away from the surface. This would provide an explanation for the absence of a very intense peak at low temperatures in the H_2 spectrum from 3,5-dimethylpyridine decomposition. If the α-pyridyl species were nearly perpendicular to the surface, the intensity of the low-temperature region of the hydrogen spectrum would be low. This is because both methyl groups would still be far removed from the surface and would likely undergo C-H bond scission at higher temperatures causing much higher intensity in the high-temperature region of the spectrum. In addition, it might be expected that 3,5-dimethylpyridine oriented perpendicular to the surface would be capable of the same reversible α-C-H bond breaking process that preceded pyridine desorption. However, the lack of 3,5-dimethylpyridine molecular desorption and the relatively flat profile of the H_2 desorption as a function of temperature suggest that the pyridine ring and the α-pyridyl ring are oriented at an acute angle with respect to the surface and that the regiospecific bond breaking is brought about through rotation about the nitrogen-nickel bond rather than bending of this bond (1).

We plan temperature-dependent studies of this methylpyridine chemistry on Ni(100) by near-edge X-ray absorption fine-structure spectra (NEXAFS). These studies may establish accurate dihedral angles formed by the metal surface plane and the ring plane of the pyridines.

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Registry No. Ni, 7440-02-0; pyridine, 110-86-1; 4-methylpyridine, 108-89-4; 2-methylpyridine, 109-06-8; 2,6-dimethylpyridine, 108-48-5; 3,5-dimethylpyridine, 591-22-0.

Intramolecular Influence of a Carboxylic Function on Platinum Blue Synthesis. A Systematic Study of Complexes Originating from Acid Amides

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Abstract: The use of acid amide as ligand for obtaining platinum blue has been investigated. While blue compounds are generally obtained by using the hydrolysis product of *cis*-dichlorodiammineplatinum(II) as platinum source, with such ligands the reaction occurs very readily using potassium tetrachloroplatinate(II). The role of the carboxylic function which offers here a primary ligating site to platinum is evidenced. The compounds obtained have been characterized by UV-visible spectral measurements, Ce(IV) oxidative titration, ESR spectroscopy, and magnetic properties. Antitumoral activity toward leukemia L1210 and sarcoma 180 is reported for two of these compounds. As a first step for this antitumor study, these compounds have been found to be inactive toward Leukemia while they present interesting activity toward Sarcoma.

Interest in the blue platinum complexes has been recently raised by the discovery that *cis*-dichlorodiammineplatinum(II) (*cis*-DDP) displays antitumor properties probably related to its interactions with DNA.[1-7] An important outcome of the study of these interactions was the isolation of a new type of platinum complexes, "the platinum-pyrimidine blues", which seemed to be very promising with regard of their high index of antitumor activity associated with a low nephrotoxicity.[8,9]

Independent of their pharmacological properties, the blue species raise many fundamental problems among which the most important was underlined by Lippert since 1979 and is related to the origin of their paramagnetic behavior.[10] It is noteworthy that the blue complexes retain their characteristics (color and paramagnetism) in solution while other mixed-valence compounds such as the violet Krogmann salts lose their color and paramagnetism in solution.

In spite of these physiological and physicochemical properties, a restricted number of blue platinum compounds has been described. Beside acetamide blue and other related amide complexes,[11,12] interest has been essentially focused on pyrimidine blues and on the α-pyridone blue, which is the only species to be obtained as monocrystal and therefore extensively studied.[13-18]

