Experimental Section

I. Materials and Instrumentation

All chemicals and solvents were obtained from Sigma-Aldrich and used as received unless otherwise noted. NMR data were collected on a Varian Inova 400 MHz (^{1}H) and 101 MHz (^{13}C) spectrometer with chemical shifts reported in ppm and J values in Hz. UV/Vis spectra were recorded on a Cary 50 UV/Vis spectrophotometer. High-resolution, fast-atom bombardment (HR-FABMS) mass spectra were recorded on a JOEL JMS-SX-102 instrument. Turbidity and hydrogen peroxide assays were conducted on a Perkin Elmer Victor 1420 plate reader.

II. Synthesis

Quinoline boronic acid, pinanediol ester (QBP). A 1-mmol portion of 8-quinolinylboronic acid was combined with 1 mmol (1*R*,2*R*,3*S*,5*R*)-(−)-pinanediol in 2 mL DMSO and 18 mL benzene. The clear colorless solution was refluxed in a Dean-Stark apparatus for 10 h. Solvent was removed by evaporation to yield a brown crystalline solid. Colorless prisms suitable for X-ray crystallography were obtained by slow evaporation from ether (65 %). ^{1}H NMR ($CDCl_3$): δ=9.04 (d, J=2.36 Hz, 1H), 8.15 (t, J=7.97, 7.97 Hz, 2H), 7.88 (d, J=8.00 Hz, 1H), 7.54 (t, J=7.44, 7.44 Hz, 1H), 7.38 (dd, J=8.04, 4.10 Hz, 1H), 4.69 (d, J=8.45 Hz, 1H), 2.47 (dd, J=14.18, 9.16 Hz, 1H), 2.31 (dd, J=9.91, 5.58 Hz, 1H), 2.24 (t, J=5.39, 5.39 Hz, 1H), 2.12 (d, J=14.81 Hz, 1H), 1.98 (m, 1H), 1.61 (s, 1H), 1.58 (s, 3H), 1.50 (d, J=10.82 Hz, 1H), 1.34 (s, 3H), 0.93 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 150.85, 137.20, 136.27, 130.59, 127.89, 125.88, 120.72, 85.79, 78.81, 51.50, 39.60, 38.24, 35.66, 28.73, 27.12, 26.55, 24.11. UV/Vis (PBS pH 7.4): $\lambda_{max}(\varepsilon)$ = 317 nm (7300 $M^{-1}cm^{-1}$); MS: *m/z* (%): 308 (100) [M^{+}]

III. Assays

Preparation of Aβ

The $A\beta_{1\text{-}42}$ peptide was purchased from Genscript and >95% pure. A portion (1 mg) of $A\beta_{1\text{-}42}$ was dissolved in 500 μL de-ionized water at pH 10 by sonicating 1 min on, 30 s off and 1 min on. The solution was filtered through a syringe filter (GE Water, Nylon, 0.22 μm, 3 mm). A second aliquot of 500 μL de-ionized water was used to rinse the filter of any residual peptide. The concentration of this stock solution was determined by the Pierce MicroBCA assay, and validated by measuring the tyrosinate absorption (295 nm, ε = 2480 $M^{-1}cm^{-1}$) at pH

12. The stock solution was portioned into aliquots and stored at -20 °C and used within 5 days of preparation.

Turbidity Assay

All solutions were prepared using Chelex-treated Hepes buffer (20 mM Hepes, 150 mM NaCl, pH 7.4). Solutions of chelator, prochelator, and metals were prepared fresh daily. Reagents were added to individual wells of a 96-well plate in the following order, with their final concentrations given in parentheses: Hepes buffer to give a final total volume of 200 μL, $Cu(Gly)_2$ (prepared from $CuCl_2$ with 2 equiv glycine) or $ZnCl_2$ (10 μM), 8HQ (10 – 20 μM), QBP (20 – 100 μM), ascorbic acid (10 μM) and lastly $A\beta_{1\text{-}42}$ (10 μM). Samples were incubated at 37 °C for 1 h with the plate lid on to minimize evaporation. After incubation, the turbidity was measured by light scattering at 405 nm on a plate reader set to collect one reading every min for 4 min with 30 s of shaking in between each reading. Added chelator or hydrogen peroxide was allowed to incubate for an additional h before a final set of measurements was made. Solution turbidity was determined by subtracting the Aβ-negative matched control from each well and averaging these values over each 4-min period.[1,2] Error bars represent the standard deviation from a minimum of 3 independent samples.

