Cytotoxic gallium complexes containing thiosemicarbazones derived from 9-anthraldehyde: Molecular docking with biomolecules

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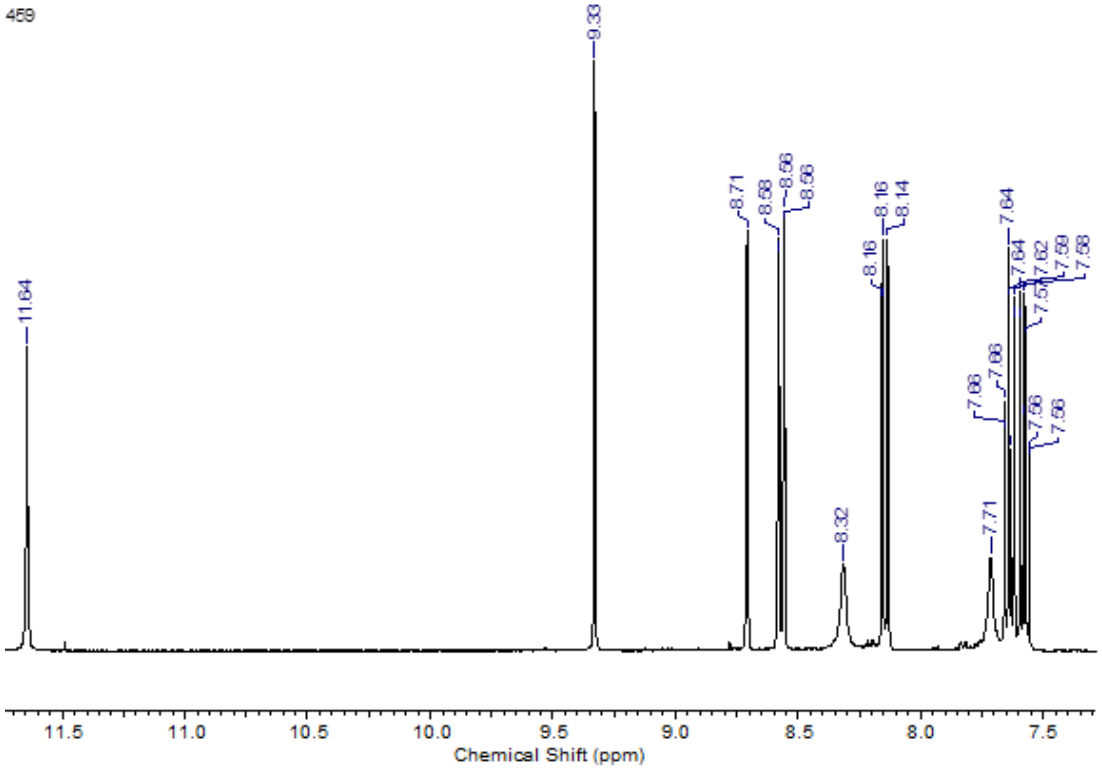
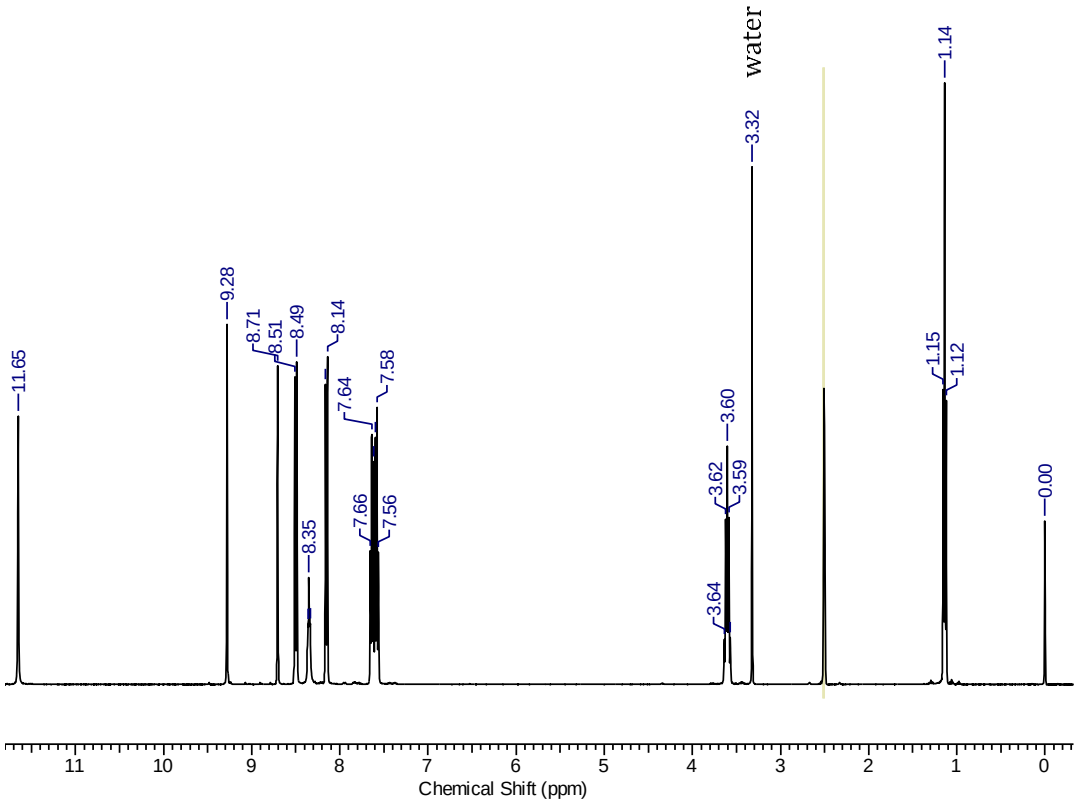
Supplemental Information

