Electronic Supplementary Material (ESI) for Metallomics

Supporting Information

for

Dual-function Triazole-pyridine Derivatives as Inhibitors of Metal-induced Amyloid-β Aggregation

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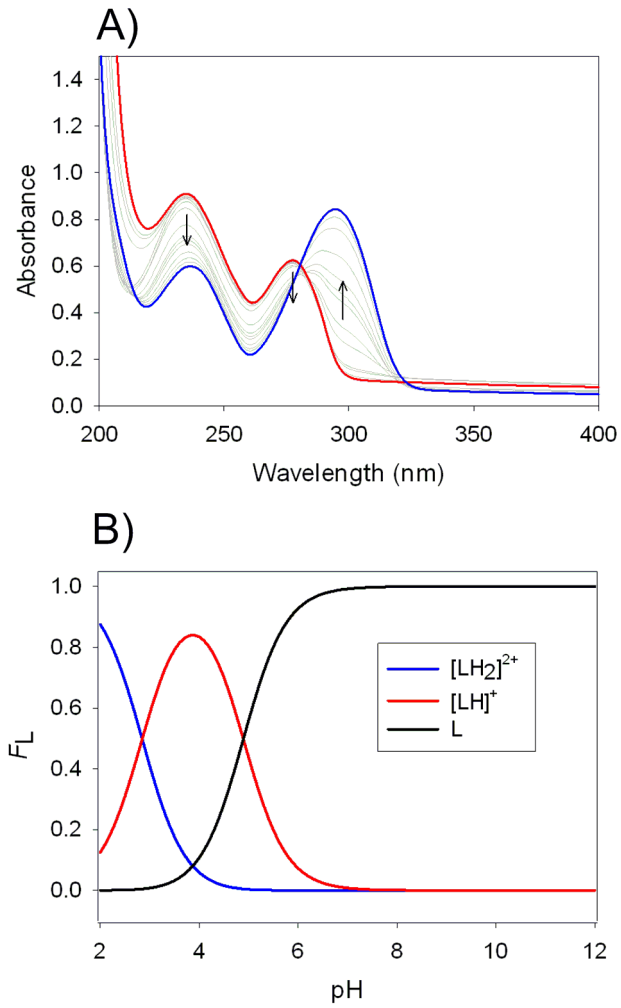


Figure S1: Variable pH UV-Vis spectra of **L1** (A) and calculated speciation diagram from pH 2 – 12 (B).

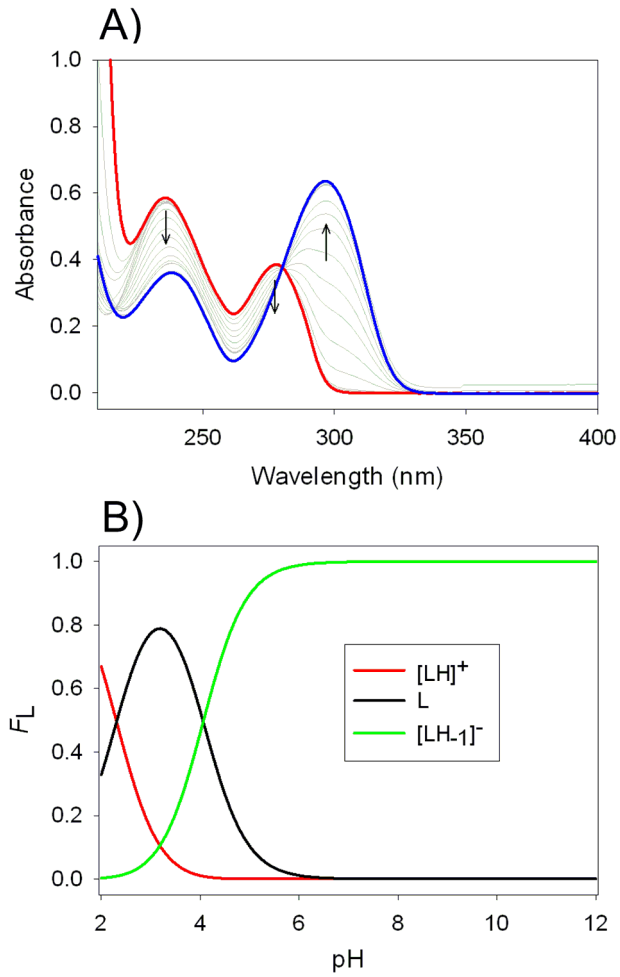


Figure S2: Variable pH UV-Vis spectra of **L3** (A) and calculated speciation diagram from pH 2 – 12 (B).

