the magnetic moment of the present system and the anti-Curie temperature dependence around room temperature can be reproduced by J values of 100–200 cm^{-1}. As an example, a set of J values of 100 cm^{-1} for the Fe(II)–Fe(III) pairs and 200 cm^{-1} for the Fe(III)–Fe(III) and Fe(II)–Fe(II) pairs gives a room-temperature μ_{eff} value of $\simeq 3.3\ \mu_B$ and very similar isotropic shifts (calculated by using $A_c/h = 1$ MHz)[34,37] for all cysteines, showing the right order of magnitude (Figure (7A). Similar results are obtained by using a set of J values of 150 cm^{-1} for two of the four possible mixed-valence pairs and 200 cm^{-1} for all the other pairs (Figure 7B). The introduction of double exchange effects[38-40] within the two mixed-valence pairs in the latter case does not yield qualitatively different results. Double exchange is undoubtedly present in these systems since Mössbauer data show mixed-valence behavior for all iron atoms. However, at the present state of knowledge it cannot be established whether double-exchange effects or intrinsic differences in J values are more responsible for the anti-Curie behavior of all the NMR signals.

In the presence of fully reduced, one-electron-oxidized, and fully oxidized species, saturation-transfer experiments are possible, and they allow us to set the lower limit of the electron-transfer rate and provide a tool for the assignment of all the signals of the various species. The limitation of this technique at the present stage is that the spectrum of the semireduced Fd is overcrowded with signals.

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Characterization of Products from [PtCl(dien)]Cl and *S*-Adenosyl-L-homocysteine. Evidence for a pH-Dependent Migration of the Platinum Moiety from the Sulfur Atom to the Amine Group and Vice Versa

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The reaction of [PtCl(dien)]Cl with *S*-adenosyl-L-homocysteine (SAH) has been followed by ^1H and ^{195}Pt NMR in the range $2 < pH < 12$. Three products are formed: the mononuclear complex [Pt(dien)SAH-*S*]$^{2+}$ (**1**), with platination of SAH at the sulfur atom, the mononuclear complex [Pt(dien)SAH-*N*]$^{+}$ (**2**), which has a Pt(dien)$^{2+}$ unit coordinated to the amine group of the homocysteine unit, and the dinuclear complex [{Pt(dien)}$_2$SAH-*S*,*N*]$^{3+}$ (**3**), which contains a Pt(dien)$^{2+}$ unit coordinated to the sulfur atom as well as a Pt(dien)$^{2+}$ unit coordinated to the amine group of the cysteine group. No coordination to the adenine unit has been observed under the present conditions. At $pH < 7$ only **1** was formed ($t_{1/2}$ = 75 min for 5 mM concentrations). At $pH > 7$, **1** spontaneously isomerizes to **2** ($t_{1/2}$ = 10 min). This process can be reversed at $pH < 5$ ($t_{1/2}$ = 2 h). At $pH > 7$ the following sequence of reactions occurs between 1 equiv of SAH and 2 equiv of [PtCl(dien)]Cl: SAH → **1** → **2** → **3**. No reaction of SAH directly leading to **2** could be detected. All three complexes react with sodium diethyldithiocarbamate (Na(ddtc)) forming, eventually, free SAH and [Pt(dien)ddtc]$^{+}$. Complexes **2** and **3** both consist of a pair of diastereomers due to different configurations at the sulfur atom. It could be proven for **1** that the interconversion of these isomers was slow on the NMR time scale at 255 K.

Introduction

Platinum–nucleic acid interactions play an important role in the mechanism of action of the antitumor agent *cis*-$PtCl_2(NH_3)_2$ (*cis*-Pt).[1,2] Therefore, research has so far mainly focused on these interactions. Sulfur-containing molecules, like proteins and peptides such as glutathione, are also known to be reactive with Pt ions.[3] It is thought that these constituents of the cytoplasm are responsible for the inactivation of *cis*-Pt and for the observed nephrotoxicity.[4-8] To understand these negative effects, it is necessary to study the chemical reactivity of Pt antitumor drugs with respect to sulfur-containing molecules.