Cytotoxicity assay

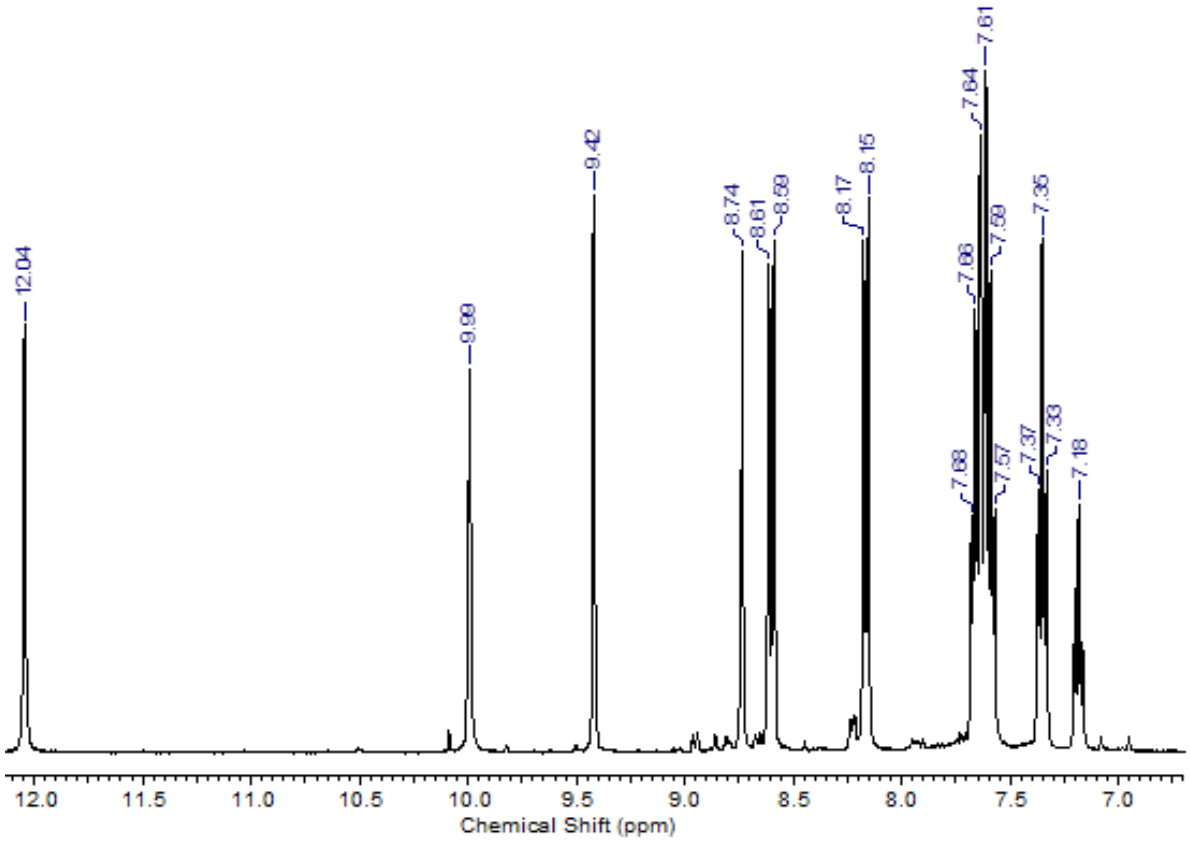
Briefly, the *in vitro* cytotoxicity of samples were assessed in tumor cells by a tetrazolium-based colorimetric assay, which takes advantage of the metabolic conversion of MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfenyl)-2H-tetrazolium, inner salt] to a reduced form that absorbs light at 490 nm. Cells were counted using a haemocytometer and were plated at 2,000 to 5,000 cells per well, depending on the cell line, in a 96-well format for 24 h prior to drug addition. Test samples and a positive control, etoposide 4 mg/mL (Sigma), were solubilized in DMSO by sonication. All samples were diluted with media to the desired treatment concentration and the final DMSO concentration per well did not exceed 0.5%. Control wells were also included on all plates. Following a 24 h, 48 h or 72 h drug-incubation period at 37 °C with serially diluted test compounds, MTS, in combination with the electron coupling agent, phenazine methosulfate, was added to the wells and cells were incubated at 37 °C in a humidified incubator for 3 h. Absorbance at 490 nm (OD490) was monitored with a spectrophotometer (SpectraMax M2, Molecular Devices Corp., operated by SoftmaxPro v.4.6 software, Sunnyvale, CA, USA) to obtain the number of surviving cells relative to control populations. The results are expressed as the median cytotoxic concentrations (IC50 values) and were calculated from six-point dose response curves using 4-fold serial dilutions. Each point on the curve was tested in triplicate. Data are expressed as mean ± SE for three replicates on each cell line.



^{1}H NMR spectrum of **1**.

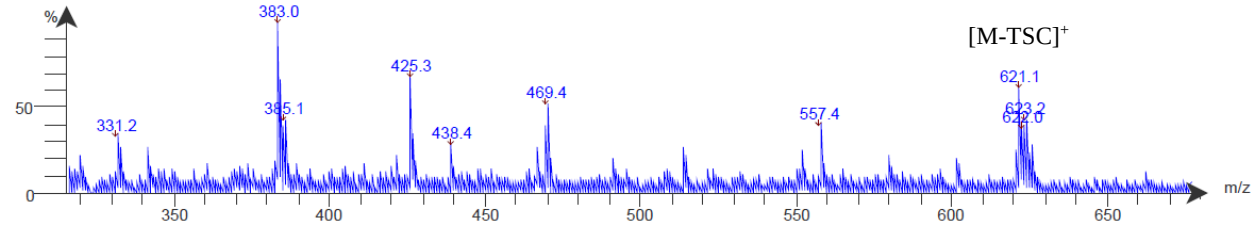


^{1}H NMR spectrum of **2**.

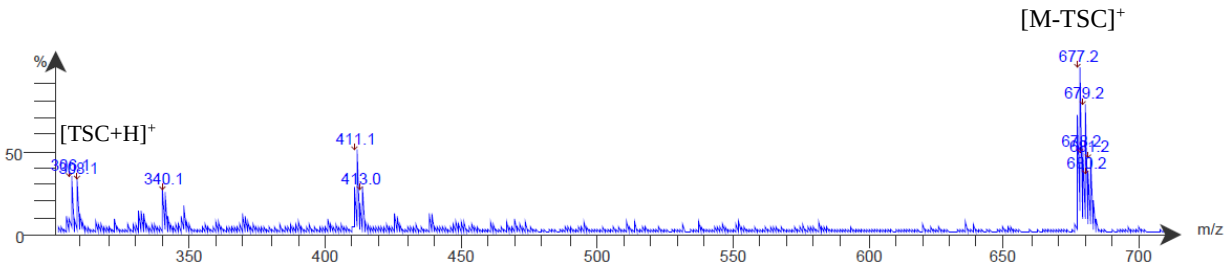


^{1}H NMR spectrum of **3**.

