Supporting information

A case of Extensive Protein Platination:

the Reaction of Lysozyme with a Pt(II) terpyridine complex

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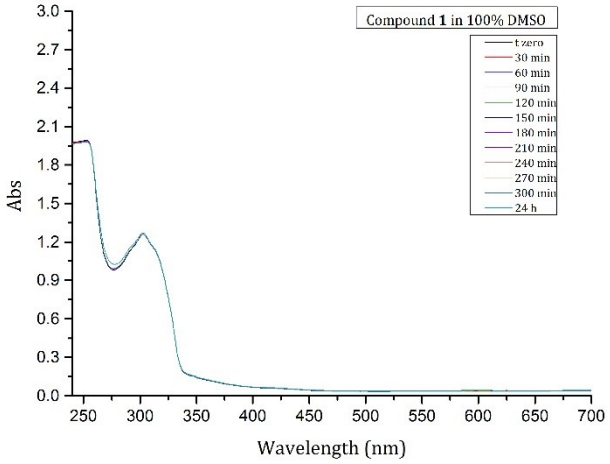
Compound 1 in 100% DMSO
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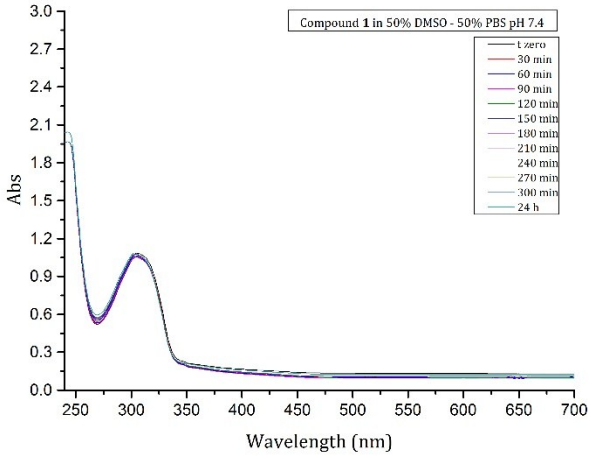
60 min
90 min
120 min
150 min
180 min
210 min
240 min
270 min
300 min
24 h
Abs
Wavelength (nm)

A


Compound 1 in 50% DMSO - 50% PBS pH 7.4
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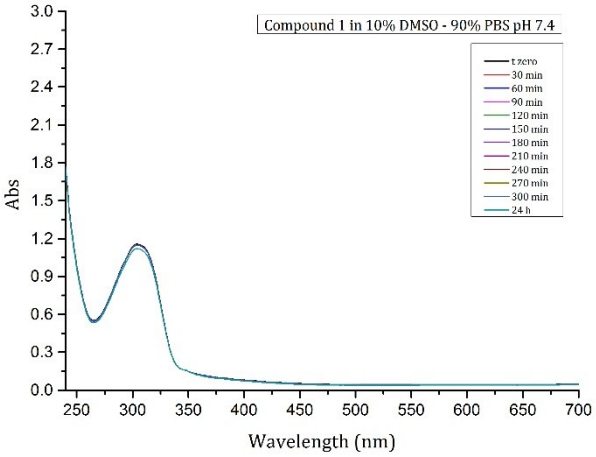
150 min
180 min
210 min
240 min
270 min
300 min
24 h
Abs
Wavelength (nm)

B


Compound 1 in 10% DMSO - 90% PBS pH 7.4
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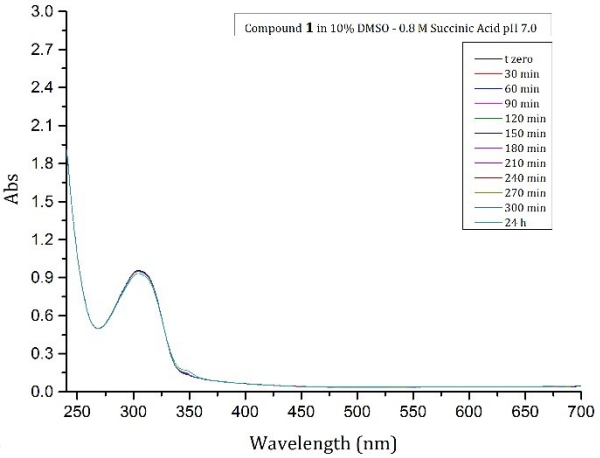
120 min
150 min
180 min
210 min
240 min
270 min
300 min
24 h
Abs
Wavelength (nm)

