1.53 (s, 1H, COD sp^3)

^{13}C NMR [ppm] (CD_2Cl_2): 174.4, 164.1 (q, $^1J_{CB}$ = 49.2 Hz, BPh_4), 152.1, 151.1, 139.9, 136.1, 136.0 (BPh_4), 135.2, 134.7, 134.6, 129.3, 126.4, 125.8, 125.7 (q, $^3J_{CB}$ = 2.7 Hz, BPh_4), 123.2, 121.8 (BPh_4),121.4, 86.0, 82.9, 65.9, 64.4, 55.2, 34.5, 31.5, 31.1, 27.7, 20.8, 18.6, 17.6

Positive ESI-HRMS M/Z: found 578.2130, calc. 578.2142 for $[C_{26}H_{31}N_3Ir]^+$ as $[M\text{-}BPh_4]^+$

Elemental Analysis: found 62.87 % C, 5.52% H, 4.49% N; calc. 62.80% C, 5.47% H, 4.32% N for $C_{50}H_{51}N_3IrB \cdot 0.9\ CH_2Cl_2$

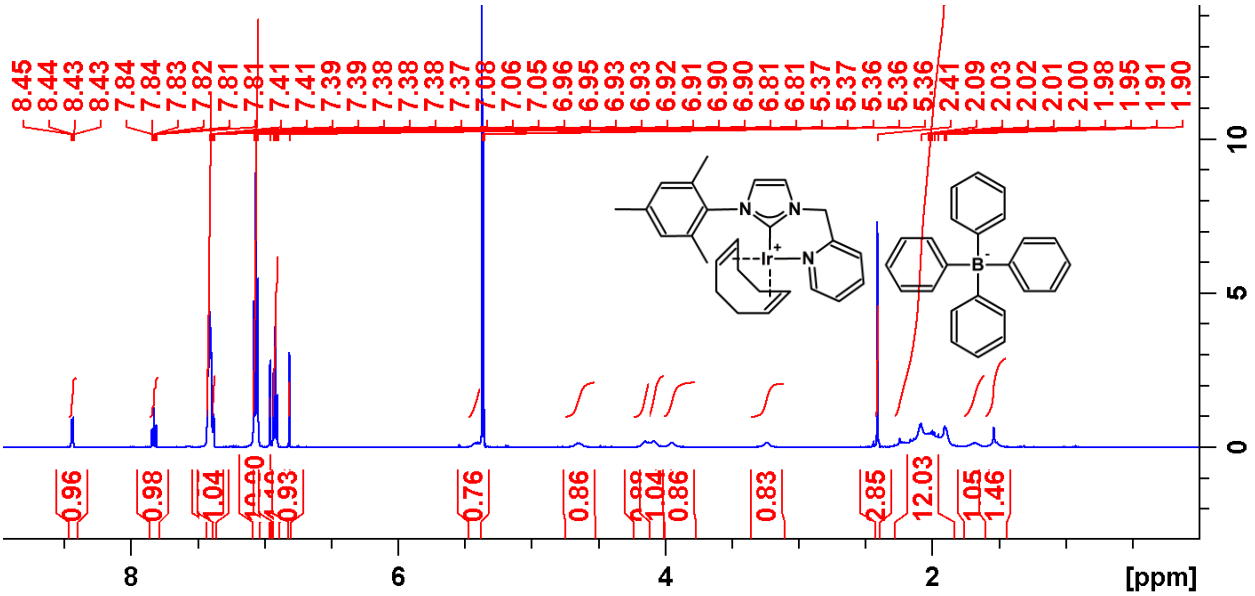


Figure S6a: ^{1}H NMR spectrum of precatalyst 2

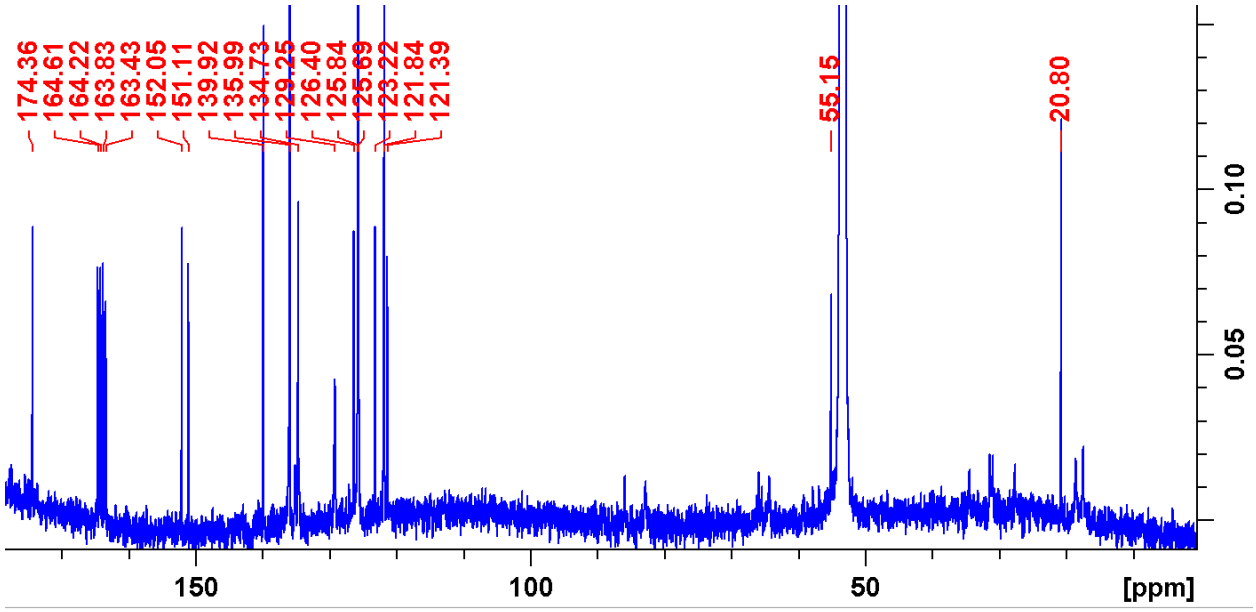


Figure S6b: ^{13}C NMR spectrum of precatalyst 2

Pre-catalyst 3: (1,5-cyclooctadiene)[1-(2,6-diisopropylphenyl)-3-(1-pyrazolyl methyl)imidazol-2-ylidene]iridium(I) tetraphenylborate

Yield: 64.1 mg or 69% as red crystals

