Cationic intermediates in oxidative addition reactions of Cl₂ to [PtCl₂(cis-1,4-DACH)]†

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Oxidative addition and reductive elimination are fundamental processes in transition-metal chemistry. New interest in this field has been generated by the exploitation of platinum(IV) complexes as antitumor drugs. The two extra ligands can be used to render these species more resistant to attack by biological nucleophiles compared to their platinum(II) counterparts, to anchor additional pharmacologically active moieties, or, finally, to target the drug to specific sites by conferring responsiveness to some type of chemotaxis. On the other hand, platinum(IV) species are considered to be prodrugs and to require reduction to Pt(II) to become active. Thus, reductive elimination promoted by biological reducing agents becomes an important issue and it too could be exploited for targeting purposes. In this paper, we investigated the oxidation step in more detail and shown that, independent of the solvent used, a solvent molecule assists the reaction by entering in a trans position with respect to the attacking oxidant. In the case of bifunctional solvent molecules, such as dimethylsulfoxide, both S- and O-coordinated species are formed, the latter being thermodynamically favored. The substitution of the axially coordinated solvent molecule by a free chloride ion is found to be quite slow in organic solvents, as well as in water. It is also shown that the intermediate solvato-species can be exploited for binding just one molecule of another substrate in the axial position.

Introduction

The oxidative addition and the reverse process, reductive elimination, are among the most fundamental reactions in transition-metal chemistry.1–3 These two-electron redox processes are also an integral part of platinum chemistry and allow the metal to move between three different oxidation states (0, +2 and +4), with the oxidative addition process being restricted to the lower oxidation states (0 and +2) and the reductive elimination to the higher oxidation states (+2 and +4).4

In the oxidative addition, a reagent, XY, removes two electrons from the metal centre (the oxidation state of which increases from M” to M”+2) and splits the X–Y bond. The newly formed X– and Y– anions coordinate to the metal centre forming two new linkages (M–X and M–Y).

The mechanism of the addition of dihalides (X₂) to platinum(II) complexes has been extensively investigated in the past.5,6 In aqueous solution, this reaction involves two consecutive processes: 1) a rapid oxidation assisted by the solvent, which leads to the formation of a trans-halidoaquaplatinum(IV) intermediate and a free halide ion and 2) an anion reaction, in which the free halide ion attacks the trans-halidoaquaplatinum(IV) intermediate to yield the trans-dihalidoplatinum(IV) final product.5–10

In a recent study concerning the oxidative addition of chlorine to the Pt(II) complex trans-[PtCl₄(5-methoxy-3,4-dihydro-2H-pyrrole-κN)] in aqueous solution, the intermediate halidoaqua species trans-[PtCl₂(OH₂)(5-methoxy-3,4-dihydro-2H-pyrrole-κN)]12+ was isolated and its X-ray structure was determined for the first time (Fig. 1).13 This intermediate aqua species, while proving the solvent assistance in the mechanism of oxidative addition, was exceptionally stable towards solvent substitution by free chloride ions. The reason for such inertness was envisaged to be due to the presence of H-bonds, between the coordinated solvent molecule and the methoxy-oxygens of the two 1-pyrroline ancillary ligands, stabilizing the intermediate Pt(IV) solvato-species.

In the present work, we extended the investigation (oxidative addition of chlorine) to [PtCl₄(cis-1,4-DACH)] (DACH = diaminocyclohexane, Fig. 1). This complex contains an isomeric form of the diamine ligand present in oxaliplatin (trans-1, R₂R₄-diaminocyclohexaneoxalatoplatinum(II)) and has been widely investigated as a potential new platinum anticancer drug. Platinum drugs (cisplatin, cis-diaminedichloroplatinum(II); carboplatin, diaminine[1,1-cyclobutane-dicarboxylato] platinum(II); and oxaliplatin) are widely used in the clinic and the prototype cisplatin still represents the only antineoplastic drug with highly curative effect in a solid malignancy, such as in testicular cancer.15,16 [PtCl₄(cis-1,4-DACH)] is toxic towards several cisplatin-resistant

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Pt(IV) complex, [PtCl4(DMSO)] and acetone. The results were rather interesting and vents, including dimethylformamide (DMF), dimethylsulphoxide (DMSO), and acetone-1,4-DACH). Preparations of fac-[PtCl4(DMSO)]Cl and [PtCl4(1,4-DACH)] were synthesized according to reported procedures.12,17

