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Coordination Compounds of Pt(II) with N-methyl Imidazole as a Ligand

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The synthesis of a number of new coordination compounds of Pt(II) with the nitrogen-donor ligand N-methyl imidazole (NMIz) is described. These compounds are cis-*$Pt(NMIz)_2X_2$, $Pt(NMIz)_2C_2O_4 \cdot H_2O$,* trans-*$Pt(NMIz)_2X_2$, $Pt(NMIz)_4X_2(H_2O)_n$ and $Pt(NMIz)_4PtX_4$ where X = Cl, Br or I and n = 0 or 2, and the mixed-valence compound $Pt(NMIz)_4PtCl_6$. The new compounds are characterised by chemical analyses, X-ray powder diffraction, vibrational spectroscopy (infrared, far-infrared and Raman spectroscopy), thermal analyses (thermogravimetry and differential thermal analysis) and proton nuclear magnetic resonance. The* cis-*dichloro and* cis-*dibromo compounds exist in several crystal forms with slightly different spectroscopic properties. When dissolved in concentrated hydrochloric acid and exposed to air, the compound $Pt(NMIz)_4PtCl_4$ is oxidised to $Pt(NMIz)_4PtCl_6$.*

Introduction

Recently we started a research program directed towards the synthesis and characterisation of coordination compounds of the platinum metals with imidazoles and pyrazoles as ligands. This type of compounds is interesting in the first place because of the possible use of certain *cis*-Pt(II) complexes as antitumor drugs [1–4]. Secondly, the interaction of platinum(II) with this type of heterocyclic nitrogen-donor ligands is of interest from the fact that "active" platinum(II) complexes like *cis*-$Pt(NH_3)_2Cl_2$ seem to bind mainly to the N_7 donor atom of the guanine bases of DNA *in vitro* [5–9]. This interaction is also postulated as a first step of the mechanism of action *in vivo* [8, 10, 11].

The synthesis and characterisation of Pt(II) and Pd(II) compounds with imidazole as the ligand has been reported [12]. It has been found recently that the complex *cis*-Pt(imidazole)$_2$Cl$_2$ shows cytostatic activity in mice bearing the tumor *L1210 leukemia* [13]. In order to study the possible influence of the hydrogen bonding capacity of the complex on the activity, compounds with N-methyl imidazole (abbreviated as NMIz) were synthesised. This paper describes the synthesis and characterisation of these compounds with several anions like Cl^-, Br^-, I^- and $C_2O_4^{2-}$.

A crystal structure determination of one of the *cis*-isomers will be published elsewhere [14]. As far as known to the authors the only other N-methyl imidazole complex of Pt(II) known in the literature, has formula *trans*-$[Pt(NH_3)_2(NMIz)_2]Cl_2 \cdot 2H_2O$, for which a crystal structure determination has been carried out [15].

Experimental

Starting Materials

Commercially available N-methyl imidazole (Merck) was used without further purification. Platinum was commercially available as the tetrachloroplatinate, K_2PtCl_4 (Drijfhout, Amsterdam). *Cis*-$Pt(DMSO)_2Cl_2$ was synthesised from K_2PtCl_4 and DMSO according to the method of Price *et al.* [16].

Synthesis of the Compounds

cis-*$Pt(NMIz)_2I_2$*

This compound was synthesised by an improved procedure according to the method of Dhara [17]. 415 mg (1 mmol) of K_2PtCl_4 was dissolved in 20 ml of water and 4 g (about 24 mmol) KI was added to yield a solution of 0.05 *M* PtI_4^{2-} and 1 *M* I^- To this solution 164 mg (2 mmol) of the ligand was added. The *cis*-compound precipitated immediately and was filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

cis-*$Pt(NMIz)_2Br_2$ and* cis-*$Pt(NMIz)_2Cl_2$*

613 mg (1 mmol) of the *cis*-diiodo compound was suspended in water and a solution of 340 mg (2 mmol) $AgNO_3$ in water was added. The suspension was stirred for one hour and the precipitate of AgI was filtered. The filtrate is supposed to contain the *cis*-diaquo species. After addition of a twentyfold

