*Supporting Information*

# Copper(I) Forms a Redox Stable 1:2 Complex with α-Synuclein N-Terminal Peptide in a Membrane-Like Environment

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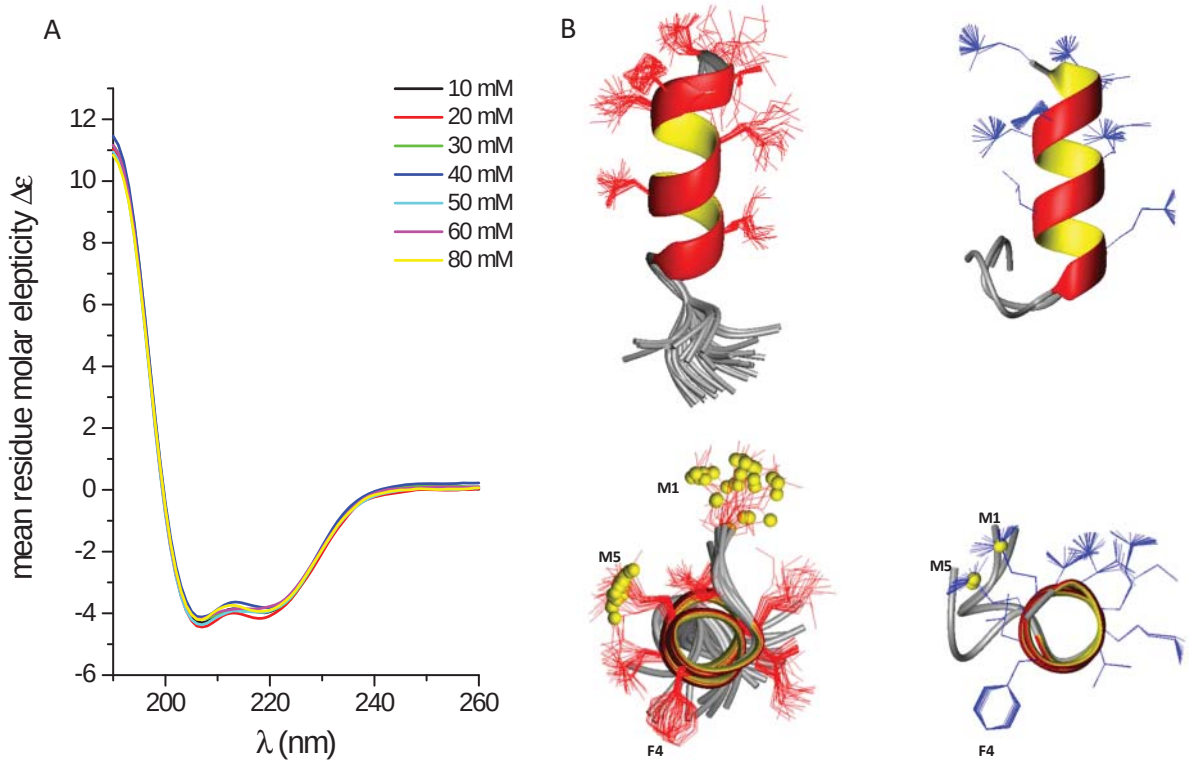



**Figure 1S**. **(A)** Far UV CD spectra of $\alpha S_{1\text{-}15}$ fragment recorded in phosphate buffer 2.0 mM in the presence of gradually increased SDS concentration (10-80 mM); the CD spectrum of Ac-$\alpha S_{1\text{-}15}$ in SDS is superimposable with that of $\alpha S_{1\text{-}15}$ and is shown in Figure 8S below. **(B)** Superimposition of the best 30 NMR structures obtained for the apo $\alpha S_{1\text{-}15}$ (left) and Ac-$\alpha S_{1\text{-}15}$ (right) fragments in the presence of 40 mM SDS. The structures are fitted on the 1-12 backbone residues and have RMSD values ($\alpha S_{1\text{-}15}$) 0.31 ± 0.15 Å and 1.12 ± 0.24 Å and (Ac-$\alpha S_{1\text{-}15}$) 0.06 ± 0.08 Å and 0.71 ± 0.26 Å for backbone and heavy atoms, respectively. The figure was created with MOLMOL 2.K.1.

