Oxidation of a [Cu_2S] Complex by N_2O and CO_2: Insights into a Role of Tetranuclearity in the Cu_Z Site of Nitrous Oxide Reductase

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General considerations

Unless otherwise specified, all reactions and manipulations were performed under purified N_2 in a glovebox or using standard Schlenk line techniques. Glassware was oven-dried prior to use. Reaction solvents (tetrahydrofuran, toluene and pentane) were sparged with argon and dried using a Glass Contour Solvent System built by Pure Process Technology, LLC, or purified by repeated freeze-pump-thaw cycles followed by prolonged storage over activated, 3-Å molecular sieves (methanol and NMR solvents). N_2O and CO_2 gas were purchased from PRAXAIR at a purity of 99.999% (5.0 UHP grade) and purified further by running through an O_2 removing catalyst column (RCI GetterMax 133T) and a drying column (Drierite). Literature methods were used to synthesize (IPr*)CuCl,[1] the free IPr* carbene,[2] (IPr*)Cu-OtBu,[3] (IPr*)Cu-SH,[3] and {(IPr*)Cu}$_2$(μ-S) (**1**),[3]. Unless otherwise specified, all other chemicals were purchased from commercial sources and used without further purification.

Physical measurements

NMR spectra were recorded at ambient temperature using Bruker Avance DPX-400 spectrometer. ^{1}H NMR chemical shifts were referenced to residual solvent peak. ^{31}P NMR chemical shifts were refrenced to external triphenylphosphine (-6.7 ppm). Elemental analyses were performed by Midwest Microlab, LLC in Indianapolis, IN. HRMS analyses were performed on Micromass 70 VSE mass spectrometer by the Mass spectroscopy Lab, SCS, University of Illinois. Single-crystal X-ray diffraction studies were performed using a Bruker PHOTON II diffractometer. Solution and refinement were accomplished with the SHELXTL suite of programs,[4] using standard methods,[5] and CIF files are included as Supporting Information.

Computational methods

All calculations were performed using Gaussian09, Revision B.01.[6] Density functional theory (DFT) calculations were carried out using a hybrid functional, BVP86, consisting of Becke's 1988 gradient corrected Slater exchange functional[7] combined with the VWNS local electron correlation functional and Perdew's 1986 nonlocal electron correlation functional.[8] Mixed basis sets were employed: the

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[3] Zhai, J.; Filatov, A. S.; Hillhouse, G. L.; Hopkins, M. D. *Chem. Sci*. **2016**, *7*, 589–595

[4] Sheldrick, G. M. *Acta Cryst.* **2008***, A64,* 112-122

[5] Müller, P. *Crystallography Reviews* **2009**, *15***,** 57–83

[6] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; ; Fox, D. J. Gaussian 09, Revision B.01; Gaussian, Inc., Wallingford, CT, **2010**.

[7] Becke, A. D. Phys. Rev. A: At., Mol., Opt. Phys. 1988, 38, 3098.

[8] Perdew, J. Phys. Rev. B: Condens. Matter Mater. Phys. 1986, 33, 8822−8824.

LANL2TZ(f) triple-ζ basis set[9,10,11]with effective core potential[12,13]was used for Cu, and the Gaussian09 internal 6-311+G(d) basis set was used for C, H, N, O and S. The bulky aryl groups of the IPr* (1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazo- 2-ylidene) ligands were truncated to methyl groups in order to minimize computational time. Frequency calculations confirmed that the optimized structures corresponded to energy minima with zero imaginary vibrational frequencies. Optimized XYZ coordinates are provided as Supporting Information.

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[9] Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 299−13.

[10] Roy, L. E.; Hay, P. J.; Martin, R. L. J. Chem. Theory Comput. 2008, 4, 1029−1031.

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[12] Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 270.

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Generation of {(IPr*) Cu}$_2$(μ-SO$_4$) (2) from (IPr*)CuCl:

In a nitrogen filled glovebox a scintillation vial was charged with IPr*CuCl (50 mg, 0.05 mmol) and Ag_2SO_4 (15 mg, 0.05 mmol). Toluene (4 mL) and methanol (2 mL) were then added. The reaction mixture was stirred at 65°C temperature for 8h, and then it was filtered through Celite. Volatiles were removed from the filtrate under reduced pressure. Then white solid was dissolved in C_6D_6, and mesitylene (0.05 mmol, 6.9 μL) was added as an internal integration standard. ^{1}H NMR integration indicated 3% conversion to **4**. Colorless single crystals suitable for X-ray diffraction studies were grown by diffusion of pentane vapors into a concentrated solution **2** in 2-methyltetrahydrofuran. Note: Due to a low yield of {(IPr*) Cu}$_2$(μ-SO$_4$) in this reaction, the single crystals used for X-ray diffraction were actually grown from a reaction mixture from **1** + CO_2 (see below). ^{1}H NMR (400 MHz, C_6D_6): δ 7.46 (s, 8H), 7.44 (s, 10H), 7.32 (s, 8H), 6.84 (s, b, 10H), 5.69 (s, 4H, NCH), 5.49 (s, 8H, CH Ph_2), 1.76 (s, 12H, CH_3).

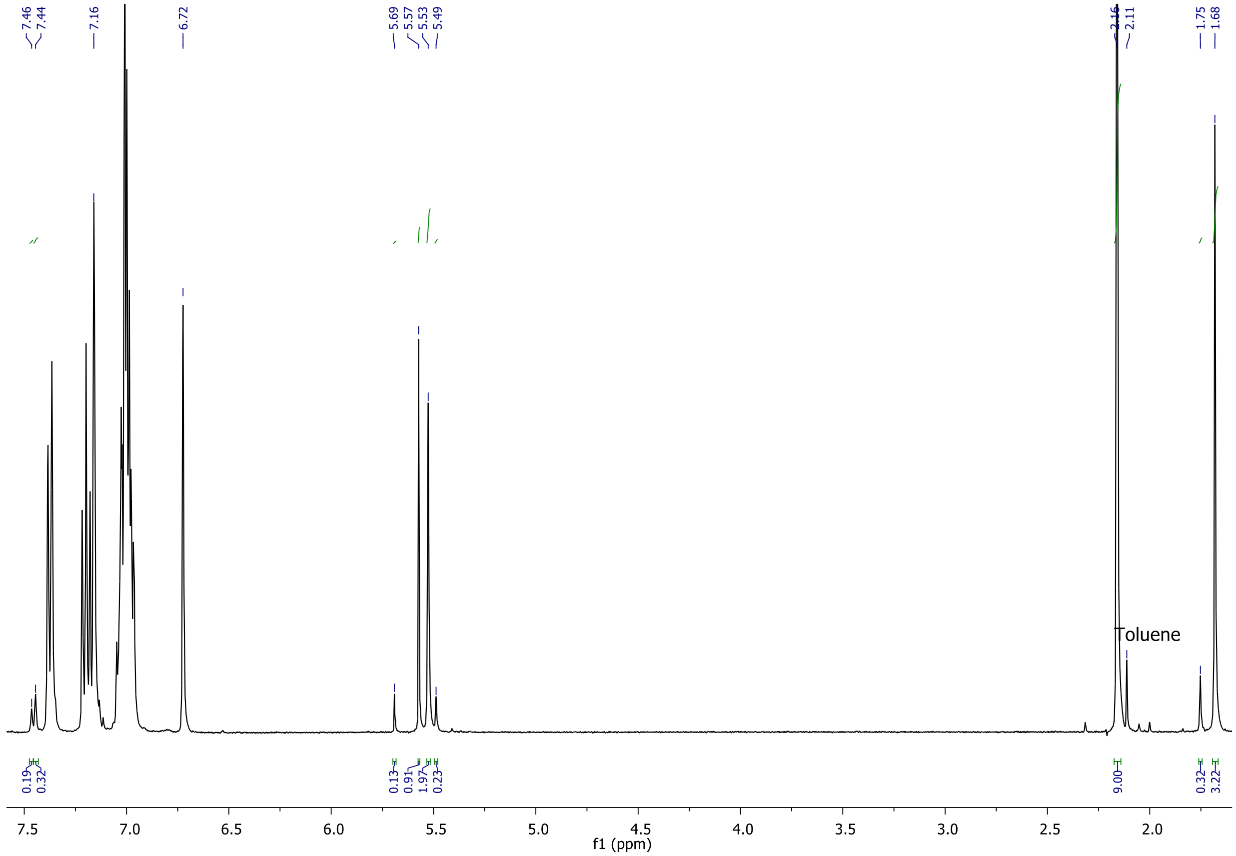


Figure S1. ^{1}H NMR spectrum of the reaction between (IPr*)CuCl and Ag_2SO_4 (C_6D_6, mesitylene internal standard).

Preparation of (IPr*)CuOH:

Inside the glovebox a 20 mL scintillation vial was charged with stir bar, (IPr*)CuCl (0.4 g, 0.39 mmol), CsOH (0.177 g, 1.18 mmol) and THF (15 mL). The reaction mixture was stirred at room temperature for 12 h, then filtered through Celite. The solvent was removed from the filtrate under reduced pressure to yield a white powder (0.373 g, 96%). Colorless single crystals suitable for X-ray diffraction studies were grown by diffusion of pentane vapors into a concentrated solution of (IPr*)CuOH in THF. ^{1}H NMR (400 MHz, C_6D_6): δ 7.50 (s, 4H), 7.48 (s, 4H, CH phenyl), 7.17-7.19 (m, 6H), 6.99-7.03 (m, 30H), 5.68 (s, 4H, CH ph$_2$), 5.54 (s, 2H, NCH), 1.73 (s, 6H, CH_3). Anal. Calcd for $C_{69}H_{57}CuN_2O$: C, 83.4; H, 5.79; N, 2.82. Found: C, 81.25; H, 5.59; N, 2.84. Repeated attempts at obtaining satisfactory combustion analysis results (with %C within ±0.4% of the calculated value) gave results with a large degree of variance, indicating either that the spectroscopically pure samples were decomposed during shipping/handling or that the compound does not combust cleanly.