C


Compound 1 in 10% DMSO - 0.8 M Succinic Acid pH 7.0
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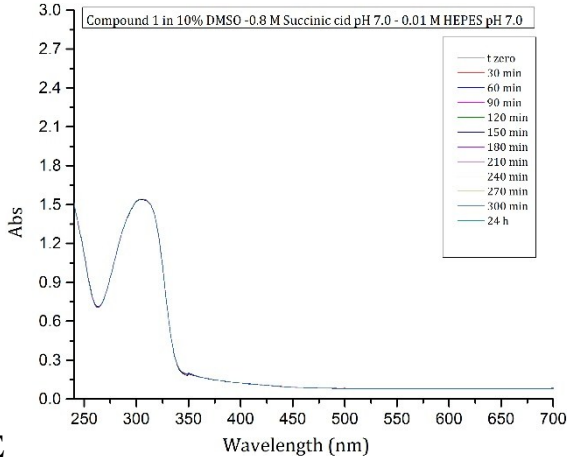
90 min
120 min
150 min
180 min
210 min
240 min
270 min
300 min
24 h
Abs
Wavelength (nm)

D


Compound 1 in 10% DMSO -0.8 M Succinic cid pH 7.0 - 0.01 M HEPES pH 7.0
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90 min
120 min
150 min
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270 min
300 min
24 h
Abs
Wavelength (nm)

E

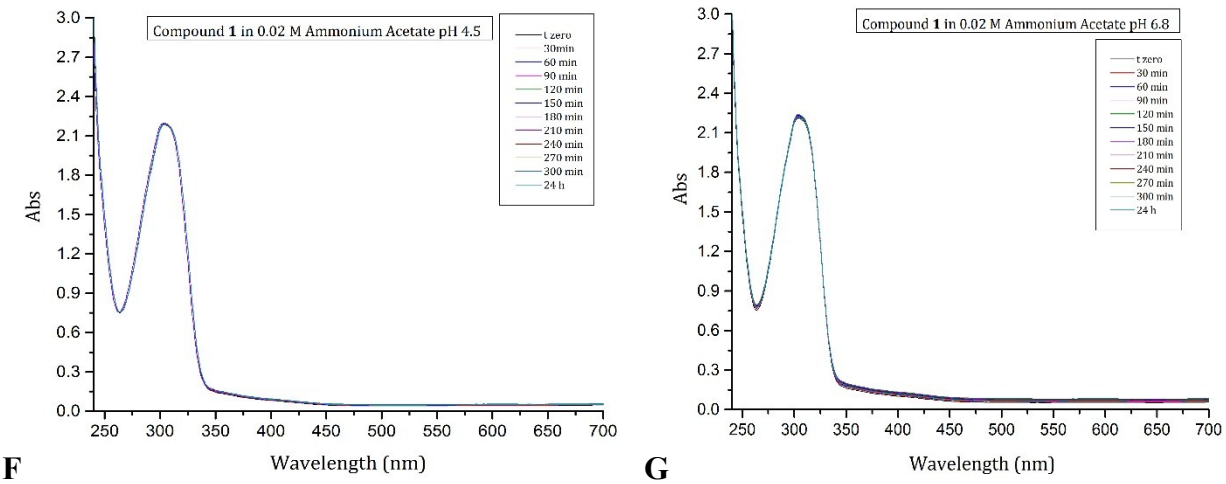

Figure S1. Time dependent UV-Vis absorption spectra of compound **1** (10^{-4} M) dissolved in A) 100% DMSO, B) 50% DMSO–50% PBS pH 7.4, C) 10% DMSO–90% PBS pH 7.4 D) 10% DMSO, 0.8 M succinic acid/NaOH pH 7.0, E) 10% DMSO, 0.8 M succinic acid/NaOH and 0.010 M HEPES pH 7.0, 15% DMSO and 0.020 M ammonium acetate F) pH 4.5 and G) pH 6.8 monitored over 24 h.