**Preparation of fac-[PtCl4(DMSO)]Cl.** [PtCl4(cis-1,4-DACH)] (52.1 mg, 0.14 mmol) was dissolved in DMF (5 mL) and the resulting solution was treated with 6 mL of CCl4 previously saturated with gaseous Cl2. The mixture was kept under stirring for one minute at room temperature and then diethylether (150 mL) was added to induce the formation of a yellow precipitate. The precipitate was filtered off, washed with Et2O and dried under vacuum. Yield: 70% (51.3 mg, 0.098 mmol). Anal. calculated for [PtCl4(cis-1,4-DACH)]Cl (C26H20N2Cl4Pt): C, 37.45; H, 1.92; N, 4.45%. Found: C, 37.4; H, 1.9; N, 4.45%.

**Preparation of fac-[PtCl4(1,4-DACH)]Cl.** [PtCl4(1,4-DACH)] (47 mg, 0.09 mmol) was dissolved in H2O (10 mL) and treated with Ag(CF3SO3)2 (23 mg, 0.09 mmol). The resulting solution was kept under stirring for one minute. After filtration of the solution, the solvent was evaporated to dryness under reduced pressure and the residue was re-crystallized from acetone to obtain fac-[PtCl4(1,4-DACH)]Cl (47 mg, 0.09 mmol). Anal. calculated for [PtCl4(1,4-DACH)]Cl (C32H20N2Cl4Pt): C, 33.8; H, 1.6; N, 4.11%. Found: C, 33.8; H, 1.6; N, 4.11%.

**Preparation of fac-[PtCl4(1,4-DACH)](OH).** [PtCl4(1,4-DACH)] (38 mg, 0.10 mmol) was suspended in a water solution (3 mL) containing potassium acetate (294 mg, 3.0 mmol) and treated with Ag(CF3SO3)2 (23 mg, 0.09 mmol). The resulting solution was kept under stirring for one minute. After filtration of the solution, the solvent was evaporated to dryness under reduced pressure and the residue was re-crystallized from acetone to obtain fac-[PtCl4(1,4-DACH)](OH) as a pale yellow solid. Yield: 90% (51.7 mg, 0.08 mmol). Anal. calculated for [PtCl4(1,4-DACH)](OH) (C32H20N2Cl4Pt): C, 34.8; H, 1.57; N, 4.11%. Found: C, 34.8; H, 1.57; N, 4.11%.

Monitoring of the oxidative addition by NMR – general procedure. 5 mg (ca. 0.01 mmol) of platinum(II) substrate ([PtCl4(cis-1,4-DACH)] or [PtCl4(en); en = ethylenediamine) were dissolved in 550 µL of solvent (DMF–d7, DMSO–d6, D2O, or acetone–d6). The resulting solution was transferred into an NMR tube and treated with 300 µL of CCl4 saturated with gaseous Cl2. 1H-NMR spectra were recorded at certain times.

**Results and discussion**

The oxidative addition of Cl2 to [PtCl4(cis-1,4-DACH)] was investigated by 1H-NMR spectroscopy at room temperature and in different solvents.
The progress of the reaction performed in deuterated \(N,N\)-dimethylformamide (DMF-\(d_7\)) is shown in Fig. 2. The \(^1\)H-NMR spectrum of a solution of \([\text{PtCl}_2(\text{cis}-1,4\text{-DACH})]\) in DMF-\(d_7\) (Fig. 2a) exhibits two pseudo-triplets (relative intensities 1:4:1) centered at 4.97 (assigned to \(\text{NH}_2\) protons) and 3.28 ppm (assigned to \(\text{H}_a\) protons) and two multiplets centered at 1.93 and 1.66 ppm (assigned to \(\text{H}_b\) of the cyclohexane ring). The pseudo-triplets at 4.97 and 3.28 ppm are generated by \(^{195}\text{Pt}–\text{H}\) coupling (\(^{195}\text{Pt}\) has a natural abundance of 33.8% and receptivity relative to \(^1\text{H}\) of \(3.4 \times 10^{-3}\)) with \(J_{\text{Pt}-\text{H}}\) coupling constants of 70 (2\(J\)) and 100 Hz (3\(J\), respectively.

