

Supporting Information for

Second-Order Biomimicry: In Situ Oxidative Self-Processing Converts Copper(I)/Diamine Precursor into a Highly Active Aerobic Oxidation Catalyst

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I. General Considerations

All commercially available compounds were purchased, and used as received unless indicated otherwise. X-band EPR data were collected using a Bruker EleXsys E500 spectrometer; all spectra were acquired at 115 K using a N₂(l) cryostat under nonsaturating conditions. In situ IR data were collected using a Mettler Toledo ReactIR ic10 with an AgX probe. ¹H and ¹³C NMR spectra were recorded on Bruker 400 or 500 MHz spectrometers. GC analyses were performed on a Shimadzu gas chromatograph (GC-2010 Plus) using a Phenomenex® Zebron™ ZB-Wax capillary column (30 m x 0.25 mm x 0.25 μm film thickness); 1.0 μL injection volume at 70 °C, which was ramped to 200 °C at a rate of 20 °C/minute, and was held at 200 °C for 2.5 minutes. Chemical shift values are given in parts per million relative to CDCl₃ (7.26 ppm for ¹H or 77.23 ppm for ¹³C).¹ NMR spectra were plotted with MestReNova v8.0.1 (Mestrelab Research S. L. 2012).

General procedure for collection of ReactIR/gas-uptake time course data:

100 mg of flame-dried 4Å molecular sieves were weighed into a two-neck flask. One neck of the flask was plugged with a rubber septum with a hole for the ReactIR probe, and the other neck was attached to a gas-uptake apparatus.² The flask was evacuated and backfilled with O₂ five times, and pressurized to a final pressure of 500 torr O₂. The flask was placed into a temperature-controlled oil bath at 27 °C, and 3 mL of 0.167 M 1-octanol was injected into the flask. After the temperature and pressure equilibrated (approximately 30 minutes), 1 mL of 0.025/0.025/0.1 M [Cu(MeCN)₄]PF₆/DBED/DMAP solution was injected to initiate the reaction. Note: The [Cu(MeCN)₄]PF₆/DBED/DMAP solution must be prepared under a N₂ atmosphere.

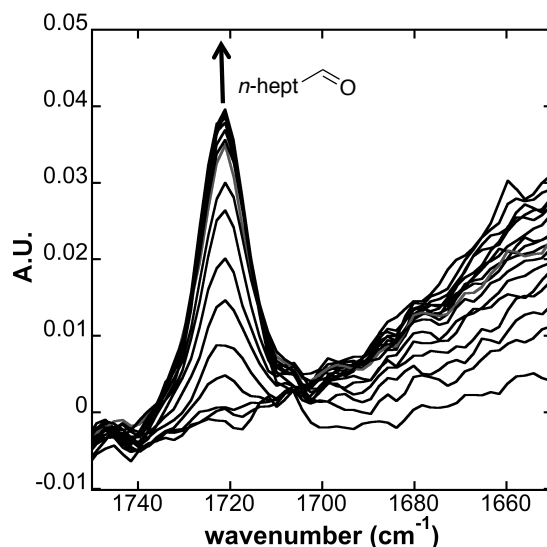


Figure S1. ReactIR data obtained for the catalytic oxidation of 1-octanol. The data were used to produce Figure 3. Concentration data were generated by conversion of absorbance data.

II. Observation of Ligand Oxidation Products

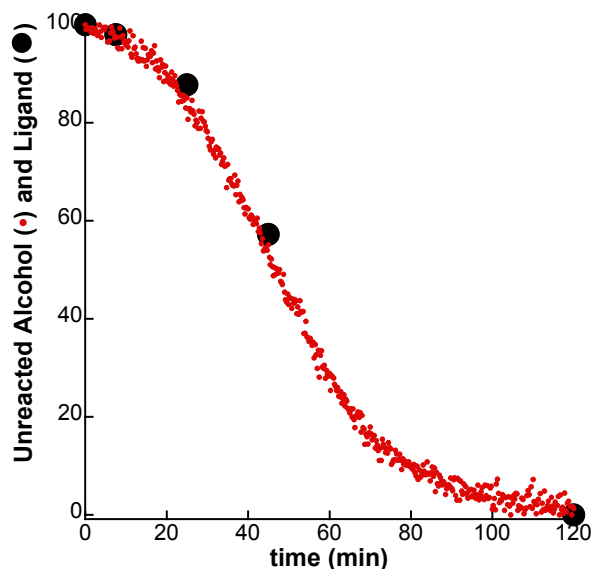


Figure S2. Comparison of 1-octanol and DBED consumption time courses. Reaction Conditions: 0.125 M 1-octanol, 6.25 mM $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$, 6.25 mM DBED, 25 mM DMAP, 100 mg 4\AA MS, 500 torr O_2 , 27 °C. Yield of 1-octanol determined by using in situ IR spectroscopy. Yield of DBED determined by ^1H NMR analysis.

Experiments Probing Ligand Oxidation Products

For consumption of DBED and production of **1**:

400 mg of flame-dried 4\AA molecular sieves were weighed into a 100 mL round-bottom flask, and the flask was sealed with a rubber septum. The flask was purged with O_2 for five minutes. 14.5 mL of 0.138 M 1-octanol was added and the solution was stirred under O_2 for 15 minutes. 1.5 mL of 0.0667/0.0667/0.267 $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DBED}/\text{DMAP}$ solution was then injected to initiate the reaction. 1 mL aliquots were taken at 7.5, 25, 45, and 120 minutes. Different workup procedures needed to be carried out to observe DBED and **1**:

For observation of DBED:

A 1 mL aliquot of the reaction mixture was removed and run through a silica plug that had been prewashed with NH_3 -saturated dichloromethane using NH_3 -saturated dichloromethane as the eluant. 1 mL of 6.25 mM 1,3,5-trimethoxybenzene was then washed through the same plug. The solvent was evaporated and the residue was subjected to ^1H NMR analysis.

For observation of **1**:

A 1 mL aliquot of the reaction mixture was removed and run through a silica plug using EtOAc as the eluant (**1** appears as a bright red band on the silica plug). 1 mL of 6.25 mM 1,3,5-trimethoxybenzene was then washed through the same plug. The solvent was evaporated and the residue was subjected to ^1H NMR analysis.

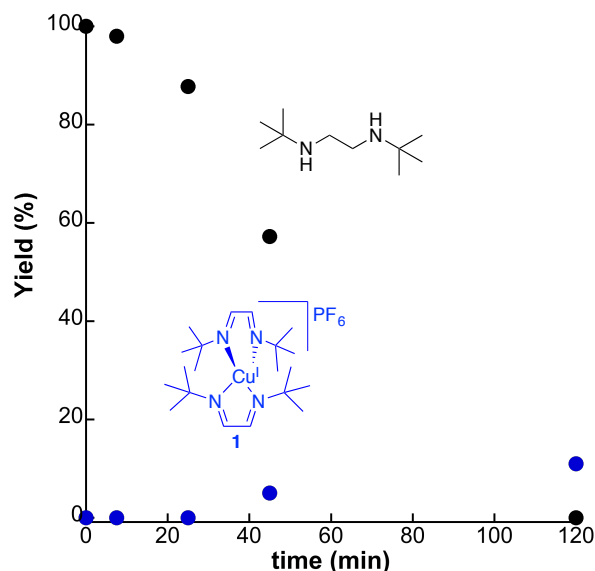


Figure S3. Ligand oxidation time course tracking the amount of **1** formed during the reaction. ^1H NMR yields relative to trimethoxybenzene standard.

For production of **2**:

200 mg of flame-dried 4Å molecular sieves were weighed into a 100 mL round-bottom flask, and the flask was sealed with a rubber septum. The flask was purged with O_2 for five minutes. 7 mL of 0.143 M 1-octanol (with 0.0715 M tetradecane as an internal standard) was added and the solution was stirred under O_2 for 15 minutes. 1 mL of 0.05/0.05/0.2 M $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DBED}/\text{DMAP}$ solution was then injected to initiate the reaction. 300 μL aliquots were taken at 7.5, 25, 45, and 120 minutes. The aliquots were filtered through alumina with DCM as the eluent and subjected to GC analysis.

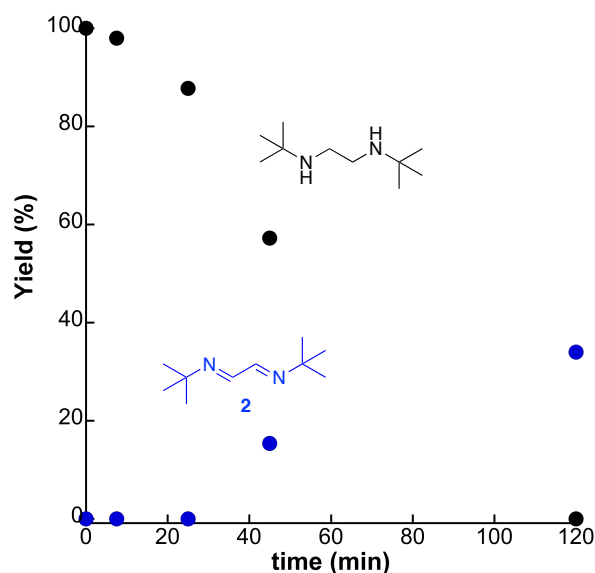


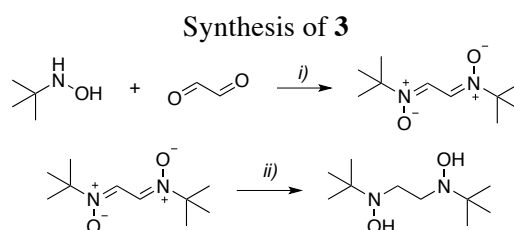
Figure S4. Ligand oxidation time course tracking the amount of **2** formed during the reaction. GC yields relative to tetradecane standard.

Independent Synthesis of 1 and 2

Synthesis of 1: Equimolar amounts of $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ and **2** were mixed in a minimal amount of MeCN. The solution immediately turned deep bright red. The solvent was removed to afford a red solid. ^1H NMR (400 MHz, CDCl_3) δ 8.39 (s, 2H), 1.35 (s, 18H). ^{13}C NMR (126 MHz, CDCl_3) δ 156.60, 59.84, 30.93. m/z (M+H): calculated = 399.2544, found = 399.2547.

Synthesis of 2: **2** was prepared according to a literature procedure.³ 3.7 mL *tert*-butyl amine was mixed with 25 mL H_2O and cooled to 0 °C. 20 mL of 40% glyoxal was added dropwise. A precipitate was immediately observed. The mixture was further stirred for 1 h. The solid was filtered and collected. It was then recrystallized from EtOH/ H_2O . The crystals were then sublimed under vacuum at approximately 40 °C. The ^1H NMR data matched the previously reported spectral parameters. ^1H NMR (400 MHz, CDCl_3) δ 7.87 (s, 2H), 1.19 (s, 18H).

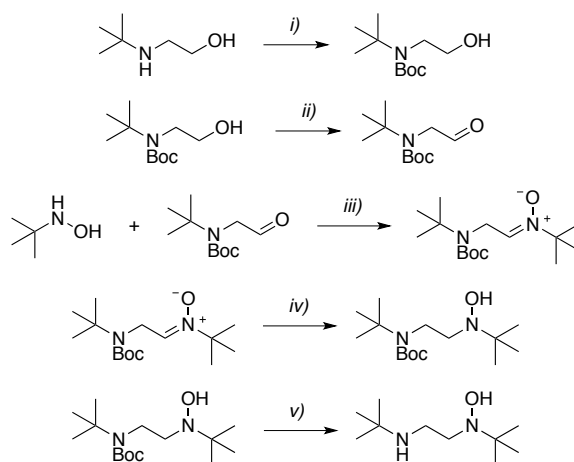
III. Synthesis of Hydroxylamine Cocatalysts



Step i: This synthesis was based on a literature procedure.⁴ 655.6 mg (4.4 mmol) *N*-(*tert*-butyl)hydroxylamine acetate was dissolved in 1 mL H_2O and added to 0.29 g of 40% solution of glyoxal in water. 466.4 mg Na_2CO_3 was added and the mixture was refluxed for 3 h. The water was evaporated and the resulting residue was suspended in 10 mL dichloromethane. The inorganic solids were removed by filtration, and the solvent was evaporated to give a white solid (271.3 mg, 31%). ^1H NMR (400 MHz, CDCl_3) δ 8.00 (s, 2H), 1.52 (s, 18H). ^{13}C NMR (101 MHz, CDCl_3) δ 125.38, 70.99, 27.94. m/z (M+H): calculated = 201.1598, found = 201.1598.

