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A DFT/ECP-Small Basis Set Modelling of Cisplatin: Molecular Structure and Vibrational Spectrum

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ABSTRACT

A DFT conformational and vibrational analysis of a single molecule of cisplatin (*cis*-[Pt(NH$_3$)$_2$Cl$_2$]) was performed by means of PW91 functional and LANL08 ECP basis set for the Pt atom. 3-21G and 3-21G* Basis sets were used for the remaining atoms. All the initially chosen conformations were found to converge to the global minimum conformation of C_{2v} symmetry with H atoms lying in the coordination plane and pointing to the Cl atoms. The computational results were compared with the newest experimental structural data and with the vibrational spectroscopic data for cisplatin, obtained by other workers. The chosen level of theory was found to describe satisfactory the molecular structure (r. m. s. of the relative deviations $\leq$ 6%) and the harmonic vibrational frequencies (r. m. s. of the relative deviations $\leq$ 5%) of cisplatin.

Keywords: Cisplatin; DFT Calculations; Basis Set; Effective Core Potential; Molecular Structure; Vibrational Analysis

1. Introduction

Cisplatin (*cis*-diamminedichloroplatinum(II)) is the first inorganic compound introduced in clinical use for the treatment of cancer [1-4]. It is a prototype of several thousands platinum [5-12] and other metal [6,8,9,13-16] coordination compounds synthesized and tested so far in the search for novel cytostatic agents with improved therapeutic characteristics with respect to the parent compound. Among them, only five more Pt(II) complexes—carboplatin, oxaliplatin, nedaplatin, lobaplatin and heptaplatin—have gained international or local marketing approval [8,17]. At present, cisplatin remains amongst the most widely used platinum chemotherapeutics, with particular effectiveness in the treatment of testicular, ovarian and bladder cancer [9,18,19].

Quantum-chemical studies of the molecular and electronic structure, and prediction of spectroscopic characteristics of pharmacologically active compounds, have always been challenging for computational chemists. Moreover, such data are quite useful for better understanding the reactivity of the drugs with physiological target molecules. Cisplatin molecule has been studied at different levels of theory using the Effective Core Potential [20] (ECP) approximation: Hartree-Fock (HF) [21-24], Møler-Plesset (MP) [22,23] and Density Functional Theory (DFT) [22-25], as well as by the all-electron DFT approach [26]. The small molecule of cisplatin serves as a useful example for testing the computational accuracy and effectiveness of different computational schemes in predicting molecular geometry and vibrational frequencies [22-25].

Although the vibrational spectra of cisplatin have been studied by many researchers [22-25,27-29], the assignment of some low-frequency bands is ambiguous. Curiously, for more than forty years, the only available experimental structure of cisplatin was that of Milburn and Truter of 1966 [30]. Last year, Weller *et al*. [31] published a re-examination of the crystal structure of cisplatin, and showed that it exists in two polymorphic modifications. They found, *inter alia*, that the values of the Pt-N bond lengths were underestimated in the earlier study. Moreover, Weller *et al*. firstly located the positions of the hydrogen atoms by neutron powder diffraction, thus revealing the orientation of the NH$_3$ groups with respect to the coordination plane.

The appearance of the more detailed and accurate structural data prompted us to perform a DFT analysis of cisplatin molecule and to compare our computational results with the new experimental data, as well as with the computational results published earlier. There is no uniform opinion in the literature concerning the optimal combination of basis sets and density functional for reproducing the structural parameters and vibrational frequencies of cisplatin. Thus, Wysokiński and Michalska [22] claim the combination of mPW1PW functional [32] and LANL2DZ basis [33-36] (all atoms) to be among the best performing theory level for predicting both geome-

try optimization and vibrations; Amado *et al.* [24] also recommend mPW1PW functional for structural and vibrational calculations. Regarding the basis sets, the combination of LANL2DZ [36] (Pt), LANL2MB [35,37] (N and Cl) and 3-21G [38,39] (H) has given the best vibrational results, whereas LANL2DZ (Pt)/CEP-4G (N and Cl)/3-21G (H) has produced the best structural parameters. Finally, Gao *et al.* [25] have found the combinations LSDA functional [40]/SDD basis set [33,41] and PBE-1PBE [42]/SDD to give the best results for structural and vibrational calculations, respectively.

Here we present our computational results on the geometry optimization and vibrational analysis of a single cisplatin molecule obtained with the Perdew-Wang exchange-correlation functional PW91 [43,44] and small basis sets for the Pt and the remaining atoms, and compare them with the new experimental data and with the computational results of other researchers.

