Articles

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Multinuclear NMR Study of Reactions of Methylphosphonic Acid, $CH_3PO_3H_2$, and (Aminoalkyl)phosphonic Acids, $NH_2(CH_2)_nPO_3H_2$ (n = 1-3), with the *cis*-Diamminediaquaplatinum(II) Cation and *cis*-Diamminedihydroxoplatinum(II)

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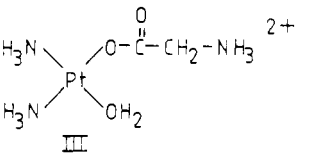
^{31}P, ^{15}N, and, in some cases, ^{195}Pt NMR spectroscopy has been used to study the reactions of *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ and *cis*-$Pt(NH_3)_2(OH)_2$ (using ^{15}N-substituted ammine) with $CH_3PO_3H_2$ (mpH$_2$) and $NH_2(CH_2)_nPO_3H_2$ (n = 1, ampH$_2$; n = 2, aepH$_2$; n = 3, appH$_2$). Each initially gives at pH 1.5 and 4 a complex in which the ligand is bound only through oxygen. At pH 4 subsequent reaction occurs to give a complex in which Pt atoms are bridged by phosphonate and hydroxo groups. With amp, further reaction occurs at pH 1.5 and 4 to give the chelate complex $Pt(NH_3)_2$(ampH-N,O)$^+$. At pH 4 an intermediate, Pt-$(NH_3)_2(\mu_{O,O'}$-amp-$N)Pt(NH_3)_2(H_2O)^{2+}$, is detected. In alkaline solution amp^{2-} gives ultimately *cis*-$Pt(NH_3)_2$(amp-N)$_2^{2-}$, while aep^{2-} gives *cis*-$Pt(NH_3)_2$(aep-N,O), and app^{2-} does not react. These differences are rationalized in terms of decreasing nucleophilicity of the ammine group of $NH_2(CH_2)_nPO_3^{2-}$ as n increases.

Introduction

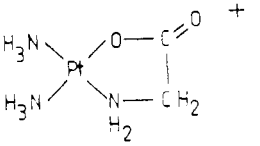
(Aminoalkyl)phosphonic acids, $NH_2(CH_2)_nPO_3H_2$,[1] are formal analogues of amino acids, $NH_2(CH_2)_nCOOH$. The most obvious difference is that the phosphonic acid group is diprotic. (2-Aminoethyl)phosphonic acid, β-ciliatine, occurs naturally in several lower life-forms.[2] The coordination chemistry of amino acids has been extensively investigated, and the behavior of the (aminoalkyl)phosphonates as ligands might be expected to show comparable diversity and richness. While it is clear from stability constant measurements involving labile metal ions that the (aminoalkyl)phosphonates can act as ligands over a wide pH range,[3-5] little is known of the structures of the complexes formed. Probably because they are usually much more soluble than complexes of amino acid analogues, very few solid complexes of (aminoalkyl)phosphonates have been prepared, and no crystal structures have yet been reported. It is therefore appropriate to study the coordination behavior of these complexes in solution, for which purpose ^{31}P NMR is a technique with obvious potential.

When ^{15}N-substituted ammine is used, ^{15}N and ^{195}Pt NMR can also greatly assist in characterizing complexes formed in solution in reactions of ammineplatinum(II) complexes.[6-10] We have recently used NMR to study the reactions of *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ (I) and *cis*-$Pt(NH_3)_2(OH)_2$ (II) with glycine (glyH).[11,12] Most notable was the formation in acid solution of a complex III in which glycine acts as an O-bound unidentate



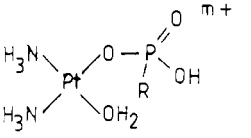
III

ligand, with rearrangement to the chelate complex IV being very



IV

slow. Also relevant to the present study is a recent investigation by NMR of the interaction between I and phosphate ion.[13] Under acid conditions (pH $\leq$1.5), V forms, in which phosphate is unidentate. At pH 3-5, a number of additional species form of which VI predominates, and these solutions eventually turn blue.



	R	m
V	OH	1
VII	CH_3	1
IX	CH_2NH_3	2
XIX	$(CH_2)_2NH_3$	2
XXIII	$(CH_2)_3NH_3$	2

For an NMR investigation of the reaction of the ligands with the platinum complexes, it is important to be able to identify peaks due to the free ligand and to know the protonation state of the ligand under the reaction conditions. We have recently reported[14] ^{31}P, ^{13}C, and ^1H NMR spectra as a function of pH for each of the ligands dealt with here: methylphosphonic acid, $CH_3PO_3H_2$

(1) Although the (aminoalkyl)phosphonic acids usually exist as zwitterions, $^+NH_3(CH_2)_nPO_3H^-$, unless this is being emphasized they will be written in the unionized form $NH_2(CH_2)_nPO_3H_2$.
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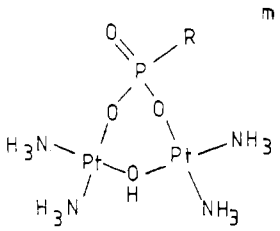


	R	m
VI	OH	1
VIII	CH_3	1
XIII	CH_2NH_3	2
XX	$(CH_2)_2NH_3$	2
XXIV	$(CH_2)_3NH_3$	2

(mpH_2); (aminomethyl)phosphonic acid, $NH_2CH_2PO_3H_2$ ($ampH_2$); (2-aminoethyl)phosphonic acid, $NH_2CH_2CH_2PO_3H_2$ ($aepH_2$); (3-aminopropyl)phosphonic acid, $NH_2(CH_2)_3PO_3H_2$ ($appH_2$). A subsequent paper[15] will deal with the reactions of more complex ligands containing nitrogen and phosphonate groups.