Step ii: The product from step i (270.3 mg, 1.35 mmol) was dissolved in 12 mL Et_2O . This solution was carefully added to 12 mL Et_2O containing 77 mg LiAlH_4 (2.02 mmol) at room temperature. The solution was stirred for 30 minutes, then an additional 77 mg LiAlH_4 was added, and the solution was stirred for 30 additional minutes. 5 mL of water was added to quench the reaction, and the aqueous layer was extracted with 25 mL Et_2O . The organics were dried over MgSO_4 and the solvent was evaporated to give a solid (204.8 mg, 74%). The solid could be used without further purification. However, it can be chromatographed on alumina using 9:1 dichloromethane/MeOH. ^1H NMR (400 MHz, CDCl_3) δ 2.94 (s, 4H), 1.13 (s, 18H). ^{13}C NMR (101 MHz, CDCl_3) δ 58.73, 50.46, 215.15. m/z (M+H): calculated = 205.1911, found = 205.1908.

Synthesis of **4**



Step i: 2-(*tert*-butylamino)ethanol (5.85 g, 50 mmol) and Boc_2O (11.6 g, 53 mmol) were mixed in 15 mL of THF. The solution was heated to 50 °C for 2 hours. The solvent was evaporated. The resulting oil was purified by silica gel chromatography using 1:1 EtOAc/hexanes to give a clear and colorless oil (6.7 g, 62%). ^1H NMR (400 MHz, CDCl_3) δ 3.66 (q, J = 5.4 Hz, 2H), 3.48 (t, J = 5.7 Hz, 2H), 3.22 (t, J = 4.8 Hz, 1H), 1.47 (s, 9H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.39, 80.18, 63.95, 55.46, 46.92, 29.76, 28.48. m/z (M+H): calculated = 218.1751, found = 218.1750.

Step ii: The product from step i (6.5 g, 30 mmol) was dissolved in MeCN (300 mL). 570 mg $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$, 324 mg 4,4'-dimethoxy-2,2'-bipyridine, 246 *N*-methylimidazole, and 42 mg 9-azabicyclo[3.3.1]nonane *N*-oxyl were added to this solution under ambient air. This solution was stirred for approximately 1 h (until the color of the solution turned from brown to green to sky blue). 300 mL of diethyl ether was added to the solution, which was then filtered through a pad of silica. The solvent was then evaporated to give a clear colorless oil. The oil was purified by silica gel chromatography in 2:1 hexane/EtOAc (the oil could be used without further purification without complications). Yield: 5.91 g, 91%. ^1H NMR (400 MHz, CDCl_3) δ 9.51 (s, 1H), 3.98 (s, 2H), 1.42 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 200.40, 155.24, 80.38, 55.59, 54.97, 29.55, 28.28. m/z (M+H): calculated = 216.1594, found = 216.1593.

Step iii: The product from step ii (4.73 g, 22 mmol) and *N*-(*tert*-butyl)hydroxylamine acetate (3.29 g, 22 mmol) were mixed in 33 mL of dichloromethane. 2.33 g Na_2CO_3 and 2.64 g of MgSO_4 were then added. The reaction was stirred overnight, and was then filtered to remove the inorganic solids. The solvent was evaporated to give a white solid (5.5 g, 87% crude yield). The 2.05 of the crude solid was purified by silica gel chromatography in dichloromethane/MeOH (10% to 20% MeOH) to give a white solid (1.93 g, 82%). ^1H NMR (400 MHz, CDCl_3) δ 6.78 (t, J = 4.5 Hz, 1H), 4.30 (d, J = 4.5 Hz, 2H), 1.48 (s, 9H), 1.44 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 155.59, 135.36, 79.92, 68.89, 55.67, 43.17, 29.57, 28.53, 27.82. m/z (M+H): calculated = 287.2329, found = 287.2324.

Step iv: 1.93 g (6.74 mmol) of the product of step iii was dissolved in 21 mL of MeOH. The solution was cooled to 0 °C, and NaBH₄ (768 mg, 20.2 mmol) was added portionwise. The reaction was then put under a N₂ atmosphere and stirred overnight. The methanol was evaporated, and the resulting solid was dissolved in 40 mL of deionized water. The aqueous solution was extracted with EtOAc (3 x 30 mL), dried over MgSO₄, and filtered. The solvent was evaporated to give an off-white solid. The solid was purified by silica gel chromatography in dichloromethane/MeOH (10% to 20% MeOH) to give an off-white solid (1.78 g, 92%). ¹H NMR (400 MHz, CDCl₃) δ 5.90 (br. s, 1H), 3.49 (t, *J* = 6.2 Hz, 2H), 2.60 (t, *J* = 6.2 Hz, 2H), 1.41 (s, 9H), 1.32 (s, 9H), 1.01 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 156.96, 79.53, 57.93, 55.04, 51.99, 43.05, 29.95, 28.58, 25.46. m/z (M+H): calculated = 289.2486, found = 289.2485.

Step v: 1.2 g (4.2 mmol) of the product from step iv was dissolved in 31 mL dichloromethane. The solution was cooled to 0 °C, and 11.3 mL trifluoroacetic acid was added. The resulting solution was stirred at room temperature for 2 h. The reaction solution was poured into a large beaker containing 415 mL sat. NaHCO₃ solution, and stirred for 30 minutes. 5 g of Na₂CO₃ was then added to ensure all of the acid was quenched. The 200 mL dichloromethane was then added, and separated from the aqueous layer using a separatory funnel. The aqueous layer was further extracted with dichloromethane (3 x 500 mL). The organic layers were combined and dried over MgSO₄, filtered, and the solvent was evaporated to give a yellow solid. The solid was purified by Al₂O₃ chromatography using 95:5 dichloromethane/MeOH. Yield 229 mg, 29%. ¹H NMR (400 MHz, CDCl₃) δ 2.99 (t, *J* = 5.8 Hz, 2H), 2.84 (t, *J* = 5.6 Hz, 2H), 1.24 (s, 9H), 1.10 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 58.31, 52.31, 50.44, 41.09, 28.87, 25.31. m/z (M+H): calculated = 189.1961, found = 189.1961.

IV. NMR Spectra for Synthesis of **3** and **4**

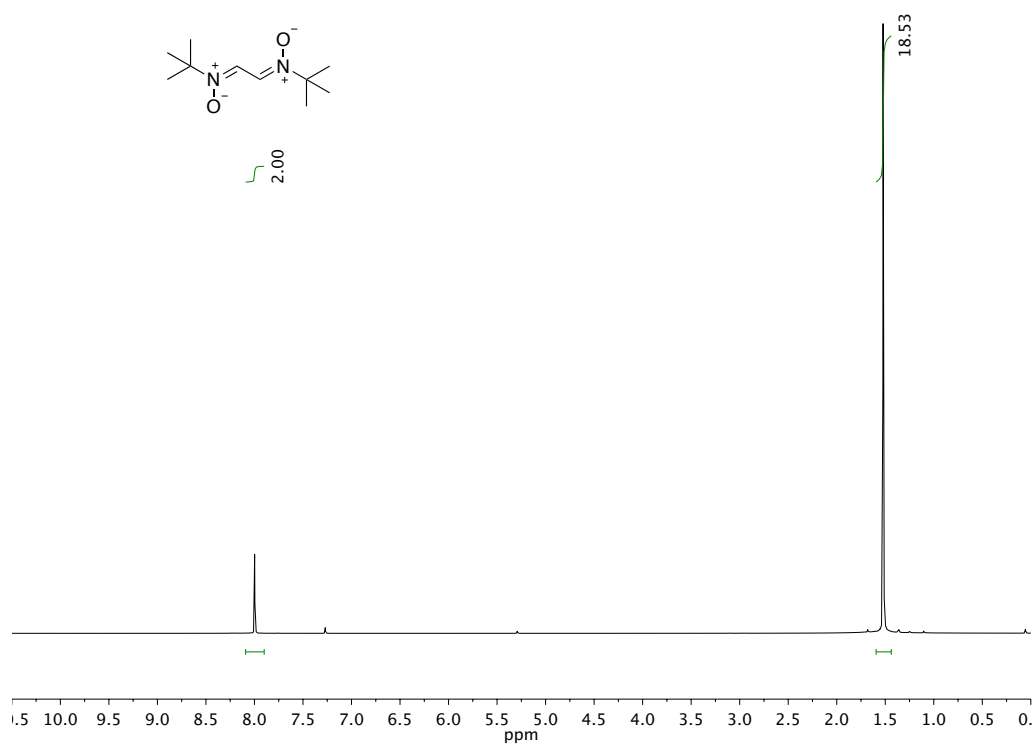


Figure S5. ^1H spectrum for the product of step i in the synthesis of **3**.

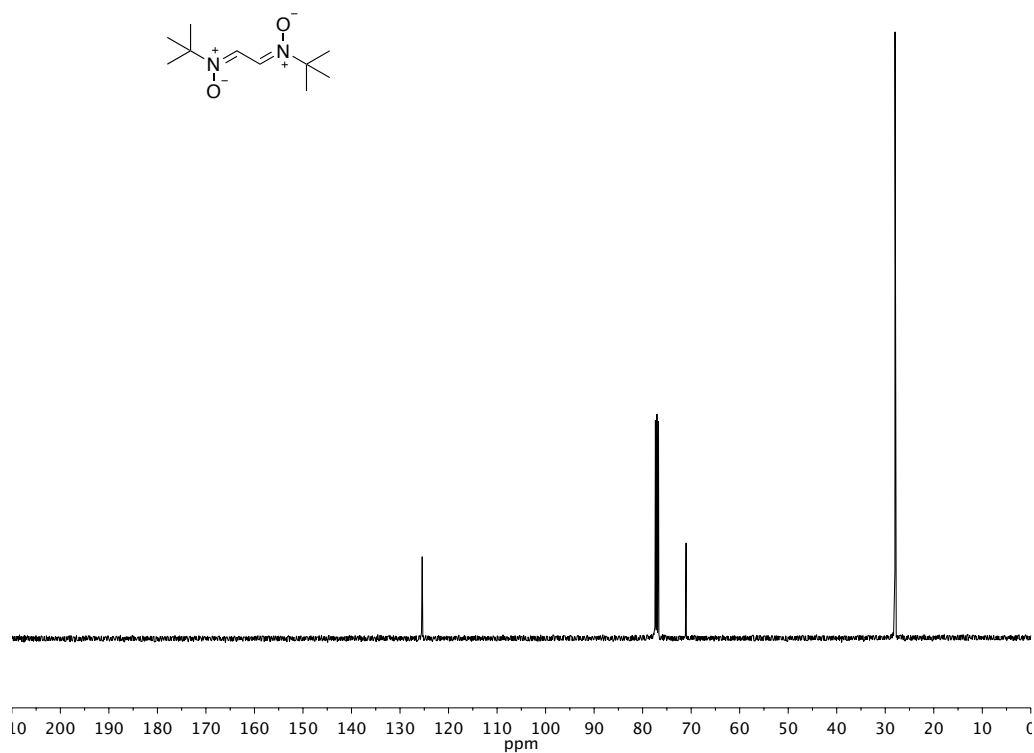


Figure S6. ^{13}C spectrum for the product of step i in the synthesis of **3**.

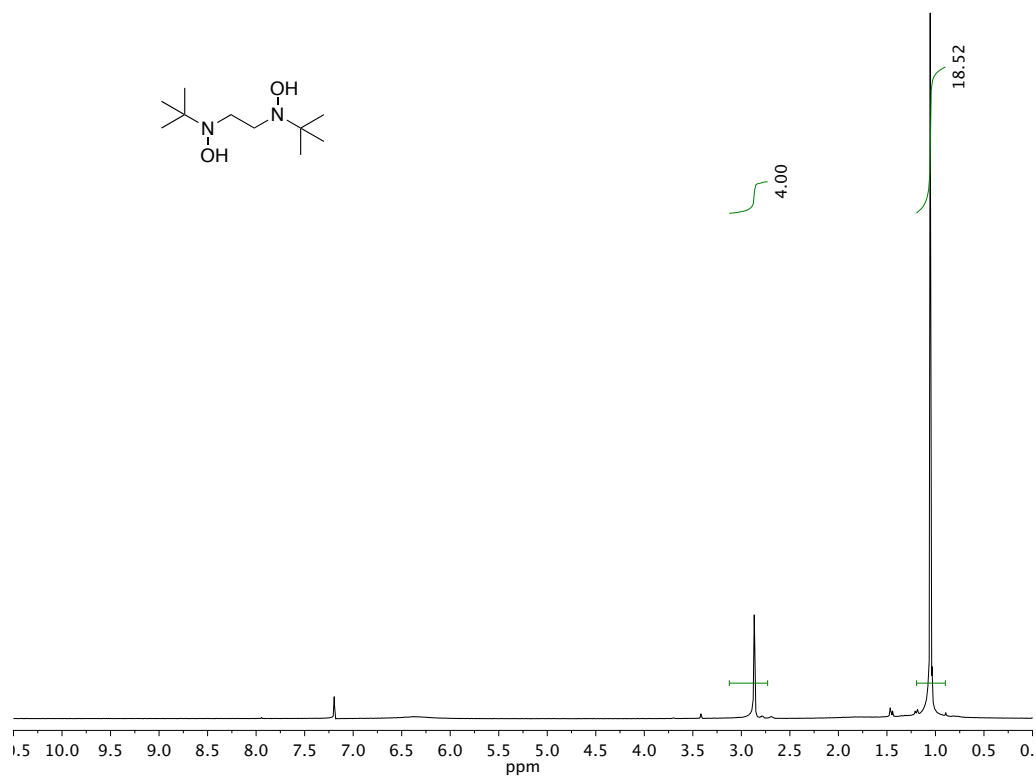


Figure S7. ¹H spectrum for **3**.