2. Methods

The DFT calculations were performed on a personal computer (2.29 GHz, 2.96 GB RAM), as well as on a HPC Cluster Platform Express 7000 (36 blades BL 280 c, dual Intel Xeon X5560 at 2.8 GHz and 24 GB RAM per blade), using the Firefly quantum chemistry package [45], which is partially based on the GAMESS (US) [46] source code. All structures were optimized using the algorithm of direct inversion in the iterative subspace and gradient convergence tolerance of 1×10^{-5} Hartree/Bohr. The final values of the maximum and r. m. s. gradients were below 8×10^{-6} and 3×10^{-6} Hartree/Bohr, respectively. The optimized structures were further subjected to vibrational analysis at the same theory level, using numerical calculation of Hessian matrix elements (displacement size 1×10^{-3} Bohr). No negative eigenvalues were obtained, thus assuring that actual maxima on the potential energy surface were located. The Hessian matrix and the total energy distribution matrix were expressed in internal coordinates (the complete set of bond lengths, bond angles, torsion angles and out-of-plain angles). The vibrational modes were visualized by means of the Molekel programme [47]. The calculated vibrational wavenumbers were compared with the FT Raman data of Amado *et al.* [24] for solid cisplatin.

The PW91 functional [43,43] was used in the DFT calculations. The relativistic ECP and associated non-contracted basis set LANL08 [48] were used for Pt atom. The H and N atoms were described by the all electron split-valence 3-21G basis set [38,39]. For the description of the Cl atoms, the 3-21G basis set and the supplemented with *d*-type functions 3-21G* basis set [49] were applied. The ECP and the basis sets were taken from the EMSL Basis Set Exchange Library [50-52].

Initial conformations and their minimization. Four conformations (*a*, *b*, *b*⁻ and *c*) differing in the torsion angles H-N-Pt-Cl around one of the N-Pt bonds were considered (**Figure 1**). Their combination in couples gives seven non-eqivalent and non-enantiomorphic conformations as depicted in **Figure 2**. Each of these starting conformations were subjected to DFT minimization and all of them were found to converge to the *a,a* comformer (C_{2v} simmetry). The calculated molecular geometry was compared with the single crystal X-ray and neutron powder diffraction data of Weller *et al.* [31] for the two polymorphic modifications of cisplatin.

All calculations concern a single molecule in gas phase. Input and output files are deposited as Supplementary material.

3. Results and Discussion

3.1. Conformational Considerations

The initial structures of cisplatin (**Figure 2**) were minimized with the two protocols: PW91/LANL08/3-21G (A) and PW91/LANL08/3-21G* (B) (*vide supra*). All of
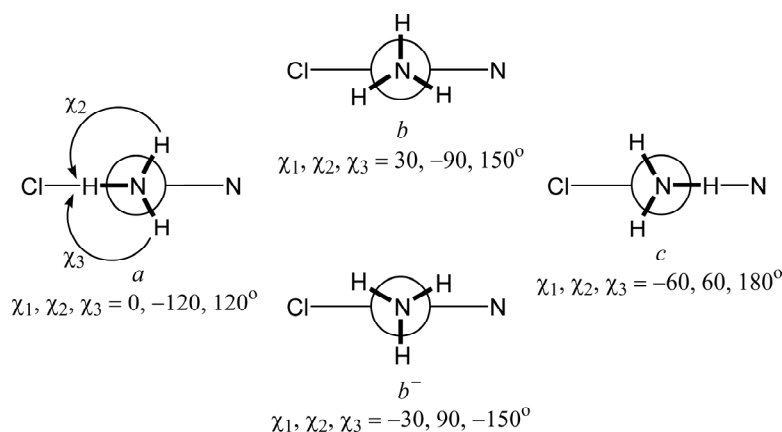

Figure 1. Newman projections along one of the N-Pt bonds for the conformations *a*, *b*, *b*⁻ and *c*, of cisplatin differing in the torsion angles χ_1, χ_2 and χ_3 (*b* and *b*⁻ are enantiomorphic).

them converged to the *a,a* conformer (**Figure 2**), with energies (corrected with the vibrational zero-point energy) of −1147.5051 and −1147.9213 Hartree, respectively. Thus, within the given level of theory, we found a single minimum on the potential energy surface of the cisplatin molecule. Amado *et al*. [23,24] have pointed out that the number of local minima (1, 2 or 3) varies with the combination of density functional and basis sets. In all cases, however, including all electron basis set DFT calculations [26], the lowest energy conformation is of the *a,a* type.