The coordination chemistry of *cis*-Pt and related platinum compounds toward methionine, cysteine, glutathione, and derivatives has already been the subject of some research. Initial binding takes place at the sulfur atom.[9,10] In these initially formed compounds, amine ligands coordinated trans to the sulfur atom become labile.[9-12] Furthermore, with respect to nucleophiles like sodium diethyldithiocarbamate, the Pt–S cysteine bond shows a high degree of stability, whereas the Pt–S methionine bond is thermodynamically labile.[12,13a,b] As a result the formed Pt–S methionine bond is cleaved.

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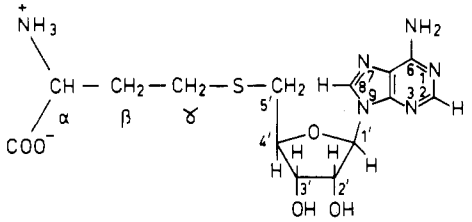
Table I. 300-MHz ^{1}H NMR data for SAH and Its Pt Complexes with [PtCl(dien)]Cl with Chemical Shifts (δ) in ppm Relative to TMA at pH* = 7.0 at 295 K

	chem shift									
compd	H8	H2	Hα	Hβ	Hγ	H1′	H2′	H3′	H4′	H5′,5″
free SAH	5.17	5.06	0.62	−1.09	−0.50	2.89	1.69	1.24	1.15	−0.16
1	5.18	5.11	0.68[a]	−0.84[a]	*b*	2.96	1.78	1.33	1.41[a]	0.32[a]
2	5.19	5.09	0.16	−1.23	−0.52	2.91	1.71	1.24	1.16	−0.16
3	5.20	5.14	a,b	−1.00[a]	*b*	2.97	1.78	1.34	1.40[a]	0.30[a]

[a] Broad signal due to the occurrence of diastereomers and an intermediate rate of interconversion. [b] Signal overlaps with those for H5′,5″ and the dien protons.

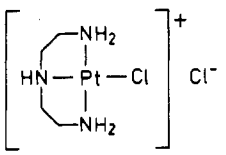
In previous studies, the reactivity of a sulfur-containing molecule has been investigated in the absence of a nucleobase. The aim of the present study is to investigate the intramolecular competition between a sulfur-containing fragment and a nucleobase. This will allow a direct comparison between the reactivity of a sulfur donor atom and a nitrogen donor atom. *S*-Adenosyl-L-homocysteine (abbreviated as SAH) appeared to be a useful model compound



SAH

to study such competitive interactions. The adenine unit is quite a reactive nucleobase in DNA with both N1 and N7 as possible coordination sites.[14] Moreover, SAH is a biologically relevant molecule, as it is the co-product of the methyl-transfer reaction by *S*-adenosyl-L-methionine (SAM).[15]

In the past especially [PtCl(dien)]Cl has proven to be ideally suited to study Pt–sulfur complexes.[12,13a] This monofunctional



[PtCl(dien)]Cl

antitumor-inactive compound is one of the few platinum complexes that is expected to form relatively stable coordination compounds with S-donor ligands (no amine release is observed) and therefore was chosen as a model for *cis*-Pt. The present compounds are the first reported metal complexes of SAH to the best of our knowledge.

Experimental Section

Starting Materials. *S*-Adenosyl-L-homocysteine and sodium diethyldithiocarbamate (Na(ddtc)) were obtained from Sigma Chemicals and used without further purification. [PtCl(dien)]Cl (dien stands for diethylenetriamine) was prepared according to Watt and Cude.[16]

NMR Measurements. The ^{1}H and ^{195}Pt (at 64.4 MHz, with a 10-mm tunable probe) NMR spectra were recorded with a Bruker WM 300 spectrometer. D_2O was used as a solvent. References were Na_2PtCl_6 for ^{195}Pt (external) and TMA (tetramethylammonium nitrate) for ^{1}H NMR. For the ^{195}Pt NMR measurements, concentrations of 100 mM were used, while for the ^{1}H NMR measurements concentrations of 5 mM were sufficient. To monitor the pH-dependent chemical shift behavior of the ^{1}H signals of the various products, the pH was adjusted with 0.1–1 M solutions of NaOD and DCl. Meter readings, reported as pH*, were not corrected for deuterium isotope effects.