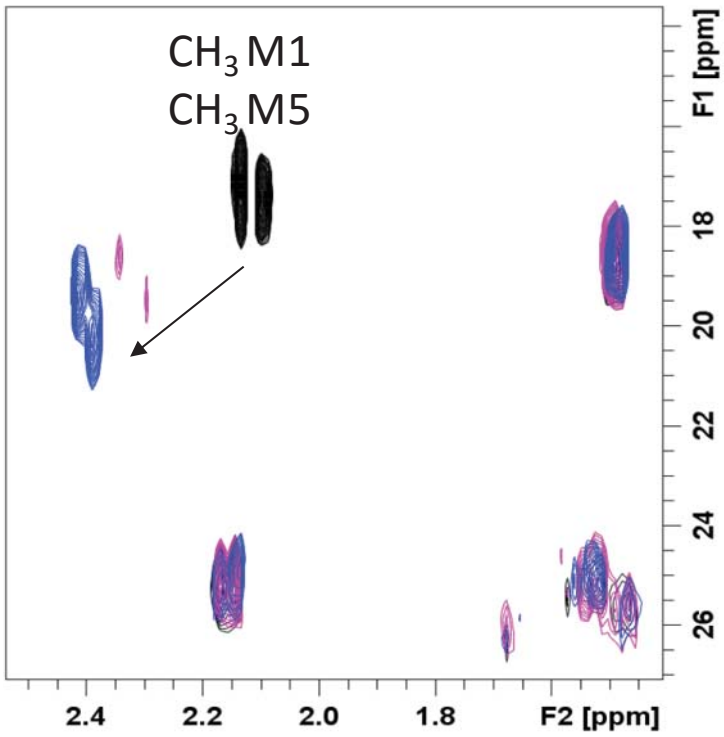



**Figure 2S.** Overlay of $^{1}H$-$^{13}C$ HSQC spectra of Ac-$\alpha S_{1\text{-}15}$ in the absence (black) and in the presence of 0.4 (magenta) or 0.6 $Ag^{I}$ (blue) equiv.

