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Supporting Information

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for

Electrochemically Protected Copper(I)-Catalyzed Azide–Alkyne Cycloaddition

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Synthesis of Ligand 2: 4-Chloromethyl benzoic acid (5 g, 29 mmol) was dissolved in DMSO (40-50 mL) and was then treated with sodium azide (5.7 g, 88 mmol) along with a small amount of sodium iodide. The reaction was stirred at room temperature and was monitored by thin layer chromatography (silica, ethyl acetate). The reaction was completed after 2 h and was worked up by addition of water, acidification with dilute hydrochloric acid, and extraction with diethyl ether. The ether extracts were washed with water to remove DMSO and then brine before drying with anhydrous $MgSO_4$ and evaporation to give 4.5 g (86%) of 4-azidomethyl benzoic acid as a white solid. The product was further washed with hexane a number of times to give a white powder with minimal loss of mass. The ^{1}H NMR spectrum (Figure S1) was clean and consistent with that reported previously.[56] ^{1}H NMR (400 MHz, $CDCl_3$) d = 4.45 (s, $-CH_2$-N- 2H), 7.44 (d, J = 8.1 Hz, aromatic), 8.14 (d, J = 8.4 Hz, aromatic).

The CuAAC reaction to prepare ligand **2** was performed as follows (Figure S2). Potassium hydrogen carbonate (0.94 g, 9.4 mmol) was dissolved in water/*t*BuOH (1:2, 15 mL). 4-Azidomethyl benzoic acid (1.5 g, 8.5 mmol) was added with stirring to dissolve, followed by tripropargylamine (0.37 g, 2.8 mmol) and sodium ascorbate (420 µL of a 1 M solution, 5 mol%). Copper sulfate (85 µL of a 1 M solution, 1 mol%) was added to initiate the reaction, which turned briefly pale green and then a lighter yellow. After a short while the solution was opalescent. The reaction was stirred overnight, and was then diluted with water and gradually acidified with glacial acetic acid to ca. pH 4. The white precipitate thus formed was collected and washed with water. The precipitate was boiled briefly in methanol (30 mL), cooled (-10°C), and filtered to give **2** as an off-white powder (1.50 g, 80%). The product can be dissolved in aqueous base and reprecipitated with acidification with glacial acetic acid if additional purification is required. ^{1}H NMR (Figure S3, 400 MHz, [D$_6$]DMSO) d = 3.63 (s, N-CH$_2$-triazole, 2H), 5.67 (s, benzylic CH$_2$, 2H), 7.34 (d, J = 6.95 Hz, aromatic, 2H), 7.90 (d, J = 6.04 Hz, aromatic, 2H), 8.12 (s, triazole CH, 1H). ^{13}C NMR (Figure S3, 100.6 MHz, [D$_6$]DMSO) 47.4 (CH$_2$-N), 53.8 (benzyl), 125.0 (triazole CH), 128.2 (aromatic), 130.2 (aromatic) , 131.0 (aromatic quat.), 141.3 (aromatic quat.) , 144.2 (triazole quat.), 167.4 (C=O).

