ABSTRACT: Complexes \(([\text{PTA})_2\text{CpRu-}\mu-\text{CN-1}\kappa\text{C}:2\kappa\text{2N}-\text{RuCp}(\text{PTA})][\text{ZnCl}_2(\text{H}_2\text{O})]\) (13), \([\text{ZnCl}_2(\text{H}_2\text{O})]-(\text{PTA-1}\kappa\text{P}:2\kappa\text{2N})-\text{(PTA)CpRu-}\mu-\text{CN-1}\kappa\text{C}:2\kappa\text{2N}-\text{RuCp}(\text{PTA})(\text{PTA})][\text{ZnCl}_2(\text{H}_2\text{O})]\) (14), \([\text{RuCp}(\text{HdmoPTA})(\text{PPh}_3)(\text{PTA})][\text{CF}_3\text{SO}_3]\) (20), \([\text{RuCp}(\text{HdmoPTA})(\text{HPTA})(\text{PPh}_3)(\text{PTA})][\text{CF}_3\text{SO}_3]\) (21), and \([\text{RuCp}(\text{dmoPTA})(\text{PPh}_3)(\text{PTA})][\text{CF}_3\text{SO}_3]\) (22) were obtained and characterized, and their crystal structure together with that of the previously published complex 18 is reported. The behavior of the 1,3,5-triaza-7-phosphatricyclo[3.3.1.1^{3,7}]decane (PTA) and 3,7-dimethyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (dmoPTA) ligands against protonation and \(\kappa\text{N}\)-coordination is discussed, on the basis of \(^{15}\text{N}\) nuclear magnetic resonance data collected on 22 different compounds, including PTA (1), HdmopTA (7H), and some derivatives as free ligands (2−6 and 8), along with mono- and polymeric complexes containing PTA and/or HdmopTA (9−22). \(^{15}\text{N}\) detection via \(^1\text{H}\)−\(^{15}\text{N}\) heteronuclear multiple bond correlation allowed the construction of a small library of \(^{15}\text{N}\) chemical shifts that shed light on important features regarding \(\kappa\text{N}\)-coordination in PTA and its derivatives.

INTRODUCTION

Today, hydrophilic phosphines are very common ligands in organometallic and coordination chemistry.\(^1\) In this class of compounds, monodentate \(m\)-monosulfonated \(\text{PPh}_3\) (\(m\)-TPPMS) and tris-\(m\)-sulfonated \(\text{PPh}_3\) (\(m\)-TPPTS) are among the most popular examples, but bidentate diphosphines and tridentate tripodal phosphines are also known and have been used.\(^1\) There are also examples of hydrosoluble cage-like phosphines such as Verkade-type phospha-amides and 1,3,5-triaza-7-phosphaadamantane (1), which was first reported in 1974 by Daigle et al. (usually abbreviated as PTA or pta; the acronym TPA and the name “monophosphaurotropine” have been also used to indicate the ligand; the IUPAC name is rarely used in the scientific literature).\(^5\) This ligand contains a soft phosphorus atom and three hard nitrogen atoms, which can be functionalized providing a large variety of derivatives (some examples are shown in Figure 1),\(^6\) useful for obtaining catalysts,\(^7\)−\(^13\) bioactive agents,\(^14\)−\(^25\) luminescent compounds,\(^26\)−\(^27\) and new materials.\(^28\)−\(^35\)

During the past several years, we have devoted a great deal of effort to synthesizing mono- and polymeric complexes containing PTA and its derivatives, affording good homogeneous catalysts for the isomerization of allylic alcohols in water\(^36\)−\(^42\) like complex 9,\(^43\) highly antiproliferative compounds\(^44\)−\(^47\) such as compounds 17−19,\(^48\)\(^49\) and hetero-

metallic polymers like 15 built via assembly of dimetallic complex 12 through metallic moieties (Figure 2).\(^50\) The simplest functionalizations of the PTA cage are mono- and bis-
N-methylation to afford the cationic ligands N-methyl-PTA (mPTA) (5) and N,N′-dimethyl-1,3,5-triaza-7-phosphaadamantane (dmPTA) (6). While the first is very stable, the latter decomposes under mild conditions, providing the ligand 3,7-dimethyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (dmoPTA) (7). Half-sandwich Ru(II) complexes containing 7 and the protonated ligand 3,7-H-3,7-dimethyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (HdmoPTA) (7H+) such as 17 and 18 (Figure 2), exhibit great antiproliferative activities and the ability to chelate a second metallic moiety through the methylated nitrogen atoms. It was shown that the chelation of a second metal, such as in the bimetallic complexes [RuCp(PPh3)2-μ-dmoPTA-1κP:2κ2N,N′-ZnCl2](CF3SO3) (19) and [RuCp(PPh3)2-μ-dmoPTA-1κP:2κ2N,N′-CoCl2]-(CF3SO3), improved the antiproliferative activity that was found to be 200 times higher than that of cisplatin for T-47D and WiDr human solid tumor cell lines.