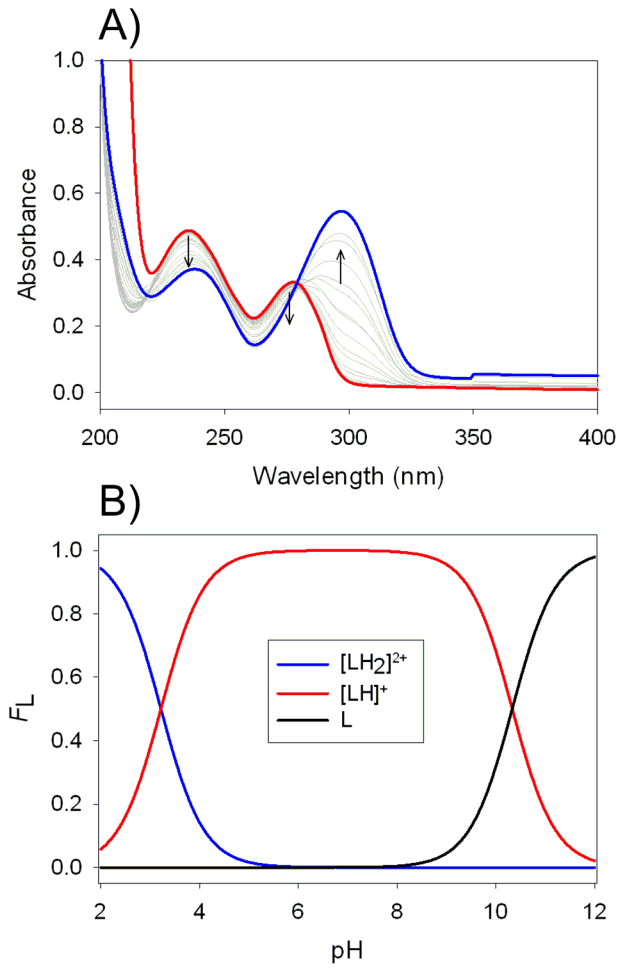


Figure S3: Variable pH UV-Vis spectra of **L4** (A) and calculated speciation diagram from pH 2 – 12 (B).

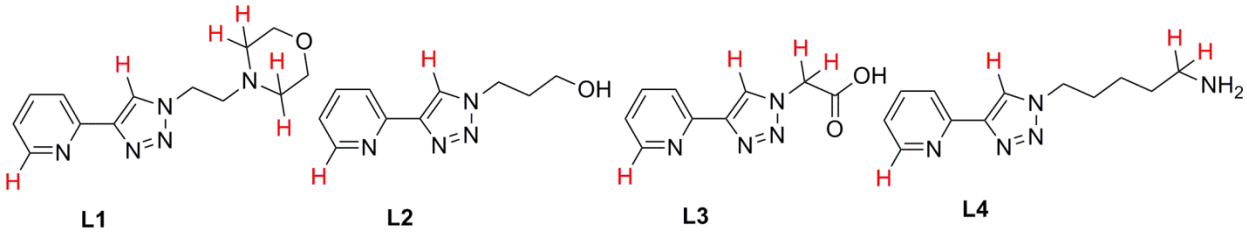


Figure S4: Hydrogen atoms (red) monitored during variable pH NMR experiments to determine solution speciation.

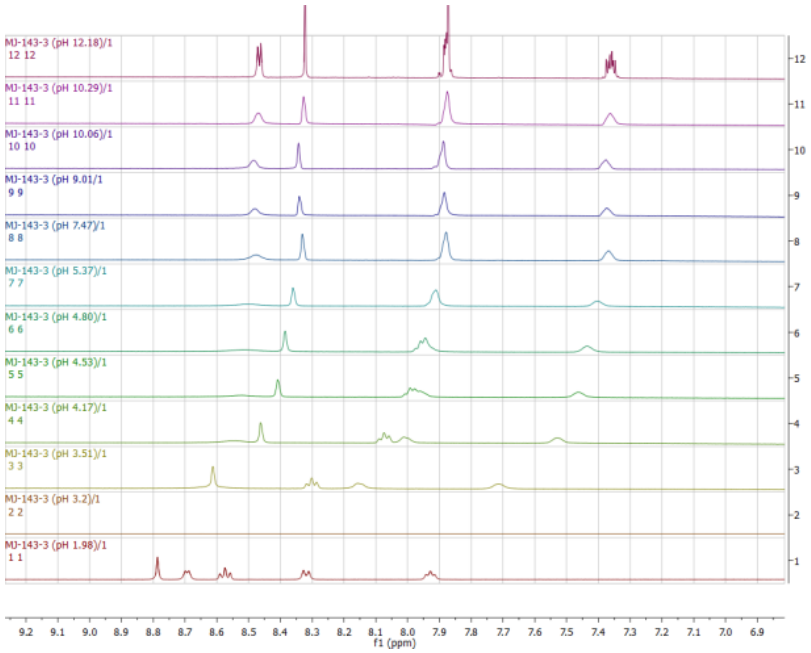


Figure S5a: Variable pH ^{1}H NMR spectra of **L2** in the aromatic region.