^{1}H NMR [ppm] (CD_2Cl_2): 7.55 (t, 1H, J = 7.9, Dipp para-H), 7.5 (br m; 1H, pyz; 8H BPh_4), 7.31 (d, 2H, J = 7.9 Hz, Dipp meta-H), 7.29 (d, 1H, J = 2.5 Hz, pyz), 7.10 (t, 8H, J = 7.4 Hz, BPh_4), 6.96 (tt, 4H, J = 7.2, 1.3 Hz, BPh_4), 6.75 (d, 1H, J = 1.9 Hz, Im), 6.73 (d, 1H, J = 1.9 Hz, Im), 6.41 (t, 1H, J = 2.5 Hz, pyz, 5.0 (br, 2H, CH_2), 4.33 (s, 2H, COD sp^2), 3.4 (br, 2H, COD sp^2), 2.15 (br m, 2H, Dipp ^{i}Pr-CH), 2.3 – 1.6 (br m, 8H, COD sp^3), 1.36 (d, 6H, J = 6.5 Hz, Dipp ^{i}Pr-CH_3), 1.08 (s, 6H, Dipp ^{i}Pr-CH_3)

^{13}C NMR [ppm] (CD_2Cl_2): 172.7, 164.1 (q, $^{1}J_{CB}$ = 49.2 Hz, BPh_4), 145.9, 141.4, 136.0 (BPh_4), 133.9, 133.4, 130.6, 125.9 (q, $^{3}J_{CB}$ = 2.7 Hz, BPh_4), 124.3, 124.1, 122.1 (BPh_4), 121.1, 108.0, 83.5, 63.6, 62.5, 32.8, 29.3, 28.5, 24.9, 24.0

Positive ESI-HRMS M/Z: found 609.2549, calc. 609.2564 for $[C_{27}H_{36}N_4Ir]^+$ as $[M\text{-}BPh_4]^+$

Elemental Analysis: found 65.98% C, 6.02% H, 6.08% N; calc. 66.00% C, 6.08% H, 6.04% N for $C_{51}H_{56}N_4IrB$

