Tetranuclear and trinuclear copper(I) pyrazolates as catalysts in copper mediated azide-alkyne cycloadditions (CuAAC)

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Supporting Information
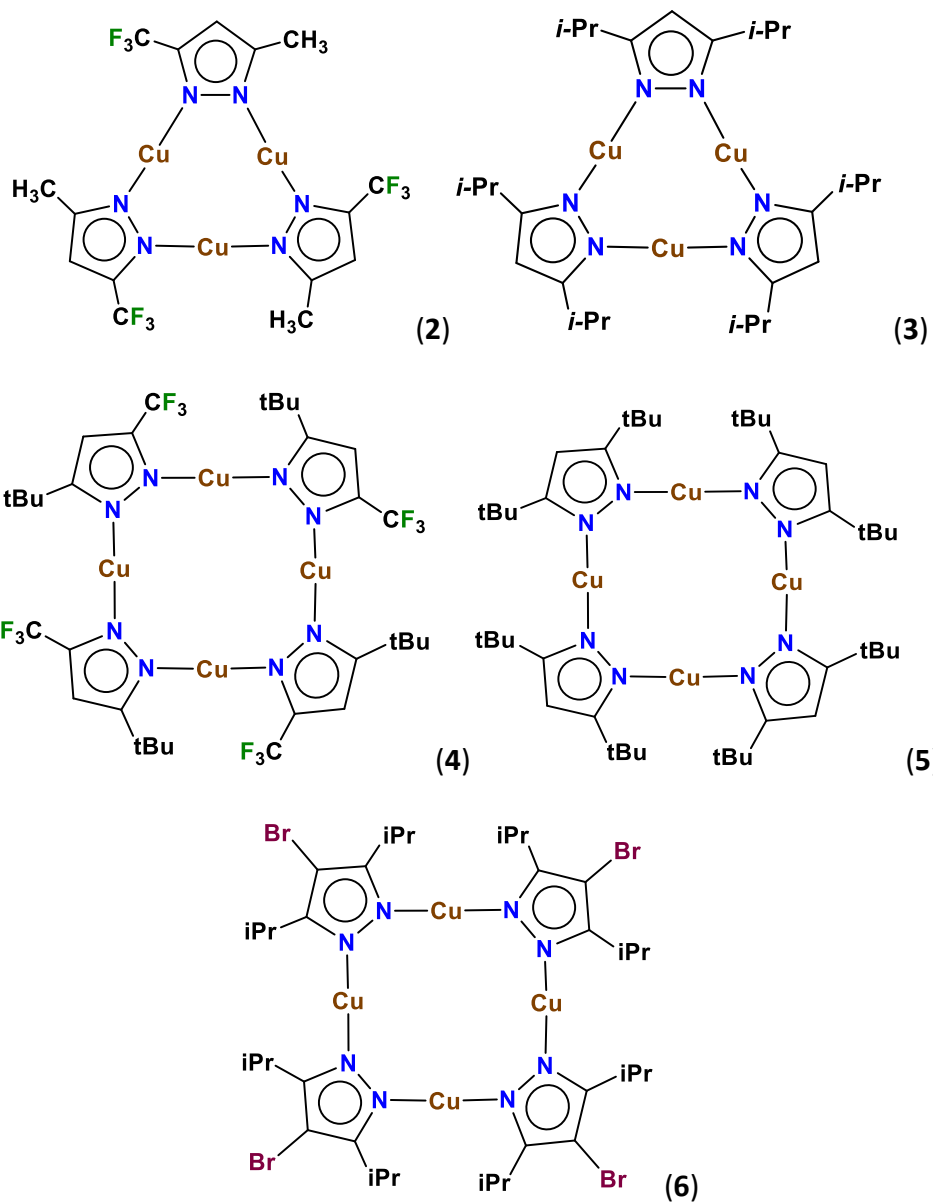
Materials and Methods

Figure S1. Copper complexes used in this work

General procedure for azide-alkyne cycloadditions

Benzyl azide, p-tolyl azide, 1-adamantyl azide, {[3,5-(i-Pr)$_2$Pz]Cu}$_3$, {[3-(CF$_3$)-5-(CH$_3$)Pz]Cu}$_3$, {[3,5-(t-Bu)$_2$Pz]Cu}$_4$, {[3-(CF$_3$)-5-(t-Bu)Pz]Cu}$_4$, and {[4-Br-3,5-(i-Pr)$_2$Pz]Cu}$_4$ were prepared via reported routes.[1-6] Solvents were purchased from commercial sources and purified before use. All other reagents were obtained from commercial sources and used as received. For all reactions, 1 mol percent (0.0075 mmol) of the catalyst was added to a vial containing 100 mg (0.75 mmol) of azide, 1 equiv. (0.75 mmol) of alkyne, and 5 mL dried dichloromethane.   Although the reagent mixing was done in open air, unnecessary exposure to air was avoided, and the samples were prepared fresh and used immediately. The resulting solutions were stirred at room temperature (20 °C) for 12 hours, unless noted otherwise. Approximately 0.1 mL of the crude mixtures were taken in an NMR tube and CDCl$_3$ was added. Samples were analyzed using NMR at 25 °C on a JEOL Eclipse 500 spectrometer (^{1}H, 500.16 MHz; ^{13}C, 125.78 MHz)to check for the presence of the desired triazole. The percent conversion was calculated by comparing the peaks of the desired 1,2,3-triazole with the peaks of the starting azide. No by-products were observed.

1-(*p*-tolyl)-4-hexyl-1*H*-1,2,3-triazole
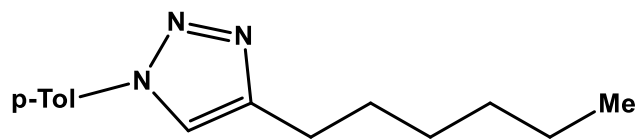
^{1}H NMR (CDCl$_3$, 500 MHz): 7.67 (s, 1H), 7.55 (d, 2H, J = 6.87 Hz), 7.23 (d, 2H, J = 6.87 Hz), 2.73 (t, 2H, J = 7.45 Hz), 2.35 (s, 3H), 1.65-1.71 (m, 2H), 1.33-1.37 (m, 2H), 1.26-1.29 (m, 4H), 0.85 (t, 3H, J = 6.87 Hz). ^{13}C{^{1}H} NMR (CDCl$_3$, 500 MHz): 149.0, 138.4, 135.0, 130.1, 120.2, 118.8, 31.6, 29.4, 29.0, 25.7, 22.6, 21.0, 14.1.

Reference: Devaborniny, P.; Ponduru, T.; Noonikara-Poyil, A.; Jayaranta, N.; Dias, H.V.R.; Acetylene and terminal alkyne complexes of copper(I) supported fluorinated pyrazolates: synthesis, structures, and transformations. *Dalton Transactions.* **2019**, *48*, 15782-15794.
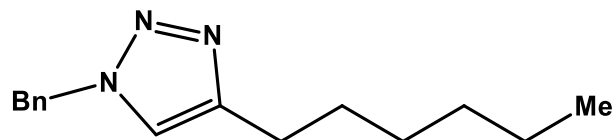
1-(*p*-tolyl)-4-phenyl-1*H*-1,2,3-triazole
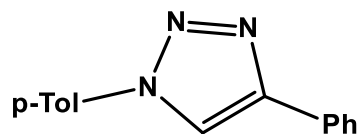
^{1}H NMR (CDCl$_3$, 500 MHz): 8.15 (s, 1H), 7.90 (d, 2H, J = 7.45 Hz), 7.65 (d, 2H, J = 8.60 Hz), 7.45 (t, 2H, J = 7.45 Hz), 7.30-7.36 (m, 3H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (CDCl$_3$, 500 MHz): 148.3, 139.0, 134.8, 130.4, 129.0, 128.4, 125.9, 120.5, 117.8, 21.2.

Reference: Meng, X.; Xu, X.; Gao, T.; Chen, B.; *Eur. J. Org. Chem.* **2010**, *2010*, 5409-5414
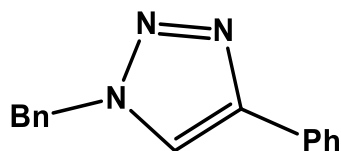
1-(benzyl)-4-hexyl-1*H*-1,2,3-triazole

^{1}H NMR (CDCl$_3$, 500 MHz): 7.32-7.38 (m, 3H), 7.23-7.27 (m, 2H), 7.17 (s, 1H), 5.49 (s, 2H), 2.68 (t, J=7.5 Hz, 2H), 1.63 (quint, J=7.5 Hz, 2 H), 1.26-1.36 (m, 6H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (CDCl$_3$, 500 MHz): 149.2, 135.2, 129.2, 128.8, 128.1, 120.6, 54.1, 31.7, 29.5, 29.1, 25.9, 22.7, 14.2.

Reference: Iwasaki, M., Yorimitsu, H., and Oshima, K.; *Chem. Asian J.* **2007**, *2*, 1430-1435.
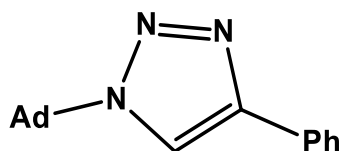
1-(benzyl)-4-phenyl-1*H*-1,2,3-triazole

^{1}H NMR (CDCl$_3$, 500 MHz): 7.77 (m, 2H), 7.65 (s, 1H), 7.32 (m, 8H), 5.53 (s, 2H). ^{13}C{^{1}H} NMR (CDCl$_3$, 500 MHz): 161.1, 140.2, 133.6, 134.5, 129.3, 129.2, 128.3, 127.3, 54.5, 54.2.

Reference: Jlalia, I., Meganem, F., Herscovici, J., Girard, C.; *Molecules.* **2009**, *14*, 528-539.