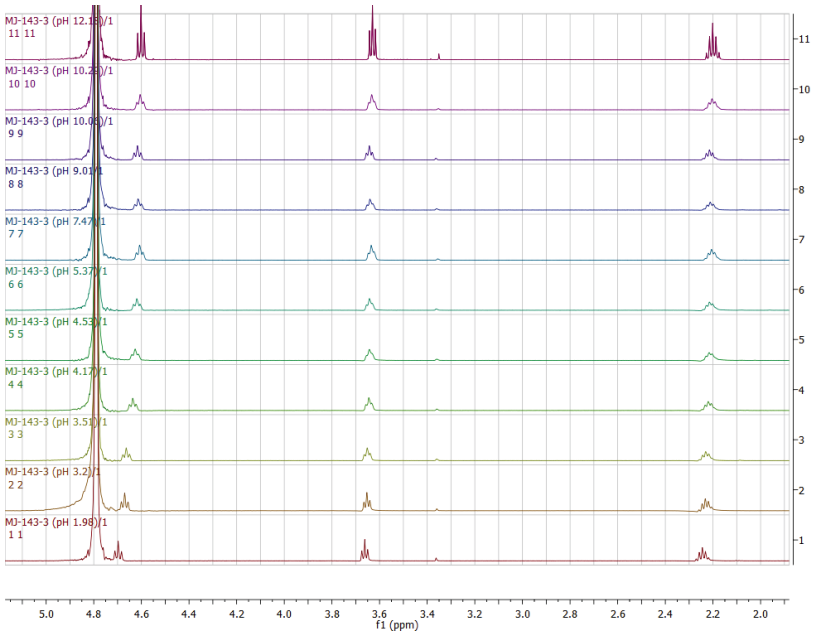


Figure S5b: Variable pH ^{1}H NMR spectra of **L2** in the alkyl region.

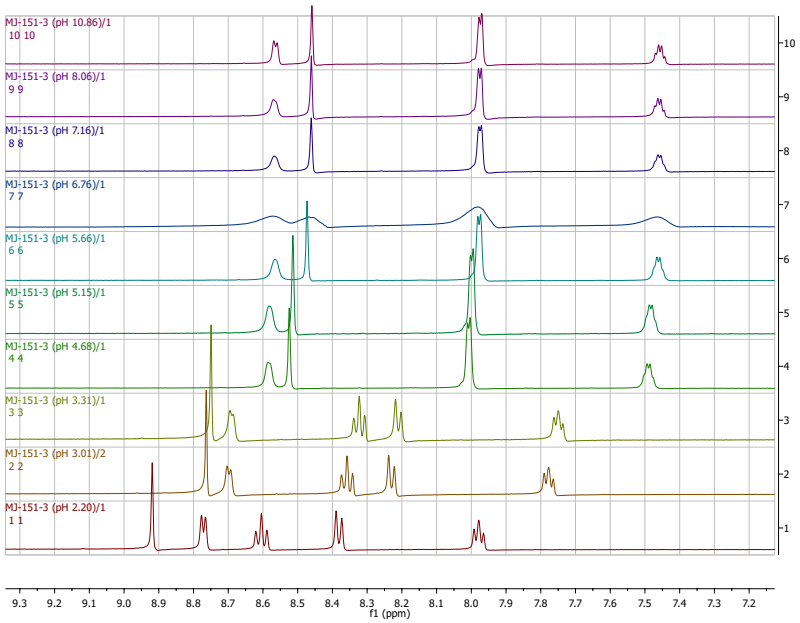


Figure S6a: Variable pH ^{1}H NMR spectra of **L1** in the aromatic region.

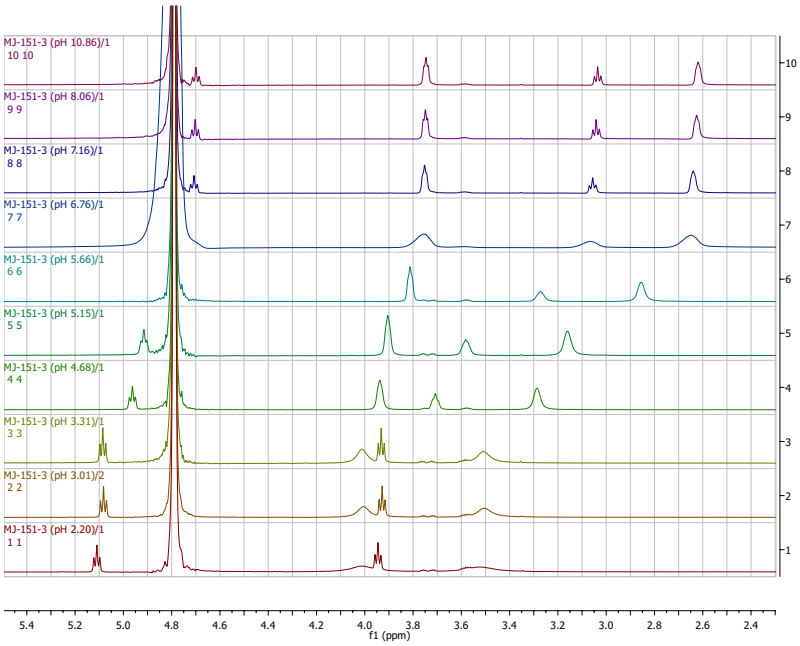


Figure S6b: Variable pH ^{1}H NMR spectra of **L1** in the alkyl region.