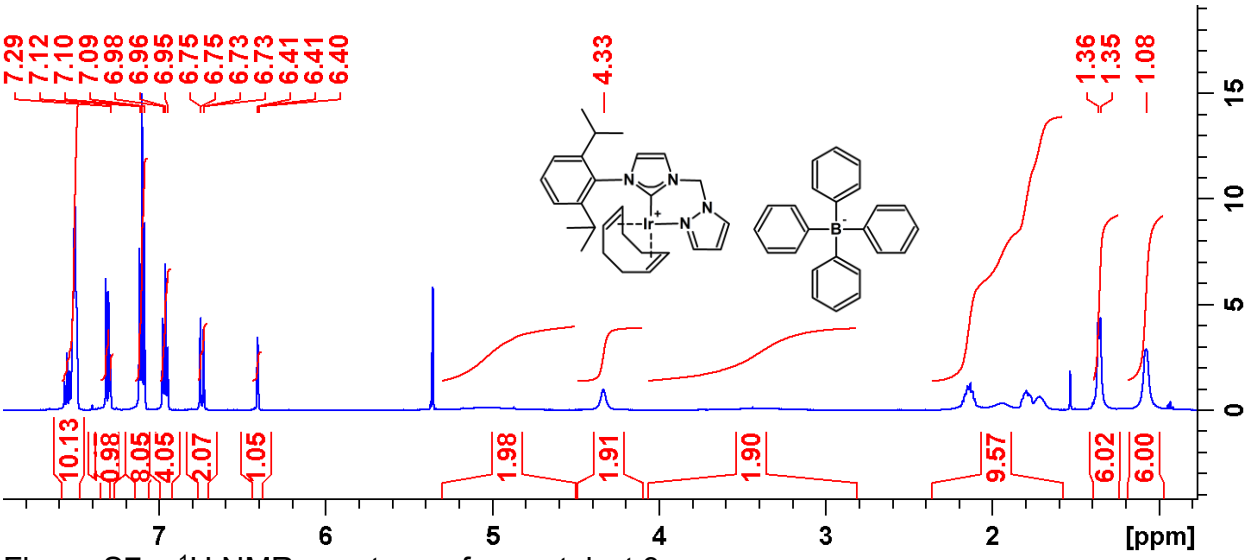


Figure S7a: ^{1}H NMR spectrum of precatalyst 3

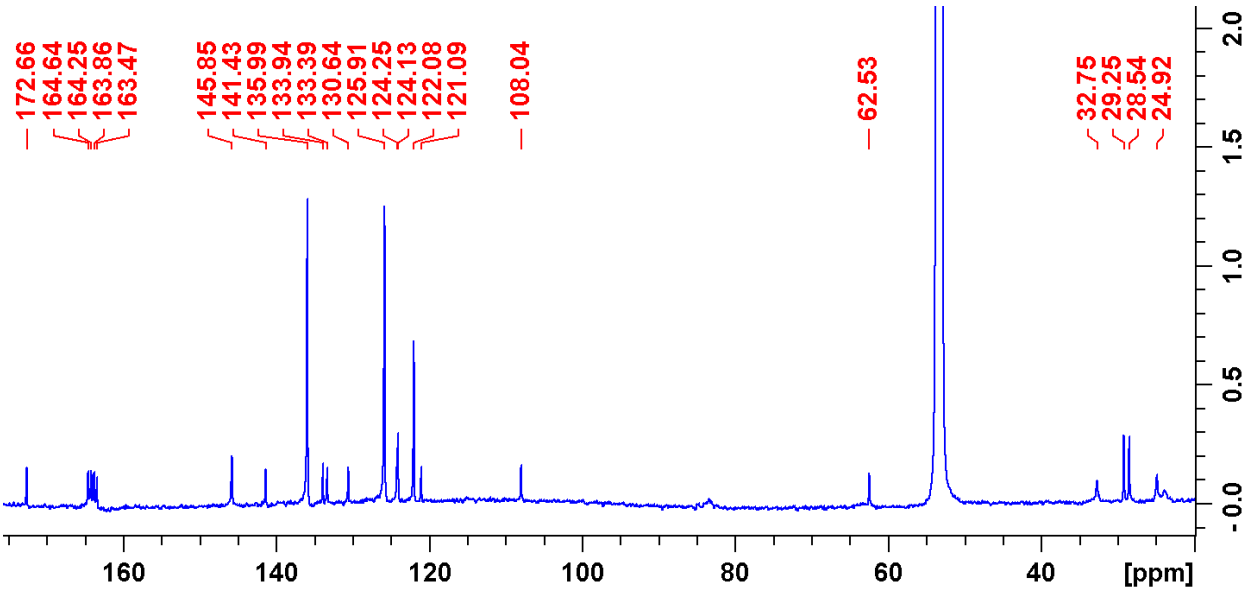


Figure S7b: ^{13}C NMR spectrum of precatalyst 3

Pre-catalyst 4: ***(1,5-cyclooctadiene)[1-(2,6-diisopropylphenyl)-3-(2-pyridylmethyl) imidazol-2-ylidene]iridium(I) tetraphenylborate***