Most of the time, the coordination of PTA and its derivatives to one metal through the phosphorus atom can be proven by 31P nuclear magnetic resonance (NMR). Nevertheless, spectroscopic characterization of κN-coordination by infrared (IR), Raman, ultraviolet–visible (UV–vis), and 1H and 13C NMR is not straightforward, and only single-crystal X-ray diffraction can provide the needed confirmation, which only ensures the N coordination only in the solid state. Thus, to obtain more information about whether and how PTA and its derivatives are coordinated by the N atoms, we thought to lean on nitrogen NMR.

The most abundant isotope of nitrogen, 14N, is quadrupolar; thus, most of the time, its detection is not practical. On the contrary, 15N has a spin of 1/2 but its natural abundance is only 0.365%; therefore, the duration for data collection for non-enriched samples is usually very long. Nevertheless, this issue can be bypassed by the detection of 15N via 1H through long-range correlation experiments, today run by using routine and robust pulse sequences as heteronuclear multiple-bond correlation (HMBC) or heteronuclear multiple quantum correlation. It is well established that 1H−15N HMBC is a very useful tool for the structural assignments in protein sequences and was also used for the characterization of natural products and the structural resolution of isomers. Also, various studies were published, including 15N-enriched coordination compounds such as bimetallic clusters, and in recent years, organometallic complexes.
were also characterized by this technique. In this work, we used the $^1H-^{15}N$ HMBC pulse sequence to investigate in solution some noncoordinated PTA derivatives (Figure 1) as well as some previously published representative Ru half-sandwich complexes displaying $k^p$- and $k^pN$-coordination (Figure 2). Additionally, the new monometallic (20–22) and polymetallic (13 and 14) complexes containing dmoPTA and/or PTA were synthesized and characterized by single-crystal X-ray diffraction, expanding the family of PTA-$k^p$N-complexes, illuminating new aspects of the coordination behavior of the PTA and dmoPTA ligand in the solid state and solution.

#### EXPERIMENTAL PROCEDURES

**Synthesis and Characterization of 13 and 14.** Trying to obtain an analogue of polymer 15 with Zn instead of Cd, we reacted bimetallic complex 12 with 3 equiv of ZnCl$_2$ in water. Immediately, a light brown precipitate formed, which was used to solve some noncoordinated PTA derivatives (Figure 1) as as well as three previously published representative Ru halfsandwich complexes displaying $k^p$- and $k^pN$-coordination (Figure 2). Additionally, the new monometallic (20–22) and polymetallic (13 and 14) complexes containing dmoPTA and/or PTA were synthesized and characterized by single-crystal X-ray diffraction, expanding the family of PTA-$k^p$N-complexes, illuminating new aspects of the coordination behavior of the PTA and dmoPTA ligand in the solid state and solution.

**EXPERIMENTAL PROCEDURES**

**Synthesis and Characterization of 20–22.** Complex [Ru$_2$(dmoPTA)(PPh$_3$)(PTA)]($CF_3$SO$_3$)$_2$ (20) was obtained in 81% yield by treatment of [RuCl$_2$(PPh$_3$)(PTA)] with AgOTf and further reaction with dmpPTA (6) at 50°C (Scheme 2). The presence of the $CF_3$SO$_3^-$ anion in the complex composition was confirmed by both its $^{13}$C($^1H$) NMR and infrared spectra. Except for the resonances assigned to PTA, the $^1H$ and $^{13}$C chemical shifts are similar to those of complex 17, supporting that the ligand dmoPTA is protonated. Its $^{31}$P($^1H$) NMR spectrum in CD$_2$OD displays the signals relative to PTA (−39.40 ppm), protonated dmoPTA (−3.99 ppm), and PPh$_3$ (46.33 ppm) in a 1:1:1 ratio as an AMX pattern and agrees with those of previously reported compounds containing these ligands.

**Crystal Structure of 13 and 14.** Complexes 13 and 14 crystallize in the $P2_1/n$ and $P1$ space groups, respectively. Selected bond lengths and angles are listed in Table 1, while a complete list can be found in Tables S7, S8, S12, and S13.