BCA Assay for Soluble Protein

Samples containing 200 μL (final volume) of 10 μM Aβ were incubated with 10 μM $Cu(Gly)_2$ or $ZnCl_2$ in the presence or absence of 20 μM 8HQ at 37 °C. After 1 h, the samples were centrifuged for 20 min at 5500 rpm and 150 μL aliquots of the supernatant solutions were removed for analysis by the Pierce MicroBCA assay by following the kit protocol.

Hydrogen Peroxide Assay

Hydrogen peroxide quantitation was done by following the general assay directions for the Amplex Red Hydrogen Peroxide/Peroxidase Assay Kit available from Invitrogen. Reagents were added to individual wells of a 96-well plate in the following order, with final concentrations given in parentheses and a final volume of 50 μL: sodium phosphate buffer (50 mM), 8HQ (50 – 200 nM), QBP (50 – 400 μM), H_2O_2 (300 nM – 5 μM), $A\beta_{1\text{-}42}$ (200 nM), ascorbic

[1] X. Huang, C. S. Atwood, R. D. Moir, M. A. Hartshorn, J-P. Vonsattel, R. E. Tanzi, A. I. Bush, *J. Biol. Chem.* **1997**, *272*, 26464-26470.

[2] T. Storr, L. E. Scott, M. L. Bowen, D. E. Green, K. H. Thompson, H. J. Schugar, C. Orvig, *Dalton Trans.* **2009**, 3034-3043.

acid (4 μM or 10 μM) and either $CuGly_2$ or $ZnCl_2$ (50 - 200 nM). In some experiments, Amplex Red (50 μM; 0.1U/mL HRP) was added immediately before incubation, while in others the 96-well plate was incubated at RT or 37 °C for 1 h before the addition of 50 μL of Amplex Red/HRP. The amount of H_2O_2 produced was quantified by comparison to a standard curve, the slope of which was recalculated at each measured time point. Separate H_2O_2 standards were used for plates in which Amplex Red was added at both time points in order to better quantify the degradation of H_2O_2.[3,4,5,6] Error bars represent standard deviation from runs done in at least triplicate.

IV. Kinetics of prochelator oxidation

The rate of oxidation of QBP to 8HQ was determined under pseudo first-order conditions with excess H_2O_2. QBP was initially dissolved in a minimal amount of methanol and then diluted into PBS buffer, pH 7.4 to a final concentration of 100 μM. Spectra were taken immediately after addition of 1-10 mM H_2O_2; at least 40 spectra were collected before 50% conversion of prochelator to chelator (Figure S1). The change in absorbance at 310 nm was used to follow the reaction. The negative slope of the linear fit of $\ln[(A-A_f)/(A_0-A_f)]$ vs time gives the rate constant k_{obs} (where A_0 and A_f are the absorbance of the intact prochelator and the final chelator product, respectively). The slope of the line through data k_{obs} vs $[H_2O_2]$ provides k ($M^{-1}s^{-1}$) (Figure S2), and was determined to be 0.25 $M^{-1}s^{-1}$ in accordance with Equation 1.

$$\text{Rate} = k[\text{QBP}][H_2O_2] \qquad \mathbf{1}$$

V. X-ray Data Collection and Structure Solution Refinement. Colorless prisms of QBP were grown by slow evaporation of ether and mounted on a cryoloop. Data were collected at 296 K on a Bruker Kappa Apex II CCD diffractometer equipped with a graphite monochromator and a $Mo_{K\alpha}$ fine-focus sealed tube (λ = 0.71073Å) operated at 1.75 kW power (50 kV, 35 mA). The detector was placed at a distance of 5.010 cm from the crystal. A total of 2655 frames were collected with a scan width of 0.5º and an exposure time of 30.0 sec/frame. The frames were integrated with the Bruker SAINT v7.12A software package using a narrow-frame integration algorithm. Empirical absorption corrections were applied using SADABS