After the addition of \(\text{Cl}_2\), the signals belonging to \([\text{PtCl}_2(\text{cis}-1,4\text{-DACH})]\) disappear completely, while new signals appear (Fig. 2b). The new signals are a multiplet centered at 7.51 ppm (integrating for 4 protons), a pseudotriplet at 3.22 ppm (\(J_{\text{Pt}-\text{H}} = 76\) Hz) (2 protons) and two multiplets centered at 2.20 and 1.89 ppm (8 protons in total). After five days, the \(^1\)H-NMR spectrum (Fig. 2c) exhibits two pseudo-triplets at 6.87 (\(J_{\text{Pt}-\text{H}} = 60\) Hz) and 3.26 ppm (\(J_{\text{Pt}-\text{H}} = 77\) Hz), integrating for 4 and 2 protons, respectively, and two multiplets centered at 2.30 and 1.75 ppm, integrating globally for 8 protons. The \(^1\)H NMR data indicate that the intermediate species (spectrum b) could be the solvato-species \(\text{fac-}[\text{PtCl}_3(\text{cis}-1,4\text{-DACH})(\text{O-DMF})]\text{Cl}\). This complex could be formed by axial coordination to the platinum atom of a chloride ion and a solvent molecule. The non-equivalence of the amine protons (two multiplets around 7.51 ppm) is in accord with this formulation. This intermediate complex slowly evolves to the tetrachlorido species \([\text{PtCl}_4(\text{cis}-1,4\text{-DACH})]\) (Fig. 2c) formed by replacement of the coordinated solvent molecule by a chloride ion and characterized by equivalent amine protons (one multiplet at 6.87 ppm). In order to confirm the interpretation of the NMR spectra, we isolated the intermediate solvato-species \(\text{fac-}[\text{PtCl}_3(\text{cis}-1,4\text{-DACH})(\text{O-DMF})]\text{Cl}\) by performing the reaction on a preparative scale in DMF (5 mL) at room temperature and, soon after the addition of excess \(\text{Cl}_2\) in \(\text{CCl}_4\) (6 mL), by precipitating the first formed complex by addition of excess...
The IR spectrum exhibits a signal at 1650 cm⁻¹, which can be assigned to the C=O stretching of a coordinated DMF, which is in agreement with literature data already reported for (DMF)Pt⁴⁺ compounds. The ESI-MS spectrum shows a peak at m/z 488 (100), which is assignable to the cation [PtCl₃(cis-1,4-DACH)(O-DMF)]⁺ (the simulated isotopic distribution for such a species was identical to the experimental one).

The ¹H-NMR spectrum (Fig. 3) in DMSO-d₆ exhibits a pseudotriplet at 8.25 ppm (Jₚt,HH = 25 Hz) and two singlets falling at 3.35 and 3.10 ppm, which can be assigned to the amidic proton and to the two methyl groups of free DMF in DMSO-d₆. The chemical shift of the Pt atom to the two methyl groups of an O-coordinated DMF is in the range typical for a Pt(IV) atom (Fig. S1 and S2, respectively). The chemical shift of the Pt atom corresponding compound with triflate as the counterion by a reaction was identical to the experimental one). The two, partially overlapping, singlets at 7.95, 2.89, and 2.73 ppm that are assigned to the amidic protons) and the three multiplets centered at 2.00, 1.87 and 1.66 ppm (Hb protons) belonging to free DMF are marked with •.

The time course of the oxidative addition of Cl₂ to [PtCl₂(cis-1,4-DACH)(O-DMF)]Cl with Ag(CF₃SO₃) in diethylether (150 mL). The obtained complex was characterized by elemental analysis, spectrometric (ESI-MS) and spectroscopic (IR and NMR) investigations.

The ¹H-NMR spectrum of [PtCl₃(cis-1,4-DACH)(O-DMF)]Cl in DMSO-d₆ in the low field region (Fig. 5, top) shows three cross-peaks (1H/¹⁵Pt)-HMQC spectra in acetone-d₆ are reported in Figs S1 and S2, respectively. The chemical shift of the Pt atom (320 ppm; Table 1) is in the range typical for a Pt(IV) atom in a PtN₂Cl₃O coordination environment.