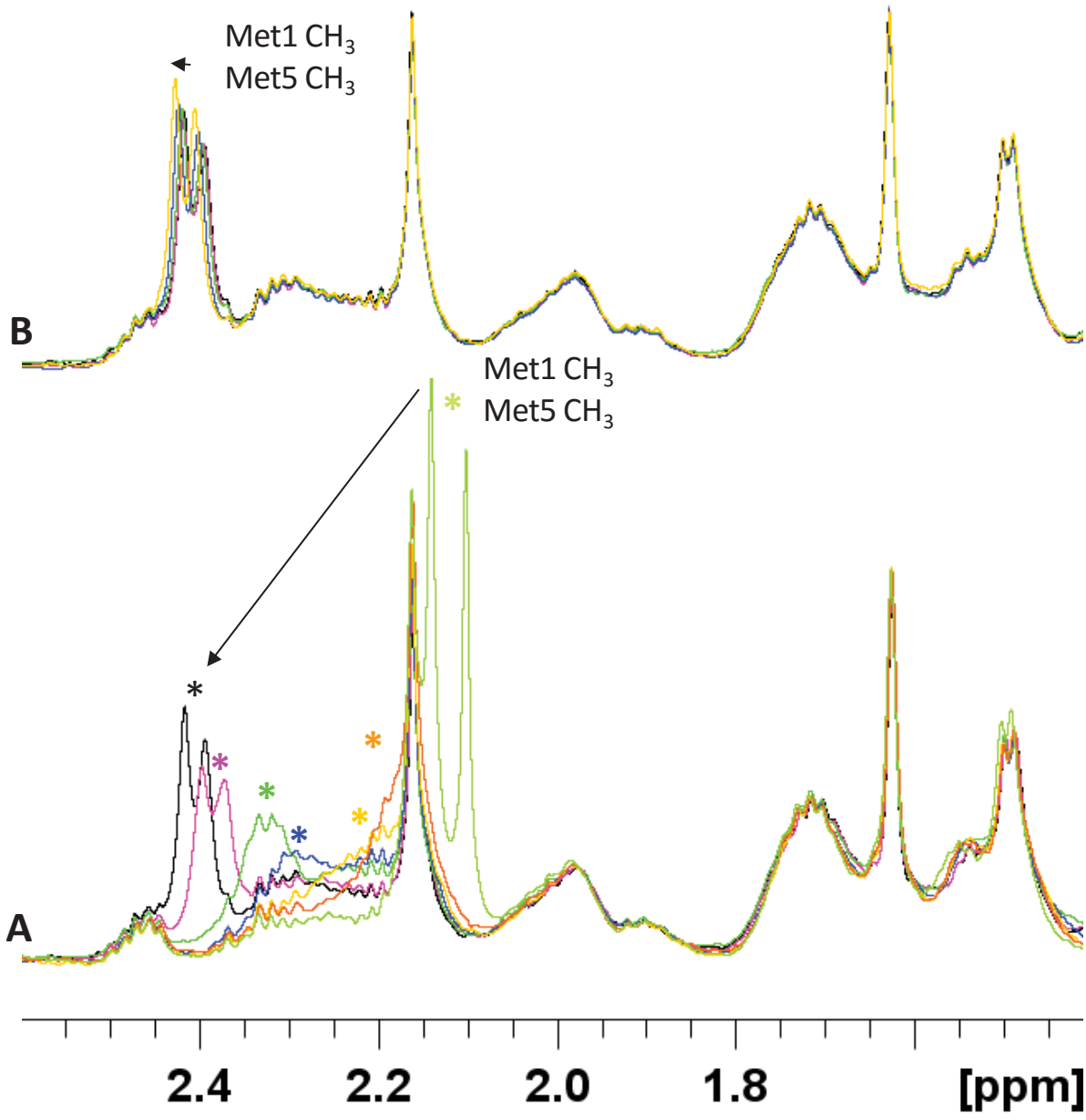



**Figure 3S.** Overlay of selected regions of $^{1}$H NMR spectra of Ac-α$S_{1-15}$ with increasing amount of $Ag^{I}$: (A) from 0.0 (yellow trace) to 0.6 (black trace) $Ag^{I}$ equiv; (B) from 0.6 to 1.1 $Ag^{I}$ equiv. The arrow show the chemical shifts of methyl groups signals (labeled with *) of Met1 and Met5.

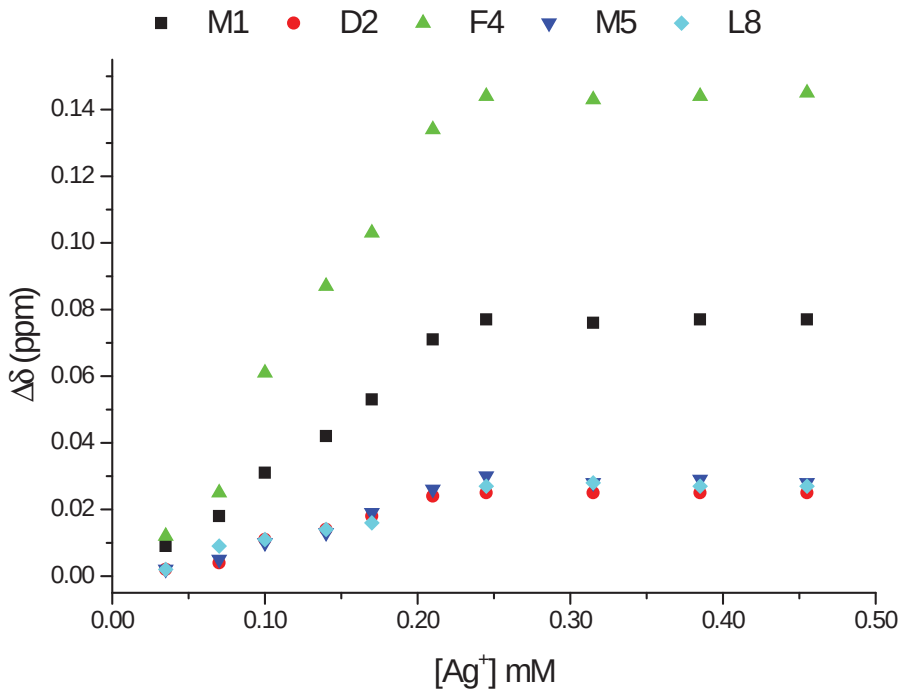



**Figure 4S**. Binding curves of Ag(I)-Ac-α$S_{1-15}$ complex as monitored by changes in the amide protons chemical shifts (Δδ) of Met1 (black squares), Asp2 (red circles), Phe4 (green triangles), Met5 (blue triangles) and Leu8 (cyan rhombs).