[3] C. Deraeve, M. Pitie, B. Meunier, *J. Inorg. Biochem.* **2006**, *100*, 2117-2126.
[4] C. Opazo, X. Huang, R. A. Cherny, R. D. Moir, A. E. Roher, A. R. White, R. Cappai, C. L. Masters, R. E. Tanzi, N. C. Inestrosa, A. I. Bush, *J. Biol. Chem.* **2002**, *277*, 40302-40308.
[5] C. Deraeve, M. Petie, H. Mazarguil, B. Meunier, *New. J. Chem.* **2007**, *31*, 193-195.
[6] C. Deraeve, C. Boldron, A. Maraval, H. Mazarguil, H. Gornitzka, L. Vendier, M. Petie, B. Meunier, **2008**, I14, *682-696.*

v2.10 and the structure was checked for higher symmetry with PLATON v1.07. The structure was solved by direct methods with refinement by full-matrix least-squares based on F2 using the Bruker SHELXTL Software Package. All non-hydrogen atoms were refined anisotropically. All hydrogen atom positions were calculated. Table S1 contains a summary of crystal data, intensity collection and structure refinement parameters. Figure S3 and Table S2 show the fully labeled structure with select bond distances and angles. CCDC 743258 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

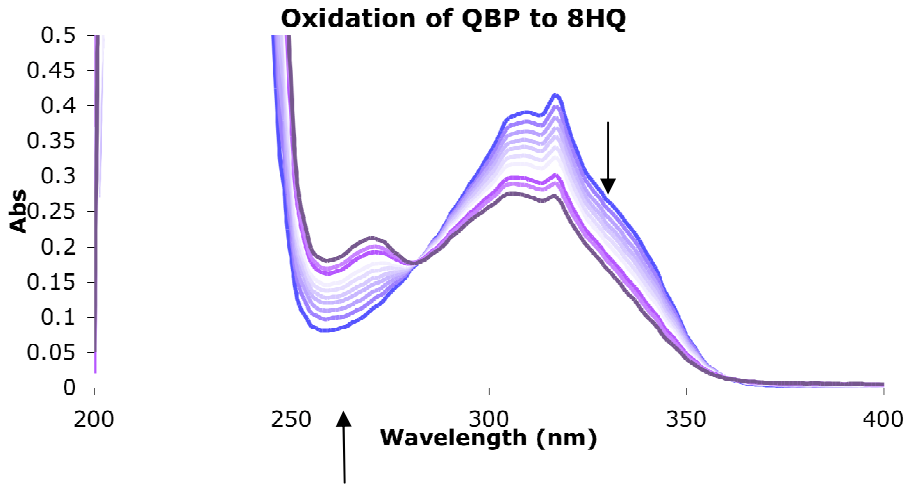

Figure S1. Oxidation of QBP to 8HQ by the addition of 4 mM H_2O_2 to 100 µM QBP in PBS buffer. These spectra represent the first 45 min of oxidation. Arrows indicate the direction of spectral change.

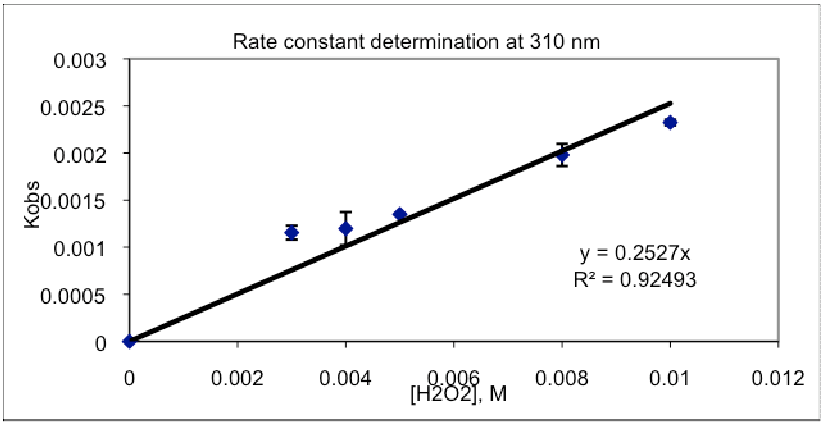

Figure S2. Plot of k_{obs} against H_2O_2 concentration to determine the rate constant for oxidation from QBP to 8HQ.

Table S1. Crystal data and structure refinement for **QBP**.