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Another relevant remark is related to the fact that almost all the compounds already described were obtained by reacting a suitable ligand with the hydrolysis products of *cis*-DDP or by hydrolyzing a dichlorobis(nitrile)platinum(II) complex.[19] A very few reports of the possibility to use K_2PtCl_4 as a platinum source appear in the literature but in this instance,the formation of a blue product only occurs when the amide is largely in excess with respect to the platinum.[20,21] The difficulty in obtaining blue species from K_2PtCl_4 is likely due to the weak coordinating ability of the amido group, which does not easily enter the coordination sphere of the metal. However, in a previous work[21] we have shown that reacting oxamic acid with $K_2[Pt(NO_3)_4]$ yields a blue compound after a time, the first step of the reaction being the formation of a yellow product in which the platinum is bonded to the carboxylic group. This is reminiscent of the data obtained by Sigel and Martin concerning the coordinating properties of the amido group.[22] According to these authors, "...a metal ion needs a primary locating site or anchor in order to chelate to the amide oxygen and, by substitution of an hydrogen, to the amide nitrogen...". The role of the carboxylic function as anchor in the complexation of peptides and proteins was particularly emphasized. In the present report we wish to demonstrate that this rationale may be extended to the platinum blues. It appears that an amidic group may easily react with K_2PtCl_4 to provide platinum blue if it has a carboxylic function in its vicinity.

Experimental Section

Measurements. The infrared spectra of the ligand and complexes were recorded on a Perkin-Elmer Model 577 spectrometer calibrated with polystyrene film, using KBr disks. Electronic spectra were recorded on a Cary 14 spectrophotometer in the 800–200-nm range.

ESR spectra were obtained with a Bruker ER.200K with a conventional X-band (9.6 GHz). The microwave frequency was calibrated with diphenylpicrylhydrazyl. All ESR spectra were recorded on frozen aqueous solutions directly on the mother solution, they were also recorded on the powdered sample in a large range of temperature.

Magnetic susceptibilities were determined by the Faraday method using a Sartorius microbalance coupled with a Drusch electromagnet. The measurements have been performed between 80 and 320 K. $Hg[Co(SCN)_4]$ was used as standard ($\chi_g = (16.44 \times 10^{-6})\mu em$ cgs). A small amount of ferromagnetism was found in the samples upon variation of the applied field at various temperatures. Magnetic susceptibility data were corrected for this ferromagnetism by extrapolation to infinite field. The experimental values have been corrected for the diamagnetism of the ligand.

The X-ray photoelectron spectroscopic measurements were obtained with an AEI ES 200B spectrometer using Mg Kα radiation (1253.6 eV) as the X-ray excitation source, the powdered samples being compressed into a copper grid. The measured binding energies were standardized by using a Au 4f $^7/_2$ binding energy of 83.5 eV.

NMR spectra were recorded on a WH 250 Bruker spectrometer operating in the Fourier transform mode and equipped with a wide-band probe (23–103 MHz).

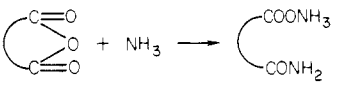
Typical parameters for ^{13}C spectra were the following: pulse width 20 μs, impulse delay 1 s; 100 accumulations were usually necessary to achieve a satisfactory signal-to-noise ratio. ^{13}C spectra were recorded directly on the reaction mixtures, a special preparation being conducted in D_2O for this purpose.

Oxidative Titration. The solution of platinum blue was decolorised by a number of oxidizing agents, this observation provides a method of estimating the formal oxidation number of platinum in these compounds. Oxidative titration was monitored by spectrophotometry and carried out with ceric sulfate solutions (5.023×10^{-3} N in 0.70 H_2SO_4), standardized by the normal procedure. The average oxidation state of the platinum atom was calculated on the basis of the percentage of platinum in the sample as determined by elemental analysis.

Antitumor Activity. Experiments were conducted on mice of 20–22-g body weight, which were about 3 months old. On day 0, mice were inoculated by intraperitoneal (ip) inoculation with 10^5 L1210 cells or with 10^6 Sarcoma 180 cells. The drug was administered on day 1 by ip inoculation, suspended in a 4 % Klucel JF (Hercules Inc.) water solution, and the concentration was adjusted for an injection of 0.1 mL per 10 g of body weight. Antitumor activity was expressed as $(T/C)100$ (significant when >125), T being the median survival time of the treated mice and C the median survival time of the control. Experiments were achieved on day 30 for Leukemia L120 and on day 60 for Sarcoma 180. The number of animals still alive at the time was recorded but not included in the calculation of T/C. The highest nonlethal dose for nontumoral animals (LD_0) was 300–500 mg/kg for **10** and 150 mg/kg for 3.