**Synthesis and Characterization of 20–22.** Complex [Ru$_2$(dmoPTA)(PPh$_3$)(PTA)]($CF_3$SO$_3$)$_2$ (20) was obtained in 81% yield by treatment of [RuCl$_2$(PPh$_3$)(PTA)] with AgOTf and further reaction with dmpPTA (6) at 50°C (Scheme 2). The presence of the $CF_3$SO$_3^-$ anion in the complex composition was confirmed by both its $^{13}$C($^1H$) NMR and infrared spectra. Except for the resonances assigned to PTA, the $^1H$ and $^{13}$C chemical shifts are similar to those of complex 17, supporting that the ligand dmoPTA is protonated. Its $^{31}$P($^1H$) NMR spectrum in CD$_2$OD displays the signals relative to PTA (−39.40 ppm), protonated dmoPTA (−3.99 ppm), and PPh$_3$ (46.33 ppm) in a 1:1:1 ratio as an AMX pattern and agrees with those of previously reported compounds containing these ligands.

**Crystal Structure of 13 and 14.** Complexes 13 and 14 crystallize in the $P2_1/n$ and $P1$ space groups, respectively. Selected bond lengths and angles are listed in Table 1, while a complete list can be found in Tables S7, S8, S12, and S13. In terms of 13, the asymmetric unit contains one molecule of trinuclear complex $[($PTA)$_2$Ru$_2$μ-μ-CN-1kC:2κ²N-Ru$_2$Cl$_2$($H_2$O)]$N$ bond in $[^1H]NMR$ spectra in D$_2$O of both complexes 13 and 14 show $H_2$O stretching and bending bands (3479 and 1623 cm$^{-1}$), respectively, which are absent in 13.

The $^{31}$P($^1H$) NMR spectra in D$_2$O of both complexes 13 and 14 display two singlets in a 1:1 ratio, at −19.8 and −22.4 ppm, respectively. This behavior agrees with the cleavage of $\Delta^{2}$P($^1H$) NMR spectrum displays the signals of PTA, dmoPTA, and PPh$_3$ at −37.54, 5.48, and 50.03 ppm, respectively, which are similar to what was observed for 18. It is also worth mentioning that the carbons of the methyl groups are inequivalent, arising at 44.19 and 44.27 ppm in the $^{13}$C($^1H$) NMR spectrum, as evidenced by its $^{1H}-^{13}$C HSQC spectrum.

**Crystal Structure of 13 and 14.** Complexes 13 and 14 crystallize in the $P2_1/n$ and $P1$ space groups, respectively. Selected bond lengths and angles are listed in Table 1, while a complete list can be found in Tables S7, S8, S12, and S13. In terms of 13, the asymmetric unit contains one molecule of trinuclear complex $[($PTA)$_2$Ru$_2$μ-μ-CN-1kC:2κ²N-Ru$_2$Cl$_2$($H_2$O)]$N$ bond in $[^1H]NMR$ spectra in D$_2$O of both complexes 13 and 14 show $H_2$O stretching and bending bands (3479 and 1623 cm$^{-1}$), respectively, which are absent in 13.

The $^{31}$P($^1H$) NMR spectra in D$_2$O of both complexes 13 and 14 display two singlets in a 1:1 ratio, at −19.8 and −22.4 ppm, respectively. This behavior agrees with the cleavage of $\Delta^{2}$P($^1H$) NMR spectrum displays the signals of PTA, dmoPTA, and PPh$_3$ at −37.54, 5.48, and 50.03 ppm, respectively, which are similar to what was observed for 18. It is also worth mentioning that the carbons of the methyl groups are inequivalent, arising at 44.19 and 44.27 ppm in the $^{13}$C($^1H$) NMR spectrum, as evidenced by its $^{1H}-^{13}$C HSQC spectrum.
The zinc atoms in 13 and 14 display a distorted tetrahedral geometry and complete the coordination spheres with three chlorides in 13 and two chlorides and one H2Oi in 14. The Zn−Cl bond lengths are comparable in both complexes (13, \(d_{Zn-Cl} = 2.244\) Å; 14, \(d_{Zn-Cl} = 2.242\) Å), similar to the typical bond lengths in the structure of zinc chloride complexes in aqueous solution \([\text{ZnCl}_2(\text{PTA})_2], d_{Zn-Cl} = 2.231\) Å; \([\text{ZnCl}_2(\mu-\text{O}≡\text{PTA})]_n, d_{Zn-Cl} = 2.198(3)\) Å; \([\text{ZnCl}_2(\text{O}≡\text{PTA})(\text{H}_2\text{O})], d_{Zn-Cl} = 2.218\) Å; \([\text{ZnCl}_2(\text{S}≡\text{PTAH})(\text{S}≡\text{PTAZnCl}_3)], d_{Zn-Cl} = 2.245\) Å), \(^{77,78,84}\) while the Zn−N bond in 13 is slightly longer than that in 14 [13, Zn1−N1 = 2.123(7) Å; 14, Zn1−N1 = 2.114(3) Å] as well as other examples of Zn−N_{PTA} bonds \([\text{ZnCl}_2(\text{PTA})_2], \text{Zn1−N1} = 2.055(3)\) Å; \([\text{ZnCl}_2(\mu-\text{O}≡\text{PTA})]_n, \text{Zn1−N1} = 2.108(16)\) Å; \([\text{ZnCl}_2(\text{O}≡\text{PTA})(\text{H}_2\text{O})], \text{Zn1−N1} = 2.093(10)\) Å; \([\text{ZnCl}_2(\text{S}≡\text{PTAH})(\text{S}≡\text{PTAZnCl}_3)], \text{Zn1−N1} = 2.085(15)\) Å]. \(^{77,78,85}\)

