Supplementary Material (ESI) for Chemical Communications
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Supplementary Information

Methionine Ligand selectively promotes monofunctional adducts between *Trans-EE* platinum anticancer drug and Guanine DNA base

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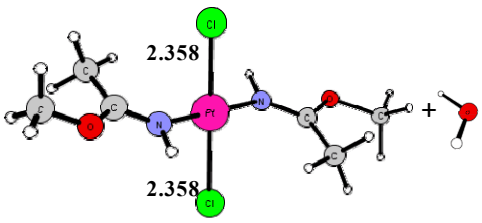
Computational Details

All calculations were performed with the Gaussian 03 [1] program at the density functional theory level, using the hybrid B3LYP functional, composed of Becke's [2] three-parameter hybrid exchange functional (B3) and the correlation functional of Lee, Yang, and Parr (LYP). [3] Geometry optimizations without symmetry constraints were carried out with a 6-31G(d) basis set for all atoms except the platinum atom, which was described by the quasi-relativistic Stuttgart-Dresden pseudopotentials [4] with the pseudo-orbital basis set augmented by a set of diffuse functions, α_s=0.0075, α_p= 0.013, and α_d=0.025, and polarization functions, α_f=0.98. [5] In order to confirm proper convergence to equilibrium and transition state geometries, vibrational frequency analysis was done on the basis of analytical second derivatives of the Hamiltonian at this level of theory. Solvent effects (ε = 80) were taken into account by the CPCM method [6] and using Klamt radii for constructing the solute cavity. [7] More accurate energies were obtained in gas phase and in solvent by performing single point calculations with the larger basis set 6-31++G(2df,2pd).

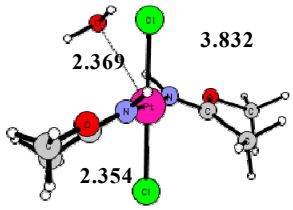
Figure -S2-

Optimized structures and selected structural parameters of the stationary points along the hydrolysis reaction paths; a) *Trans-EE* and b) *Trans-EE/Met;*

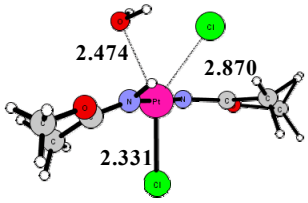
a)



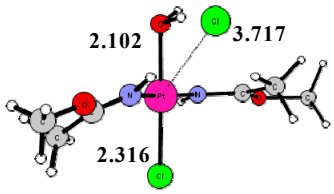
Separated Reagents (R)



Intermediate (INT_1)



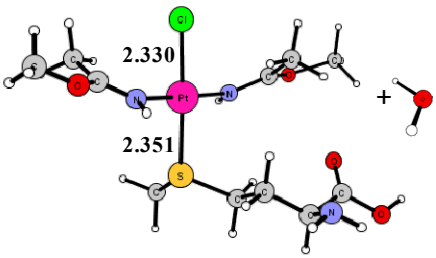
Transition State (TS_1)



Product (P)

Imaginary frequency: -151.595*i* cm $^{-1}$

b)



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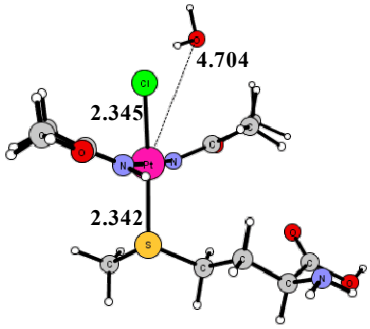

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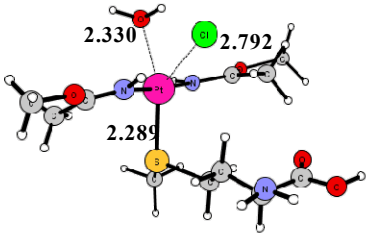
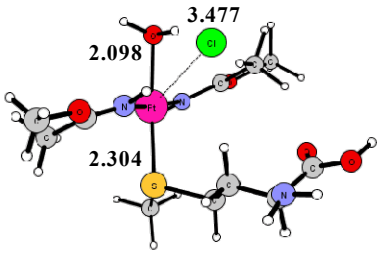