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excess of NaBr or NaCl respectively, the *cis*-dibromo compound or the *cis*-dichloro compound precipitated. The product was filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

$Pt(NMIz)_2C_2O_4 \cdot H_2O$

A suspension of the *cis*-dichloro complex in a concentrated solution of a large excess $K_2C_2O_4 \cdot H_2O$ was boiled for a few minutes. After cooling the complex crystallized as white needles. The crystals were filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

$Pt(NMIz)_4Cl_2 \cdot 2H_2O$

420 mg (1 mmol) *cis*-$Pt(DMSO)_2Cl_2$ was dissolved in 2 ml of water containing an excess of the ligand. This solution was boiled for a few minutes. After cooling and addition of a mixture of dimethylformamide and acetone white crystals appeared. The crystals were filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

$Pt(NMIz)_4Br_2 \cdot 2H_2O$

A tenfold excess of N-methyl imidazole was added to a concentrated solution of *cis*-$Pt(NMIz)_2Br_2$ in DMF. When the solution had become colourless acetone was added and the desired compound crystallized as white needles. The crystals were filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

$Pt(NMIz)_4I_2$

To a concentrated solution of *cis*-$Pt(NMIz)_2I_2$ in acetone a large excess of the ligand was added. After 2 days the desired complex crystallized. The crystalline material was filtered, washed with acetone and dry diethyl ether and dried *in vacuo* at room temperature.

trans-$Pt(NMIz)_2X_2$ *with* $X = Cl, Br$ *and* I

These compounds were prepared by heating the corresponding complexes with four ligands at 130 °C *in vacuo* (10 mmHg) during a few days, according to the procedure of Watt *et al.* [18].

$Pt(NMIz)_4PtX_4$ *with* $X = Cl, Br$ *and* I

These compounds were prepared by mixing aqueous solutions of the appropriate cations and anions in equimolar amounts. compounds precipitated immediately. The precipitates were filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature. The solutions of $PtBr_4^{2-}$ and PtI_4^{2-} were prepared by adding a sixfold excess of KBr or KI resp. to a solution of $PtCl_4^{2-}$ in water (0.05 *M*).

$Pt(NMIz)_4PtCl_6$

When $Pt(NMIz)_4PtCl_4$ was dissolved in concentrated hydrochloric acid, and exposed to air, after a few days bright red crystals appeared analysing as $Pt(NMIz)_4PtCl_6$. The same compound could be synthesised by reaction of K_2PtCl_6 and $Pt(NMIz)_4Cl_2$ in water. The crystals were filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

Physical Methods

Chemical analyses were carried out using standard methods. Infrared spectra of the compounds, pressed in KBr discs and as Nujoll mulls were recorded on a Beckman Acculab instrument (4000–250 cm^{-1}). No decomposition of the compounds occurs in KBr as can be seen from the spectra recorded in nujoll mull, which are identical with those recorded in KBr. Far-infrared spectra of the compounds pressed in polyethylene discs were recorded on a Beckman IR 720 interferometer (500–20 cm^{-1}). Raman spectra of $Pt(NMIz)_4Cl_2 \cdot 2H_2O$, $Pt(NMIz)_4Br_2 \cdot 2H_2O$ and *cis*-$Pt(NMIz)_2Cl_2$ were recorded on a Ramanor HG2S instrument (University of Amsterdam) using a CRL type CR 5 Argon laser (wavelength 514.5 nm). X-ray powder diffraction photographs were obtained with a Guinier-de Wolff camera using CuKα radiation. High temperature X-ray powder diffraction patterns, thermogravimetric measurements and differential thermal analyses were carried out as described elsewhere [19].

Proton NMR spectra were recorded on a Varian T-60 instrument. The spectra of *cis*-$Pt(NMIz)_2Br_2$ and *cis*-$Pt(NMIz)_2I_2$ were recorded in DMF and the spectrum of *cis*-$Pt(NMIz)_2Cl_2$ was taken in DMSO, whereas the spectra of the other compounds were recorded in D_2O.