With regard to the intermolecular contacts, in the crystal packing of 13, there is no interaction worth mentioning, while in 14, each tetrametallic moiety of 14 is connected to four neighboring complexes via the O1 and N6 atoms, forming hydrogen-bonded layers along the reciprocal b*-e* plane (Figure 4).
Crystal Structure of 18, 21, and 22. Complex [RuCp-(PPh3)3(dmoPTA-κP)]((CF3SO3)-CHCl3 (18) was previously prepared and published by us40 but single crystals suitable for X-ray diffraction were obtained only recently by diffusion of Et2O vapor into a solution of the complex in chloroform, giving chloroform-solvated (18·CHCl3). Single crystals of complexes [RuCp(HdmoPTA)(PPh3)(HPTA)]((CF3SO3)3·3H2O (21·H2O) and [RuCp(dmoPTA)(PPh3)(PTA)]·(CF3SO3)·MeOH (22·MeOH) were obtained by slow evaporation of a solution of the corresponding complex in water and methanol, respectively. Selected bond distances and angles for the three complexes are listed in Table 2, and complete lists of bond lengths and angles are provided in Tables S9–S11 and S14–S16. The asymmetric unit of complex 18·CHCl3 contains a [RuCp(PPh3)3(dmoPTA-κP)]+ molecule, one CF3SO3−, and one CHCl3. The coordination sphere of the ruthenium atom displays a pianostool geometry and is constituted by a nη3-Cp, two PPh3 ligands, and one dmoPTA ligand (Figure 5). Bond distances between the metal and the Cp centroid and phosphine P atoms are similar to those found for similar complexes (Table 2).46,86–88 The dmoPTA ligand is distorted (C1–P1–C2 = 102.15°; C1–P1–C3 = 95.86°; C2–P1–C3 = 94.84°), and the distance between the CHN atoms [N1–N2 = 3.609(4) Å] is significantly larger than the distance for the equivalent protonated complex (2.80 Å). Comparison of the crystal structure of 18·CHCl3 with its protonated form also shows that protonation of dmoPTA causes an extension of the three Ru–P bonds [Δa(Ru1–P1) = +0.0023 Å, Δa(Ru1–P2) = +0.0119 Å, and Δa(Ru1–P3) = +0.0326 Å].48

Complexes 21 and 22 are constituted by the same complex moiety: a nη3-Cp bonded to the Ru, which completes its coordination geometry by one κP-PTA, one PPh3, and one κP-dmoPTA. Nevertheless, in 21, PTA and dmoPTA are monoprotonated, its composition being [RuCp(PPh3)(HPTA-κP)]+, while in 22, these ligands are deprotonated, its composition being [RuCp(PPh3)(PTA-κP)]+ (dmoPTA-κP)−. Figure 5). In both 21 and 22, the counterions are CF3SO3−, which are disordered in the lattice. The bond lengths and angles in complexes 21 and 22 are similar and fall in the ranges found for related complexes.46–89 Nevertheless, it is important to point out that the Ru–PdmoPTA bond in 21 [Ru–P1 = 2.8281(14) Å] is significantly shorter than that in 22 [Ru–P1 = 2.3066(8) Å] and 18 [Ru–P1 = 2.3187(9) Å]. The same tendency is also observed for the Ru–PTA bond in 21 [Ru–P2 = 2.2838(13) Å], which is shorter than that in 22 [Ru–P2 = 2.3099(8) Å] and similar to the Ru–PdmoPTA bond for this complex. Also, the Ru–PPh3 bond length is somewhat different in the three complexes [18, 2.3541(8) and 2.3564(9) Å; 21, 2.3433(12) Å; 22, 2.3116(8) Å]. The longest Ru–P bond observed in 18 is reasonable, due to the steric effect exerted by the PPh3 ligands, which also provoke a large distortion of the coordination geometry, as reflected by the angles between ligands [18, P1–Ru1–P2 = 95.44(3)°; P2–Ru1–P3 = 105.94(3)°; P1–Ru1–P3 = 94.27(3)°]. Nevertheless, compared to what found in dmoPTA–ZnCl2 complex 19, the Ru–PPh3 bond length is only somewhat shorter in the protonated complex 21 and significantly shorter in deprotonated complex 22. The cone angles90 of the HdmoPTA and dmoPTA ligands calculated from the crystal structure are only slightly different, ~103° for 21 and ~106° for 22, leading to a similar angle between