1-(adamantyl)-4-phenyl-1*H*-1,2,3-triazole

^{1}H NMR (CDCl$_3$, 500 MHz): 7.84 (d, 2H, J = 7.6 Hz), 7.83 (s, 1H), 7.41 (t, 2H, J = 7.6 Hz), 7.31 (t, 1H, J = 7.6 Hz), 2.29 (s, 9H), 1.82 (s, 6H).

Reference: Chtchigrovsky, M., Primo, A., Gonzalez, P., Molvinger, K., Robitzer, F. Q., Taran, F.; *Angewandte Chemie International Edition*. **2009**, *48*, 5916-5920.

trans-amide 1,4-disubstituted triazole

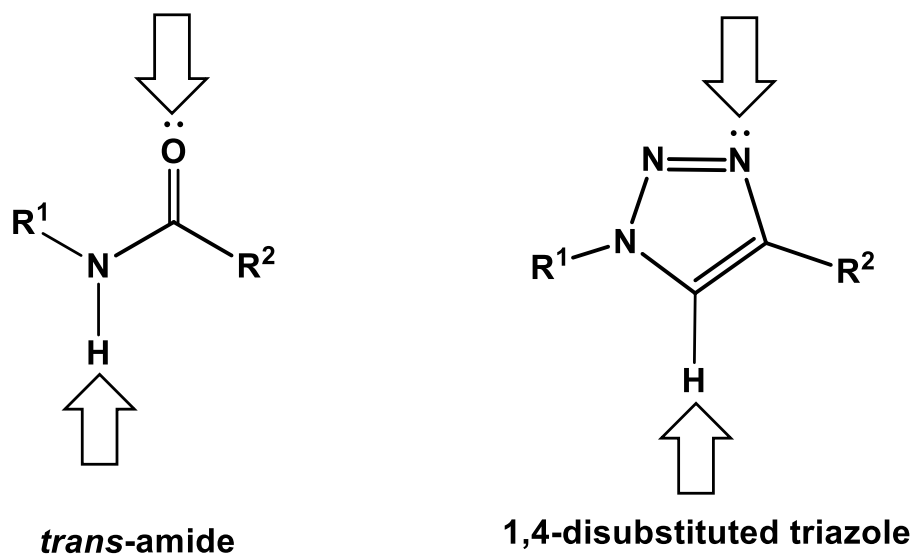**Figure S2.** Similarities between *trans*-amide and 1,4-disubstituted triazoles[7]

The 1,4-disubstituted 1,2,3-triazole serves as a good model for bioactive amides due to numerous similarities. For example, the lone pair on the nitrogen of the triazole mimics the hydrogen bond accepting character of the carbonyl on the amide, while the triazole C(5)-H mimics the hydrogen bond donor character of the amide N-H.

Vapor Pressure Osmometry

Molecular weight data were obtained using a KNAUER Vapor Pressure Osmometer K-7000 with EuroOsmo 7000 software. A reference measurement was run before performing all sample measurements by attaching a droplet pure solvent on each thermistor and performing AUTOZERO. Solutions of the test samples were prepared fresh and the exposure to air was minimized. To run a sample measurement, a droplet of solution was placed on one thermistor while pure solvent remained on the other. The concentration of each sample was entered for every single run and at least three osmograms were recorded at each concentration. The software automatically calculated an average value once two or more readings were selected. To avoid contamination, it was also important to rinse the sample thermistor with pure solvent when moving from one concentration to another. The drop size was kept as constant and equal as possible on both thermistors. To provide saturated atmosphere around the thermistors, the chamber contained a reservoir and wick. The difference in vapor pressure between the two droplets caused in the difference in temperature at each thermistor.

Chloroform was used as the solvent. The instrument was operated at 30 °C (the minimum working temperature suggested for the solvent) and commercially available benzil was used as the standard for calibration. A calibration curve was constructed by measuring prepared solutions of benzil in chloroform in the concentration range 5-50 mmol/kg. The minimum concentration was always kept above the suggested minimum value (3 mmol/kg) given in the manual (K-7000 VPO). EuroOsmo software was used to draw graphs and calculate the calibration constant (K_{calib}).

A similar procedure was followed to obtain measurements and calculate a sample constant (K_{sample}) for copper pyrazolate samples. The sample concentration was entered for each run and at least three concentrations were examined within each range. At least three measurements from each concentration were used in calculations to calculate the molecular weight. Since VPO is a sensitive instrument, other thermal sources and losses could contribute to the observed results. Electrical current flowing through the thermistors results in self-heating, which is kept as small as possible but cannot be eliminated entirely. To minimize the error, each sample measurement was repeated at least four times. Additionally, each entire experiment was repeated at least twice to confirm the accuracy of the values.

Table S1. Actual and calculated molecular weights for tetranuclear copper(I) pyrazolate catalysts.

Catalyst	Concentration range (mmol/kg)	Actual MW (g/mol)	Observed MW (g/mol)
{[3,5-(t-Bu)$_2$Pz]Cu}$_4$ (**5**)	4-12	971	985
{[3-(CF$_3$)-5-(t-Bu)Pz]Cu}$_4$ (**4**)	4-10	1019	900
{[4-Br-3,5-(i-Pr)$_2$Pz]Cu}$_4$ (**6**)	4-12	1174	1058
{[3,5-(i-Pr)$_2$Pz]Cu}$_3$ (**3**)	4-10	644	685
{[3,5-(CF$_3$)$_2$Pz]Cu}$_3$ (**1**)	4-10	800	529

A comparison of Vapor Pressure Osmometry data to the data from NMR spectroscopic data of {[3-(CF₃)-5-(t-Bu)Pz]Cu}₄ (4).
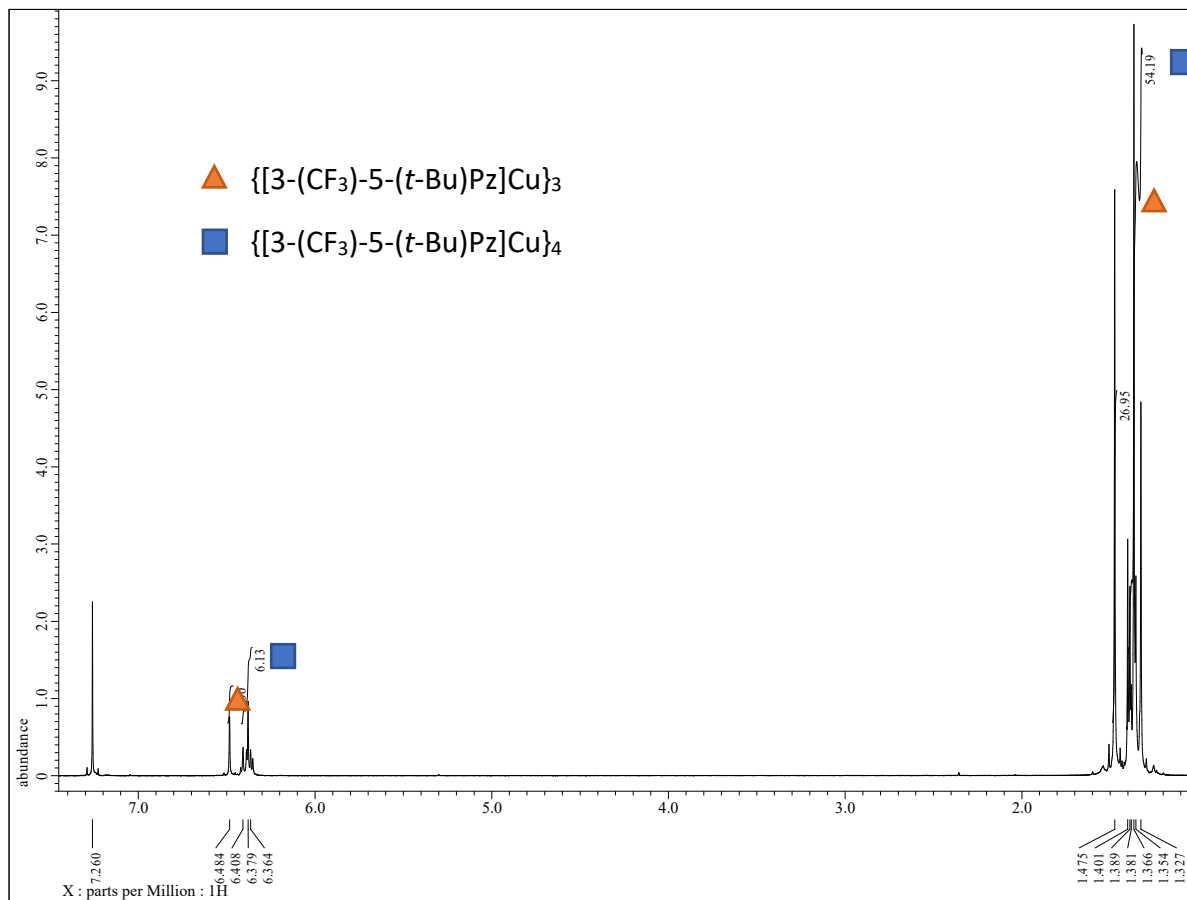

Figure S3. ^{1}H NMR spectrum of 6 mmol/kg solution of {[3-(CF₃)-5-(t-Bu)Pz]Cu}₄ (**4**) in CDCl₃ at room temperature. In agreement with spectrum in ref 5.

The ^{1}H NMR spectrum for {[3-(CF₃)-5-(t-Bu)Pz]Cu}₄ in CDCl₃, Figure S3, has a singlet at 6.48 ppm (3.00 H) and a multiplet in the region 6.36-6.41 ppm (6.13 H). Both of these correspond to the hydrogen on C4 of the pyrazolates, and were attributed to two isomers of the complex. Similarly two sets of peaks were seen in the ^{1}H NMR at 1.33-1.47 ppm corresponding to the *tert*-butyl CH₃ peaks for two isomers of the complex. Using this information combined with the calculated molecular weight in chloroform from VPO data, we were able to assign the singlets at

6.48 ppm and 1.47 ppm, notated with triangles, to the trinuclear isomer and the peaks at 6.36-

6.41 ppm and 1.33-1.40 ppm, notated with squares, to the tetranuclear isomer (Calculation 1).