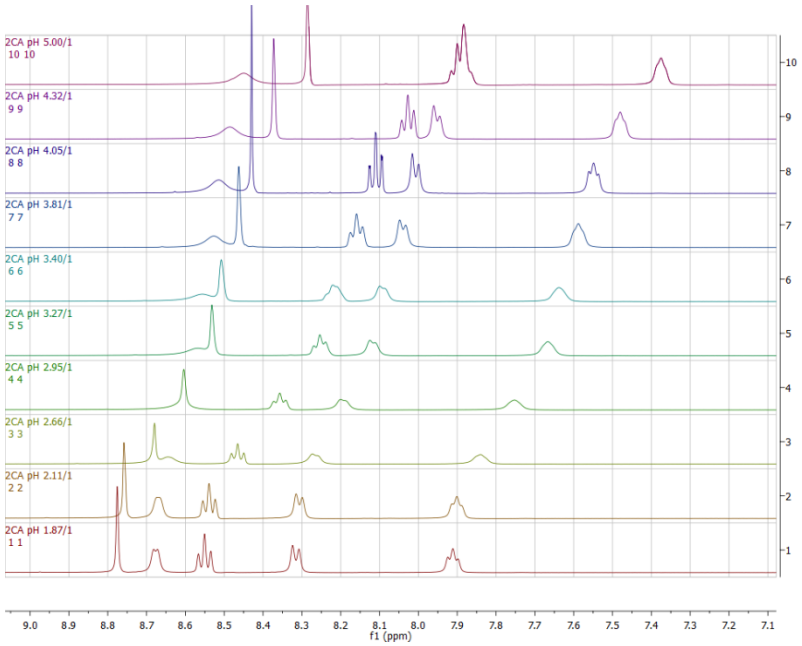


Figure S7a: Variable pH ^{1}H NMR spectra of **L3** in the aromatic region.

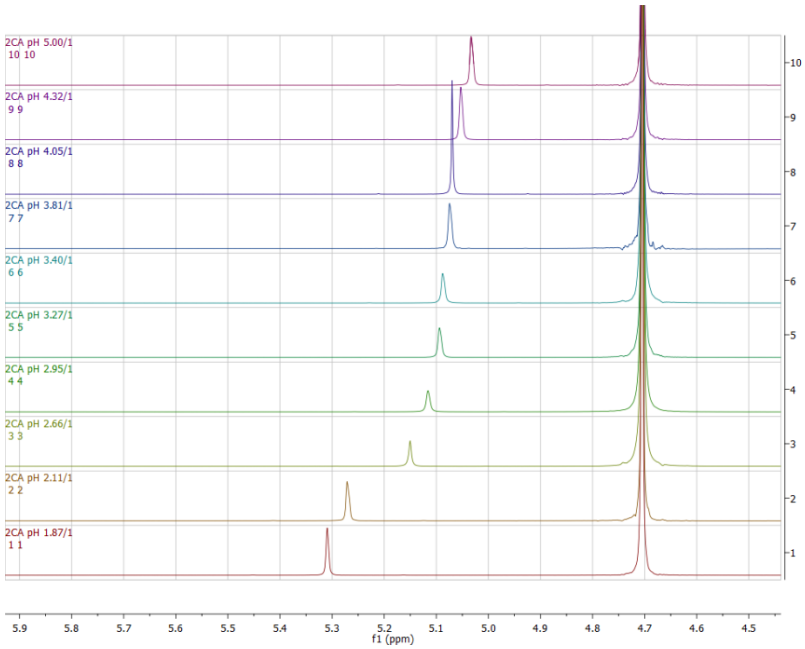


Figure S7b: Variable pH ^{1}H NMR spectra of **L3** in the alkyl region.

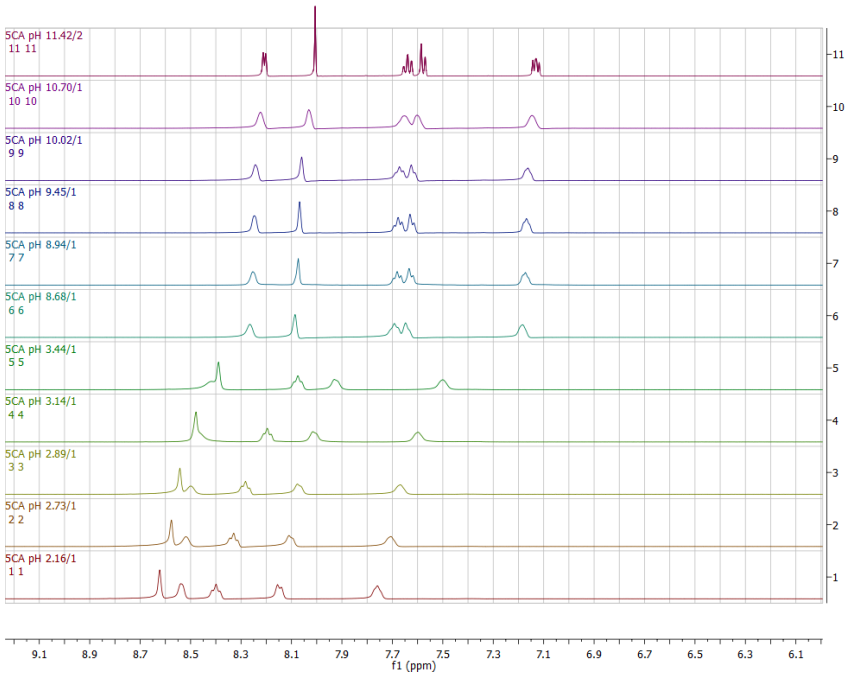


Figure S8a: Variable pH ^{1}H NMR spectra of **L4** in the aromatic region.

