Supporting Information

Protein Samples

Samples of purified amine oxidase were obtained from D. M. Dooley at Montana State University. The copper amine oxidase from *Arthrobacter globiformis* was expressed and purified as a fusion protein with a C-terminal *Strep*-tag II peptide. The procedures for expression and isolation of AGAO are described by Juda et al.[1]

Synthesis

General

Aryl halides, TMS-acetylene, Pd and Cu catalysts were obtained from commercially available sources. Fluka "puriss" diethylamine, diisopropylamine and THF were used in the cross-coupling reactions. Gas chromatography/mass spectra (GC-MS) were collected on an Agilent Technologies instrument. Electrospray mass spectrometry (ES-MS) and atmospheric pressure chemical ionization were performed on a Hewlett Packard 1100 series instrument in the Caltech Environmental Analysis Center. NMR spectra were collected on Varian 300MHz or 600 MHz instruments.

General procedures for Pd cross-coupling reactions

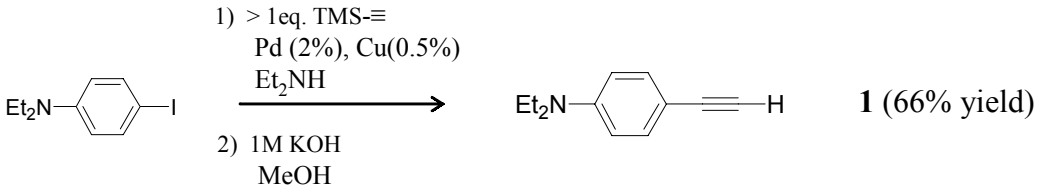
The thiol oligomer was synthesized by means of Sonogashira Pd catalyzed cross-coupling reactions[2] with modifications to procedures previously described for these types of oligomers.[3,4] The synthesis is outlined in Scheme S1. The general procedure is as follows: $(Ph_3P)_2PdCl_2$ (2%) and CuI (0.5%) were added to a deoxygenated solution of the aryl halide and acetylene-terminated compound in a pressure tube. Diethylamine was generally used as the solvent. The pressure tube was sealed and the reaction mixture was sonicated for 12 hours. The solvent was removed in vacuo and the product purified by flash chromatography (EM Science silica gel, 230-400 mesh). For the final coupling involving addition of the acetyl-protected iodothiophenol, 2% Pd and 5.5% CuI were used as catalysts, and a mixture of 1:1 THF / diisopropylamine was used as the solvent. TMS deprotection reactions were carried out with 1 M KOH in MeOH. Products of each reaction were confirmed by MS and NMR.[5]

Synthesis of 1-iodo-4-thioacetylbenzene: The thiol starting material was synthesized by modification of procedures previously described.[3] To a solution of 5 g of diiodobenzene (15 mmol) in ether (15 mL) at -78 ºC was added dropwise 17.7 mL of *t*-BuLi (1.7M solution in pentane, 30 mmol) under Ar. The solution was stirred at -78 ºC for 30min, and then warmed to 0 ºC for 15 min. The solution was then recooled to -78 ºC and a suspension of 0.55g of sulfur powder (2.14 mmol) in 40 mL THF was added. The mixture was stirred for 15 min at -78 ºC and warmed to 0 ºC for 30 min. After recooling to -78 ºC again, 1.9 mL of acetyl chloride (27 mmol) was added. The reaction was allowed to warm to room temperature overnight. The mixture was extracted with CH_2Cl_2, the organic layer collected, and the solvent removed in vacuo. The product was then purified by column chromatography using 2:1 hexane/CH_2Cl_2. $R_f = 0.25$; 67% yield.