Yield: 60.5 mg or 64% as red cubic crystals

^{1}H NMR [ppm] (CD_2Cl_2): 8.41 (ddd, 1H, J = 5.6, 1.5, 0.8 Hz, pyd), 7.81 (td, 1H, J = 7.7, 1.5, pyd), 7.57 (t, 1H, J = 7.8, Dipp para-H), 7.43 (br m, 8H, BPh_4), 7.38 (ddd, 1H, J = 7.7, 5.6, 1.5 Hz, pyd), 7.35 (ddd, 1H, J = 7.7, 1.5, 0.8 Hz, pyd), 7.33 (br, 2H, Dipp meta-H), 7.08 (t, 8H, J = 7.5 Hz, BPh_4), 6.93 (tt, 4H, J = 7.5, 1.3 Hz, BPh_4), 6.91 (d, 1H, J = 1.9 Hz, Im), 6.84 (d, 1H, J = 1.9 Hz, Im), 5.38 (d, 1H, J = 14.7 Hz, CH_2), 4.56 (d, 1H, J = 14.7 Hz, CH_2), 4.11 (s, 1H, COD sp^2), 4.03 (s, 1H, COD sp^2), 3.94 (s, 1H, COD sp^2), 3.10 (s, 1H,

COD sp^2), 2.51 (m, 1H, Dipp ^{i}Pr-CH), 2.3 – 1.8 (br, m, 6H, COD sp^3), 1.89 (m, 1H, Dipp ^{i}Pr-CH), 1.68 (br, 1H, COD sp^3), 1.53 (br, 1H, COD sp^3; s, 3H, Dipp ^{i}Pr-CH_3), 1.25 (s, J = 5.1 Hz, 6H, Dipp ^{i}Pr-CH_3), 0.93 (s, J = 6.0, 3H, Dipp ^{i}Pr-CH_3)

^{13}C NMR δ [ppm] (CD_2Cl_2): 174,1, 164.0 (q, $^{1}J_{CB}$ = 49.2 Hz, BPh_4), 152.2, 151.0, 146.2, 145.6, 140.0, 136.0 (BPh_4),133.9, 130.5, 126.3, 125.9, 125.7 (q, $^{3}J_{CB}$ = 2.7 Hz, BPh_4), 124.4, 124.2, 124.0, 121.9 (BPh_4), 121.5, 85.8, 82.1, 65.2, 63.4, 55.1, 34.1, 21.3, 31.0, 28.7, 28.3, 27.8, 25.9, 25.8, 24.0, 22.5

Positive ESI-HRMS M/Z: found 618.2575, calc. 618.2588 for $[C_{29}H_{37}N_3Ir]^+$ as $[M\text{-}BPh_4]^+$

Elemental Analysis: found 67.69% C, 6.11% H, 4.59% N; calc. 67.79% C, 6.12% H, 4.47% N for $C_{53}H_{57}N_3IrB$