Reactions. All reactions (5 mM concentrations of SAH) in D_2O were carried out in the NMR tube over the pH range 2–12 and were followed by ^{1}H NMR as a function of time at 295 K. For the low-temperature measurements, the pH of the solution of [Pt(dien)SAH-*S*]$^{2+}$ (**1**) was first adjusted to 4.2; the Pt compound was then lyophilized and finally dissolved in 75% CD_3OD/D_2O. For the ^{195}Pt NMR measurements, [Pt(dien)SAH-*S*]$^{2+}$ (**1**) was prepared separately by mixing SAH (77 mg, 0.2 mmol) with [PtCl(dien)]Cl (74 mg, 0.2 mmol) in 100 mL of H_2O at pH = 4. After 8 h, the sample was lyophilized. After the sample was dissolved in 2 mL of D_2O, the ^{195}Pt chemical shift was measured. Sample solutions of [Pt(dien)SAH-*N*]$^+$ (**2**) and [{Pt(dien)}$_2$SAH-*S*,*N*]$^{3+}$ (**3**) for the ^{195}Pt NMR measurements were obtained by preparing these compounds in the NMR tube by using complex **1** as a starting compound. All three complexes were afterward characterized by ^{1}H NMR spectroscopy. All the reported $t_{1/2}$ values were measured by integration (concentrations of 5 mM were used; estimated error is 10–15%) of the intensities of proton signals of both reaction products and starting compounds.

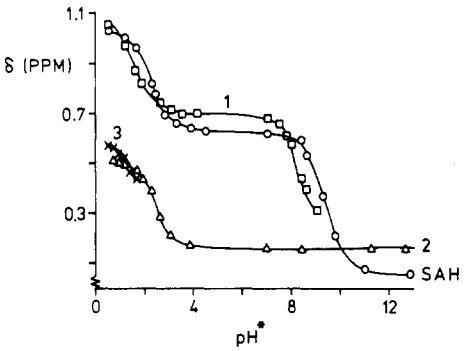


Figure 1. Chemical shifts (δ) of the Hα protons of free SAH (○), **1** (□), **2** (△), and **3** (×) as a function of pH* at 295 K. Chemical shifts are given in ppm relative to TMA. The signals of **1** and **3** could not be followed over the whole pH range due to their broadness and overlap with H5′,5″ and the dien protons.

Results

General Observations. Three complexes were formed between [PtCl(dien)]Cl and SAH under different conditions: two mononuclear complexes (**1** and **2**) and one dinuclear complex (**3**). Unless indicated otherwise, all complexes are stable in aqueous solutions for at least 12 h. All of the proton resonances of **1–3** can be assigned on the basis of chemical shift values and their pH dependence, spin multiplicities, and decoupling patterns and by comparison to the spectrum of free SAH. The assignment of the proton resonances of SAH was found to be consistent with that of Stolowitz et al.[17]

Characterization of Complexes 1–3. The chemical shift differences of the protons H2 and H8, which are due to complexation of Pt(dien)$^{2+}$ to SAH, are all smaller than 0.1 ppm over the pH range 2–12 (see Table I). Coordination of Pt(dien)$^{2+}$ to N7 would produce at pH = 7 a downfield shift of about 0.6 ppm and about 0.15 ppm of H8 and H2, respectively, while coordination of Pt(dien)$^{2+}$ to N1 would produce a downfield shift of about 0.5 ppm of H2.[14] None of these effects is observed; in fact, maximal shifts of 0.08 ppm were found. Therefore, it is concluded that in all three complexes no coordination to the N1 or N7 of the adenine unit takes place.