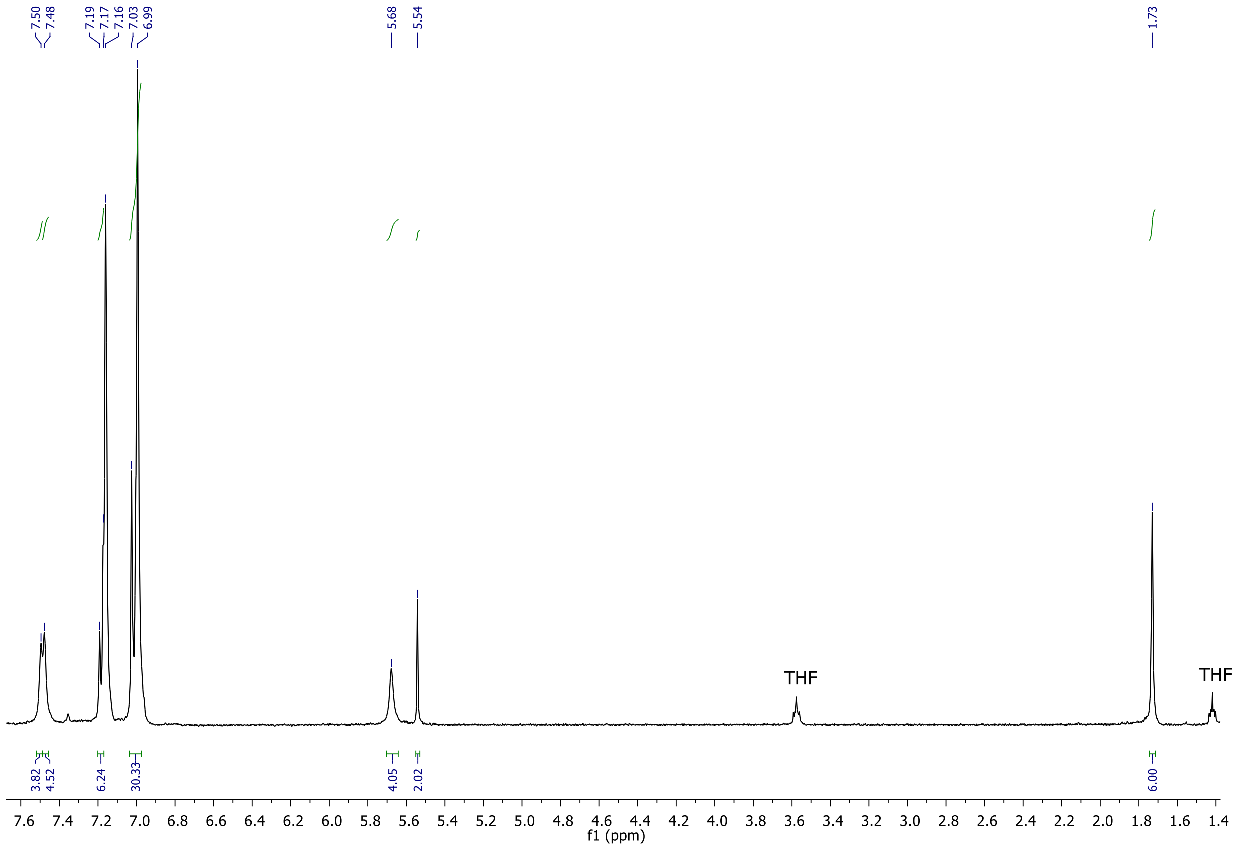


Figure S2. ^{1}H NMR spectrum of (IPr*)CuOH in C_6D_6.

Preparation of {(IPr*) Cu}$_2$(µ-O) (3) from (IPr*)CuOH:

Inside the glovebox a 50-mL Schlenk flask was charged with stir bar, (IPr*)CuOH (0.7 gr, 0.7 mmol), molecular sieves (3 g) and toluene (15 mL). The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The reaction mixture was stirred at 65°C for 6 h under N_2. After 6 h the reaction was cooled down to room temperature and was transferred inside the glovebox. The reaction was filtered through plug of Celite. Solvent was removed from the filtrate under reduced pressure to yield a white powder (0.35g, 25 %). ^{1}H NMR (400 MHz, C_6D_6): δ 7.44 (s, 8H), 7.42 (s, 10H), 7.30 (t, J=7.6 Hz, 18H), 7.09 (t, J=7.3 Hz, 12H), 6.93-7.0 (m, 56H), 5.59 (s, 8H, CH ph$_2$), 5.43 (s, 4H, NCH), 1.78 (s, 12H, CH_3). HRMS (ESI) calcd. for $[C_{138}H_{112}N_4OCu+H]^+$: 1967.7506 Found: 1967.7472

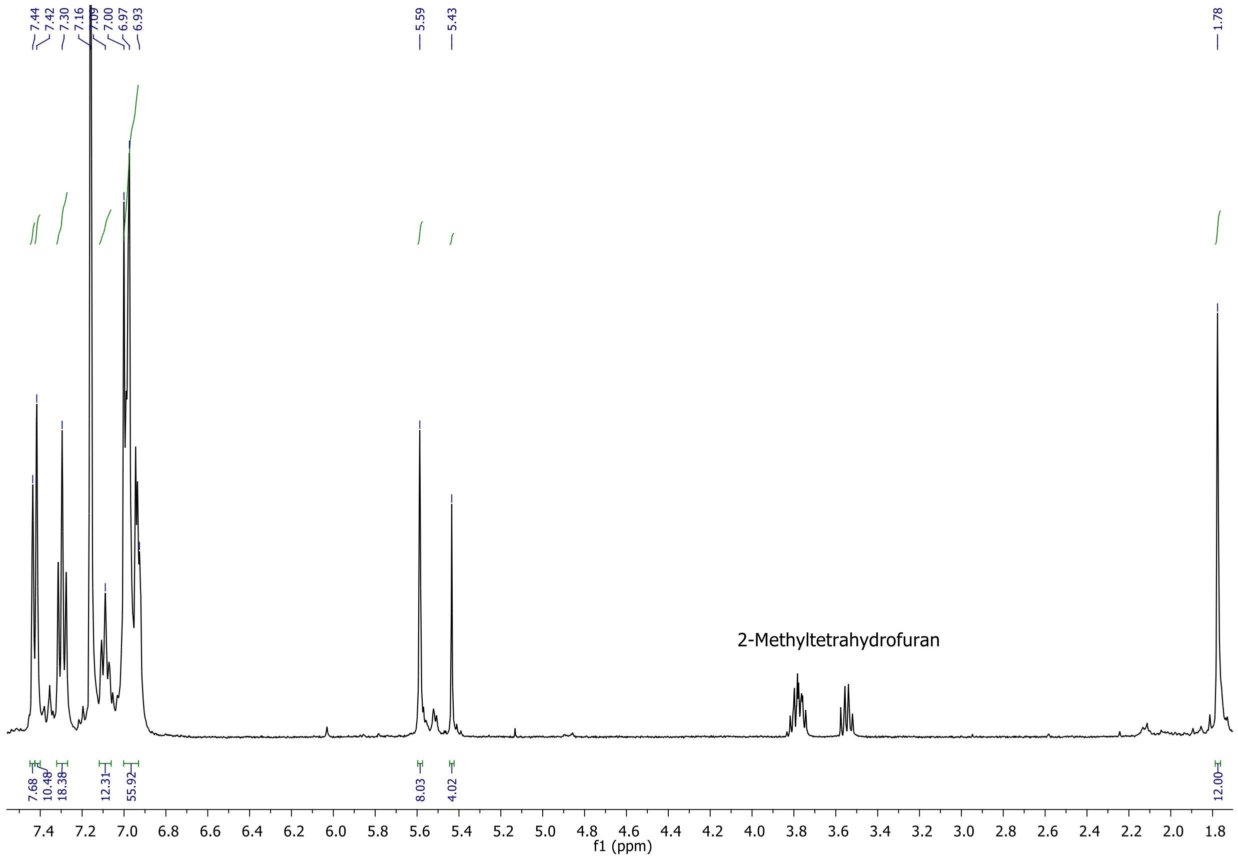


Figure S3. ^{1}H NMR spectrum of **3** in C_6D_6.

Preparation of {(IPr*)Cu}$_2$(μ-CS$_3$) (4):

In a nitrogen filled glovebox a scintillation vial was charged with **1** (15 mg, 0.0075 mmol) and stir bar. Benzene-*d*$_6$ (3 mL) was added, followed by CS$_2$ (0.46 µL, 0.007mmol). The reaction mixture was stirred at room temperature for 1 h then ^{1}H-NMR was taken to confirm complete conversion to **4**. Solvent was removed under reduced pressure to yield a pink powder (14 mg, 96 %). Pink single crystals suitable for X-ray diffraction studies were grown by diffusion of pentane vapors into concentrated solution of **4** in THF. ^{1}H NMR (400 MHz, C$_6$D$_6$): δ 7.54 (s, 6H), 7.52 (s, 10 H) 7.23-7.19 (m, 16H), 7.06 (s, 8H), 6.91-6.97 (m, 52), 5.69 (s, 8H, CH ph$_2$), 5.57 (s, 4H, NCH), 1.75 (s, 12H, CH$_3$). HRMS (ESI) calcd. for [C$_{139}$H$_{112}$N$_4$S$_3$Cu$_2$ +H]$^+$: 2059.6719 Found: 2059.6707.

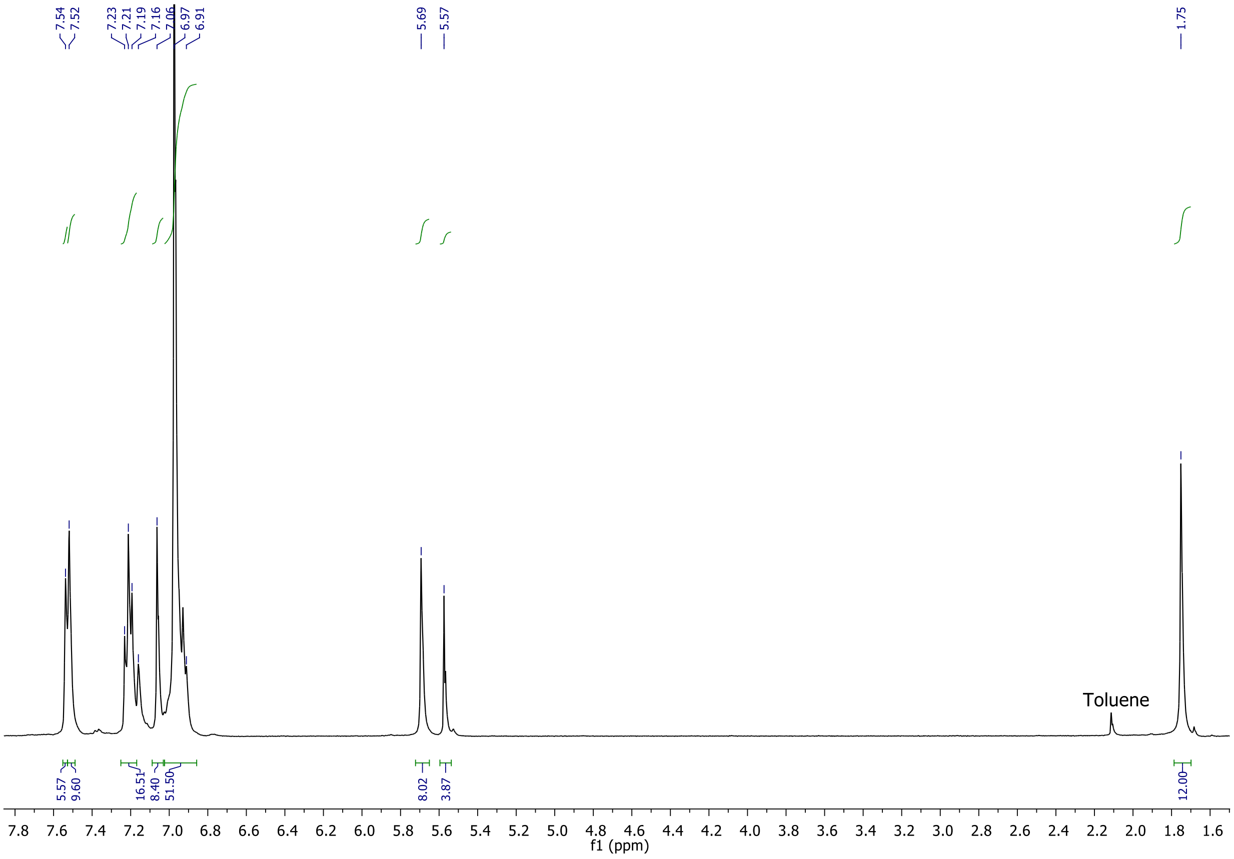


Figure S4. ^{1}H NMR spectrum of **4** in C$_6$D$_6$.

Reaction of IPr*carbene with CO_2:

In a nitrogen filled glovebox a 50 mL Schlenk flask was charged with IPr* (40 mg, 0.044 mmol) and stir bar. Then C_6D_6 (4 mL) was added. The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The solution was degassed by three freeze-pump-thaw cycles and backfilled with CO_2 (1 atm). The reaction mixture was stirred for 24 h at room temperature under CO_2, and then volatiles were removed under reduced pressure. The resulting solid was analyzed by ^{1}H NMR. ^{1}H NMR (400 MHz, C_6D_6): δ 7.85 (d, J= 7.6 Hz, 8H), 7.22 (t, J= 7.7Hz, 8H), 7.04 (t, J= 7.4 Hz, 4H), 6.87-6.93 (m, 24H), 6.03 (s, 4H, $CHPh_2$), 5.02 (s, 2H, NCH), 1.60 (s, 6H, Me).