This provides a calculated molecular weight based on NMR of 917 g/mol, and observed molecular

weight (based on VPO) of 900 g/mol. Similar results were obtained when calculations were done

using the peak integration values for the *tert*-butyl CH_3 peaks. As a further confirmation, when

molecular weights were calculated using the opposite NMR peak assignments (i.e., a ratio of

2.6 Cu_3 : 1 Cu_4 is used), a molecular weight of 834 g/mol was obtained, which does not agree

with the observed molecular weight based on VPO. Overall, VPO results are in good agreement

with NMR data. In agreement with previous NMR data.

Calculation 1. Assuming the peak at 6.48 (3.00 H) corresponds to the trinuclear isomer, and the

peaks at 6.36-6.41 (6.13 H) correspond to the tetranuclear isomer.

$$\frac{3.00\ H}{3\ H} = 1\ Cu_3 \qquad \frac{6.13\ H}{4\ H} = 1.5\ Cu_4$$

$$\boldsymbol{1\ Cu_3 : 1.5\ Cu_4}$$

$$Calculated\ molecular\ weight\ using\ this\ ratio\!:$$

$$Molecular\ weight\ of\ Cu_3 = 764.2\frac{g}{mol} \quad Molecular\ weight\ of\ Cu_4 = 1018.9\frac{g}{mol}$$

$$\frac{\left(1 \times 764.2\frac{g}{mol}\right) + \left(1.5 \times 1018.9\frac{g}{mol}\right)}{(1 + 1.5)} = \boldsymbol{917\frac{g}{mol}}$$

A comparison of Vapor Pressure Osmometry data to the data from NMR spectroscopic data of {[4-Br-3,5-(i-Pr)₂Pz]Cu}₄ (5).
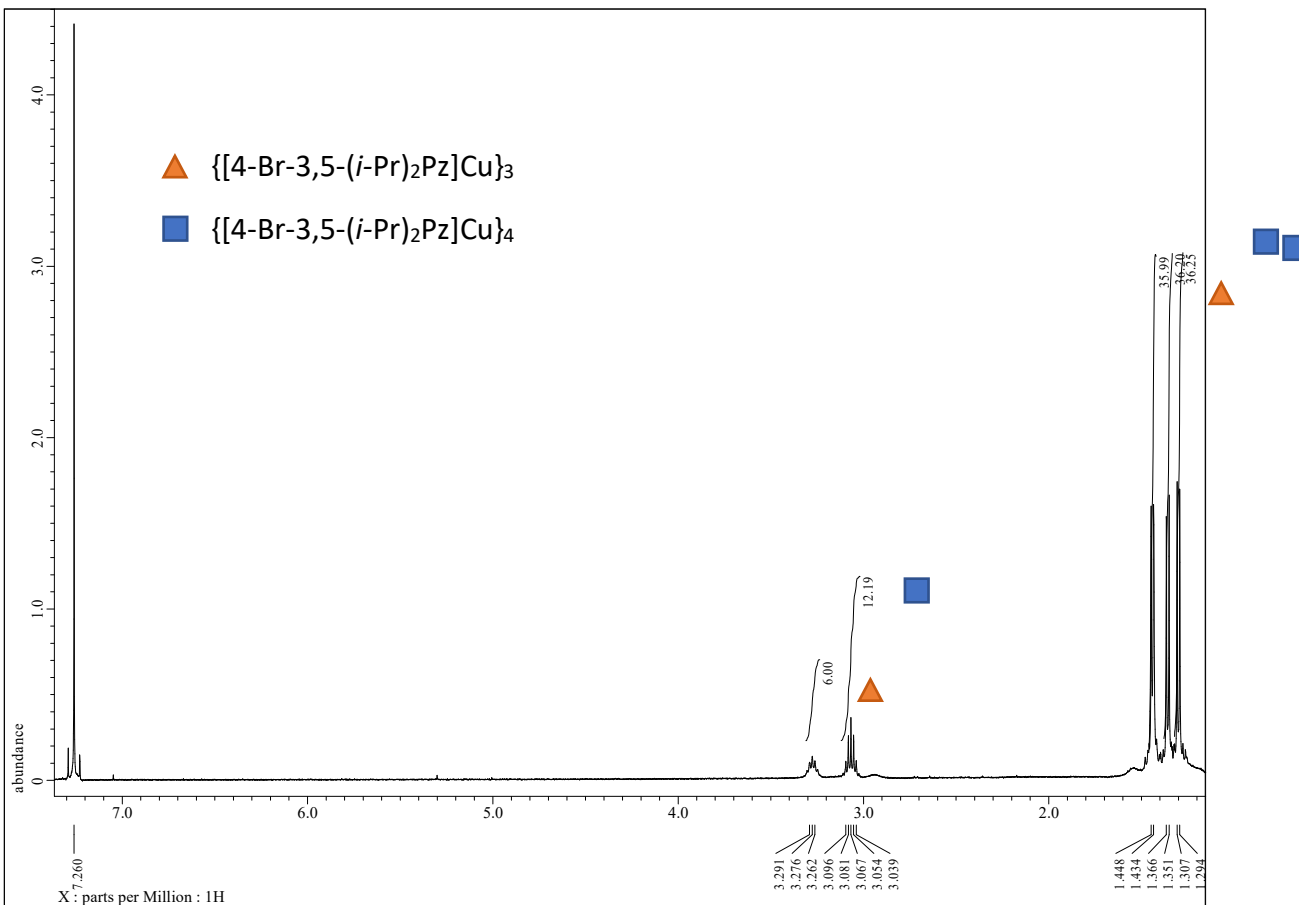
Figure S4. ¹H NMR spectrum of 6 mmol/kg solution of {[4-Br-3,5-(i-Pr)₂Pz]Cu}₄ (**5**) in CDCl₃, at room temperature. In agreement with spectrum in ref 5.

The ¹H NMR spectrum for {[4-Br-3,5-(i-Pr)₂Pz]Cu}₄ in CDCl₃, Figure S4, indicates that there is a mixture of isomers present. There is a septet at 3.28 ppm (6.00 H) and a second septet at 3.07 ppm (12.2 H). They correspond to the C*H* hydrogen of the *iso*-propyl groups on the pyrazolates. There are also doublets at 1.44 ppm (36 H), 1.35 ppm (36 H), and 1.30 ppm (36 H). Using this information combined with the molecular weight in chloroform from VPO data, we were again able to assign the peaks at 3.28 ppm and 1.44 ppm, notated with triangles, to the

trinuclear isomer and the peaks at 3.07 ppm, 1.35 ppm and 1.30 ppm, notated with squares, to the tetranuclear isomer (Calculation 2). This provides a calculated molecular weight of 1057 g/mol based on NMR data and observed molecular weight of 1058 g/mol based on VPO data, which is a remarkably close agreement. These calculations were also done using the peak integration values for the *iso*-propyl CH_3 signals, giving very similar results. As a final confirmation, when molecular weight was calculated using the opposite peak assignments (i.e., a ratio of 2.65 Cu_3 : 1 Cu_4), a molecular weight of 960 g/mol was obtained, which does not correspond closely to the observed molecular weight.

Calculation 2. Assuming the peak at 3.28 (6.00 H) corresponds to the trinuclear isomer, and the peak at 3.07 (12.2 H) corresponds to the tetranuclear isomer.

$$\frac{6.00\ H}{6\ H} = 1\ Cu_3 \qquad \frac{12.2\ H}{8\ H} = 1.5\ Cu_4$$

$$\mathbf{1\ Cu_3 : 1.5\ Cu_4}$$

Calculated molecular weight using this ratio:

$$Molecular\ weight\ of\ Cu_3 = 881.0\ \frac{g}{mol} \quad Molecular\ weight\ of\ Cu_4 = 1174.7\ \frac{g}{mol}$$

$$\frac{\left(1 \times 881.0\ \frac{g}{mol}\right) + \left(1.5 \times 1174.7\ \frac{g}{mol}\right)}{(1 + 1.5)} = \mathbf{1057\ \frac{g}{mol}}$$

Due to instrument limitations, the concentration range examined in VPO is higher than the actual catalyst concentration used in the reactions. However, we observed in ^{1}H NMR the ratio of isomers, 1 Cu_3 : 1.5 Cu_4, is the same at both the higher VPO concentrations and lower catalytic concentration. Thus, the VPO data serves as a good model for the solution behavior of the catalysts despite the concentration differences.