Experimental Section

Starting Materials. *cis*-$Pt(NH_3)_2(ONO_2)_2$ and solutions of *cis*-$Pt(NH_3)_2(OH)_2$ (containing either [^{14}N]- or [^{15}N]ammine) were prepared as previously described.[9,12,13] $^{15}NH_4Cl$ (99.0% ^{15}N) was supplied by Novachem, Melbourne, Australia. Ligands were used as supplied, methylphosphonic acid from Alfa and the (aminoalkyl)phosphonic acids from Sigma.

NMR Spectra. Instrumentation and general techniques were as previously described.[12-14] All chemical shifts are reported positive to lower shielding. Referencing was as follows: ^{31}P (40.3 MHz) to 85% H_3PO_4 in a coaxial capillary; ^{15}N (10.1 MHz) to the $^{15}NH_4^+$ signal of 5 M $^{15}NH_4{}^{15}NO_3$ in 2 M HNO_3 in a coaxial capillary; ^{195}Pt (21.4 MHz) to a separate sample of 0.5 g of Na_2PtCl_6 dissolved in 2 mL of H_2O. Probe temperature was 28 °C.

All spectra were ^{1}H-decoupled, and were recorded in H_2O. No extensive use was made of ^{1}H NMR in this work. The methylene protons of coordinated amp exchanged readily with solvent deuterium for most of its complexes if dissolved in D_2O.

Typical NMR Experiment. Details are given for one reaction carried out in an NMR tube. A 0.200-g sample of *cis*-$Pt(^{15}NH_3)_2(ONO_2)_2$ (0.57 mmol) was dissolved in 2 mL of warm water, and the pH was adjusted to 1.5 by using 0.1 M HNO_3. A 0.063-g (0.57-mmol) sample of (aminomethyl)phosphonic acid was dissolved in 2 mL of water, and the pH was adjusted to 1.5 with 0.1 M HNO_3. The solutions were mixed at room temperature, and reactions were monitored by ^{31}P, ^{15}N, and ^{195}Pt NMR. As required, further pH adjustments were made by using 0.1 M HNO_3 or 0.1 M NaOH solution.

pH Measurements. Routine measurements were made with Merck narrow-range indicator strips. More accurate measurements were made by using a TPS 1852 MV digital pH-multivoltmeter.

Results

Reactions of the ligands with the platinum complexes were studied in aqueous solution by ^{31}P, ^{195}Pt, and ^{15}N NMR. NMR data are given in Table I. A solution of *cis*-$Pt(^{15}NH_3)_2(ONO_2)_2$ in water shows peaks due to *cis*-$Pt(^{15}NH_3)_2(H_2O)_2^{2+}$ (I) (for ^{195}Pt a 1:2:1 triplet at −1583.7 ppm; for ^{15}N a singlet with satellites at −85.83 ppm, $^1J(^{195}Pt-^{15}N)$ = 390.6 Hz),[9,13] with much weaker peaks due to *cis*-$Pt(^{15}NH_3)_2(ONO_2)(H_2O)^+$,[13] which are ignored in the subsequent discussion. When the pH of this solution is rapidly raised above 8, peaks due to *cis*-$Pt(^{15}NH_3)_2(OH)_2$ (II) are observed (δ_{Pt} −1572, triplet; δ_N −76.9, ^1J(Pt–N) = 293 Hz).[9,13] It is difficult to follow reactions in the pH range 5.5–8.0 because of the formation of hydroxo-bridged species $[Pt(^{15}NH_3)_2(\mu\text{-}OH)]_n^{n+}$ (n = 2, 3) over this pH range.[9]

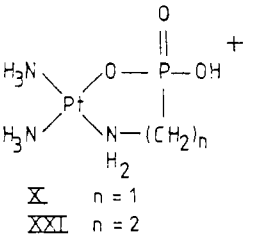
Reactions of I with Methylphosphonic Acid, mpH_2. When aqueous solutions containing equimolar amounts of *cis*-$Pt(^{15}NH_3)_2(H_2O)_2^{2+}$ (I) and mpH_2 were mixed, and pH immediately adjusted to 2.5, a new peak slowly grew in the ^{31}P NMR spectrum at 35.18 ppm, with no resolved Pt–P coupling, and two new singlets, just resolved from the peak due to I, grew in the ^{15}N spectrum (−85.93, −85.69 ppm). The ^{195}Pt spectrum showed a 1:2:1 triplet at −1495.3 ppm, with J(Pt–N) = 383 Hz. These values may be compared with those for the phosphato complex *cis*-$Pt(^{15}NH_3)_2(OPO_3H_2)(H_2O)^+$ (V) (see Table I).[13] The methylphosphonate complex is therefore assigned as *cis*-$Pt(^{15}NH_3)_2(OPO_2HCH_3)(H_2O)^+$ (VII) with the Pt–N coupling constants trans to mpH^- and H_2O so similar that a 1:2:1 triplet rather than a doublet of doublets was observed in the ^{195}Pt NMR spectrum. No further change occurred in this solution with time.