Preparation and Characterization of the Complexes. The starting materials, K_2PtCl_4, all the anhydrides, and some of the acid amides studied such as oxamic acid, succinamic acid, and orotic and isoorotic acid were purchased from Aldrich Chemical Co. and used without further purification.

Preparation of the Acid Amide Ligands. The ligands were prepared according to the following scheme:



Dry ammonia is bubbled through a saturated solution of the dicarboxylic anhydride in 2,2-dimethoxypropane. A white precipitate forms immediately. It is collected, washed with water, and leached with boiling acetone to remove any dicarboxylic acid formed.

Further purification of the ligand was achieved on a Sephadex-type EAE A25 columns, the elution being performed with acidic solutions more and more acidic.

The purity of the ligand was checked by chromatography.

Synthesis of the Complexes. In a typical synthesis, 1×10^{-3} mol of the ligand was dissolved in the minimum amount of water saturated with N_2 and allowed to react with K_2PtCl_4 (1×10^{-3} mol). The pH was kept constant (7.2) by adding 1 N KOH. The blue species was formed within a few hours and even within a few minutes if the reaction mixture is heated to 40 °C. It was collected by precipitation with an ethanol/ether (80/20) mixture, redissolved in water, and reprecipitated. This process was repeated several times. Finally, the blue compound was dried in vacuo.

Precipitation would also be obtained by adding an acidic solution to the reaction mixture, but in this instance, analytical data reveal the presence of unreacted ligand which is precipitated together with the complex.

Results and Discussion

With a view to foresee all the possibilities of this type of ligand, we have considered an extensive set of acid amides offering different structural patterns, i.e.: (i) linear aliphatic acid amides, $NH_2CO(CH_2)_nCOOH$, oxamic acid ($n = 0$), malonamic acid ($n = 1$), succinamic acid ($n = 2$), glutaramic acid ($n = 3$) (products **1–4**); (ii) substituted aliphatic acid amides, 3-methylglutaramic acid, 3,3-dimethylglutaramic acid, 3,3-diphenylglutaramic acid, and 3,3-tetramethyleneglutamaric acid (products **5–8**); (iii) alicylic acid amides, 1-carboxy-2-(aminocarboxyl)cyclobutane, *cis*-1-carboxy-2-(aminocarboxyl)-2-cyclohexane; and *trans*-1-carboxy-2-(aminocarboxyl)cyclohexane (products **9–11**); (iv) unsaturated cyclic acid amides, 1,2,3,6-tetrahydrophthalamic acid (product **12**); (v) aromatic acid amides, phthalamic acid (product **13**), 2-carboxy-2′-(aminocarboxyl)-1,1′-biphenyl (product **14**), 3-oxaglutaramic acid (product **15**), and also acid amides whose amidic functions are implied in an heterocycle such as orotic isoorotic acid (products **16** and **17**).

Figure 1 collects the most unusual products. However, owing to the difficulties in separating isomers, we have limited our work to symmetric acid amides.

Synthesis and Analytical Data. The blue compounds have been prepared by reacting K_2PtCl_4 in aqueous medium with the acid amide ligands and the blue species appear within a very short period, in marked contrast with the behavior of systems involving separate acid and amide. We have probed that, in such systems, the blue color only appears when a large excess of amide (acetamide) is used, irrespective of the presence of acid (acetic acid).