In complex **1**, the chemical shifts of the protons Hα (see Figure 1) and Hβ still depend on pH, which clearly indicates that no coordination has occurred at the amino or the carboxyl group. The protons that are nearest to the sulfur atom, show the largest

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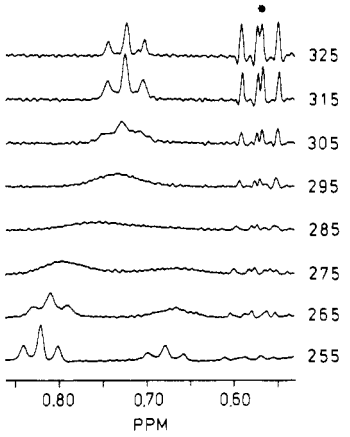

Figure 2. Chemical shift of the Hα proton of complex **1** as a function of temperature (K), showing the appearance of diastereomers upon cooling (in 75% CD_3OD/D_2O). Peaks at the asterisk correspond to free SAH, which is formed due to the thermodynamic lability of the Pt–S bond at higher temperatures. Chemical shifts are given in ppm relative to TMA.

Table II. Ionization Constants (as pK_a) of the Amino and Carboxyl Groups of SAH and Its Pt Complexes As Determined by ^1H NMR Spectroscopy (in D_2O)

compd	pK_a(amino)	pK_a(carboxyl)
free SAH	9.4 (0.1)	2.2 (0.1)
1	8.6 (0.3)	1.5 (0.1)
2		2.4 (0.1)
3		1.7 (0.3)

downfield shifts upon platination (see Table I) and in addition exhibit broadening of their signals. Both observations indicate that a $Pt(dien)^{2+}$ unit is coordinated to the sulfur atom and that $[Pt(dien)SAH\text{-}S]^{2+}$ (**1**) is formed. Broadening is most likely the result of the occurrence of a pair of diastereomers due to different configurations about the sulfur and an intermediate rate of interconversion at room temperature on the NMR time scale. At low pH values (pH < 1.8) the broadened signals sharpen up; this process is reversible on raising the pH again. The explanation for this could be that the protonation of the carboxyl group causes some kind of conformational change, resulting in smaller differences between the pair of diastereomers. If the temperature (in 75% CD_3OD/D_2O) were lowered, the rate of interconversion could be retarded sufficiently to allow separate sets of signals to be observed. The reversible change in the ^1H NMR spectrum observed by changing the temperature is ascribed to the inversion of the pyramidal configuration at the platinum-coordinated sulfur atom (see Figure 2). At 255 K, separate sets of signals are observed for each isomer. There appears to be some chiral discrimination, since the ratio between the two sets of peaks is about 1:2. At this moment we cannot relate this ratio to particular structural differences. It should be mentioned, however, that synthetic *S*-adenosyl-L-methionine consists also of a pair of diastereomers with unequal populations.[17] Because it is out of the scope of this study and no significant new information would be obtained, no attempts have been made to determine the accurate energy of activation for the inversion of configuration. For this kind of pyramidal inversions at sulfur values of about 60 kJ/mol are most often found.[18] When the temperature is raised, some SAH and [PtCl(dien)]Cl are formed (this in fact shows the thermodynamic lability of this Pt–methionine bond). Although the liberation of $Pt(dien)^{2+}$ at high temperature occurs also to some extent in pure D_2O, it is significantly faster in 75% CD_3OD/D_2O.

The acidity of the amino group and the carboxyl group upon $Pt(dien)^{2+}$ coordination to the sulfur atom is increased, respectively,

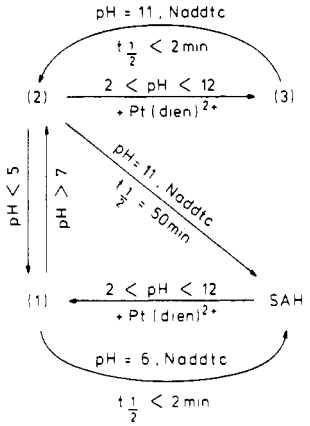

Figure 3. Formation scheme of the complexes of SAH and their interconversions as a function of pH, as well as decomposition reactions with Na(ddtc). Concentrations of SAH, [PtCl(dien)]Cl, and Na(ddtc) are 5 mM.

by ±0.8 and ±0.7 log units (see Table II). This is consistent with the electron-withdrawing effect of the Pt electrophile at the sulfur atom and is in agreement with findings in Pt–nucleotide complexes.[1,2]