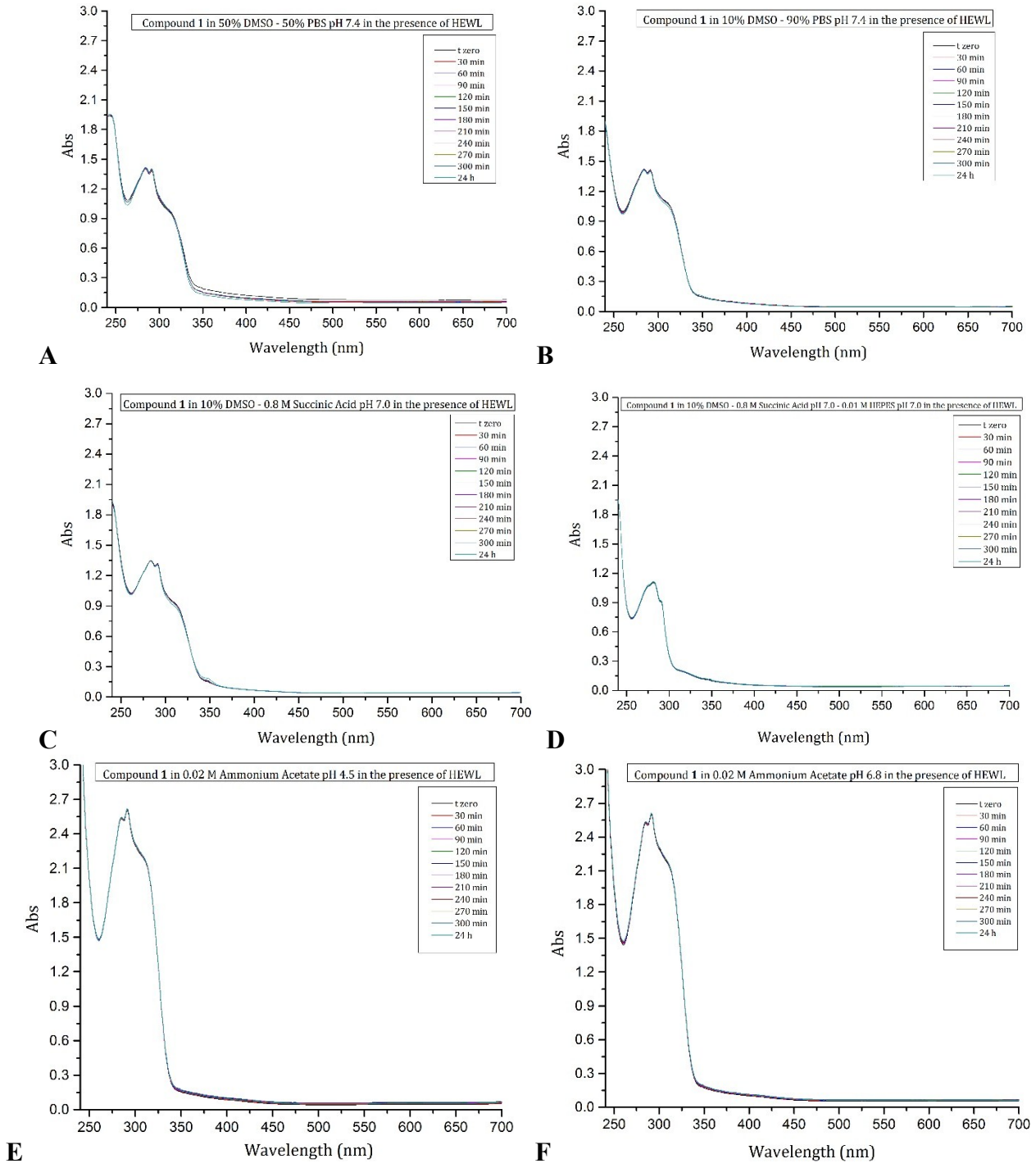

Figure S2. Time dependent UV-Vis absorption spectra of compound **1** (10^{-4} M) dissolved in A) 50% DMSO–50% PBS pH 7.4, B) 10% DMSO–90% PBS pH 7.4, C) 10% DMSO – 0.8 M succinic acid/NaOH at pH 7.0, D) 10% DMSO–0.8 M succininc acid/NaOH, 0.010 M HEPES at pH 7.0, E) 15% DMSO and 0.02 ammonium acetate pH 4.5 and F) pH 6.8 in the presence of HEWL in 3:1 metal to protein ratio, monitored over 24 h.