When the pH was increased to 4.5, a new set of peaks slowly grew, to become after several hours the major peaks in solution. The ^{15}N NMR spectrum showed two singlets with satellites, indicating that the two ^{15}N nuclei are nonequivalent. One Pt–N coupling constant, 339.8 Hz, corresponded to ammine trans to bridging hydroxide (cf. 342 Hz in $[Pt(^{15}NH_3)_2(\mu\text{-}OH)]_2^{2+}$ [9]), and the other, 363.3 Hz, to ammine trans to a deprotonated mp^{2-} ligand. This species is assigned as $[Pt(^{15}NH_3)_2]_2(\mu\text{-}OH)(\mu\text{-}mp)^+$ (VIII). The NMR parameters may be compared with those for the phosphate analogue, VI (Table I). The major difference is the observation of resolved platinum coupling (26.9 Hz) in the ^{31}P NMR spectrum of the methylphosphonate complex VIII. If the complex is a dimer, the ^{31}P spectrum should show a 1:8:16:8:1 pattern, from the superposition of spectra from isotopomers with 0, 1, and 2 ^{195}Pt nuclei. The weak outermost lines were difficult to observe with certainty, but the intensities of the other peaks corresponded to those above. As expected, the peaks due to VIII were independent of pH over the pH range 1.0–8.0. In acid solution, peaks due to VIII decreased over a period of hours, while those due to VII and I increased.

When solutions were allowed to stand near pH 4, they slowly turned blue, but the formation of the blue color was very much slower than in the corresponding reaction of I with phosphate-[13,16-18]

Reactions of I with (Aminomethyl)phosphonic Acid, $ampH_2$ (Scheme I). When aqueous solutions of *cis*-$Pt(^{15}NH_3)_2(H_2O)_2^{2+}$ (I) and $ampH_2$ were mixed at pH 1.5, a new set of peaks grew over several hours, which were assigned to *cis*-$Pt(^{15}NH_3)_2(ampH_2\text{-}O)(H_2O)^{2+}$ (IX). The NMR parameters (Table I) are very similar to those for *cis*-$Pt(^{15}NH_3)_2(mpH)(H_2O)^+$ (VIII). In particular, the ^{195}Pt chemical shift, −1490.8 ppm, is in the region expected for platinum(II) bound by two N atoms and two O atoms,[6,9,13] so that the N atom of the (aminomethyl)phosphonate ligand is not coordinated. This is analogous to the formation of *cis*-$Pt(NH_3)_2(glyH\text{-}O)(H_2O)^{2+}$ (III) from I and glycine in acid solution.[11,12]

When this solution was allowed to stand at pH 1.5 for four weeks, a new set of NMR peaks appeared in ^{31}P and ^{15}N spectra, and peaks due to IX began to decrease. The ^{15}N spectrum showed two singlets with satellites. A peak at −87.04 ppm, with ^1J(Pt–N) = 362.6 Hz, could be assigned to ammine trans to phosphonate. The second peak at −65.12 ppm, with ^1J(Pt–N) = 306.6 Hz, corresponds to ammine trans to a nitrogen donor.[6-13,19] These peaks were assigned to the chelate complex $Pt(^{15}NH_3)_2(ampH\text{-}N,O)^+$ (X). The ^{195}Pt spectrum of this solution showed no peaks



X n = 1
XXI n = 2

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Table I. NMR Data[a]

compd	structure	pH	δ_P	J(Pt–P)	δ_N	J(Pt–N)[b]	ligand trans to NH_3	δPt[c]
$Pt(NH_3)_2(OPO_3H_2)(H_2O)^{+}$[d]	V	1.5	5.75	26.8	−86.46	377.2	OPO_3H_2	−1502.1
					−85.54	392.6	H_2O	
$[Pt(NH_3)_2]_2(\mu_{O,O'}\text{-}PO_4H)(\mu\text{-}OH)^{+}$[d]	VI	4.0	7.91	<8	−83.38	366	PO_4H	−1480.6
					−79.30	342	OH	
$Pt(NH_3)_2(mpH\text{-}O)(H_2O)^{+}$	VII	2.5	35.18	<8	−85.93[e]	383[f]	O	−1495.3 (t)
					−85.69[f]	383[f]	O	
$[Pt(NH_3)_2]_2(\mu_{O,O'}\text{-}mp)(\mu\text{-}OH)^{+}$	VIII	4.5	35.91	26.9	−83.12	363.3	O(mp)	−1489.3 (dd)
					−79.44	339.8	OH	
$Pt(NH_3)_2(ampH_2\text{-}O)(H_2O)^{2+}$	IX	1.5	20.83	<8	−85.25	383[f]	O	−1490.8 (t)
					−86.31	383[f]	O	
$[Pt(NH_3)_2]_2(\mu_{O,O'}\text{-}ampH)(\mu\text{-}OH)^{2+}$	XIII	4.0	23.07	19.5	−84.33	372.0	O(amp)	−1464.3 (dd)
					−79.25	343.3	OH	
$Pt(NH_3)_2(ampH\text{-}N,O)^{+}$	X	1.5	45.96	119.6	−65.12	306.6	N	
					−87.04	362.6	O	
$Pt(NH_3)_2(amp\text{-}N,O)$	XI	12.5	39.84	95.2	−64.30	281.0	N	
					−84.77	341.8	O	
$Pt(NH_3)_2(\mu_{O,O'}\text{-}amp\text{-}N)Pt(NH_3)_2(H_2O)^{2+}$	XIV	4.0	51.05	112.3	−66.48	331.7	N	−1489.4 (Pt_B, dd)[g]
					−86.12	356.9	O(amp)	
					−86.51	356.5	O(amp)	
					h			
$PtCl_2(amp\text{-}N,O)^{2-}$	XV	7.0	42.75	117.2				
$Pt(NH_3)_2(amp\text{-}N)(OH)^{-}$	XVII	12.5	12.23	141.6	−64.83	280.3	N	
					−77.46	294.9	OH	
$Pt(NH_3)_2(amp\text{-}N)_2^{2-}$	XVI	12.5	11.99	112.3	−64.30	281.3	N	
$Pt(NH_3)_2(ampH\text{-}N)_2$	XVIII	1.5	16.41	119.7	−65.22	283.7	N	
$Pt(NH_3)_2(aepH_2\text{-}O)(H_2O)^{2+}$	XIX	1.5	29.31	<8	−85.39[e]	386[f]	O	−1487.3 (t)
					−85.88[e]	386[f]	O	
$[Pt(NH_3)_2]_2(\mu_{O,O'}\text{-}aepH)(\mu\text{-}OH)^{2+}$	XX	4.0	31.12	26.9	−83.41	367.2	O(aep)	−1465.0 (dd)
					−79.11	342.3	OH	
$Pt(NH_3)_2(aepH\text{-}N,O)^{+}$	XXI	1.5	27.09	25.6	−59.17	290.0	*N*	
					−85.54	361.8	O	
$Pt(NH_3)_2(aep\text{-}N,O)$	XXII	11.5	26.10	37.8	−58.69	286.1	N	
					−83.36	334.9	O	
$Pt(NH_3)_2(appH_2\text{-}O)(H_2O)^{2+}$	XXIII	1.5	34.45	<8	*e*	379	O	−1487.6 (t)
$[Pt(NH_3)_2]_2(\mu_{O,O'}\text{-}appH)(\mu\text{-}OH)^{2+}$	XXIV	4.0	35.66	29.0	−83.17	363.7	O(app)	−1460.9 (dd)
					−79.11	340.3	OH	