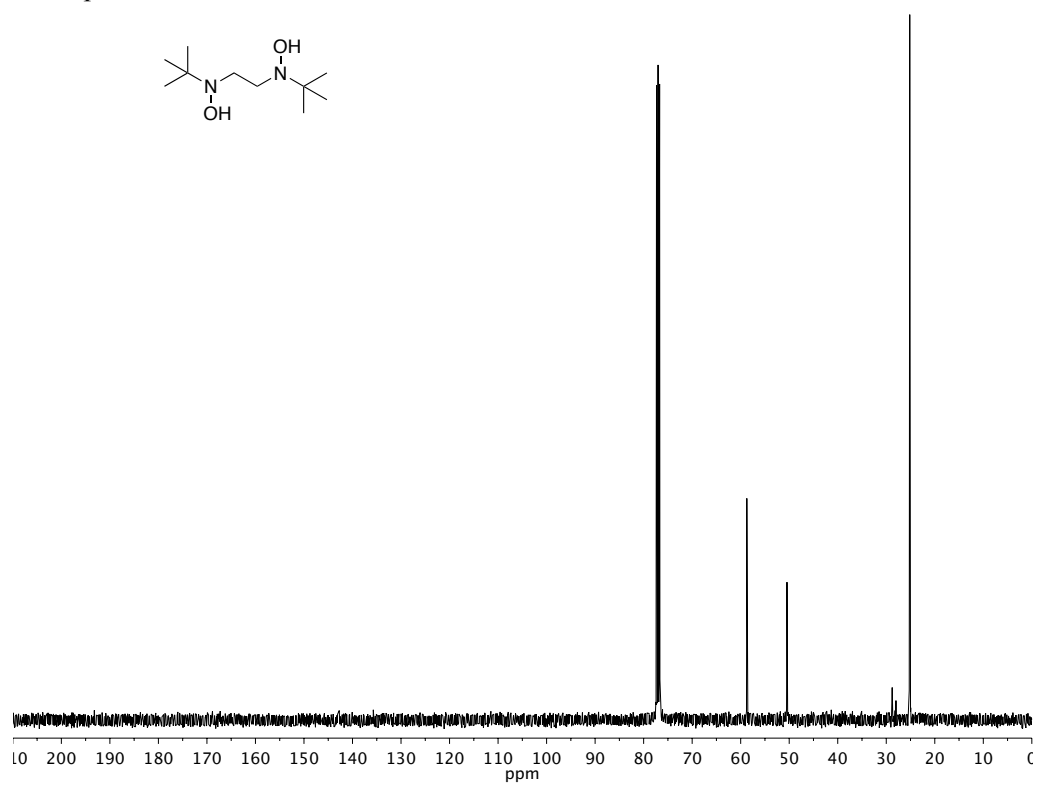


Figure S8. ¹³C spectrum for **3**.

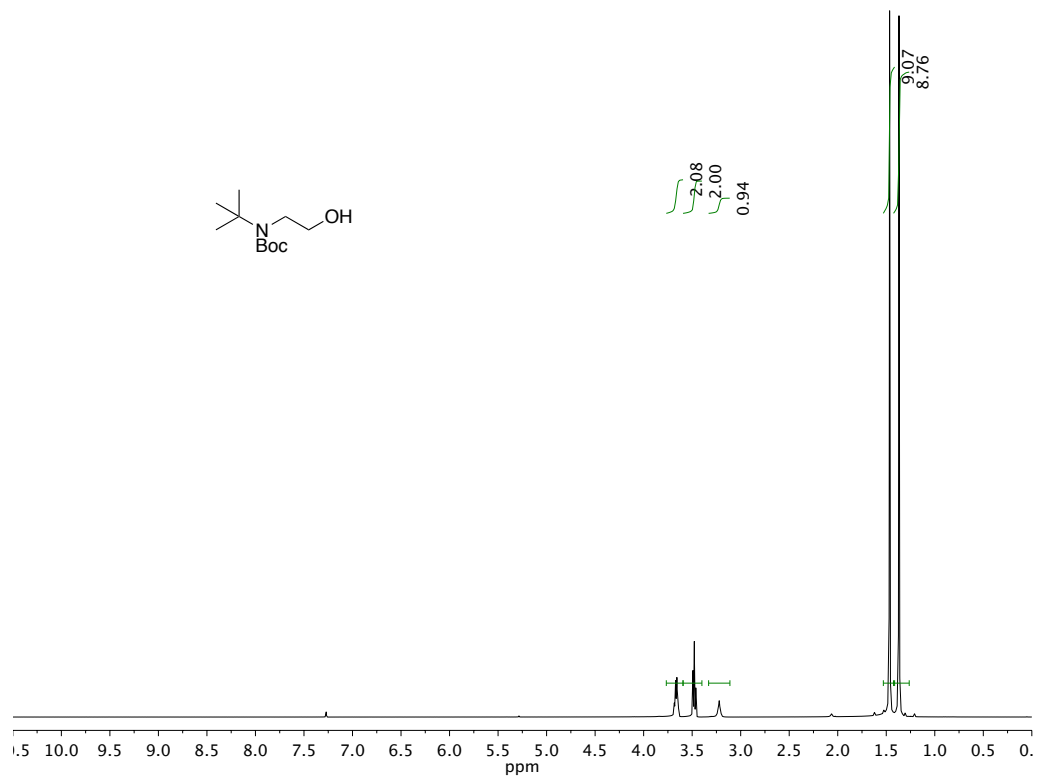


Figure S9. ¹H spectrum for the product of step i in the synthesis of **4**.

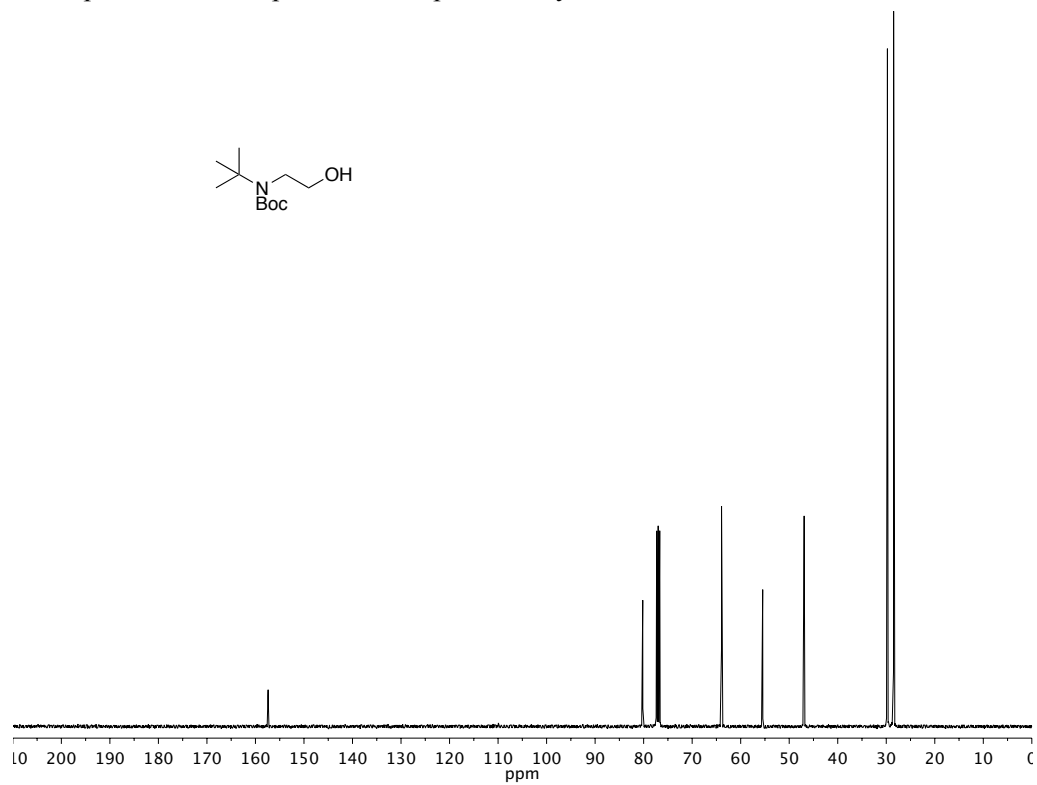


Figure S10. ¹³C spectrum for the product of step i in the synthesis of **4**.

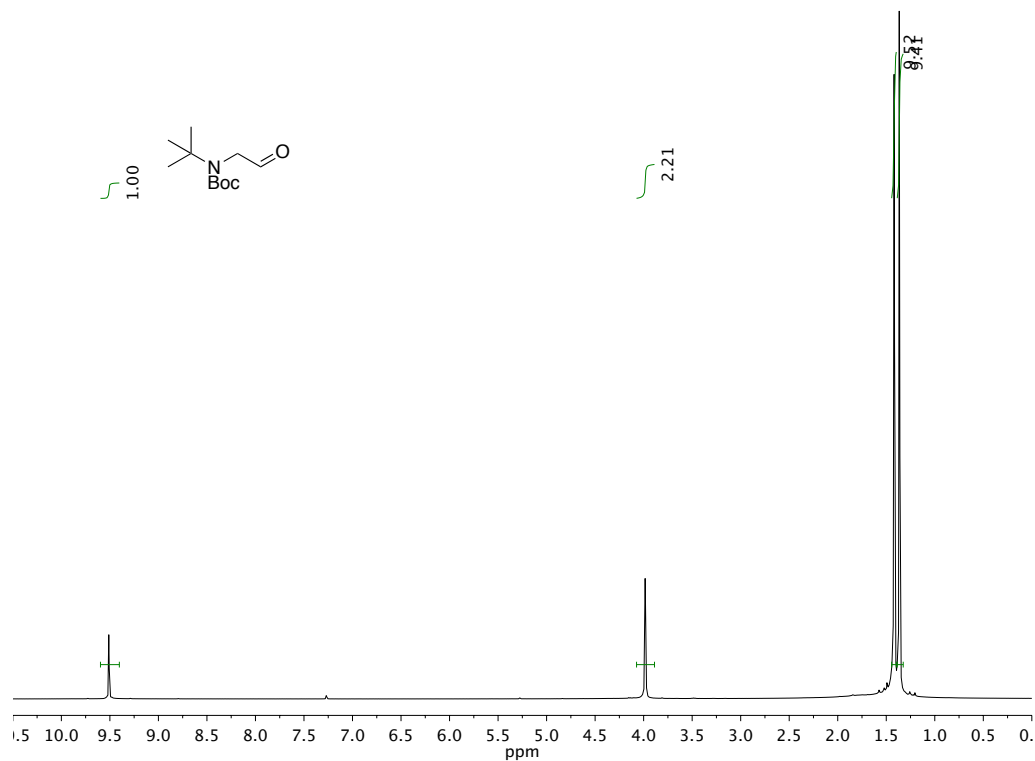


Figure S11. ¹H spectrum for the product of step ii in the synthesis of **4**.