The ¹H-NMR spectrum of [PtCl₃(cis-1,4-DACH)(O-DMF)]Cl in DMSO-d₆ exhibits a pseudotriplet at 8.25 ppm (Jₚt,HH = 25 Hz) and two singlets falling at 3.35 and 3.10 ppm, which can be assigned to the amidic proton and to the two methyl groups of an O-coordinated DMF, respectively. The two, partially overlapping, pseudotriplets around 7.43 ppm (amine protons), the pseudotriplet at 2.80 ppm (Jₚt,HH = 80 Hz, H₄ protons) and the three multiplets centered at 2.00, 1.87 and 1.66 ppm (Hb protons) belong to the cis-1,4-DACH ligand. The given assignments are fully supported by the 2D COSY spectrum (data not shown). Additionally, the spectrum shows three very weak singlets at 7.95, 2.89, and 2.73 ppm that are assigned to the amido proton and to the two methyl groups of free DMF in DMSO-d₆ solution, respectively. The intensity of these latter signals increases with time with a concomitant decrease in the intensity of the peaks assigned to coordinated DMF. As already anticipated, the coordinated solvent DMF molecule is slowly replaced by the chloride present in solution as a counterion. In order to abrogate this latter reaction and stabilize the solvato-species fac-[PtCl₃(cis-1,4-DACH)(O-DMF)]⁺, we synthesized the corresponding compound with triflate as the counterion by a reaction of fac-[PtCl₃(cis-1,4-DACH)(O-DMF)]Cl with Ag(CF₃SO₃) in water solution. A thorough characterization of fac-[PtCl₃(cis-1,4-DACH)(O-DMF)](CF₃SO₃) was accomplished by IR and NMR and is reported in the Electronic Supplementary Information (¹H and [¹⁵Pt]-HMOC spectra in acetone-d₆ are reported in Figs S1 and S2, respectively).

The 1H-NMR spectrum (Fig. 3) in DMSO-d₆ exhibits a pseudotriplet at 8.25 ppm (Jₚt,HH = 25 Hz) and two multiplets centered at 1.66 and 1.45 ppm (H₄ protons) belonging to the cis-1,4-DACH ligand. After the addition of Cl₂ (Fig. 4b), the signals of the starting complex immediately disappear and two new sets of signals (marked by A and B) appear. A exhibits two multiplets centered at 7.30 (see discussion below) and 6.48 ppm, a pseudotriplet at 3.13 ppm (Jₚt,HH = 86 Hz), a multiplet centered at 2.24 ppm and a singlet falling at 1.74 ppm. B exhibits a multiplet centered at 7.18 ppm (integrating for slightly more than 4 protons), a pseudotriplet at 2.81 ppm (Jₚt,HH = 75 Hz, integrating for 2 protons) and three multiplets centered at 2.00, 1.85 and 1.58 ppm (8 protons). Moreover this spectrum shows also a very weak pseudotriplet at 6.66 ppm (Jₚt,HH = 62 Hz) and a doublet at 6.10 ppm, assigned to the amine and methylenic protons, respectively, of the final oxidation product [PtCl₄(cis-1,4-DACH)]. A was a transient species and disappeared after ca. 3 h, transforming into B (Fig. 4c), while B was longer lived and disappeared after 17 days, giving the final product [PtCl₄(cis-1,4-DACH)]. A 2D-COSY experiment (Fig. S3) recorded soon after the addition of Cl₂ to [PtCl₃(cis-1,4-DACH)] showed a cross peak between a signal at ca. 7.30 ppm (partially overlapping with the more intense signal at 7.18 ppm belonging to species B) and the signal at 6.48 ppm of set A. This cross-peak clearly indicates that species A has another signal falling at 7.30 ppm, which, together with the signal at 6.48 ppm, belongs to chemically non-equivalent amine protons. The 2D-COSY spectrum also shows an intense cross-peak between the multiplet at 7.18 ppm (amine protons) and the signal at 2.81 ppm (methylenic protons) of set B.