[a] All ammine complexes are ^{15}N-substituted and are cis. Chemical shifts are in ppm to lower shielding from the references given in the Experimental Section. Coupling constants are in Hz. [b] Unless otherwise noted, J(Pt–N) was measured from the ^{15}N NMR spectrum. [c] Key: d, doublet; t, triplet. [d] From ref 13. [e] Overlaps with peak from I. [f] Measured from ^{195}Pt spectrum. [g] Peak due to Pt_A not detected. [h] Peak due to NH_3 trans to H_2O probably obscured by peak from I.

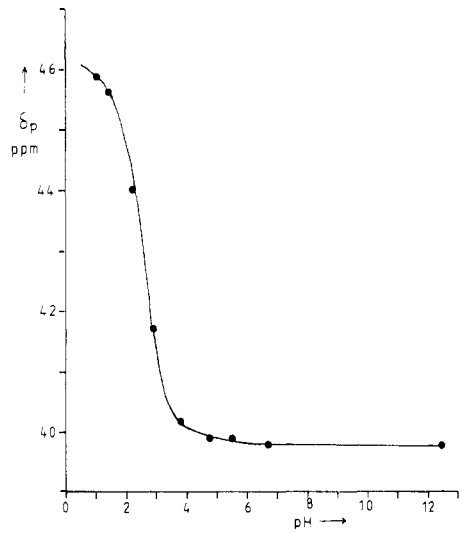


Figure 1. Effect of pH on ^{31}P NMR chemical shift for an H_2O solution of $Pt(NH_3)_2(ampH\text{-}N,O)^{+}$ (X).

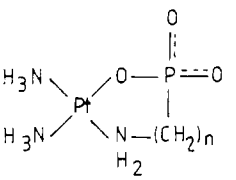
near −1500 ppm. X would be expected to give a multiplet to higher shielding,[6,12] broadened due to partial decoupling from the quadrupolar ^{14}N nucleus.

The ^{31}P spectrum of X showed a singlet with satellites at 45.96 ppm, a large shift to lower shielding compared with the free ligand or the complex IX, with ligand bound through oxygen only. Substantial deshielding is usually observed when phosphorus is incorporated in a five-membered ring.[20] The Pt–P coupling constant, 119.6 Hz, is very much larger than in complexes in which the ligand is bound only through oxygen, so the coupling is probably dominated by the contribution through the Pt–N–C–P pathway.

At pH 1.5, after 8 weeks at room temperature, only peaks due to X (and any excess free ligand) were present, and no other reactions were observed.

The presence of an acid proton on the chelate complex under these conditions is indicated from a plot of δ_P against pH (Figure 1), from which the pK_a of X may be determined as 2.5 (cf. $NH_3CH_2PO_3H_2$, $pK_{a1} = 0.44$, $pK_{a2} = 5.39$[4,21]). The ammine ^{15}N nuclei trans to N and O became less shielded on ligand deprotonation, and Pt–N coupling constants decreased, indicating that trans influences of the amp ligand donor groups increase.[19]

Attempts to isolate solid complexes from these solutions were unsuccessful. At pH 7, when the chelate complex should exist predominantly as the nonelectrolyte $Pt(NH_3)_2(amp\text{-}N,O)$ (XI),



