

Supplementary Figures

Multivalency in the Inhibition of Oxidative Protein Folding by Arsenic (III)

Species

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Figure S1: Reaction schemes for synthesizing multivalent arsenicals. Panels A-C depict the synthetic schemes for BA-1, BA-2 and TA-1 respectively.

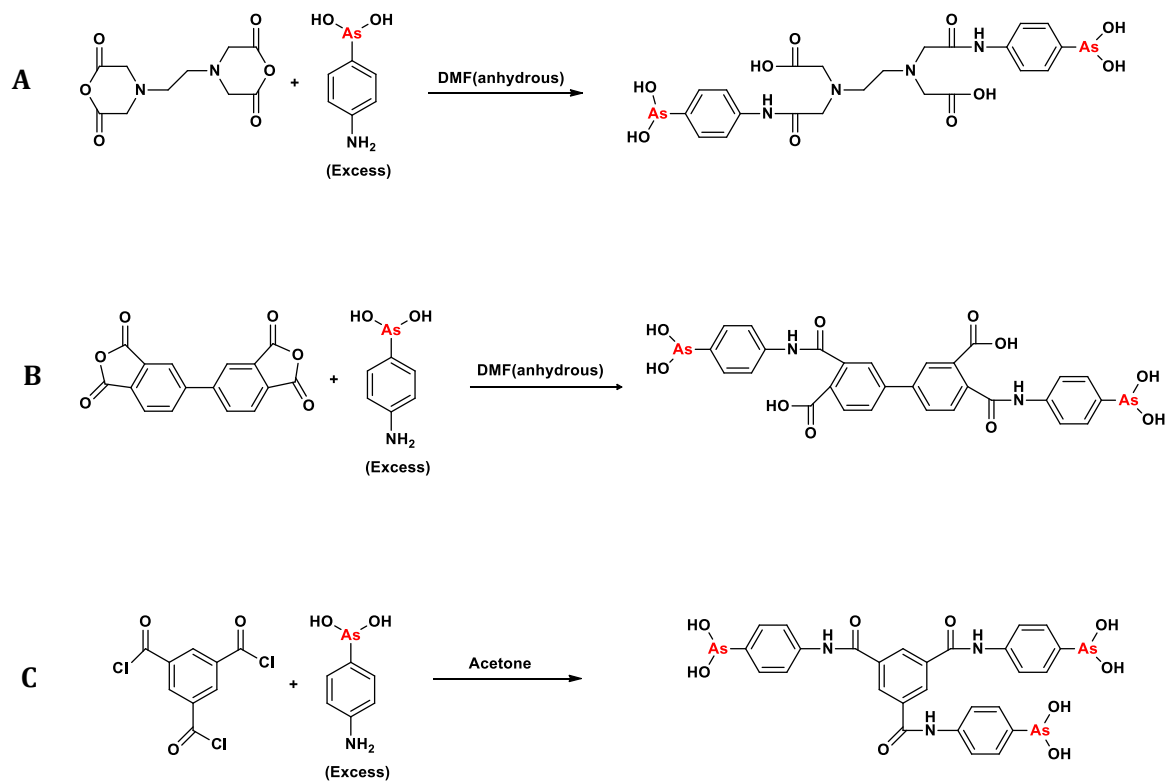


Figure S2: Arsenicals BA-1, BA-2 and TA-1 do not markedly delay the onset of light scattering following reduction of insulin by TCEP. Insulin (50 μM in 50 mM phosphate buffer, pH 7.5, containing 1 mM EDTA) was mixed with 5 mM TCEP in presence of MVAs. The onset of turbidity was observed at 600 nm (panel A). The lag times are also presented as a bar graph in panel B with control (no arsenical), black; BA-1 (5 μM), pink; BA-2 (5 μM), blue; TA-1 (3.33 μM) green.