Identification code	md114	
Empirical formula	$C_{19}H_{22}BNO_2$	
Formula weight	307.19	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	*P*2(1)	
Unit cell dimensions	*a* = 7.604(2) Å	α = 90°.
	b = 7.693(2) Å	β = 101.258(6)°.
	c = 14.673(4) Å	γ = 90°.
Volume	841.8(4) $Å^3$	
Z	2	
Density (calculated)	1.212 Mg/m^3	
Absorption coefficient	0.077 mm^{-1}	
F(000)	328	
Crystal size	0.31 x 0.12 x 0.08 mm^3	
Crystal color and habit	colourless prism	
Diffractometer	Bruker SMART Apex II	
Theta range for data collection	3.31 to 23.91°.	
Index ranges	-8<=*h*<=8, -8<=*k*<=6, -16<=*l*<=16	
Reflections collected	8315	
Independent reflections	2210 [R(int) = 0.0622]	
Observed reflections (I > 2sigma(I))	1805	
Completeness to theta = 23.91°	94.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9939 and 0.9766	
Solution method	SHELXS-97 (Sheldrick, 2008)	
Refinement method	SHELXL-97 (Sheldrick, 2008)	
Data / restraints / parameters	2210 / 1 / 208	
Goodness-of-fit on F^2	0.907	
Final *R* indices [I>2σ(I)]	*R*1 = 0.0404, *wR*2 = 0.1304	
R indices (all data)	*R*1 = 0.0600, *wR*2 = 0.1604	
Absolute structure parameter	-1(2)	
Largest diff. peak and hole	0.221 and -0.182 e.$Å^{-3}$	

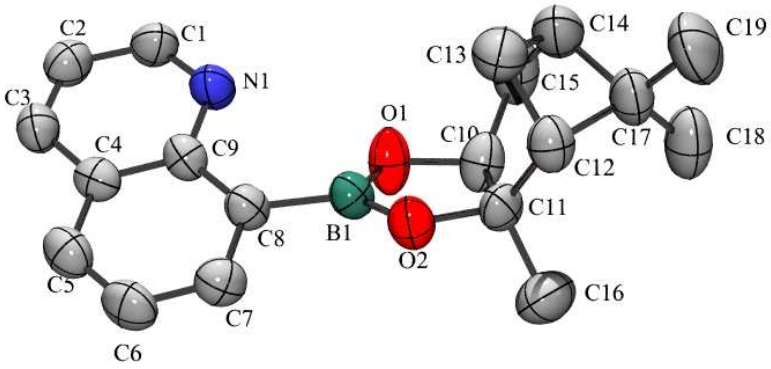

Figure S3. Xray crystal structure of **QBP**. Thermal ellipsoids are shown at 50% probability and hydrogen atoms are omitted for clarity.

Table S2. Bond lengths [Å] and angles [°] for **QBP**.

B(1)-O(2)	1.355(5)	C(9)-H(9A)	0.9300
B(1)-O(1)	1.357(4)	C(10)-C(11)	1.500(6)
B(1)-C(2)	1.541(6)	C(10)-C(12)	1.524(4)
N(1)-C(9)	1.310(5)	C(10)-C(16)	1.549(4)
N(1)-C(1)	1.373(4)	C(11)-H(11A)	0.9600
O(1)-C(10)	1.453(5)	C(11)-H(11B)	0.9600
O(2)-C(16)	1.428(5)	C(11)-H(11C)	0.9600
C(1)-C(6)	1.412(5)	C(12)-C(13)	1.521(7)
C(1)-C(2)	1.418(5)	C(12)-C(17)	1.546(5)
C(2)-C(3)	1.374(4)	C(12)-H(12A)	0.9800
C(3)-C(4)	1.398(5)	C(13)-C(14)	1.515(7)
C(3)-H(3A)	0.9300	C(13)-H(13A)	0.9700
C(4)-C(5)	1.346(6)	C(13)-H(13B)	0.9700
C(4)-H(4A)	0.9300	C(14)-C(15)	1.509(7)
C(5)-C(6)	1.414(4)	C(14)-C(17)	1.542(6)
C(5)-H(5A)	0.9300	C(14)-H(14A)	0.9800
C(6)-C(7)	1.406(5)	C(15)-C(16)	1.533(6)
C(7)-C(8)	1.341(5)	C(15)-H(15A)	0.9700
C(7)-H(7A)	0.9300	C(15)-H(15B)	0.9700
C(8)-C(9)	1.387(6)	C(16)-H(16A)	0.9800
C(8)-H(8A)	0.9300	C(17)-C(18)	1.506(8)