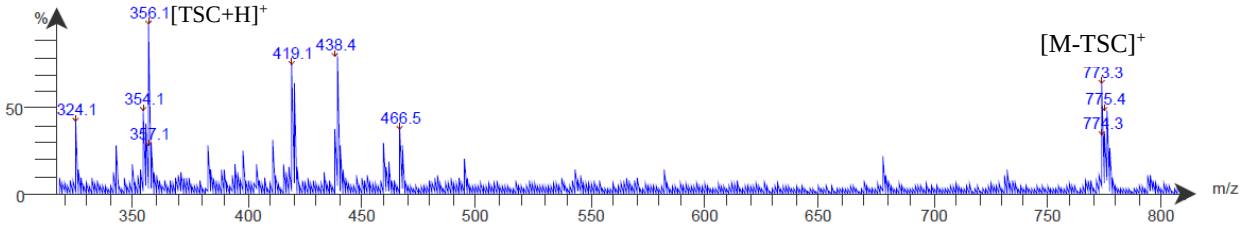
Complex **1**



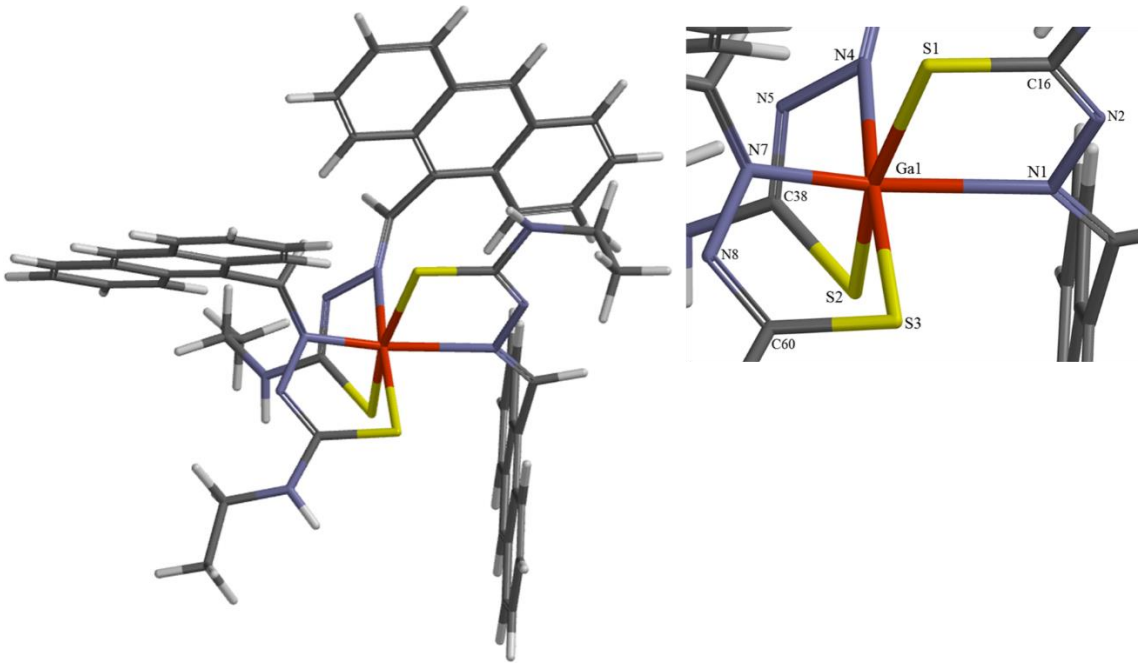
Complex **2**



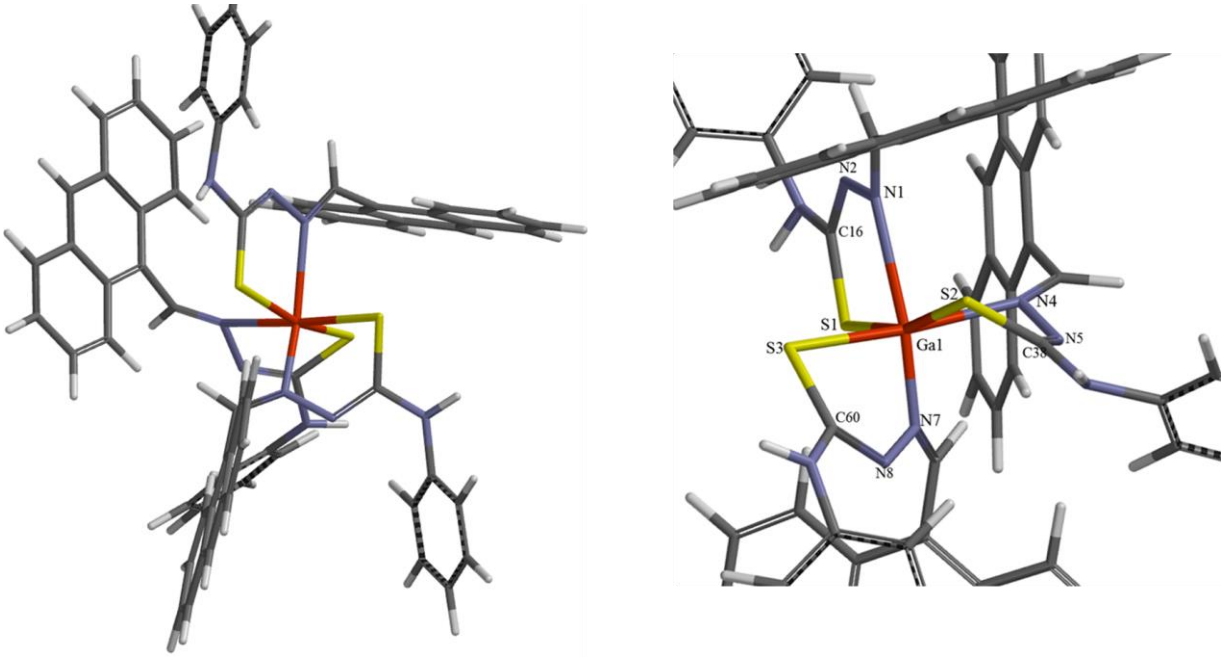
Complex **3**



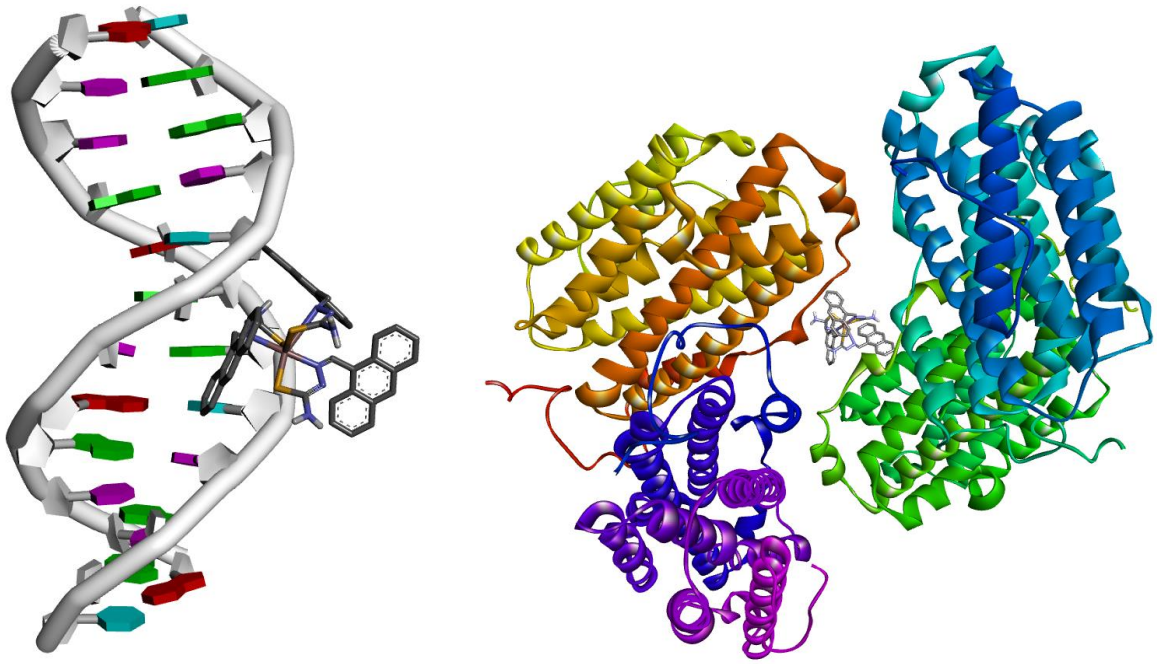
ESI-MS for the complexes



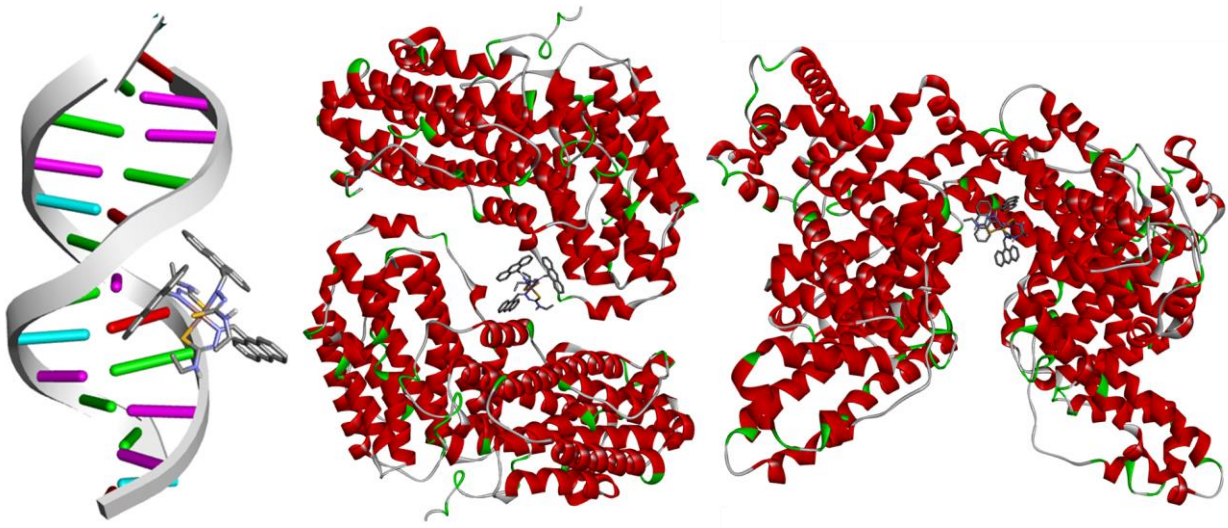
Calculated structure for $Ga(EtATSC)_3$, **2**