Methods A and B give the same set of torsion angles around the N-Pt bonds (0, −117, 117). The calculated torsion angles are compared (**Table 1**) with the experimental data of Weller *et al*. [31] about the *α*- and *β*-polymorphs of cisplatin, the later containing two crystallographically non-equivalent molecules. As seen, in the solid state the torsion angles vary considerably, and no one conformation resembles enough the gas-phase minimum-

energy conformation of *a,a* type. This is a consequence of the extended intermolecular H-bonding network of N-H···Cl type [31]. Thus, it seems in the solid state the conformational preferences are governed by the H-bonding rather than by the torsion potential.

3.2. Bond Lengths and Bond Angles

The bond lengths and bond angles calculated by computational methods A and B are compared with the averaged structural data for the two crystal modifications of cisplatin [31]. The relative deviations of the individual structural parameters, as well as the arithmetic mean (*s*) and root mean square deviations (*S*) are summarized in **Table 2**. The accuracy obtained by the chosen theory levels is similar to or slightly better than that reported by Amado *et al*. [23,24]. Adding *d*-orbitals on the Cl atoms (method B) gives somewhat better overall description of the bond lengths and angles. The application of method
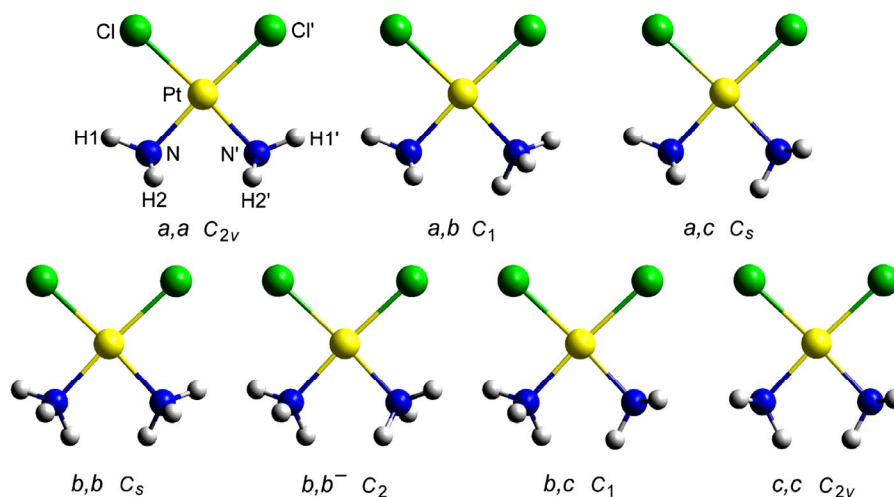

Figure 2. View of the seven non-equivalent and non-enantiomorphic conformations of cisplatin arising from the combination of the conformations *a*, *b*, *b̄* and *c* in couples. Each of them was subjected to DFT minimization.

Table 1. Torsion angles (deg) for cisplatin.

Torsion angle	Experimental[a]			Calcd. A[b]	Calcd. B[c]
	α-Poly-morph	*β*-Polymorph			
		Molec. *a*	Molec. *b*		
H1NPtCl	20.3	39.8	−37.5	0.0	0.0
H2NPtCl	−101.2	−98.2	81.9	−117.1	−117.1
H3NPtCl	130.4	142.5	−153.0	117.1	117.1
H1'N'PtCl'	−39.5	−9.6	16.8	0.0	0.0
H2'N'PtCl'	86.1	112.2	−106.2	117.1	117.1
H3'N'PtCl'	−154.7	−131.7	124.2	−117.1	−117.1

[a]Data from [31]; [b]Values calculated at PW91/LANL08/3-21G level; [c]Values calculated at PW91/LANL08/3-21G* level.

Table 2. Bond lengths (Å) and bond angles (deg) for cisplatin.

Geometric parameter	Experimental[a]	Calcdulated A[b]	Relative deviation A[c]	Calcdulated B[d]	Relative deviation B[e]
Pt-N	2.054	2.088	0.016	2.094	0.019
Pt-Cl	2.318	2.374	0.024	2.323	0.002
N-Pt-N	90.2	100.2	0.111	99.8	0.106
N-Pt-Cl	88.9	81.7	−0.081	82.1	−0.076
Cl-Pt-Cl	91.9	96.4	0.049	96.1	0.046
N-H	1.00	1.04	0.04	1.04	0.04
H-N-H	107	110	0.03	110	0.03
H-N-Pt	111	109	−0.02	109	−0.02
			$s_A = 0.05$[f]		$s_B = 0.04$[f]
			$S_A = 0.06$[g]		$S_B = 0.05$[g]