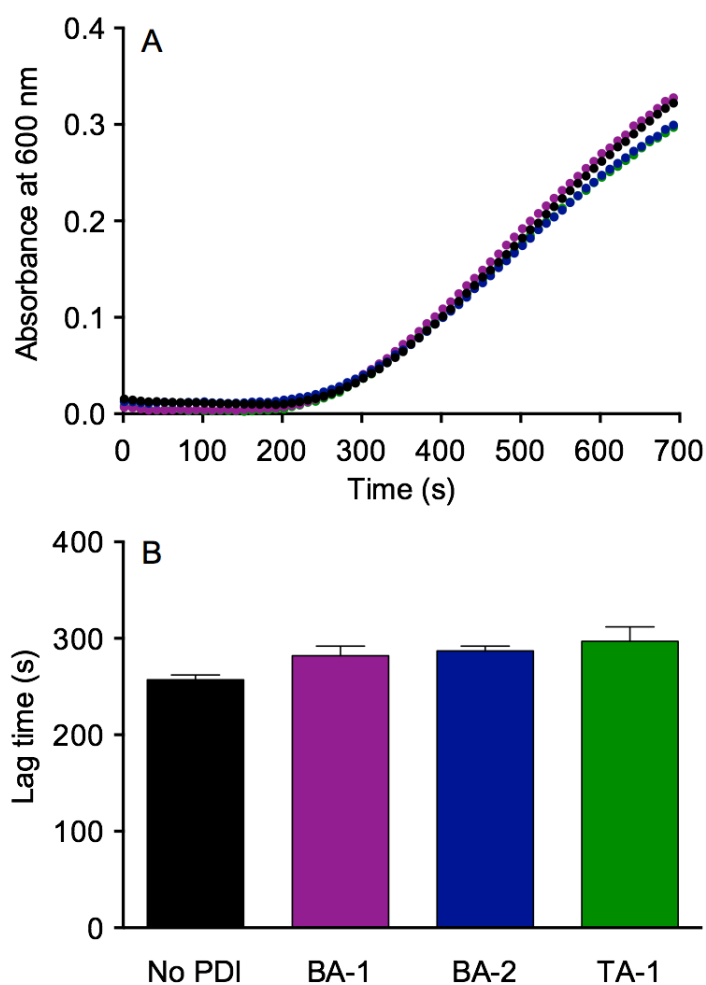


Figure S3: Spectrophotometric determination of the dissociation constant for the binding of BA-2 and TA-1 to reduced PDI. Panel A: The solid line for BA-2 binding to 1 μM of reduced PDI was fit to a stoichiometry of 1.0 ± 0.11 and a K_d of $56 \text{ nM} \pm 36 \text{ nM}$ (see Methods). Panel B: The binding of TA-1 was fit to a stoichiometry of 0.89 ± 0.08 and a K_d of $100 \pm 32 \text{ nM}$.

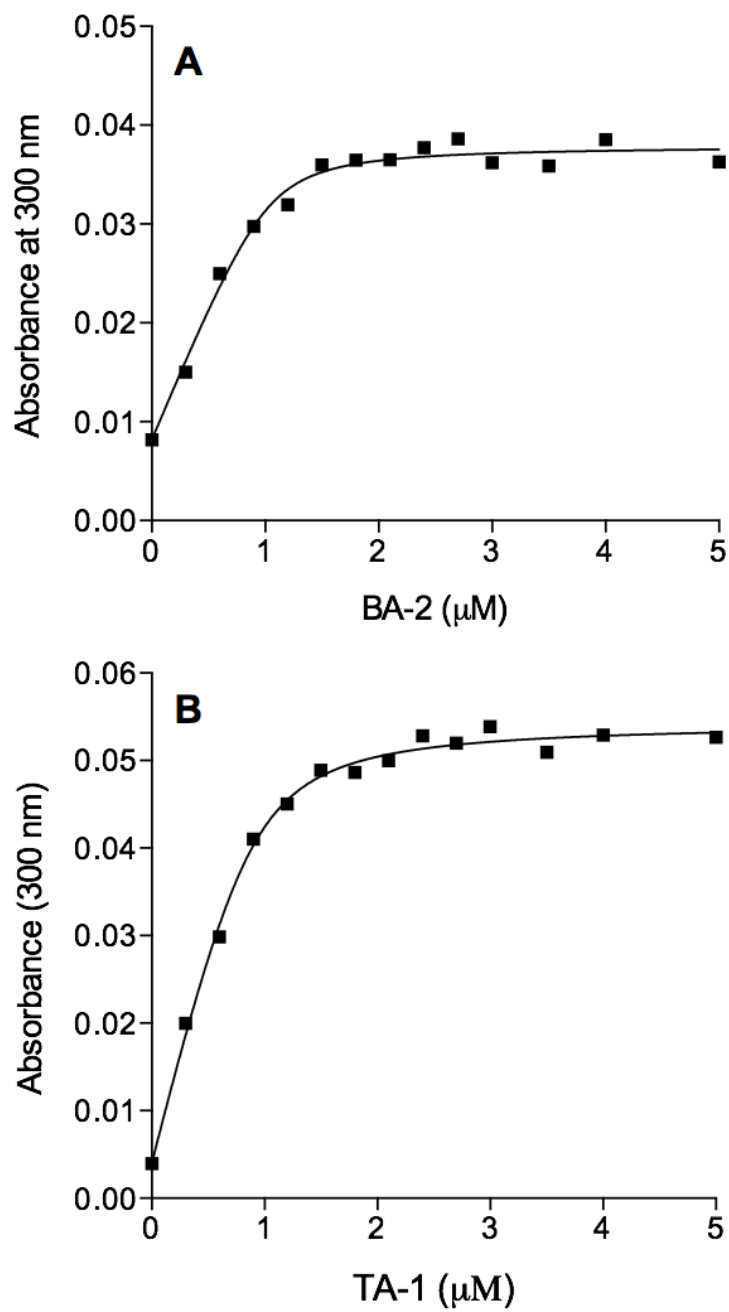


Figure S4: Transmission electron microscopy of reduced RNase treated with multivalent arsenicals. Reduced RNase (50 μM in 50 mM potassium phosphate buffer, pH 7.5, containing 1 mM EDTA and 1 mM TCEP) was incubated with 5 μM BA-1 (panel A), BA-2 (panel B) and 3.33 μM of TA-1 (panel C) overnight at 4 $^{\circ}\text{C}$. TEM imaging shows fibril formation with all multivalent arsenicals. Reduced RNase in absence of any arsenical does not show fibril like structures (panel D).