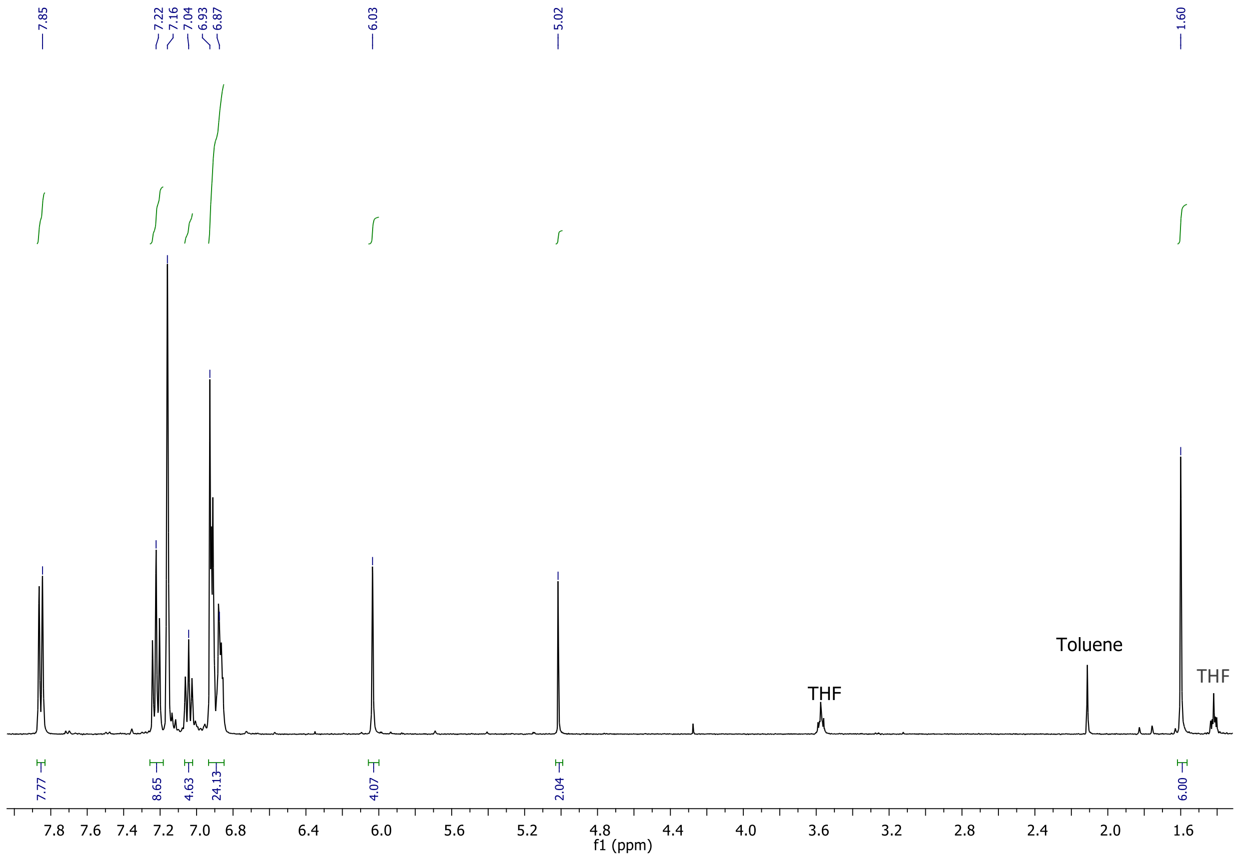
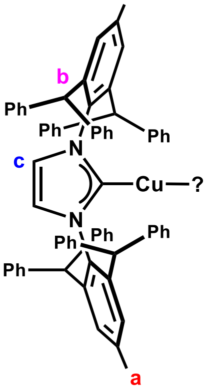


Figure S5. ^{1}H NMR spectrum of IPr*·CO_2 in C_6D_6.

Reaction of {(IPr*) Cu}$_2$(μ-S) with N_2O:

In a nitrogen filled glovebox, **1** (50 mg, 0.025 mmol) was dissolved in C_6D_6 (6 mL) and pipette-filtered through Celite into a scintillation vial. This solution was transferred to a Schlenk flask. The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The solution was degassed by three freeze-pump-thaw cycles and backfilled with N_2O (1 atm). The reaction mixture was exposed to N_2O for 24 h at room temperature. ^{1}H NMR analysis at this point showed that six different species had formed, with compound **2** as the main product of the reaction. Compound **8** (see Table S1) was found to be an intermediate which can convert to compound **2** upon further exposure to N_2O. The presence of N_2O is necessary for this conversion, as established by observing that when the reaction was stopped after 24 h and then was stirred under N_2 for 5 days the conversion of **8** to **2** was not observed. The same results were observed in C_6H_6. C_6D_6 was used as the reaction solvent to facilitate monitoring by NMR.



Identity	Species	a	b	c
{(IPr*)Cu}$_2$(μ-SO_4)	Compound 2	1.76	5.49	5.69
{(IPr*) Cu}$_2$(μ-O)	Compound 3	1.78	5.44	5.59
Intermediate	Compound 8	1.75	5.58	5.62
Minor impurity	Compound 9	1.74	5.56	5.64
Minor impurity	Compound 10	1.82	5.14	6.04
Minor impurity	Compound 11	1.68	5.53	5.55

Table S1. ^{1}H NMR chemical shifts for different species formed in the N_2O reaction

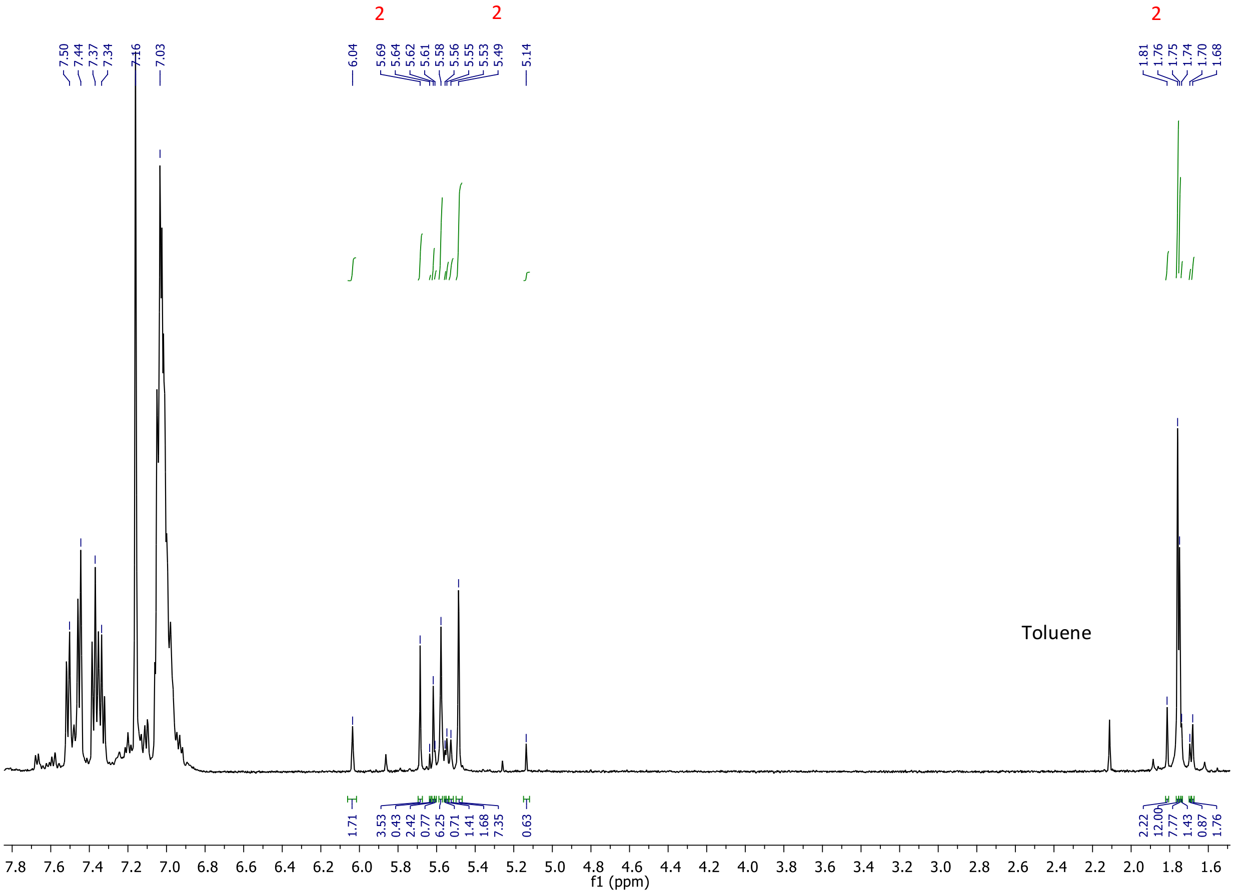
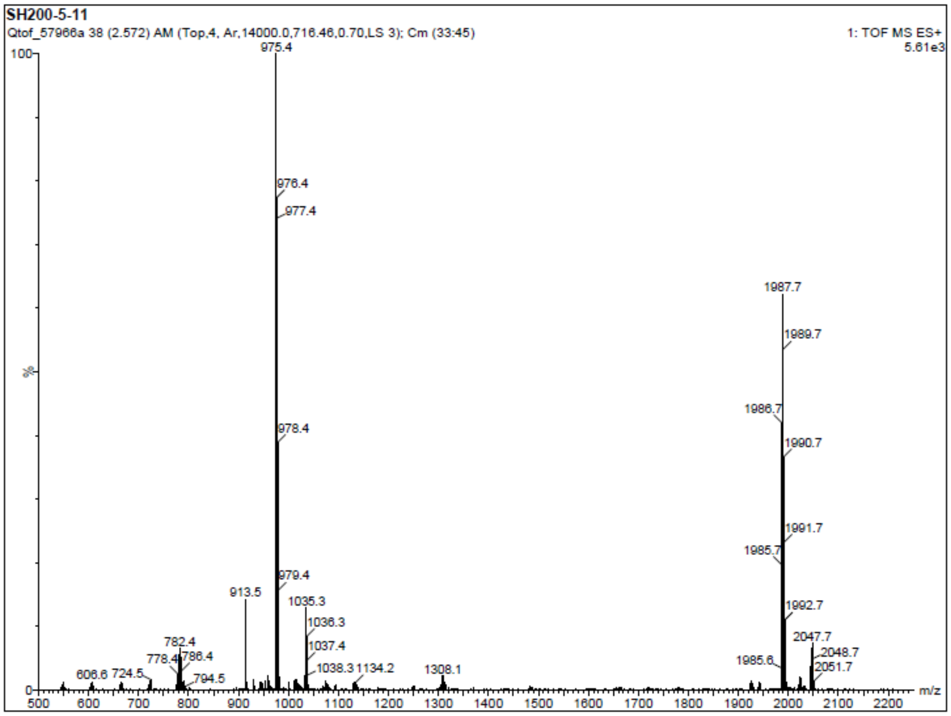