Kinetics, General Methods

Following methods similar to previous reports,[8, 9] the desired amount of 1-octyne (0.75, 1.5, 3.75, 15.0, or 30.0 mmol) was added to the corresponding equivalent of benzyl azide (0.75, 1.5, 3.75, 15.0, or 30.0 mmol) in a vial. Dried dichloromethane was added to reach a total volume of 5 mL. The copper(I) pyrazolate catalyst was then added in the desired mol percent (0.0075 mmol – 0.0375 mmol). Although the samples were prepared and mixed in open air, samples were prepared fresh and used without delay and the exposure to air was kept at a minimum level. The vials were closed and the resulting mixtures were stirred in a 16 °C water bath. An approximately 0.1 mL aliquot was taken in an NMR tube every 30 minutes, $CDCl_3$ was added, and the sample was analyzed via ^1H NMR for the presence of the desired 1,2,3-triazole.
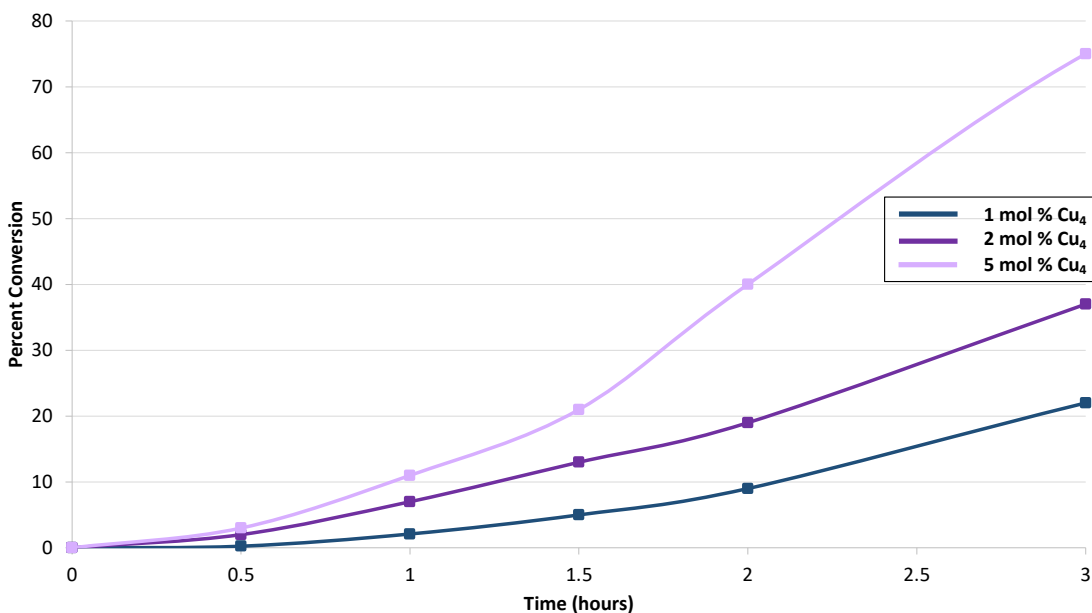
Dependence on {[3,5-(t-Bu)$_2$Pz]Cu}$_4$ concentration

Figure S5. Percent conversion vs. time for reactions with 0.75 mmol benzyl azide, 0.75 mmol 1-octyne, and 1 – 5 mol percent of {[3,5-(t-Bu)$_2$Pz]Cu}$_4$ catalyst.

Table S2: Rate calculations for various equivalents of $\{[3,5-(t\text{-Bu})_2\text{Pz}]\text{Cu}\}_4$ at t = 1 hour where [Benzyl azide] = 0.15 M, [1-octyne] = 0.15 M, and total volume is 5 mL.

Entry	$[Cu_4]$ (M)	Percent Conv.	[Triazole] (M) = [Benzyl azide]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.0015	2.1	0.0032	0.0032
2	0.0030	3.7	0.0071	0.0071
3	0.0075	10	0.0165	0.0165

Calculation of order in $[Cu_4]$ 0.0075 mmol – 0.0375 mmol (1 – 5 mol percent).

$$\frac{rate_1}{rate_2} = \frac{[Cu_4]_1^z}{[Cu_4]_2^z} \equiv \frac{0.0032}{0.0071} = \frac{[0.0015]^z}{[0.0030]^z}$$

$$\ln\left(\frac{0.0032}{0.0071}\right) = z\ln\left(\frac{0.0015}{0.0030}\right)$$

$$z = 1.16$$

$$\frac{rate_2}{rate_5} = \frac{[Cu_4]_2^z}{[Cu_4]_5^z} \equiv \frac{0.0071}{0.0165} = \frac{[0.0030]^z}{[0.0075]^z}$$

$$\ln\left(\frac{0.0071}{0.0165}\right) = z\ln\left(\frac{0.0030}{0.0075}\right)$$

$$z = 0.93$$

$$z_{average} = 1.05$$

Confirmation by graphing ln(rate) vs. ln([Cu$_4$]) for 1 – 5 mol percent, where slope = z (order with respect to Cu$_4$)

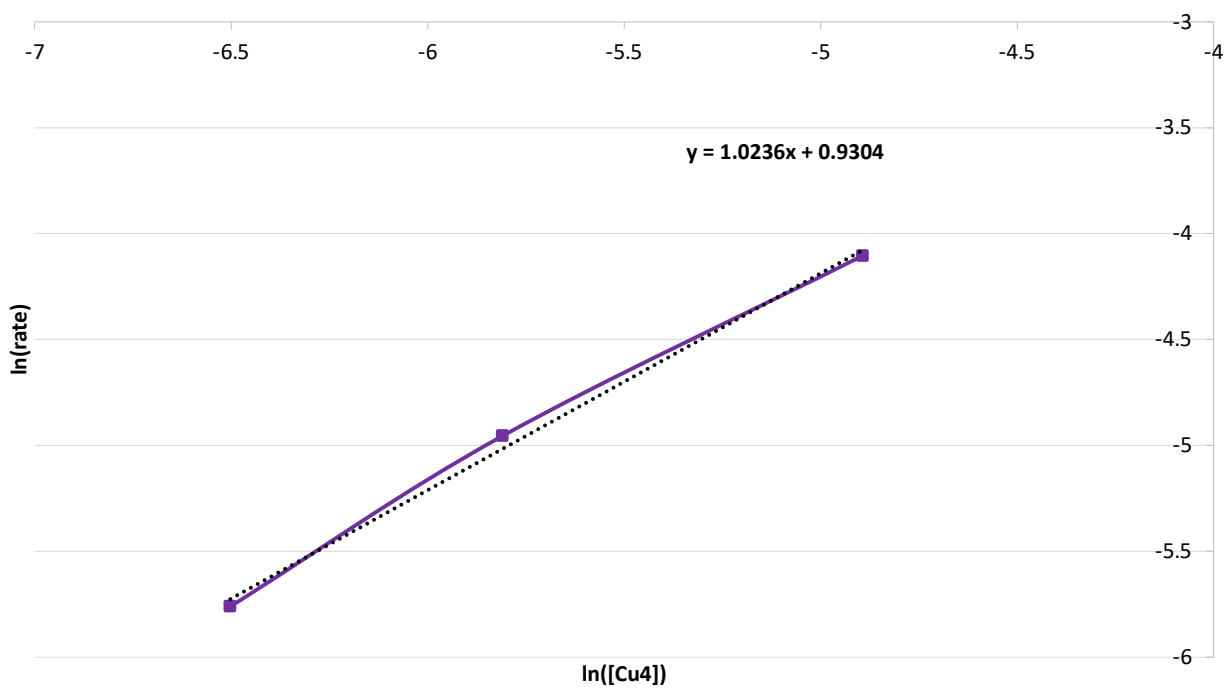**Figure S6.** ln(rate) vs. ln([Cu$_4$]) for reactions with 0.75 mmol benzyl azide, 0.75 mmol 1-octyne, and 1 – 5 mol percent of {[3,5-(t-Bu)$_2$Pz]Cu}$_4$ catalyst.

Dependence on 1-octyne concentration

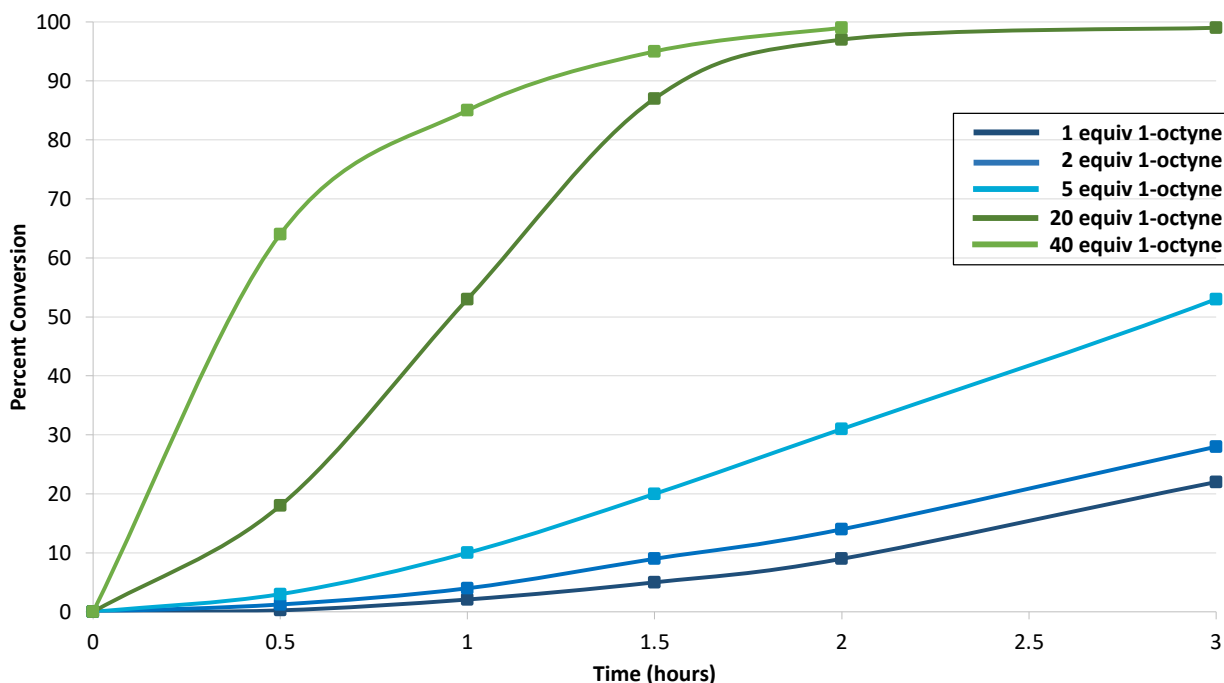**Percent conversion vs. time using various amounts (1 – 40 equivalents) of 1-octyne.**

Figure S7. Percent conversion vs. time for reactions with 0.75 mmol benzyl azide, 0.0075 mmol of $\{[3,5-(t\text{-Bu})_2\text{Pz}]\text{Cu}\}_4$ catalyst, and 0.75 – 30 mmol of 1-octyne.

Table S3. Rate calculations for various equivalents of 1-octyne at t = 1 hour where [Benzyl azide] = 0.15 M, [Cu$_4$] = 0.0015 M, and total volume is 5 mL.