Transition State (TS_1)



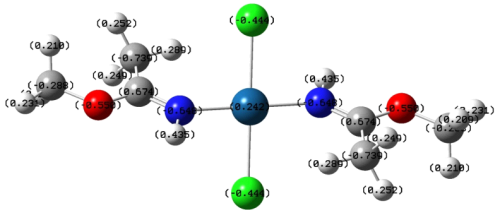
Product (P)

Imaginary frequency: -111.195*i* cm $^{-1}$

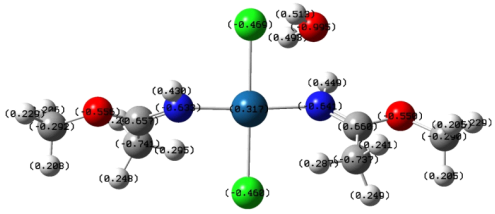
Figure -S3-

Natural Bond charges of the stationary points located along the hydrolysis paths for a) *Trans-EE* and b) *Trans-EE/Met* complexes;

a)



Reagent (R)



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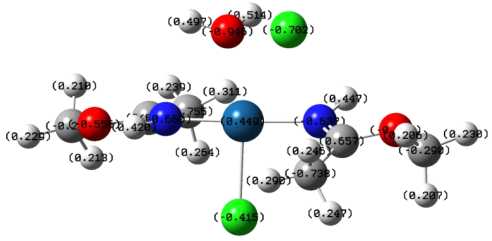
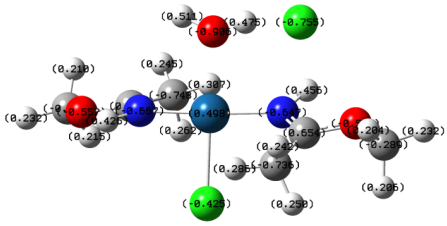
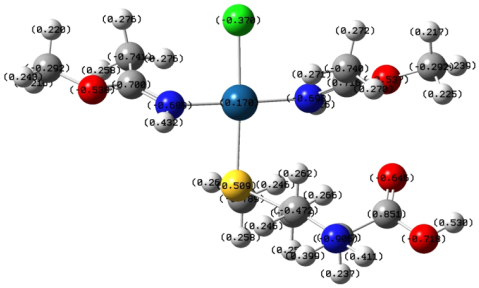


Transition State (TS_1)

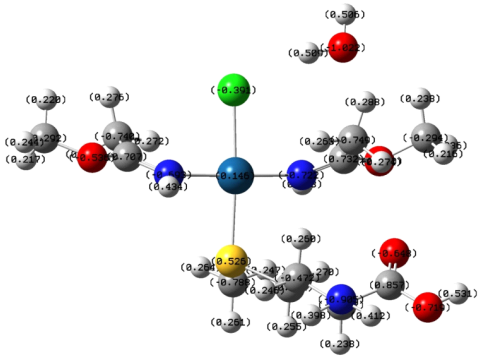


Product (P)

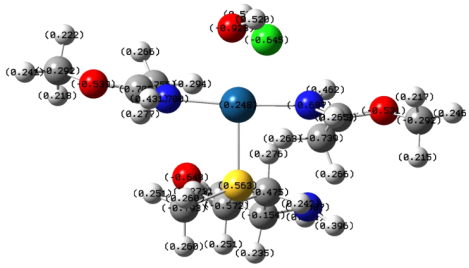
b)



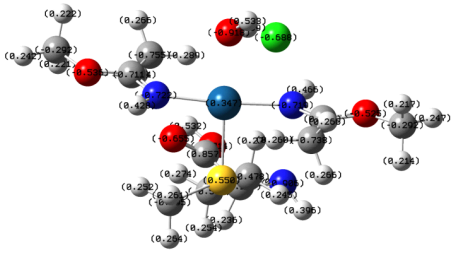
Reagent (R)



Intermediate (INT_1)



Transition State (TS_1)



Product (P)