[a]Averaged data for α- and β-polymorphs of cisplatin [31]; [b]Averaged calculated values at PW91/LANL08/3-21G level (a_{cldA}); [c]Relative deviation (δa_A) of the calculated (a_{cldA}) from the experimental (a_{exp}) value: $\delta a_A = (a_{cldA} - a_{exp})/a_{cldA}$; [d]Averaged calculated values at PW91/LANL08/3-21G* level (a_{cldB}); [e]Relative deviation (δa_B) of the calculated (a_{cldB}) from the experimental (a_{exp}) value: $\delta a_B = (a_{cldB} - a_{exp})/a_{cldB}$;

[f]Arithmetic mean of the relative deviations' modules: $s_A = \dfrac{1}{N}\sum_{i=1}^{N}\left|\delta a_{Ai}\right|$, $s_B = \dfrac{1}{N}\sum_{i=1}^{N}\left|\delta a_{Bi}\right|$, N = number of geometric parametes; [g]Root mean

square of the relative deviations: $S_A = \left(\dfrac{1}{N}\sum_{i=1}^{N}\delta a_{Ai}^2\right)^{1/2}$, $S_B = \left(\dfrac{1}{N}\sum_{i=1}^{N}\delta a_{Bi}^2\right)^{1/2}$.

B results in Pt-Cl bond length very close to the experimental (2.323 vs. 2.318 Å, respectively), but worsens the results for the Pt-N bond as compared to method A. Both protocols overestimate the values of the angles N-Pt-N and N-Pt-Cl, and underestimating the N-Pt-Cl value with respect to the experimental data [31], the discrepancy being largest for N-Pt-N (ca. 10°). The same trend has been noticed in the HF [23] and DFT [23-25] results with other ECP basis sets, and even when all-electron bases were applied [26]. These results can be explained by the existence of *intra*molecular interactions (H-bonds) Cl⋯H-N which open the angles N-Pt-Nand Cl-Pt-Cl [23-26]. Indeed, the distances Cl⋯H calculated by the A and B schemes are short: 2.354 and 2.349 Å, respectively. In the solid state it seems, however, that the *inter*molecular H-bonding network [31] leads to conformational changes which diminish the effect of the *intra*molecular Cl⋯H-N contacts.

3.3. Vibrational Analysis

The number of the normal vibrations of a single cisplatin molecule is 27, distributed in C_{2v} point group as follows: $9A_1 + 5A_2 + 8B_1 + 5B_2$. All of them are Raman active vibrations. The assignments of the vibrational spectra of cisplatin available in the literature [22-25], are made under the approximation of a single molecule, and the effects of the solid state have not been considered. Because of comparability considerations, here we also hold to this approach. In **Table A** of the Supplementary material,

however, a factor group analysis of the number and symmetry of the expected vibrational modes in the crystalline state is given.

In **Tables 3** and **4**, the harmonic vibrational modes of cisplatin calculated by methods A and B, respectively are compared with the experimental Raman sprecrtroscopic data of Amado *et al.* [24]. The coores- pondence between the theoretical and experimental wave number is good even without scaling, the r. m. s. of the relative deviations (*S*) being 4.5%. Following the approach of other workers [22-25], the vibrational modes were divided in groups and the wavenumbers scaled. The individual scaling factors ($\tilde{v}_{exp}/\tilde{v}_{cld}$) within each group were averaged to obtain the group scaling factor σ (see the footnotes d-f to **Table 3**). For both protocols A and B, we have applied grouping into three sets with the corresponding scaling factors as follows: 1) $\delta_a(NH_3)$ B_1, $\rho(NH_3)$ A_2 and $\delta(N\text{-}Pt\text{-}tN) - \sigma_1 = 0.92$; 2) $v_a(NH_3)$, $\delta_a(NH_3)$ A_1, $\delta_a(NH_3)$ A_2, $\delta_s(NH_3)$, $\rho(NH_3)$ A_1, $\rho(NH_3)$ B_2, $\rho(NH_3)$ B_1, $v(Pt\text{-}Cl)$ and $\pi_s(Pt) - \sigma_2 = 0.97$; 3) $v_s(NH_3)$, $\delta_s(NH_3)$, $v(Pt\text{-}N)$ and $\delta(N\text{-}Pt\text{-}Cl) - \sigma_3 = 1.03$. The scaled wave numbers fit closely to the experimental data as indicated from the arithmetic mean (*s*) and the r. m. s. (*S*) of the relative deviations: 1.1% and 1.4%, respectively (**Tables 3** and **4**). The former was included for better comparison with the data of Amado *et al.* [24] who use this parameter. Our *s*-value (1.1%) is the same as the value obtained by them from HF calculations and is slightly better as compared with the analogous values (1.3% and 1.5%) from their DFT calculations [24]. Our calculations show interchange of the order of the

Table 3. Calculated (PW91/LANL08/3-21G) normal vibrational modes (wavenumbers $\tilde{\nu}$, cm^{-1}) of cisplatin molecule, compared with the experimental data.