C(17)-C(19)	1.543(6)	C(19)-H(19A)	0.9600
C(18)-H(18A)	0.9600	C(19)-H(19B)	0.9600
C(18)-H(18B)	0.9600	C(19)-H(19C)	0.9600
C(18)-H(18C)	0.9600		

O(2)-B(1)-O(1)	112.3(4)	O(1)-C(10)-C(11)	106.5(3)
O(2)-B(1)-C(2)	126.3(3)	O(1)-C(10)-C(12)	107.1(3)
O(1)-B(1)-C(2)	121.3(3)	C(11)-C(10)-C(12)	113.8(3)
C(9)-N(1)-C(1)	117.7(3)	O(1)-C(10)-C(16)	102.7(3)
B(1)-O(1)-C(10)	110.0(3)	C(11)-C(10)-C(16)	115.3(4)
B(1)-O(2)-C(16)	109.3(2)	C(12)-C(10)-C(16)	110.3(3)
N(1)-C(1)-C(6)	120.6(3)	C(10)-C(11)-H(11A)	109.5
N(1)-C(1)-C(2)	118.9(3)	C(10)-C(11)-H(11B)	109.5
C(6)-C(1)-C(2)	120.5(2)	H(11A)-C(11)-H(11B)	109.5
C(3)-C(2)-C(1)	117.3(3)	C(10)-C(11)-H(11C)	109.5
C(3)-C(2)-B(1)	118.5(3)	H(11A)-C(11)-H(11C)	109.5
C(1)-C(2)-B(1)	124.1(2)	H(11B)-C(11)-H(11C)	109.5
C(2)-C(3)-C(4)	122.8(3)	C(13)-C(12)-C(10)	108.6(3)
C(2)-C(3)-H(3A)	118.6	C(13)-C(12)-C(17)	88.4(3)
C(4)-C(3)-H(3A)	118.6	C(10)-C(12)-C(17)	113.7(3)
C(5)-C(4)-C(3)	119.9(3)	C(13)-C(12)-H(12A)	114.5
C(5)-C(4)-H(4A)	120.1	C(10)-C(12)-H(12A)	114.5
C(3)-C(4)-H(4A)	120.1	C(17)-C(12)-H(12A)	114.5
C(4)-C(5)-C(6)	120.7(3)	C(14)-C(13)-C(12)	86.2(4)
C(4)-C(5)-H(5A)	119.6	C(14)-C(13)-H(13A)	114.3
C(6)-C(5)-H(5A)	119.6	C(12)-C(13)-H(13A)	114.3
C(7)-C(6)-C(1)	118.4(3)	C(14)-C(13)-H(13B)	114.3
C(7)-C(6)-C(5)	122.8(3)	C(12)-C(13)-H(13B)	114.3
C(1)-C(6)-C(5)	118.8(3)	H(13A)-C(13)-H(13B)	111.4
C(8)-C(7)-C(6)	119.8(3)	C(15)-C(14)-C(13)	108.9(3)
C(8)-C(7)-H(7A)	120.1	C(15)-C(14)-C(17)	110.1(4)
C(6)-C(7)-H(7A)	120.1	C(13)-C(14)-C(17)	88.7(3)
C(7)-C(8)-C(9)	118.4(3)	C(15)-C(14)-H(14A)	115.4
C(7)-C(8)-H(8A)	120.8	C(13)-C(14)-H(14A)	115.4
C(9)-C(8)-H(8A)	120.8	C(17)-C(14)-H(14A)	115.4
N(1)-C(9)-C(8)	125.1(3)	C(14)-C(15)-C(16)	113.2(3)
N(1)-C(9)-H(9A)	117.5	C(14)-C(15)-H(15A)	108.9
C(8)-C(9)-H(9A)	117.5	C(16)-C(15)-H(15A)	108.9