Figure -S4-

Selected calculated Wiberg bond index for Pt-$Cl_{leaving\ group}$ and Pt-O_{water} during the hydrolysis reactions for a) *Trans-EE* and b) *Trans-EE/Met* complexes;

	Pt-Cl(leaving)			*Pt-O(water)*		
	***INT*$_1$**	**TS$_1$**	**P**	***INT*$_1$**	**TS$_1$**	**P**
Trans-EE	0.6798	0.3227	0.0333	0.0089	0.2037	0.3981
Trans-EE/Met	0.7265	0.3934	0.0772	0.0022	0.2677	0.3934

Figure -S5-

Homo-Lumo molecular orbital plots for the stationary points along the hydrolysis reaction path for *Trans-EE* compound. a) Reactant b)Transition state c) Product

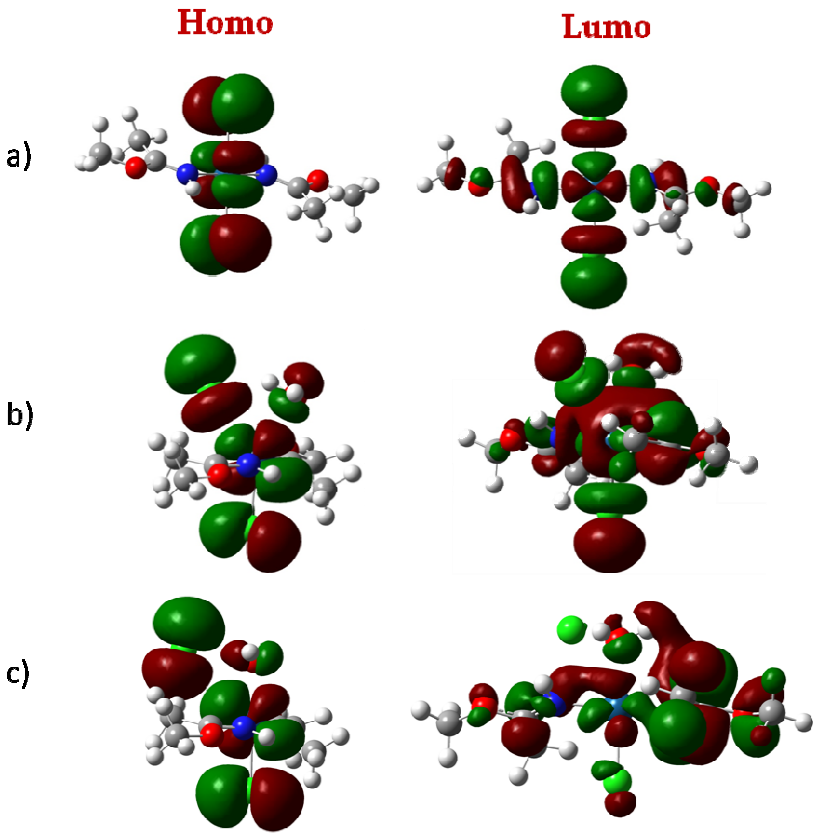


Figure -S6-

Homo-Lumo Molecular orbital plots for the stationary points along the hydrolysis path for *Trans-EE/Met* compound. a) Reactant b)Transition state c) Product

