Supplementary material

Figure S1

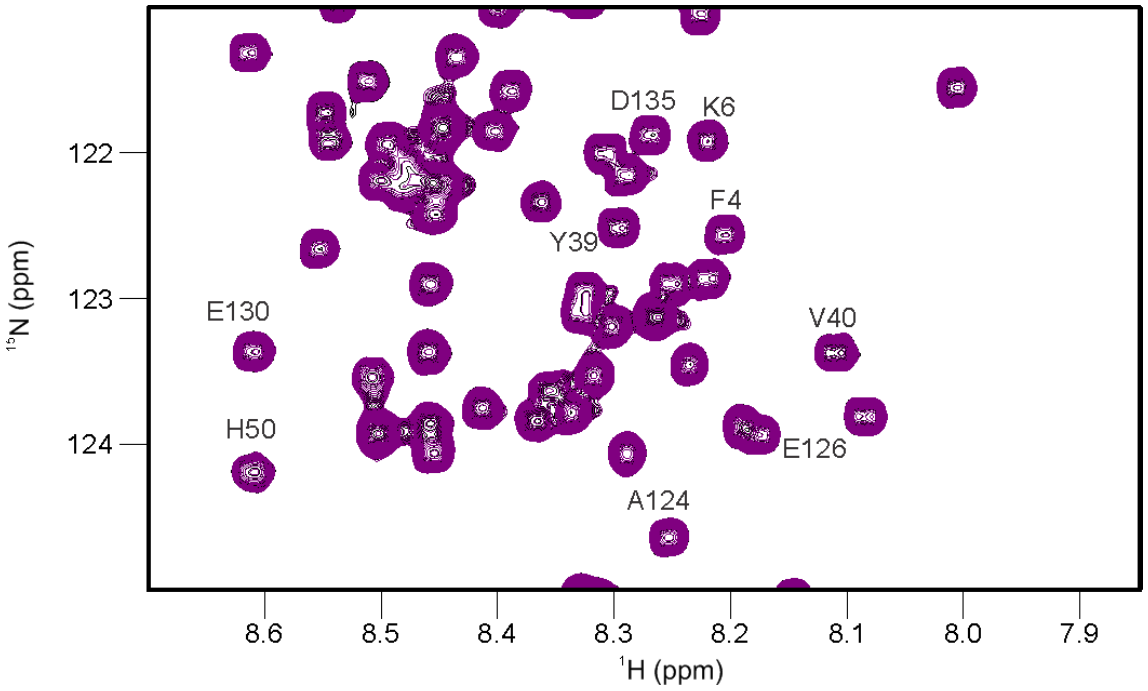

Figure S1. Overlaid contour plots of ^{1}H-^{15}N HSQC spectra of 100 μM αS in the absence (black) and presence (purple) of 50 μM [Al(H_4PcTS)Cl]. No broadening or chemical shift perturbations were detected even at high ligand:αS ratios (5:1). ^{1}H-^{15}N HSQC spectra were recorded at 15 °C using ^{15}N isotopically enriched αS (100 μM) samples.