$\tilde{\nu}_{exp}$ [a]	$\tilde{\nu}_{cld}$ [b]	$\Delta\tilde{\nu}$ [c]	$\delta\tilde{\nu}$ [d]	κ [e]	σ [f]	$\tilde{\nu}_{cld\sigma}$ [g]	$\Delta\tilde{\nu}_{\sigma}$ [h]	$\delta\tilde{\nu}_{\sigma}$ [i]	Assignment[j], TED[k], %
3309	3394 3393	85	0.026	0.97	0.97	3292	−17	−0.005	ν_a(NH$_3$) B_2, A_2 100ν(NH)
3287	3327 3327	40	0.012	0.99	0.97	3227	−60	−0.018	ν_a(NH$_3$) A_1, B_1 100ν(NH)
3211	3133 3133	−78	−0.024	1.02	1.03	3227	16	0.005	ν_s(NH$_3$) B_1, A_1 100ν(NH)
1648	1682	34	0.021	0.98	0.97	1631	−17	−0.010	δ_a(NH$_3$) B_2 59δ(HNPt+HNH) + 40t(NPt)
1628	1676	48	0.029	0.97	0.97	1626	−2	−0.001	δ_a(NH$_3$) A_2 58δ(HNPt + HNH) + 41t(NPt)
1601	1649	48	0.030	0.97	0.97	1599	−2	−0.001	δ_a(NH$_3$) A_1 65δ(HNPt + HNH) + 35t(NPt)
1537	1641	4	0.068	0.94	0.92	1510	−27	−0.018	δ_a(NH$_3$) B_1 65δ(HNPt + HNH) + 35t(NPt)
1316	1266	−50	0.038	1.04	1.03	1304	−12	−0.009	δ_s(NH$_3$) A_1 100δ(HNPt + HNH)
1295	1265	−30	−0.023	1.02	1.03	1303	8	0.007	δ_s(NH$_3$) B_1 100δ(HNPt + HNH)
824	860	36	0.044	0.96	0.97	834	10	0.012	ρ(NH$_3$) A_1 75δ(HNPt) + 24t(NPt)
811	834	23	0.028	0.97	0.97	809	−2	−0.002	ρ(NH$_3$) B_1 75δ(HNPt) + 24t(NPt)
789	802	13	0.016	0.98	0.97	778	−11	−0.014	ρ(NH$_3$) B_2 88δ(HNPt) + 10t(NPt)
724	791	67	0.092	0.91	0.92	728	4	0.005	ρ(NH$_3$) A_2 88δ(HNPt) + 11t(NPt)
524	510	−14	−0.027	1.03	1.03	525	1	0.002	ν_s(PtN) A_1 100ν(PtN)
508	506	−2	−0.004	1.00	1.03	521	13	0.026	ν_a(PtN) B_1 99ν(PtN)
323	338	6	0.046	0.96	0.97	328	5	0.015	ν_s(PtCl) A_1 95ν(PtCl)
317	327	10	0.031	0.97	0.97	317	0	0.000	ν_a(PtCl) B_1 98ν(PtCl)
255	240	−15	−0.059	1.06	1.03	247	−8	−0.031	δ(NPtCl) B_1 97δ(NPtCl)
210	233	23	0.109	0.90	0.92	214	4	0.019	δ(NPtN) A_1 61δ(NPtN) + 34δ(NPtCl)
no data	180								t_a(PtN) A_2 93t(PtN)
no data	178								t_s(PtN) B_2 99t(PtN)
162	165	3	0.0185	0.98	0.97	160	−2	−0.012	π_s(NPtCl) B_2 70δ_{op}(NPtCl) + 28t(PtN)
no data	144								δ(ClPtCl) A_1 72δ(ClPtCl) + 13δ(NPtCl) + 12δ(NPtN)
no data	122								π_a(NPtCl) A_2 63δ_{op}(NPtCl) + 35t(PtN)
		$s^l = 0.037$ $S^m = 0.045$					$s_\sigma^l = 0.011$ $S_\sigma^m = 0.014$			