Figure S6. ^{1}H NMR spectrum resulting from reaction of {(IPr*) Cu}$_2$(μ-S) with nitrous oxide for 24 h (no internal standard).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Qtof_57966a 38 (2.572) AM (Top,4, Ar,14000.0,716.46,0.70,LS 3); Cm (33:45)
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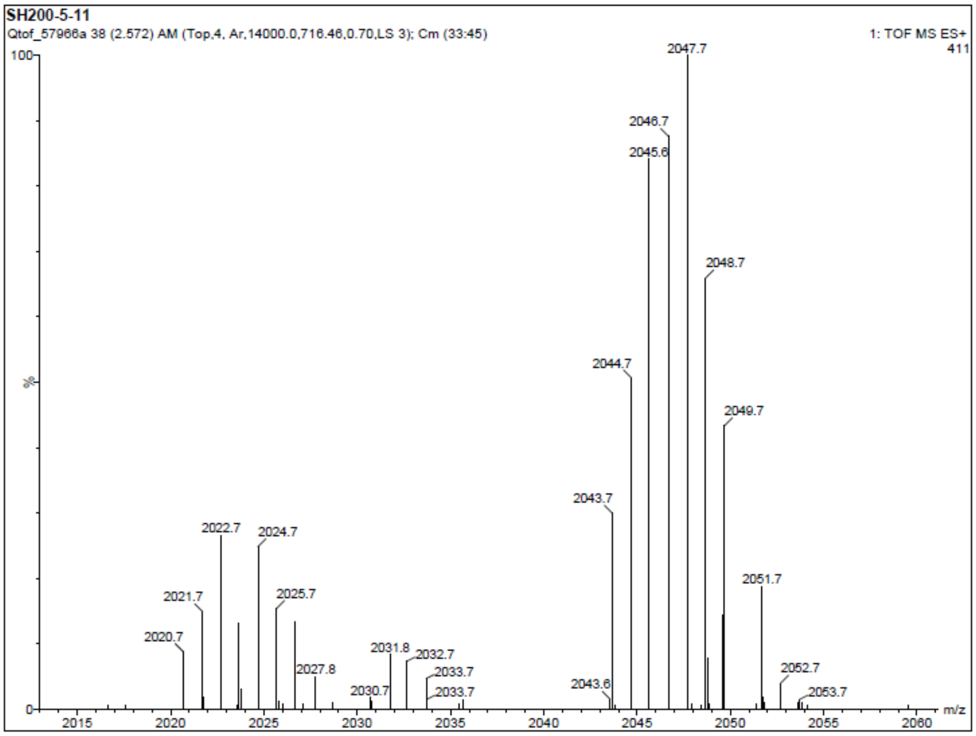


Figure S7.ESI mass spectra resulting from reaction of {(IPr*) Cu} $_2$(μ-S) with nitrous oxide for 24h.

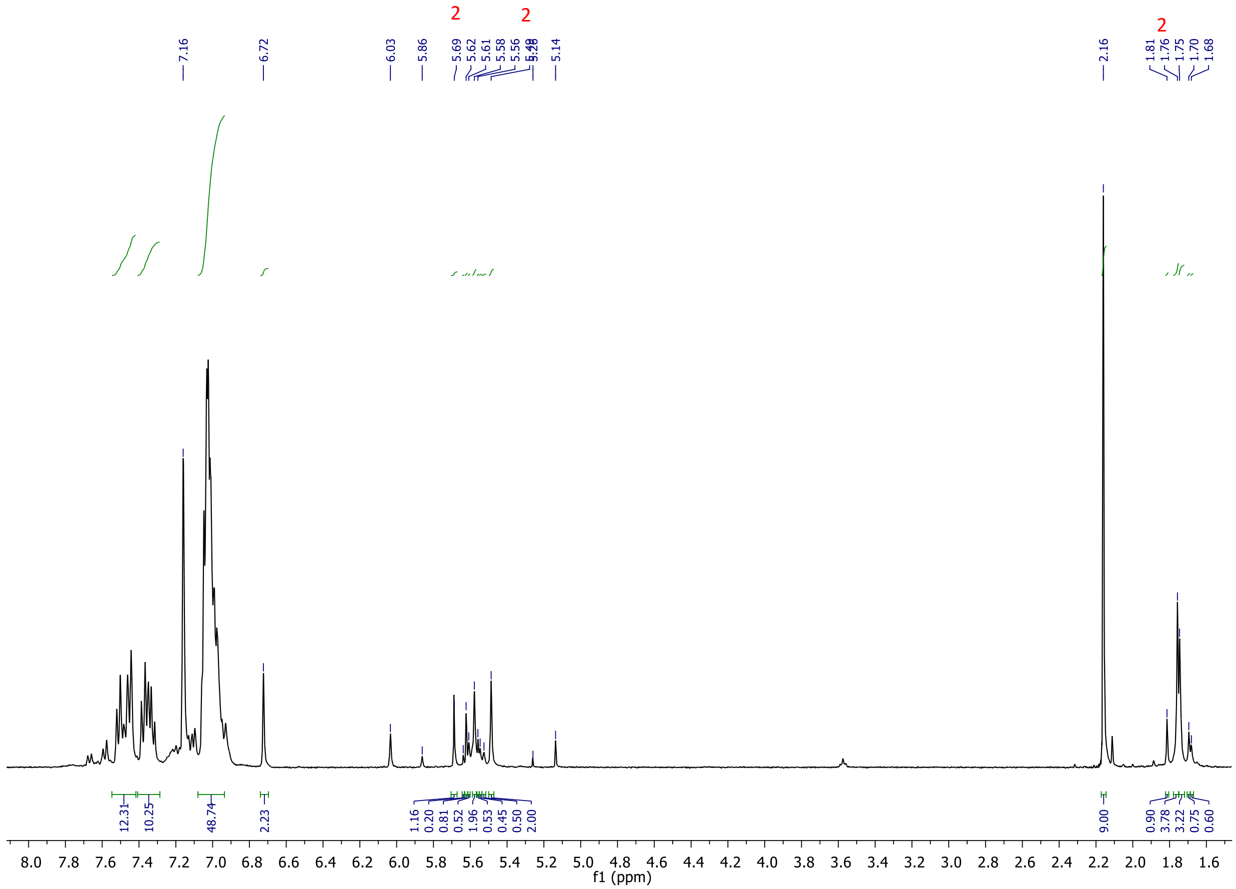


Figure S8. ^{1}H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide for 24 h. ^{1}H NMR integration indicated 32% conversion to **2**.

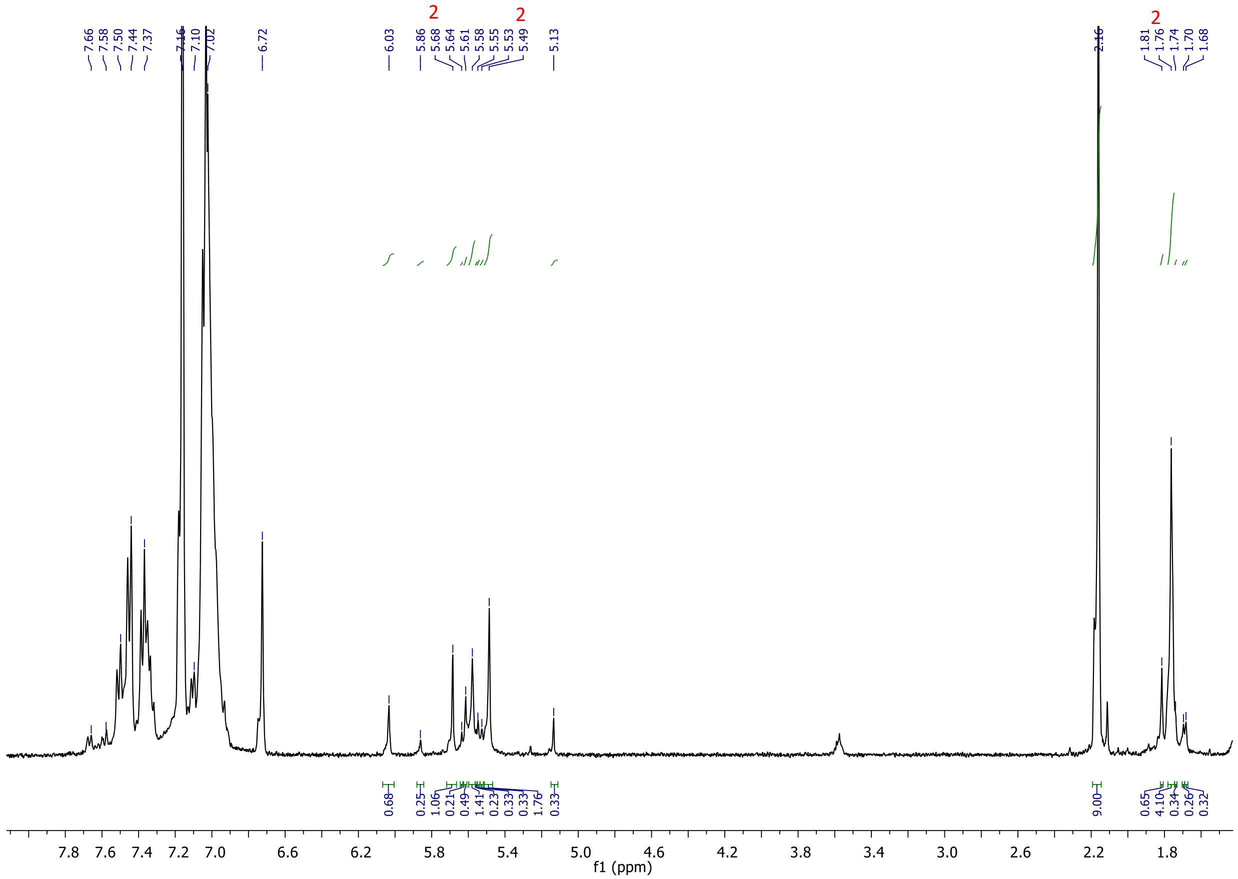


Figure S9. ^{1}H NMR spectrum resulting from reaction of $\{(\mathrm{IPr^*})\mathrm{Cu}\}_2(\mu\text{-S})$ with nitrous oxide for 60 h. After 60 h, all the peaks that belong to compound **8** had disappeared and the integration of the compound **2** had increased relative to an internal standard.

