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Coordination Compounds of Pt(II) and Pd(II) with Imidazole as a Ligand. New Synthetic Procedures and Characterization

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The synthesis and characterization of a number of new coordination compounds of Pt(II) and Pd(II) with the nitrogen-donor ligand imidazole (IzH) is described. These compounds are cis-$Pt(IzH)_2X_2$, trans-$Pt(IzH)_2X_2$, $Pt(IzH)_4X_2$, trans-$Pd(IzH)_2X_2$, $Pd(IzH)_4X_2$ *where X = Cl, Br or I and* $Pt(IzH)_4PtX_4$, $Pd(IzH)_4PdX_4$ *where X = Cl or Br, and* cis-$Pd(IzH)_2X_2$ *where X = Cl, Br or* $X_2 = C_2O_4$, *as well as* $Pt(IzH)_2(Iz)_2$ *and* $Pd(Iz)_2$ *where Iz is the imidazolato anion. The new compounds are characterized by chemical analyses, X-ray powder diffraction photographs, vibrational spectroscopy (infrared- and far-infrared spectroscopy) and proton nuclear magnetic resonance.*

The metal(II) ions are in all cases coordinated in a square-planar geometry. In $Pd(Iz)_2$ *a polymeric structure exists with bidentate, bridging imidazolato anions.*

Introduction

In 1969 Rosenberg and co-workers described the ability of *cis*-$Pt(NH_3)_2Cl_2$ and some related complexes to inhibit the growth of certain tumours in mice [1]. The anti-tumour activity of *cis*-platinum complexes with certain N-donor ligands and anions like Cl^-, malonate, SO_4^{2-} is now well established [2, 3]. The cytostatic effect of these platinum complexes is thought to be due to a direct reaction of the platinum complex with the DNA in the cell [3, 4]. The most important interaction seems to be the binding to the N-7 atom of the guanine bases, as a first step in the mechanism of action [4, 5].

Thus far only a few complexes with aromatic heterocyclic N-donor ligands have been investigated for possible anti-tumour activity [6]. Complexes of the platinum group metals with imidazoles and pyrazoles are hardly investigated in contradiction to the numerous compounds with first row transition metals described in the literature [7]. As far as Pt and Pd are concerned, only a few compounds with imidazole [8], N-methyl imidazole [9], benzimidazole [10] and 3,5-dimethyl pyrazole [11] are described.

Therefore we have undertaken a systematic investigation of the synthesis, characterization and cytostatic activity of Pt and Pd complexes with imidazoles and pyrazoles as ligands.

This paper describes the detailed synthesis and the characterization of Pt(II) and Pd(II) compounds with imidazole (abbreviated as IzH). A preliminary report of this work, as well as a paper on Pt(II) complexes with N-methyl imidazole have appeared recently [12, 13].

Experimental

Starting Materials

Imidazole was commercially available and used without further purification. Platinum and Palladium were commercially available as the tetrachloroplatinate, K_2PtCl_4 and as palladium chloride $PdCl_2$, respectively (Drijfhout, Amsterdam). The following compounds were synthesized by known procedures: *cis*-$Pt(DMSO)_2Cl_2$ [14], PdI_2 [15], $K_2Pd(C_2O_4)_2 \cdot 2H_2O$ [16]. Palladium bromide was synthesized from $PdCl_2$ by repeated evaporation of a solution of $PdCl_2$ in concentrated HBr. The product was heated at 200 °C to constant weight.

Physical Methods

Chemical analyses were carried out using standard methods. Infrared spectra, far-infrared spectra, X-ray powder diffraction photographs, NMR spectra and conductivity data were obtained as described elsewhere [13].

The proton NMR spectra and the conductivity data of the neutral complexes were obtained in DMF as the solvent. In case of the complexes containing four imidazole ligands the conductivity data and the NMR spectra were obtained in water.

Synthesis of the Compounds

cis-$Pt(IzH)_2I_2$

This compound was synthesized 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 136 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(IzH)$_2$Br$_2$ and* cis-*Pt(IzH)$_2$Cl$_2$*

585 mg (1 mmol) of the *cis*-diiodo compound was suspended in a 1 *M* solution of $NaNO_3$ 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 excess of NaBr or NaCl respectively, the *cis*-dibromo or the *cis*-dichloro compound precipitated. The product was filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature. The *cis*-dibromo compound could also be synthesized by the method described above for the *cis*-diiodo compound. In this case recrystallization from a mixture of DMF and water is necessary, because of possible contamination of the product with $Pt(IzH)_4PtBr_4$.