Table 2. Selected Bond Lengths and Angles for 18, 21, and 22

| atoms       | bond length (Å) | bond angle (deg) |
|-------------|-----------------|------------------|
|             | 17              | 18              | 21              | 22              |
| Ru1 P1      | 2.321(1)        | 2.3187(9)       | 2.2821(14)      | 2.3066(8)       |
| Ru1 P2      | 2.366(1)        | 2.3541(8)       | 2.2838(13)      | 2.3009(8)       |
| Ru1 P3      | 2.389(1)        | 2.3564(9)       | 2.3433(12)      | 2.3116(8)       |
| N1 N2       | 2.800(6)        | 3.609(4)        | 2.670(8)        | 3.565(4)        |
| P1 P2       | 96.58(4)        | 95.44(3)        | 95.65(5)        | 95.95(3)        |
| P1 P3       | 97.53(4)        | 94.27(3)        | 97.09(5)        | 94.12(3)        |
| P2 P3       | 103.30(4)       | 105.94(3)       | 97.14(4)        | 98.64(3)        |

*a For the sake of comparison, the values obtained for 17 were also added. From ref 48.*

Figure 5. Thermal ellipsoid representations of the cationic portion of the crystal structures of 18, 21, and 22. Their relevant bond lengths, plane angles, and torsion angles are listed in Table 2, which also includes the data of 17 for the sake of comparison (structure not shown). Anions, solvent molecules, and hydrogen atoms connected to carbons have been omitted for the sake of clarity.
ligands \[21, \text{P}_1\text{Ru}_{1}\text{P}_3 = 97.09(5)°, \text{P}_1\text{Ru}_{1}\text{P}_2 = 95.65(5)°\] and \[22, \text{P}_2\text{Ru}_{1}\text{P}_3 = 97.14(5)°; \text{P}_2\text{Ru}_{1}\text{P}_3 = 95.95(3)°, \text{P}_2\text{Ru}_{1}\text{P}_1 = 94.12(3)°, \text{P}_2\text{Ru}_{1}\text{P}_3 = 98.64(3)°\]. The distance between the CH$_3$N$_{dmoPTA}$ atoms is 2.670(8) Å for 21, where the ligand is protonated, whereas for the deprotonated ligand in 22, it is 3.565(4) Å, which is like that found in 18. The protonation of PTA in 21 is localized on the N4 atom, which is part of a network of hydrogen bonds with water molecules and triflate anions (Figure 6).

It is important to additionally consider the effect of the deprotonation of the HdmoPTA ligand in complexes 18 and 22. When the CH$_3$N$_{dmoPTA}$ atoms are not H-bridged, the bottom rim of the triazaphosphaadamantine-like cage opens through an inversion about one of the methylated nitrogen atoms, which moves away from their lone pairs from each other. Given that in 18 and 22 the molecules are not connected by a network of hydrogen bonds, the greater N1–N2 length in 18 and 22 may suggest that their distance is susceptible to the steric hindrance of the surrounding ligands, which in 18 imposes a larger separation between the methyl groups (Figure 7). Intending to predict the N′−N″ chelation behavior of the dmoPTA ligand, we find these data shed light on the possibility of chelating also metals with a van der Waals radius larger than those of Zn, Ni, and Co, which are the only examples of dmoPTA-$\kappa$N′,N″-coordinated metals obtained to date.\textsuperscript{89,93}

### RESULTS AND DISCUSSION

$^{15}$N Chemical Shifts of 1−22 via $^{1}$H−$^{15}$N NMR Long-Range Correlations. $\delta^{15}$N of the Free Ligands. The adamantane-like phosphines and derivatives studied by $^{1}$H−$^{15}$N long-range NMR correlations are displayed in Figure 1. Considering that selected metal-free triazaphosphines 1−3 display $C_{3v}$ symmetry, while for ligands 4−8 is $C_{2v}$, in the first group only the cross peak due to three magnetically equivalent nitrogen atoms is expected, while for the second, two different signals should be found; the respective nitrogen atoms are numbered according to Figure 8. The obtained $\delta^{15}$N values for compounds 1−8 are summarized in Figure 8 and Table S1. As expected, only a $^{15}$N signal was observed for 1 in D$_2$O that arises at 24.6 ppm, which is the expected region for a tertiary amine.\textsuperscript{94} When the phosphorus atom is functionalized, the $^{15}$N resonance of the PTA suffers inductive deshielding, as seen for 2 and 3. Upon methylation of the phosphorus atom, compound 2 is obtained, which displays a singlet at 42.9 ppm, while oxidation of the phosphorus, which gives 3, shifts the signal to 64.3 ppm.