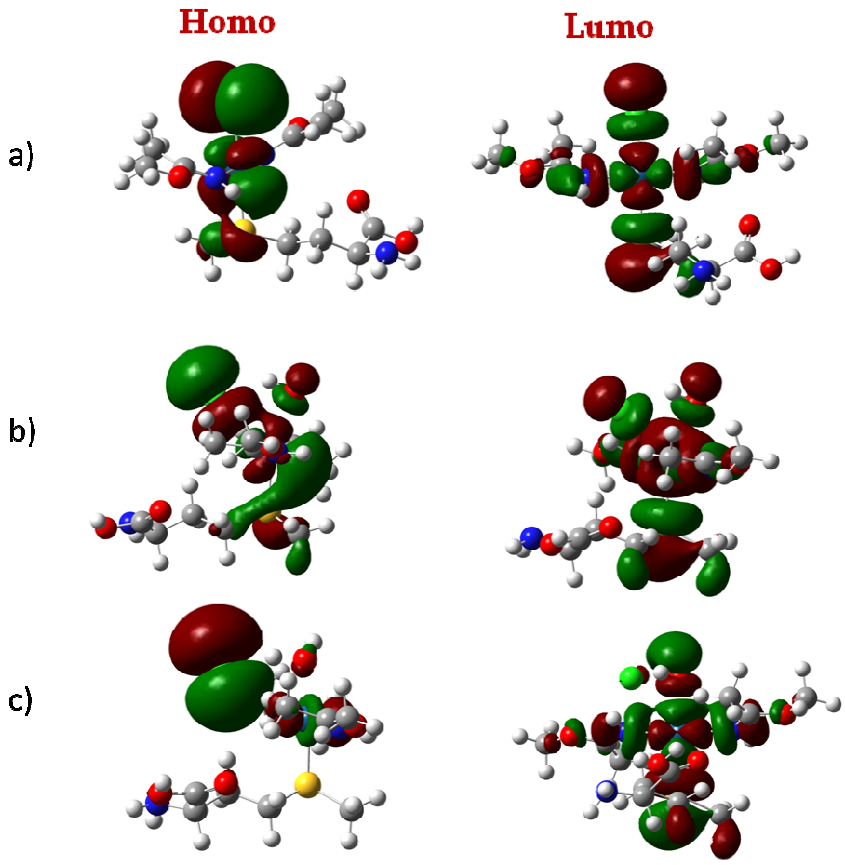
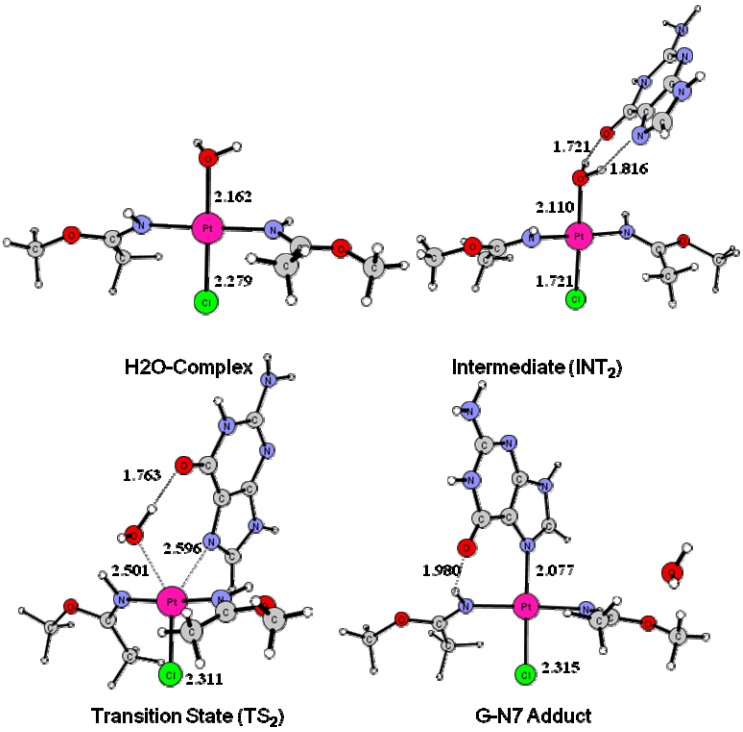


Figure -S7-

Optimized structures and selected geometric parameters of the stationary points for the binding of Guanine base to a) *Trans-EE and b)Trans-EE/Met;*

a)



b)

