Supplementary Information

Fate of cisplatin and its main hydrolysed forms in the presence of thiolates: a comprehensive computational and experimental study

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For any inquiry regarding optimised structures of the systems shown in this work, please contact the corresponding author (Bruno Cardey - *bruno.cardey@univ-fcomte.fr*).

A. Raman experimental setup

The Raman spectroscopy experimental setup includes a Spectra Physics Nd:YAG laser model LAB-170-10 delivering pulses with a duration of about 5 ns at a repetition rate of 10 Hz. The spectra were recorded using the second harmonic emission wavelength (532 nm). The samples were placed in a 1 cm x 1 cm quartz cell and were irradiated with a 10 mm diameter laser beam at an equivalent power density of 30 mW.mm^{-2}. The scattered light was detected at 90 degrees using a Roper Scientific spectroscopy system including a Spectra Pro 2500i monochromator with a maximum resolution of 0.035 nm and a PIMAX-1024-RB CCD camera (Princeton Instruments). The camera intensifier was synchronously gated over the laser pulse duration in order to maximize the signal to noise ratio. The Rayleigh scattered light was eliminated using a notch filter with a 300 cm^{-1} bandwidth and an optical density at 532 nm of 6. The system wavelength calibration was tested by detecting the N_2 Raman band at 2331 cm^{-1} which was reproduced with an error of less than 1 cm^{-1}.

B. Full input file including the optimised structure of TS45 (double job: DFT optimisation and frequencies, followed by MP2 optimisation)

```
%nprocshared=16
%mem=4GB
%chk=TScys-nh3cysnbid.chk
# b3lyp/genecp opt(TS,noeigentest,calcfc) freq scrf=read

preopt2

-1 1
Pt      -0.674019000     -0.798108000      0.086227000
N        0.445925000     -1.945076000      1.745168000
H        0.027684000     -2.845094000      1.989819000
H        1.396522000     -2.125534000      1.408867000
N       -0.765184000     -2.568482000     -1.028140000
H        0.178210000     -2.952171000     -1.132401000
H       -1.337676000     -3.294593000     -0.591123000
H        0.513493000     -1.411378000      2.614705000
H       -1.128830000     -2.437768000     -1.974651000
S       -0.642284000      1.077076000      1.318295000
H       -1.813904000      2.446940000     -0.317035000
H       -2.512622000      2.626283000      1.326383000
C       -2.111023000      1.905652000      0.598160000
C       -3.159572000      0.858668000      0.244480000
N       -2.486964000     -0.183911000     -0.596612000
C       -4.322845000      1.518565000     -0.537561000
O       -4.240860000      1.463044000     -1.807206000
H       -3.526970000      0.365367000      1.156479000
O       -5.214412000      2.083330000      0.165672000
H       -3.130617000     -0.977649000     -0.678292000
H       -2.453368000      0.221684000     -1.542106000
S        1.775459000     -0.688556000     -0.773735000
C        2.582695000      0.391649000      0.448816000
H        2.285266000      0.078425000      1.466816000
H        2.237899000      1.431149000      0.312870000
C        4.113359000      0.370558000      0.365119000
N        4.622171000      1.322856000      1.425257000
H        4.042368000      1.336144000      2.270408000
H        5.588140000      1.119404000      1.700784000
O        4.661036000      2.235136000     -0.997224000
C        4.647758000      0.956762000     -0.972666000
O        5.003291000      0.147057000     -1.868610000
H        4.520265000     -0.628222000      0.568744000
H        4.608946000      2.246439000      0.947643000

H  N  C  O  0
aug-cc-pvdz
****
```

```
S  0
aug-cc-pvtz
****
Pt 0
sdd
****
Pt     0
F   1   1.00
      0.44300000              1.0000000
F   1   1.00
      1.323000              1.0000000
****

Pt  0
sdd

ModifySph

Pt 2.021
S 1.8

--Link1--
%nprocshared=16
%mem=4GB
%chk=TScys-nh3cysnbid.chk
# mp2/genecp genchk guess=read scrf=check opt(TS,noeigentest,readfc) geom=allcheck
```

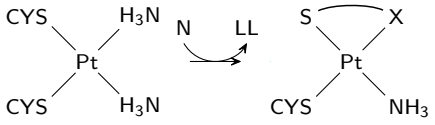
C. Full input file including the optimised structure of TS1 with glutathione (ONIOM calculation)