Simple protonation of 1 affords compound 4 that displays a singlet due to fast proton exchange. This peak is shifted by only 0.1 ppm in D$_2$O with respect to 1, which is the usual behavior for sp$^3$ nitrogen.\textsuperscript{95} Nevertheless, this fact indicates the large difference in the chemical shift between the phosphorus in $^{31}$P NMR, which is approximately 1 order of magnitude larger.\textsuperscript{96} Methylation of one of the nitrogen atoms of 1 affords the ligand mPTA (5), which displays the $\delta^{15}$N signal corresponding to quaternary nitrogen N$^1$ that moved by only 0.2 ppm to a higher field with respect to 1. On the contrary, the tertiary nitrogens N$^2$ suffer a dramatic inductive effect, arising at 34.8 ppm in D$_2$O. Therefore, the nonsubstituted PTA nitrogen atoms in 5 are shifted by almost +10 ppm with respect to 1 but $-9$ ppm with respect to P-methylated regioisomer 2. These results show that the functionalization of the PTA at the phosphorus atom leads to a $\Delta\delta^{31}$N much more pronounced than that at the nitrogen. Further N methylation of 5 gives rise to N,N$^′$-dimethylated derivative 6, usually known as dmPTA, whose CH$_3$N$^′$ and N$^2$-$\delta^{15}$N are found at 41.2 and 47.1 ppm, respectively, in acetone-\textit{d}$_6$, showing how these atoms are markedly deshielded by the second methylation. The $\Delta\delta^{31}$N$^1$ and $\Delta\delta^{31}$N$^2$ between 6 and 5 are larger ($\Delta\delta^{31}$N$^1$ = +18.1 ppm, and $\Delta\delta^{31}$N$^2$ = +12.9 ppm) than those between 5 and 1, due to the inductive effect produced by the quaternary nitrogen atoms, which is doubled in 6 and reciprocally exercised by both N$^1$. It is interesting to point out that the mono- and dimethylation of 1 produce a similar effect on the $\delta^{31}$P chemical shift.

Derivatives obtained by functionalization of PTA at the two nitrogen atoms suffer, under the appropriate conditions, the
Figure 8. $\delta^{15}$N values for compounds 1–8.

It is important to evidence that the solvent polarity also has a slight influence on the chemical shift of the N atoms of the studied compounds. In terms of 2, the $^{15}$N signal is linearly shielded with a decrease in solvent polarity, while compound 1 displays a different behavior: it suffers shielding when the more polar DMSO-$d_6$, rather than acetone-$d_6$, is used, but in D$_2$O, the signal is deshielded by 0.5 ppm concerning acetone-$d_6$. This behavior, which is shown also by 5, can be tentatively addressed considering the possible involvement of the phosphorus atom in hydrogen bonding, which could induce the deshielding of the N$_{PTA}$ atoms in a manner similar to but less intense than that caused by the methylation of the P$_{PTA}$ atom.

$\delta^{15}$N of Metal Complexes Containing Ligands 1, 4, and 5. The $^1$H–$^{15}$N HMBC of complex [RuCl$_2$(PTA)$_2$] (9), which contains two equivalent PTA ligands, is characterized by a correlation at 40.2 ppm in D$_2$O that is relative to its six equivalent nitrogen atoms, together with another set of cross-peaks at 39.3 ppm. This additional signal can be assigned to complex [RuCl$_2$(PTA)$_2$(D$_2$O)]$^+$ (10) that is in equilibrium with 9 in water. The $\delta^{15}$N$^-$ of 11 was determined to be shifted by 3.5 ppm to 9 (Figure 9). As observed in 4, only one $^{15}$N resonance is observed, due to fast proton exchange.

A new step in complexity is represented by diruthenium complex 12, which was synthesized by the reaction of 9 with a half-equivalent of KCN. The $^{15}$N resonances for 12 arise in the same chemical shift range as 9. Additionally, two singlets are observed at 40.8 and 41.8 ppm corresponding with N$^\prime$ and N$^\prime\prime$ atoms, respectively (see Figure 9), which are due to the asymmetry of the cyanide bridge making the {RuCp(PTA)$_2$}$^+$ moieties inequivalent. N$^\prime$ corresponds to the nitrogen atoms of the PTA bonded to the Ru-CN fragment, and N$^\prime\prime$ to those of the PTA bonded to the Ru-NC.