Pt(IzH)$_4$I$_2$

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

Pt(IzH)$_4$Br$_2$

A threefold excess of imidazole was added to a concentrated solution of *cis*-$Pt(IzH)_2Br_2$ in DMF. After heating the solution at 50–60 °C for 30 minutes the solution was cooled and diluted with acetone. A white precipitate was formed. The product was filtered, washed with acetone and dry diethyl ether and dried *in vacuo* at room temperature.

Pt(IzH)$_4$Cl$_2$

420 mg (1 mmol) *cis*-$Pt(DMSO)_2Cl_2$ was dissolved in three ml DMF and heated at 70 °C. A threefold excess of the ligand was added and the solution was heated for 30 minutes. The solution was cooled and diluted with acetone upon which a white precipitate was formed. The product was filtered, washed with acetone and dry diethyl ether and dried *in vacuo* at room temperature.

Pt(IzH)$_4$PtX$_4$ with X = Cl or Br

These compounds were synthesized by mixing aqueous solutions of the $Pt(IzH)_4^{2+}$ cations and the PtX_4^{2-} anions in equimolar amounts. The compounds precipitated immediately. The precipitates were filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature. The solution of $PtBr_4^{2-}$ was prepared by adding a tenfold excess of NaBr to a solution of $PtCl_4^{2-}$ in water.

Pt(IzH)$_2$(Iz)$_2$

538 mg (1 mmol) $Pt(IzH)_4Cl_2$ was dissolved in 50 ml water. To this solution 2 ml of a 4 *N* ammonia solution was added. The resulting white suspension was heated on a water bath for one hour, and filtered. The product was washed with water, ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

trans-*Pt(IzH)$_2$Cl$_2$*

538 mg (1 mmol) $Pt(IzH)_4Cl_2$ was dissolved in 3 ml DMF containing 1 g tetraethylammoniumchloride. The solution was refluxed for 15 minutes. To the yellow solution sufficiently hydrochloric acid was added to bind the free ligand molecules. After cooling the solution was diluted with 25 ml 2 *N* HCl. A yellow crystalline product separated. The product was filtered, washed with water, ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

trans-*Pt(IzH)$_2$Br$_2$*

627 mg (1 mmol) $Pt(IzH)_4Br_2$ was dissolved in 3 ml DMF containing 1 g tetraethylammoniumbromide. The solution was refluxed for 15 minutes. To the yellow solution sufficiently hydrobromic acid was added to bind the free ligand molecules. After cooling the solution was diluted with 25 ml of a 1 *M* NaBr solution in water. A yellow crystalline product separated. The product was filtered, washed with water and dried at 60 °C.

trans-*Pt(IzH)$_2$I$_2$*

To a solution of 491 mg (1 mmol) *trans*-$Pt(IzH)_2Br_2$ in acetone a small excess of NaI was added. The white precipitate of NaBr was filtered. The filtrate was diluted with toluene. Upon standing the product crystallized after one day. Instead of toluene a solution of NaI in water could also be used to precipitate the compound. The product was washed with water (or toluene if this was used to precipitate the compound) and dried at 60 °C.

Pd(IzH)$_4$X$_2$ with X = Cl or Br

1 mmol PdX_2 was dissolved in 2 ml DMF containing a few drops of conc. HX on a water bath. The solution was diluted with acetone (50 ml). Addition of an excess of the ligand (sufficient to neutralize the added HX and to form the complex) resulted in a white precipitate. The product was filtered, washed with acetone and dry diethyl ether and dried *in vacuo* at room temperature.

Pd(IzH)$_4$I$_2$

360 mg (1 mmol) PdI_2 was suspended in a solution of 136 mg (2 mmol) imidazole in acetone. The

suspension was stirred until most of the PdI_2 was dissolved. The solution was filtered and is supposed to contain *trans*-$Pt(IzH)_2I_2$. To the filtrate an excess of the ligand was added. The desired compound precipitated immediately. The product was filtered, washed with dry diethyl ether and dried *in vacuo* at room temperature.

$Pd(IzH)_4PdX_4$ with X = Cl or Br

1 mmol PdX_2 was dissolved in 25 ml of a 2 *M* solution of NaX in water. This solution was mixed with a solution of 0.95 mmol $Pd(IzH)_4X_2$ in water. The compounds precipitated immediately. The products were filtered, washed with water and dried at 60 °C.