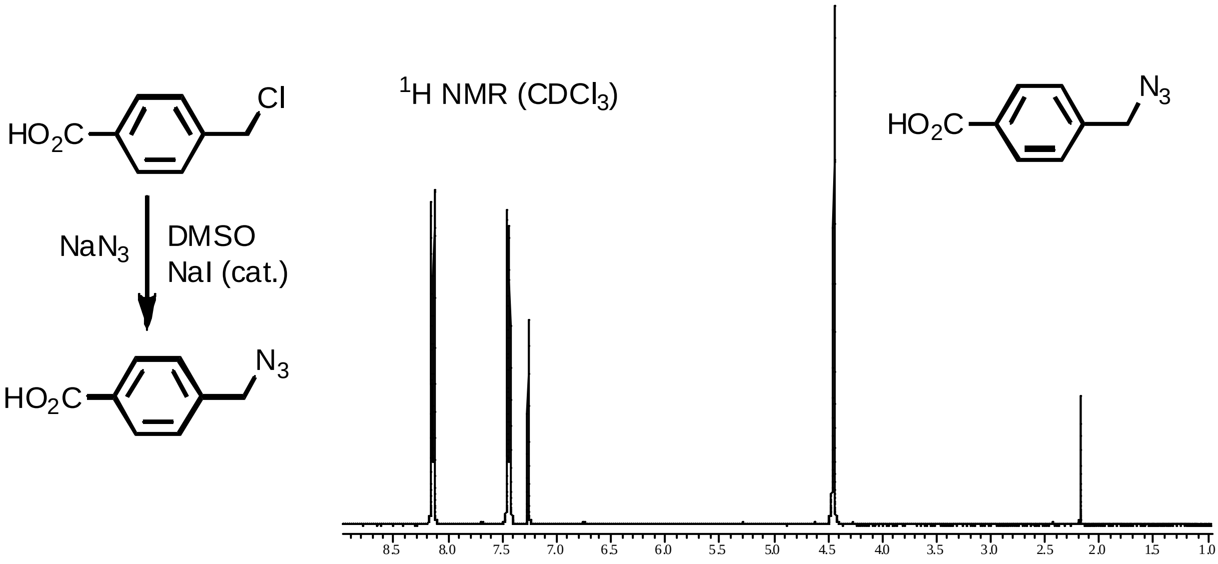

Figure S1. Synthesis and ^{1}H NMR spectrum of azidomethyl benzoic acid.

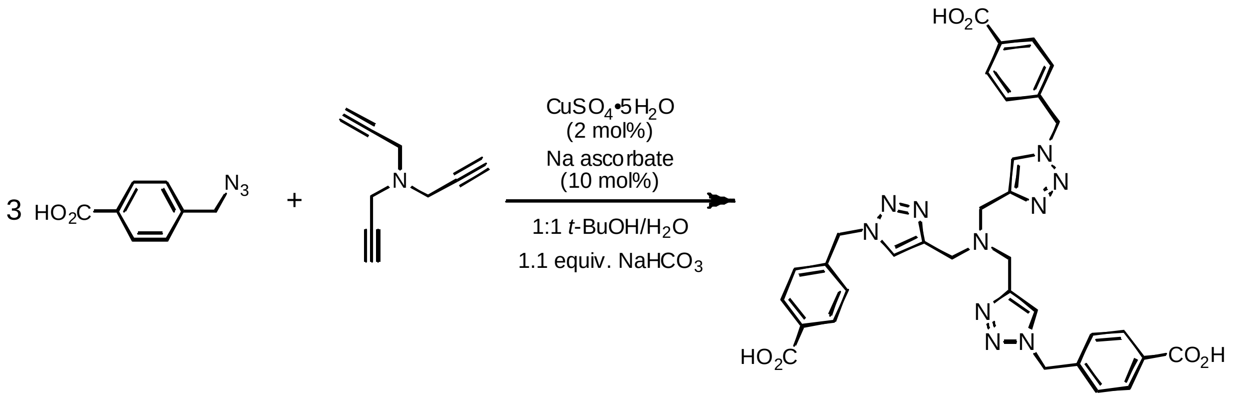

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Figure S2. Synthesis of ligand **2**.