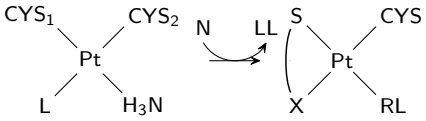
```
%nprocshared=16
%mem=4GB
# opt(TS,noeigentest,calcfc,Maxcycles=60,Maxstep=15) freq ONIOM(mp2/genecp:b3lyp/
genecp) scrf=read scf=xqc

Title Card Required

-2 1  -1 1  -1 1
Pt      -2.996864000     -1.487320000     -0.032849000  H
N       -4.447155000     -0.338870000      0.761319000  H
H       -4.321094000      0.631525000      0.458760000  H
H       -5.410989000     -0.612277000      0.556352000  H
N       -4.301505000     -2.422688000     -1.303903000  H
H       -5.042133000     -2.945062000     -0.831385000  H
H       -4.750144000     -1.772496000     -1.952881000  H
H       -4.323877000     -0.358730000      1.778632000  H
H       -3.771750000     -3.094623000     -1.865662000  H
Cl      -1.347519000     -2.862454000     -0.924571000  H
C        6.590568000     -1.265323000     -0.467740000  L
H        7.220051000     -0.403145000     -0.696025000  L
C        5.132285000     -0.980873000     -0.861333000  L
H        5.073770000     -0.894055000     -1.951726000  L
H        4.502037000     -1.829759000     -0.567018000  L
C        4.582610000      0.314651000     -0.250766000  L
H        5.249945000      1.149577000     -0.502655000  L
H        4.557147000      0.246808000      0.838634000  L
C        6.775017000     -1.671591000      1.032332000  L
C        3.209605000      0.664187000     -0.818370000  L
O        2.964509000      0.578166000     -2.032498000  L
O        7.036360000     -2.899014000      1.223428000  L
O        6.638245000     -0.763558000      1.879338000  L
N        7.110104000     -2.444808000     -1.263294000  L
H        6.490720000     -2.739213000     -2.020766000  L
H        8.036397000     -2.275969000     -1.659457000  L
N        2.302913000      1.104233000      0.084683000  L
H        2.547859000      1.128169000      1.066920000  L
C        0.942354000      1.532791000     -0.255166000  L H 30 1.0 1.0
C       -0.055126000      0.390791000     -0.035720000  H
H        0.295709000     -0.490597000     -0.599613000  H
H       -0.085086000      0.113010000      1.031261000  H
C        0.636562000      2.749799000      0.631777000  L
O        0.817611000      2.685622000      1.862244000  L
H        0.948900000      1.817574000     -1.309633000  L
N        0.201451000      3.852861000      0.006597000  L
H        0.045416000      3.867582000     -0.997095000  L
C       -0.172521000      5.086964000      0.676948000  L
```

```
H       -0.979635000      4.906909000      1.397371000  L
H        0.675322000      5.491997000      1.240695000  L
C       -0.646600000      6.143010000     -0.352312000  L
O       -0.966419000      7.263371000      0.130510000  L
O       -0.673600000      5.793608000     -1.567049000  L
H        7.184465000     -3.190519000     -0.526232000  L
S       -1.767724000      0.764087000     -0.582237000  H
Cl      -1.985827000     -1.388618000      2.290807000  H

H  N  C O Cl 0
6-31++G(d,p)
****
S 0
6-311++G(d,p)
****
Pt 0
sdd
****
Pt     0
F   1   1.00
      0.44300000              1.0000000
F   1   1.00
      1.323000              1.0000000
****

Pt  0
sdd

ModifySph

Pt 2.021
S 1.8

H  N  C  O  Cl 0
aug-cc-pvdz
****
S 0
aug-cc-pvtz
****
Pt 0
sdd
****
Pt     0
F   1   1.00
      0.44300000              1.0000000
F   1   1.00
      1.323000              1.0000000
****

Pt  0
```

```
sdd

H  N  C O Cl 0
6-31++G(d,p)
****
S 0
6-311++G(d,p)
****
Pt 0
sdd
****
Pt     0
F   1   1.00
      0.44300000              1.0000000
F   1   1.00
      1.323000              1.0000000
****

Pt  0
sdd
```