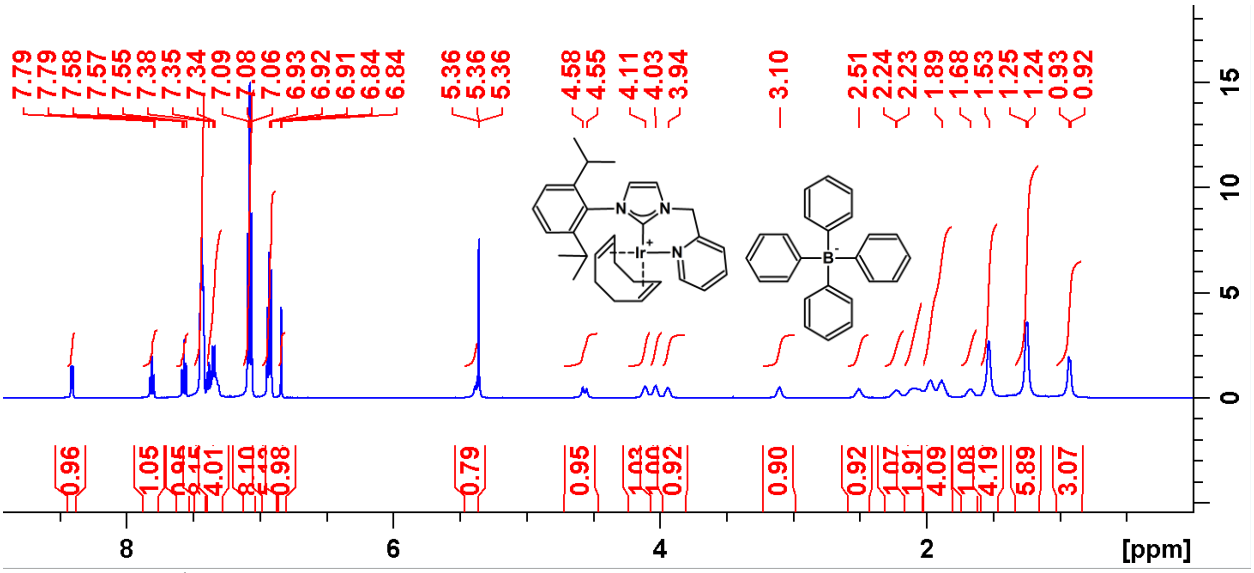


Figure S8a: ^{1}H NMR spectrum of precatalyst 4

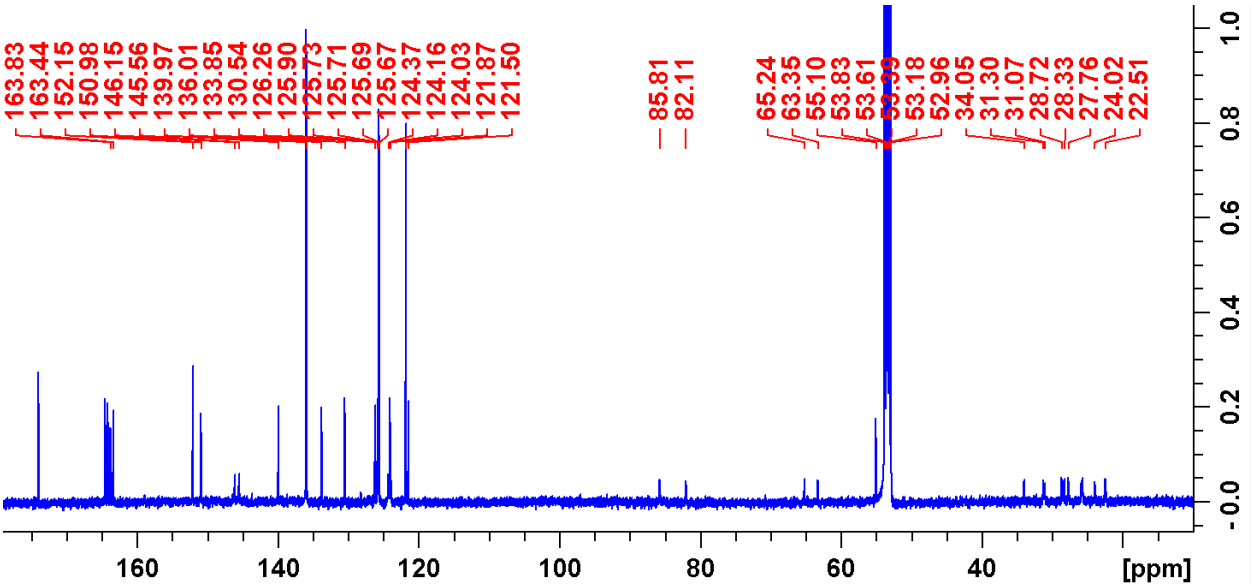


Figure S8b: ^{13}C NMR spectrum of precatalyst 4

Sample Preparation

Under argon atmosphere, a correct weight of [Ir(COD)(κC,N-NHC)]BPh_4 pre-catalysts and 20 µL of a premade 1 M 2,4-diaminopyrimidine substrate (Sigma-Aldrich, St. Louis, MO)/methanol-d4 (Cambridge Isotope, Tewksbury, MA) solution were added to 0.380 mL methanol-d4. This amount of pre-catalyst was not completely soluble in the methanol. The entire sample was transferred to a 5 mm O.D. thick-wall NMR tube (P/N 524-PP-7, Wilmad, Vineland, NJ), modified with an adapter for tubing connection. After full activation, the final solution contained 5 mM catalyst and 50 mM substrate. For the sample with trimethoprim, the concentrations of catalyst and trimethoprim were 3.5 and 35 mM respectively due to solubility limitation of trimethoprim.

Parahydrogen generation

H_2 gas (UN1049, Coastal Welding Supply, Beaumont, TX) was enriched in the para spin state by cooling the gas in a heat exchanger immersed in liquid nitrogen (T = ~77 K), while in contact with Fe_3O_4 (Sigma-Aldrich) serving as a spin-flip catalyst. The para-hydrogen content was determined by comparing ortho-hydrogen NMR signals of the para-enriched gas ($S_{p\text{-}H2}$) with signals of non-para enriched gas at room temperature (S_{H2}). The fraction of para-H_2 in the enriched gas was calculated by the equation $f_{p\text{-}H2} = 1 - (3S_{p\text{-}H2}) / (4S_{H2})$, resulting in f_{pH2} ~ 50%. (Caution: Hydrogen gas is flammable and can create an explosive mixture with air. The hydrogen gas was delivered to the instrument with a system that includes a provision for automatically turning off the gas flow in case of an excessive flow rate, pressure, or on-time.)