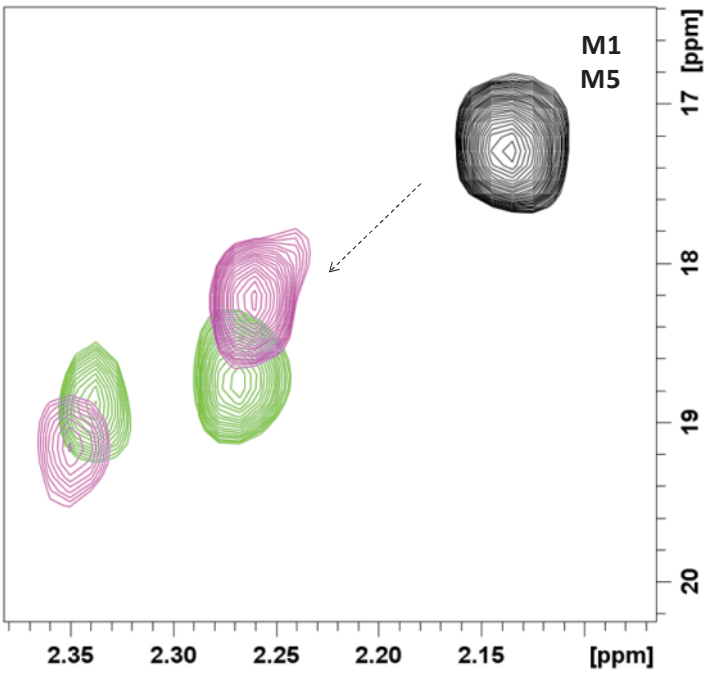



**Figure 5S**. Overlay of $^{1}H$-$^{13}C$ HSQC spectra of α$S_{1-15}$ in the absence (black) and in the presence of 0.9 $Cu^{I}$ (magenta) or 0.9 $Ag^{I}$ (green) equiv.