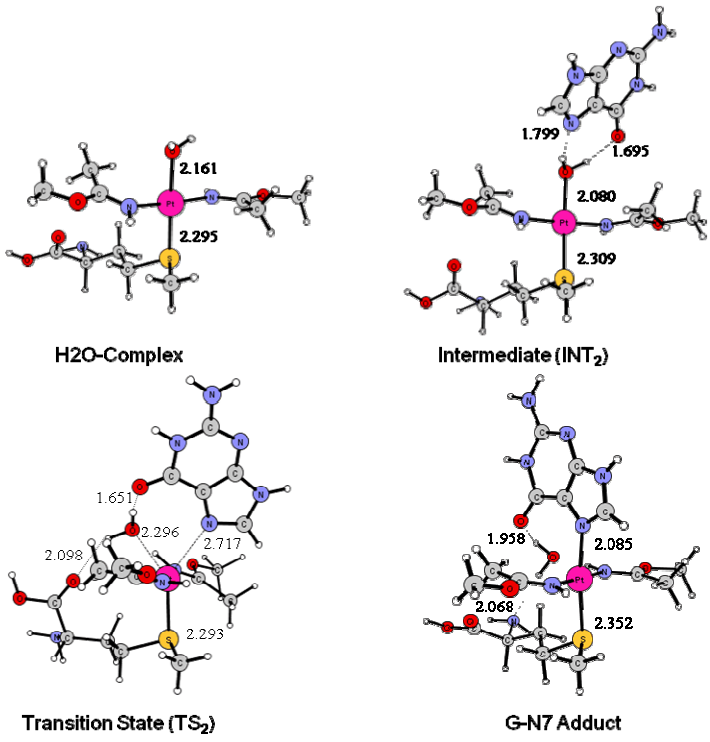


Figure -S8-

Homo-Lumo molecular orbital plots and G-N7 lone-pairs energies for a)*Trans-EE* and b) *Trans-EE/Met* transition state structures;

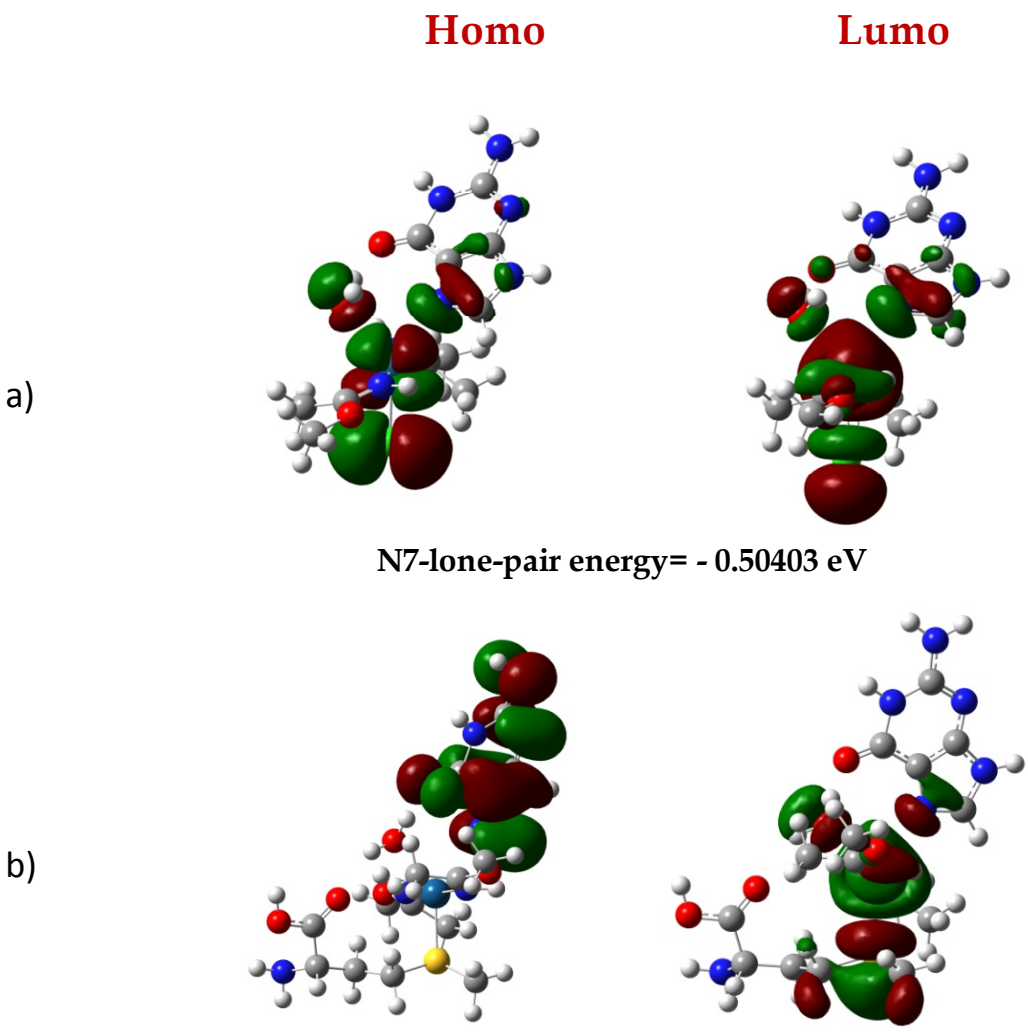
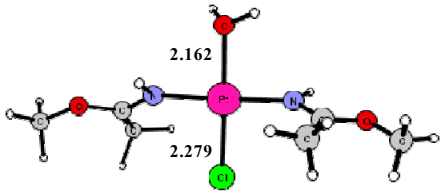