Figure S2

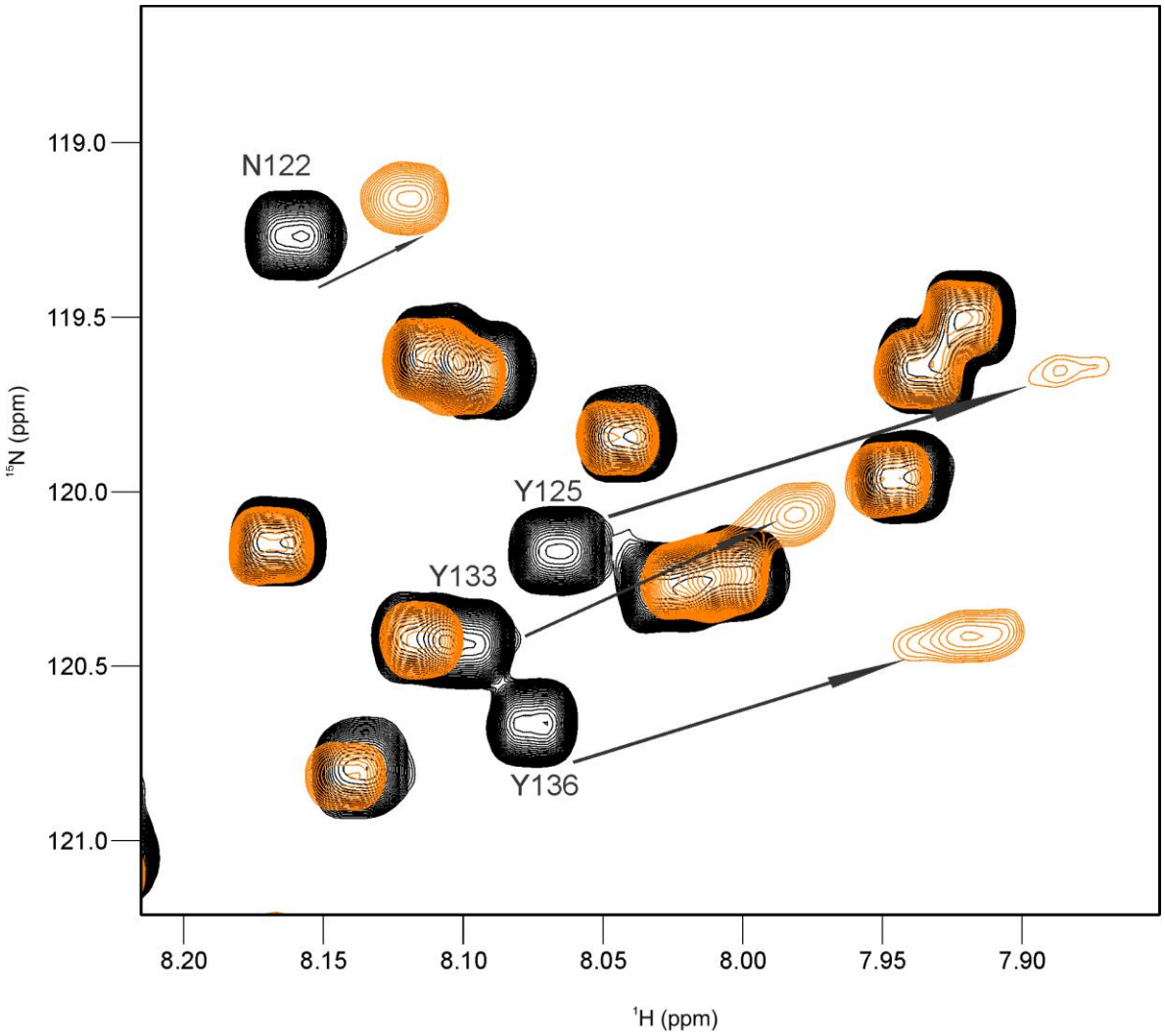

Figure S2. Overlaid contour plots of ^{1}H-^{15}N HSQC spectra of 100 μM αS in the absence (black) and presence (orange) of 50 μM [$H_2PrTPCl_4$]. Aromatic residues located at the C-terminus of αS (Y-125, Y-133 and Y-136) are the main anchoring residues for [$H_2PrTPCl_4$] binding to the protein. ^{1}H-^{15}N HSQC spectra were recorded at 15 °C using ^{15}N isotopically enriched αS (100 μM) samples.