The time course of the Cl₂ addition reaction performed in DMSO is very similar to that performed in DMF-d₆. However, there are two intermediate Pt⁴⁺ species (A and B) with a DMSO molecule coordinated to the metal center (and not just one as in the case of DMF). Since DMSO is a bifunctional molecule capable of coordinating to platinum through either the oxygen or the sulphur atoms, it is not surprising that we observe two intermediate species in solution (Fig. 4). It should be noted that the signals of species B look very similar to those of fac-[PtCl₃(cis-1,4-DACH)(O-DMF)]Cl in the same solvent (Fig. 3). This could be a first indication that species B contains O-coordinated DMSO. In order to gain further support for the conclusion that species B contains O-bonded DMSO, we performed a [¹H-¹⁵Pt] HMOC 2D experiment on a newly prepared sample. The [¹H-¹⁵Pt] HMOC 2D spectra (two different spectral regions of ¹⁵Pt were considered) recorded soon after addition of Cl₂ are reported in Fig. 5. The ¹⁵Pt low field region (Fig. 5, top) shows three cross-peaks (¹H-¹⁵Pt) at 7.20/~918, 6.54/~918 and 3.13/~918 ppm (the splitting of the last cross-peak is due to an insufficient decoupling power on the...
Fig. 4 Top, scheme of the reaction. Bottom, $^1$H-NMR spectra: (a), [PtCl$_2$(cis-1,4-DACH)] in DMSO-$d_6$; (b), soon after addition of Cl$_2$; (c), after ca. 3 h; (d), after 17 days. The asterisks indicate residual solvent peaks.

hetero-nucleus during acquisition). These cross-peaks correlate the $^1$H peaks assigned to species A to a Pt atom falling at −918 ppm (Table 1). The $^{195}$Pt high field region (Fig. 5, bottom) shows two sets of resonances. One set (less intense) contains two split cross-peaks ($^1$H/$^{195}$Pt) centered at 6.66/−120 and 2.88/−120 ppm, which are characteristic of the [PtCl$_4$(cis-1,4-DACH)] end product of the oxidation reaction. The second set (more intense) contains two split cross-peaks ($^1$H/$^{195}$Pt) centered at 7.17/430 and 2.81/430 ppm (Table 1), which correlate the $^1$H peaks assigned to species B to a Pt atom falling at 430 ppm and, hence, less shielded with respect to the Pt atom of species A. 430 ppm is very close to the value found for the compound with O-coordinated DMF (320 ppm in acetone-$d_6$, Table 1), therefore we conclude that B corresponds to the intermediate species with O-bonded DMSO and, consequently, A should correspond to an intermediate species with S-bonded DMSO. It is expected that a S-coordinated DMSO
The Cl₂ oxidative addition to [PtCl₂(cis-1,4-DACH)] was also investigated in acetone-d₆ and the progress of the reaction is reported in Fig. 6. The ¹H-NMR spectrum recorded before the addition of the oxidant (Fig. 6a) exhibits a broad signal (pseudotriplet) at 4.52 ppm (J₁₆ = 80 Hz) assigned to the aminic protons, a pseudotriplet at 3.43 ppm (J₁₆ = 96 Hz) assigned to the H₆ protons and two multiplets at 1.99 and 1.74 ppm assigned to the eight H₈ protons of the cyclohexane ring. An impurity of [PtCl₂(cis-1,4-DACH)], present in the sample of [PtCl₄(cis-1,4-DACH)], gives the broad signal at 6.13 ppm (amine protons), the pseudotriplet at 3.54 ppm (H₈ protons) and the two multiplets at 2.38 and 1.86 ppm (H₁₀ protons). After the addition of Cl₂ (Fig. 6b) the intensities of the signals assigned to [PtCl₂(cis-1,4-DACH)] immediately increase, however, weak signals of an intermediate species are also visible. They consist of two broad signals falling at 7.62 and ca. 6.25 ppm (the latter appears as a shoulder of the intense peak at 6.13 ppm belonging to [PtCl₄(cis-1,4-DACH)]) and a multiplet at 2.48 ppm. After 3 h, the signals of this intermediate species disappear completely (Fig. 6c) and the spectrum only shows the signals belonging to [PtCl₂(cis-1,4-DACH)].