In complex **2**, the chemical shifts of the protons Hα (see Figure 1), Hβ, and Hγ depend on pH at pH < 5 but are independent of pH at higher pH values. This clearly indicates that $Pt(dien)^{2+}$ is coordinated to the amino group, forming $[Pt(dien)SAH\text{-}N]^+$ (**2**). The only resonances that shift significantly upon Pt coordination are those of Hα and Hβ (see Table I). These upfield shifts originate from the replacement of a proton by a less polarizing $Pt(dien)^{2+}$. The small decrease of the acidity of the carboxyl group upon $Pt(dien)^{2+}$ coordination to the amino group by ±0.2 log units (see Table II) can be explained in a similar way. The decrease of the acidity as a result of the replacement of a proton by a platinum atom has already been reported in $[Pt(dien)(mAdenosine\text{-}N1)]^+$[14] and in $[\{Pt(NH_3)_3\}_2(\mu\text{-}eGua\text{-}N1,N7)]^{3+}$.[19]

In complex **3**, similar observations can be seen as in complex **1**, indicating coordination of $Pt(dien)^{2+}$ to the sulfur atom (vide supra). No attempts have been made to detect the two different configurations about sulfur as done for **1**. As in **1**, the broadened signal sharpens at pH < 1.8. Due to the broadness of the signal of Hα and its overlap with H5′,5″ and the dien protons, it was impossible to detect this signal at pH > 2 (see Figure 1). However, the signal of Hβ could be detected up to pH 8.5. As in **2**, the chemical shift of this proton still depends on pH below pH 5, but is independent of pH above pH 7 (data not shown). This confirms that in addition to a $Pt(dien)^{2+}$ unit coordinated to the sulfur atom of SAH a second $Pt(dien)^{2+}$ unit is coordinated, this time to the amino group, forming the dinuclear species $[\{Pt(dien)\}_2SAH\text{-}S,N]^{3+}$ (**3**).

It is interesting to note that the chemical shifts depicted in Table I are internally consistent. This means that the chemical shifts of protons in **3** can be calculated from those in SAH, **1**, and **2** (within 0.02 ppm). This observation strongly suggests that there are no major conformational differences for SAH in going from **1** to **2** and to **3**, in agreement with the fact that the coupling constants of the ribose ring protons in SAH, **1**, **2**, and **3** are all about the same. This implies that the ribose ring in species **1**, **2**, and **3** has a C3′-exo configuration, just as in free SAH.[17]

S-Adenosyl-L-methionine (SAM) is reported to be fairly unstable in aqueous solution, leading to several degradation products,[20] most likely originating from the presence of the sulfonium center. Compounds **1** and **3**, both have a Pt(II)–S bond, which can in a sense be compared with the $CH_3\text{–}S^+$ bond in SAM. To exclude the possibility of an incorrect identification, due to formation of degradation products as in SAM, the Pt–SAH

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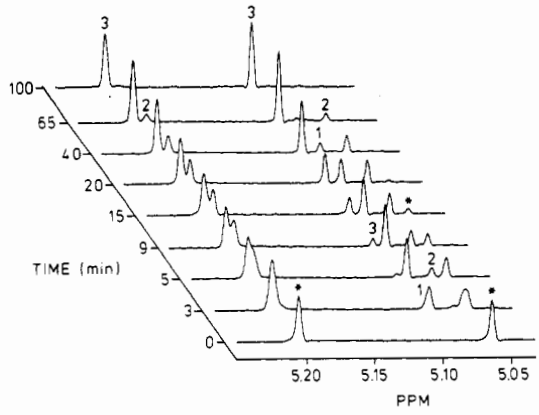

Figure 4. Aromatic region of the ^{1}H NMR spectrum of the reaction between SAH (5 mM) with 2.5 equiv of [PtCl(dien)]Cl as a function of time (pH* = 11). Chemical shifts are given in ppm relative to TMA. Signals between 5.05 and 5.12 ppm correspond to the H2 proton; signals between 5.20 and 5.22 ppm correspond to the H8 proton. * = free SAH; 1 = species **1**; 2 = species **2**; 3 = species **3**.