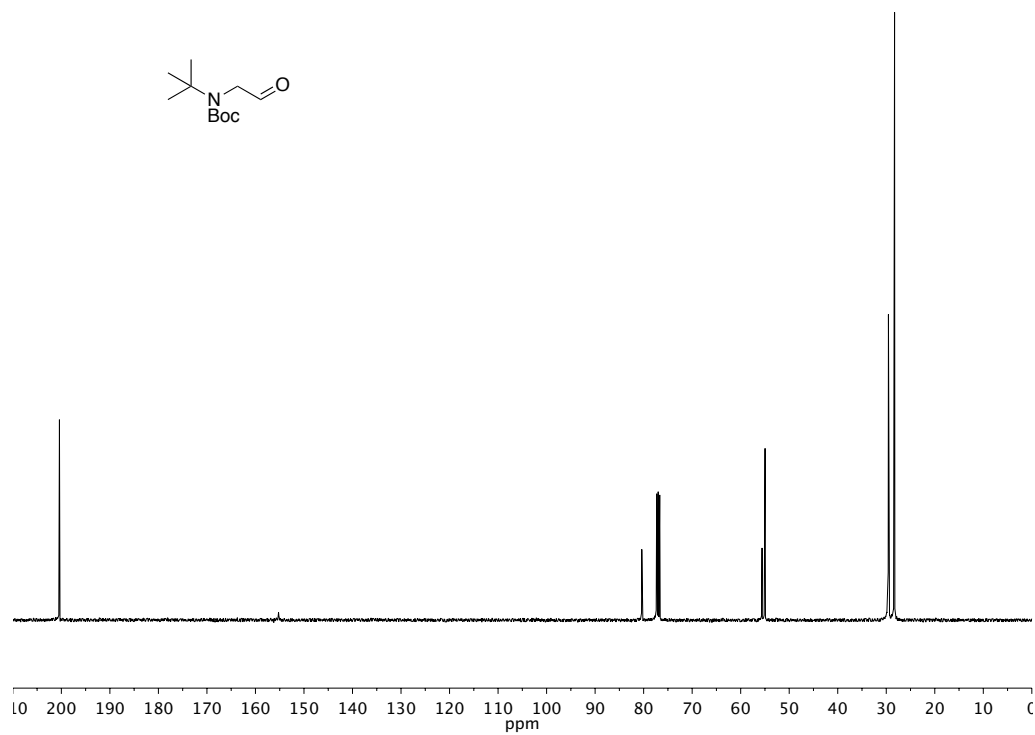


Figure S12. ¹³C spectrum for the product of step ii in the synthesis of **4**.

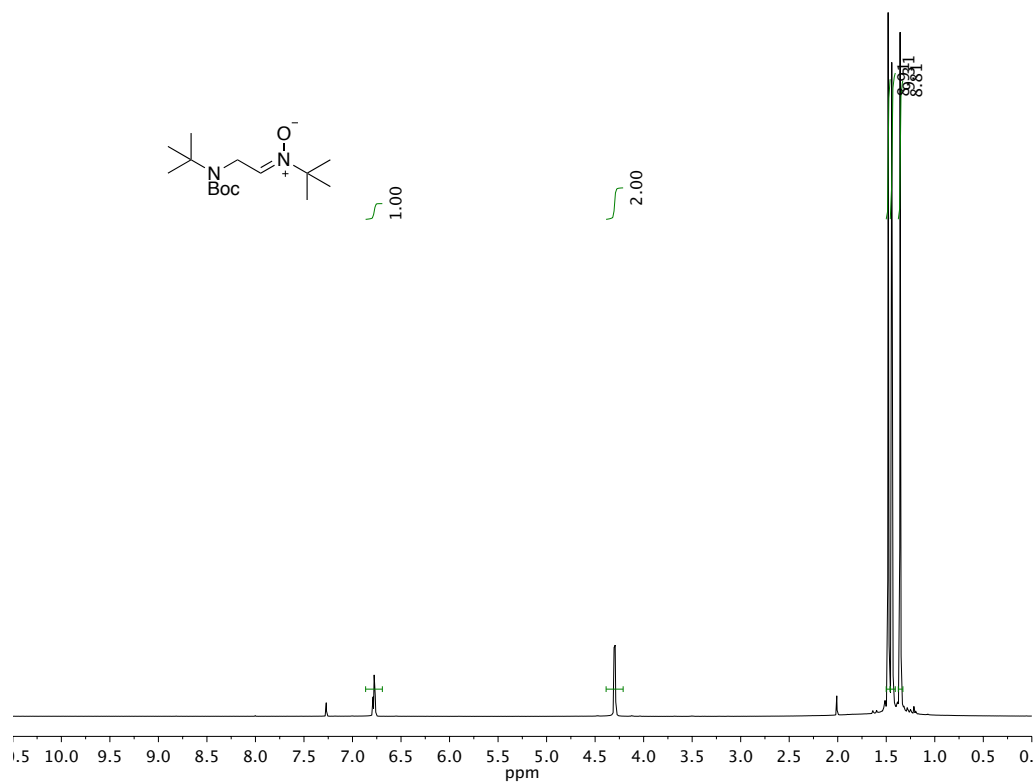


Figure S13. ¹H spectrum for the product of step iii in the synthesis of **4**.

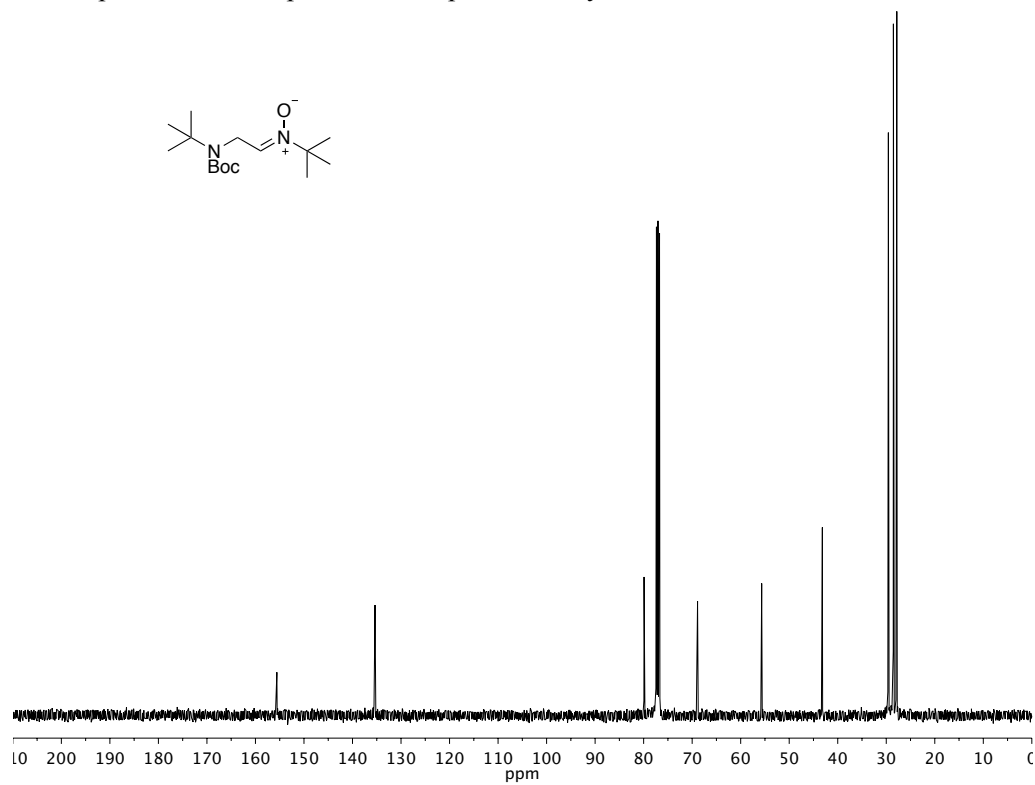


Figure S14. ¹³C spectrum for the product of step iii in the synthesis of **4**.

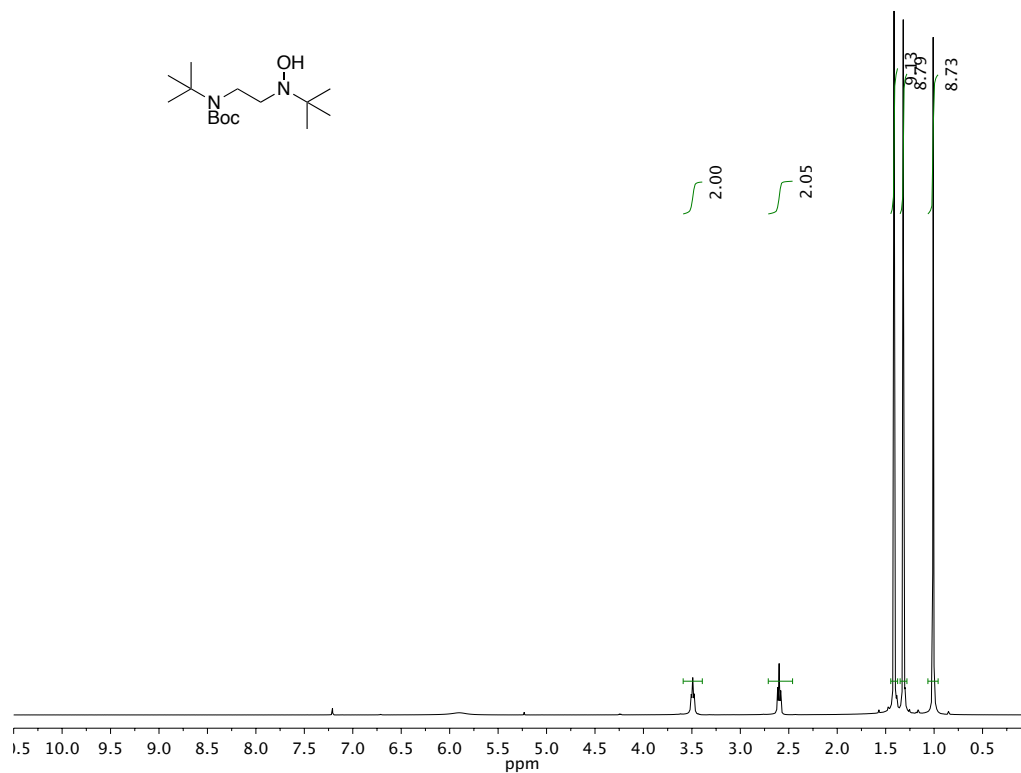


Figure S15. ¹H spectrum for the product of step iv in the synthesis of **4**.

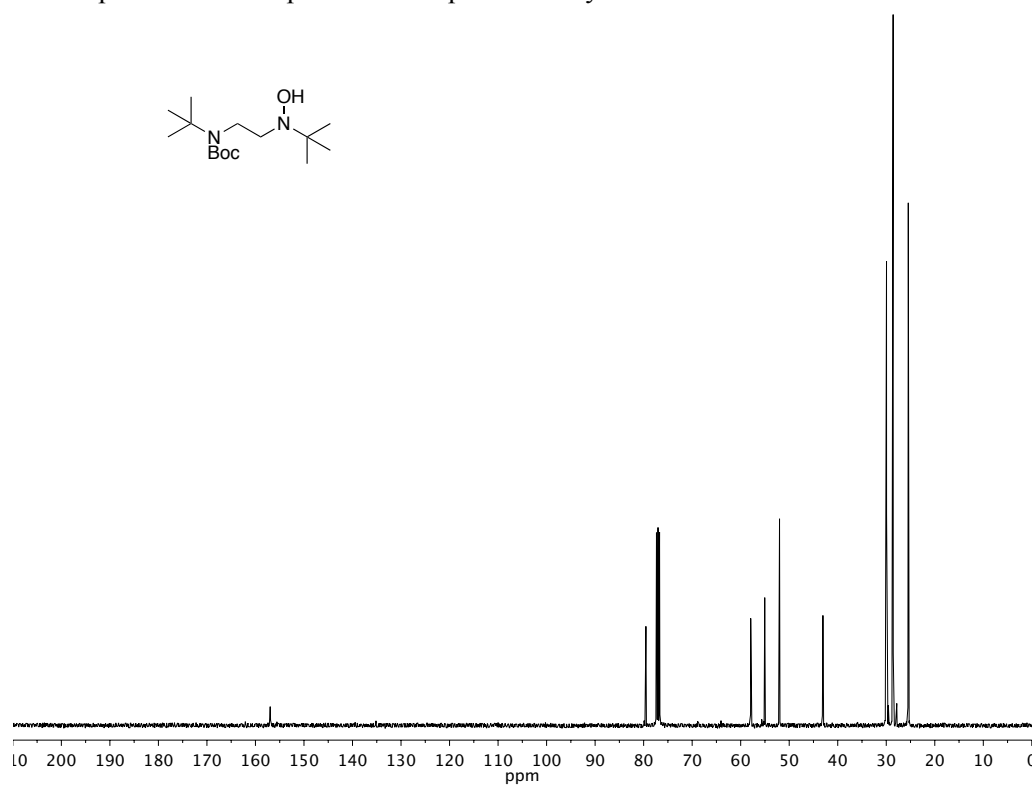


Figure S16. ¹³C spectrum for the product of step iv in the synthesis of **4**.