[a]Experimental Raman wavenumbers [24]; [b]Theoretical values; [c]Deviation of the theoretical values from the experimental ones: $\Delta\tilde{\nu} = \tilde{\nu}_{cld} - \tilde{\nu}_{exp}$; [d]Relative deviation of the theoretical values from the experimental ones: $\delta\tilde{\nu} = (\tilde{\nu}_{cld} - \tilde{\nu}_{exp})/\tilde{\nu}_{exp}$; [e]Individual scaling factor: $\kappa = \tilde{\nu}_{exp}/\tilde{\nu}_{cld}$; [f]Group scaling factor: $\sigma_i = \frac{1}{N}\sum_{j=1}^{n_i}\kappa_{ij}$, where n_i is the number of the individual scaling factors in the i-th group. Thus $\sigma_1 = 0.92$ for δ_a(NH$_3$) B_1, ρ(NH$_3$) A_2 and δ(NPtN); $\sigma_2 = 0.97$ for ν_a(NH$_3$), δ_a(NH$_3$) A_1, δ_a(NH$_3$) A_2, δ_s(NH$_3$), ρ(NH$_3$) A_1, ρ(NH$_3$) B_2, ρ(NH$_3$) B_1, ν(PtCl) and π_s(NPtCl); $\sigma_3 = 1.03$ for ν_s(NH$_3$), δ_s(NH$_3$), ν(PtN) and δ(NPtCl); [g]Theoretical scaled values; [h]Deviation of the theoretical scaled values from the experimental ones: $\Delta\tilde{\nu}_{\sigma} = \tilde{\nu}_{cld\sigma} - \tilde{\nu}_{exp}$; [i]Relative deviation of the theoretical scaled values from the experimental ones: $\delta\tilde{\nu}_{\sigma} = (\tilde{\nu}_{cld\sigma} - \tilde{\nu}_{exp})/\tilde{\nu}_{exp}$; [j]Notations for the modes: ν—stretching, δ—bending, ρ—rocking, π—out-of-plane bending, t—torsion; The indices s and as stand for symmetric and asymmetric respectively, and the index op denotes out-of-plane; [k]Total energy distribution over internal coordinates; [l]Arithmetic mean of the relative deviations' modules: $s = \frac{1}{N}\sum_{t=1}^{N}|\delta\tilde{\nu}_i|$; $s_\sigma = \frac{1}{N}\sum_{t=1}^{N}|\delta\tilde{\nu}_{\sigma i}|$; $N = 27$ is the number of vibrational modes;

[m]Root mean square of the relative deviations: $S = \frac{1}{N}\left(\sum_{t=1}^{n}\delta\tilde{\nu}_i^2\right)^{1/2}$, $S_\sigma = \frac{1}{N}\left(\sum_{t=1}^{n}\delta\tilde{\nu}_{i\sigma}^2\right)^{1/2}$.

Table 4. Calculated (PW91/LANL08/3-21G*) normal vibrational modes (wavenumbers $\tilde{\nu}$, cm^{-1}) of cisplatin molecule, compared with the experimental data[a].