$Pd(IzH)_2(C_2O_4)$

396 mg (1 mmol) $K_2Pd(C_2O_4)_2 \cdot 2H_2O$ was dissolved in 75 ml water. To the clear yellow solution a solution of 136 mg (2 mmol) imidazole in 15 ml water was added. The imidazole solution was adjusted to pH 6 with diluted HNO_3. The desired compound precipitated as a yellow product. The product was filtered, washed with water, ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

cis-*$Pd(IzH)_2Cl_2$*

A suspension of $Pd(IzH)_2C_2O_4$ in concentrated HCl was stirred for three hours. The suspension was filtered and the product washed with water, ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

cis-*$Pd(IzH)_2Br_2$*

266 mg $PdBr_2$ (1 mmol) was suspended in 10 ml ethanol containing 1 g NaBr and stirred for 1 hour at 60 °C. The excess NaBr and undissolved material was filtered. To the filtrate a solution of 136 mg (2 mmol) imidazole in 10 ml ethanol was slowly added. The resulting orange-yellow precipitate was filtered, washed with ethanol and dry diethyl ether and dried *in vacuo* at room temperature.

trans-*$Pd(IzH)_2Cl_2$*

177 mg (1 mmol) $PdCl_2$ was dissolved in 5 ml DMF while heating on a water bath. To this solution 136 mg (2 mmol) imidazole dissolved in 20 ml acetone was added. The solution was heated on the water bath for 30 minutes. Then the solution was evaporated to dryness. The product was dissolved in acetone and an equal volume of toluene was added. After standing for a few days a yellow product crystallized. The product was filtered, washed with toluene and dry diethyl ether and dried *in vacuo* at room temperature.

The same compound could also be synthesized by heating a solution of $Pd(IzH)_4Cl_2$ in 6 *N* HCl for a few hours. The *trans* compound crystallized after cooling the solution. The product was filtered and washed with water and dried at 60 °C.

trans-*$Pd(IzH)_2Br_2$*

This product could also be synthesized by the method in DMF described for *trans*-$Pd(IzH)_2Cl_2$.

Trans-$Pd(IzH)_2Br_2$ could also be prepared by heating a solution of $Pd(IzH)_4Br_2$ in 100 ml water adjusted to pH 1 with a 2 *N* HBr solution. The yellow crystalline precipitate was filtered, washed with water and dried at 60 °C. If necessary the compound can be recrystallized from a mixture of acetone and toluene.

trans-*$Pd(IzH)_2I_2$*

360 mg (1 mmol) PdI_2 was dissolved in 25 ml acetone containing 2.1 mmol NaI. To this solution 136 mg (2 mmol) imidazole was added. The solution was stirred for one hour and filtered if necessary. The filtrate was evaporated to dryness. The crude product which still contained NaI was washed with water to remove this NaI. The product was dissolved in acetone and an equal volume of toluene was added. After a few days bright red crystals were formed. The crystals were filtered, washed with toluene and dry diethyl ether and dried *in vacuo* at room temperature.

$Pd(Iz)_2$

177 mg (1 mmol) $PdCl_2$ was dissolved in 20 ml of a 4 *N* ammonia solution while heating on a water bath. To this solution 2.1 mmol imidazole was added. The solution was further heated on the water bath for two hours. A white precipitate was formed. The product was filtered, washed with water, acetone and dry diethyl ether and dried *in vacuo* at room temperature.