It may be emphasized that the pH must be kept constant during the course of the reaction. Otherwise, deprotonation of the ligands induces a lowering of the pH, which causes a simultaneous pre-

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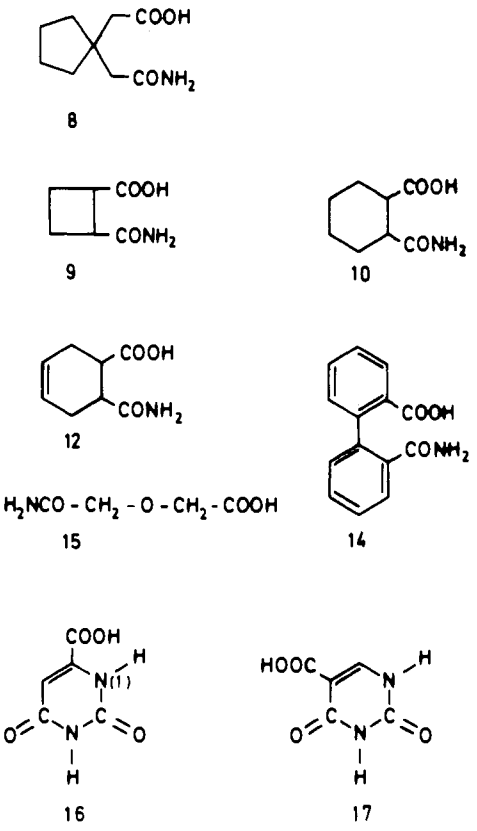

Figure 1.

Table I. Analytical Data Related to the Blue Platinum Acid Amide Complex

compd	% C	% H	% N	% Pt	% Cl	% K[a]	Pt/L ratio
1	5.1	0.4	3.0	41.7	22.8	16.8	1
2	10.4	1.1	4.1	53.7	7.2		1
3	11.0	2.8	3.3	45.0	12.6		1
4	15.8	2.6	3.7	51.2	4.3		1
5	18.2	2.9	3.6	48.2	5.3		1
6	20.5	3.3	3.5	46.8	4.6		1
7	36.5	3.1	2.5	36.2	4.8		1
8	24.2	3.4	3.1	43.5	5.0		1
9	17.3	2.8	3.4	45.2	8.8	5.1	1
10	23.1	3.3	3.6	45.8	4.1		1
11	23.4	3.3	3.6	45.7	6.8		1
12	22.4	2.1	3.1	47.2	4.8		1
13	20.7	1.9	3.0	42.1	8.3	6.7	1
14	43.8	3.1	3.6	25.2	2.9		2
15	11.3	3.6	4.2	46.9	6.9	4.3	1
16	14.2	1.2	6.6	46.1	2.1	9.2	1
17			no blue				

[a] If no percentage is reported, its value is <1% or 0.

cipitation of the blue species and the unreacted ligand. Besides, the blue complexes are destroyed in basic media so that it is essential to maintain the pH at a value of ca. 7.0.

It is well-known that acid amide may also be obtained through hydrolysis of the corresponding imide. Owing to the difficulty in preparing imide, this route was discarded. However, in the case of succinimide, we have shown that the ligand reacts readily with K_2PtCl_4 to yield a blue complex. However, considering the ^{13}C spectra of the complex it appears that during the reaction process the ligand has been converted to succinamic acid, the complexing being actually an acid amide blue.[23]

Analytical data related to the blue complexes are reported in Table I. It appears that all the products, except the complex obtained from 2-carboxy-2'-(aminocarboxyl)-1,1'-biphenyl (**14**), are characterized by a ratio of ligand to platinum equal to 1.[24] Due to the difficulties in differentiating between the various forms of the ligands—i.e., between H_2O and OH^- or between LH_2, LH^-, and L^{2-} (LH_2 representing the acid amide in its neutral form)—it is not obvious to propose a detailed formulation that would be consistent with the actual oxidation state of the platinum. Similarly, the potassium content may depend on a slight variation of pH during the precipitation phase leading to a complex in which the carboxylate function is either free or ionized.