Pre-catalyst activation and SABRE experiments

All SABRE experiments were conducted with mixtures described in the sample preparation section. The pre-catalysts were activated by pressurizing samples with 827 kPa H_2 at 65 ^oC. NMR spectra of these mixtures were measured over time; the activation of catalysts was concluded from the disappearance of pre-catalyst signals and the appearance of active catalyst, cyclooctane, and cyclooctene signals. For SABRE experiments, the p-H_2 gas was introduced into the sample through an array of four capillary tubes (360 µm outer diameter, 150 µm inner diameter; P/N 062569, Trajan, Ringwood, Australia). The gas flow rate was monitored using a mass flow meter (M-10SLPM-D, Alicat Scientific, Marana, AZ), and was adjusted by a metering valve (SS-SS4-VH, Swagelok, Solon, OH) to a flow rate of 0.5 standard liter per minute at a pressure of 827 kPa. Subsequently, the gas flow was diverted, and the sample sealed by switching two air actuated three-way valves (SS-41GXS2, Swagelok). The magnetic field was produced by an electromagnet (22 cm diameter, 28 cm length), with a current of up to 5 A from a DC power supply (6553A, Hewlett Packard, Palo Alto, CA). Magnetic fields for polarization transfer were tested in the range of 1 – 10 mT. Fields were confirmed using a Gauss meter (5170, F.W. Bell, Milwaukie, OR). A sample enclosure within the electromagnet was heated by a stream of air (FTS System TC-84, SP Scientific, Warminster, PA). Temperatures were tested in the range of 25 – 65 ^oC. The temperatures were confirmed using an electronic thermometer (HH2001A, Omega Technologies, Westlake Village, CA). After 5 minutes, para-hydrogen was bubbled through the sample for 15 seconds, and the sample was manually transferred within 5 s to a 9.4 T NMR spectrometer (Ultrashield 400 Plus magnet, Bruker Biospin, Billerica, MA) containing a pre-shimmed broadband observe probe (Bruker Biospin). ^1H NMR spectra were measured after a π/2 radio-frequency excitation pulse with an amplitude of γB_1 = 22.7 kHz. The SABRE enhancements were determined as the integrated signal ratios of SABRE experiments compared to non-hyperpolarized NMR spectra from experiments obtained at 298.2 K.

Different amounts of time were required to activate the pre-catalysts 1 – 4 under the same conditions (Table 1). A higher steric hindrance and electron donation of the bidentate NHC ligands caused faster pre-catalyst activation. The emergence of cyclooctane and cyclooctene were found as the hydrogenated products of cyclooctadiene from the pre-catalysts. Cyclooctene concentrations were estimated at <1 mM, *i.e.* <10% of catalysts or <2% of 2,4-diaminopyrimidine. Because of the relatively low concentration and no evidence of iridium complexes involving cyclooctene in NMR spectra, it is expected that the presence of cyclooctene did not affect the SABRE hyperpolarization of 2,4-diaminopyrimidine or trimethoprim.

Dissociation rates of bound ligands

The aromatic protons of bound 2,4-diaminopyrimidine were identified from ^{1}H NMR spectra (Figure 2) and ^{1}H-^{1}H COSY spectra (Figure S9). A series of EXSY-type experiments was conducted with various mixing times between 50 and 200 ms. Selective excitation was applied at the chemical shift of aromatic protons of the equatorially bound substrates. The ratios of integrated NMR signals of bound and free substrates were fitted to the equations 1. Fitting was performed using Python software, version 3.7 (Python Software Foundation, www.python.org). The fitting results are summarized in Table S2.