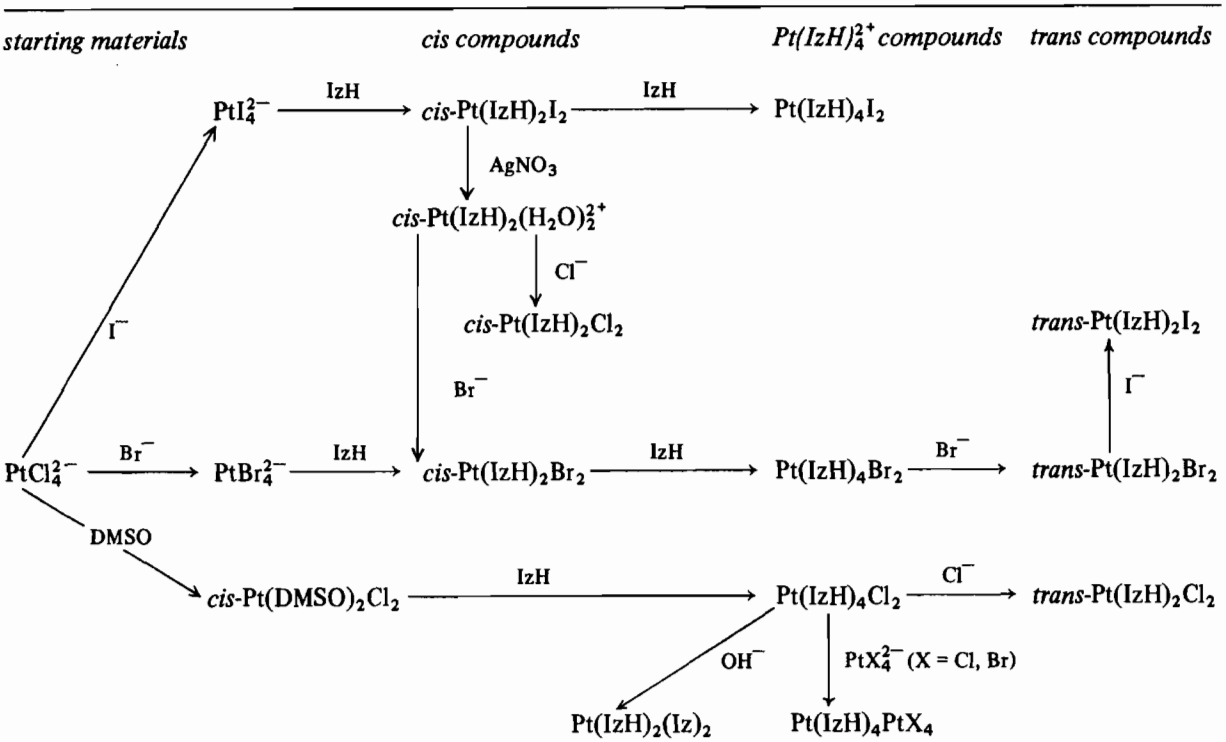
Results and Discussion

General

The synthetic methods employed are outlined in Schemes 1 and 2. Some remarks can be made on these methods.

The *cis*-platinum compounds could be synthesized directly from K_2PtX_4 by reaction with the ligand in case of X = Br or I. For X = Cl no reaction occurred. The *cis*-dichloro compound could be prepared from the *cis*-diiodo compound by reaction with silver nitrate and subsequent addition of Cl^-. The Pt compounds containing four imidazole ligands could easily be prepared from the *cis*-compounds or from *cis*-$Pt(DMSO)_2Cl_2$. The *trans* platinum compounds could not be synthesized by reaction of the $Pt(IzH)_4X_2$ compounds with concentrated HX in water because of the rapid formation of Pt(IV) compounds due to air oxidation. Reaction in non-aqueous solvents, however resulted in the pure *trans* compounds. With Pt an unusual halogen-free compound of formula

Scheme 1. Synthetic procedures for the several platinum compounds.



$Pt(IzH)_2(Iz)_2$ could be prepared in which two of the imidazole ligands are deprotonated. The compound is very stable probably because of the very strong hydrogen bonds (*vide infra*). An analogous palladium compound could not be synthesized however. All attempts resulted in the formation of the palladium imidazolato compound, $Pd(Iz)_2$. For the synthesis of the $Pd(IzH)_4X_2$ compounds it was possible to make use of the fact that the PdX_2 salts are soluble in DMF, which is not the case for the corresponding platinum compounds.