Coordination Sites and Complexation Process. An acid amide has two potential coordination sites, and it has been established that, with some metals such as copper, the carboxylic function only is implied in the complexation process.[25] The complexation site in acid amide platinum blues has been studied by ^{13}C NMR spectroscopy, a special preparation being conducted in D_2O for this purpose. As expected,[37] valuable ^1H NMR spectra have not been obtained, the paramagnetic species contributing to the observed resonance broadening but the enlargement of the ^{13}C resonances is not large enough to preclude observation of well-separated signals. However, the use of this spectroscopy is limited by the low solubility of most of the complexes. We discuss here the data obtained for succinamic acid blue; very similar data have been obtained for some of the other complexes.[26]

In the free ligand, we observed four lines at, respectively, 31.61, 32.08, 179.6, and 181.3 ppm. The former may be unambiguously related to methylenic carbon while the latter are attributable to carbonyl groups. Considering the literature,[27] the most shielded signal (179.6 ppm) may be due to the amidic function and the other (181.3 ppm) to the carboxylic acid carbon. Complexation induces an important shielding of the signal related to the amidic function (δ 163.3) while the carboxylic signal is practically not affected. These effects are consistent with (i) coordination of the amidic function leading to a lowering of the double-bond character of its carbonyl bond and (ii) the occurrence of free carboxylic function. This is further supported by the observation of the characteristic IR absorption of free carboxylic group. Moreover, the chemical behavior of the blue species, i.e., precipitation at low pH and formation of bimetallic complexes by addition of copper(II) ions to their preparative mixtures, is characteristic of free acid group.[28]

However, the carboxylic function is likely implied in the early steps of the reaction. This has been fully demonstrated in the case of oxamic acid.[29] Complementary evidences are gained from a comparative study of the complexation of orotic and isoorotic acids. Actually, orotic acid yields a blue species whereas isoorotic acid affords only a brown complex. It has been shown[30] that, in the case of orotic acid, an intermediate complex with the formula $K_2[Pt(LH)_2]$ (the free ligand being represented by LH_3) may be isolated. Spectroscopic data point to a coordination of the ligand through its deprotonated N(1) site and carboxylate group. A rearrangement then occurs within the coordination sphere to yield finally the blue complex which involves chelation of the metal to the amidic oxygen and adjacent nitrogen.[31] Such a rearrangement is not conceivable in the case of isoorotic acid so that complexation stops at the first step and yields a "classical" complex. It may

(23) Arrizabalaga, P.; Castan, P.; Laurent, J.-P. *J. Am. Chem. Soc.* **1984**, *106*, 1300–1303.

(24) Regarding the latter complex, it is interesting to underline that it is the only one to be purple and not blue.

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(26) Values of ^{13}C NMR chemical shifts for the carbonyl groups of the blue compounds (the ligand values are in parentheses): **9** $\delta(C{=}O)_{acid}$ = 186.3 (185.6), δ $(C{=}O)_{amide}$ = 168.7 (1756); **10** $\delta(C{=}O)_{acid}$ = 186.7 (185.9), $\delta(C{=}O)_{amide}$ = 170.8 (176.7).

(27) Williamson, K. L.; Hasan, M. V.; Clutter, D. R. *J. Magn. Reson.* **1978**, *30*, 367–371. Hasan, M. V. *Org. Magn. Reson.* **1980**, *14*, 447–450. Newmark, R. N.; Hill, J. H. *J. Magn. Reson.* **1976**, *21*, 1–7.

(28) The bimetallic nature of these compounds has been proved by analytical data. In each case, the copper to platinum ratio is 1/1. However, all attempts to obtain crystals failed.

(29) Arrizabalaga, P.; Castan, P.; Laurent, J.-P. *Transition Met. Chem. (Weinheim, Ger.)* **1980**, *5*, 204–206.

(30) Arrizabalaga, P.; Castan, P.; Laurent, J.-P. *Inorg. Chim. Acta*, in the press.