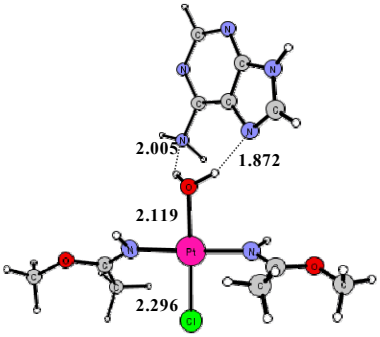
Figure -S9-

Optimized structures and selected geometric parameters of the stationary points for the binding of Adenine base to a)*Trans-EE* and b) *Trans-EE/Met;*

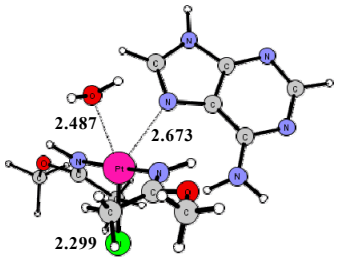
a)



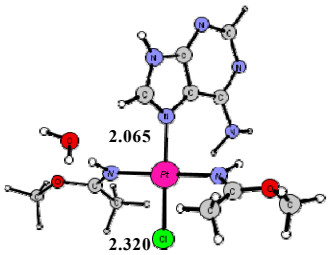
H2O-Complex



Intermediate (INT_2)

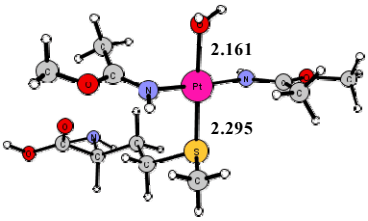


Transition State (TS_2)

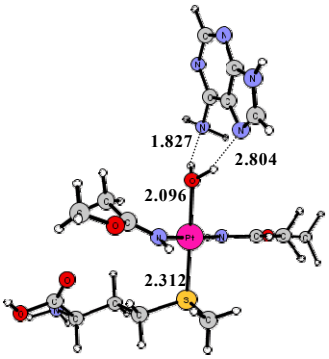


A-N7 Adduct

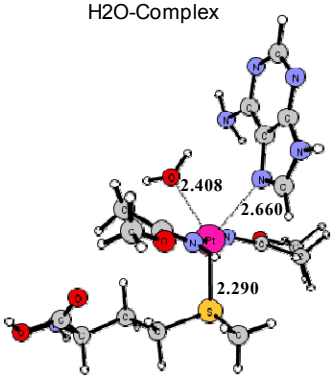
b)



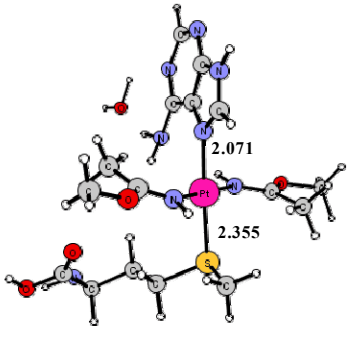
H2O-Complex



Intermediate (INT_2)