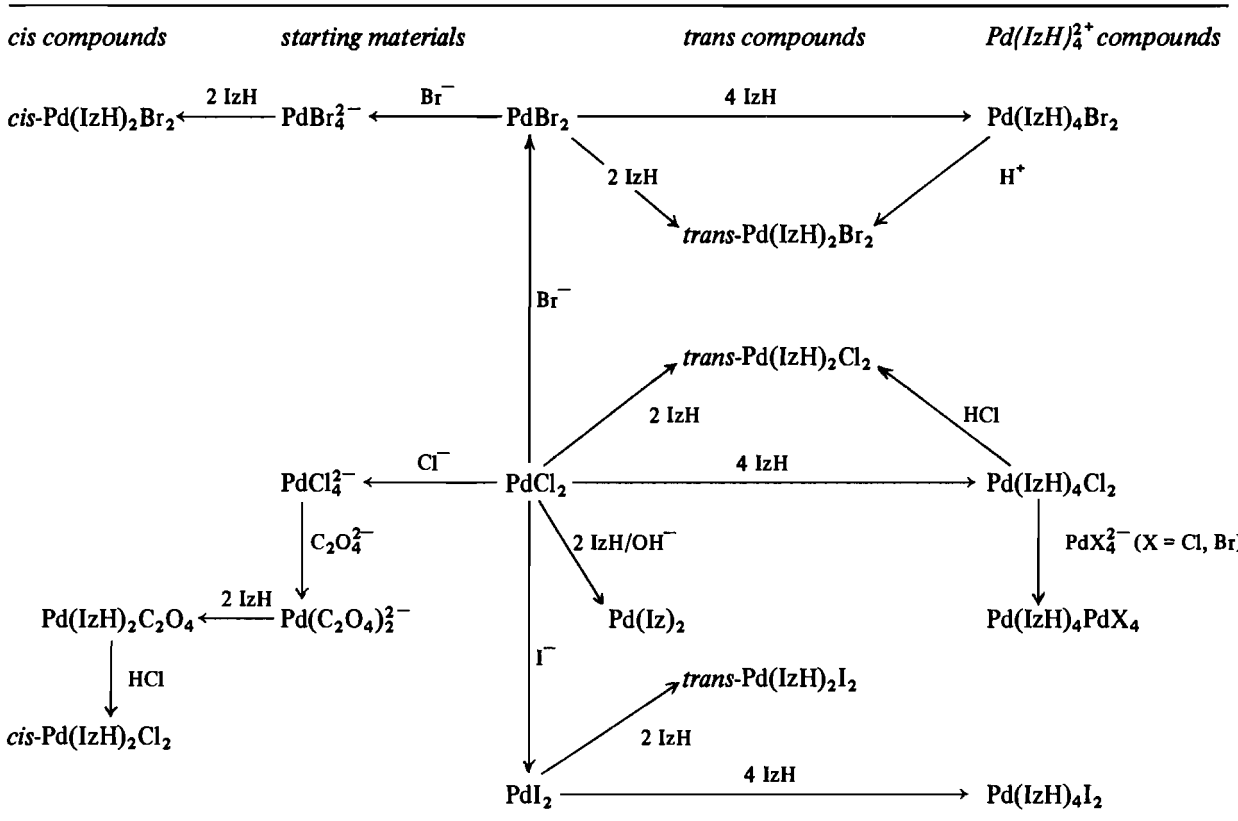
The $Pd(IzH)_4PdX_4$ (X = Cl, Br) compounds are rather unstable. High X^- concentrations are necessary to prevent isomerisation to the *trans* compounds. These compounds dissolve in acetone with formation of the *trans* compounds. Compounds containing the MI_4^{2-} anion with M = Pt or Pd could not be obtained in a pure form as in the case of Pt(N-methyl imidazole)$_4PtI_4$ [13].

The *cis*-palladium compounds were difficult to synthesize because of rapid isomerisation to the *trans* isomers. The *cis*-dichloro compound could be obtained by reaction of the oxalato compound with concentrated HCl. The *cis*-dibromo compound could be obtained by reaction of IzH with $PtBr_4^{2-}$ in ethanol. The insolubility of *cis*-$Pd(IzH)_2Br_2$ in ethanol apparently prevents the isomerisation to the *trans* isomer. This shows that in this system first the *cis* compounds are formed which then rapidly isomerise to the *trans* compounds. The *cis*-diiodo compound could not be obtained because of the extremely rapid isomerisation reaction. However when *cis*-$Pd(IzH)_2Br_2$ is reacted with $AgNO_3$ in DMF at −50 °C and the precipitate of AgBr is filtered, followed by addition of NaI and the reaction mixture is poured into toluene, one can obtain a very small amount of the *cis*-diiodo compound. Its infrared spectrum is identical with that of *cis*-$Pt(IzH)_2I_2$. This unusual method has to be investigated in more detail.

The *trans* palladium compounds could easily be obtained by reaction of PdX_2 salts with two equivalents of the ligand in DMF or acetone. Only with the chloro compound was it necessary to heat the solution for half an hour to ensure that isomerisation to the *trans* compound is complete.

Table I lists the compounds with their colour, analytical data, conductivity data and X-ray and infrared isomorphism. The analytical data are in good agreement with the suggested formulae. The conductivity data are in good agreement with the expected non-electrolytic behaviour for the *cis* and *trans* compounds and with the values for 1:2 electrolytes for the $M(IzH)_4X_2$ compounds. The X-ray powder diffraction photographs showed that all the *cis* compounds are mutually isomorphous. The $M(IzH)_4X_2$ compounds are also isomorphous including the

Scheme 2. Synthetic procedures for the several palladium compounds.



corresponding Ni compounds [18]. In the series of *trans* compounds and $M(IzH)_4MX_4$ compounds only the compounds with the same anion are isomorphous. The *cis* and *trans* compounds are readily soluble in polar organic solvents like DMF although the *cis* palladium compounds isomerise to the *trans* compounds (see ^{1}H-NMR spectra). The $M(IzH)_4X_2$ compounds are readily soluble in water in the case of X = Cl and Br and insoluble in the case of X = I. The $Pd(IzH)_4PdX_4$ compounds are readily soluble in DMF and acetone with rapid formation of the *trans* compounds. All other compounds are insoluble both in water and in organic solvents.

Infrared Spectra

The infrared spectra of the new compounds show the absorptions due to ligand vibrations [19]. The same type of alterations on complexation of the ligand are observed as in the case of N-methyl imidazole [13].