The conductivity of 0.001 *M* solutions of the compounds was measured with a Philips PR 9501 conductivity bridge. The solvents used were DMF for the *cis*-compounds and water for the compounds containing four N-methyl imidazole ligands.

Results and Discussion

General

Table I lists the compounds with their colours, analytical and conductivity data. The analytical data are in good agreement with the suggested formulae. The conductivity data of the *cis* and *trans* compounds are in good agreement with the expected non-electrolytic behaviour. The conductivity data of the compounds containing four N-methyl imidazole ligands are in agreement with the expected values for 1:2 electrolytes. The X-ray powder diffraction photographs and the infrared spectra of the *cis*-dichloro and *cis*-dibromo complexes showed that the *cis*-

TABLE I. The NMIz Complexes with Their Colour and Analytical and Conductivity Data.

Compounds	Colour	%C		%H		%N		λ^h cm^2 ohm^{-1} mol^{-1}
		Found	Calc.	Found	Calc.	Found	Calc.	
cis-$Pt(NMIz)_2Cl_2$	l. yellow	22.4	22.3	2.9	2.8	13.0	13.0	2.3
cis-$Pt(NMIz)_2Br_2$	l. yellow	18.6	18.5	2.4	2.3	10.8	10.8	2.4
cis-$Pt(NMIz)_2I_2$	yellow	15.6	15.7	2.0	2.0	9.7	9.1	3.0
$Pt(NMIz)_2C_2O_4 \cdot H_2O$[a]	white	25.9	25.8	2.9	3.0	12.1	12.0	2.1
trans-$Pt(NMIz)_2Cl_2$	l. yellow	22.6	22.3	2.8	2.8	13.0	13.0	2.0
trans-$Pt(NMIz)_2Br_2$[b]	l. yellow	19.0	18.5	2.6	2.3	10.7	10.8	2.9
trans-$Pt(NMIz)_2I_2$[c]	yellow	15.6	15.7	2.0	2.0	9.2	9.1	7.2
$Pt(NMIz)_4Cl_2 \cdot 2H_2O$	white	30.5	30.5	4.6	4.4	17.7	17.8	203
$Pt(NMIz)_4Br_2 \cdot 2H_2O$[d]	white	27.0	26.7	3.6	3.9	15.3	15.6	261
$Pt(NMIz)_4I_2$[e]	white	24.7	24.7	3.0	3.1	14.4	14.4	204
$Pt(NMIz)_4PtCl_4$	pink	22.3	22.3	2.7	2.8	13.0	13.0	g
$Pt(NMIz)_4PtBr_4$	cream	18.7	18.5	2.3	2.3	10.8	10.8	g
$Pt(NMIz)_4PtI_4$	l. green	15.9	15.7	1.9	2.0	8.9	9.1	g
$Pt(NMIz)_4PtCl_6$[f]	l. red	20.3	20.6	2.6	2.6	12.0	12.0	g

[a] %Pt found 42.0 calc. 41.9. [b] %Pt found 37.2 calc. 37.6. [c] %Pt found 31.3 calc. 31.8. [d] %Pt found 27.4 calc. 27.1. [e] %Pt found 25.0 calc. 25.1. [f] %Pt found 41.3 calc. 41.9, %Cl found 23.0 calc. 22.9. [g] Insufficiently soluble in organic solvents. [h] In DMF or water, see experimental part.

dichloro complex exists in four different crystal forms and the *cis*-dibromo complex exists in two different crystal forms. The different crystal forms have completely different X-ray powder diffraction patterns and different infrared spectra as well as slightly different far-infrared spectra. The details of these differences and the X-ray structure of one of the crystal forms of the *cis*-dichloro complex will be described elsewhere [14].

The X-ray powder diffraction patterns of *trans*-$Pt(NMIz)_2Br_2$ and *trans*-$Pt(NMIz)_2I_2$ are almost identical. The compounds $Pt(NMIz)_4PtBr_4$ and $Pt(NMIz)_4PtI_4$ also have very similar line patterns. As far as known to the authors only one other solid PtI_4^{2-} compound is known in the literature, *i.e.* $Pt(NH_3)_4PtI_4$ [20].