XI n = 1
XXII n = 2

or at pH 3, when it would be present as $Pt(NH_3)_2(ampH\text{-}N,O)^{+}$

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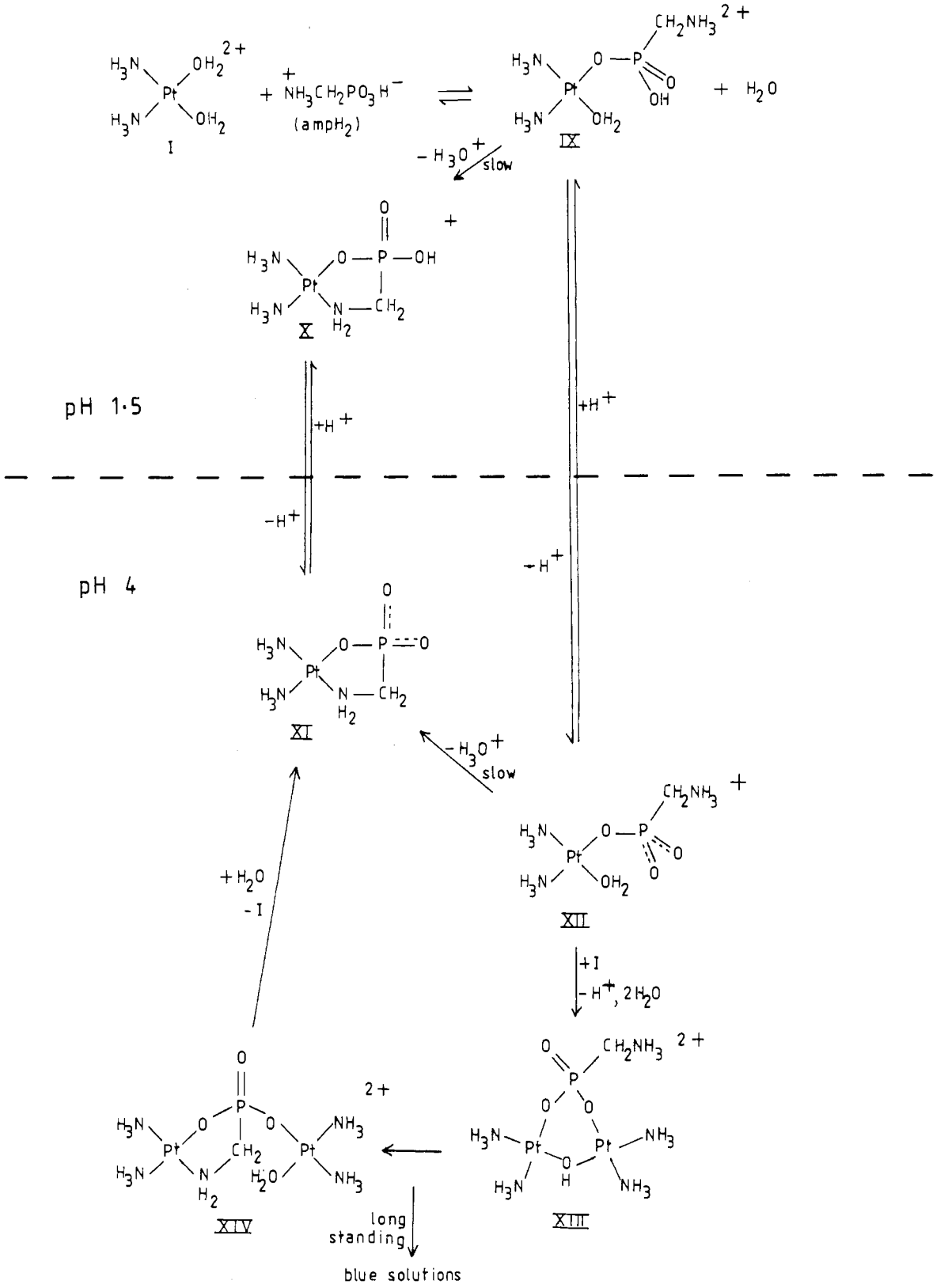
Scheme I



(X) with perchlorate or nitrate as counterions, no solids crystallized from concentrated solutions. This contrasts with the facile isolation of $[Pt(NH_3)_2(gly\text{-}N,O)]NO_3$ from the corresponding glycinate system.[12] Only when all solvent was removed was a solid obtained, mixed with inorganic salts.

When the reaction between I and the ligand was carried out at pH 4 a more complex sequence of reactions occurred. A series of ^{31}P spectra run at different times after the initial mixing of solutions are shown in Figure 2. As at lower pH, the first set of peaks to appear corresponded to *cis*-$Pt(NH_3)_2(ampH_2\text{-}O)(H_2O)^{2+}$ (IX). These peaks passed through a maximum in intensity then began to decrease as a second set of peaks slowly grew. After 3 days, with the pH maintained at 4, this new complex was the major species in solution (^{31}P spectrum, Figure 2b). The ^{195}Pt spectrum for this species was a sharp doublet of doublets at −1464.3 ppm, indicating that the platinum atom was bound only to oxygen donors. The spectrum was very similar to that of $[Pt(^{15}NH_3)_2](\mu\text{-OH})(\mu\text{-mp})^+$ (VIII). The ^{15}N spectrum (Table

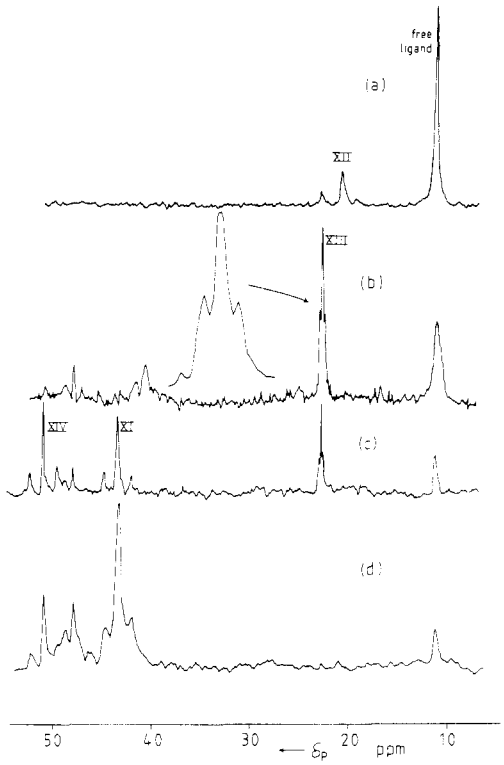
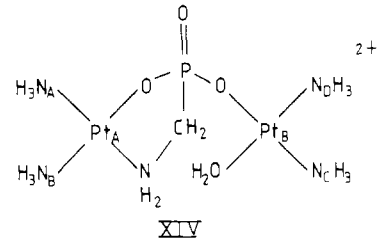


Figure 2. Changes with time in the ^{1}H-decoupled ^{31}P NMR spectrum of a solution obtained by mixing *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ and $ampH_2$ in the molar ratio 2:1 at pH 4: (a) 2 h; (b) 24 h; (c) 1 week; (d) 1 month. Roman numerals refer to the labels in Scheme I.