Table I also shows the isomorphism in the infrared spectra of the different classes of compounds.

The infrared spectrum of $Pt(IzH)_2(Iz)_2$ shows two very strong and broad absorption bands at 2550 and 1900 cm^{-1} which are tentatively assigned to N–H stretching vibrations. The very low frequencies of these vibrations with respect to the other compounds suggests extremely strong hydrogen bonding in this compound. Such a strong binding might occur in case of species like Pt–Iz–H–Iz–Pt. Unfortunately no crystals suitable for X-ray analysis could be obtained. In the infrared spectrum of $Pd(Iz)_2$, as expected, no absorption bands due to N–H stretching vibrations are observed.

In the spectrum of $Pd(IzH)_2C_2O_4$ four oxalate vibrations could be assigned at 1680, 1415, 900 and 545 cm^{-1}, in agreement with bidentate coordination of the oxalate ion [20]. The other oxalate absorptions could not be observed due to ligand vibrations in the same region.

Far-infrared Spectra

Table II gives the wave numbers of the absorption bands in the spectra of the compounds in the 450–100 cm^{-1} region.

The M–Halogen stretching frequencies can easily be assigned because of their high intensity. No attempts have been made to assign M–ligand vibrations, because of the fact that even in pyridine complexes where isotope substitution studies have been

TABLE I. The Imidazole Compounds with Their Colour, Analytical Data, Conductivity Data and X-Ray and IR Isomorphism.

Compounds	Colour	%C found (calc.)	%H found (calc.)	%N found (calc.)	Conductivity[d] $cm^2\ ohm^{-1}\ mol^{-1}$	Isomorphism	
						X-ray	IR
cis-$Pt(IzH)_2Cl_2$	1. yellow	18.0 17.9	2.3 2.0	13.6 13.9	11.3	I	A
cis-$Pt(IzH)_2Br_2$[a]	yellow	14.6 14.7	1.6 1.6	11.4 11.4	7.4	I	A′
cis-$Pt(IzH)_2I_2$	yellow	12.3 12.3	1.3 1.4	9.6 9.6	5.8	I	A″
cis-$Pd(IzH)_2Cl_2$	1. yellow	23.3 23.0	2.7 2.6	17.5 17.9		I	A
cis-$Pd(IzH)_2Br_2$	orange-yellow	18.2 17.9	2.0 2.0	13.7 13.9	15.1	I	A′
$Pd(IzH)_2C_2O_4$	yellow	29.1 29.1	2.5 2.4	16.9 17.0			
trans-$Pt(IzH)_2Cl_2$	yellow	17.9 17.9	2.1 2.0	14.1 13.9		II	B
trans-$Pt(IzH)_2Br_2$[b]	yellow	14.6 14.7	1.6 1.6	11.4 11.4	3.9	III	B′
trans-$Pt(IzH)_2I_2$	yellow	12.6 12.3	1.5 1.4	9.6 9.6		IV	B″
trans-$Pd(IzH)_2Cl_2$	yellow	23.0 23.0	2.7 2.6	17.7 17.9	9.6	II	B
trans-$Pd(IzH)_2Br_2$	orange-yellow	18.0 17.9	2.1 2.0	13.5 13.9	14.3	III	B′
trans-$Pd(IzH)_2I_2$	dark-red	14.6 14.5	1.6 1.6	11.3 11.3	16.1	IV	B″
$Pt(IzH)_4Cl_2$	white	26.8 26.8	3.2 3.0	20.8 20.8	191	V	C
$Pt(IzH)_4Br_2$[c]	white	22.5 23.0	2.6 2.6	17.6 17.9		V	C′
$Pt(IzH)_4I_2$	white	20.1 20.0	2.3 2.2	15.3 15.5		V	C″
$Pd(IzH)_4Cl_2$	white	32.3 32.1	3.9 3.6	24.7 24.9	209	V	C
$Pd(IzH)_4Br_2$	white	26.7 26.8	3.2 3.0	20.9 20.8		V	C′
$Pd(IzH)_4I_2$	white	23.0 22.8	2.6 2.6	17.8 17.7		V	C″
$Pt(IzH)_4PtCl_4$	pink	17.9 17.9	2.1 2.0	13.8 13.9		VI	D
$Pt(IzH)_4PtBr_4$	creme	15.0 14.7	1.7 1.6	11.4 11.4		VII	D′
$Pd(IzH)_4PdCl_4$	red	22.8 23.0	2.8 2.6	17.4 17.9		VI	D
$Pd(IzH)_4PdBr_4$	dark-red	17.8 17.9	2.1 2.0	13.7 13.9		VII	D′
$Pt(IzH)_2(Iz)_2$	white	30.9 31.0	3.3 3.0	23.7 24.1			
$Pd(Iz)_2$	white	30.0 30.0	3.1 2.5	22.6 23.3			

[a]%Pt found 40.1, calc. 39.7. [b]%Pt found 39.8, calc. 39.7. [c]%Pt found 31.0, calc. 31.1. [d]10^{-3} *M* solution.