binding was reversed by sodium diethyldithiocarbamate (Na(ddtc)). Na(ddtc) is known to be very effective in dissociating Pt–methionine type bonds in particular.[12] All the Pt exchange reactions with Na(ddtc) (Figure 3) were carried out under pH conditions at which **1–3** are stable themselves. Both **1** and **3** react with Na(ddtc) with a typical $t_{1/2}$ value[12] for dissociation of a Pt–methionine bond forming respectively SAH and **2**. In addition, **2** reacts also with another equivalent of Na(ddtc), although more slowly ($t_{1/2}$ = 50 min), forming SAH. In all three reactions [Pt(dien)ddtc]$^+$, a species reported earlier,[12] could be detected by NMR. These results prove that in **1–3** the original structure of SAH has remained intact and that no degradation reactions have occurred.

Formation and Interconversion of Complexes 1–3. Figure 3 describes the formation of the complexes **1–3** as a function of pH. At pH < 7, only **1** could be detected, even in the presence of an excess of [PtCl(dien)]Cl. On the other hand, at pH > 7 a sequence of reactions occurs. At first **1** is formed, which isomerizes readily to **2**. On addition of a further equivalent of Pt(dien)$^{2+}$, finally **3** is formed. This pH-dependent reactivity between SAH and Pt(dien)$^{2+}$ can best be explained by the presence of a deprotonated amino group at high pH values. Although the coordination of Pt to sulfur is still kinetically strongly favored, resulting in the formation of **1**, thermodynamically the Pt–methionine bond is labile, in the presence of nucleophiles. For instance Na(ddtc) "liberates" and binds the coordinated Pt(dien)$^{2+}$ from **1** and **3** (vide supra). The most likely mechanism for the isomerization of **1** → **2**, therefore, is an intramolecular migration of the Pt(dien)$^{2+}$ from the sulfur atom to the nucleophilic amino group, resulting in the thermodynamically favored product **2**. No internal migration of the Pt(dien)$^{2+}$ unit to the adenine N1 or N7 is observed. Most likely, the adenine base cannot be oriented in close proximity to the platinum, which would be necessary for such an isomerization reaction. In **2**, the sulfur atom is still available for Pt coordination. Therefore, upon addition of another Pt(dien)$^{2+}$ unit, at any pH, **3** is formed. In **3**, the Pt–S bond is relatively stable at pH = 11, mainly because now there is no further internal N-donor nucleophile within reach. In Figure 4 the sequence of reactions between SAH and 2.5 equiv of [PtCl(dien)]Cl at pH = 11, as observed by ^{1}H NMR, is depicted. Although no coordination to the adenine base was observed, the isolated chemical shift values of its H2 and H8 protons makes them ideally useful for species identification. Finally, no direct reaction of SAH leading to **2** could be observed.

^{195}Pt NMR appeared to be a useful technique for studying this kind of interconversion reactions. The value of the Pt chemical shift is highly dependent on the set of donor atoms.[21] The ^{195}Pt NMR spectrum of **1** shows a singlet at −3358 ppm, which is characteristic for a PtN_3S complex with a tridentate N_3 ligand.[13a] When the pH of the sample is raised (pH = 11), a new signal grows in with time (δ = −2935 ppm), whereas the original signal disappears. The position of this signal is in agreement with a PtN_4 complex, containing a tridentate N_3 ligand, like in **2**. The 208 ppm upfield shift compared to that of free [PtCl(dien)]Cl agrees with the chemical shift difference observed on going from $[PtCl(NH_3)_3]^+$ to $[Pt(NH_3)_4]^{2+}$ (Δ = 227 ppm).[21] Upon addition of a second equivalent of [PtCl(dien)]Cl, two new signals appear at −2938 and −3362 ppm, which can be ascribed to the dinuclear platinum complex **3**, with one signal corresponding to PtN_4 and the other to the PtN_3S unit. The positions of these signals are similar to those of complex **1** and **2**, indicating a rather small effect of the Pt(dien)$^{2+}$ units on the shift. Neither for **1** nor for **3** could separate signals from different diastereomers be detected. The two resonances expected for the diastereomers are probably not resolved due to the broadness (500–600 Hz) of the signals as reported for a comparable complex.[13a] Apparently, the fast relaxation of the ^{14}N nucleus in the dien ligand results in severe broadening of the ^{195}Pt resonance.[22] For the recently reported monofunctional complexes $[PtCl_3(thioether)]^-$ the diastereomers could be detected by ^{195}Pt NMR with a observed splitting of 6–35 ppm.[23]