C(14)-C(15)-H(15B)	108.9	C(19)-C(17)-C(12)	109.8(4)
C(16)-C(15)-H(15B)	108.9	C(17)-C(18)-H(18A)	109.5
H(15A)-C(15)-H(15B)	107.7	C(17)-C(18)-H(18B)	109.5
O(2)-C(16)-C(15)	110.7(4)	H(18A)-C(18)-H(18B)	109.5
O(2)-C(16)-C(10)	105.4(3)	C(17)-C(18)-H(18C)	109.5
C(15)-C(16)-C(10)	115.8(3)	H(18A)-C(18)-H(18C)	109.5
O(2)-C(16)-H(16A)	108.2	H(18B)-C(18)-H(18C)	109.5
C(15)-C(16)-H(16A)	108.2	C(17)-C(19)-H(19A)	109.5
C(10)-C(16)-H(16A)	108.2	C(17)-C(19)-H(19B)	109.5
C(18)-C(17)-C(14)	119.4(4)	H(19A)-C(19)-H(19B)	109.5
C(18)-C(17)-C(19)	108.4(4)	C(17)-C(19)-H(19C)	109.5
C(14)-C(17)-C(19)	110.8(4)	H(19A)-C(19)-H(19C)	109.5
C(18)-C(17)-C(12)	122.1(4)	H(19B)-C(19)-H(19C)	109.5
C(14)-C(17)-C(12)	84.4(3)		

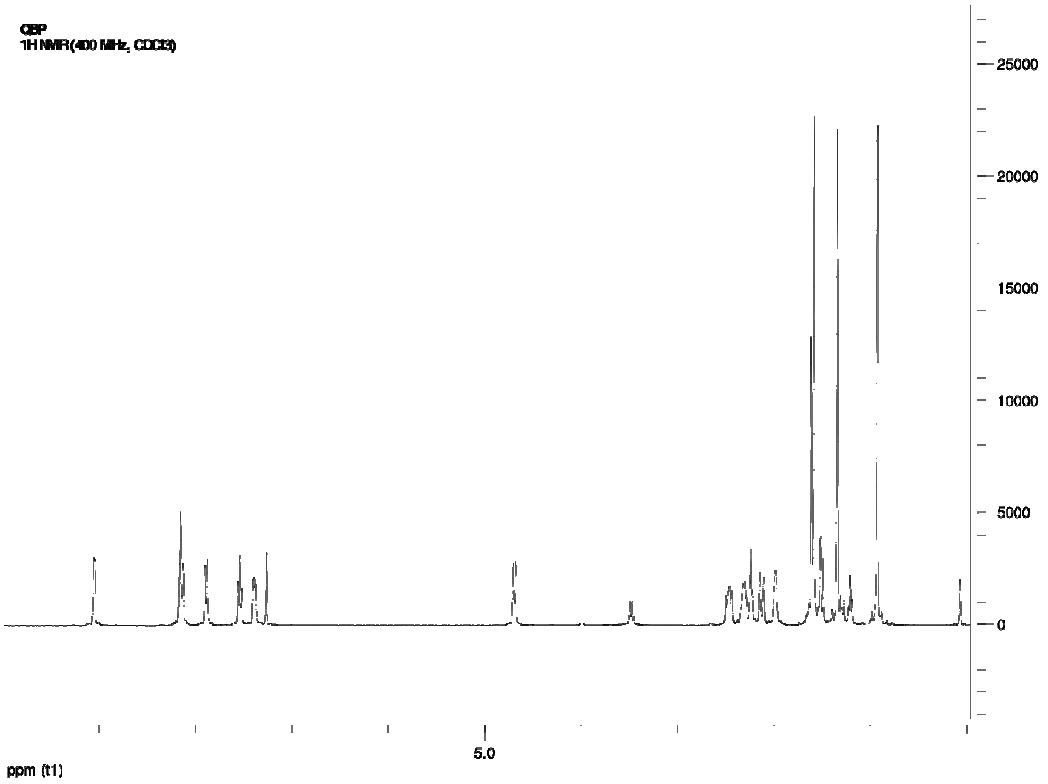

Figure S4. ^{1}H NMR spectrum of QBP in $CDCl_3$. The peaks at δ 3.58 and 1.21 are due to residual ether from crystallization.