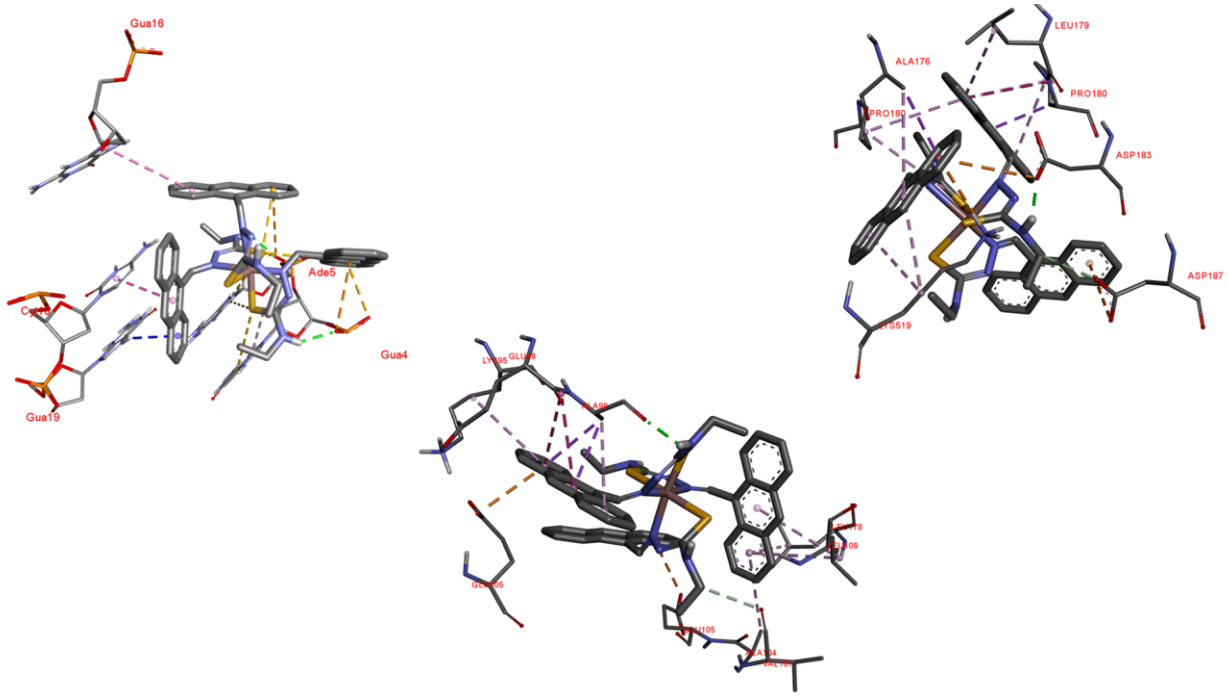
Calculated structure for $Ga(PhATSC)_3$, **3**



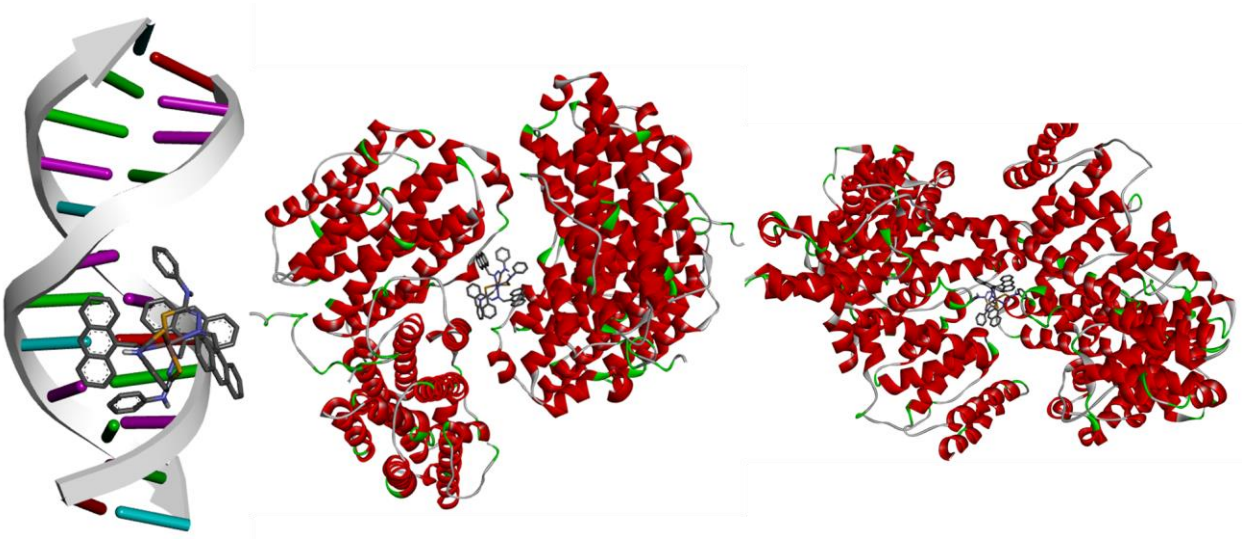
Secondary pose for the binding of $Ga(ATSC)_3$, **1**, to DNA (left) and ribonucleotide reductase (RNR) (right)



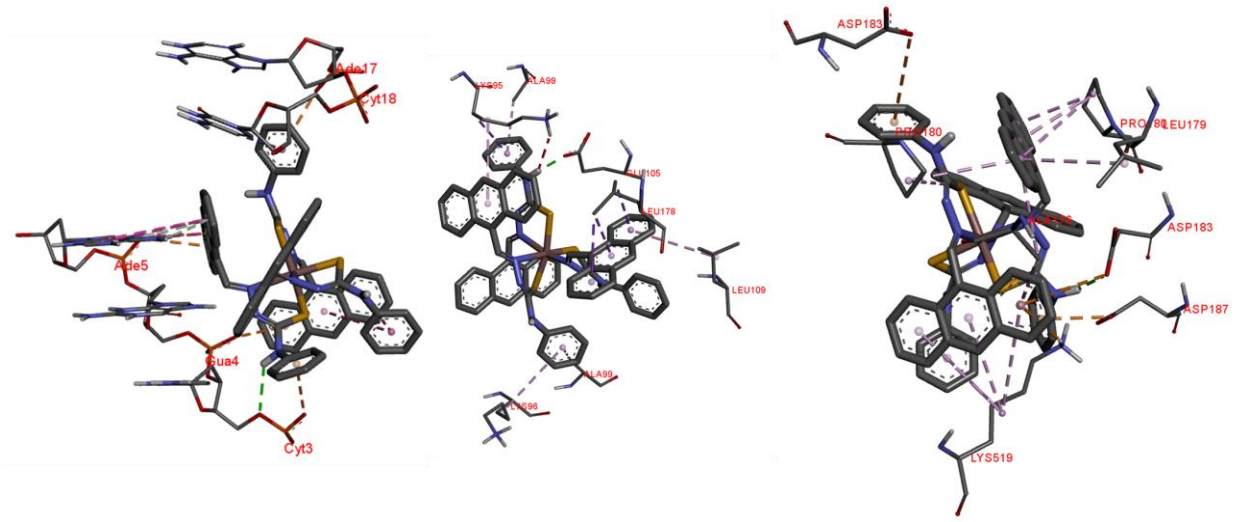
Docked poses for the interaction of $Ga(EtATSC)_3$, **2**, with DNA, RNR and HSA.