Table III. $t_{1/2}$ Values as Determined by ^{1}H NMR (Concentrations of Compounds 5 mM; Estimated Errors 10–15%) of the Conversion of SAH into Complexes **1–3** at pH* = 4 and 11

reacn	$t_{1/2}$ pH = 4	$t_{1/2}$ pH = 11
SAH → **1**	75 min	15 min[a]
1 → **2**		10 min
2 → **3**	1 h[a]	30 min
2 → **1**	2 h	

[a] Estimated error is 50%, due to the occurrence of side reactions (see text).

At pH < 5, **2** slowly isomerizes back to **1** (see Table III). However, some side reactions also occur, leading to up to 20% of products that could not be characterized. The mechanism of this isomerization can be considered as an intramolecular migration of the Pt(dien)$^{2+}$ unit. In an acidic medium, assisted by the nucleophilic sulfur atom, the Pt–N bond becomes labile, and subsequently the amino group will protonate. The nearby sulfur atom will now bind to Pt(dien)$^{2+}$. The fact that no free SAH could be detected during this reaction and the fact that **3** under the same acidic conditions was stable for 12 h are in favor of this mechanism.

The determination of the $t_{1/2}$ values (Table III) for the formation of **1–3** at pH = 4 and pH = 11 was rather straightforward, except for the conversion of SAH → **1** at pH = 11 and of **2** → **3** at pH = 4. The latter products show side reactions at these pH values (i.e. **1** → **2** at pH = 11 and **2** → **1** at pH = 4). The $t_{1/2}$ of SAH → **1** at pH = 11 was therefore estimated as the time in which the amount of free SAH was equal to the total amount of **1** + **2**.

Some interesting observations can be deduced from Table III. There is a factor of 5 difference in size for the $t_{1/2}$ values of SAH → **1** at pH = 4 and pH = 11. This can be interpreted in terms of an electrostatic repulsion of the protonated amino group at pH = 4. A similar electrostatic repulsion of the NH_2 coordinated Pt(dien)$^{2+}$ can be used to explain the difference in reactivity of SAH → **1** and **2** → **3** at pH = 11.

Discussion

Although Pt–adenine interactions in DNA are probably not primarily responsible for the antitumor activity of various Pt compounds, adenine is also a reactive nucleobase[1,2] and therefore interesting to study in competitive binding experiments in comparison with other cellular ligands. The absence of any Pt(dien)$^{2+}$

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coordination to the N7 or N1 atom of the adenine base in SAH agrees with the high kinetic affinity of Pt for the sulfur atom.[9,10] It is therefore not unlikely that significant amounts of platinum antitumor compounds will bind to sulfur-containing biomolecules. In fact *cis*-Pt is known to bind to plasma proteins and glutathione, and methionine-containing Pt(II) metabolites have been isolated from the urine of patients receiving *cis*-Pt.[24,25]

Given the absence of any binding to the adenosine unit, the Pt-coordination chemistry of SAH can now be reduced to that of a modified methionine molecule, under the assumption that the $Pt(dien)^{2+}$ coordination to the homocysteine is not sterically affected by the adenosine unit. The coordination chemistry of *cis*-Pt to methionine has recently been described by Appleton et al.[10] They also reported a high affinity for and an initial binding at the thioether sulfur. The subsequent chelating steps resulted in both *cis*-$[Pt(NH_3)_2$(met-*S*,*N*)$]^+$ and *cis*-$[Pt(NH_3)_2$(met-*S*,*O*)$]^{2+}$.[10] The formation of this six-membered chelate ring in *cis*-$[Pt(NH_3)_2$(met-*S*,*N*)$]^+$ already indicates that the amino group can be located in close proximity to the platinum, which in our case is a requirement for isomerization of **1** → **2**. Therefore a pentacoordinated transition state $[Pt(dien)SAH\text{-}S,N]^+$ is likely to occur.