The formation of $Pt(NMIz)_4PtCl_6$ from $Pt(NMIz)_4PtCl_4$ in concentrated hydrochloric acid must be due to air oxidation. The compounds formed from $Pt(NMIz)_4PtCl_4$ in HCl and from $Pt(NMIz)_4^{2+}$ and $PtCl_6^{2-}$ are completely identical, as deduced from X-ray powder diffraction patterns. The compounds with formula $Pt(NMIz)_4X_2 \cdot nH_2O$ with X = Cl, Br, I and n = 0 or 2 are readily soluble in water but are insoluble in organic solvents. The compounds $Pt(NMIz)_4PtX_4$ with X = Cl, Br, J are insoluble in all common solvents.

Infrared Spectra

The infrared spectra show the absorptions due to ligand vibrations [21]. On complexation with Pt(II) the ligand absorptions show in general three types of alterations.

1) Most absorptions bands are slightly shifted upon complexation. These shifts are always smaller than 20 cm^{-1}. The only exception is the ring stretching vibration at 909 cm^{-1} in the spectrum of the free ligand which appears at about 960 cm^{-1} in the spectra of the complexes, characteristic for coordination of N-alkyl imidazoles [22].

2) In some compounds certain absorption bands are split.

3) A few absorption bands in the spectra of the complexes have a decreased intensity compared with the free ligand.

In agreement with the observed X-ray patterns the spectra of the following pairs of compounds are very similar: *trans*-$Pt(NMIz)_2Br_2$ and *trans*-$Pt(NMIz)_2I_2$; $Pt(NMIz)_4Cl_2 \cdot 2H_2O$ and $Pt(NMIz)_4Br_2 \cdot 2H_2O$; $Pt(NMIz)_4PtBr_4$ and $Pt(NMIz)_4PtI_4$.

In the spectrum of the oxalato complex absorption bands due to vibrations of the oxalate ion occur at 1710, 1665, 1385, 1235, 895, 810, 550 and 450 cm^{-1}. These values are in agreement with a bidentate coordination of the oxalate ion to platinum [23].

Far-infrared and Raman Spectra (450–100 cm^{-1} region)

Table II gives the wavenumbers of the absorption bands in the far-infrared spectra of the compounds in the 450–100 cm^{-1} region. The Pt–halogen stretch-

TABLE II. Far Infrared Spectra of the Compounds (450–100 cm^{-1}).

Compounds	Pt–Halogen Stretchings	Other Vibrations	
		Ligand	Pt–X Bendings and Pt–L Stretchings and Bendings
cis-$Pt(NMIz)_2Cl_2$^{a}	333s, 320s	386w	288w, 265w, 208w, 163w, 110m, br.
cis-$Pt(NMIz)_2Br_2$^{a}	223s, 210s	385	269m, 247m.
cis-$Pt(NMIz)_2I_2$	166m, br.	375w	249m, 230s.
$Pt(NMIz)_2C_2O_4 \cdot H_2O$	–	400w	377s, 358m, 308s, 283w, 271m, 223m, 213m, 197m, 154w, 120w, br.
trans-$Pt(NMIz)_2Cl_2$	341s, 335s	400m	290m, 283m, 271m, 234m, 210m, 179m, 172m, 133m, 128sh, 100m.
trans-$Pt(NMIz)_2Br_2$	226s	395m	301w, 272m, 250m, 212m, 111m.
trans-$Pt(NMIz)_2I_2$	179s	395w	297vw, 270w, 219m, 113sh.
$Pt(NMIz)_4Cl_2 \cdot 2H_2O$		397m, 378m	314w, 273w, 261m, 239w, 203s, br, 173s, vbr, 118s, br, 100s, br.
$Pt(NMIz)_4Br_2 \cdot 2H_2O$		401m, 390m	315vw, 282w, 270w, 263w, 220vw, 200vw, 100br.
$Pt(NMIz)_4I_2$		404m	317w, 299w, 265m, 242w, 219s, 204m, 100s.
$Pt(NMIz)_4PtCl_4$	320sh, 310vs	397m	274w, 264w, 207w, br, 173m, 152s.
$Pt(NMIz)_4PtBr_4$	226s	400 vw	278w, 267w, 108m.
$Pt(NMIz)_4PtI_4$	184s	390vw	272w, 263w, 216w, 209m.
$Pt(NMIz)_4PtCl_6$	322vs	398w	287w, 245w, 233w, 213w, 198w, 143w, 100m.