$\tilde{\nu}_{exp}$	$\tilde{\nu}_{cld}$	$\Delta\tilde{\nu}$	$\delta\tilde{\nu}$	κ	σ	$\tilde{\nu}_{cld\sigma}$	$\Delta\tilde{\nu}_\sigma$	$\delta\tilde{\nu}_\sigma$	Assignment, TED, %
3309	3394 3394	85	0.026	0.97	0.97	3292	−17	−0.005	$\nu_a(NH_3)$ B_2, A_2 $100\nu(NH)$
3287	3329 3329	42	0.013	0.99	0.97	3229	−58	−0.018	$\nu_a(NH_3)$ A_1, B_1 $100\nu(NH)$
3211	3137 3136	−74	−0.023	1.02	1.03	3231	20	0.006	$\nu_s(NH_3)$ B_1, A_1 $100\nu(NH)$
1648	1682	34	0.021	0.98	0.97	1631	−16	−0.010	$\delta_a(NH_3)$ B_2 $59\delta(HNPt + HNH) + 40t(NPt)$
1628	1676	48	0.029	0.97	0.97	1626	−2	−0.001	$\delta_a(NH_3)$ A_2 $58\delta(HNPt + HNH) + 41t(NPt)$
1601	1649	48	0.030	0.97	0.97	1599	−2	−0.001	$\delta_a(NH_3)$ A_1 $65\delta(HNPt + HNH) + 35t(NPt)$
1537	1641	104	0.068	0.94	0.92	1510	−27	−0.018	$\delta_a(NH_3)$ B_1 $65\delta(HNPt + HNH) + 35t(NPt)$
1316	1259	−57	−0.043	1.04	1.03	1297	−19	−0.014	$\delta_s(NH_3)$ A_1 $100\delta(HNPt + HNH)$
1295	1256	−39	−0.030	1.03	1.03	1294	−1	−0.001	$\delta_s(NH_3)$ B_1 $100\delta(HNPt + HNH)$
824	853	29	0.035	0.97	0.97	827	3	0.004	$\rho(NH_3)$ A_1 $75\delta(HNPt) + 24t(NPt)$
811	826	15	0.018	0.98	0.97	801	−10	−0.012	$\rho(NH_3)$ B_1 $75\delta(HNPt) + 24t(NPt)$
789	797	8	0.010	0.99	0.97	773	−16	−0.020	$\rho(NH_3)$ B_2 $88\delta(HNPt) + 10t(NPt)$
724	785	61	0.084	0.92	0.92	722	−2	−0.003	$\rho(NH_3)$ A_2 $88\delta(HNPt) + 11t(NPt)$
524	503	−21	−0.040	1.04	1.03	518	−6	−0.011	$\nu_s(PtN)$ A_1 $100\nu(PtN)$
508	499	−9	−0.018	1.02	1.03	514	6	0.012	$\nu_a(PtN)$ B_1 $99\nu(PtN)$
323	343	20	0.062	0.94	0.97	333	10	0.031	$\nu_s(PtCl)$ A_1 $96\nu(PtCl)$
317	330	13	0.041	0.96	0.97	320	3	0.009	$\nu_a(PtCl)$ B_1 $99\nu(PtCl)$
255	241	−14	−0.055	1.06	1.03	248	−7	−0.027	$\delta(NPtCl)$ B_1 $97\delta(NPtCl)$
210	231	21	0.100	0.91	0.92	212	2	0.009	$\delta(NPtN)$ A_1 $60\delta(NPtN) + 35\delta(NPtCl)$
no data	179								$t_a(PtN)$ A_2 $92t(PtN)$
no data	178								$t_s(PtN)$ B_2 $99t(PtN)$
162	168	6	0.037	0.96	0.97	163	1	0.006	$\pi_s(NPtCl)$ B_2 $70\delta_{op}(NPtCl) + 28t(PtN)$
no data	147								$\delta(ClPtCl)$ A_1 $72\delta(ClPtCl) + 13\delta(NPtCl) + 12\delta(NPtN)$
no data	122								$\pi_a(NPtCl)$ A_2 $63\delta_{op}(NPtCl) + 35t(PtN)$
		$s = 0.039$ $S = 0.045$					$s_\sigma = 0.011$ $S_\sigma = 0.014$		

[a]The notations are the same as in **Table 3**.

δ(N-Pt-Cl) and δ(N-Pt-N) modes as compared to the data of Amado *et al.* [23,24], and conform with the earlier assignments of Pavankumar *et al.* [21]. The other discrepany concerns the order of π_s(N-Pt-Cl) and δ(Cl-Pt-Cl) modes: our results correlate the experimental band at 162 cm^{-1} [23,24] with π_s(N-Pt-Cl), whereas δ(Cl-Pt-Cl) vibration should be expected at *ca.* 140 cm^{-1} (**Tables 3** and **4**).

As concerns the two protocols, adding *d*-orbitals to Cl atoms (protocol B), slightly worsens the fit to the experimental wavenumbers, especially with respect to the *v*(Pt-N) and *v*(Pt-Cl) vibrations. The shape of the skeletal vibrations of cisplatin molecule is visualized in **Figure 3**. Selected harmonic force constants for cisplatim molecule are presented in **Table 5**. In agreement with the finding that adding *d*-orbitals to the Cl atoms shortens the bond Pt-Cl and lengthens the bond Pt-N (cf. **Table 2**), it is seen that it also strengthens the former and weakens the

later, judging by the force constants given in **Table 5**.

Typically the tasks on geometry optimization and vibrational analysis take totally 15 min on a PC.