The same experiment (oxidative addition of Cl₂ to [PtCl₂(cis-1,4-DACH)]) was repeated at 203 K. The ¹H-NMR spectrum taken soon after the addition of Cl₂ is reported in Fig. S5†. The spectrum exhibits, in addition to the signals of [PtCl₂(cis-1,4-DACH)], two multiplets at 7.70 and 6.90 ppm and two multiplets at ca. 2.35 and 2.16 ppm (the latter two signals partially overlapping with the signal at 2.23 ppm). Most likely, the signals at 7.70 and 6.90 ppm belong to the amionic protons of an intermediate Pt⁰ species with different axial ligands. The same species should have H₆ protons overlapping with those of the [PtCl₄(cis-1,4-DACH)] end product, and three multiplets (of relative intensities 2.2:4) for the H₁₀ protons (the first two falling at 2.35 and 2.16 ppm and the third one overlapping with the signal at 1.88 ppm). The given assignment is also supported by a 2D-COSY experiment performed at 203 K (Fig. S6†). The ¹³C-NMR spectrum recorded at 203 K, soon after addition of Cl₂ to [PtCl₂(cis-1,4-DACH)] in acetone-d₆, is reported in Fig. S7†. The spectrum shows a species with a Pt chemical shift of 281 ppm (Table 1), which is compatible with a [PtCl₄(cis-1,4-DACH)(O-acetone)]⁰ intermediate. Therefore, similar to the case of the oxidative reaction carried out in DMF and DMSO solutions, the reaction performed in acetone also leads to an intermediate Pt⁰ solvato-species of formula fac-[PtCl₄(cis-1,4-DACH)(O-acetone)]⁰. The instability of the intermediate species containing a coordinated acetone molecule prevented its isolation.

Finally, Cl₂ addition to [PtCl₂(cis-1,4-DACH)] was investigated in water (Fig. 7). The ¹H-NMR spectrum (Fig. 7a) of a solution of [PtCl₂(cis-1,4-DACH)] in D₂O exhibits a broad pseudotriplet (partially overlapping the residual solvent signal) at 4.91 ppm, a pseudotriplet at 3.19 ppm (J₁₆ = 104 Hz) assigned to H₆ protons and a singlet at 1.74 ppm assigned to the eight equivalent H₈ protons of the cyclohexane ring. After addition of Cl₂ (Fig. 7b), the signals belonging to [PtCl₂(cis-1,4-DACH)] disappear and the signals of a new species appear. They consist of a broad signal at 7.01 ppm, assigned to the amionic protons of the Pt⁰ aquo-species, a pseudotriplet at 3.16 ppm and two multiplets centered at 2.10 and 1.88 ppm (indicated by •H). After 24 h (Fig. 7c), the ligand cannot be invoked for explaining the greater stability of the O-bonded DMSO intermediate.

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aminic signal at 7.01 ppm disappears (due to the exchange with deuterium of the solvent) and a new peak appears at 3.11 ppm (indicated by $\uparrow$H$_a$). The intensity of this latter peak grows with time simultaneously with the decrease in intensity of the peak at 3.16 ppm. After 5 days (Fig. 7d), the main peak is that falling at 3.11 ppm ($J_{H,H} = 82$ Hz). Also, the peaks near 2.10 and 1.90 ppm undergo some changes, particularly in their relative intensities, which was initially ca. 2:6 and becomes 4:4 at the end of the reaction. This is in accord with the intermediate species having three $H_a$ peaks of relative intensities 2:2:4 (the latter two peaks overlapping one another) as a consequence of the difference in axial ligands, while the tetrachlorido end product with equivalent axial ligands gives only two multiplets for the $H_a$ protons (4:4 relative intensities), falling at 2.13 and 1.82 ppm.

The formation of the intermediate species fac-[PtCl$_3$(cis-1,4-DACH)(D$_2$O)]$^+$, with a coordinated D$_2$O trans to chloride, was confirmed by a 2D [$^1$H–$^{195}$Pt] HMQC experiment. The 2D [$^1$H–$^{195}$Pt] HMQC spectrum (Fig. 8), recorded soon after the addition of Cl$_2$, shows the presence of two sets of cross-peaks ($^1$H/$^{195}$Pt). The first set, less shielded on the Pt axis, has cross-peaks at 7.01/303 and 3.16/303 ppm, while the second set has cross-peaks at 6.88/273 and 3.11/273 ppm. A second experiment, performed some time later, showed a decrease in the intensity of the cross-peaks belonging to the species with the