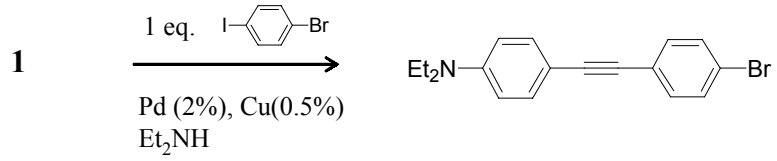
Deprotection of thiol group: The acetyl group was removed from the oligomer (**3**) to yield the final thiol oligomer (**4**), according to procedures described by Stoltz et al. in the synthesis of nicandrenones.[6] To a deoxygenated solution of **4** (20 mg, 0.047 mmol) in toluene at -78 ºC was added dropwise 160 μL of diisobutylaluminum hydride (DIBAL, 1 M in toluene, 0.16 mmol). After 5 min the reaction mixture was treated with 100 μL of MeOH followed by 600 mg of $Na_2SO_4 \bullet 10H_2O$ and 120 mg of celite. The mixture was allowed to warm to room temperature and the mixture filtered through a plug of celite. The solvent was removed from the filtrate under vacuum, and the solid used without further purification. (56% yield).

Characterization of thiol oligomer (4):
1H NMR (600 MHz, CD_2Cl_2): δ 1.17 (t, 6H) 3.38 (q, 4H), 3.64 (s, 1H), 6.63 (d, 2 H), 7.26 (d, 2 H), 7.35 (d, 2H), 7.4 (d, 2H), 7.46 (q, 4H).
ES-MS: [m+1] = 382.

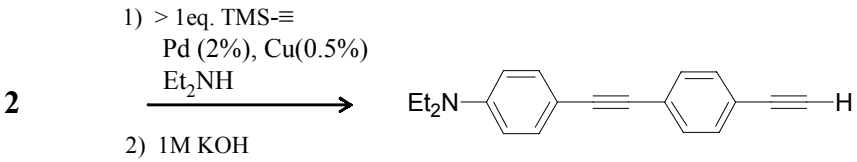
Scheme S1: Molecular Wire Synthesis



1 (66% yield)

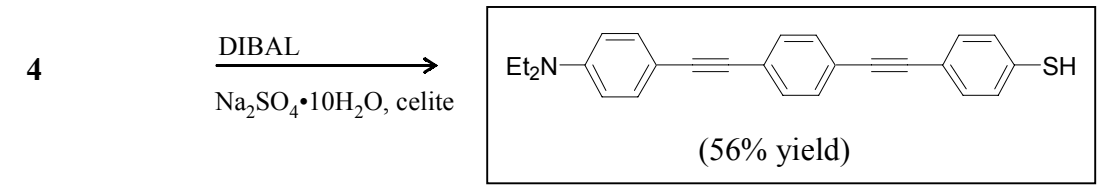


2 (95% yield)



3 (86% yield)

4 (43% yield)