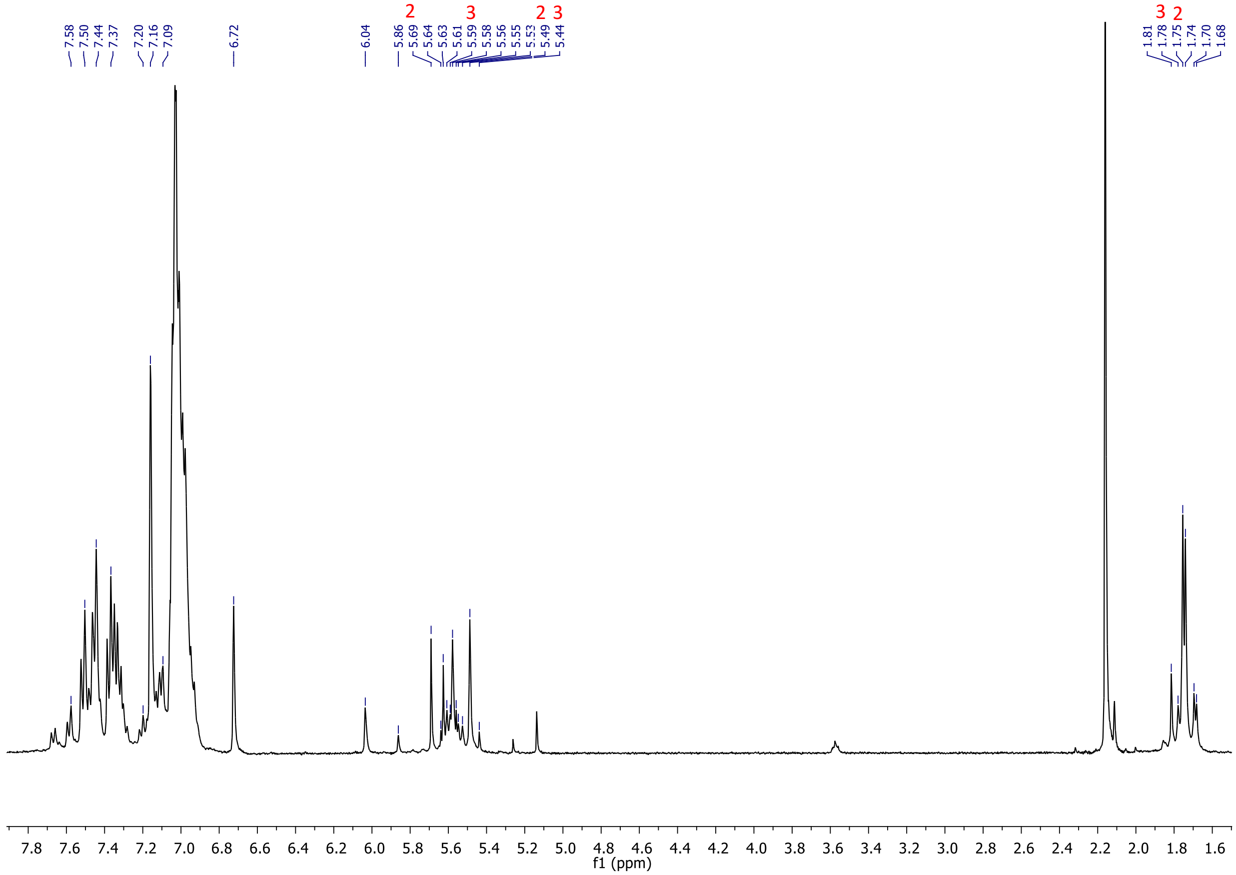


Figure S10. ^{1}H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide for 24 h, then under N_2 for 5 d. No conversion of compound **8** to compound **2** was observed under N_2. ^{1}H NMR integration indicated 26% conversion to **2**, 5% conversion to **3** under these conditions.

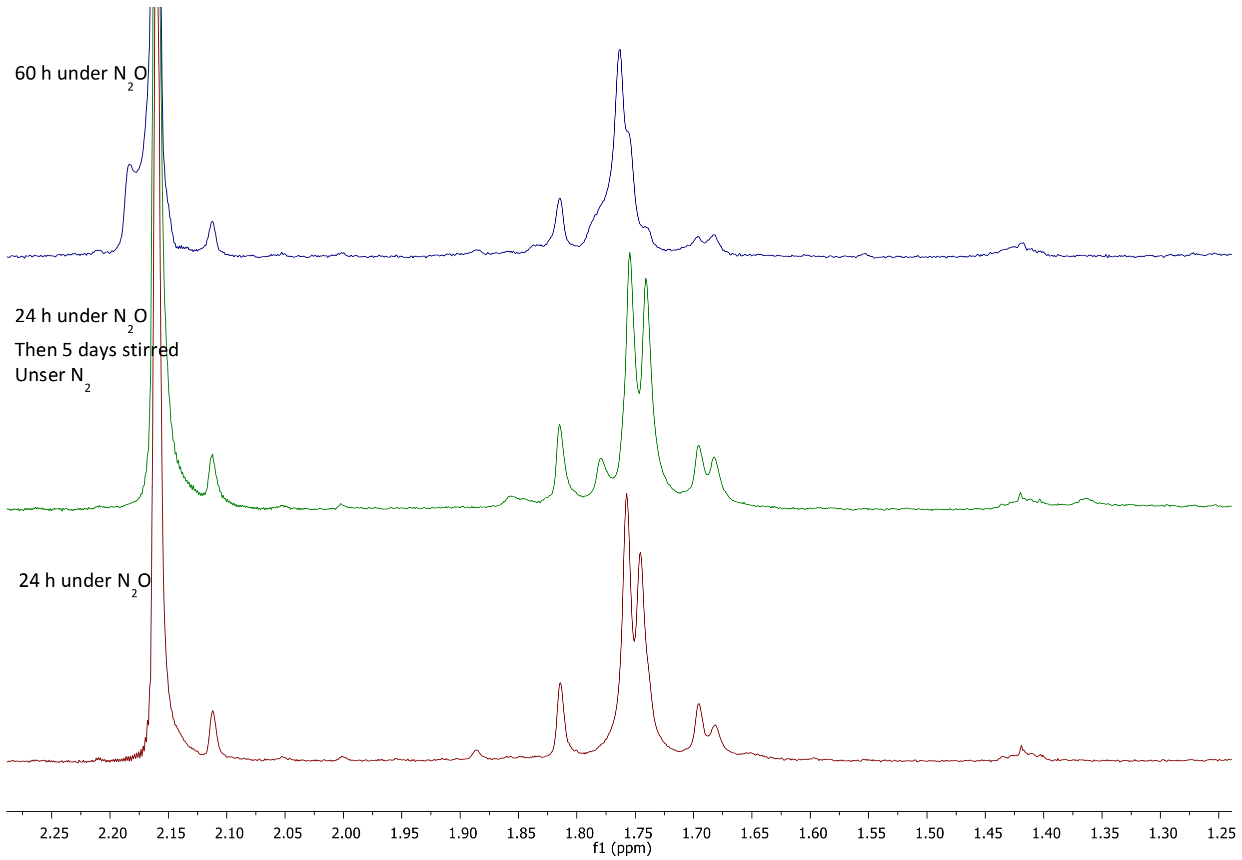


Figure S11. Comparison of ^{1}H NMR spectra resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide in three different conditions: 24 h under N_2O (red), 60 h under N_2O (blue), and 24 h under N_2O followed by stirring under N_2 for 5 days (green).

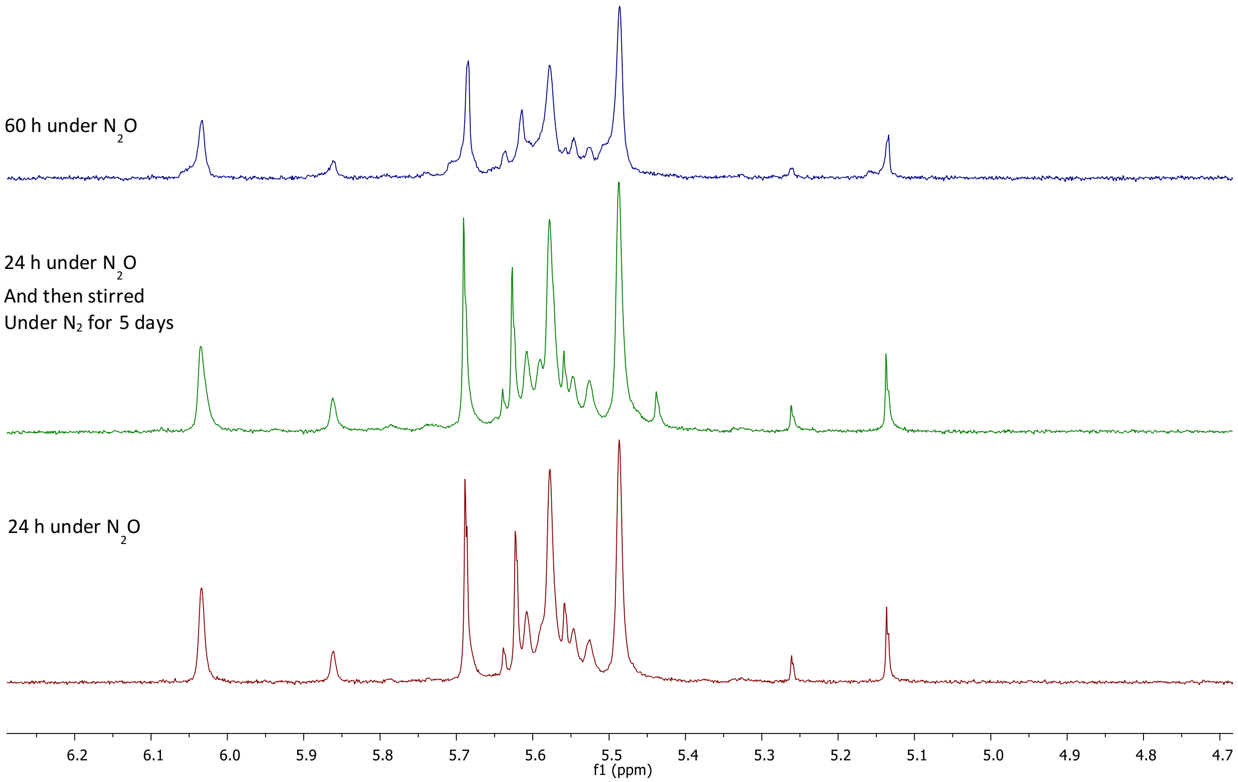


Figure S12. Comparison of ^{1}H NMR spectra resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide in three different conditions: 24 h under N_2O (red), 60 h under N_2O (blue), and 24 h under N_2O followed by stirring under N_2 for 5 days (green).

Reaction of {(IPr*)Cu}$_2$(μ-S) with N_2O in the presence of PPh_3:

In a nitrogen filled glovebox a scintillation vial was charged with {(IPr*)Cu}$_2$(μ-S) (30 mg, 0.0151 mmol) and triphenyphosphine (4 mg, 0.0151 mmol), and then C_6D_6 (6 mL) was added. This solution was transferred to a 50-mL Schlenk flask. The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The solution was degassed by three freeze-pump-thaw cycles and backfilled with N_2O (1 atm). After 24 h the reaction flask was transferred into the glovebox and mesitylene (2μL, 0.0151 mmol) was added as an internal integration standard. ^1H NMR and ^{31}P NMR spectra were taken. ^1H NMR integration indicated 19% conversion to **2**, 17% conversion to **3**.

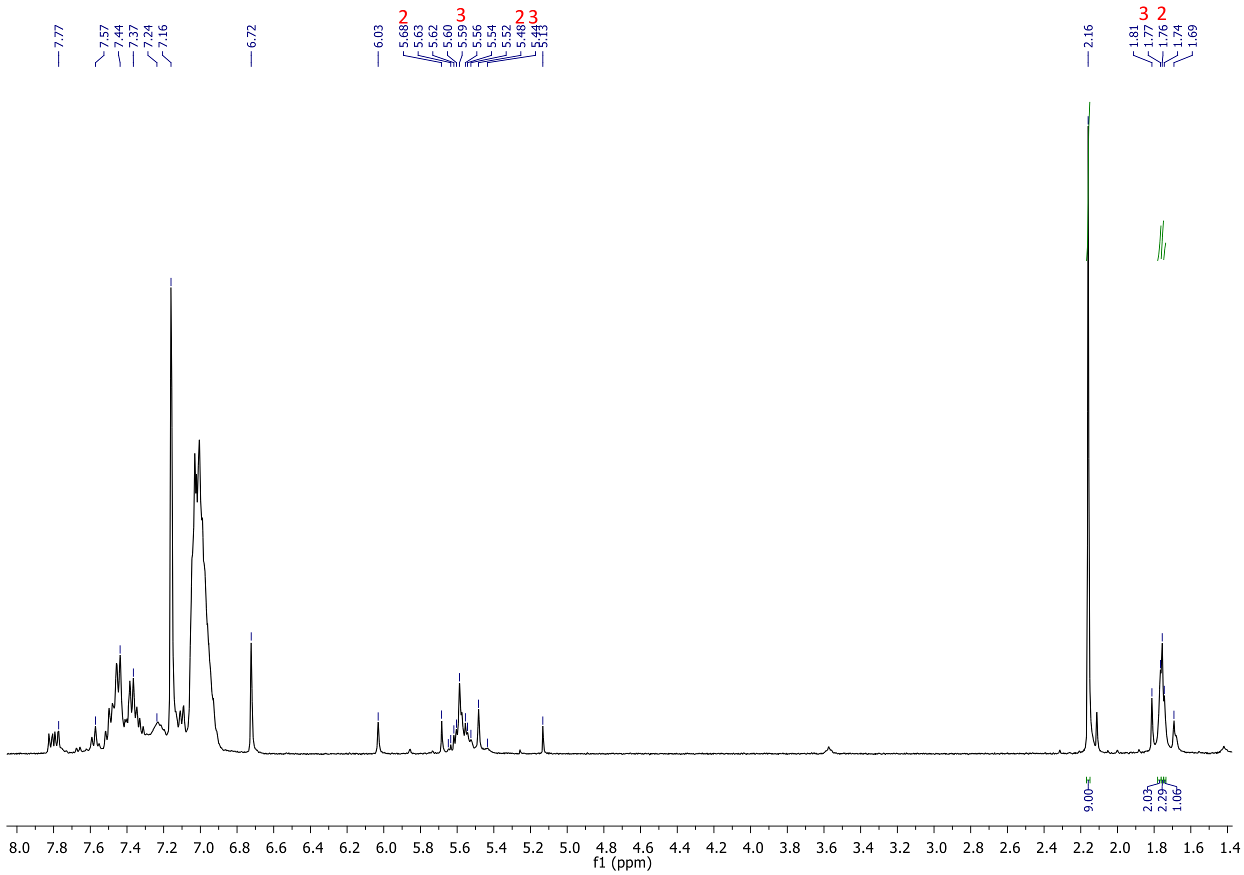


Figure S13. ^1H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide in the presence of PPh_3 for 24h.