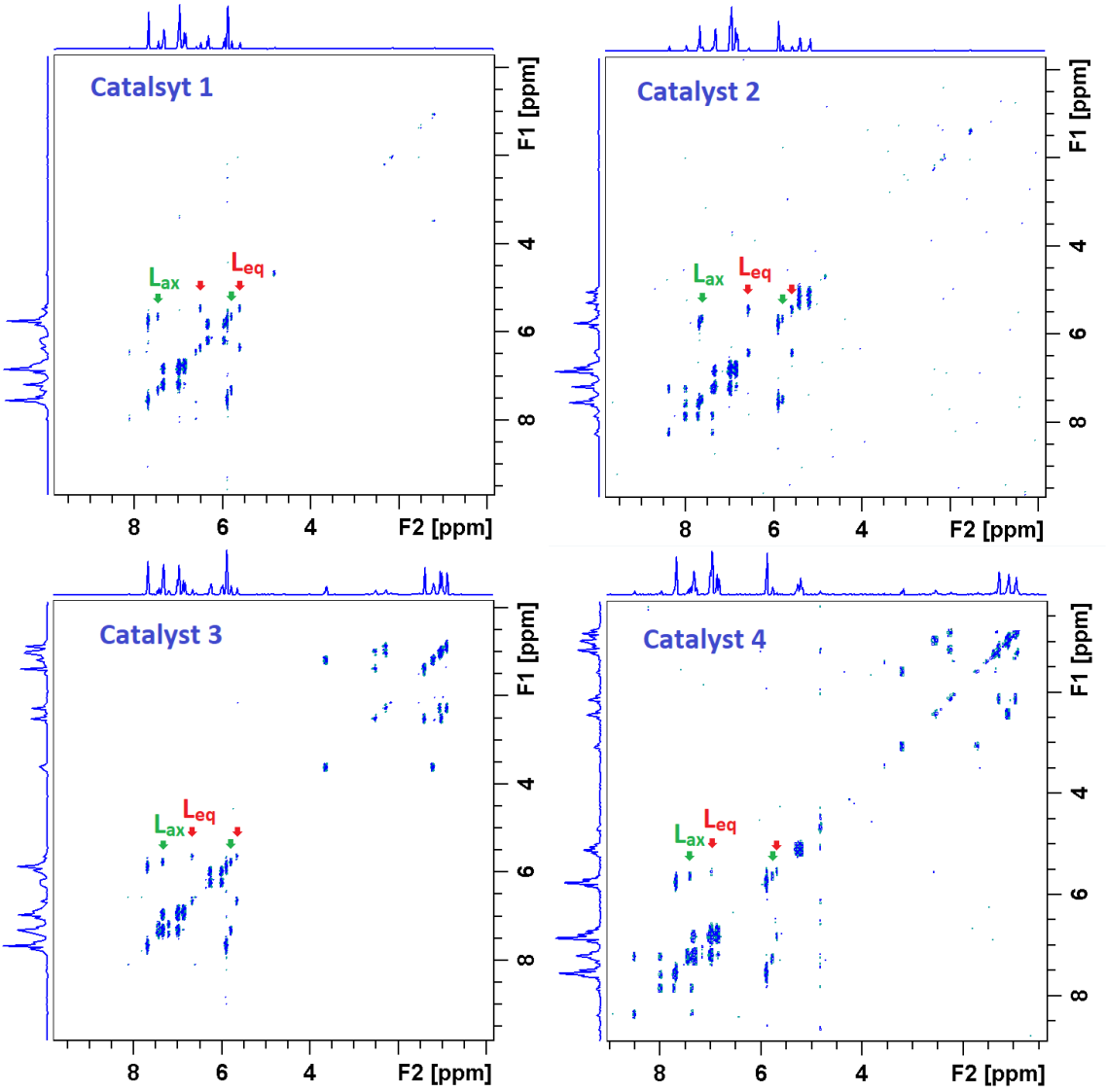
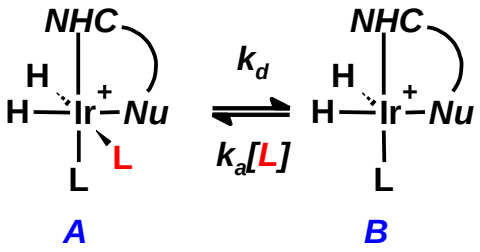


Figure S9. ^{1}H-^{1}H COSY spectra of 5 mM SABRE active catalysts 1 – 4 with 50 mM 2,4-diaminopyrimidine in methanol-d4.



$$\frac{d[L]_{bound}}{dt} = \frac{d[A]}{dt} = -k_d[A] + k_a[B][L]_{free}$$

$$\frac{d[L]_{free}}{dt} = \frac{d[B]}{dt} = +k_d[A] - k_a[B][L]_{free} \qquad (1)$$

$$\frac{k_d}{k_a[B]_{eq}} = \frac{[L]_{free,eq}}{[A]_{eq}}$$

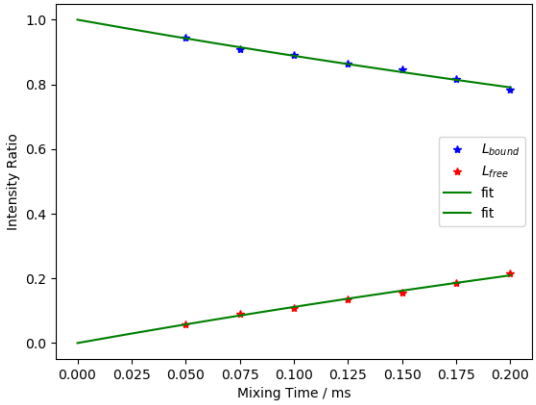


Figure S10. an example of fitting results using the equations 1 for 5 mM SABRE active catalyst 4 and 50 mM 2,4-diaminopyrimidine in methanol-d4.

Table S2: Dissociation rate constants (k_d) of equatorially bound 2,4-diaminopyrimidine for catalysts 1 – 4 at different temperatures.