Entry	[1-octyne] (M)	Percent Conv.	[Triazole] (M) = [Benzyl azide]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.15	2.1	0.0032	0.0032
2	0.30	3.7	0.0056	0.0056
3	0.75	10	0.015	0.015
4	3.0	53	0.0795	0.0795
5	6.0	85	0.128	0.128

Calculation of order in [1-octyne] 0.75 mmol – 3.75 mmol (1 – 5 equivalents).

$$\frac{rate_1}{rate_2} = \frac{[alkyne]_1^y}{[alkyne]_2^y} \equiv \frac{0.0032}{0.0056} = \frac{[0.15]^y}{[0.30]^y}$$

$$\ln\left(\frac{0.0032}{0.0056}\right) = y\ln\left(\frac{0.15}{0.30}\right)$$

$$y = 0.82$$

$$\frac{rate_2}{rate_5} = \frac{[alkyne]_2^y}{[alkyne]_5^y} \equiv \frac{0.0056}{0.015} = \frac{[0.30]^y}{[0.75]^y}$$

$$\ln\left(\frac{0.0056}{0.015}\right) = y\ln\left(\frac{0.30}{0.75}\right)$$

$$y = 1.09$$

$$y_{average} = 0.95$$

Confirmation by graphing ln(rate) vs. ln([alkyne]) for 1 – 5 equivalents, where slope = y (order with respect to alkyne)
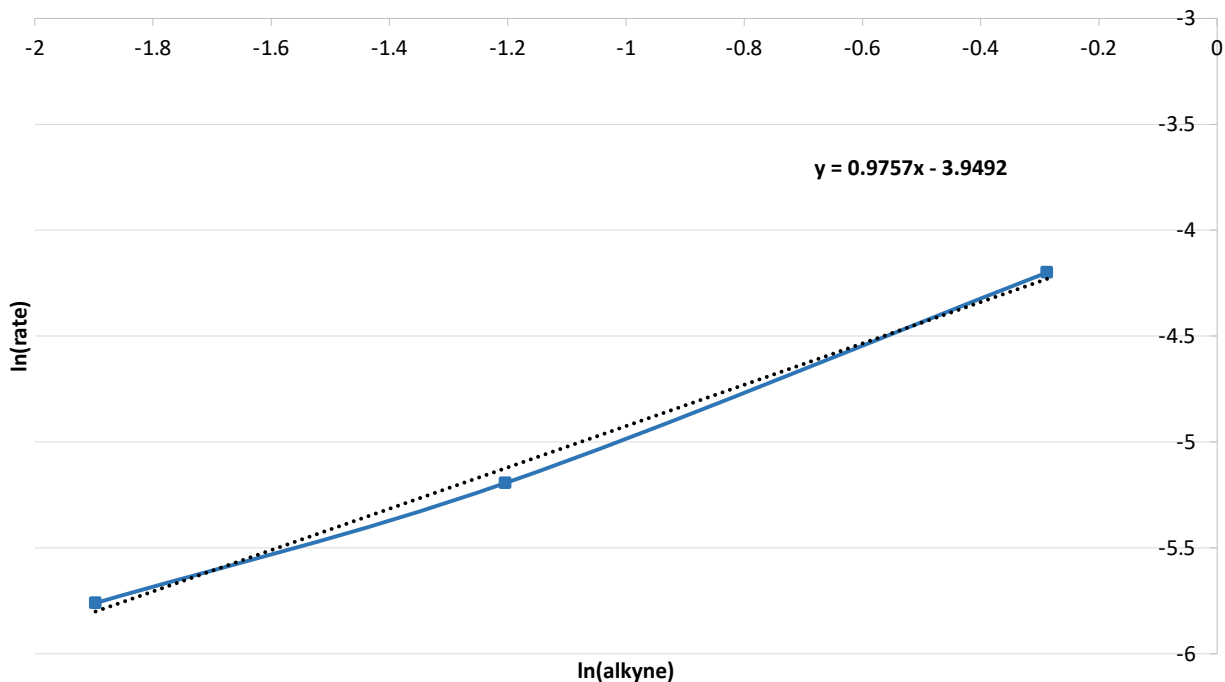

y = 0.9757x - 3.9492

Figure S8. ln(rate) vs. ln([1-octyne]) for reactions with 0.75 mmol benzyl azide, 0.0075 mmol of {[3,5-(t-Bu)$_2$Pz]Cu}$_4$ catalyst, and 0.75 – 3.75 mmol of 1-octyne.

Table S4. Confirmation of 1-octyne order under pseudo first order conditions: [benzylazide] = 6.0 M, [Cu₄] = 0.0015 M, and total volume is 5 mL.

Entry	[1-octyne] (M)	Percent Conv.	[Triazole] (M) = [1-octyne]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.15	1.5	0.0023	0.0023
2	0.30	1.7	0.0051	0.0051
3	0.75	1.75	0.0131	0.0131

y = 1.0924x - 4.0023
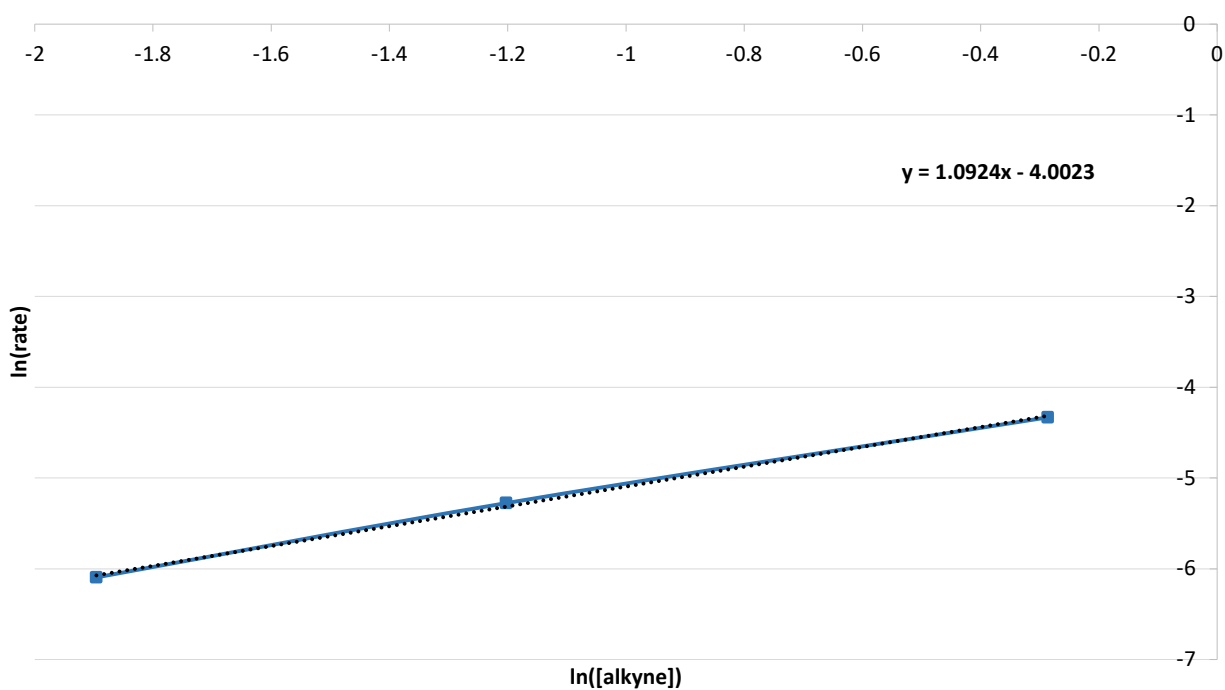
Figure S9. ln(rate) vs. ln([1-octyne]) for reactions with 30.0 mmol benzyl azide, 0.0075 mmol of {[3,5-(t-Bu)$_2$Pz]Cu}$_4$ catalyst, and 0.75 – 3.75 mmol of 1-octyne.

Calculation of order in [1-octyne] 15 mmol – 30 mmol (20 – 40 equivalents).

$$\frac{rate_{20}}{rate_{40}} = \frac{[alkyne]_{20}^{y}}{[alkyne]_{40}^{y}} \equiv \frac{0.080}{0.128} = \frac{[3.0]^{y}}{[6.0]^{y}}$$

$$\ln\left(\frac{0.080}{0.128}\right) = y\ln\left(\frac{3.0}{6.0}\right)$$

$$y = 0.68$$

Confirmation by graphing ln(rate) vs. ln([alkyne]) for 20 – 40 equivalents, where slope = y (order with respect to alkyne)
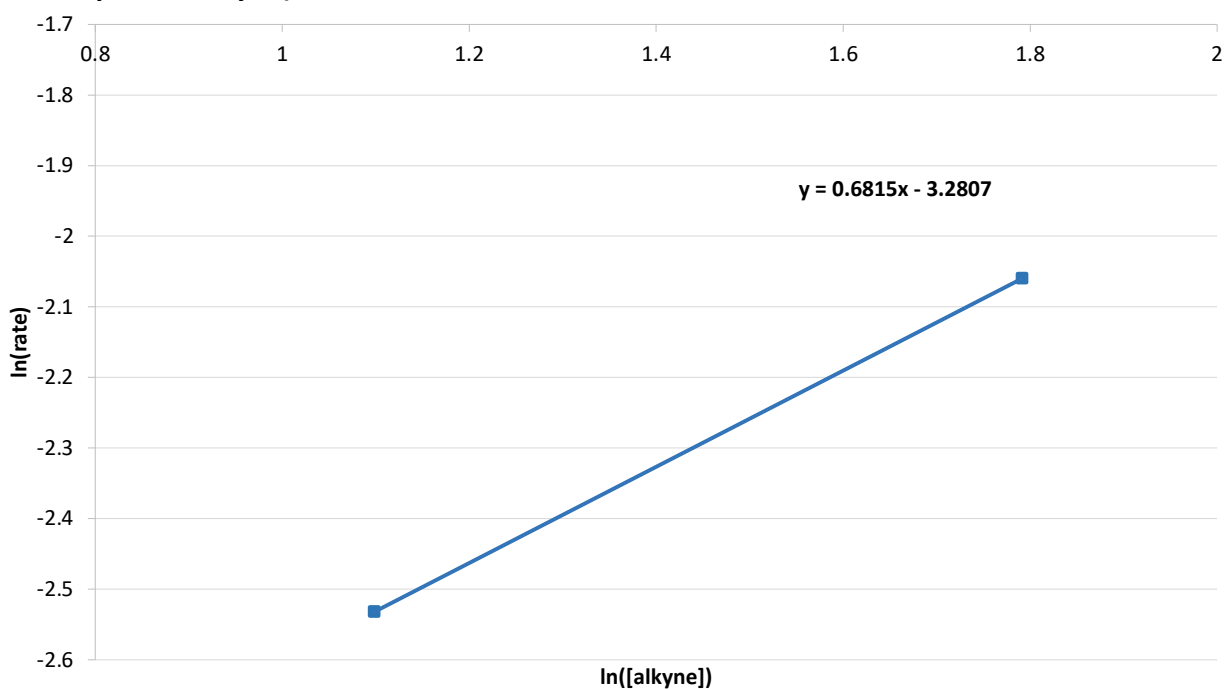