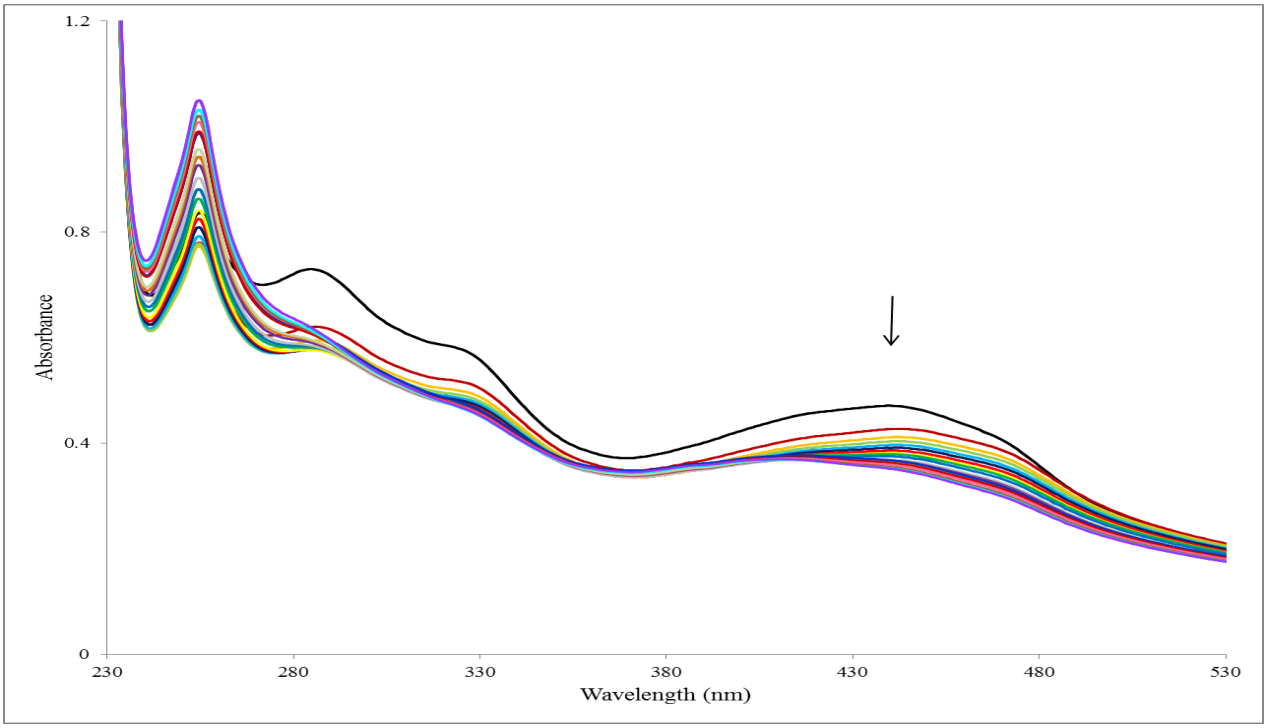
Binding groups involved in the docked poses for the interaction of $Ga(EtATSC)_3$, **2**, with DNA, RNR and HSA.



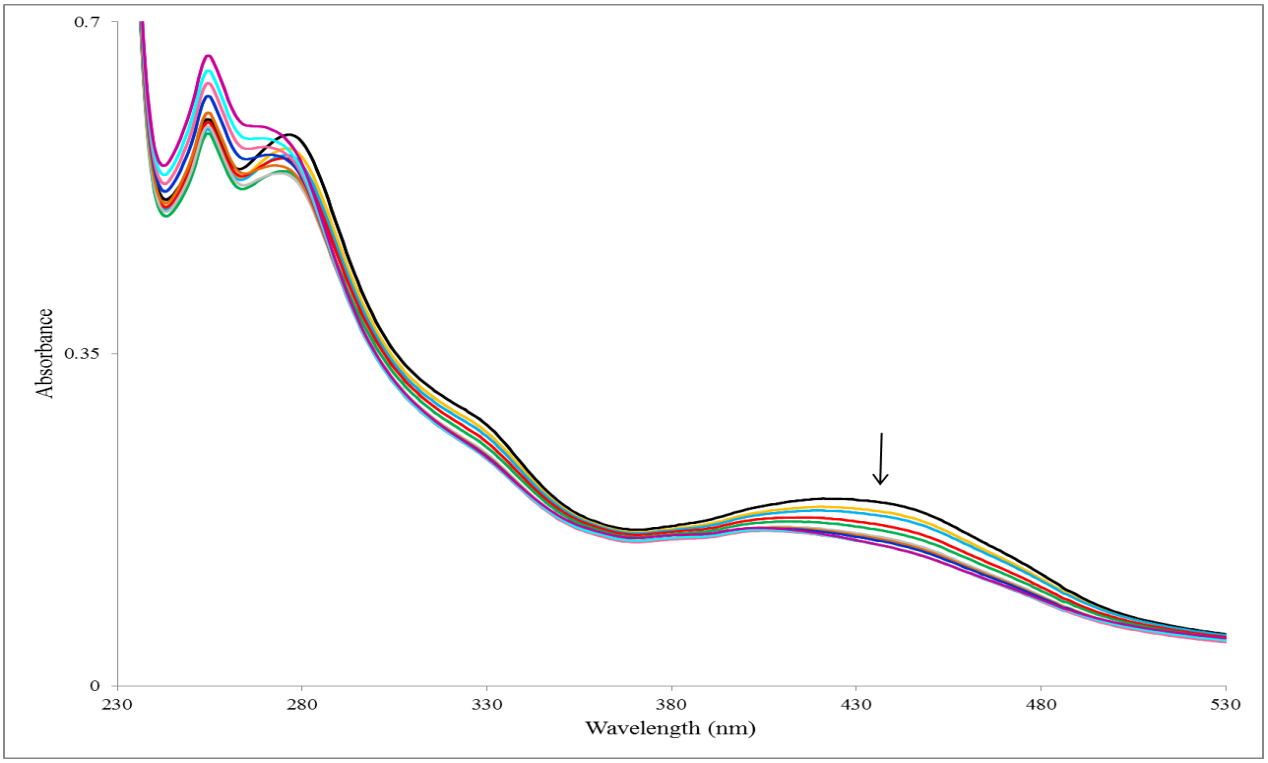
Docked poses for the interaction of $Ga(PhATSC)_3$, **3**, with DNA, RNR and HSA.