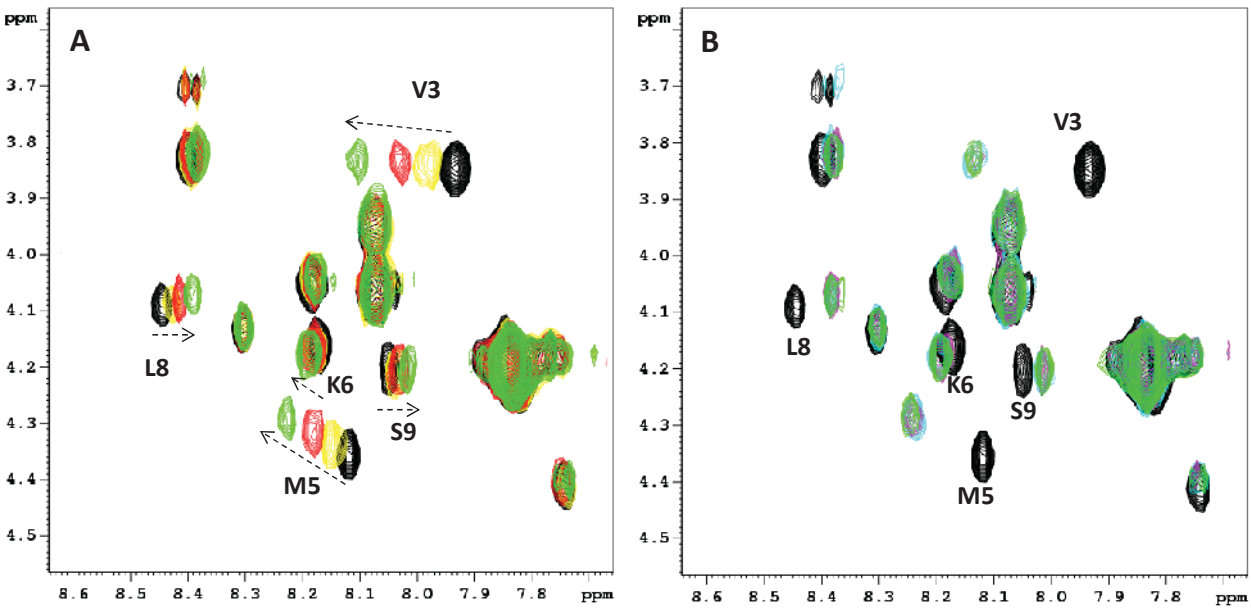



**Figure 6S**. (A) Overlaid $^{1}$H-$^{1}$H TOCSY spectra of $\alpha S_{1-15}$ with variable amounts of $Ag^{I}$: 0 equiv. (black), 0.15 equiv. (yellow), 0.25 equiv. (red), 0.5 equiv. (green). (B) Overlaid $^{1}$H-$^{1}$H TOCSY spectra of $\alpha S_{1-15}$ with variable amounts of $Ag^{I}$: 0 equiv. (black), 0.5 equiv. (green), 0.75 equiv. (cyan), 1.0 equiv. (magenta). The amide protons of Met1 and Asp2 were not detectable for both peptides because of solvent exchange effects.

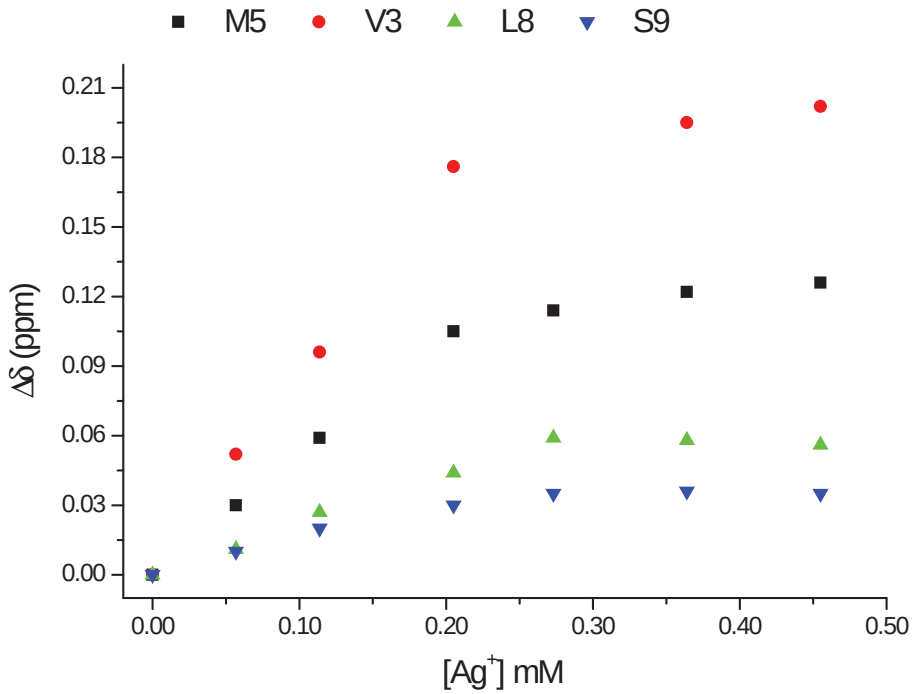



**Figure 7S**. Binding curves of Ag(I)-$\alpha S_{1-15}$ complex as monitored by changes in the amide protons chemical shifts (Δδ) of Met5 (black squares), Val3 (red circles) Leu8 (green triangles) and Ser9 (blue triangles).