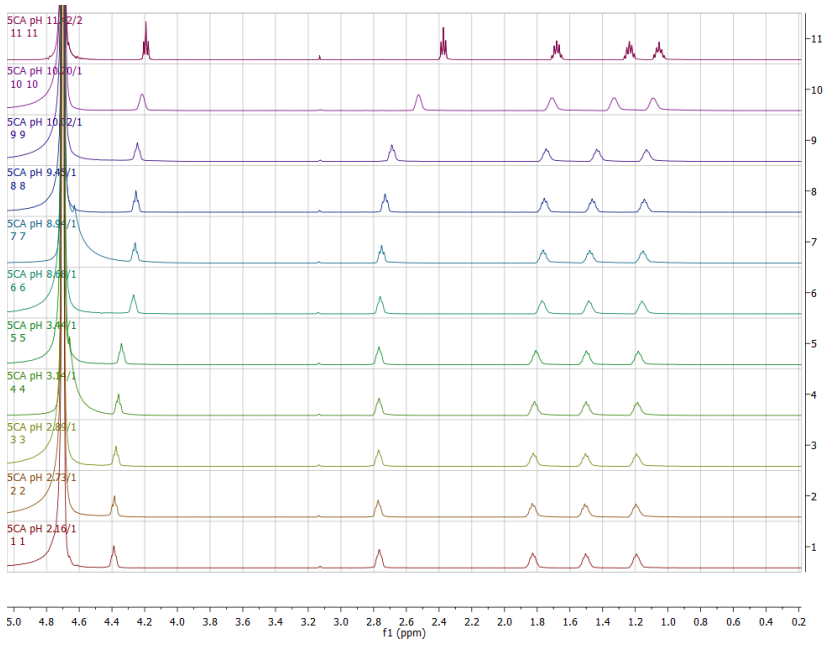


Figure S8b: Variable pH ^{1}H NMR spectra of **L4** in the alkyl region.

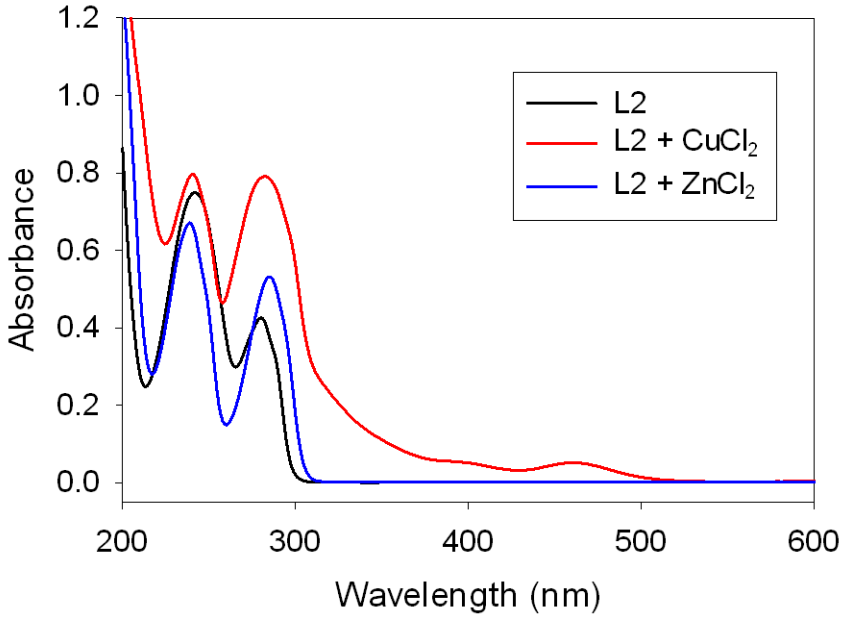


Figure S9: UV-Vis spectra of **L2** (50 μM, black) incubated with metal ions (25 μM) in CH_3CN [**L2** + 1 equiv $CuCl_2$ (red) or $ZnCl_2$ (blue)].

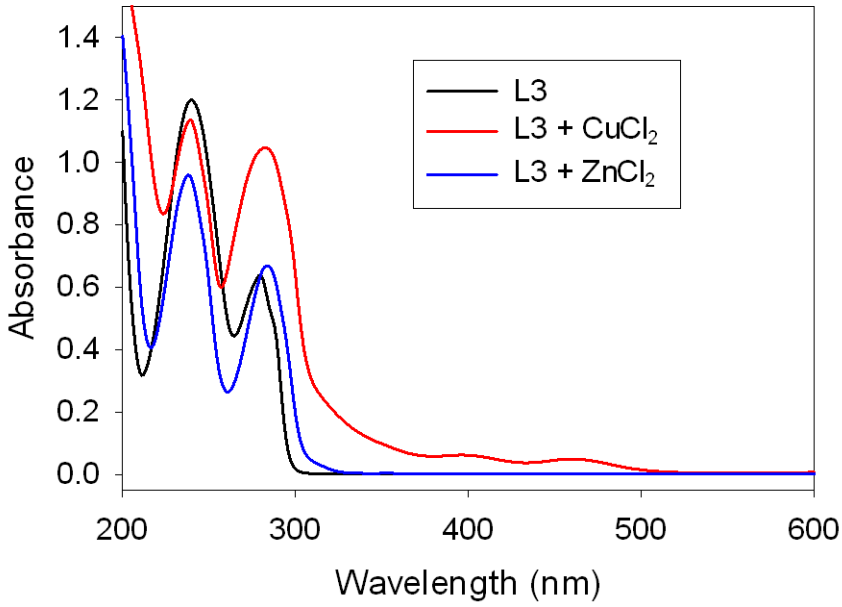


Figure S10: UV-Vis spectra of **L3** (50 μM, black) incubated with metal ions (25 μM) in CH_3CN [**L3** + 1 equiv $CuCl_2$ (red) or $ZnCl_2$ (blue)].