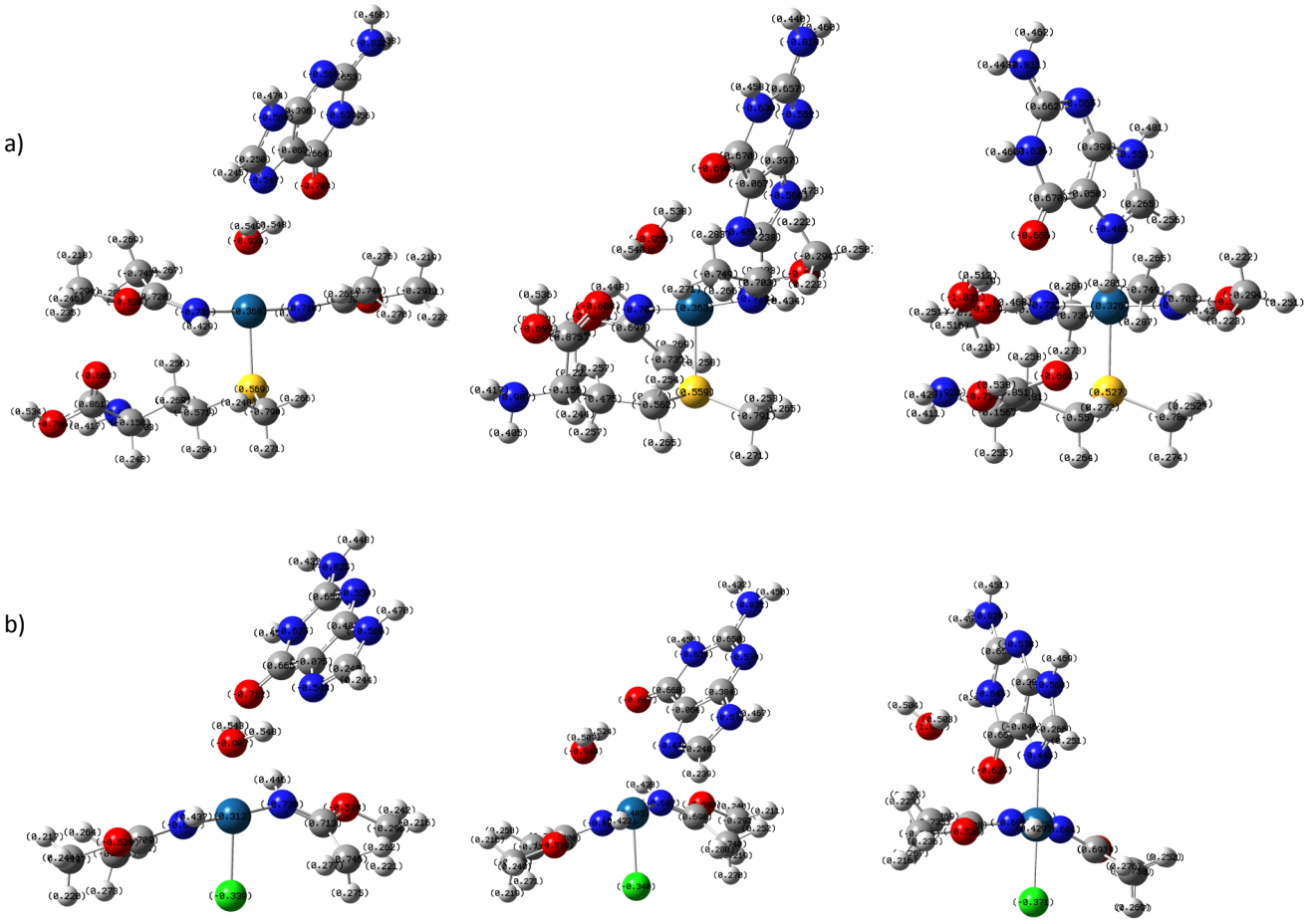
Transition State (TS_2)



A-N7 Adduct

Figure -S10-

Natural Bond charges of the stationary points of the reaction with Guanine base a) *Trans-EE* and b) *Trans-EE/Met* complexes;



References

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