Catalyst 1		**Catalyst 2**		**Catalyst 3**		**Catalyst 4**		**Catalyst 4 + trimethoprim**	
T / °C	**k_d / s^{-1}**	**T / °C**	**k_d / s^{-1}**	**T / °C**	**k_d / s^{-1}**	**T / °C**	**k_d / s^{-1}**	**T / °C**	**k_d / s^{-1}**
45	0.37 ± 0.06	40	0.53 ± 0.01	35	0.83 ± 0.04	30	1.23 ± 0.08	40	0.78 ± 0.04
50	0.76 ± 0.03	45	1.05 ± 0.08	40	1.6 ± 0.1	35	2.4 ± 0.2	45	1.363 ± 0.003
55	1.3 ± 0.2	50	1.90 ± 0.05	45	3.2 ± 0.3	40	4.6 ± 0.5	50	2.43 ± 0.02

Determination of T_1 relaxation values

Experiments for determining T_1 relaxation were determined using a pulse sequence π-t_{mix}-π/2-acq. The mixing time, t_{mix}, was varied from 0.1 s to 60 s. The NMR spectra were processed and analyzed using Bruker Topspin software, version 4.0.6. The averaged T_1 relaxation times were 10.3 ± 0.2 s and 10.2 ± 0.2 s for the ortho and meta protons of 2,4-diaminopyrimidine, respectively. For the pyrimidinyl and phenyl protons of trimethoprim, the T_1 relaxation times were 2.33 ± 0.05 s and 2.18 ± 0.01 s, respectively.

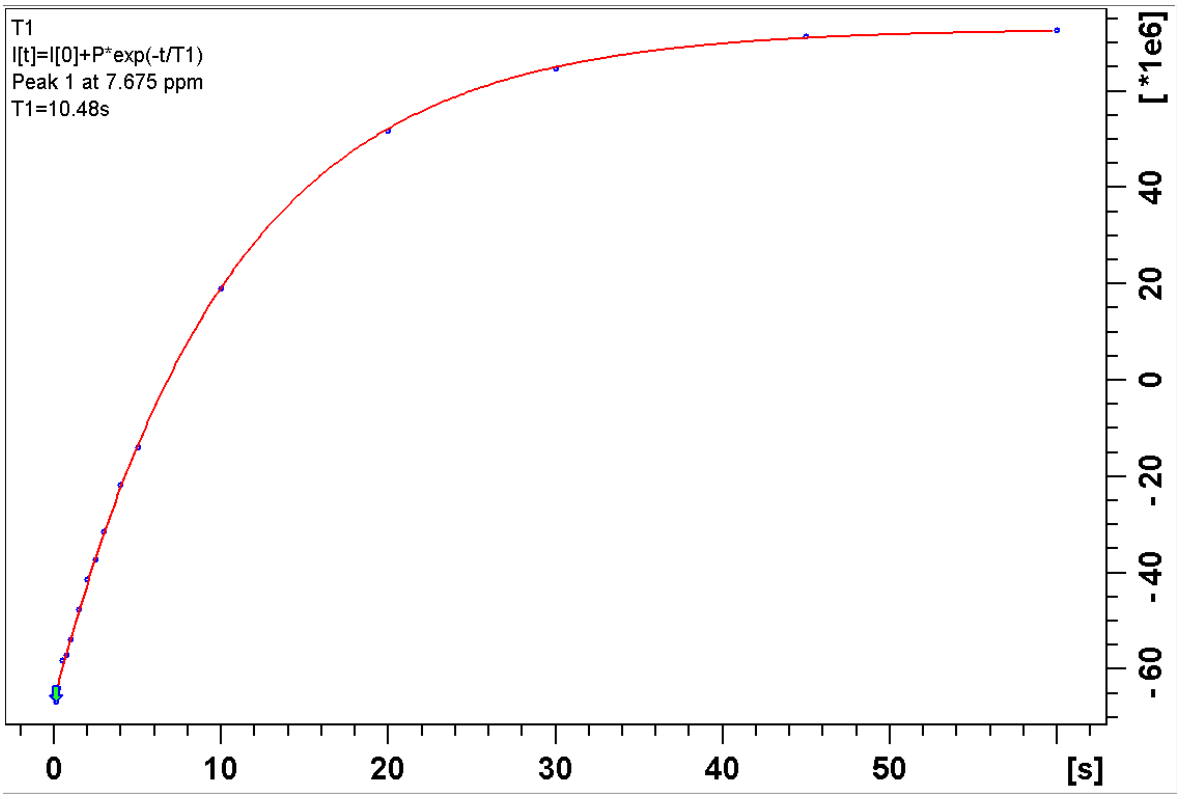


Figure S11. An example of fitting results to determine the T_1 relaxation value of the ortho proton of 2,4-diaminopyrimidine

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