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

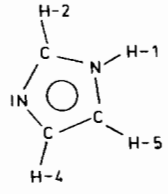
Compounds	M–Halogen Stretchings	Other Vibrations M–X Bendings and M–Ligand Stretchings and Bendings
cis-$Pt(IzH)_2Cl_2$	329vs, 322vs	295m, 281m, 261w, 238m, 170m, 132m
cis-$Pt(IzH)_2Br_2$	217vs, 205vs	293w, 279m, 227m
cis-$Pt(IzH)_2I_2$	175m, 167m	282w, 267w
cis-$Pd(IzH)_2Cl_2$ [a]	339vs, 335vs	282s, 264s, 250m, 225m, 175m, 130m, br, 110m, br
cis-$Pd(IzH)_2Br_2$	210vs, 192s	310s, 300s, 240m
$Pd(IzH)_2C_2O_4$	–	382vs, 347vs, 263s, 255s, 238m, 231m, 148m, 129s, 126s, br, 110sh
trans-$Pt(IzH)_2Cl_2$	350s	287m, 244w, 186m, 133m
trans-$Pt(IzH)_2Br_2$	228vs	312m, 285m, 128m
trans-$Pt(IzH)_2I_2$	180s	100w
trans-$Pd(IzH)_2Cl_2$	373vs	310vs, 270s, br, 240m, 192s, 146m, 134vs, 125m, 106m, 94s
trans-$Pd(IzH)_2Br_2$	220vs	322s, 305m, 272m, 130w
trans-$Pd(IzH)_2I_2$	182vs	301m, 272w, 105m, br
$Pt(IzH)_4Cl_2$	–	325w, 315w, 277s, 267m, 196m, 160vs, br, 137vs, 92s
$Pt(IzH)_4Br_2$		310w, 272m, 257w, 195w, 126s, 97m
$Pt(IzH)_4I_2$		318w, 306m, 267s, 256w, 193vw, 118vs, 98s
$Pd(IzH)_4Cl_2$		349s, 306m, 252s, 182sh, 106vs, br, 139vs, 92vs
$Pd(IzH)_4Br_2$		344s, 301m, 246m, 124vs, 96 vs
$Pd(IzH)_4I_2$		340m, 298m, 242m, 117s, 99m, 83m
$Pt(IzH)_4PtCl_4$	313vs	324m, sh, 257w, 251w, 181m, 150m
$Pt(IzH)_4PtBr_4$	234vs	317m, br, 265w, 124w
$Pd(IzH)_4PdCl_4$	323vs	346sh, 233m, 181m, br, 153s
$Pd(IzH)_4PdBr_4$	252s	340m, 310w, 238m, 121w
$Pt(IzH)_2(Iz)_2$		335m, 307m, 298w, 282sh, 266s, 254m, 138s, br
$Pd(Iz)_2$		385s, br

[a] Recorded at liquid nitrogen temperature.

carried out, a definite assignment is still very difficult [21]. The presence of two M–Halogen stretching frequencies (A_1 and B_1 under C_{2v} symmetry) in the spectra of the *cis* compounds confirms their geometry. In the case of *cis*-$Pd(IzH)_2Cl_2$ the splitting of the Pd–Cl stretching vibration is very small and could only be detected at liquid nitrogen temperature. The presence of one M–Halogen stretching vibration (B_{3u} under D_{2h} symmetry) in the spectra of the *trans* compounds is in agreement with their structure. The spectra of the compounds with formula $M(IzH)_4MX_4$ with M = Pt and Pd and X = Cl, Br show one strong M–Halogen stretching vibration just as expected for the square planar MX_4^{2-} ions (E_u under D_{4h} symmetry). The absence of Pt–Halogen stretching vibrations in the spectra of the other compounds confirms that in these compounds the metal ions are only coordinated to imidazole molecules. The strong absorption band in the spectrum of $Pd(IzH)_4Cl_2$ at 349 cm^{-1} cannot be assigned to a Pd–Cl stretching vibration, because of the fact that this band also occurs in the spectra of the other $Pd(IzH)_4X_2$ compounds with X = Br, I. The behaviour of this compound as a 1:2 electrolyte in solution also supports this view.