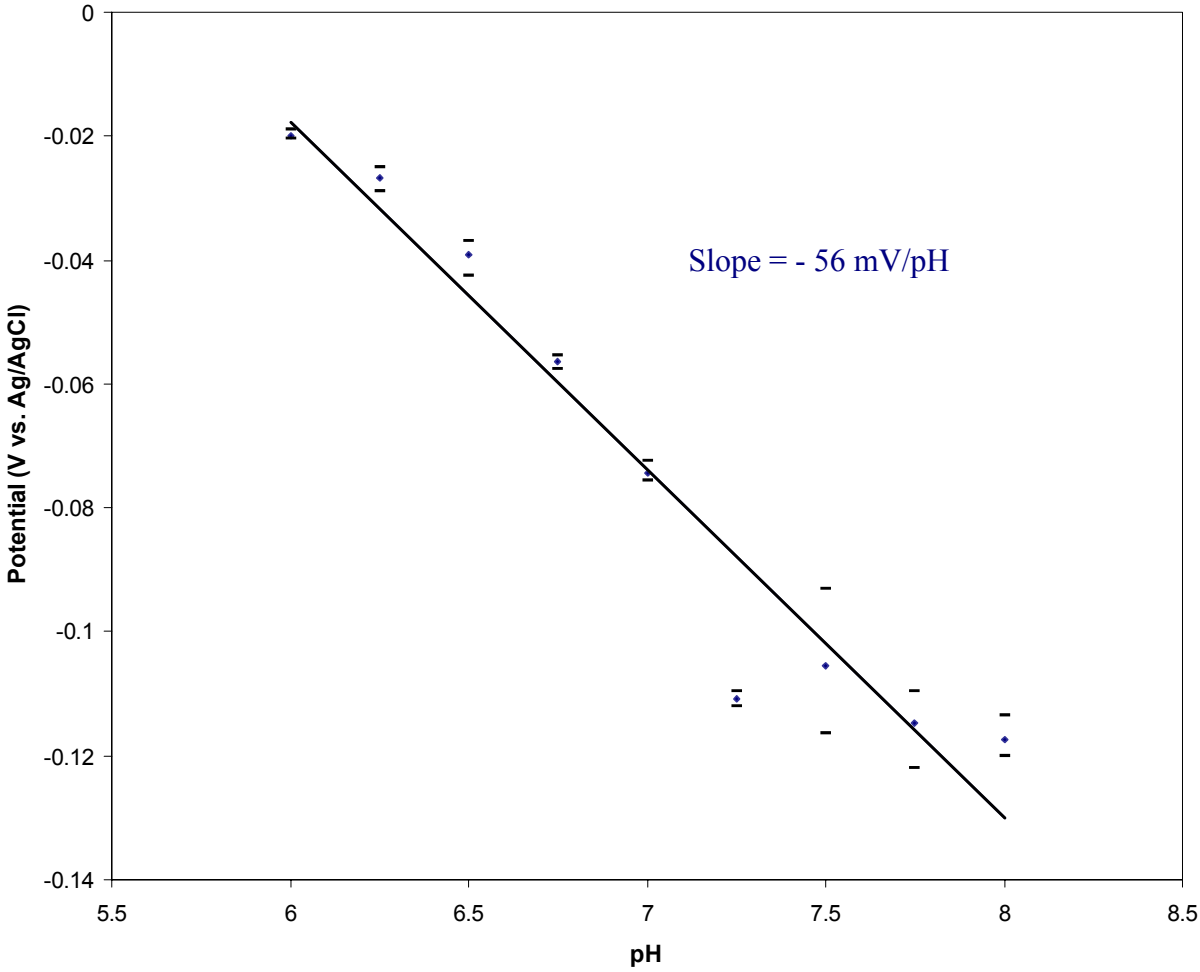


(56% yield)

Binding Studies

Binding constants for several phenyl alkynyl oligomers were estimated from fluorescence quenching studies as well as substrate inhibition studies. The oligomers have emission maxima of ~ 400 nm in aqueous solution. The topaquinone cofactor of AGAO (λ_{max} = 480 nm) can thus serve as a quencher of the fluorescence and provides an indication of binding of these molecules within the protein channel. In addition, substrate inhibition experiments were performed by measuring the rate of O_2 consumption by the enzyme in the presence of the oligomers using phenethylamine as the substrate. Further details regarding these experiments can be found in Reference 5.

Electrochemistry: pH vs. E^0 dependence



Plot showing the variation of the AGAO reduction potential with pH. All measurements were made in 10 mM KP_i using DEA-OPE-SH modified Au-bead electrodes. The scan rate was 100 mV/s, slope = –56 mV/pH. The average values from several measuremnts are shown by data points (♦). Minimum and maximum values observed for each pH value are indicated by the solid lines (—).

(1) Juda, G. A.; Bollinger, J. A.; Dooley, D. M. *Protein Expression and Purification* **2001**, *22*, 455-461.
(2) Sonogashira, K.; Yasuo, T.; Hagihara, N. *Tet. Lett.* **1975**, *50*, 4467-4470.
(3) Pearson, D. L.; Tour, J. M. *J. Org. Chem* **1997**, *62*, 1376-1387.
(4) Hsung, R. P.; Chidsey, C. E. D.; Sita, L. R. *Organometallics* **1995**, *14*, 4808-4815.
(5) Hess, C. R. In *Chemistry*; California Institute of Technology: Pasadena, 2002.
(6) Stoltz, B. M.; Kano, T.; Corey, E. J. *J. Am. Chem. Soc.* **2000**, *122*, 9044-9045.