y = 0.6815x - 3.2807

Figure S10. ln(rate) vs. ln([1-octyne]) for reactions with 0.75 mmol benzyl azide, 0.0075 mmol of {[3,5-(t-Bu)$_2$Pz]Cu}$_4$ catalyst, and 15.0 – 30.0 mmol of 1-octyne.

Dependence on benzyl azide concentration

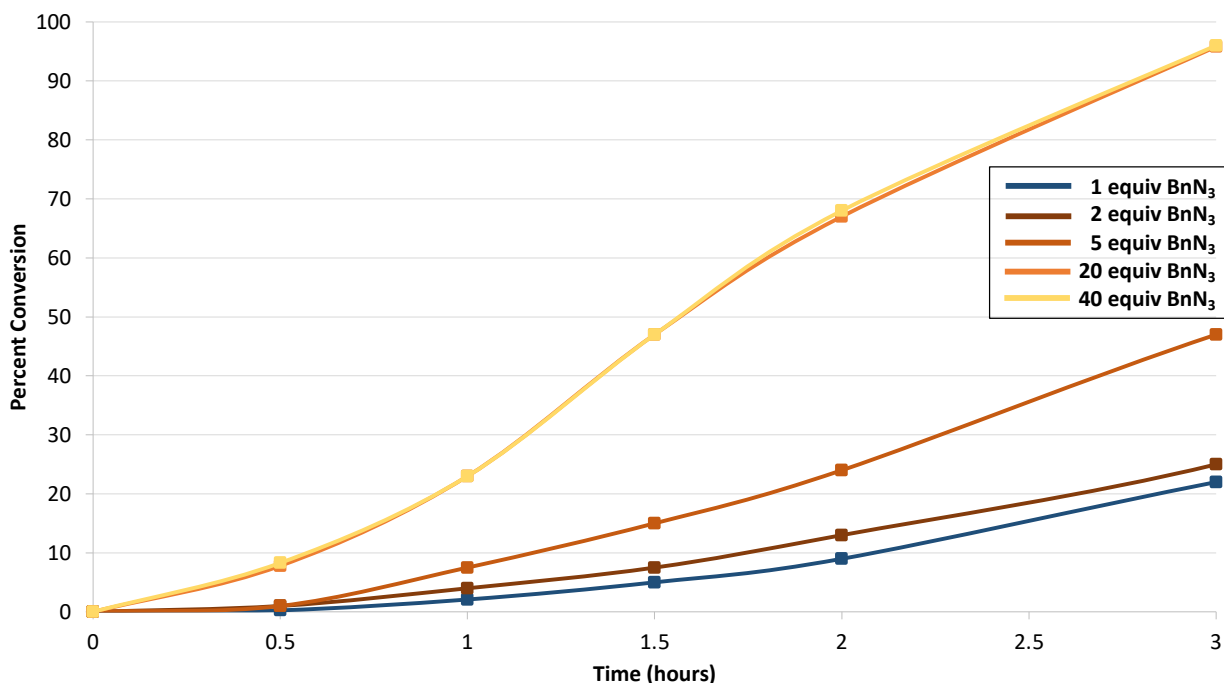**Percent conversion vs. time using various amounts (1 – 40 equivalents) of benzyl azide.**

Figure S11. Percent conversion vs. time for reactions with 0.75 mmol 1-octyne, 0.0075 mmol of

$\{[3,5-(t\text{-Bu})_2\text{Pz}]\text{Cu}\}_4$ catalyst, and 0.75 – 30 mmol of benzyl azide.

Table S5. Rate calculations for various equivalents of benzyl azide at t = 1 hour where [1-octyne] = 0.15 M, [Cu₄] = 0.0015 M, and total volume is 5 mL.

Entry	[Benzyl azide] (M)	Percent Conv.	[Triazole] (M) = [1-octyne]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.15	2.1	0.0032	0.0032
2	0.30	3.7	0.0056	0.0056
3	0.75	7.5	0.0113	0.0113
4	3.0	23	0.0341	0.0341
5	6.0	23	0.0345	0.0345

Calculation of order in [Benzylazide] 0.75 mmol – 3.75 mmol (1 – 5 equivalents).

$$\frac{rate_1}{rate_2} = \frac{[azide]_1^x}{[azide]_2^x} \equiv \frac{0.0032}{0.0056} = \frac{[0.15]^x}{[0.30]^x}$$

$$\ln\left(\frac{0.0032}{0.0056}\right) = x \ln\left(\frac{0.15}{0.30}\right)$$

$$x = 0.82$$

$$\frac{rate_2}{rate_5} = \frac{[azide]_2^x}{[azide]_5^x} \equiv \frac{0.0056}{0.0113} = \frac{[0.30]^x}{[0.75]^x}$$

$$\ln\left(\frac{0.0056}{0.0113}\right) = x \ln\left(\frac{0.30}{0.75}\right)$$

$$x = 0.77$$

$$x_{average} = 0.79$$

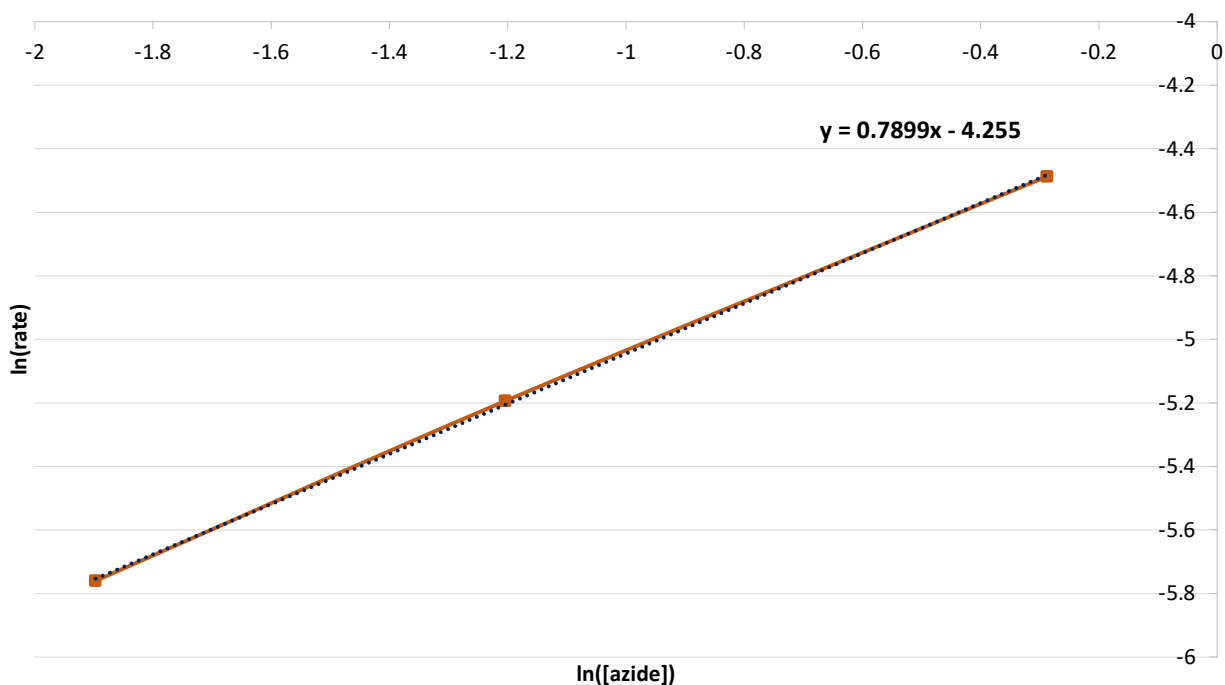**Confirmation by graphing ln(rate) vs. ln([azide]) for 1 – 5 equivalents, where slope = x (order with respect to azide)**

Figure S12. ln(rate) vs. ln([benzyl azide]) for reactions with 0.75 mmol 1-octyne, 0.0075 mmol of

{[3,5-(t-Bu)$_2$Pz]Cu}$_4$ catalyst, and 0.75 – 3.75 mmol of benzyl azide.

Table S6. Confirmation of benzyl azide order under pseudo first order conditions: [1-octyne] = 6.0 M, [Cu$_4$] = 0.0015 M, and total volume is 5 mL.