D. Thermodynamical data for $B_{2,1}$ S,O (and S,N) bidentations

		S,X bidentation	
LL	#reac	(CysO)	(CysN)
NH_{3trans}	26	**21,7** *6,8*	**18,1** *-4,2*

			S,X bidentation	
L	LL	#reac	(CysO)	(CysN)
Cl^-	Cl^-	27	**17,4** *1,9*	**12,1** *-11,3*
	NH_{3trans}	28	**19,2** *8,3*	**14,2** *-7,9*
OH^-	OH^-	29	**26,8** *15,8*	**17,3** *-0.3*
	NH_{3trans}	30	**21,5** *7,0*	**14,6** *-9,9*
H_2O	H_2O	31	**7,6** *-13,5*	**17,0** *-16,5*
	NH_{3trans}	32	**19,1** *5,7*	**13,0** *-8,1*

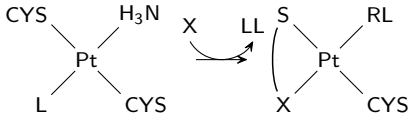
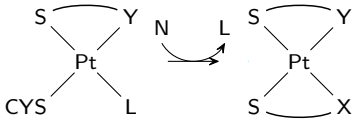
			S,X bidentation	
L	LL	#reac	(CysO)	(CysN)
Cl^-	Cl^-	33	**10,4** *-5,6*	**11,6** *-18,1*
	NH_{3cis}	34	**23,8** *5,8*	**21,7** *-10,8*
OH^-	OH^-	35	**4,9** *9,2*	**26,5** *-1,8*
	NH_{3cis}	36	**15,1** *1,0*	**26,5** *-7,8*
H_2O	H_2O	37	**3,6** *-24,5*	**2,1** *-32,7*
	NH_{3cis}	38	**23,8** *1,7*	**24,6** *-8,7*

Table 1 Gibbs free energy barriers (in bold) and Gibbs free energies of reaction (in italics) of bidentation $B_{2,1}$, given in kcal.mol^{-1}. The different parts refer to the type of reactant.

E. Thermodynamical data for $B_{2,2}$ S,O (and S,N) bidentations

			S,X bidentation	
Y	L	#reac	(CysO)	(CysN)
COO^-	Cl^-	55	**14,6** *-2,1*	**18,9** *-10,3*
	OH^-	56	**27,4** *13,2*	**24,2** *1,2*
	H_2O	57	**3,6** *-14,9*	**9,7** *-25,0*
	NH_{3trans}	58	**20,7** *4,3*	**18,8** *-7.4*
NH_2	Cl^-	59 / 47	**17,9** *-1,3*	**17,1** *-13,2*
	OH^-	60 / 48	**29,2** *11,9*	**25,2** *-0,5*
	H_2O	61 / 49	**4,8** *-17,0*	**10,5** *-26,9*
	NH_{3trans}	62 / 50	**19,6** *1,9*	**20,6** *-9,0*

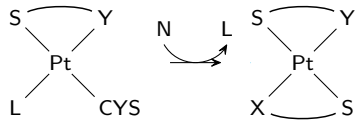
			S,X bidentation	
Y	L	#reac	(CysO)	(CysN)
COO^-	Cl^-	63	**26,1** *-4,9*	**19,5** *-16,5*
	OH^-	64	**40,5** *14,7*	**30,5** *-1,7*
	H_2O	65	**12,9** *-20,3*	**9,1** *-35,6*
	NH_{3cis}	66	**35,3** *6,5*	**24,2** *-10,0*
NH_2	Cl^-	67 / 51	**24,8** *-3,1*	**19,7** *-17,8*
	OH^-	68 / 52	**34,5** *10,9*	**36,9** *4,8*
	H_2O	69 / 53	**8,2** *-19,0*	**13,7** *-30,8*
	NH_{3cis}	70 / 54	**26,7** *4,9*	**26,2** *-8,8*

Table 2 Gibbs free energy barriers (in bold) and Gibbs free energies of reaction (in italics) of bidentation $B_{2,2}$, given in kcal.mol^{-1}. Part I (above) refers to the cis reactant and part II to the trans reactant.