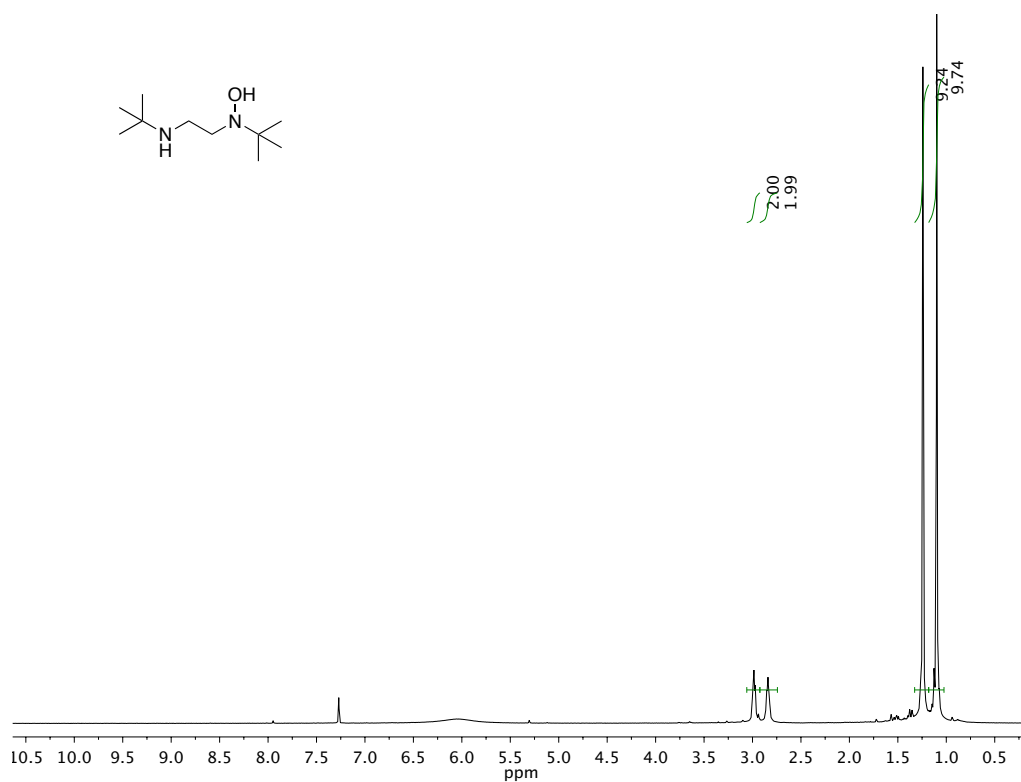


Figure S17. ¹H spectrum for **4**.

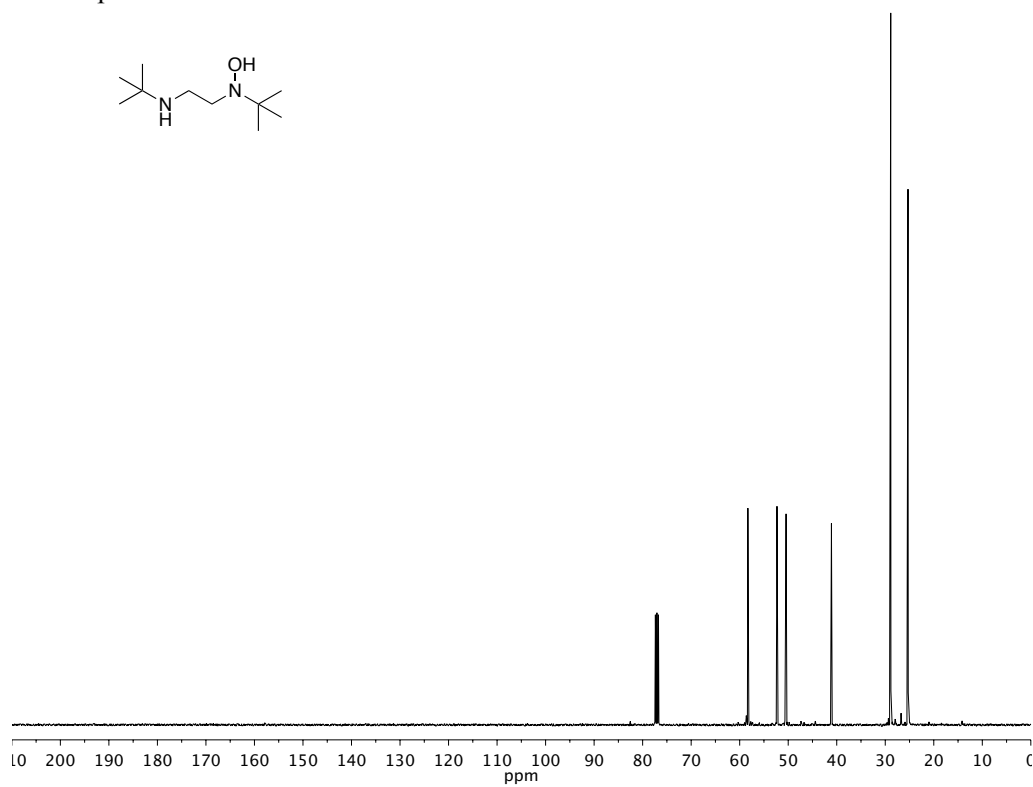


Figure S18. ¹³C spectrum for **4**.

V. Methods for Gas-Uptake Kinetics

Each set of data was collected using a 6-well gas uptake apparatus which holds individually calibrated 25 mL round bottom flasks, each connected to a pressure transducer designed to measure the gas pressure within each sealed reaction vessel.² Five vessels contained various reaction mixtures, and the sixth well used as a solvent control for variations in pressure. The apparatus was evacuated and filled with O₂ to a pressure of 800 torr five times. The pressure was established at pressure of 500 torr O₂ and the flasks heated to 27 °C. A solution of alcohol was added via syringe through a septum, and the pressure and temperature allowed to equilibrate. When the pressure and temperature stabilized, a solution of catalyst was added via syringe through a septum. It is very important that the Cu solution is not oxidized prior to initiating the reaction. [Cu(MeCN)₄]PF₆ is relatively stable under air for < ~30 min; however, solutions of [Cu(MeCN)₄]PF₆ with DBED and/or DMAP must be prepared under an inert atmosphere. Details for the alcohol and catalyst solutions used in each experiment are below. Data were acquired using custom software written within LabVIEW (National Instruments).

A. Kinetic Competence of TEMPO as a nitroxyl cocatalyst under the reaction conditions.

Solution A: 93.1 mg 1-octanol (0.143 M) and 5.6 mg TEMPO (0.00714 M) in 5 mL dichloromethane.

Solution B: 37 mg [Cu(MeCN)₄]PF₆ (0.05 M), 17.2 mg DBED (0.05 M), and 49 mg DMAP (0.2 M) in 2 mL dichloromethane.

Flask	Solution A (mL)	Solution B (mL)	Solution C (mL)	Solution D (mL)	Solution E (mL)	Solution F (mL)	Solvent
1	-	-	-	-	-	-	4
2	3.5	0.5	0	0	0	0	0

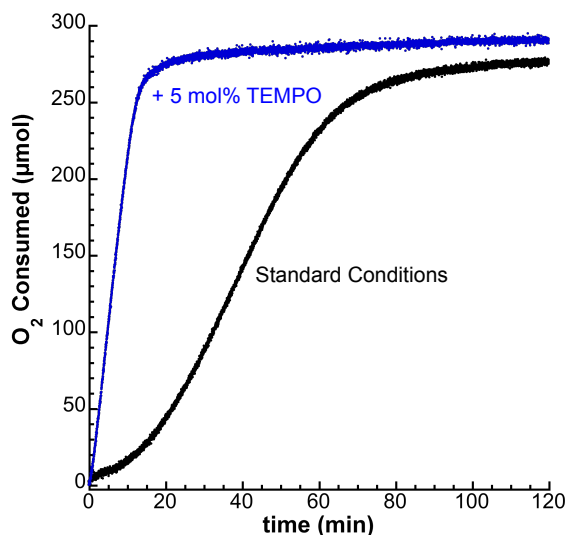


Figure S19. O₂-uptake time course data comparing reactions with and without added TEMPO. Reaction Conditions: 0.125 M 1-octanol, 6.25 mM [Cu(MeCN)₄]PF₆, 6.25 mM DBED, 25 mM DMAP, 6.25 mM TEMPO in blue trace, 100 mg 4Å MS, 500 torr O₂, 27 °C.

B. Kinetic Competence of **3** and **4**.

Solution A: 541.8 mg 1-octanol (0.167 M), and 100.7 mg DMAP, 25 mL dichloromethane.

Solution B: 62 mg $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$ (0.0833 M) in 2 mL dichloromethane.

Ligand Solution: Solution A: 12.2 mg DBED 2 mL dichloromethane, Solution B: 9.2 mg **3** in 1.5 mL dichloromethane, Solution C: 9.2 mg **3** and 10.1 mg DBED in 1.5 mL dichloromethane, Solution D: 10.9 mg **4** in 1.5 mL dichloromethane, or Solution E: 10.9 mg **4** and 10.1 mg DBED in 1.5 mL dichloromethane (all 0.0357 M).

Flask	Solution A (mL)	Solution B (mL)	Ligand Solution (mL)	Solvent
1	-	-	-	4
2	3	0.3	0.7 (Solution A)	0
3	3	0.3	0.7 (Solution B)	0
4	3	0.3	0.7 (Solution C)	0
5	3	0.3	0.7 (Solution D)	0
6	3	0.3	0.7 (Solution E)	0

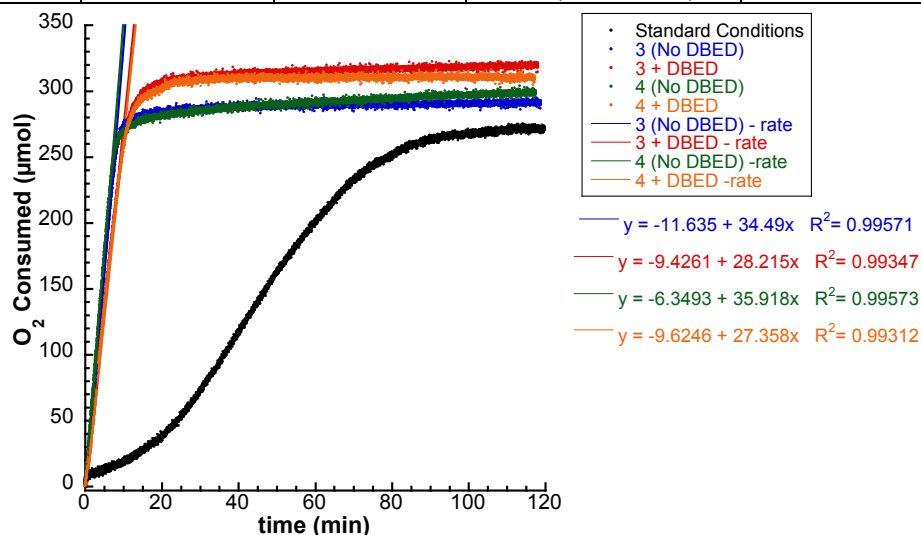


Figure S20. O₂-uptake time course data comparing reactions with and without added hydroxylamines **3** and **4** in the presence or absence of DBED. Reaction Conditions: 0.125 M 1-octanol, 6.25 mM $[\text{Cu}(\text{MeCN})_4]\text{PF}_6$, 6.25 mM DBED and/or **3** or **4**, 25 mM DMAP, 100 mg 4Å MS, 500 torr O₂, 27 °C.

VI. Synthesis/Characterization of Deuterated Alcohols for KIE Experiments

Benzylalcohol- d_1 This procedure was adapted based upon literature procedure.⁵ 750 mg (7.1 mmol) of benzaldehyde was massed into a 100 mL round-bottom flask equipped with a Teflon™ stirbar. 12.5 mL of MeOD was added and the solution was cooled in an ice bath. 321 mg NaBD₄ (7.6 mmol) was added portion-wise over ~10 min as solid. The reaction was monitored by TLC until all of the starting material was consumed. The reaction was quenched with 50 mL saturated NH₄Cl. The resulting solution was extracted with EtOAc (3 x 30 mL) and dried over MgSO₄. The solvent was removed under reduced pressure and the resulting oil was purified by silica gel column chromatography (3:1 hexane:ethyl acetate). The solvent was removed under reduced pressure, giving a clear and colorless oil (640.4 mg, 83%). The deuterium incorporation was determined to be > 98% by ¹H NMR.