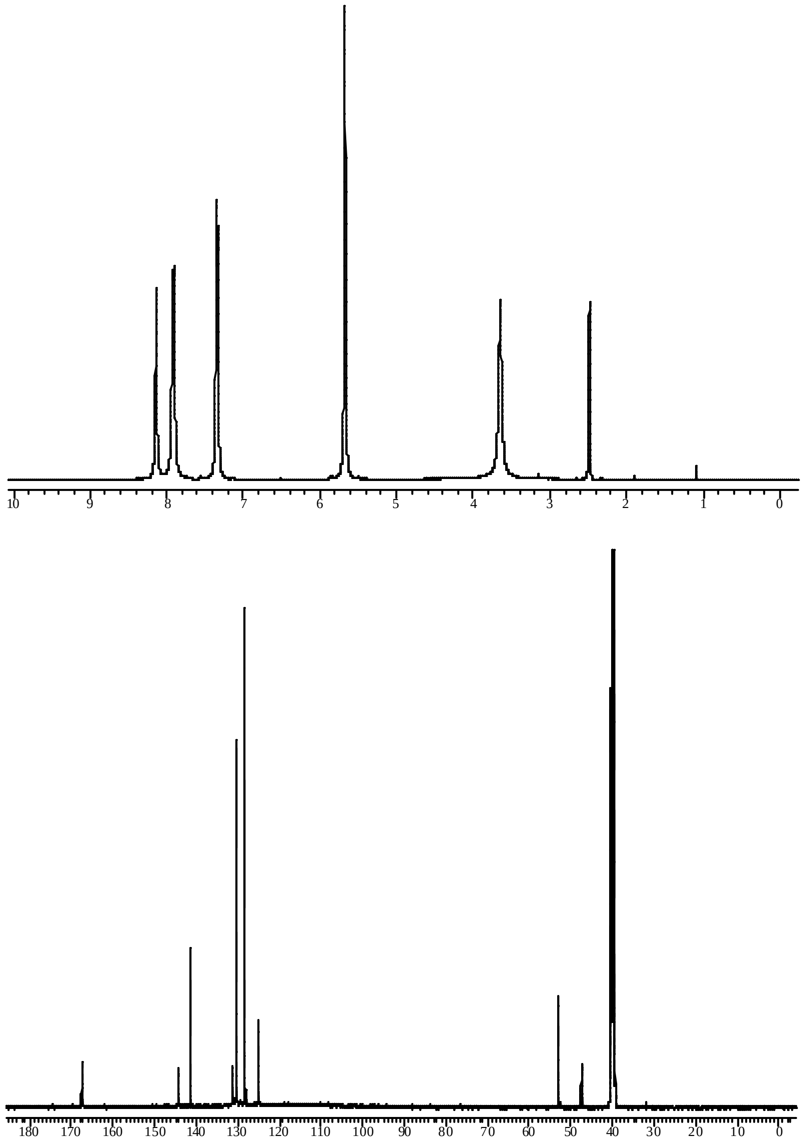

Figure S3. ^{1}H NMR spectrum (top) and ^{13}C NMR spectrum (bottom) of ligand 2, both in [D_6]DMSO.

Additional Electrochemical Data

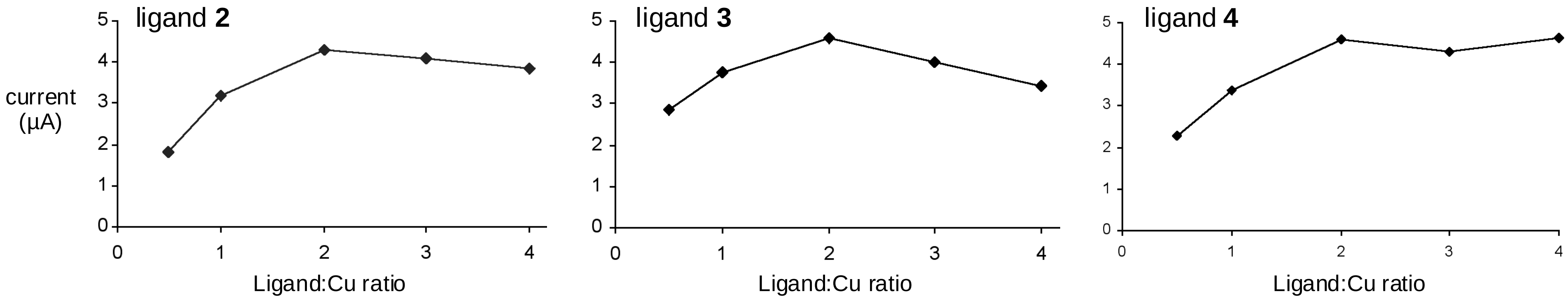

Figure S4. Peak current titration curves with increasing ligand concentration.