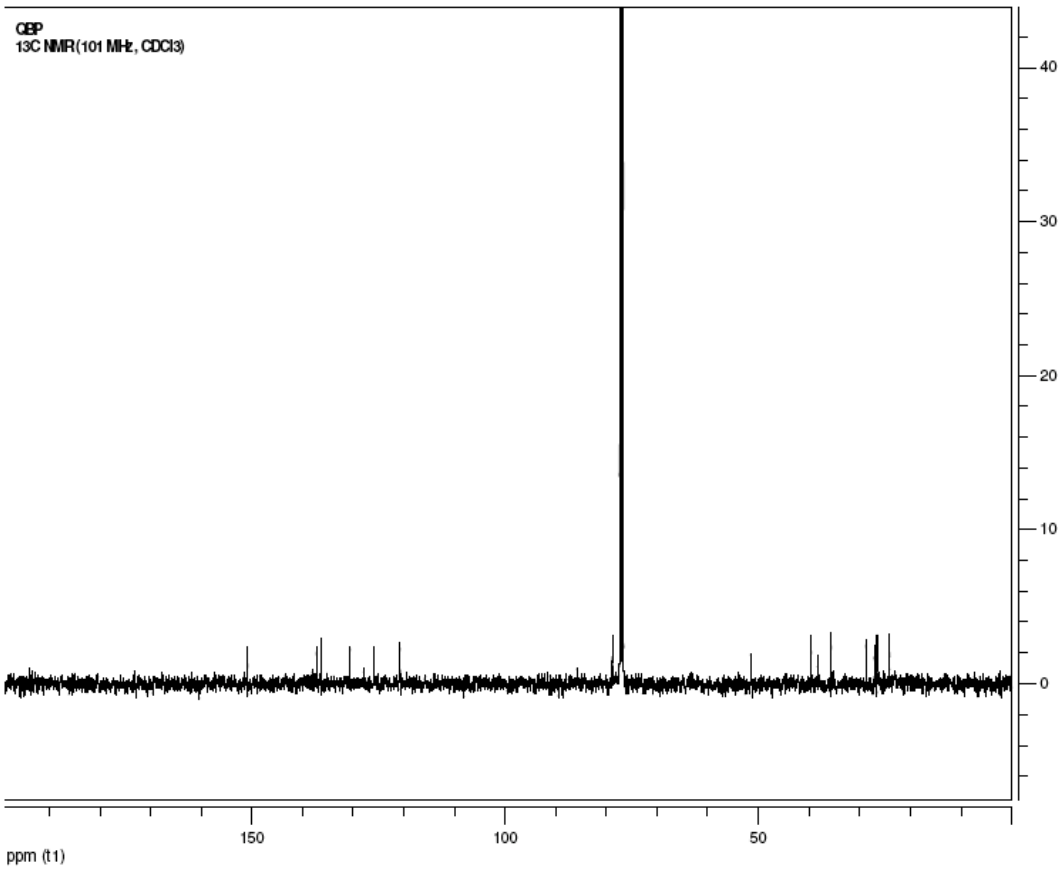

Figure S5. ^{13}C NMR spectrum of **QBP** in $CDCl_3$.

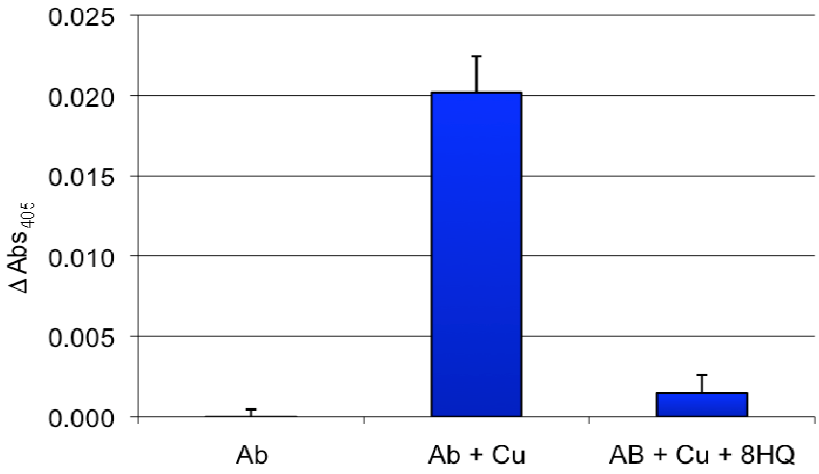

Figure S6. 10 μM Aβ and 10 μM $Cu(Gly)_2$ were incubated for 1 h at 37 °C. The turbidity of the solution was measured by the difference in absorbance at 405 nm. 20 μM 8HQ was added. The decrease in turbidity was nearly instantaneous, but was allowed to incubate for an additional hour with no significant change.