The coordination of one [ZnCl$_3$]$^-$ moiety or two {ZnCl$_2$(H$_2$O)}$^+$ moieties to the nitrogen atoms of 12 leads to trimetallic complex 13 and tetrametallic complex 14, respectively. The absence of multiplicity in their $^{31}$P($^1$H) NMR resonances suggests that the N–Zn bond is cleaved upon dissolution. This assumption can be also supported by their identical $\delta^{15}$N values (41.1 and 42.7 ppm in D$_2$O and 41.4 and 43.5 ppm in DMSO-$d_6$), very similar to those of 12.

Under adequate reaction conditions, polymeric complexes such as 15 can be obtained from 12, in which two PTA-N bonds are coordinated to two different {CdCl$_3$}$_2^-$ units. The $^1$H–$^{15}$N HMBC of this polymer provides identical correlations with respect to 12–14, supporting previous evidence that indicates that upon dissolution in water the Cd–N bonds are cleaved.

Finally, complex 16, which contains the methylated ligand mPTA (5), shows the resonances relative to methylated atom N$^\prime$ and nonmethylated N$^\prime\prime$ in DMSO-$d_6$ arising at 37.7 and 44.7 ppm, respectively. The differences in the chemical shift between the coordinated and free ligand ($\Delta\delta^{15}$N$^\prime$ = 14.6 ppm, and $\Delta\delta^{15}$N$^\prime\prime$ = 10.9 ppm) are in the range found for the complexes containing 1. Also, it is interesting to point out that N$^\prime$ resonates at a frequency similar to that of the protonated species 11.

In general, the $^{15}$N resonances for complexes 9–16 (Table S2) and compound 2 appear in a very narrow chemical shift range, suggesting that P methylation of the PTA and the $\kappa^P$-coordination to the ruthenium produce a similar deshielding effect.
Figure 9. $\delta^{15}N$ values for compounds 9–16.

Figure 10. $\delta^{15}N$ values for compounds 17–19.
\( \delta^{15}N \) of Metal Complexes Containing Ligand dmoPTA (7). Generally, to avoid possible side reactions caused by the chelating nitrogen atoms, the complexes containing dmoPTA (7) are obtained employing 6 as a proligand. Under reaction conditions, once 6 is \( \kappa^2P \)-coordinated, it usually undergoes solvolysis of the CH₂ bridging the ammonium groups and converts into phosphate 7 in its protonated form, \( 7H^+ \), which occurs when \([\text{Ru-Cp}(\text{HdmoPTA})(\text{PPh}_3)_2](\text{CF}_3\text{SO}_3)_2 \) (17) is synthesized. The \( ^1H-^{15}N \) HMBC spectrum of 17 displays two correlations at 45.3 and 47.5 ppm (CD₃OD), which are slightly susceptible to solvent changes (Figure 10). The presence of just two sets of correlations in the \( ^1H-^{15}N \) HMBC spectrum supports the idea that the proton is shared between the two methylated nitrogen atoms \( N^3 \). The deprotonation of 17 affords 18 and displaces the \( N^1 \) chemical shift to 33.7 ppm in CD₃OD (Table S3). Also, \( N^2 \) is slightly shielded and resonates at 42.1 ppm. Surprisingly, after coordination to the Ru center, the \( \delta^{15}N \) values of 7 do not vary as much as observed for ligands 1 and 5.

Ligand 7 can coordinate a variety of metallic centers through its methylated nitrogen atoms, affording bimetallic complexes whose antiproliferative activity is usually much higher than those of the monometallic parent compounds and cisplatin. This is the case for the complex \([\text{Ru-Cp}(\text{PPh}_3)_2-\mu-\text{dmoPTA-1kP-2x²N₈N³-ZnCl₂}](\text{CF}_3\text{SO}_3)_2 \) (19), which is 5 times more potent than 18 and 425 times more potent than cisplatin on WiDr colon cancer cells. The chelation of the \{ZnCl₂\} moiety closes the bottom rim of the dmoPTA ligand and deshields both \( N^1 \) and \( N^2 \), which in CDC₁₃ appear at 41.1 and 47.8 ppm, respectively, near the observed signals for 6 in acetone-\( \text{d}_6 \). The trend shown by the \( \delta^{15}N \) values of compounds 17–19 is revealed to be very significant to assess the coordination of a second metallic unit to \( \text{CH}_2\text{N}_2\text{dmoPTA} \). The \( \Delta\delta^{15}P \) of the singlets found for 17 and 19 is only 1.2 ppm, while the \( \delta^{15}N \) of their methylated nitrogen differs by 4.21 ppm, making it easier to distinguish whether dmoPTA is protonated or coordinated to a metal.