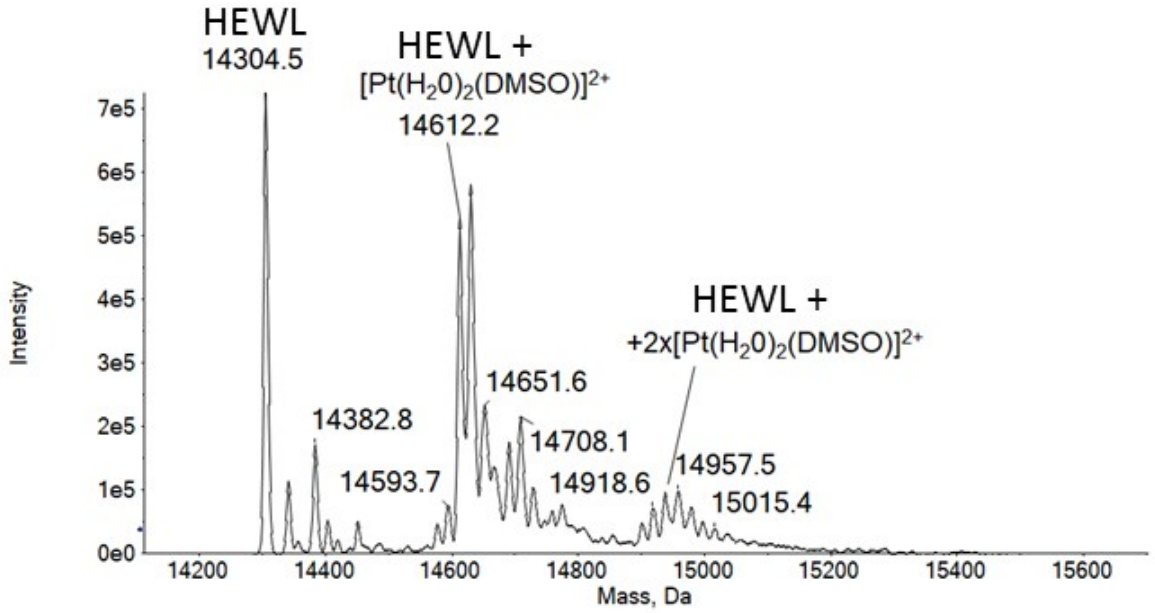

Figure S3. Deconvoluted ESI mass spectra of HEWL (10^{-4} M) treated with compound 1 in 1 : 3 protein to metal ratio. Spectra were registered after 24 h of incubation at 37 °C, in the presence of 3% DMSO and 20 mM ammonium acetate pH 6.8.

Table S1:
Comments on uninterpreted peaks of electron density (> 5 σ) in the structure deposited under the accession code 6g5y

Peak 1	The presence of this peak could suggest an additional Pt site, i.e. as a split site with Pt B4, but this Pt site is close to the binary axis, and thus there are already two Pt centres in those positions.
Peak 2	The presence of this peak could suggest the Pt B1 occupancy isn't quite correct. However, a deeper inspection of the e.d. map reveals that the positive peak does not correspond to the Pt position and is not on the plane where the Pt ligands are placed. The existence of this peak suggests the presence of a solvent molecule alternative to the Pt containing fragment. We have tried to interpret this peak with a water molecule, which is already present as alternative to Pt centre in our model, but a positive peak in the Fo-Fc map still remains.
Peak 3	The presence of this peak could suggest the Pt B4 occupancy isn't quite correct. Interpretation of the electron density map in this region is rather difficult due to fact that the Pt centre is in close proximity to the binary axis. In this site, Pt occupancy has been refined to 0.40 and B-factor value is 41.3 $Å^2$. Due to the proximity of the Pt centre to the symmetry axis the occupancy value of this atom cannot exceed the value of 0.50. Refinements indicate that when Pt has an occupancy equal to 0.50, Rfactor and Rfree does not significantly change, although Rfree marginally increase in both isotropic and anisotropic refinements (ΔRfactor=+0.0002, ΔRfree=+0.0002 in the anisotropic refinement and ΔRfactor=-0.0005, ΔRfree=+0.0014 in the isotropic refinement), B-value increases to 45.4 $Å^2$ and the map is not so different for that obtained when the occupancy is equal to 0.4. Thus we decided to fix the occupancy to 0.40.
Peak 4 Peak 5	The presence of these peaks could suggest that Pt B2 occupancy and the assignment of water 112 is not correct. After anisotropic refinement it is clear that the positive peak is on the water ligand and not on the Pt centre. This would indicate that the ligand interpreted as water could be something else. We cannot exclude this possibility, however, the water molecule is at 3.3 Å distance from the N of Ile88, at 4.0 Å distance from the CB atom of the side chain of Ala11, and in short contact with CB atom of the side chain of Ile88 (3.4 Å). This suggests that it is not possible to interpret this peak as a bulkier ligand such as DMSO and since there are no Cl^- or other monoatomic anions in the experimental conditions that have been used to form the protein-Pt adduct we decided to interprete the peak as a water molecule.
Peak 6 Peak 7	These peaks are not present in the map calculated after anisotropic refinement