SAH and analogues with modifications at the sugar moiety, at the amino acid residue, or at the purine ring are known to be potent inhibitors of biological methylation reactions catalyzed by *S*-adenosylmethionine-dependent methyltransferases.[26] This points to the possibility that compounds inhibiting these reactions can be pharmacologically active. The three metal complexes of SAH, described above, exemplify a complete new area of analogues of this compound. Therefore studies of the inhibition of this class of enzymes by these three Pt complexes may be worthwhile.

The first three metal complexes of SAH have been described in the present study. The results show that SAH, when reacting with Pt compounds, has a pronounced kinetic preference for the thioether linkage. The initially formed product isomerizes at pH > 7 to yield a thermodynamically favored product in which $Pt(dien)^{2+}$ is coordinated to the NH_2 group. This process can be reversed at pH < 5. The high reactivity of the Pt-S methionine bond toward nucleophiles is confirmed by its reaction with Na(ddtc). Ongoing studies are dealing with the coordination chemistry of [PtCl(dien)]Cl with synthetic *S*-guanosyl-L-homocysteine. In that case the reactivity of the sulfur atom can be directly studied and compared with the reactivity of N7 of the very reactive guanine.

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Spectroscopic Studies of Cyclometalated Platinum(II) Complexes: Superposition of Two Different Spectroscopic Species in the Electronic Spectra of a Single Crystal of [Pt(bpm)$(CN)_2$] (bpm = 2,2'-Bipyrimidine)

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The influence of temperature ($1.9 \le T \le 80$ K) and applied magnetic fields ($0 \le H \le 6$ T) on the optical properties of a single crystal of [Pt(bpm)$(CN)_2$] (bpm = 2,2'-bipyrimidine) is reported. These properties are due to two different kinds of chains (α and β) in the crystal. Chain α consists of quasi-isolated complexes with alternating Pt-Pt distances of 4.178 and 3.438 Å; chain β has a dimeric structure with Pt-Pt distances of 4.581 and 3.269 Å. At $T = 1.9$ K a luminescence exhibiting a sharp-line structure in the high-energy range and a broad weakly structured band in the low-energy range has been observed. The emission indicates a superposition of the electronic transitions in the α and β chains. When a magnetic field $\mathbf{H} \| \mathbf{a}$ is raised from $H = 0$ to 6 T, the intensity of the $\mathbf{E} \| \mathbf{a}$ polarized fine-structure lines increases by a factor of ~70. An applied magnetic field $\mathbf{H} \perp \mathbf{a}$ provides an increase of the $\mathbf{E} \perp \mathbf{a}$ and $\mathbf{E} \| \mathbf{a}$ polarized dimer emission by factors of 5 and 4, respectively. Both effects are explained by a magnetic field induced mixing of the lowest excited state with higher states. Crystallographic data for [Pt(bpm)$(CN)_2$]: triclinic, space group $P\bar{1}$, $a = 7.261$ (1) Å, $b = 10.828$ (1) Å, $c = 14.387$ (1) Å, $\alpha = 88.54$ (1)°, $\beta = 82.78$ (1)°, $\gamma = 74.07$ (1)°, $V = 1072.34$ Å^3, $Z = 4$, $D_x = 2.51$ g·cm^{-3}, μ(Cu Kα) = 249.0 cm^{-1}, $R = 0.025$ and $R_w = 0.033$ for 344 variables and 4411 reflections with $I > 3\sigma(I)$.

Introduction

During recent years, several efforts have been made to understand the photochemistry, photophysics, and electrochemistry of cyclometalated transition-metal complexes and related compounds.[1-7] Several of these systems can be employed as light-absorption sensitizers (LAS) and/or as light-emission sensitizers (LES) for the interconversion between light energy and chemical energy. Depending on the central ion and the ligands, the energetically lowest excited states of these systems were assigned to metal-centered (LF) states, ligand-centered (LC) states, or metal-to-ligand charge-transfer (MLCT) states.[8-15] Sometimes merely a variation of the solvent changes the type of the lowest

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