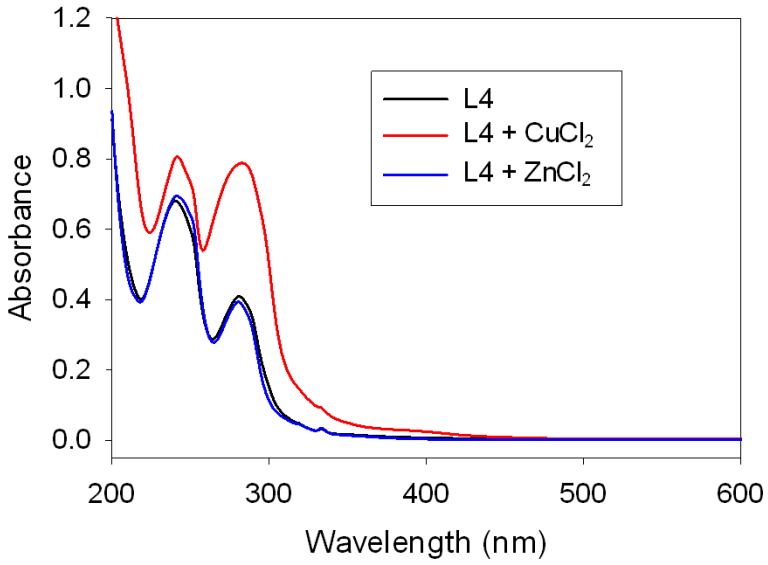


Figure S11: UV-Vis spectra of **L4** (50 μM, black) incubated with metal ions (25 μM) in CH_3CN [**L4** + 1 equiv $CuCl_2$ (red) or $ZnCl_2$ (blue)].

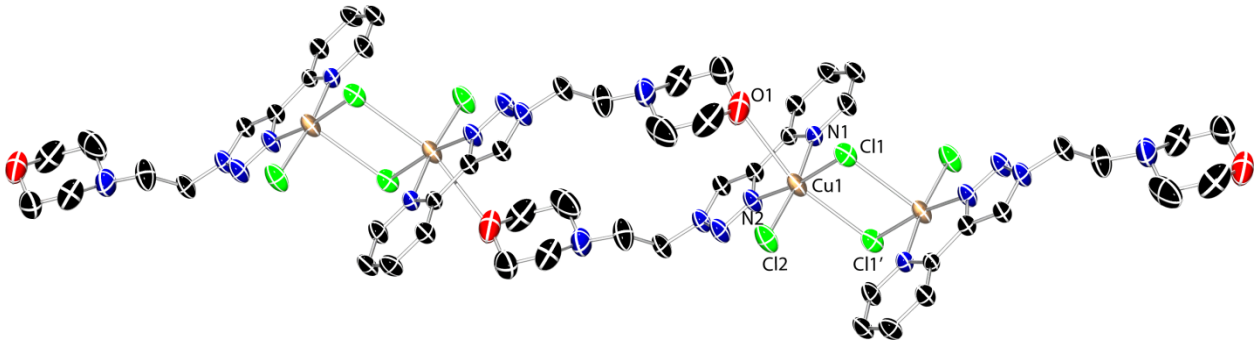
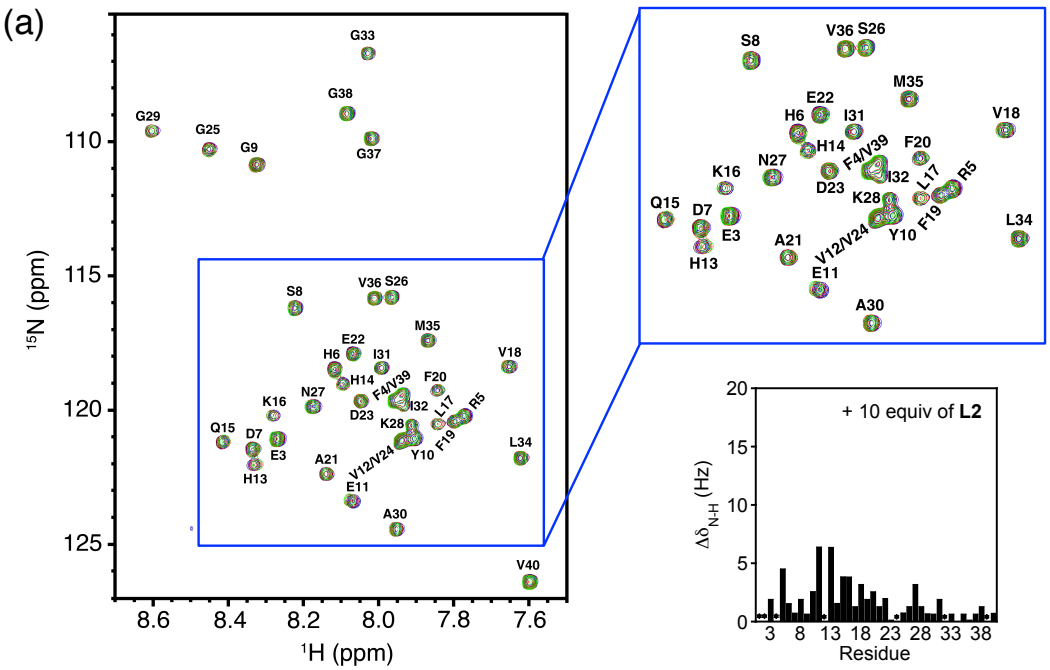
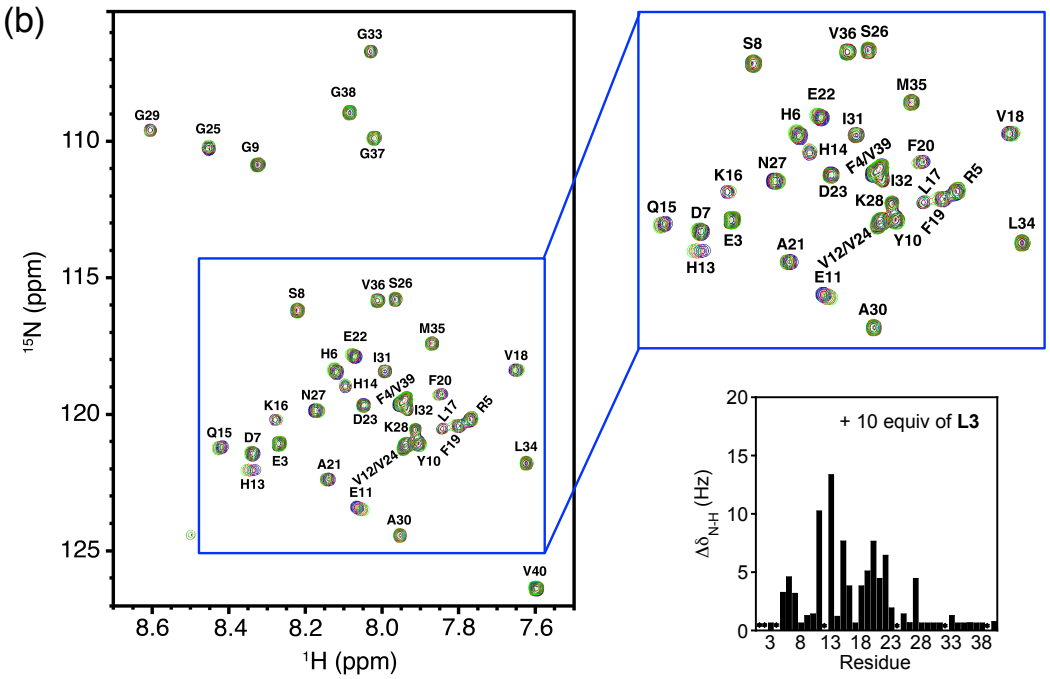