I) was also very similar to that of VIII, leading to the assignment of this species as $[Pt(^{15}NH_3)_2]_2(\mu\text{-OH})(\mu_{O,O'}\text{-ampH})^{2+}$ (XIII). δ_P (23.07 ppm) was to higher shielding than in VIII (35.91 ppm), probably as a result of the proximity of the positively charged amine group. The relative intensities of the "satellite" and central peaks (inset, Figure 2b are as expected for a dimeric structure. J(Pt–P), 19.5 Hz, is much lower than would be expected if there were a Pt–N–C–P coupling route (see above). Since XIII has two $Pt(NH_3)_2$ units but only one phosphonate group, peaks due to XIII are more pronounced relative to those from monomeric species present in the ^{195}Pt and ^{15}N spectra than in the ^{31}P spectrum.

Peaks due to the monomeric chelate complex, $Pt(^{15}NH_3)_2$(amp-*N*,*O*) (XI), slowly grew with time, and after several weeks of standing, this was the major complex present (Figure 2d). Various weak peaks, many transient, were observed in the spectra, and some of these appear in Figure 2b,c. One set of peaks, however, became relatively intense in the spectra, passing through a maximum after about a week (depending on proportions of the original reactants) and then slowly disappearing as peaks due to XI grew. The ^{31}P NMR spectrum showed a 1:4:1 singlet with satellites at 51.05 ppm, with J(Pt–P) = 112.3 Hz. The low shielding would be expected if the phosphorus atom is incorporated in a five-membered ring. The large coupling constant indicates that there is a Pt–N–C–P coupling route to one Pt atom. Since this species was present only when mixed with I, XI, and XIII, careful examination of spectra was required to assign its ^{195}Pt and ^{15}N peaks. Three singlets, with accompanying satellites, of equal intensity could be assigned to this species in the ^{15}N spectrum. Peaks at −86.12 and −86.51 ppm, each with ^1J(Pt–N) = 357 Hz, would correspond to ammine trans to phosphonate, and a peak at −66.48 ppm, ^1J(Pt–N) = 332 Hz, to ammine trans to coordinated nitrogen.

From these data, the structure of this species was assigned as $Pt(^{15}NH_3)_2(\mu_{O,O'}\text{-amp-}N)Pt(^{15}NH_3)_2(H_2O)^{2+}$ (XIV), in which the ligand forms a chelate ring through coordination of the N atom and one phosphonate O atom to one Pt atom, with a bridge to a second Pt atom through another phosphonate O atom. The ^{15}N spectrum of this compound would be expected to show peaks due



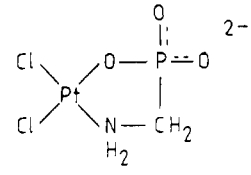
XIV

to ammine trans to nitrogen (N_A), phosphonate (N_B, N_C), and water (N_D). The last peak was not observed in our spectra, but it would be expected to occur very close to that due to *cis*-$Pt(^{15}NH_3)_2(H_2O)_2^{2+}$ (I) and was probably obscured. No ^{195}Pt resonance assignable to Pt_A (expected to be broadened by coordination to ^{14}N) was observed, but a doublet of doublets was observed at −1489.4 ppm, as expected for Pt_B, coordinated by two ammine ligands and two O donors.

If our assignment is correct, XIV is an intermediate in the conversion of $[Pt(NH_3)_2]_2(\mu_{O,O'}\text{-ampH})(\mu\text{-OH})^{2+}$ (XIII) to the chelate complex, XI. *cis*-$Pt(NH_3)_2(ampH_2\text{-}O)(H_2O)^{2+}$ (IX) will also slowly convert directly to XI.

After several weeks of standing at pH 4.5, these solutions turned blue.

Reaction of a solution of K_2PtCl_4 with $ampH^-$ at pH 7 caused a peak with satellites to grow in the ^{31}P NMR spectrum. The chemical shift (42.75 ppm) and high Pt–P coupling constant (117.2 Hz) were consistent with formation of a five-membered chelate ring, and the complex was assigned as $PtCl_2$(amp-*N*,*O*)$^{2-}$ (XV).