(31) Tentative determination of carbonyl complexation site by means of ^{13}C NMR spectroscopy failed due to the poor solubility of this platinum blue.

Table II. Experimental Values for the Blue Compounds

compd	λ_{max}, nm	ϵ, M_{Pt}^{-1} cm^{-1}	$g_\perp$	$g_\parallel$	$10^{-4}\chi_A$, cgs[a]	μ_{eff}, μ_B	OS[b]
1	650	329	2.5	2.0	2.15	0.72	2.5
2	655	405	2.39	1.99			
3	625	450	2.42	1.99	16.6	1.97	2.5
4	670	405	2.39	1.98	0.45	0.32	2.3
5	675	480	2.43	1.97			
6	660	520	2.45	1.98	3.7	0.94	2.6
7	680	920	2.37	1.98	5.1	1.10	2.3
8	680	1100	2.44	1.97	8.6	1.42	2.8
9	710	670	2.44	1.98			
10	655	2890	2.36	1.98	5.6	1.15	2.7
11	655	1990	2.36	1.98	4.3	1.01	
12	680	1120	2.37	1.97			
13	590	480	2.43	1.98			
14	720	350	2.41	1.99			2.8
15	670	475	2.33	2.03			
16	625	580	2.47	1.97	3.2	0.87	2.3

[a] Experimental data have been corrected for diamagnetism estimated from Pascal's constants. [b] Platinum oxidation state.

be emphasized that, at least in the case of orotic acid, this process is slightly different from that of Sigel and Martin.

Antitumor Activities. To date, the study of the antitumor activity of these new blue compounds is still in progress. However, some primary results may be presented. All the products already tested are quite uneffective against leukemia L1210 whatever the schedule used for administrating the drug. However, promising results were achieved concerning Sarcoma 180, but the antitumoral activity depends strongly on the ligand implied in the blue compound. Thus, a significant activity is exhibited by the succinamic acid blue (**3**) toward solid Sarcoma 180. A T/C of ca. 150% is found for one single intraperitoneal injection. The best results so far are related to the 1,2,3,6-tetrahydrophthalamic acid blue (**10**) for which a $T/C > 335\%$ is obtained with the cure of half the animals. These data may be favorably compared to those obtained by Rosenberg et al.[8] with pyrimidine blues, the best result being obtained for the 5,6-dimethyluracil blue (% ILS = 100, T/C ca. 200).

Properties Related to the Mixed-Valence Character of Acid Amide Blues. It is generally accepted that the known blue species enter the large family of mixed-valence compounds. However, difficulties have been encountered to obtain a more precise definition of these complexes. For instance, it would be anticipated that a suitable analysis of some of their properties would allow them to be classified into one of the three Robin and Day classes depending on the extend of interaction between the two valence states.[32]

The mixed-valence character of our blue species is obviously deduced from redox titrations (cf. experimental data). The data reported in Table II show that the average oxidation state of the platinum is always higher than 2 but less than 3. It may be underlined that these values are related to samples prepared according to the very same process since the oxidation state depends markedly on the preparative conditions (reactant concentrations, pH, temperatures,...). This certainly explains the large variations of the oxidation state already mentioned for a similar product.[33] Such variations might be related to the fact that, upon changing experimental conditions, either the delocalized electron or the metal in its higher oxidation state may be implied in more or less long oligomeric chains.

X-ray photoelectron spectroscopy (XPS) has been previously used in the study of mixed-valence complexes. However, thee are only two reports of its application to platinum blues, and the data are conflicting. Two sets of signals have been observed by Burness[34] in the spectrum of its oxamate blue while the spectrum of the α-pyridone blue reported by Lippard et al.[35] displays only one doublet. The XPS spectra of the succinamic acid blue (**3**) comprises two doublets of unequal intensities (3/1) indicative of the occurrence of two oxidation states which are recognized on the basis of the binding energies as platinum(II) and platinum(IV), respectively. This would lead to an average oxidation state of 2.5, which agrees well with the values deduced from oxidative titration, 2.5 ± 0.1.