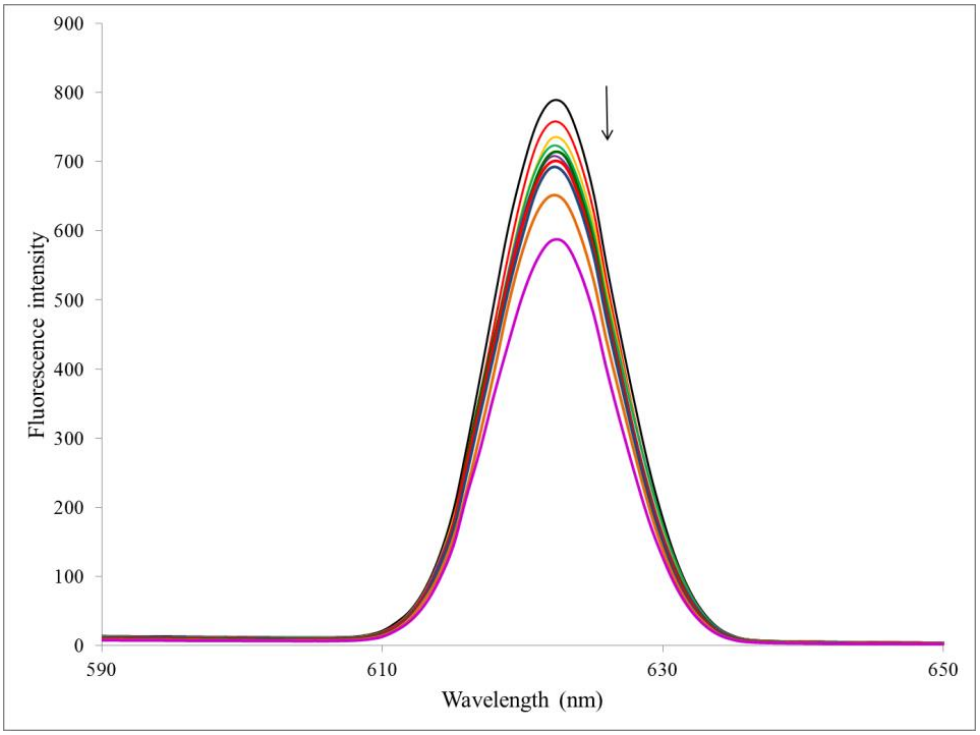
Binding groups involved in the docked poses for the interaction of $Ga(PhATSC)_3$, **3**, with DNA, RNR and HSA.



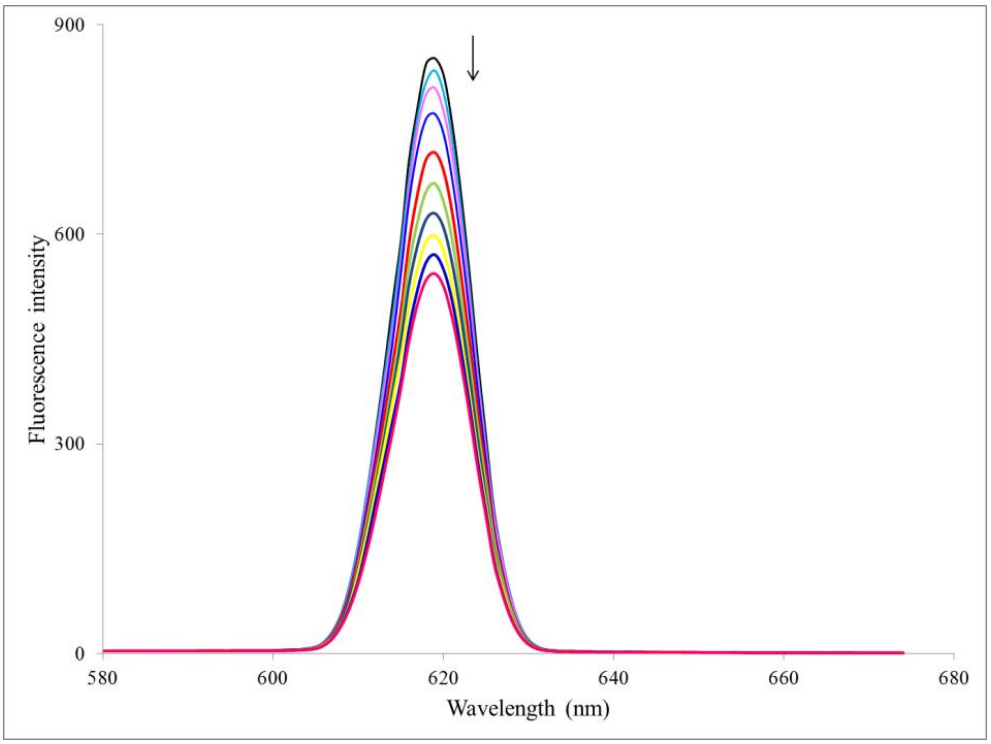
Electronic absorption spectral changes of complex **2** on titration with ct-DNA. [Ga] = 100 μM, [DNA] = 0 - 19 μM. Arrow indicates the change upon increasing DNA concentration



Electronic absorption spectral changes of complex **3** on titration with ct-DNA. [Ga] = 100 μM, [DNA] = 0 - 20 μM. Arrow indicates the change upon increasing DNA concentration.



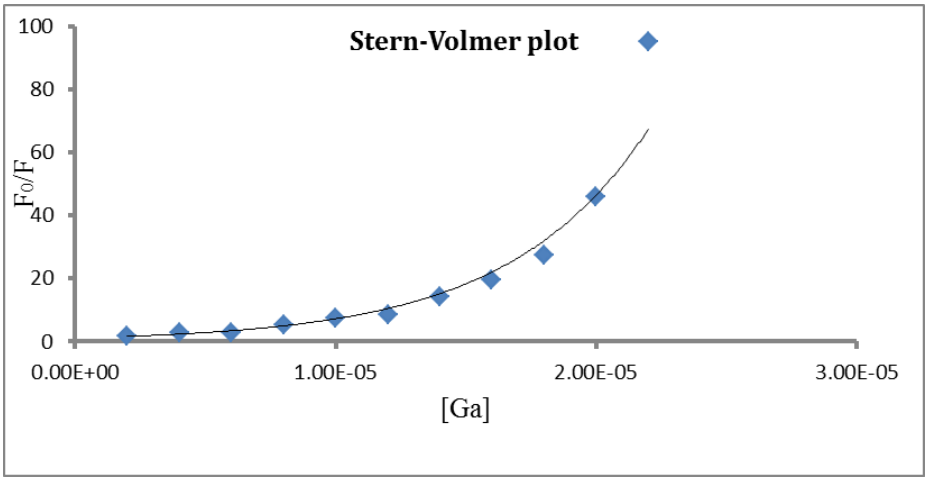
Emission spectra of complex **2** in the absence and presence of increasing amounts of ct-DNA, λ_{ex} = 311 nm, [**2**] = 10 μM, [DNA] = 0, 2, 4, 6, 10, 18, 22, 26, 28, 30, 32 μM. Temperature = 303 K.



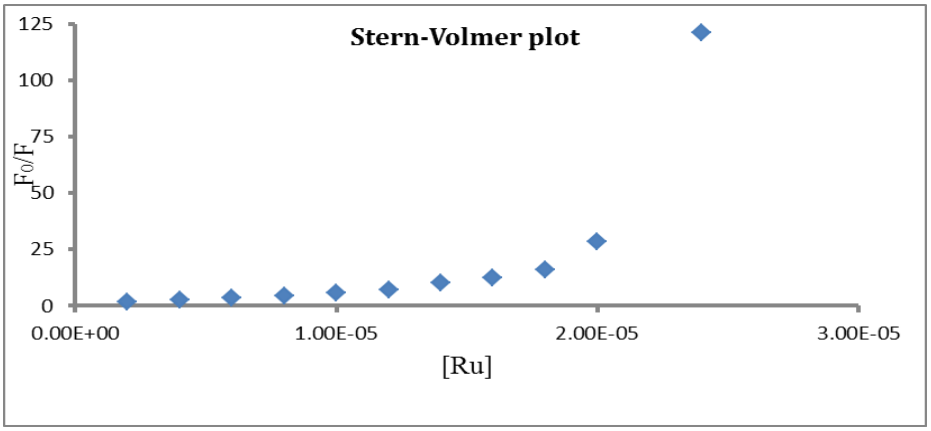
Emission spectra of complex **3** in the absence and presence of increasing amounts of ct-DNA, λ_{ex} = 311 nm, [**3**] = 10 μM, [DNA] = 0, 4, 6, 8, 10, 12, 14, 16, 18, 20 μM. Temperature = 303 K.