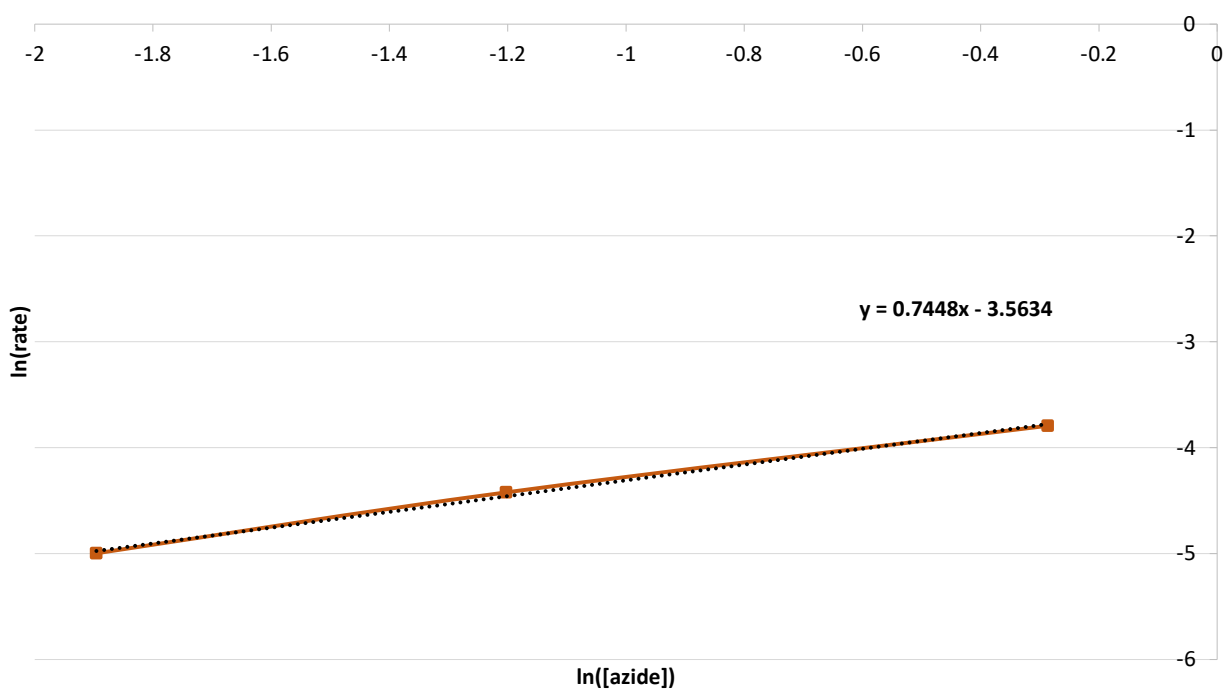| Entry	[Benzylazide] (M)	Percent Conv.	[Triazole] (M) = [benzylazide]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.15	4.5	0.0034	0.0032
2	0.30	4	0.0060	0.0056
3	0.75	3	0.0113	0.0113

Figure S13. ln(rate) vs. ln([benzyl azide]) for reactions with 30.0 mmol 1-octyne, 0.0075 mmol of {[3,5-(*t*-Bu)$_2$Pz]Cu}$_4$ catalyst, and 0.75 – 3.75 mmol of benzyl azide.

Calculation of order in [Benzylazide] 15 mmol – 30 mmol (20 – 40 equivalents).

$$\frac{rate_{20}}{rate_{40}} = \frac{[azide]_{20}^x}{[azide]_{40}^x} \equiv \frac{0.0341}{0.0345} = \frac{[3.0]^x}{[6.0]^x}$$

$$\ln\left(\frac{0.0341}{0.0345}\right) = x\ln\left(\frac{3.0}{6.0}\right)$$

$$x = 0.02$$

Confirmation by graphing ln(rate) vs. ln([azide]) for 20 – 40 equivalents, where slope = x (order with respect to azide)

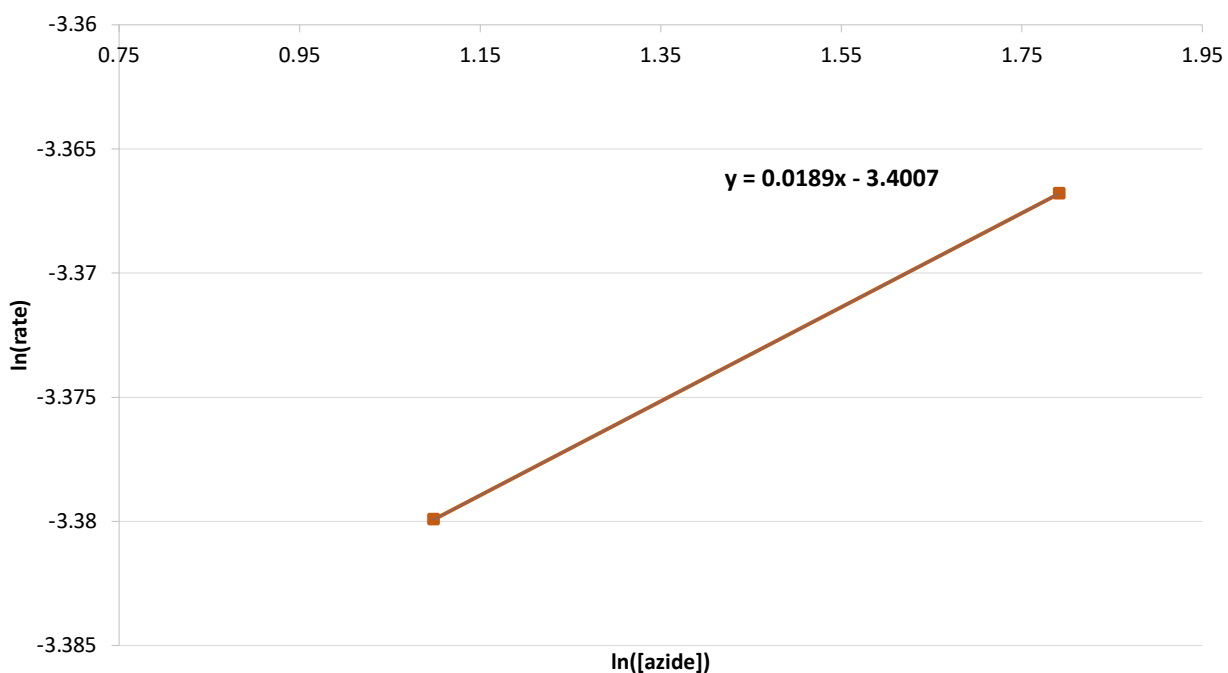**Figure S14.** ln(rate) vs. ln([benzyl azide]) for reactions with 0.75 mmol 1-octyne, 0.0075 mmol of

{[3,5-(*t*-Bu)$_2$Pz]Cu}$_4$ catalyst, and 15.0 – 30.0 mmol of benzyl azide.

Dependence on {[3-(CF$_3$)-5-(t-Bu)Pz]Cu}$_4$ concentration

Table S7. Rate calculations for various equivalents of {[3-(CF$_3$)-5-(t-Bu)Pz]Cu}$_4$ at t = 1 hour where [Benzyl azide] = 0.15 M, [1-octyne] = 0.15 M, and total volume is 5 mL.

Entry	[Cu$_4$] (M)	Percent Conv.	[Triazole] (M) = [Benzyl azide]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.0015	17	0.023	0.023
2	0.0030	32	0.048	0.048
3	0.0075	69	0.104	0.104

Calculation of order in [Cu$_4$] 0.0075 mmol – 0.0375 mmol (1 – 5 mol percent).

$$\frac{rate_1}{rate_2} = \frac{[Cu_4]_1^z}{[Cu_4]_2^z} \equiv \frac{0.023}{0.048} = \frac{[0.0015]^z}{[0.0030]^z}$$

$$\ln\left(\frac{0.023}{0.048}\right) = z \ln\left(\frac{0.0015}{0.0030}\right)$$

$$z = 0.91$$

$$\frac{rate_2}{rate_5} = \frac{[Cu_4]_2^z}{[Cu_4]_5^z} \equiv \frac{0.048}{0.104} = \frac{[0.0030]^z}{[0.0075]^z}$$

$$\ln\left(\frac{0.048}{0.104}\right) = z \ln\left(\frac{0.0030}{0.0075}\right)$$

$$z = 0.84$$

$$z_{average} = 0.88$$

Confirmation by graphing ln(rate) vs. ln([Cu_4]) for 1 – 5 mol percent, where slope = z (order with respect to Cu_4)

y = 0.8688x + 1.9908
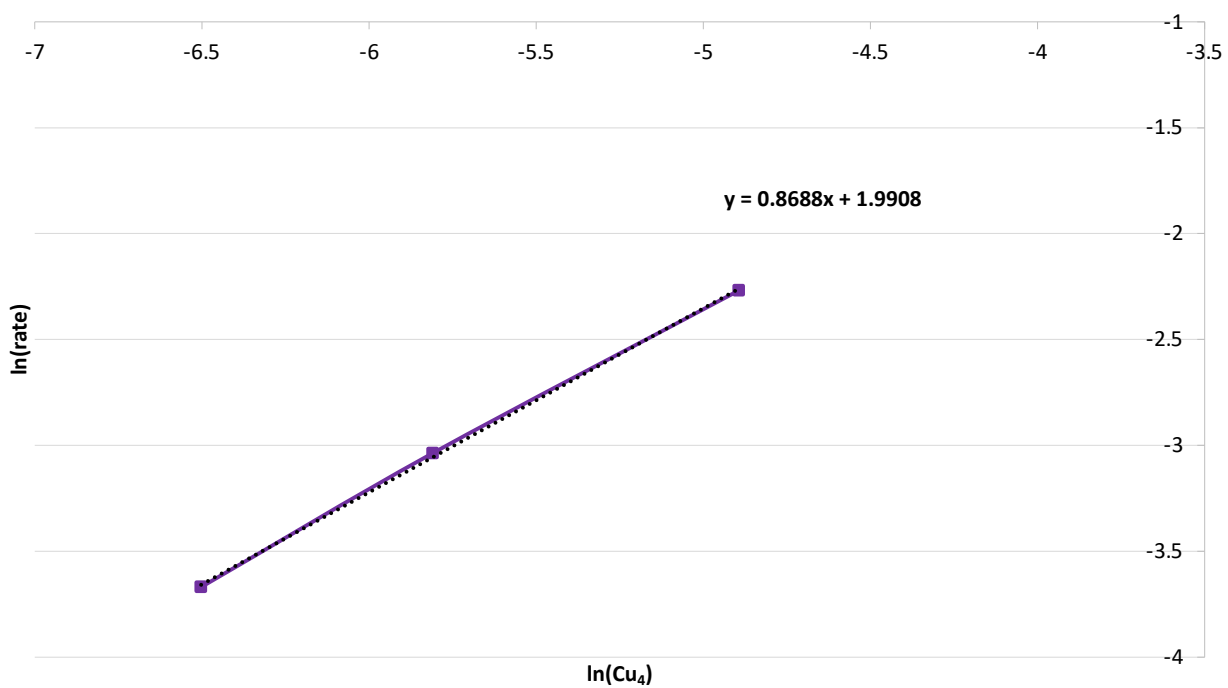
Figure S15. ln(rate) vs. ln([Cu_4]) for reactions with 0.75 mmol 1-octyne, 0.75 mmol of benzyl azide, and 1 – 5 mol percent of {[3-(CF_3)-5-(t-Bu)Pz]Cu}$_4$ catalyst.