Table III. Valence Delocalization Parameter (α) Calculated by Hush's Model

compd	ν	ϵ	Δ	g	α
1	15380	329	8100	1	0.097
	id	id	id	2	0.048
10	15270	2890	8300	1	0.293
	id	id	id	2	0.146
α-pyridone blue	14700	60	5830	1	0.036

As with other blue species, the visible spectra of the acid amide blues show a broad transition in the region of 600–700 nm. Whereas the position of the maximum is seemingly characteristic of the ligand, the extinction coefficient is primarily affected by the conditions of synthesis and measurement (pH value, nature of anions, etc...). One of the differences actually observed in the spectral properties of these compounds when compared to the platinum blues already described is their stability with respect to chlorine. The α-pyridone blue is stable only in the absence of such an anion and discharged its blue color upon addition of the chloride ion. In contrast with Lippard's blue, the platinum acid amide blues seem to be quite stable although more or less chloride is actually present in the formula of these products. Furthermore, no significant change has been observed over 1 year, either in the position or in the intensity of the blue transition. However, the observed characteristic absorption is in close correspondence with the mixed-valence character of the complex, while the oxidative titration with the ceric ion determined the disappearance of the blue color.

With this in mind, it is tempting to apply Hush's model[36] for these complexes. This has been previously done in the case of phthalimide blue[33] complexes. However, we must previously precise the limitations of this theory: the formula derived by Hush described characteristics of the mixed-valence transition band on the basis of a weak interaction model where the number of metallic atoms is limited to two. If such conditions are not fulfilled, Hush's model may only perform a tentative approximation.

Consequently, the valence delocalization parameter α, which measures the extend of electron delocalization between the two metallic centers in two different oxidation states, may be calculated by eq 1, where ϵ_{max} is the molar extinction coefficient, ν the

$$\alpha^2 = (4.24 \times 10^{-4})\epsilon_{max}\Delta/(\nu d^2 g^2) \quad (1)$$

absorption frequency of the intervalence band, d the internuclear distance, g the difference in the oxidation state of the two metal centers, and Δ the half-band width.

Both the band width and the band position are directly related to temperature, and the relation reported below is consequently limited to measurements obtained at 300 K. The half-band width is further related to the frequency of the intervalence band by the relation

$$\nu = \Delta^2/2310 \quad (2)$$

which is in fact limited to the case of $g = 1$. However, when $g = 1$ and 2, we used preferably the Δ values deduced from experimental data. The value used for d was deduced from stuctural investigation of the α-pyridone blue, i.e., 2.778 Å. Calculations of α have been performed for the oxamic acid blue (**1**) (ν = 15380 cm^{-1}, ϵ = 329 cm^{-1} M^{-1}, and Δ = 8100 cm^{-1}) and for complex **10** (ν = 15270 cm^{-1}, ϵ = 2890 cm^{-1} M^{-1}, and Δ = 8300 cm^{-1}), which both present the two extreme values for ϵ.

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The results obtained for the valence delocalization parameter α are reported in Table III, which clearly shows the failure of Hush's model to describe the delocalization occurring in platinum blues. Actually, the only well-characterized complex, the α-pyridone blue, exhibits a very weak value for α which implies localized states while X-ray structural determination as well as experimental data reveal electron delocalization over several platinum atoms.[15-17,35] Since all the parameters used in this calculation possess the same magnitude order except ϵ, the latter appears to be preeminent in the determination of the α values. The unusual sensibility of ϵ to experimental conditions leading to large uncertainty in the extinction coefficient thus prevents any tentative calculation using ϵ as the significant parameter.