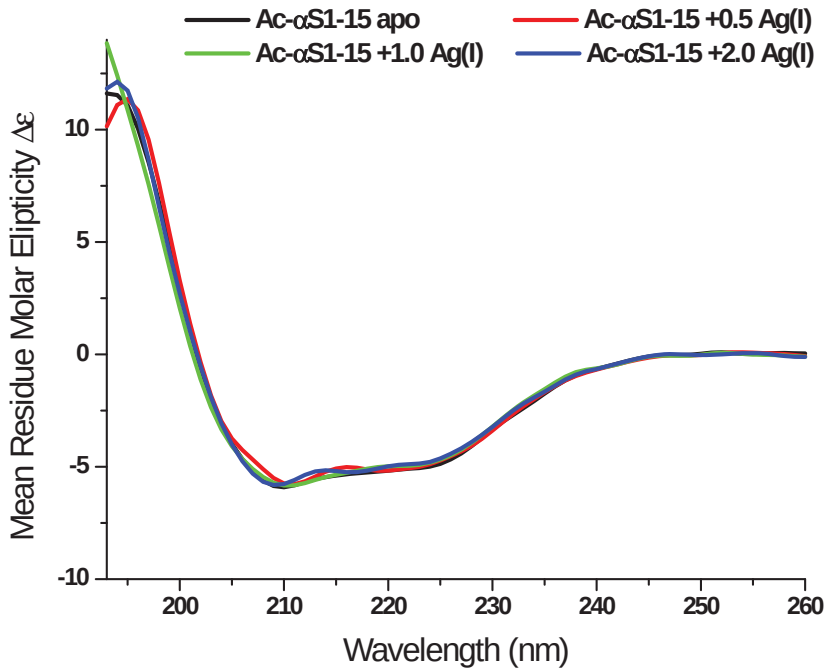



**Figure 8S.** CD spectral titration in the far-UV range of Ac-$\alpha S_{1-15}$ with $Ag^{I}$ ions, in phosphate buffer 2.0 mM, in the presence of 40 mM SDS.

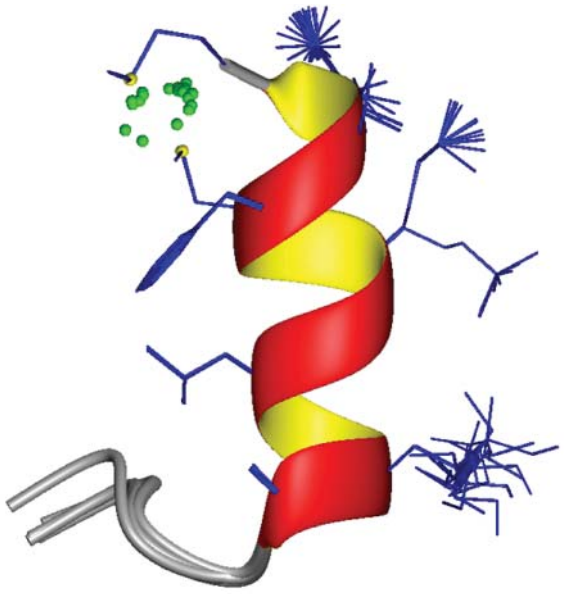


**Figure 9S.** Superimposition of the best 30 NMR structures of Ac-$\alpha S_{1-15}$ bound to $Ag^{I}$, in the presence of 40 mM SDS. The structures are fitted on the 1-12 backbone residues and have RMSD values 0.20 ± 0.19 Å and 1.10 ± 0.29 Å for backbone and heavy atoms respectively. $Ag^{I}$ and Met thioether groups are shown as green and yellow spheres, respectively Figure was created with MOLMOL 2.K.1.