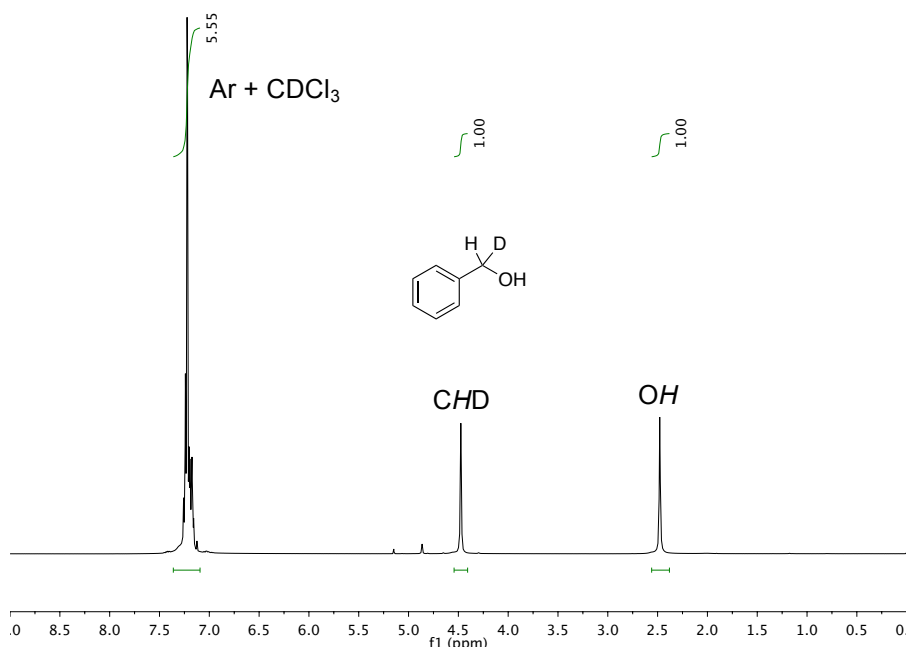


Figure S21. ¹H NMR spectrum of benzylalcohol- d_1 .

VII. Methods and Data for Determination of KIE Values

KIE values were determined by using quantitative ¹H NMR analysis. The intramolecular competition KIE was determined by comparing the integration of the *HCO* (δ 10.1) and the *ortho CH* in benzaldehyde using the equation:

$$\text{KIE} = \text{int}(\delta 7.9)/2 - \text{int}(\delta 10.1).$$

Full analysis is presented below, showing the yield of *H*- and *D*-aldehyde, remaining starting material, and mass balance.

(A) [Cu(MeCN)₄]PF₆/DBED/DMAP catalyst system intramolecular competition KIE 37.5 mg of flame-dried 4Å molecular sieves was weighed into an 8 mm culture tube, which was then sealed with a rubber septum and placed in an oil bath at 27 °C. The tube was then purged with O₂ for 5 min. 1 mL of 0.1875 M benzylalcohol- d_1 in dichloromethane was then added. 0.5 mL 18.75/18.75/75 mM [Cu(MeCN)₄]PF₆/DBED/DMAP in dichloromethane was added to this solution to initiate the reaction. After 2 h, the solution was filtered through a silica plug using EtOAc eluent. The solvent was evaporated and the resulting oil was subjected to ¹H NMR analysis using a 30 second delay time.

Table S1. ^1H NMR integrations used to determine intramolecular competition KIE for $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DBED}/\text{DMAP}$ aerobic alcohol oxidation.

a	Relative Integration				yield H ald	yield D ald	RSM	KIE
	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	23.4%	76.4%	0.0%	3.26
	1.00	8.52	21.33	0.0	Mass balance: 99.9%			
b	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1.00	8.72	21.01	0.0	23.8%	80.0	0.0%	3.36
					Mass balance: 103.8%			
c	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1.00	8.53	21.4	0.0	23.4%	76.3%	0.0%	3.27
					Mass balance: 99.7%			

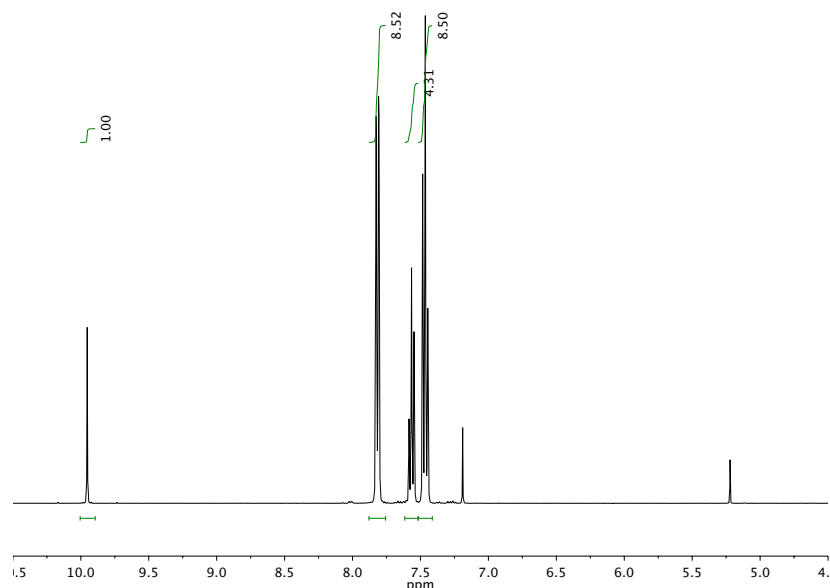


Figure S22. Representative ^1H NMR spectrum used to generate data in Table S1.

(B) [Cu(MeCN)₄]PF₆/3/DMAP catalyst system intramolecular competition KIE 37.5 mg of flame-dried 4Å molecular sieves was weighed into an 8 mm culture tube, which was then sealed with a rubber septum and placed in an oil bath at 27 °C. The tube was then purged with O₂ for 5 min. 1 mL of 0.1875 M benzylalcohol-*d*₁ in dichloromethane was then added. 0.25 mL of a 18.75 mM solution of **3** in dichloromethane was added to this solution, followed immediately by 0.25 mL of a 18.75/75 mM solution of [Cu(MeCN)₄]PF₆/DMAP in dichloromethane. After 10 minutes, the solution was filtered through a silica plug using EtOAc eluent. The solvent was evaporated and the resulting oil was subjected to ¹H NMR analysis using a 30 second delay time.

Table S2. ¹H NMR integrations used to determine intramolecular competition KIE for [Cu(MeCN)₄]PF₆/3/DMAP catalyst system intramolecular competition KIE.

a	Relative Integration				yield H ald	yield D ald	RSM	KIE
	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	22.8%	77.4%	0.0%	3.40
	1.00	8.79	21.93	0.0	Mass balance: 100.2%			
b	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1.00	8.48	21.21	0.0	23.6%	76.4%	0.0%	3.24
					Mass balance: 100.0%			
c	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1.00	8.60	21.37	0.0	23.4%	77.2%	0.0%	3.30
					Mass balance: 100.6%			

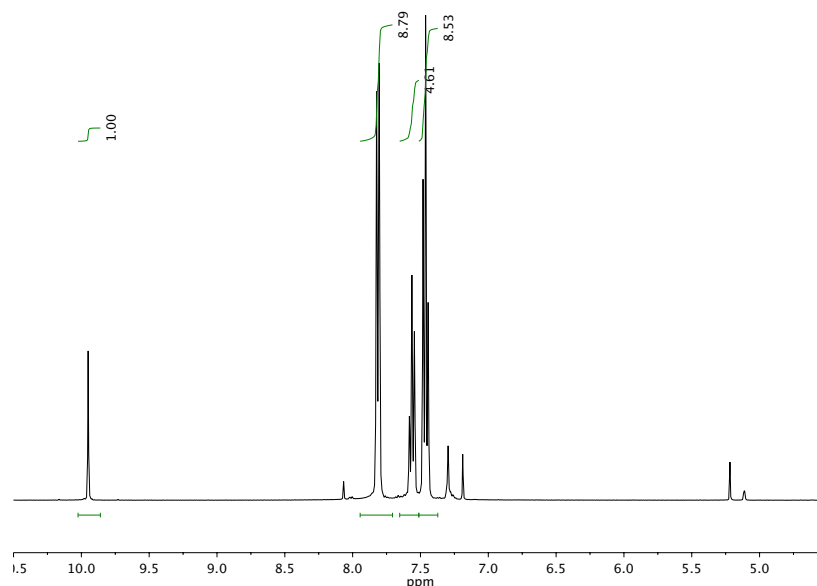


Figure S23. Representative ¹H NMR spectrum used to generate data in Table S2.

(C) [Cu(MeCN)₄]PF₆/4/DMAP catalyst system intramolecular competition KIE 37.5 mg of flame-dried 4Å molecular sieves was weighed into an 8 mm culture tube, which was then sealed with a rubber septum and placed in an oil bath at 27 °C. The tube was then purged with O₂ for 5 min. 1 mL of 0.1875 M benzylalcohol-*d*₁ in dichloromethane was then added. 0.25 mL of a 18.75 mM solution of **4** in dichloromethane was added to this solution, followed immediately by 0.25 mL of a 18.75/75 mM solution of [Cu(MeCN)₄]PF₆/DMAP in dichloromethane. After 10 minutes, the solution was filtered through a silica plug using EtOAc eluent. The solvent was evaporated and the resulting oil was subjected to ¹H NMR analysis using a 30 second delay time.

Table S3. ¹H NMR integrations used to determine intramolecular competition KIE for [Cu(MeCN)₄]PF₆/4/DMAP catalyst system intramolecular competition KIE.

a	Relative Integration				yield H ald	yield D ald	RSM	KIE
	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	23.5%	74.5%	2.1%	3.19
	1.00	8.37	21.27	0.09	Mass balance: 100.5%			
b	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1	8.70	21.53	0.05	23.2%	77.8%	1.1%	3.35
					Mass balance: 101.0%			
c	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1.00	8.71	21.82	0.04	22.9%	76.9%	0.9%	3.36
					Mass balance: 100.7%			

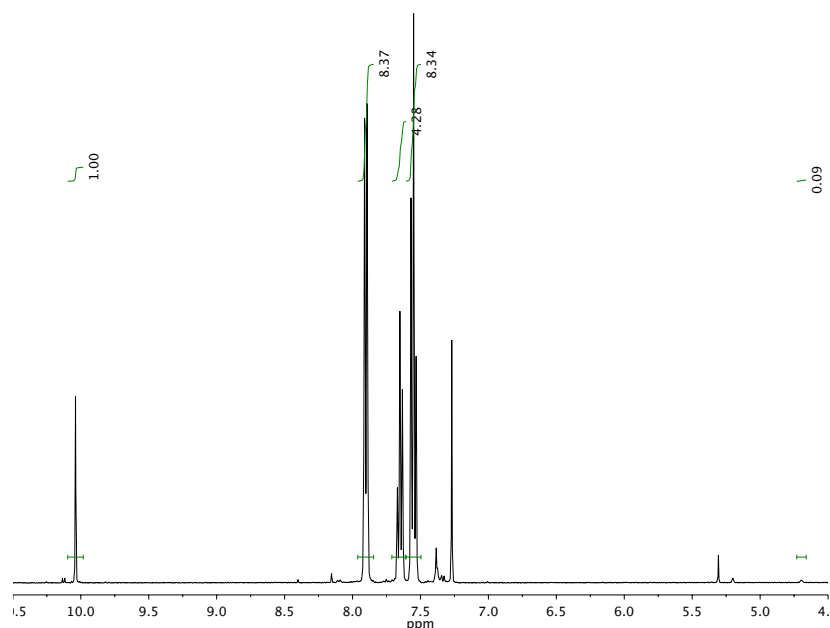


Figure S24. Representative ¹H NMR spectrum used to generate data in Table S3.

(D) [Cu(MeCN)₄]OTf/^{MeO}bpy/NMI/ABNO catalyst system intramolecular competition KIE 0.6 mL of a MeCN solution containing 0.167 M benzylalcohol-*d*₁ and 0.00167 M ABNO was added to an 8 mm culture tube. 0.4 mL of a MeCN solution containing 0.0125/0.0125/0.025 M [Cu(MeCN)₄]OTf/^{MeO}bpy/NMI was added to initiate the reaction. The reaction turned red brown within seconds. After 30 minutes, the solution was filtered through a silica plug using EtOAc eluent. The solvent was evaporated and the resulting oil was subjected to ¹H NMR analysis using a 30 second delay time.