Figure S12: Extended solid state packing of [Cu(**L1**)Cl_2] showing weak interactions of axially bound Cl ligand from another Cu centre and oxygen from a separate morpholine moiety.





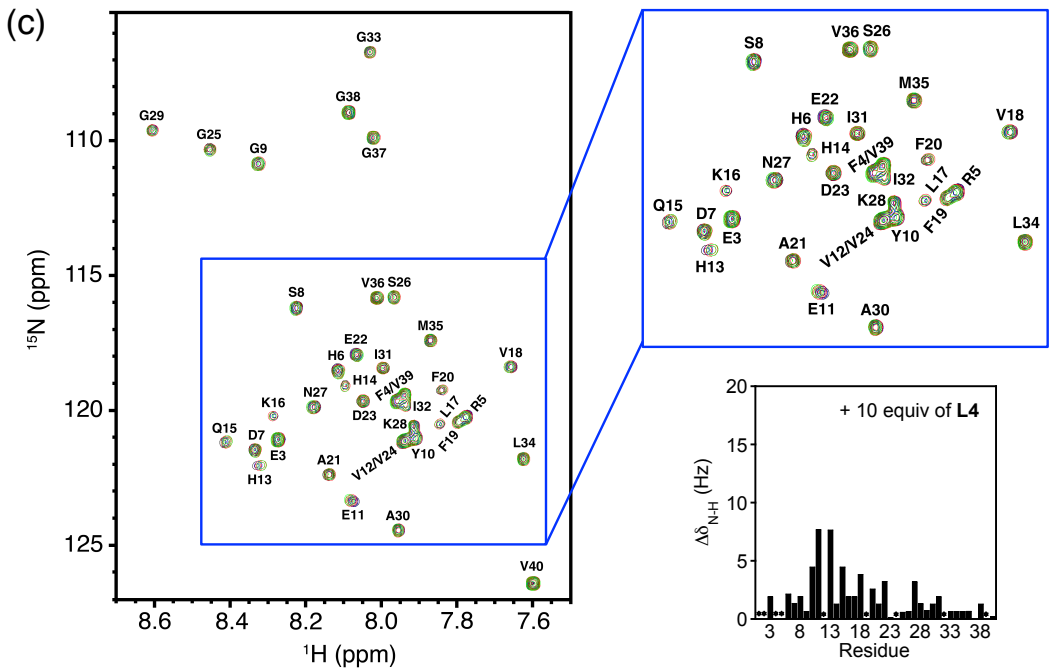


Figure S13: 2D ^{1}H-^{15}N TROSY-HSQC NMR spectra of (a) **L2**, (b) **L3**, and (c) **L4** against ^{15}N-labeled A$\beta_{1\text{-}40}$ in the presence of SDS micelles (200 mM SDS-d_{25}, 20 mM NaPi, pH 7.3, 7% v/v D_2O). Chemical shifts are depicted with increasing equivalents of corresponding ligands, indicated by: black (0 equiv), blue (1 equiv), red (5 equiv), and green (10 equiv). Plots of calculated ^{1}H and ^{15}N chemical shifts of A$\beta_{1\text{-}40}$ in the presence of 10 equivalents of the corresponding ligand calculated from Eq. 1 are shown. Peaks that could not be resolved due to overlap or absence are indicated by an asterisk (*).

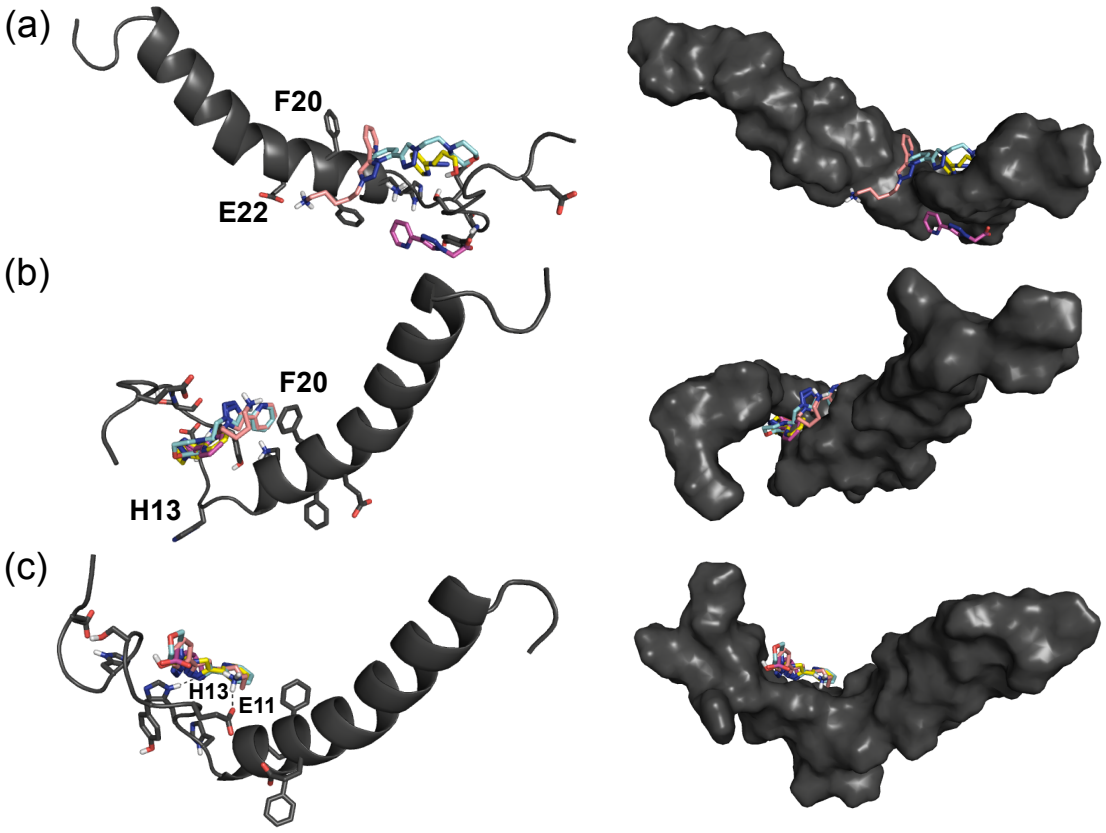


Figure S14: Docking of small molecules with $A\beta_{1\text{-}40}$ monomer in the presence of SDS (PDB 1BA4) predicted by AutoDock Vina. Cartoon (left) and surface (right) depictions of **L1** (light blue), **L2** (yellow), **L3** (carboxylate form, magenta), and **L4** (protonated form, light pink) are shown. a) Conformation B; b) Conformation C; c) Conformation D. Potential hydrogen bonding contacts between the ligands and receptors are indicated with a dashed line (1.9 – 2.3 Å).

Table S1: Predicted binding affinities generated by docking simulations using AutoDock Vina with small molecules **L1** – **L4** against $A\beta_{1-40}$ structure (PDB 1BA4). The structures used for docking are in their expected protonation state under physiological conditions (*i.e.*, **L1** and **L2** are neutral, **L3** is in carboxylate form, **L4** is protonated).

	1BA4			
	L1 (kcal/mol)	**L2** (kcal/mol)	**L3** (kcal/mol)	**L4** (kcal/mol)
A	-5.4	-4.6	-5.3	-5.1
B	-4.8	-4.4	-4.6	-4.5
C	-4.9	-4.4	-4.5	-4.2
D	-5.1	-5.0	-4.8	-4.6