vw = very weak; w = weak; m = medium; s = strong; vs = very strong; br = broad.

[a] The spectrum of one crystal form has been tabulated; details about the other modifications will be published elsewhere [14] (see also text).

TABLE III. Raman Spectra (450–100 cm^{-1}).

Compounds	Ligand Bands	Other Absorption Bands
$Pt(NMIz)_4Cl_2 \cdot 2H_2O$	392vw, 377w, 247sh	281m^{a}, 240m^{a}, 205m^{b}, 160s
$Pt(NMIz)_4Br_2 \cdot 2H_2O$	390w, 377m, 260w	280m^{a}, 240m^{a}, 207m^{b}, 190sh, 150s, br
cis-$Pt(NMIz)_2Cl_2$	390w, 250w	335s^{c}, 325sh^{c}, 290m^{a}, 260m^{a}, 190w, br, 170s

[a] These vibrations may be assigned to Pt–ligand stretchings. [b] These vibrations may be assigned to Pt–ligand bendings. [c] These vibrations may be assigned to Pt–Cl stretchings.

ing frequencies can easily be assigned because of their large intensity. The low intensity of the Pt–ligand vibrations hampered the assignment of these vibrations. A ligand vibration around 400 cm^{-1} is also assigned.

The presence of two Pt–halogen stretching vibrations (A_1 and B_1 under C_{2v} symmetry) in the spectra of the *cis* complexes confirmed their geometry. The presence of one Pt–halogen stretching vibration (B_{3u} under D_{2h} symmetry) in the spectra of the *trans* complexes is in agreement with their structure. The small splitting of the Pt–Cl stretching vibration in the spectrum of *trans*-$Pt(NMIz)_2Cl_2$ may be due to a crystal packing effect. The spectra of the compounds with formula $Pt(NMIz)_4PtX_4$ with X = Cl, Br, I, show one strong Pt–halogen stretching vibration as expected for the PtX_4^{2-} ions (E_u under D_{4h} symmetry). All of the crystal forms of the *cis*-dichloro and *cis*-dibromo compounds show the expected two Pt–halogen stretching vibrations thus confirming the *cis* geometry for all the compounds.

The Raman spectra of some compounds have also been recorded. The wavenumbers of the bands in the 450–100 cm^{-1} region are listed in Table III. The Raman spectrum of *cis*-$Pt(NMIz)_2Cl_2$ shows rather broad bands. The bands at 335 cm^{-1} and 325 cm^{-1} can be assigned to the two Pt–Cl stretching vibrations (A_1 and B_1). The other bands in the spectrum of *cis*-$Pt(NMIz)_2Cl_2$ and the bands in the spectra of the compounds containing four N-methyl imida-

TABLE IV. Chemical Shifts[a] and ^{195}Pt–Proton Coupling Constants[b] from the ^{1}H-NMR Spectra of the *cis* Compounds and of the Compounds Containing four N-methyl Imidazole Ligands[c].