Reaction of HSA with the complexes:

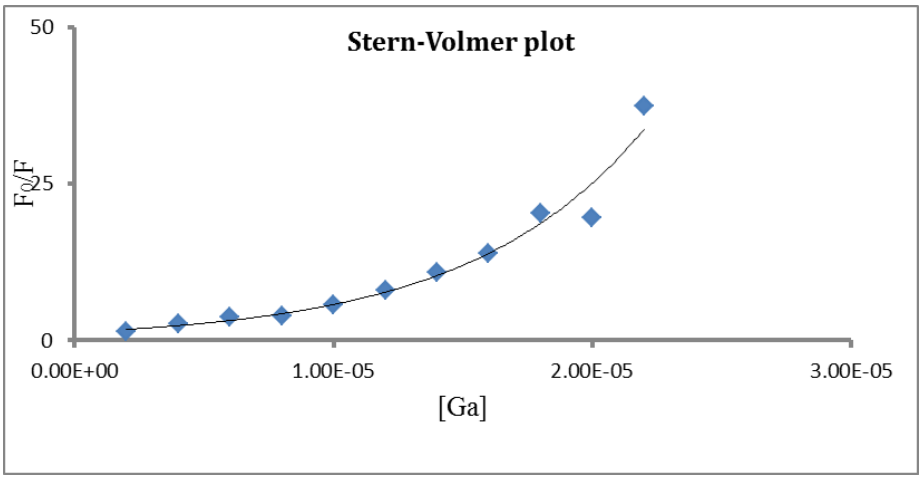
1 at 308K



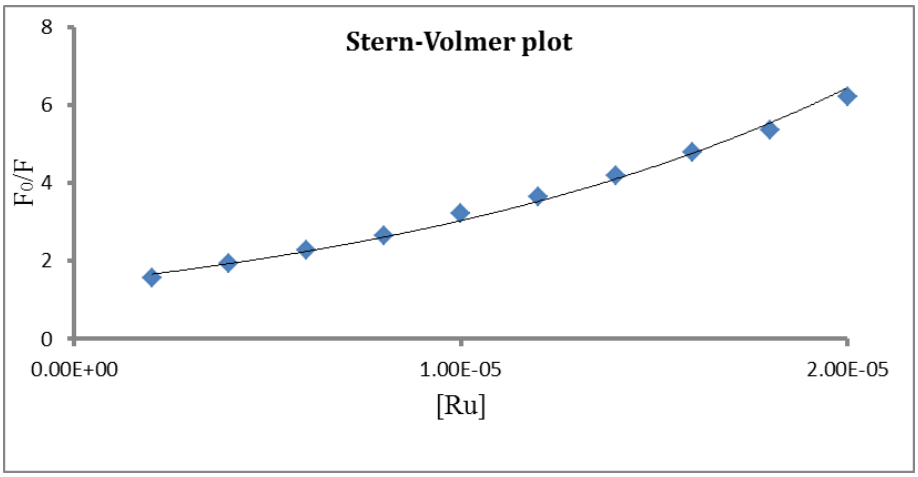
2 at 298K



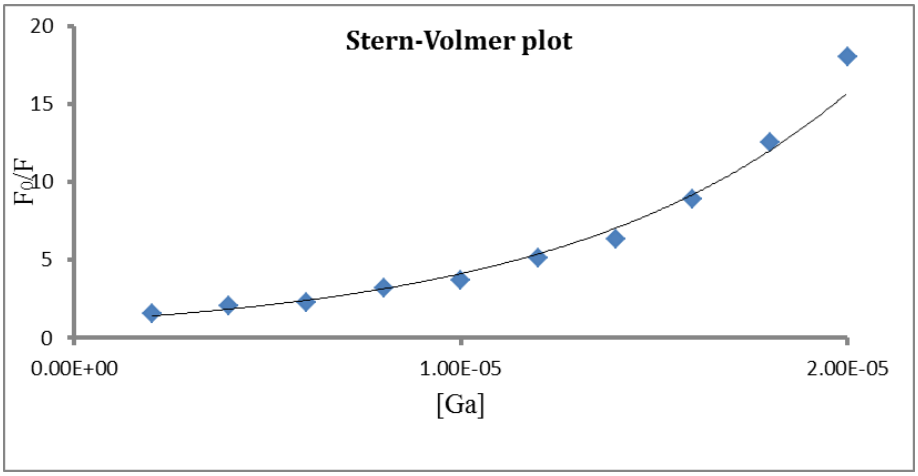
2 at 303K



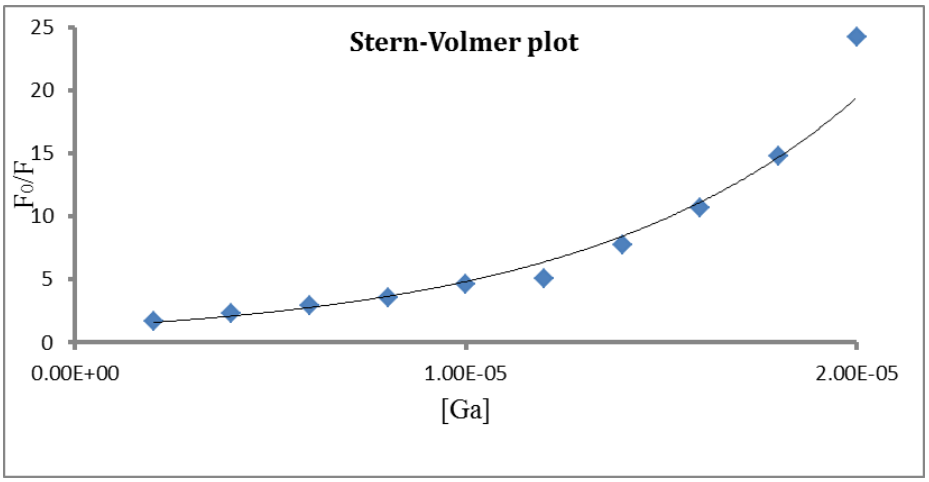
3 at 298K

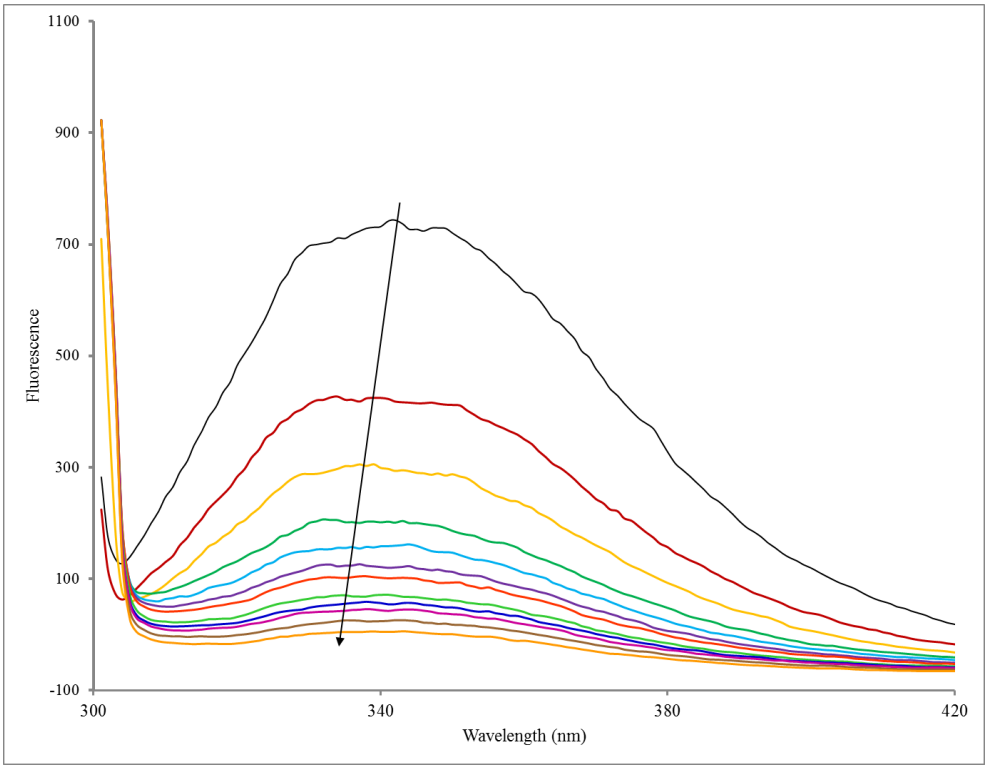


3 at 303K