Table S4. ¹H NMR integrations used to determine intramolecular competition KIE for [Cu(MeCN)₄]OTf/^{MeO}bpy/NMI/ABNO catalyst system intramolecular competition KIE.

a	Relative Integration				yield H ald	yield D ald	RSM	KIE
	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	25.9%	72.7%	0.0%	2.81
	1.00	7.62	19.34	0.0	Mass balance: 98.5%			
b	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1	7.93	19.61	0.0	25.5%	75.6%	0.0%	2.97
					Mass balance: 101.1%			
c	Ald (δ 10.1)	Ald (δ 7.9)	Ar tot	CHD (δ 4.7)	yield H ald	yield D ald	RSM	KIE
	1.00	6.93	17.38	0.0	28.8%	70.9%	0.0%	2.47
					Mass balance: 99.7%			

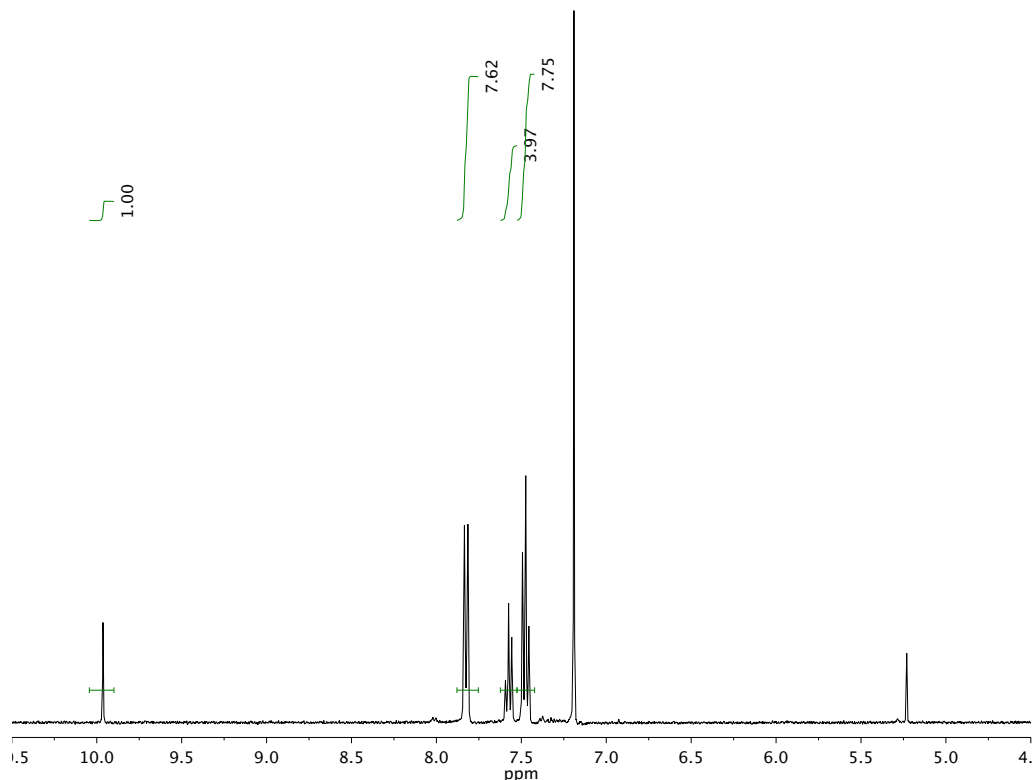


Figure S25. Representative ¹H NMR spectrum used to generate data in Table S3.

VIII. Methods and Data for Determination of Selectivity Values

A. Selectivity Experiments for **3** and **4**

100 mg of flame-dried 4Å molecular sieves were weighed into a 100 mL round-bottom flask, and the flask was sealed with a rubber septum. The flask was purged with O₂ for five minutes. After this, 3 mL of a dichloromethane solution containing 0.0833 M (0.167 M total) 1-octanol and 1-phenylethanol, and 0.066 M mesitylene was syringed into the flask. The solution was stirred in an oil bath set at 27 °C for 15 minutes. 0.5 mL of a 0.05 M solution of **3** or **4** was then added, followed quickly by 0.5 mL of a solution containing 0.05/0.2 M [Cu(MeCN)₄]PF₆/DMAP, which initiated the reaction. Aliquots were taken each minute. The aliquots were passed through a silica plug using EtOAc as an eluent, and then subjected to GC analysis using mesitylene as an internal standard.

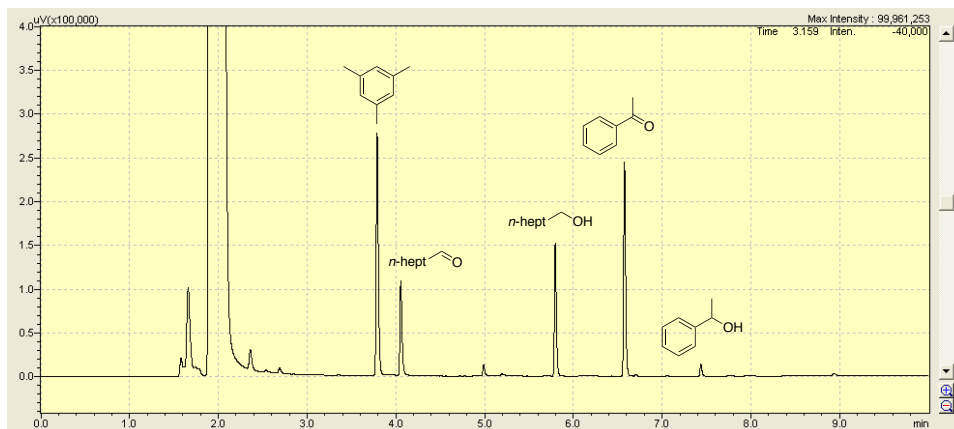


Figure S26. Representative GC chromatogram for selectivity experiments. The data correspond to the $t = 2$ min time point for the selectivity experiment using **4** as a cocatalyst.

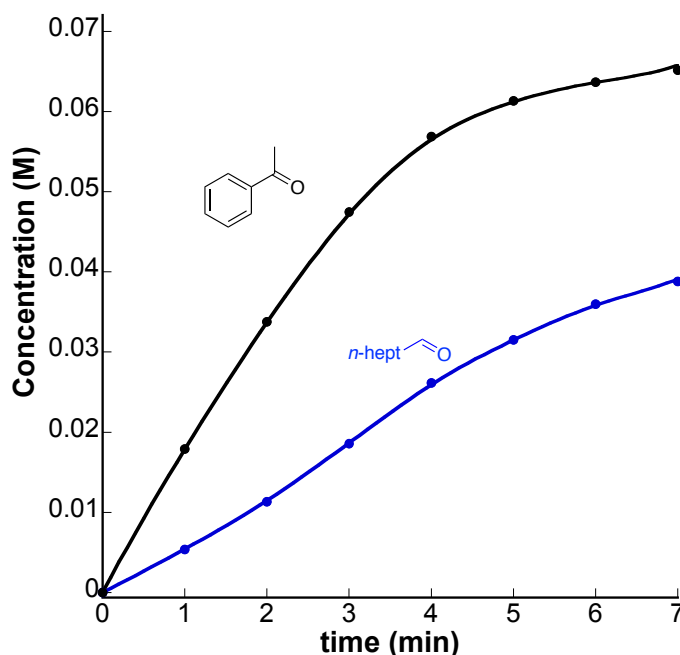


Figure S27. GC timecourse analyzing the selectivity between 1-octanol and 1-phenylethanol for [Cu(MeCN)₄]PF₆/DMAP/**3** catalyst system. Selectivity value in Figure 5C corresponds to the $t = 3$ min. timepoint.

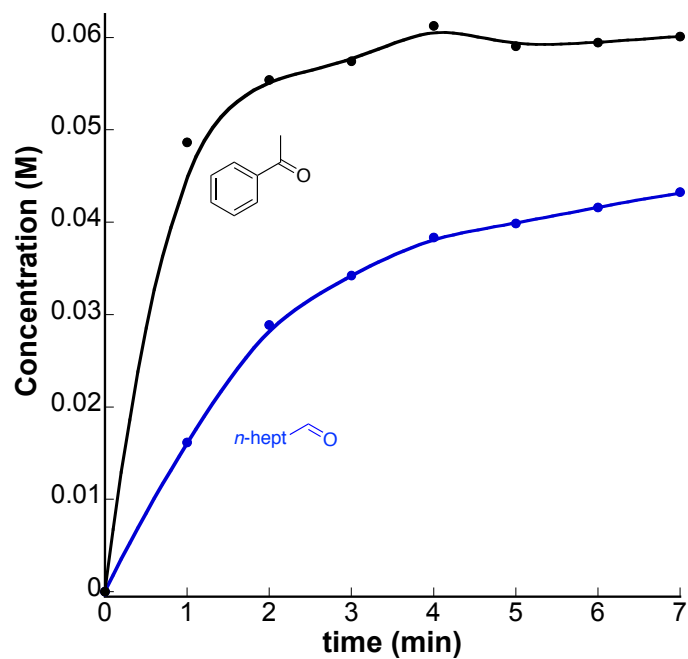


Figure S28. GC timecourse analyzing the selectivity between 1-octanol and 1-phenylethanol for $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DMAP}/\mathbf{4}$ catalyst system. Selectivity value in Figure 5C corresponds to the $t = 1$ min. timepoint.

B. Selectivity Experiment for ABNO

A 100 mL round-bottom flask sealed with a septum was purged with O₂ for five minutes. After this, 6.5 mL of a MeCN solution containing 0.0615 M of 1-octanol and 1-phenylethanol, 0.0308 M mesitylene, and 0.00123 M ABNO was added. The solution was stirred for 15 minutes, and then 1.5 mL of a 0.0267/0.0267/0.0534 M [Cu(MeCN)₄]OTf/MeO^{bpy}/NMI solution in MeCN was added to initiate the reaction. Aliquots were taken and passed through a silica plug using EtOAc as an eluent and subjected to GC analysis.

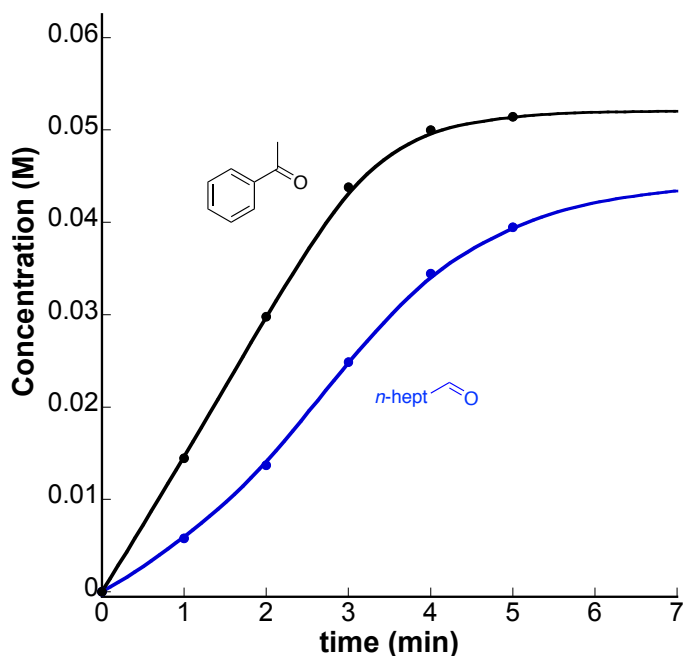


Figure S29. GC timecourse analyzing the selectivity between 1-octanol and 1-phenylethanol for [Cu(MeCN)₄]OTf/MeO^{bpy}/NMI/ABNO catalyst system. Selectivity value in Figure 5C corresponds to the $t = 3$ min. timepoint.

IX. EPR Spectroscopic Studies

A. Experimental Procedure to Generate Spectra in Figure 4

A 100 mL round-bottom flask containing a magnetic stir bar and 400 mg flame-dried 4Å molecular sieves was placed in an oil bath at a controlled temperature of 27 °C. The flask was evacuated and backfilled with O₂ five times, and brought to a final pressure of 500 torr O₂. 14 mL of 0.143 M 1-octanol solution in dichloromethane was then added to the flask. To initiate the reaction, 2 mL of 49.5/49.5/198 mM [Cu(MeCN)₄]PF₆/DBED/DMAP solution in dichloromethane was added. 400 µL aliquots were taken at 7.5, 15, 45 and 120 minutes after injection, and were flash-frozen in liquid nitrogen to prevent further reactivity. EPR simulations were performed using the Easy Spin program.⁶

B. Experimental Procedure to Generate Spectra in Figure 5B

A 100 mL round-bottom flask containing a magnetic stir bar and 100 mg flame-dried 4Å molecular sieves was placed in an oil bath at a controlled temperature of 27 °C. The flask was evacuated and backfilled with O₂ five times, and brought to a final pressure of 500 torr O₂. 3 mL of a dichloromethane solution containing 0.167 M 1-octanol and 0.084 M mesitylene was then added to the flask. To initiate the reaction, 0.5 mL of a solution containing 50 mM **4** and 200 mM DMAP in dichloromethane and 0.5 mL of a 50 mM [Cu(MeCN)₄]PF₆ solution in dichloromethane were added sequentially. 500 µL aliquots were taken at 2.5, 5, 7.5 minutes after injection. 350 µL was flash-frozen in liquid nitrogen to prevent further reactivity and used for EPR analysis. The remaining 150 µL was filtered through a silica plug and assayed by GC for octanal production (Figure S28).