Compounds	H^2	J_{Pt-H^2}	H^4	J_{Pt-H^4}	H^5	J_{Pt-H^5}	$-CH_3$
NMIz in CCl_4	7.20		6.83		6.77		3.62
NMIz in DMF-d_7	7.57		7.07		6.92		3.68
NMIz in DMSO-d_6	7.58		7.10		6.92		3.67
NMIz in D_2O	7.52		6.98		6.98		3.63
$Pt(NMIz)_4Cl_2 \cdot 2H_2O$	7.77	19.0	6.85	24	7.13	7	3.75
$Pt(NMIz)_4Br_2 \cdot 2H_2O$	7.80	19.5	6.88	24	7.17	7	3.75
$Pt(NMIz)_4I_2$	7.85	19.5	6.92	24	7.17	7	3.75
cis-$Pt(NMIz)_2Cl_2$	8.07	22	6.85	23	7.23	9	3.72
cis-$Pt(NMIz)_2Br_2$	8.20	20	7.00	22	7.30	7	3.85
cis-$Pt(NMIz)_2I_2$	8.23	20	7.00	24	7.33	7	3.82

[a] Chemical shifts in ppm. [b] Coupling constants in Hz. [c] Data for some other ligands and Pt complexes; benzimidazole: H^2 = 8.35; *cis*-$Pt(benzimidazole)_2I_2$: H^2 = 8.72, J_{Pt-H^2} = 22.5 Hz; 3,5-dimethyl pyrazole (DMPz): H^4 = 5.77; *cis*-$Pt(DMPz)_2I_2$: H^4 = 6.00, J_{Pt-H^4} = 9.6 Hz.

zole ligands are due to ligand vibrations, Pt–ligand vibrations and skeletal deformations of the ligand with respect to the rest of the complex. The strong analogy in the spectra of the compounds containing four imidazole ligands, confirms that these compounds indeed have a similar structure.

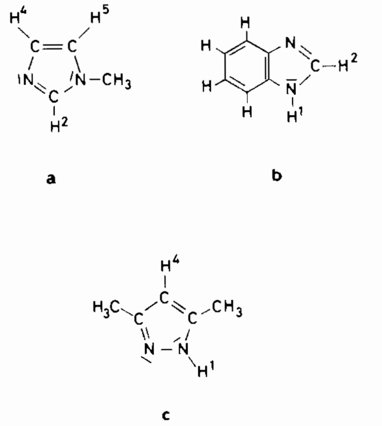
Thermal Analyses

The decomposition of the complexes with four NMIz ligands into the *trans* complexes (see experimental part, synthesis of the *trans* complexes) has been studied with the aid of thermogravimetry, differential thermal analysis and high temperature X-ray powder diffraction. The TG and DTA curves of the complexes $Pt(NMIz)_4Cl_2 \cdot 2H_2O$ and $Pt(NMIz)_4Br_2 \cdot 2H_2O$ can only be interpreted on the basis of a simultaneous loss of ligand and water molecules. The TG curve of $Pt(NMIz)_4I_2$ clearly shows the loss of two ligand molecules per molecule of the complex (calculated weight loss 21.1%, found 20.5%). In the DTA curve a very sharp peak at about 200 °C is observed which represents the ΔH value for the reaction: $Pt(NMIz)_4I_2(s) \rightarrow$ *trans*-$Pt(NMIz)_2I_2(s)$ + 2NMIz (g). The measured ΔH value is 24.5 kcal/mol of ligand. This value is close to those found for Ni(II)–NMIz complexes [24].

In the high-temperature Guinier–de Wolff photograph the decomposition of $Pt(NMIz)_4I_2$ into *trans*-$Pt(NMIz)_2I_2$ can be observed from 150–170 °C. In the high-temperature Guinier–de Wolff photographs of $Pt(NMIz)_4Cl_2 \cdot 2H_2O$ and $Pt(NMIz)_4Br_2 \cdot 2H_2O$ several transitions are observed, but the product in the highest temperature region before melting, undoubtedly is the *trans* compound.

Proton Nuclear Magnetic Resonance

Table IV lists the chemical shifts [in ppm with respect to internal TNP (sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)-propionate) or TMS] of the ring and $-CH_3$ protons of the N-methylimidazole molecule both in the complexes and as the free ligand in various solvents. Also listed are the coupling constants of the ring protons with the ^{195}Pt isotope, which is present for about 34% in natural platinum. No observable coupling of the methyl protons with ^{195}Pt appears to occur. For comparison the *cis*-diiodo complexes of benzimidazole and 3,5-dimethylpyrazole have also been synthesised [25] and their ^{1}H-NMR spectra recorded. The spectral parameters



a b

c

Numbering schemes for the ring protons in N-methylimidazole (a), benzimidazole (b), and 3,5-dimethyl pyrazole (c).

of the ring protons of the five-membered azole rings of these complexes are also listed in Table IV. The other signals in the spectra of these complexes have been omitted for the present purpose. The numbering schemes for the azole rings are presented on the preceding page.