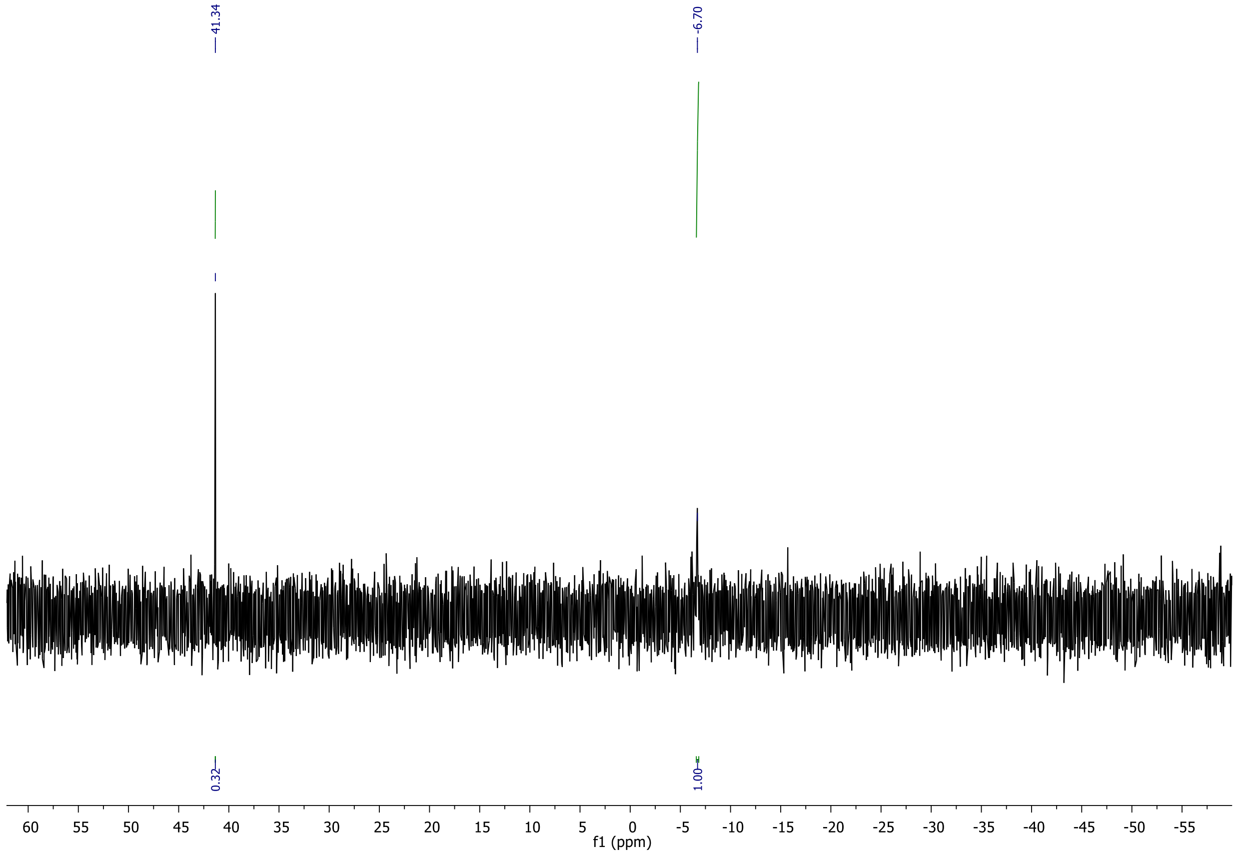


Figure S14. ^{31}P NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide in the presence of PPh_3 for 24h.

Reaction of {(IPr*) Cu} $_2$(μ-S) with N_2O and addition of PPh_3 after 24h:

In a nitrogen filled glovebox a scintillation vial was charged with {(IPr*)Cu}$_2$(μ-S) (30 mg, 0.0151 mmol), and then C_6D_6 (6 mL) was added. This solution was transferred to a 50-mL Schlenk flask. The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The solution was degassed by three freeze-pump-thaw cycles and backfilled with N_2O (1 atm). The reaction mixture was exposed to N_2O for 24 h at room temperature. After 24 h the schlenk flask was transferred inside the glovebox and triphenyphosphine (4 mg, 0.0151 mmol) and mesitylene (2μL, 0.0151 mmol) were added to the solution. The reaction was stirred under N_2 for 1h and then ^{1}H-NMR and ^{31}P-NMR spectra were taken.

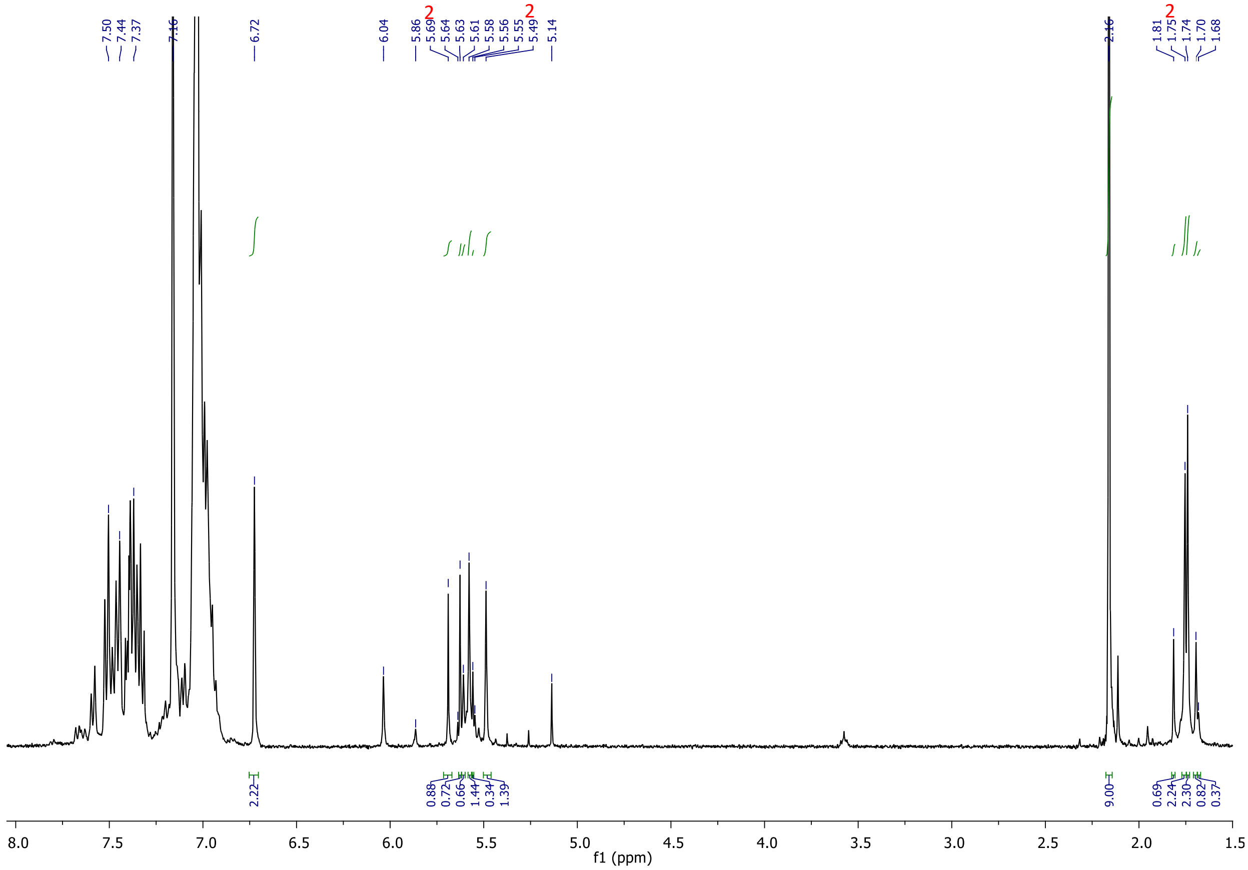


Figure S15. ^{1}H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide for 24h and then addition of PPh_3.

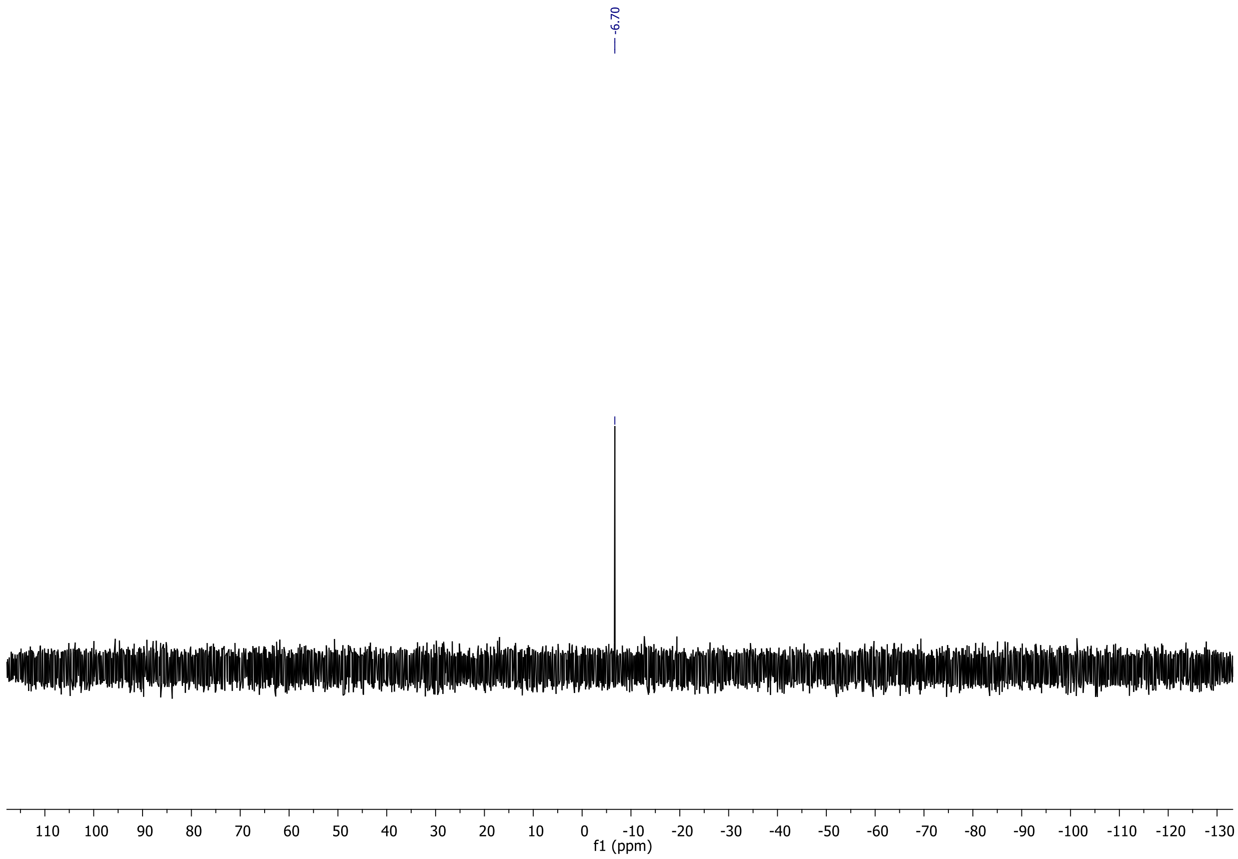


Figure S16. ^{31}P NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with nitrous oxide for 24 h and then addition of PPh$_3$ and stirring for 1 h.