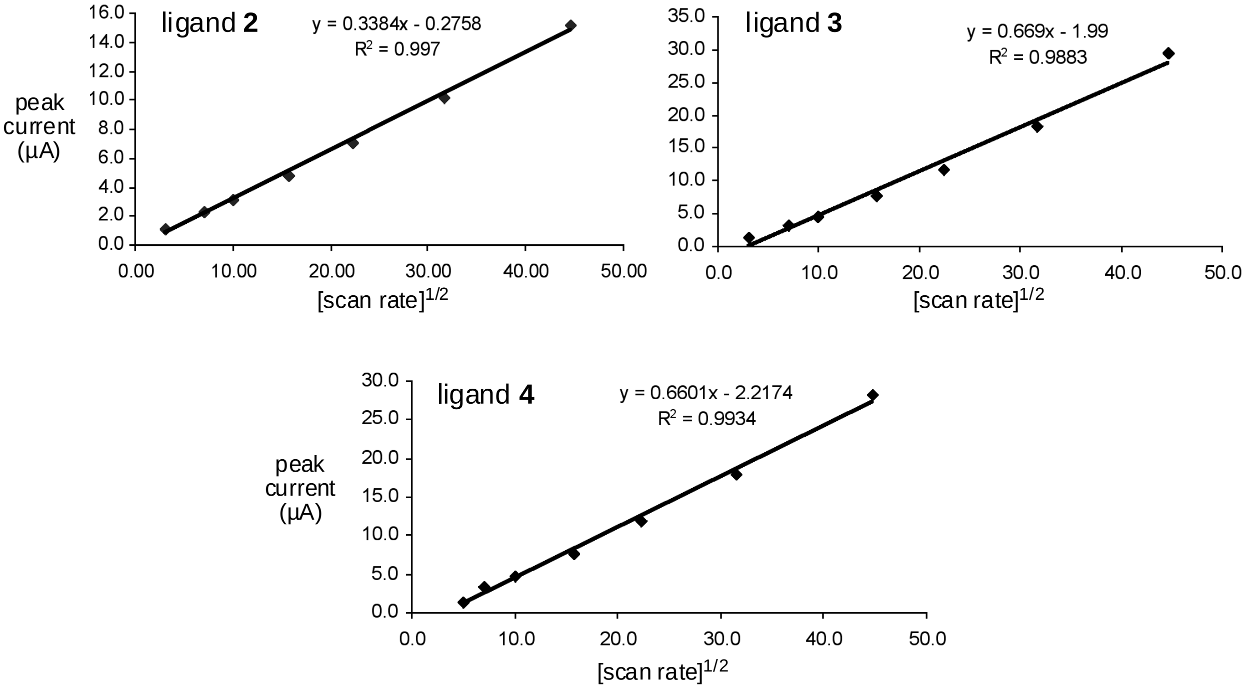

Figure S5. Peak current vs. (scan rate)$^{1/2}$ for the copper-ligand complexes. The linear relationships indicate diffusion controlled electrode reactions.

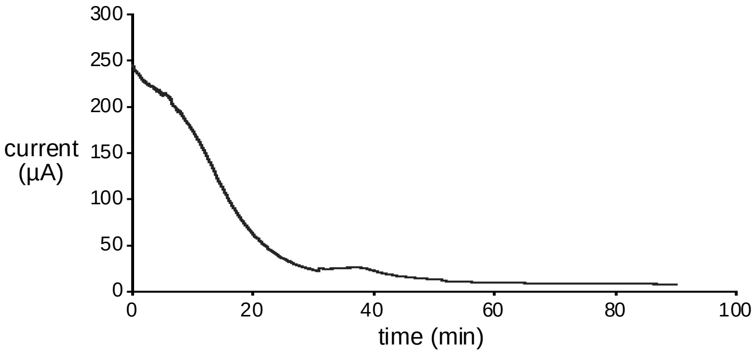

Figure S6. Exemplary current-time trace for bulk electrolysis with Cu•32.