The assignment of the ring proton resonances in the spectrum of the free ligand follows from the spectra of the free ligand in the presence of different amounts of a Lanthanide Shift Reagent ($Eu(fod)_3$). The signals of the H^2 and H^4 protons show larger shifts than the signal of the H^5 proton, just as expected from the larger distance of the H^5 proton to the coordinating N^3 atom. The position of the H^2 proton is determined by comparison with the spectrum of imidazole, where the H^4 and H^5 protons are equivalent, giving rise to a single signal. The values of the ring proton chemical shifts are dependent upon the solvent used as can be seen from Table IV. These solvent effects have roughly the same magnitude as found for pyridine and substituted pyridines [26].

The assignment in the spectra of the complexes is based on the magnitude of the coupling constant between the ring protons and ^{195}Pt. In general the magnitude of these coupling constants decreases with increasing number of bonds between the proton and the platinum atom for this type of heterocyclic aromatic rings. For example the coupling constants in pyridine complexes are $J(^{195}Pt–^1H_o)$ = 33Hz and $J(^{195}Pt–^1H_m)$ = 10 Hz, for *ortho* (H_o) and *meta* (H_m) protons respectively [27, 28]. The coupling of ^{195}Pt with the H^2 proton in the benzimidazole complex is 22.5 Hz. About the same value (26 Hz) is found by Theophanides [9] in platinum–purine nucleoside complexes for the coupling constant of ^{195}Pt coordinated at the N^7 atom with the proton at C^8. In these complexes the platinum ion and the proton are separated by the same number of chemical bonds as is the case for the platinum ion and the H^2 and H^4 protons in the NMIz compounds.

The coupling of ^{195}Pt with the H^4 proton in the 3,5-dimethyl pyrazole complex is 9.6 Hz. In this complex the same number of chemical bonds between platinum and the proton occurs as is the case for the H^5 proton in the N-methyl imidazole complexes. By comparison of the above data with the data of the N-methyl imidazole complexes the signals in the spectra of these complexes can be assigned. The signal at the lowest field can be assigned to the H^2 proton (coupling constant of about 20 Hz). The next signal at higher field shows a coupling constant of about 8 Hz and is therefore assigned to the H^5 proton. The third signal in this region is assigned to the H^4 proton which again has a large coupling constant of about 24 Hz.

Table IV shows that all signals are shifted upon complexation. These shifts must be due to several effects like the electric field effect caused by complexation, π-bonding and temperature independent paramagnetism of the platinum ion [26]. Only the signals of the H^2 and H^5 protons show larger shifts on complexation than the shifts due to solvent effects on the free ligand. Because of the asymmetry of the N-methyl imidazole molecule all ring protons are affected in a different way. The result is a downfield shift for the H^2, H^5 and $-CH_3$ protons. The shifts of the H^4 proton are comparable in magnitude with the solvent effect.

The spectra of the compounds not listed in Table IV could not be recorded because of their low solubility in the common NMR solvents. Until now it was not possible to obtain ^{13}C-NMR spectra with signals of sufficient intensity to allow interpretation.

Conclusions

The anti-tumor properties of the *cis*-dichloro complex are currently being investigated. Comparison of the activity of the imidazole and the N-methyl imidazole complexes may give some information about the effect of hydrogen bonding on the activity. Further studies will include complexes with sterically hindered ligands like 2-methyl imidazole and 1,2-dimethyl imidazole and also naturally occurring ligands like the amino acid histidine and derivatives. Such a study may deliver more information about the relationship between structure and activity and the mechanism of action of the *cis*-Pt(II) complexes.

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