Magnetic Properties. Examination of the ESR spectra shows the acid amide blue complexes to be paramagnetic. Their powder or aqueous solution spectra display the same pattern, i.e., two signals at ca. 2800 and 3400 G. The large g shifts $g_{\parallel} \simeq 1.97-2.03$ and $g_{\perp} = 2.33-2.47$ suggest considerable spin-orbit coupling of an odd-electron, which is typical of paramagnetic heavier metals. The different g values are very similar to those observed for other platinum blues studied in solution[16,37] and as powders[38] and to those of Pt(IV)-doped Magnus' green salt[39] or irradiated Pt(II) complexes.[40] The measured g values are described by a d_{z^2} hole state (z taken along the Pt chain axis) with admixture of the degenerate d_{xz}, d_{yz} state. The lack of any discernible hyperfine structure in the powder and solution spectra deserves further comments. It is unlikely that this may be attributed to the oligomeric character of the species since hyperfine patterns have been observed in the spectra of several blue complexes derived from lactam ligands. We feel that this behavior would be related to an enlargement of the resonance lines due to a coupling of the spin with the ^1H nucleus of the coordinated NH group.

Considering their magnetic susceptibility, the acid amide blues may be viewed as simple Curie paramagnets. However, varying the applied magnetic field causes a slight but significant amount of ferromganetism to be detected. Similar observations have been previously reported concerning the α-pyridone blue and the uracil blues, and it has been concluded that the ferromagnetism was attributable to impurities.[17-41] The extrinsic or intrinsic origin of this particular behavior is not an obvious problem, but it may be recalled that ferromagnetism is recognized as an intrinsic property of some mixed-valence complexes.[42]

The susceptibilities reported in Table II were corrected for ferromagnetism. These values are expected to provide informations on the number of odd electrons through consideration of their related magnetic moments. At this stage, one is faced with the problem of choosing the number of monomeric units to which the magnetic moment would be related. The values quoted in Table II are related to one platinum atom. As a matter of fact, blue complexes are known to be oligomers, but their size remains undetermined except in one case. Furthermore, this difficulty is increased by the fact that the effective moment does not linearly depend on the number of monomer untis while the susceptibility χ_A does.[43] Furthermore, it should be recalled that the high spin-orbit coupling evidenced by EPR can cause metal ions of the third transition series to have magnetic moments that cannot be easily interpreted in terms of number of unpaired electrons and hence give the oxidation state. At least, one has to acknowledge that a paramagnetic polymeric structure involving platinum atoms with an oxidation state higher than 2.5 implies that more than one odd electron is present. So, the interpretation of the magnetic properties (EPR spectra and susceptibility values) is not straightforward, and structural data are prerequisite.

Conclusion

The present work evidences that K_2PtCl_4 may be a suitable precursor in the synthesis of platinum blues in so far as the second reactant possesses not only the necessary amido group but also a carboxylic group to afford a primary ligating site to platinum. However, this acidic function is released in the blue products obtained at the end of the reaction. In view of obtaining platinum blues and more specifically those expected to be used as antitumor drugs, we believe the use of K_2PtCl_4 as a platinum source more advantageous: (i) the reaction is often very fast with an acid amide since the blue color appears within a few hours (at room temperature) or even a few minutes (at 60 °C); (ii) with respect to their analytical definition, physical properties, and pharmacological activity, the samples are almost identical from, batch to batch if the preparative scheme is rigorously complied with (temperature, pH, reaction time, process used to precipitate the sample, etc...); (iii) *cis*-DDP or its hydrolysis products are known to give blue polymers by photochemical reactions[44,45] which may disturb the process studied and are partly responsible for the resulting properties; (iv) similarly, small amounts of nonreacted *cis*-DDP, owing to its great anticancer activity, may influence pharmacological investigations.

As for the ligands, we would like to emphasize the fact that the blue species obtained from acid amides contain a free carboxylic function which offers the opportunity to prepare bimetallic materials. Work is in progress so far to characterize platinum-copper polymers and to study magnetic interactions between copper(II) and the unusual paramagnetic platinum.

Registry No. K_2PtCl_4, 10025-99-7.

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