4. Conclusion and Perspective

The DFT computational protocol involving the PW91 exchange-correlation functional, the relativistic ECP and associated non-contracted basis set LANL08 for description of the Pt atom and 3-21G or 3-21G* basis sets for the remaining atoms, gives satisfactory results for the
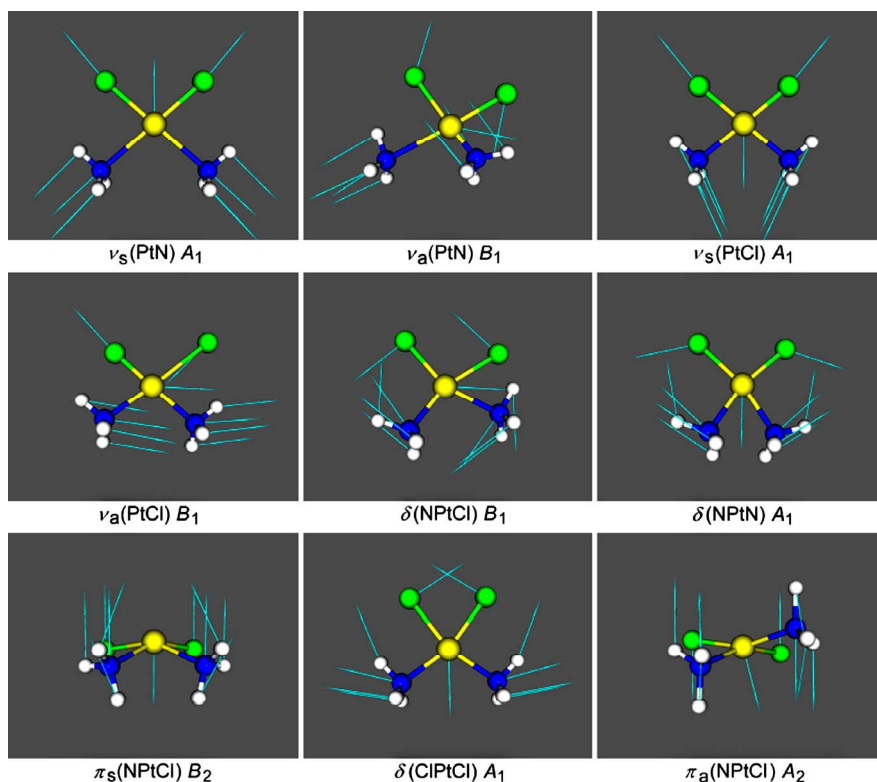
Figure 3. View of the nine skeletal vibrations of cisplatin molecule with their symmetry. The arrows represent the displacement vectors. The vibrational modes were visualized with the aid of Molekel programme using the Firefly output.

Table 5. Selected harmonic force constants[a] for cisplatin.

Internal coordinate	Force constant, A[b]	Force constant, B[c]
Pt-N stretching	2.473	2.409
Pt-Cl stretching	1.950	2.010
N-Pt-N in-plane bending	0.638	0.634
N-Pt-Cl in-plane bending	1.138	1.134
Cl-Pt-Cl in-plane bending	0.627	0.628
N-Pt-N/N-Pt-Cl off-diagonal	−0.213	−0.208
N-Pt-N/Cl-Pt-Cl off-diagonal	−0.211	−0.217
N-Pt-Cl/N'-Pt-Cl' off-diagonal	−0.715	−0.720
N-Pt-Cl out-of-plane bending	0.021	0.021

[a]Units: mdyn·Å^{-1} for the stretching and mdyn·Å·rad^{-2} for the bending and off-diagonal bending-bending force constants; [b]PW91/LANL08/3-21G level; [c]PW91/LANL08/3-21G* level.

equilibrium geometry of cisplatin molecule. The calculated wave numbers of the normal vibrations of the molecule are in very good agreement with the experimental data. The procedure used seems to be a good compromise between accuracy and computational resources. It will be used for DFT modelling of other platinum complexes that are of interest as potential cytostatic agents, and in particular towards some of the newly synthesized in our laboratory Pt(II) [53] and Pt(IV) complexes with sulfonamide ligands.

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Appendix

Factor Group Analysis of the Vibrations of Crystalline Cisplatin

Weller *et al.* [31] found that cisplatin exists in two polymorphs: low-temperature α- and high-temperature β-modifications. The crystals of both forms are triclinic, space group $P\tilde{1}$ with two and four asymmetric molecules for the α- and β-form, respectively. The relation between the point, site and factor group symmetry for both crystal forms is: $C_1 \rightarrow C_1 \rightarrow C_i$, respectively. A factor group analysis of the number and symmetry of the vibrational modes [54] of the two polymorphs is given in **Table A**.

Table A. Factor group analysis for the crystals of α- and β-polymorphs of cisplatin.

Polymorph	Number of the vibrations					
	Total	Intra-molecular	Intra-unit cell	Unit cell translations (acoustic modes)	Unit cell rotations	Molecular librations
α ($Z = 2$)	66	$27A_g + 27A_u$	$1A_g$	$3A_u$	$2A_g$	$3A_g + 3A_u$
β ($Z = 4$)	132	$54A_g + 54A_u$	$3A_g + 3A_u$	$3A_u$	$3A_g$	$6A_g + 6A_u$