Dependence on {[3,5-(CF$_3$)$_2$Pz]Cu}$_3$ concentration

Table S8. Rate calculations for various equivalents of {[3,5-(CF$_3$)$_2$Pz]Cu}$_3$ at t = 1 hour where [Benzyl azide] = 0.15 M, [1-octyne] = 0.15 M, and total volume is 5 mL.

Entry	[Cu$_3$] (M)	Percent Conv.	[Triazole] (M) = [Benzyl azide]*((% conv.)/100)	Rate = d[Triazole]/dt
1	0.0015	1	0.0045	0.0045
2	0.0030	4	0.0165	0.0165
3	0.0075	13	0.0630	0.0630

Calculation of order in [Cu$_4$] 0.0075 mmol – 0.0375 mmol (1 – 5 mol percent).

$$\frac{rate_1}{rate_2} = \frac{[Cu_4]_1^z}{[Cu_4]_2^z} \equiv \frac{0.0045}{0.0165} = \frac{[0.0015]^z}{[0.0030]^z}$$

$$\ln\left(\frac{0.0045}{0.0165}\right) = z \ln\left(\frac{0.0015}{0.0030}\right)$$

$$z = 1.87$$

$$\frac{rate_2}{rate_5} = \frac{[Cu_4]_2^z}{[Cu_4]_5^z} \equiv \frac{0.0165}{0.0630} = \frac{[0.0030]^z}{[0.0075]^z}$$

$$\ln\left(\frac{0.0165}{0.0630}\right) = z \ln\left(\frac{0.0030}{0.0075}\right)$$

$$z = 1.46$$

$$z_{average} = 1.67$$

Confirmation by graphing ln(rate) vs. ln([Cu_3]) for 1 – 5 mol percent, where slope = z (order with respect to Cu_3)
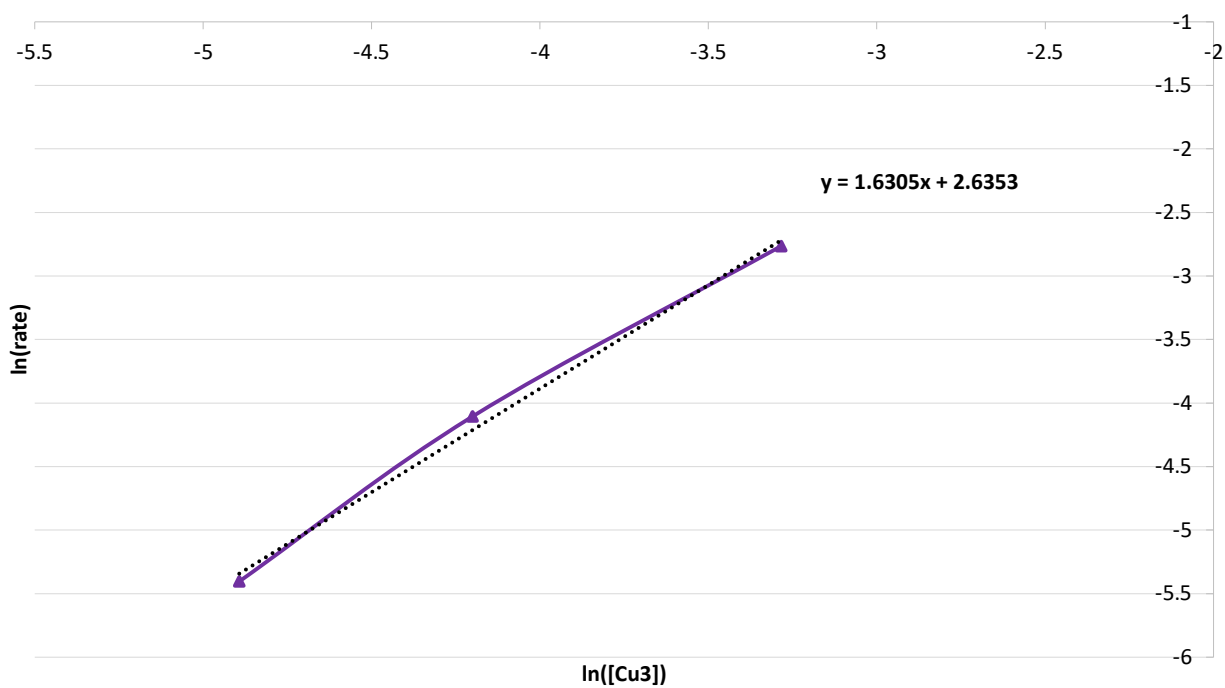

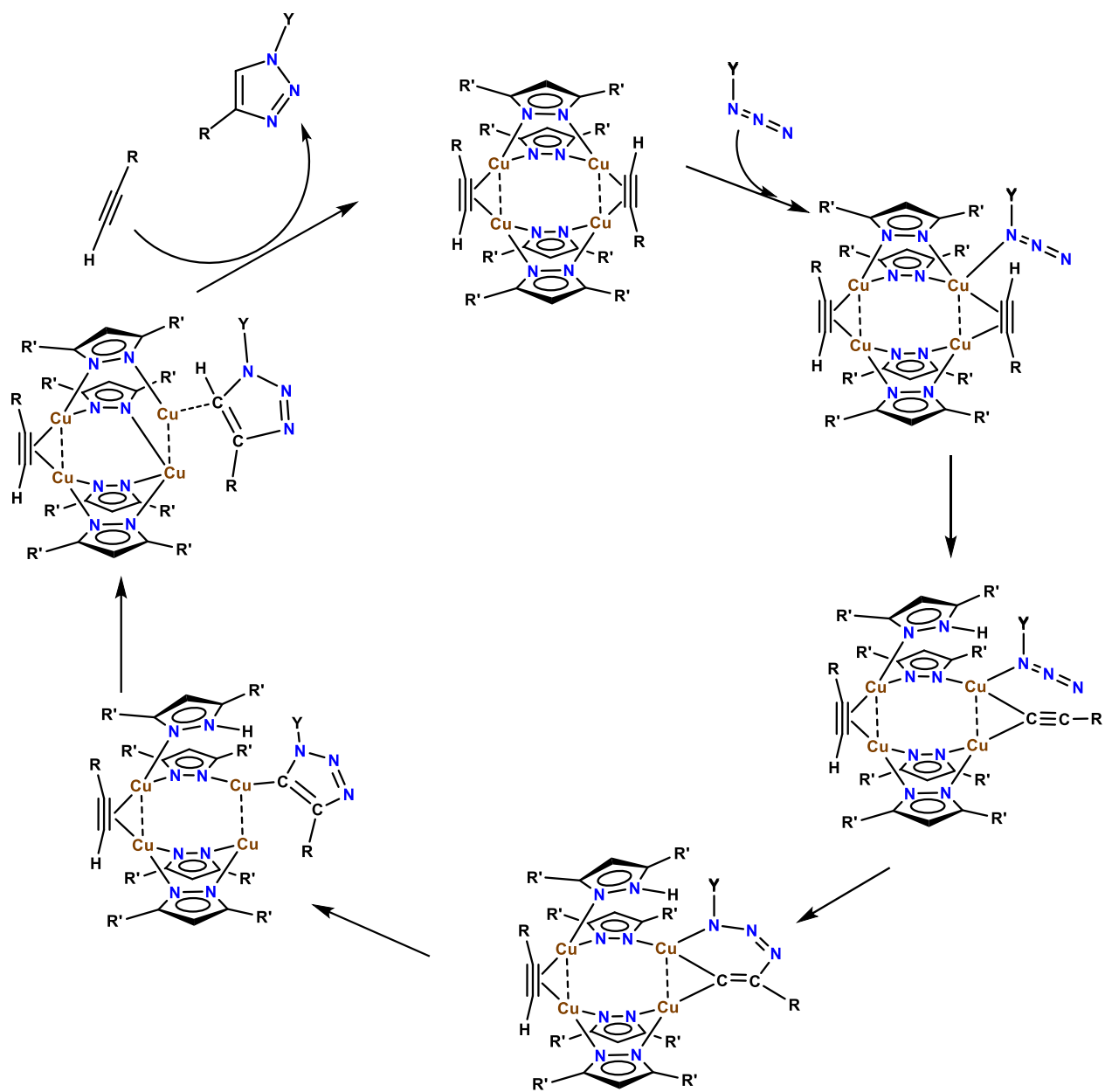**Figure S16.** ln(rate) vs. ln([Cu_3]) for reactions with 0.75 mmol 1-octyne, 0.75 mmol of benzyl azide, and 1 – 5 mol percent of {[3,5-$(CF_3)_2Pz$]Cu}$_3$ catalyst.

Figure S17. Mechanism proposed by Larionov, Totov and co-workers[8] for azide-alkyne cycloadditions catalyzed by trinuclear copper(I) pyrazolate {[3,5-(CF₃)₂Pz]Cu}₃

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