Reaction of {(IPr*) Cu} $_2$(μ-S) with CO_2:

In a nitrogen filled glovebox, {(IPr*)Cu}$_2$(μ-S) (50 mg, 0.025 mmol) was dissolved in C_6D_6 (6 mL) and pipette-filtered through Celite into another scintillation vial. This solution was transferred to a 50-mL Schlenk flask. The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The solution was degassed by three freeze-pump-thaw cycles and backfilled with CO_2 (1 atm). The reaction mixture was exposed to CO_2 for 24 h at room temperature. After 24 h five different species had formed according to ^{1}H NMR analysis, with compound **2** as the main product of the reaction. ^{1}H NMR integration indicated 33% conversion to **2**.

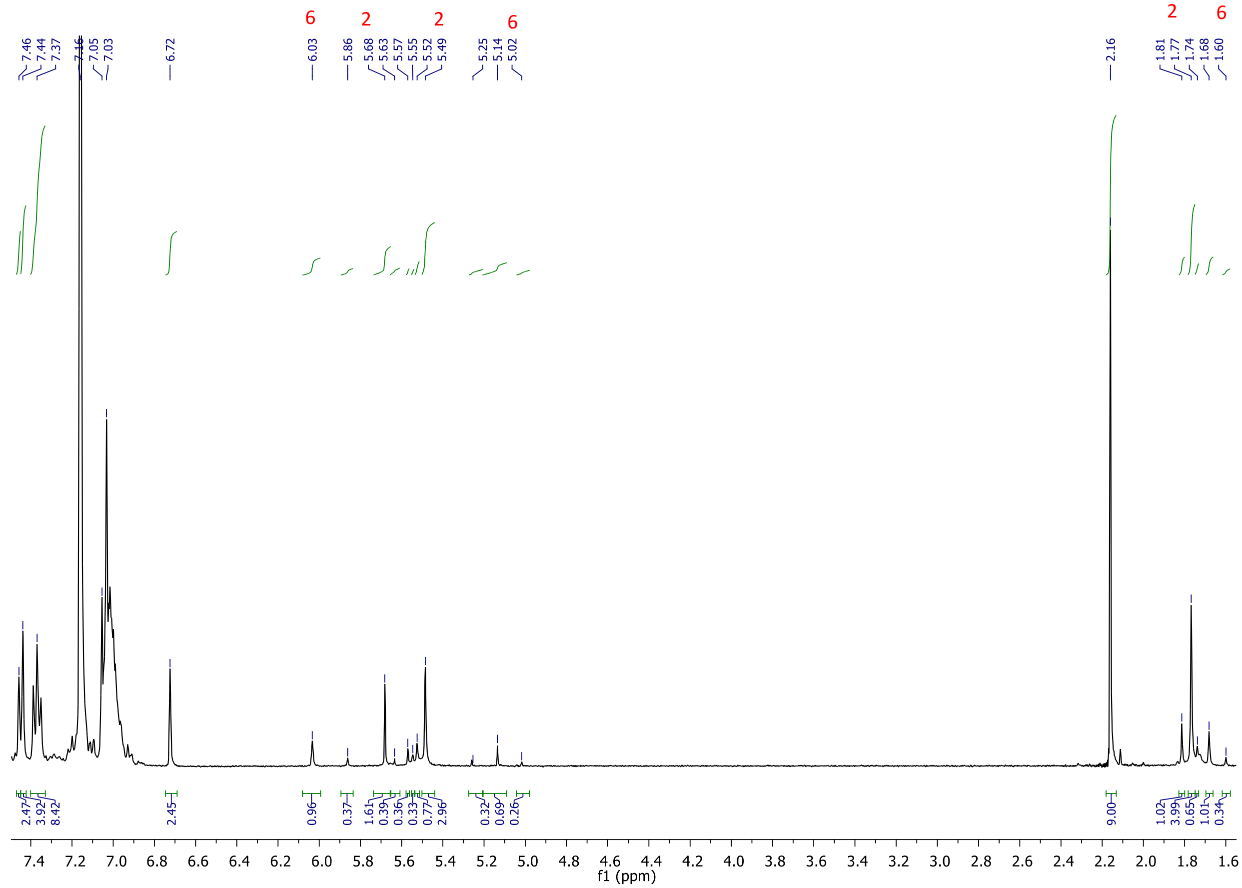
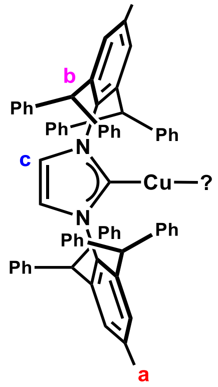


Figure S17. ^{1}H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with carbon dioxide for 24 h



Identity	Species	a	b	c
{(IPr*)Cu}$_2$(μ-SO$_4$)	Compound 2	1.76	5.49	5.69
(IPr)*·CO$_2$	Compound 6	1.60	5.02	6.03
Minor impurity	Compound 9	1.74	5.56	5.64
Minor impurity	Compound 10	1.82	5.14	6.04
Minor impurity	Compound 11	1.68	5.53	5.55

Table S2. ^{1}H NMR chemical shifts for different species formed in the CO$_2$ reaction

Reaction of {(IPr*) Cu} $_2$(μ-S) with CO_2 in the presence of PPh_3:

In a nitrogen filled glovebox a scintillation vial was charged with {(IPr*)Cu}$_2$(μ-S) (30 mg, 0.0151 mmol) and triphenyphosphine (4 mg, 0.0151 mmol), and then C_6D_6 (6 mL) was added. This solution was transferred to a 50-mL Schlenk flask. The Schlenk flask was taken out of the glovebox and connected to a Schlenk line. The solution was degassed by three freeze-pump-thaw cycles and backfilled with CO_2 (1 atm). The reaction mixture was exposed to CO_2 for 24 h at room temperature. After 24 h ^{1}H-NMR and ^{31}P-NMR were taken.^{1}H NMR integration indicated 31% conversion to **2**.

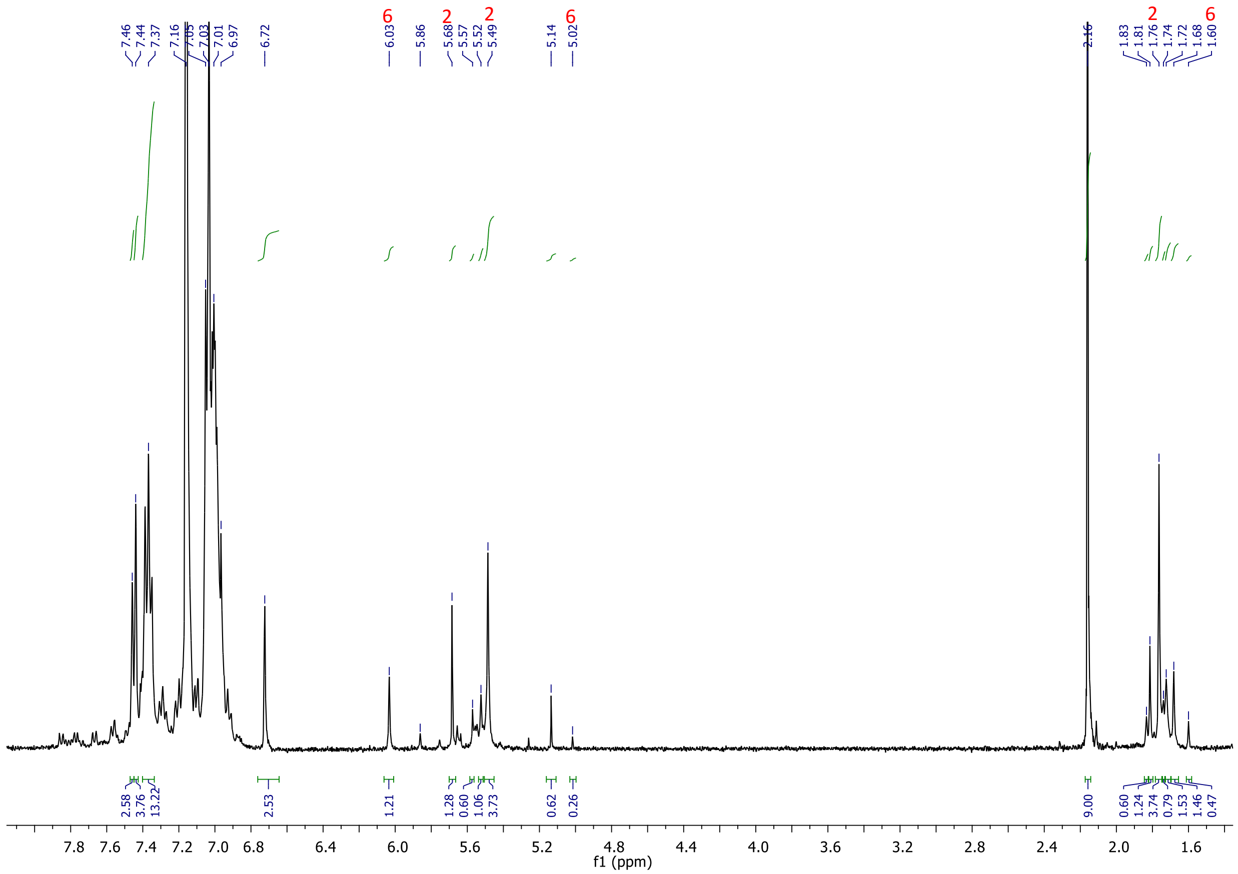


Figure S18. ^{1}H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with carbon dioxide in the presence of PPh_3 for 24 h.