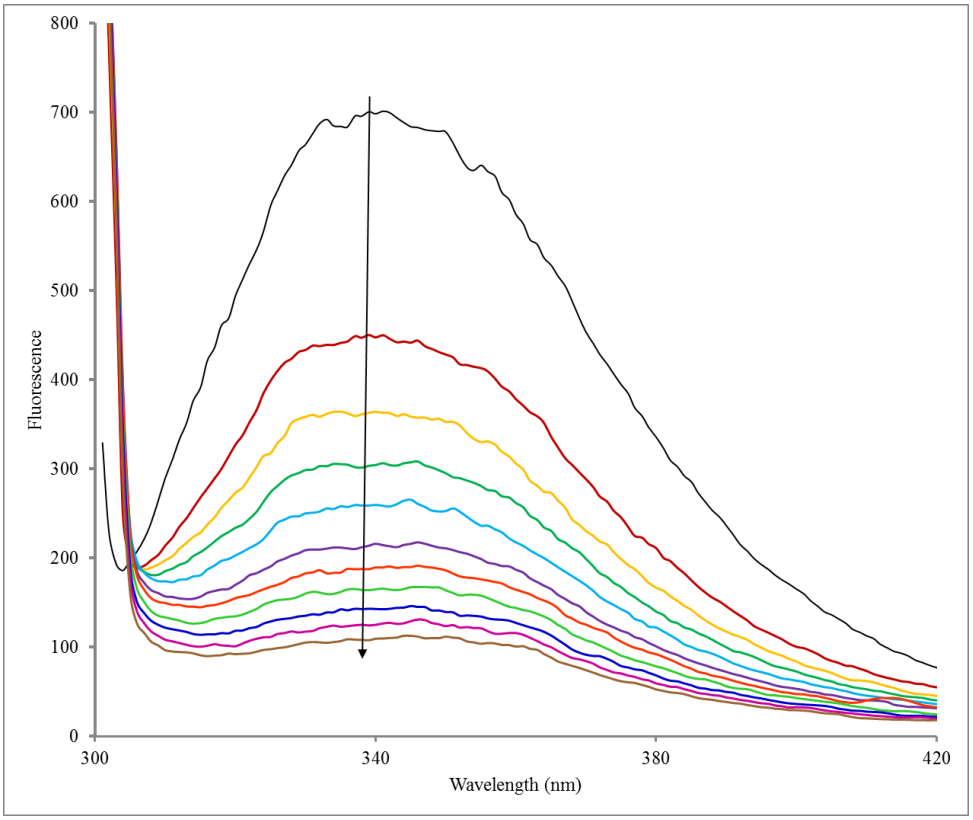


3 at 308K

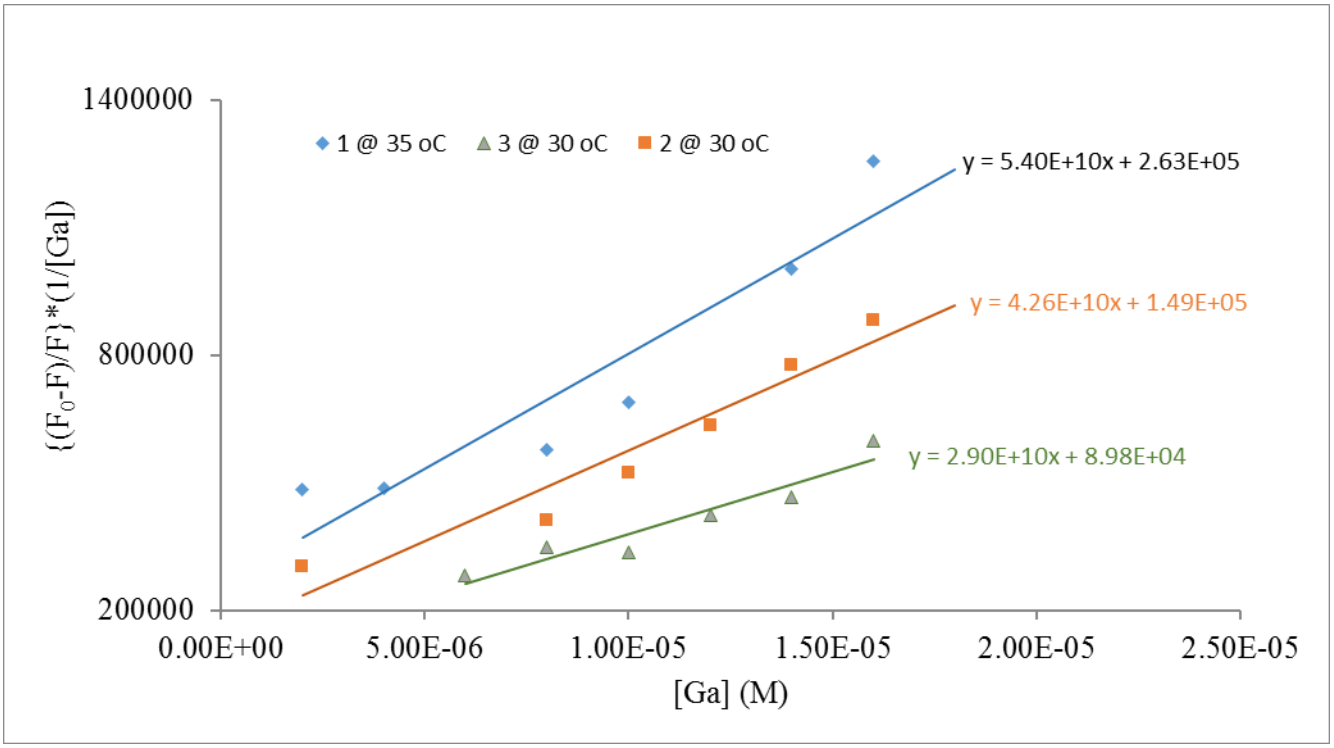




Emission spectra of HSA in the presence of various amounts of **2**.



Emission spectra of HSA in the presence of various amounts of **3**.



Analysis of the titration data according to equation 4 in text