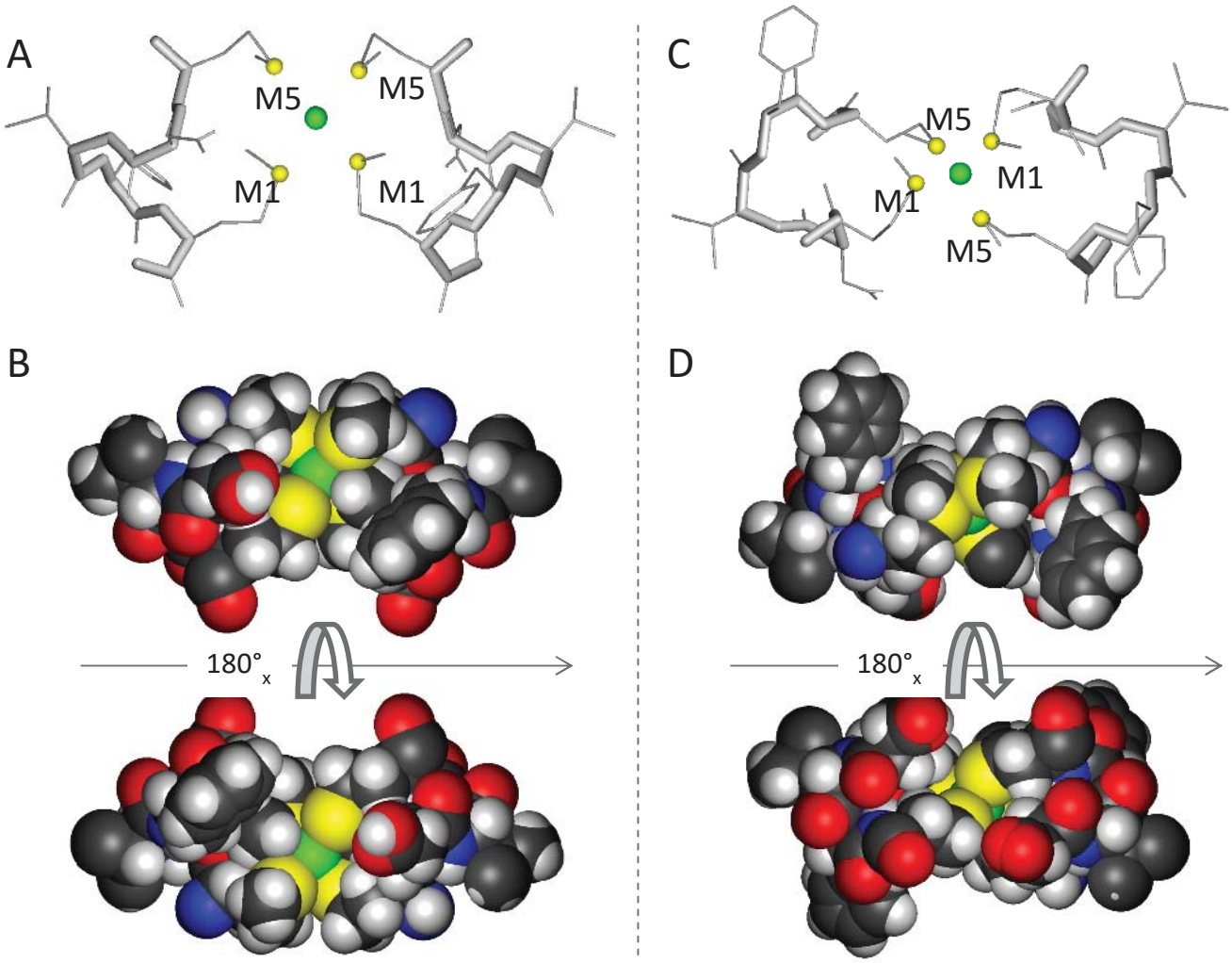



**Figure 10S.** Expanded view of the proposed Cu(I) site in the parallel (A, C) or antiparallel (B, D) dimeric Ac-$\alpha S_{1\text{-}15}$ structures.