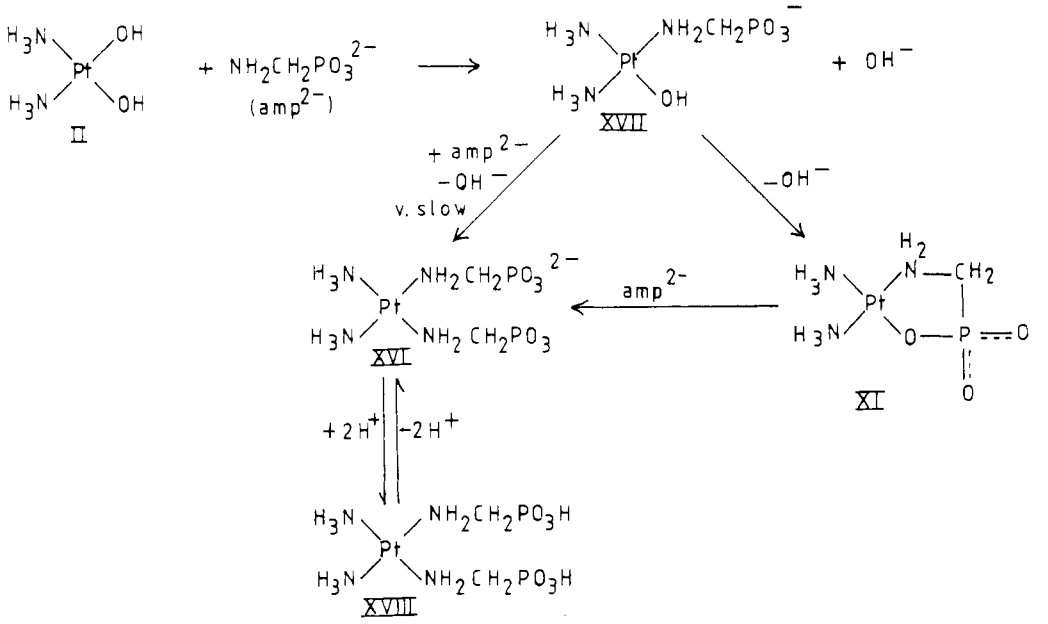
XV

Reaction of *cis*-$Pt(NH_3)_2(OH)_2$ (II) with amp^{2-} (Scheme II). When solutions of *cis*-$Pt(^{15}NH_3)_2(OH)_2$ (II) and amp^{2-} were mixed at pH 12.5, reaction was very slow, but after 1 week of standing, three sets of peaks, in addition to those from the starting materials, were detected. One set of peaks was easily assigned to the chelate complex $Pt(^{15}NH_3)_2$(amp-*N*,*O*) (XI), previously prepared via acidic solutions. The species that ultimately predominated if excess amp^{2-} was used showed a singlet with satellites at 11.99 ppm in the ^{31}P spectrum. The large Pt–P coupling constant, 112.3 Hz, indicated a Pt–N–C–P coupling route, and the phosphorus nucleus did not show the deshielding expected if there were a chelate ring. The ^{15}N NMR spectrum showed one singlet with satellites. δ_N (−64.30 ppm) and ^1J(Pt-N) (281.3 Hz) both correspond to ammine trans to coordinated nitrogen.[6,9,19] This species was assigned as *cis*-$Pt(^{15}NH_3)_2(amp\text{-}N)_2^{2-}$ (XVI), in which two amp^{2-} ligands are bound unidentate through nitrogen. The remaining species gave a singlet with satellites in the ^{31}P spectrum (12.23 ppm, ^3J(Pt–N–C–P) = 141.6 Hz) and two singlets with satellites in the ^{15}N spectrum, at −77.46 ppm, ^1J(Pt–N) = 294.9 Hz, corresponding to ammine trans to hydroxide[6,9,20] and at −64.83 ppm, ^1J(Pt–N) = 280.3 Hz, corresponding to ammine trans to nitrogen. This compound was assigned as *cis*-$(^{15}NH_3)_2$(amp-*N*)$(OH)^-$ (XVII). Even if only 1 mol of amp^{2-} is used per 1 mol of II, $Pt(NH_3)_2(amp\text{-}N)_2^{2-}$ (XVI) and II are, after several weeks, the only species remaining in solution. This would be expected if the reaction sequence is as shown in Scheme II, with ring closure in *cis*-$Pt(NH_3)_2$(amp-*N*)$(OH)^-$ (XVII) and attack by amp^{2-} on the chelate complex $Pt(NH_3)_2$(amp-*N*,*O*) (XI) both fast relative to initial reaction of II with amp^{2-}.

These reactions are similar to those between II and glycine.[12] No colored solutions were obtained on standing.

When acid was added to a solution of XI, XVI, and XVII, to reduce the pH quickly from 12.5 to 1.5, the chelate complex XI protonated to $Pt(NH_3)_2$(ampH-*N*,*O*)$^+$ (X). *cis*-$Pt(NH_3)_2$(amp-*N*)$(OH)^-$ (XVII) immediately underwent a ring closure reaction

Scheme II



to give the chelate complex X. Peaks of *cis*-Pt($^{15}NH_3$)$_2$(amp-*N*)$_2^{2-}$ (XVI) shifted, presumably owing to protonation to *cis*-Pt($^{15}NH_3$)$_2$(ampH-*N*)$_2$ (XVIII) (Table I).

Reactions of (2-Aminoethyl)phosphonic Acid, aepH$_2$, with I and II. At pH 1.5, aepH$_2$ with I gave the complex *cis*-Pt(NH$_3$)$_2$(aepH$_2$-*O*)(H$_2$O)$^{2+}$ (XIX) analogous to *cis*-Pt(NH$_3$)$_2$(ampH$_2$-*O*)(H$_2$O)$^{2+}$ (IX) and with similar NMR parameters (Table I). However, there was no subsequent reaction to form a chelate complex under these conditions at room temperature. When the solution was heated at 80 °C, the chelate complex Pt(NH$_3$)$_2$(aepH-*N*,*O*)$^+$ (XXI) did form slowly. This assignment was based primarily on the observation of two singlets with satellites in the ^{15}N NMR spectrum; at −85.54 ppm, ^1J(Pt–N) = 361.8 Hz, assigned to ammine trans to phosphonate oxygen, and at −59.17 ppm, ^1J(Pt–N) = 290.0 Hz, assigned to ammine trans to nitrogen. Since the chelate ring is now six-membered, the phosphorus nucleus is more shielded (25.66 ppm) than in the five-membered ring of X. The Pt–P coupling constant, 25.6 Hz, is also much smaller, since, as well as the Pt–O–P path, there is now a four-bond Pt–N–C–C–P pathway, rather than the three-bond pathway in X. Addition of alkali to increase the pH to 11.5 caused changes in the spectra from deprotonation of XXI to Pt($^{15}NH_3$)$_2$(aepH-*N*,*O*)$^+$ (XXI).