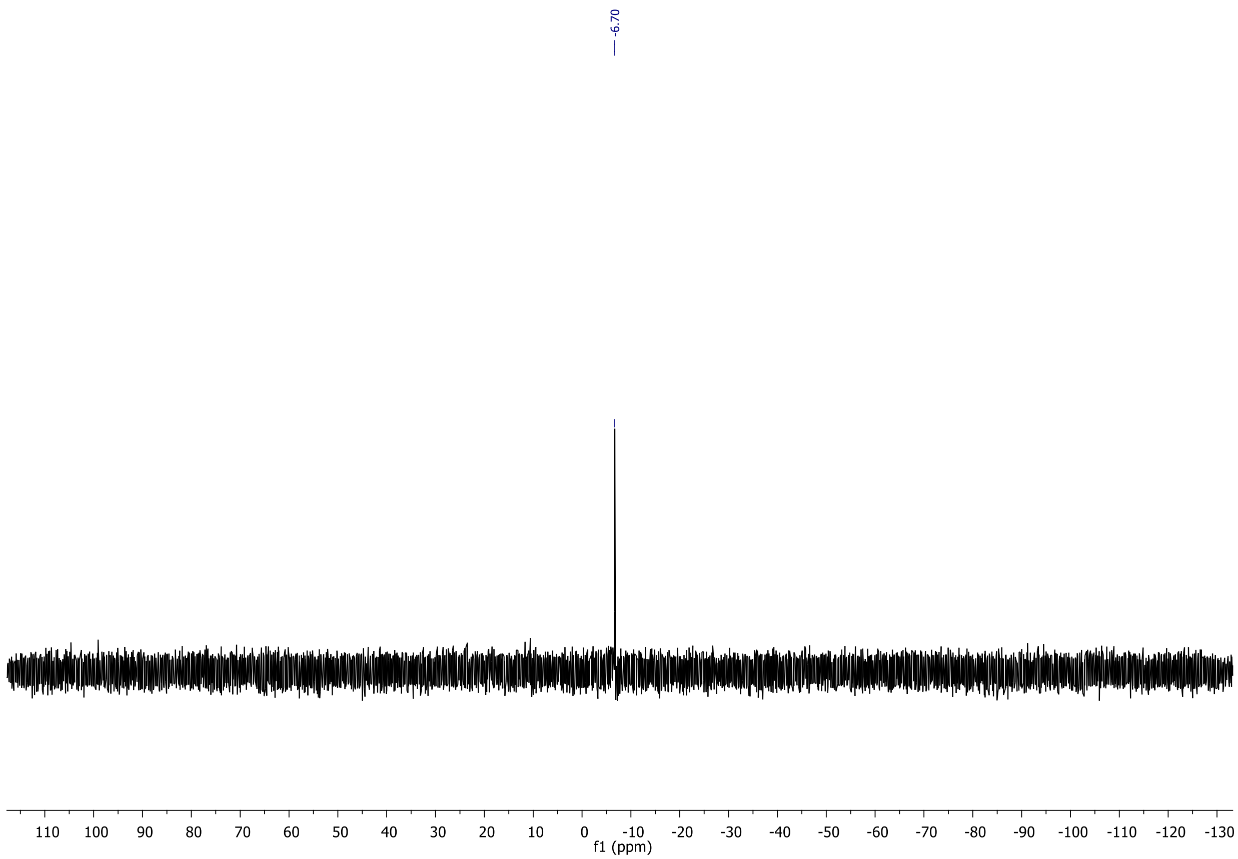


Figure S19. ^{31}P NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with carbon dioxide in the presence of PPh$_3$ for 24 h.

Reaction of {(IPr*)Cu}$_2$(μ-S) with PPh$_3$:

In a nitrogen filled glovebox a scintillation vial was charged with {(IPr*)Cu}$_2$(μ-S) (10 mg, 0.005 mmol) and triphenyphosphine (1.3 mg, 0.005 mmol) and then C_6D_6 (2 mL) was added. The reaction mixture was stirred at room temperature for 24h then ^{1}H-NMR and ^{31}P-NMR were taken, which indicated that no reaction had occured.

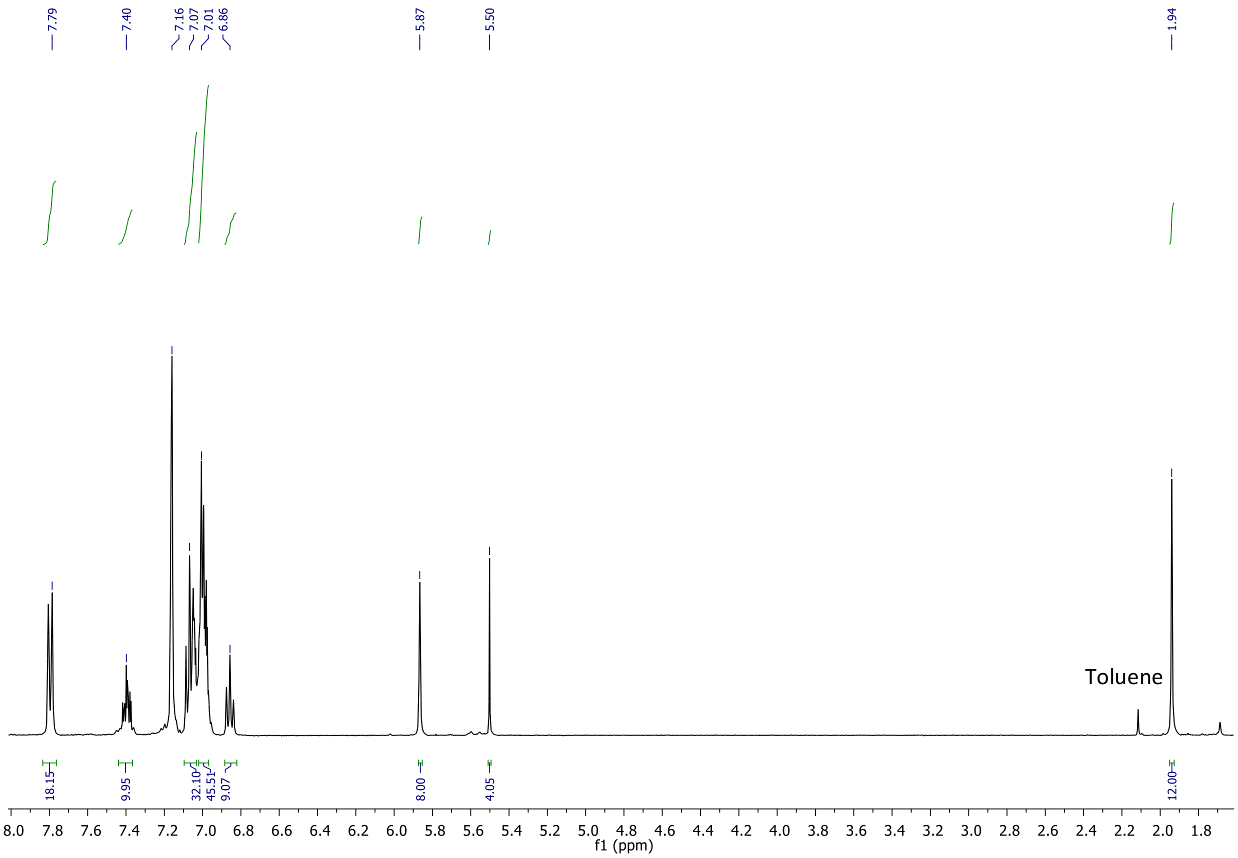


Figure S20. ^{1}H NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with PPh$_3$ for 24 h.

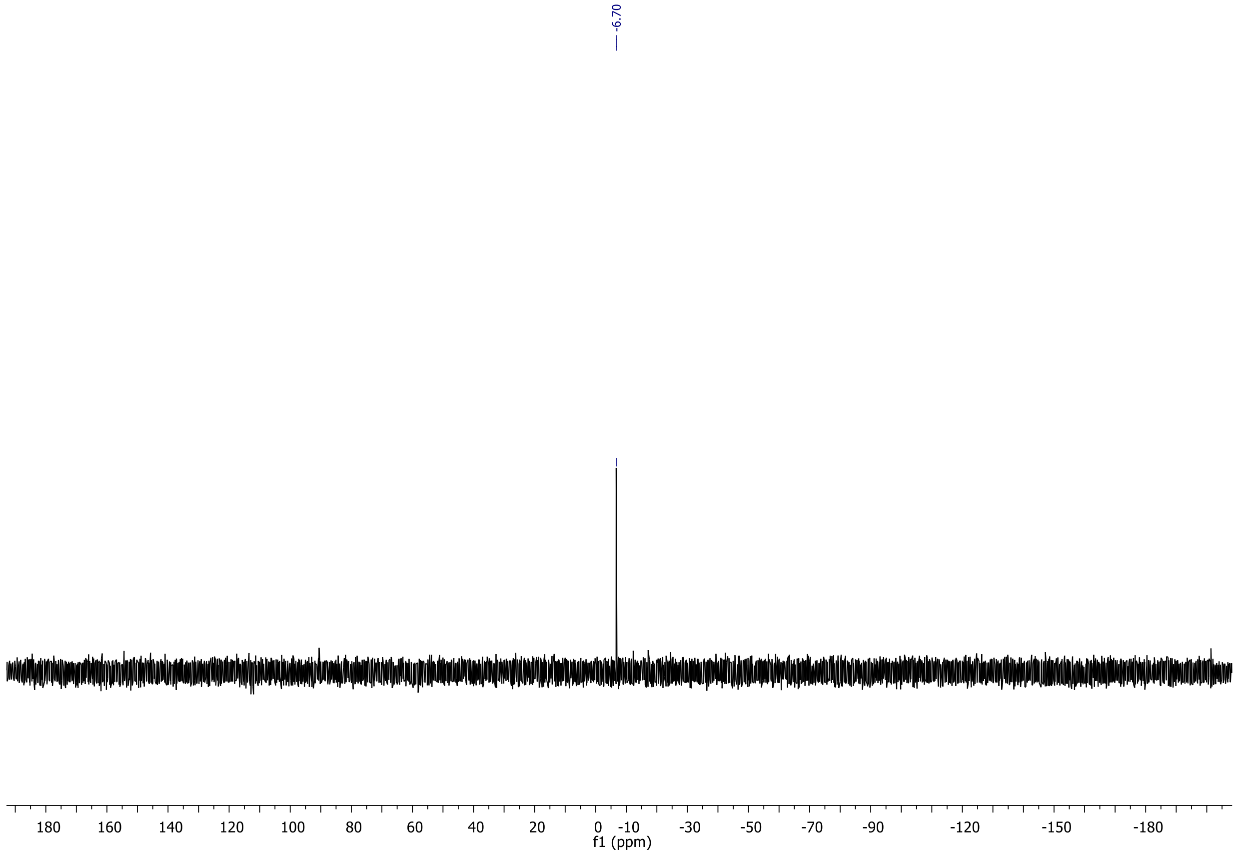


Figure S21. ^{31}P NMR spectrum resulting from reaction of {(IPr*)Cu}$_2$(μ-S) with PPh_3 for 24 h.

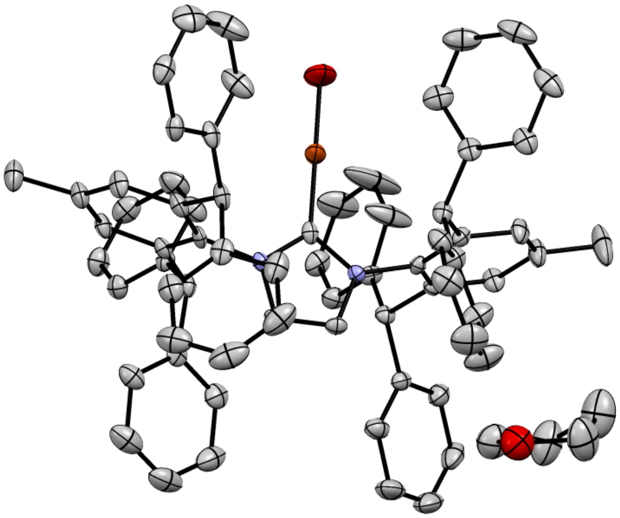


Figure S22. Solid-state structure of (IPr*)CuOH·THF determined by X-ray crystallography. Hydrogen atoms, including the O-H hydrogen located in the Fourier difference map, are omitted for clarity.