Figure S3

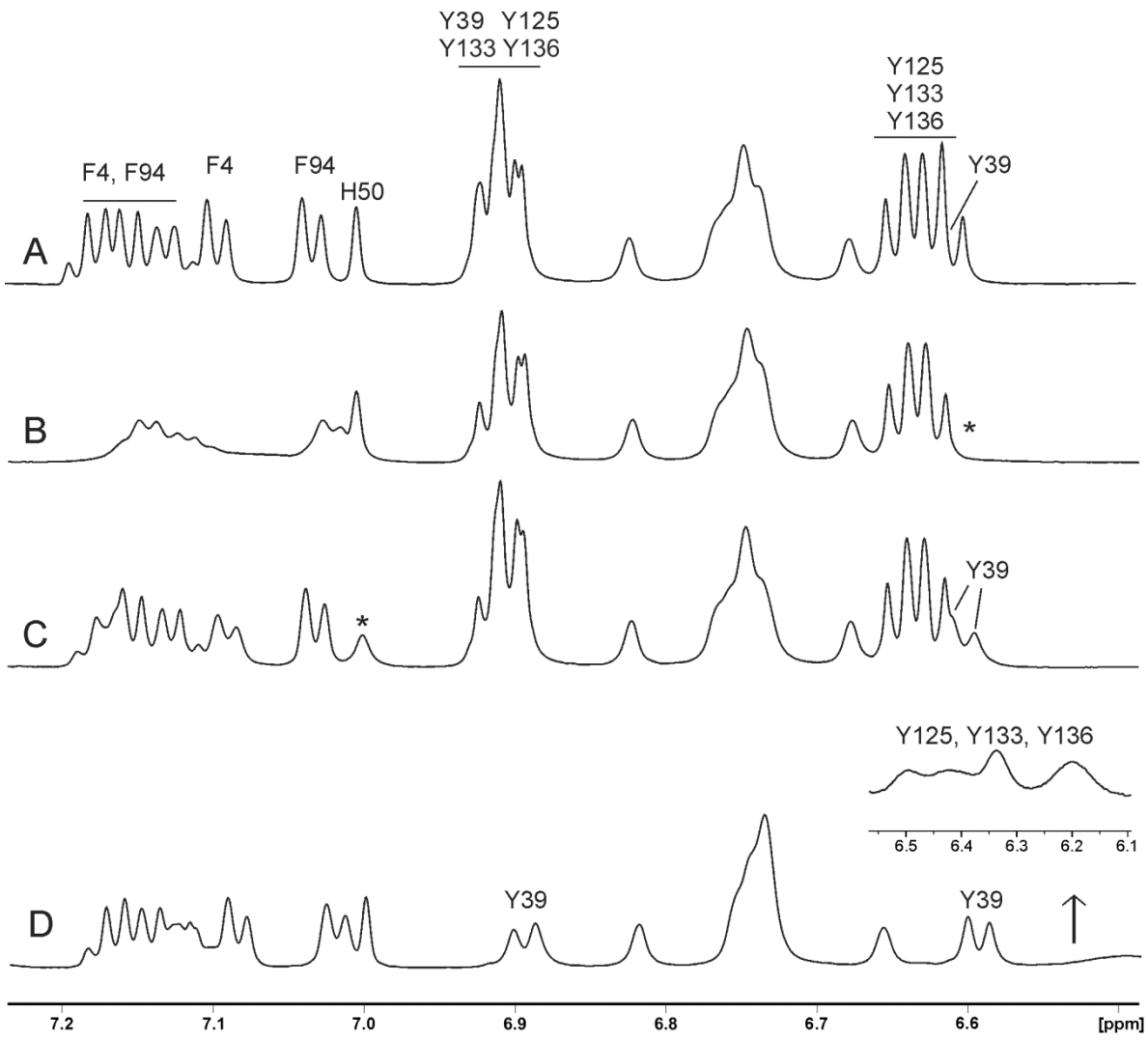

Figure S3. ^{1}H NMR of aromatic side chains of αS in the presence of phthalocyanines and [H_2PrTPCl_4]. Spectra were registerted at 15 ºC in buffer A of samples of **A)** 100 µM of αS, and in the presence of 50 µM of **B)** [Na4(H2PcTS)], **C)** [Zn(H_4PcTS)] and **D)** [H_2PrTPCl_4]. Asterisk in Figure S3B indicates the broadening beyond detection of Tyr-39 resonances upon addition of [Na4(H2PcTS)]. Asterisk in Figure S3C indicates the significant broadening induced by [Zn(H_4PcTS)] on the His-50 resonances. Insert in Figure S3D indicates the significant and selective chemical shift displacements induced by the presence of [H_2PrTPCl_4] on the C-terminal Tyr resonances.