At pH 4, XIX did react further to form [Pt(NH$_3$)$_2$]$_2$($\mu_{O,O'}$-aepH)(μ-OH)$^{2+}$ (XX), again analogous to the amp compound with similar NMR parameters. With time this became the dominant complex in solution, but there was again no further reaction to form chelate complexes analogous to X and XIII.

At pH 12.5 no reaction between II and aep^{2-} was observed over several weeks. When the pH was lowered to 11.5, significant reaction occurred over 1 week to the chelate compound Pt($^{15}NH_3$)$_2$(aep-*N*,*O*) (XXII). No peaks assignable to complexes containing aep^{2-} bound only through nitrogen were observed.

Reaction of (3-Aminopropyl)phosphonic Acid, appH$_2$, with I and II. As with the other ligands, I with appH$_2$ at pH 1.5 gave the complex with the ligand bound through oxygen, *cis*-Pt($^{15}NH_3$)$_2$(appH$_2$-*O*)(H$_2$O)$^{2+}$ (XXIII), but no further reaction occurred, even with heating at 90 °C. At pH 4, [Pt($^{15}NH_3$)$_2$]$_2$($\mu_{O,O'}$-appH)(μ-OH)$^{2+}$ (XXIV) slowly formed, but no peaks due to chelate complexes were observed, even with heating.

In contrast to the behavior of other ligands, no reaction was observed between II and app^{2-} over the pH range 9–12 over several weeks.

Discussion

At low pH (1.5) the reaction of I with ampH$_2$ is very similar to that with glyH,[11,12] with an initial "metastable" O-bound complex, I, slowly reacting to form a chelate complex, X. In less strongly acidic solutions (pH 4), however, the behavior of the phosphonate ligand is more complex than that of the carboxylate ligand, because of the greater tendency of the phosphonate group to bridge two Pt atoms.

In alkaline solution, amp^{2-} reacted with II under conditions (pH 12.5) where no detectable reaction occurred with gly$^-$. The increased negative charge on the ligand may enhance the nucleophilicity of nitrogen in amp^{2-}. The reactions that do occur at pH 9–11 for glycine[12] are, overall, similar to those for amp^{2-}.

Despite the increased size of the chelate ring, Pt(NH$_3$)$_2$(aepH-*N*,*O*)$^+$ (XXI) is clearly the thermodynamically most stable species in acidic solutions derived from I and aepH$_2$. The O-bound species, *cis*-Pt(NH$_3$)$_2$(aepH$_2$-*O*)(H$_2$O)$^{2+}$ (XIX) and [Pt(NH$_3$)$_2$]$_2$($\mu_{O,O'}$-aepH)(μ-OH)$^{2+}$ (XX) are less reactive toward ring closure than their amp analogues, probably because there is a lower probability that the longer −(CH$_2$)$_2$NH$_3^+$ chain will fold in the manner required to effect ring closure. Similar considerations would apply to the app analogue.

The differing results for the different ligands of the reactions in alkaline solution are probably due mainly to the decrease in nucleophilicity of the amine end of the anions NH$_2$(CH$_2$)$_n$PO$_3^{2-}$ as *n* increases, since increasing chain length would decrease the inductive effect of the negatively charged phosphonate group on the amine. amp^{2-} (*n* = 1) is the most nucleophilic, and is able to attack *cis*-Pt(NH$_3$)$_2$(OH)$_2$ (II), *cis*-Pt(NH$_3$)$_2$(amp-*N*)(OH)$^-$ (XVII), and Pt(NH$_3$)$_2$(amp-*N*,*O*) (XI) at pH 12.5, to give *cis*-Pt(NH$_3$)$_2$(amp-*N*)$_2^{2-}$ (XVIII) as the ultimate product. aep^{2-} (*n* = 2) is less reactive, and requires a lower pH (small proportions of *cis*-Pt(NH$_3$)$_2$(OH)(H$_2$O)$^+$ present) for reaction to occur, presumably to give initially the undetected complex *cis*-Pt(NH$_3$)$_2$(aep-*N*)(OH)$^-$. Ring closure occurs to Pt(NH$_3$)$_2$(aep-*N*,*O*) (XXII) rather than reaction with more aep^{2-}. The ligand is also insufficiently reactive to attack the Pt–O bond of the chelate complex, which slowly becomes the predominant species. app^{2-} (*n* = 3) is less reactive still, and no reaction with II was observed.

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Registry No. I, 20115-64-4; II, 99829-34-2; V, 91994-75-1; VI, 91994-78-4; VII, 99829-35-3; VIII, 99829-36-4; IX, 99829-37-5; X, 99837-56-6; XI, 99829-38-6; XIII, 99829-39-7; XIV, 99829-40-0; XV, 99829-41-1; XVI, 99829-42-2; XVII, 99829-43-3; XVIII, 99829-44-4; XIX, 99829-45-5; XX, 99829-46-6; XXI, 99829-47-7; XXII, 99829-48-8; XXIII, 99829-49-9; XXIV, 99829-50-2; ^{195}Pt, 14191-88-9; ^{15}N, 14390-96-6.