Proton Nuclear Magnetic Resonance

Table III lists the chemical shifts (in ppm with respect to internal TMS or TNP, sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)-propionate) of the ring C-H protons of the imidazole molecule both in a few complexes and as a free ligand in various solvents. In case of the platinum compounds the coupling constants of the C-H ring protons with the ^{195}Pt isotope, which occurs for about 34% in natural platinum, are also listed. The signal of the N-H proton in the spectra of the neutral complexes was too broad for accurate determination of its position.



Numbering scheme of the imidazole ring

The values of the ring proton chemical shifts of the free ligand show roughly the same solvent dependence as found for N-methyl imidazole and pyridines [13, 22]. The assignment of the signals in the spectrum of the free ligand follows from the 1:2 intensity ratio of the H-2 and H-4/H-5 signals because of the equivalence of the H-4 and H-5 protons due to the N-H proton exchange in solution.

The assignment of the signals in the spectra of the platinum compounds is very straight forward with the

TABLE III. Chemical Shifts[a] and ^{195}Pt–Proton Coupling Constants[b] from the ^{1}H NMR Spectra of Some Pt and Pd Compounds and of the Free Ligand.

Compounds	H^2	J_{Pt-H^2}	H^4	J_{Pt-H^4}	H^5	J_{Pt-H^5} [c]
IzH in $CDCl_3$	7.76		7.16		7.16	
IzH in DMF-d_7	7.82		7.13		7.13	
IzH in D_2O	7.80		7.18		7.18	
cis-Pt(IzH)$_2$Cl$_2$	8.20	20	7.02	24	7.37	7
cis-Pt(IzH)$_2$Br$_2$	8.20	20	7.04	23	7.33	5
cis-Pt(IzH)$_2$I$_2$	8.27	22	7.08	23	7.32	5
trans-Pt(IzH)$_2$Br$_2$	8.30	19.5	7.38	22	7.27	[d]
Pt(IzH)$_4$Cl$_2$	7.93	20	7.00	22	7.30	7
				H^4, H^5		
trans-Pd(IzH)$_2$Cl$_2$	8.23			7.37 7.25		
trans-Pd(IzH)$_2$Br$_2$	8.25			7.37 7.23		
trans-Pd(IzH)$_2$I$_2$	8.27			7.30		
cis-Pd(IzH)$_2$Cl$_2$	8.08			6.92[e]		
cis-Pd(IzH)$_2$Br$_2$	8.12			6.95[e]		

[a]Chemical shifts in ppm. [b]Coupling constants in Hz. [c]These small values are rather inaccurate (±2 Hz). [d]Could not be detected. [e]Only one of the two expected signals could be observed; see also text.

aid of the ^{195}Pt–^{1}H coupling constants, which are known to be dependent on the number of bonds between the Pt atom and the proton (13, and references therein). The signal at the lowest field with a large ^{195}Pt–^{1}H coupling constant is assigned to the H-2 proton. The signal at higher field with a large ^{195}Pt–^{1}H coupling constant is assigned to the H-4 proton. The remaining signal in this region with a smaller ^{195}Pt–^{1}H coupling constant is assigned to the H-5 proton.

In the spectra of the palladium compounds it was impossible to distinguish the signals of the H-4 and H-5 protons due to the absence of metal–proton coupling constants. The spectra of the *cis* palladium complexes recorded immediately after dissolution already showed the presence of significant amounts of the *trans* isomers (60% for the chloro compound and 80% for the bromo compound). After 24 hours the spectra showed only the presence of the *trans* isomers. This shows that quite rapid isomerisation occurs in DMF. One of the signals of the *cis* isomer could not be observed due to overlap with the signals of the H-4 and H-5 protons of the *trans*-isomer.

As compared to the spectrum of the free ligand the signals of all the protons in all compounds are shifted to lower field with the exception of the signal of the H-4 proton in the *cis*-platinum compounds and the signal of either the H-4 or H-5 proton in the *cis*-palladium compounds.

These observations as well as the magnitude of the ^{195}Pt–^{1}H coupling constants are very similar to those found for the N-methyl imidazole complexes [13]. The changes in chemical shifts on complexation are due to several effects like the electric field effect caused by complexation, π-bonding and temperature independent paramagnetism of the metal ions [22].

Final Remarks

The cytostatic activity of the *cis*-dichloro complexes of imidazole and other substituted imidazoles and pyrazoles has been investigated. None of the compounds showed much more than marginal activity [23]. The presence of -NH_2 donor groups seems to be essential for high activity.

Future papers will deal with complexes of 2-methyl imidazole, 1,2-dimethyl imidazole and pyrazole, as well as with bidentate ligand systems such as histamine and other chelating diamines [24].

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