Figure S4

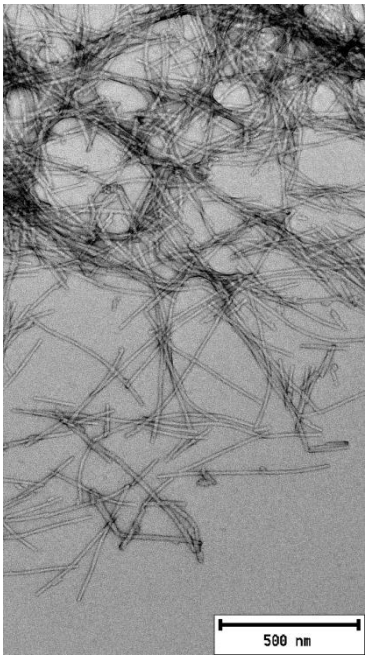

Figure S4. Representative negative stain EM image of αS aggregates (100 μM samples) generated in presence of 100 μM [Al(H_4PcTS)Cl].

Figure S5

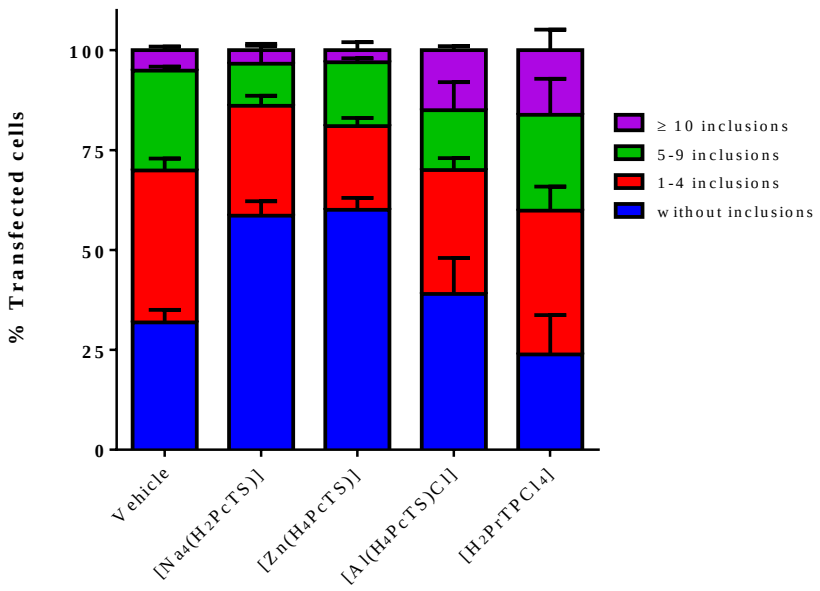

Figure S5. Quantification of αS inclusions formation in cultured cells. Human H4 neuroglioma cells were co-transfected with plasmids encoding SynT and synphilin-1, and inclusion formation was assessed 48 hours post-transfection. Cells were incubated in the absence (vehicle) and presence of the studied tetracyclic compounds (10 μM). Transfected cells were detected and scored based on the pattern of αS inclusions, classified in different groups: 1 to 4 inclusions, 5 to 9 inclusions and equal to/more than 10 inclusions. Results were expressed as the percentage of the total number of transfected cells obtained from three independent experiments. At least 50 cells were scored per experiment (n=3).