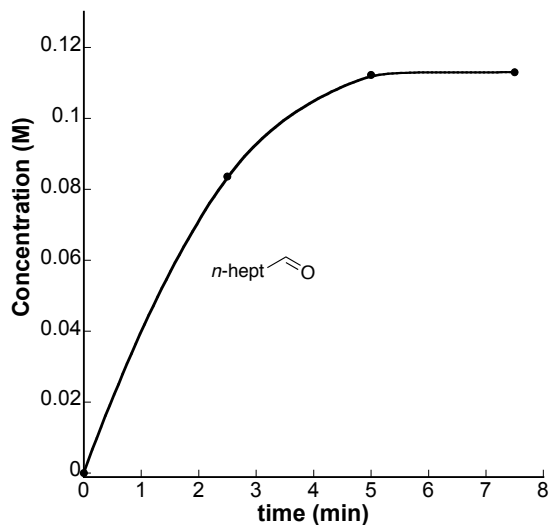


Figure S30. Time course data for octanal formation during the EPR experiment described above. The EPR spectrum in Figure 5B corresponds to the t = 5 minutes point.

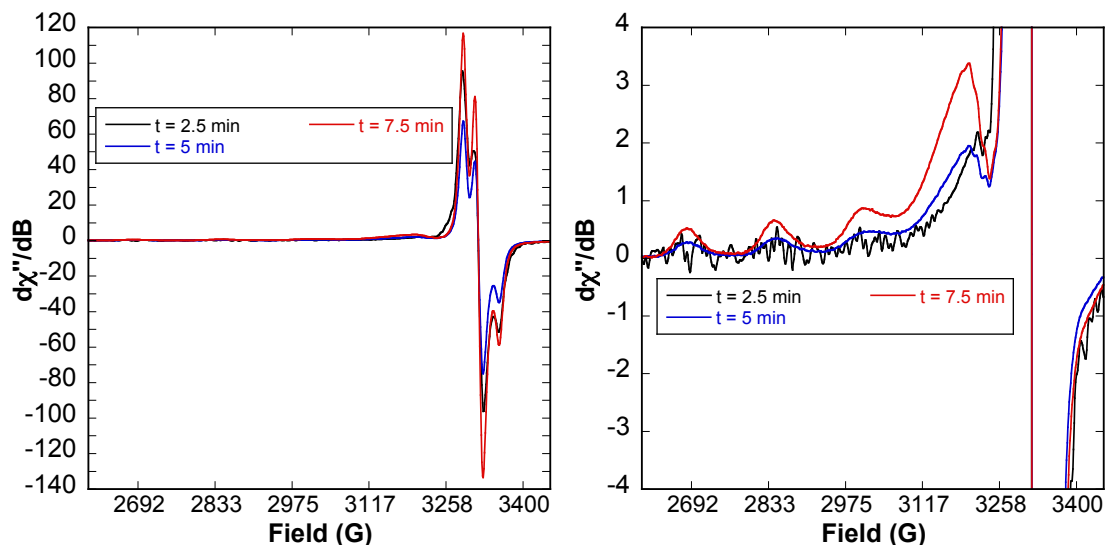


Figure S31. Evolution of the intensity of the organic radical (left) and Cu^{II} (right) EPR signals during the oxidation of 1-octanol catalyzed by 5 mol% $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\mathbf{4}$ and 20 mol% DMAP.

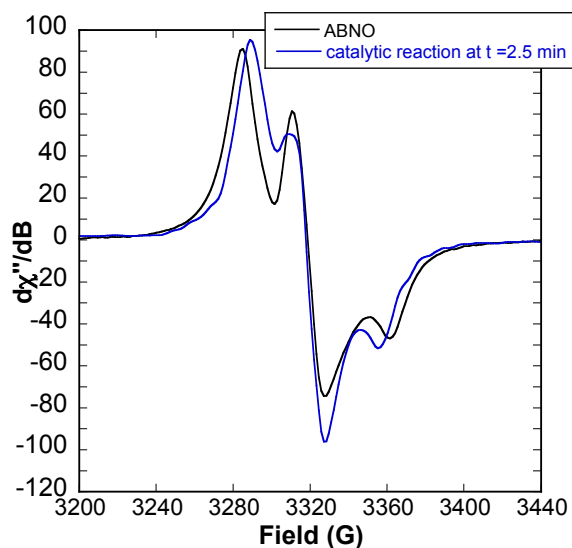


Figure S32. EPR spectra of 0.5 mM ABNO in CH_2Cl_2 (intensity multiplied by 18) and the reaction mixture during the oxidation of 1-octanol catalyzed by 5 mol% $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\mathbf{4}$ and 20 mol% DMAP at $t = 2.5$ minutes. Spectra collected at 115 K.

C. EPR Simulations

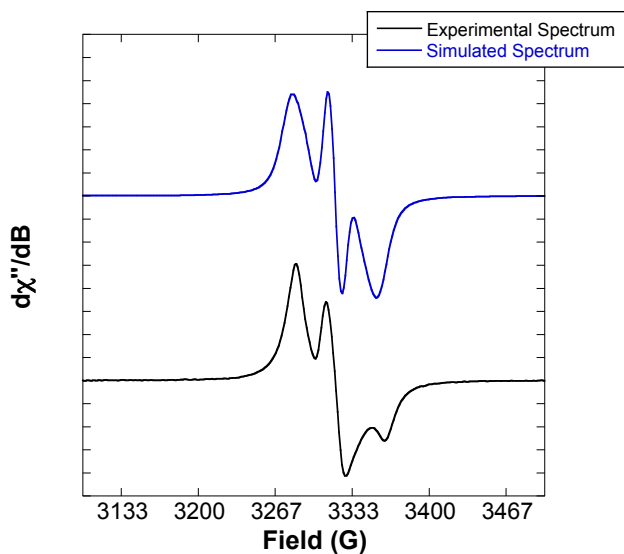


Figure S33. Simulated (blue) and experimental (black) EPR spectra of 0.5 mM ABNO in CH_2Cl_2 .

Simulation parameters:

Species 1 [^{14}N]:

$g = 2.03$

$A_{x,y}(\text{N}) = 40 \text{ MHz}$; $A_z(\text{N}) = 105 \text{ MHz}$

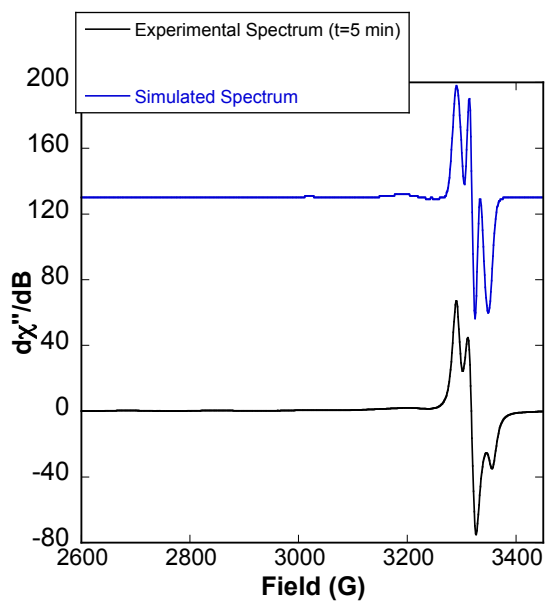


Figure S34. Simulated (blue) and experimental (black) EPR spectra for the oxidation of 1-octanol catalyzed by 5 mol% $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\mathbf{4}$ and 20 mol% DMAP at $t = 5$ minutes.

Simulation parameters:

Species 1 [Cu , ^{14}N , ^{14}N]:

$g_x = 2.04$; $g_y = 2.07$; $g_z = 2.265$

$A_{x,y}(\text{Cu}) = 25 \text{ MHz}$; $A_z(\text{Cu}) = 535 \text{ MHz}$

$A_{x,y}(\text{N}) = 40 \text{ MHz}$; $A_z(\text{N}) = 30 \text{ MHz}$

Species 2 [^{14}N]:

$g = 2.02$; $g_z = 2.21$

$A_{x,y}(\text{N}) = 33 \text{ MHz}$; $A_z(\text{N}) = 85 \text{ MHz}$

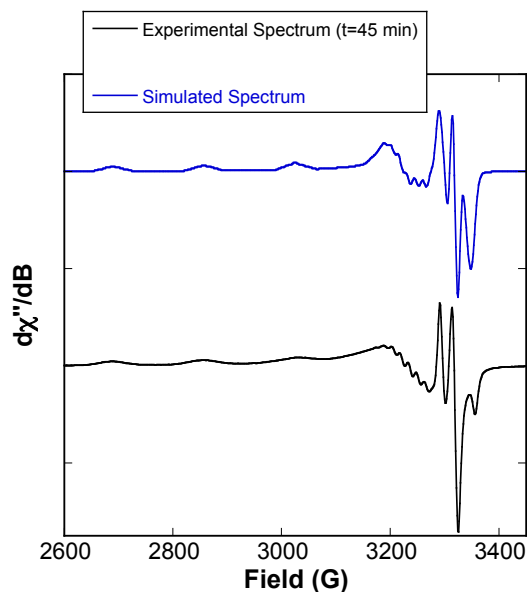


Figure S35. Simulated (blue) and experimental (black) EPR spectra for the oxidation of 1-octanol catalyzed by 5 mol% $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DBED}$ and 20 mol% DMAP at $t = 45$ minutes.

Simulation parameters:

Species 1 [Cu , ^{14}N , ^{14}N]:

$g_x = 2.04$; $g_y = 2.07$; $g_z = 2.26$

$A_{x,y}(\text{Cu}) = 25 \text{ MHz}$; $A_z(\text{Cu}) = 530 \text{ MHz}$

$A_{x,y}(\text{N}) = 40 \text{ MHz}$; $A_z(\text{N}) = 30 \text{ MHz}$

Species 2 [^{14}N]:

$g = 2.002$

$A_{x,y}(\text{N}) = 33 \text{ MHz}$; $A_z(\text{N}) = 85 \text{ MHz}$

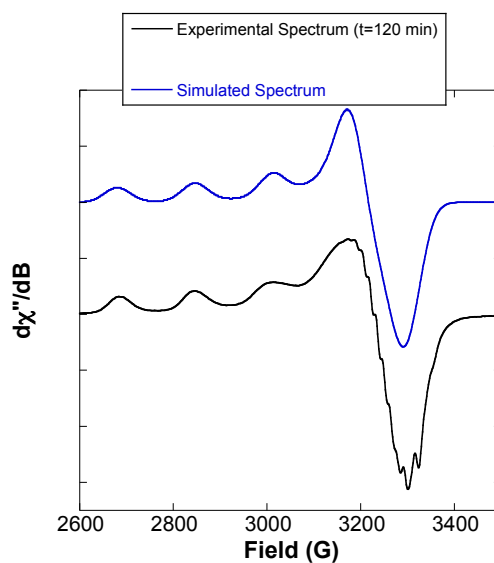


Figure S36. Simulated (blue) and experimental (black) EPR spectra for the oxidation of 1-octanol catalyzed by 5 mol% $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DBED}$ and 20 mol% DMAP at $t = 120$ minutes.

Simulation parameters:

Species 1 $[\text{Cu}, ^{14}\text{N}, ^{14}\text{N}]$:

$g_x = 2.05$; $g_y = 2.08$; $g_z = 2.27$

$A_{x,y}(\text{Cu}) = 25 \text{ MHz}$; $A_z(\text{Cu}) = 525 \text{ MHz}$

$A_{x,y}(\text{N}) = 40 \text{ MHz}$; $A_z(\text{N}) = 30 \text{ MHz}$

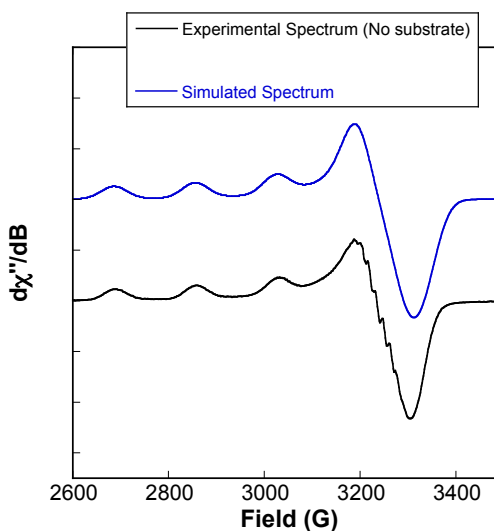


Figure S37. Simulated (blue) and experimental (black) EPR spectra for 6.25 mM $[\text{Cu}(\text{MeCN})_4]\text{PF}_6/\text{DBED}$ and 25 mM DMAP under an O_2 atmosphere.

Simulation parameters:

Species 1 $[\text{Cu}, ^{14}\text{N}, ^{14}\text{N}]$:

$g_x = 2.03$; $g_y = 2.07$; $g_z = 2.26$

$A_{x,y}(\text{Cu}) = 25 \text{ MHz}$; $A_z(\text{Cu}) = 535 \text{ MHz}$

$A_{x,y}(\text{N}) = 40 \text{ MHz}$; $A_z(\text{N}) = 30 \text{ MHz}$

IX. References

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