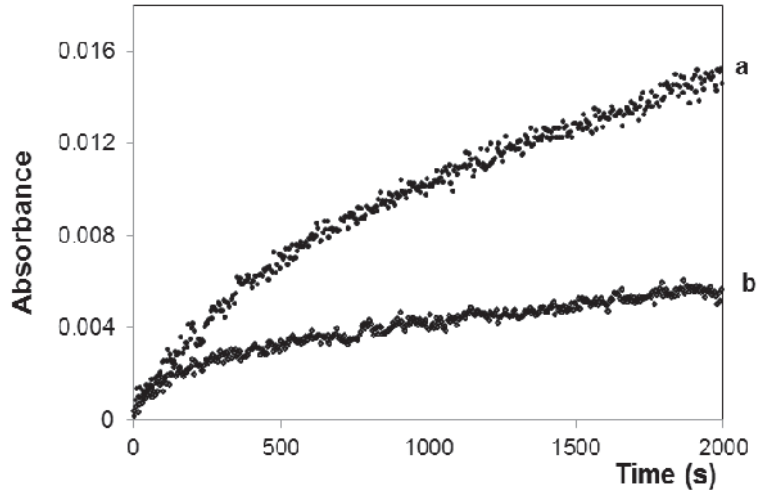



**Figure 11S.** Kinetic profiles at 475 nm of (a) autoxidation of DA (3 mM) in 50 mM Hepes buffer at pH 7.4, and (b) with the addition of SDS (20 mM) in the reaction medium.

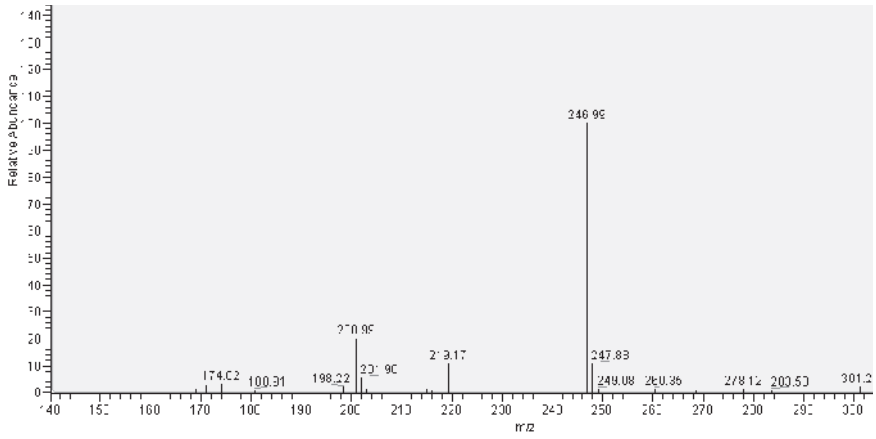
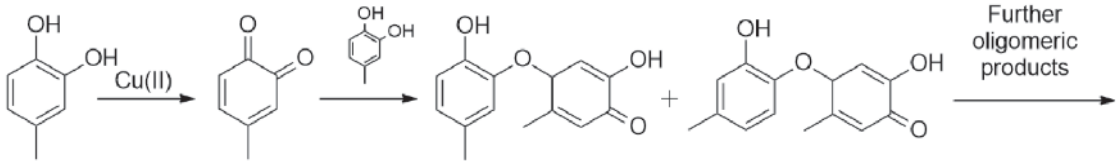



**Figure 12S.** ESI-MS (200°C, 5V, MeOH) of the addition product, resulting from MC oxidation.




**Scheme 1S** – Proposed reaction mechanism for copper(II) promoted oxidation of MC.

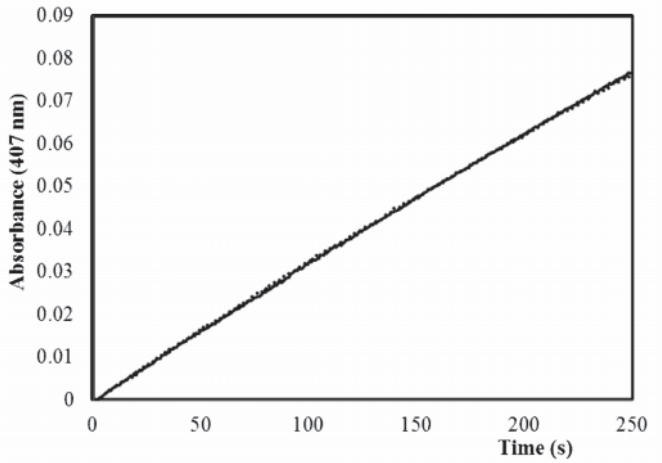



**Figure 13S**. Kinetic profiles at 407 nm for the oxidation of DTBC (3 mM) in methanol/50 mM Hepes buffer at pH 7.4 (80:20 v/v) and 25 °C in the presence of copper(II) (25 μM) and SDS (20 mM) (dotted line), and with the addition of 2 equiv. of Ac-αSyn15 (black line).