Characterization of Virus-Like Particles

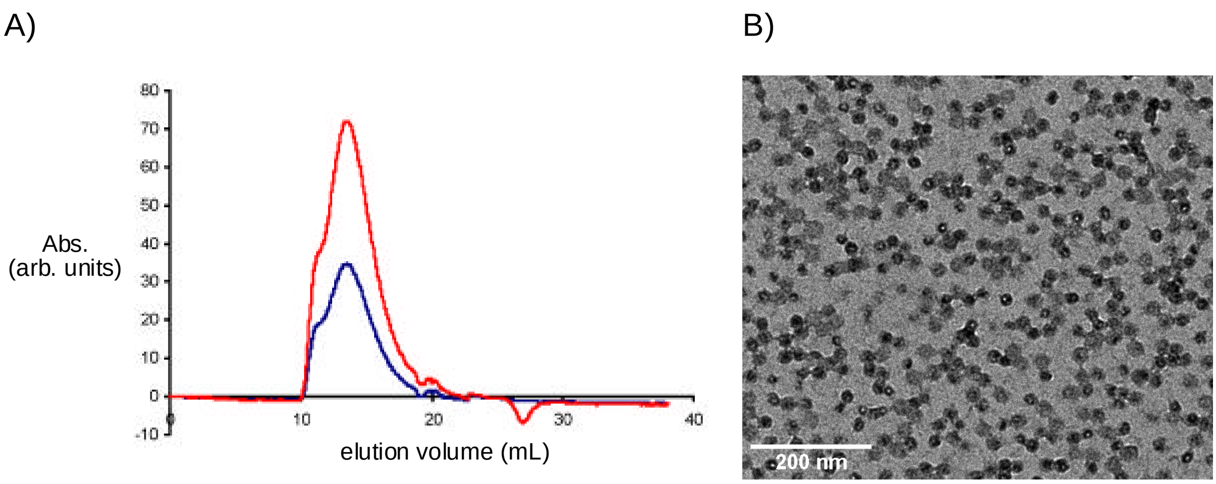

Figure S7. (A) Size-exclusion FPLC (Superose-6) and (B) transmission electron micrograph of product **7** isolated following electrochemical CuAAC reaction.

Quantitative LC-MS analysis (Table 1)

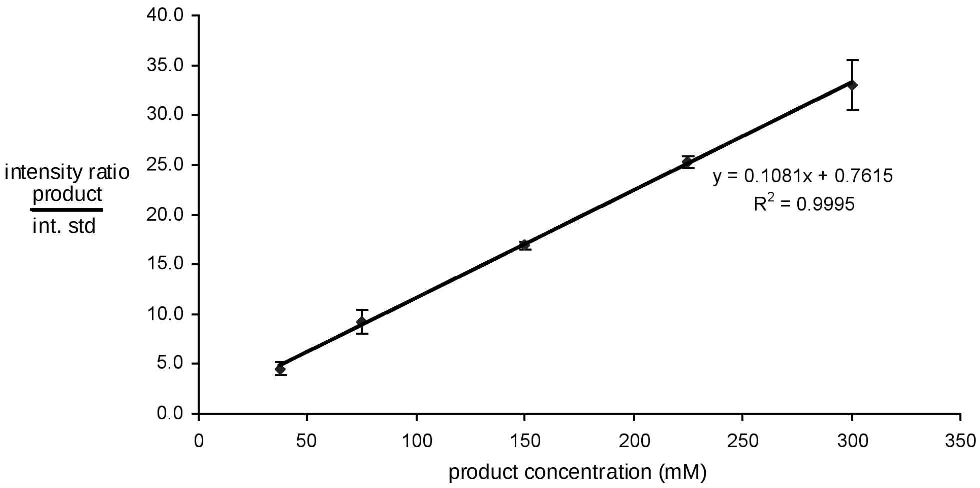

Figure S8. Calibration curve for LC-MS analysis (Agilent 1100 MSD, G1946D system), performed with a 35 mm Agilent Zorbax 1.8µm SB-C18 column.