Fig. 6  Top, scheme of the reaction. Bottom, $^1$H-NMR spectra: (a), [PtCl$_2$(cis-1,4-DACH)] in acetone-d$_6$; (b), soon after addition of Cl$_2$ in CCl$_4$; (c), after 3 h. The asterisks indicate residual solvent peaks.
less shielded Pt atom (303 ppm). Therefore, the latter experiment fully supports the formation of an intermediate species with the formula \( \text{fac-PtCl}_3(cis-1,4\text{-DACH})(\text{D}_2\text{O})^+ \), the platinum nucleus of which resonates in the range of frequencies typical of a PtN\(_2\)Cl\(_3\)O set of donor atoms (303 ppm, Table 1). As expected, in the tetrachlorido end product the Pt nucleus resonates at higher field (~273 ppm) because of the greater shielding effect of an additional chloride in the PtN\(_2\)Cl\(_4\) coordination environment.

In an attempt to prepare in one pot a Pt(IV) species with non-equivalent axial ligands, we performed the oxidative addition of Cl\(_2\) to [PtCl\(_2\)(cis-1,4-DACH)] in water in the presence of excess potassium acetate. The hope was that the acetate anion could compete with the solvent in coordinating to platinum trans to the attacking Cl\(_2\). The reaction led to the instantaneous formation of a precipitate, which was isolated and characterized. It turned out to be a Pt(IV) species with non-symmetrical axial ligands, but these were Cl\(^-\) and OH\(^-\) (the characterization of \( \text{fac-PtCl}_3(cis-1,4\text{-DACH})(\text{OH})^+ \) is reported in the Supplementary Material, Figs S8 and S9†). Most probably, the basic environment created by the acetate anion has fostered deprotonation of the Pt(IV) chlorido-aqua species. Although the reaction did not lead directly to the expected product (the mixed chlorido–acetato species), the obtained hydroxido species could be converted to the acetato species by reaction with acetic anhydride.
measurements. Fully characterized by elemental analysis, ESI-MS, NMR and IR.

ligand substitution in 6-coordinate complexes takes place by a
and water and 1 hour for acetone. Under normal conditions,

This journal is acknowledged for the syntheses of Pt(iv) species with just one molecule of another substrate.

Conclusion

The results obtained in this work have fully confirmed the general mechanism proposed for the oxidative addition of chlorine to a platinum(II) substrate and have shown that, independently from the solvent used, a solvent molecule assists the reaction by entering in trans position with respect to the attacking oxidant.

While such a mechanism was initially proposed only for oxidative addition to platinum(II) complexes performed in aqueous solution, our NMR investigations carried out in deuterated DMF, DMSO and acetone demonstrate that, in all cases, a solvent molecule is involved in the reaction mechanism. For the first time, the solvent-coordinated intermediate fac-[PtCl2(cis-1,4-DACH)(O-DMF)]Cl has been isolated as a pure solid and fully characterized by elemental analysis, ESI-MS, NMR and IR measurements.

The Cl2 addition reaction performed in DMSO has shown that the intermediate solvato species undergoes a rather unusual shift from cis to O-coordination of DMSO. Such a change in configuration does not depend upon the steric requirements of the ancillary ligand (it was observed in the cis-1,4-DACH, as well as in the en complex). However, the octahedral complexes are, per se, quite crowded. Therefore, we believe that the driving force to the shift from S- to O-coordination of DMSO is the release of interligand steric crowding in the latter configuration. It is interesting to note that the rate of isomerization is quite slow. At this stage of the investigation, we cannot say if there is a kinetic preference for S-coordination followed by a thermodynamic preference for O-coordination, or whether it is just a memory effect of the initial disposition of the DMSO molecule sitting on the axial position of the platinum(II) substrate when the attack by Cl2 takes place. In this latter hypothesis, an initial ratio of 1:1 between S- and O-bonded DMSO is to be expected.

The slow rate with which the solvato-species converts to the chlorido species is quite surprising: a rough estimate of the half-life for the anation reaction is 7 days for DMF, 2 days for DMSO and water and 1 hour for acetone. Under normal conditions, ligand substitution in 6-coordinate complexes takes place by a dissociative mechanism and, therefore, we have to conclude that the weakest coordinating solvent is, by far, acetone.

We have also shown that the intermediate solvato-species can be exploited for the synthesis of Pt(iv) species with just one molecule of another substrate.

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