Complexes 20–22 (Figure 11) contain the ligand PPh₃ and the neutral or protonated PTA and dmoPTA, providing an ideal platform for studying the effect of selective protonation on the \( \delta^{15}N \) of metal complexes containing these aminophosphines. The synthesis of these complexes starts from \([\text{Ru-Cp}(\text{PPh}_3)_2](\text{PTA})\] by abstraction of the chloride with AgCF₃SO₃ and subsequent reaction with dmPTA (6). The resulting complex \([\text{Ru-Cp}(\text{HdmoPTA})(\text{PPh}_3)_2](\text{PTA})](\text{CF}_3\text{SO}_3)_2 \) (20) displays three sets of \( ^{31}N \) atoms that are enumerated in Figure 11. Their chemical shifts show how the presence of the PTA shields the nitrogen atoms of HdmoPTA, producing in CD₃OD differences in chemical shifts to \( 17 \) of \( \Delta\delta^{15}N^1 = 0.8 \) ppm and \( \Delta\delta^{15}N^2 = -1 \) ppm (Table S4). The nitrogen atom \( N^3 \) of the PTA appears at 41.9 ppm (Figure 11), which is close to those obtained for complexes 9, 10, and 12 in D₂O. Complex 20 is susceptible to additional protonation on the PTA, but its HdmoPTA can be deprotonated into dmoPTA. The complex containing the protonated PTA ligand (21) was obtained by the addition of 1 eq of CF₃SO₂H to a solution of 20 in CD₃OD. The \( ^1H-^{15}N \) HMBC spectrum of the resulting complex shows how the protonation shifts the \( ^{31}P \) multiplet corresponding to PTA to \( -27.09 \) ppm (\( \Delta\delta^{31}P = +12.3 \) ppm) and shields the \( N^3 \) resonance by a magnitude similar to \( -31.9 \) ppm (\( \Delta\delta^{15}N^3 = -10.0 \) ppm) with regard to 20. Also, the two \( ^{15}N \) signals corresponding to HdmoPTA appear at higher fields than in 20: that for \( \delta^{15}N^1 \) at 41.5 ppm and that for \( \delta^{15}N^2 \) at 44.1 ppm. Complete deprotonation of 20 employing BuOK affords complex 22 that shows a slight deshielding of \( N^3 \) to 42.7 ppm, while dmoPTA-N¹ and N² appear at 31.7 and 39.7 ppm, respectively, being shielded with respect to the corresponding signals in both 20 and 21, which follow the observed trend for 17 and 18, respectively.

### CONCLUSIONS

To shed light on the behavior of PTA and dmoPTA ligands upon \( \kappa^N \)-coordination and N protonation, ruthenium half-sandwich complexes 13, 14, 21, and 22 were synthesized and characterized by multinuclear NMR, IR, and single-crystal X-ray diffraction. Complexes 13 and 14 are nice examples of the complexes containing the PTA ligand as the linker between metals, providing heterometallic complexes. Both complexes, trimetallic 13 and tetrametallic 14, possess terminal tetrahedral zinc centers \( \kappa^N \)-coordinated to one or two PTA ligands, being new examples of \( \kappa^P \)Nmultidentation of the PTA in the solid state. It was shown that, like other previously published complexes containing PTA-\( \kappa^P \)N ligands, the Zn–N bond is...
not stable in solution. Complexes 21 and 22 are monometallic species containing PPh₃, PTA, and dmoPTA in different protonation states. Their characterization by single-crystal X-ray diffraction confirmed that, upon deprotonation, dmoPTA undergoes a deep conformational change that leads to the separation of the methylated amino groups. The ¹⁵N chemical shifts of PTA and a representative variety of its derivatives as well as complexes (compounds 1–22) were studied by ¹H–¹⁵N HMBC NMR in various solvents. This study can be of general help to chemists working with ligands 1–8 and was performed to obtain more information about the behavior of the coordination sites of PTA and derivatives in solution. The studies supported the instability of PTA-κN multimetallic complexes in solution because of the cleavage of the PTA-κN-M bond, such as observed for 13–15, and revealed it to be important and complementary to ³¹P{¹H} NMR in assessing the dmoPTA-κN,N coordination in complexes, such as shown for 17–22.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/10.1021/acs.inorgchem.1c03831.

Experimental procedures, NMR data, and X-ray crystallographic data of 13, 14, 18, 21, and 22 (PDF)

Accession Codes

CCDC 2126899 and 2126904–2126907 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Author

Antonio Romerosa — Área de Química Inorgánica-CIESOL, Universidad de Almería, 04120 Almería, Spain; orcid.org/0000-0002-6285-9262; Email: romerosa@ual.es

Authors

Andrés Alguacil — Área de Química Inorgánica-CIESOL, Universidad de Almería, 04120 Almería, Spain; orcid.org/0000-0002-3305-7033
Franco Scalambra — Área de Química Inorgánica-CIESOL, Universidad de Almería, 04120 Almería, Spain; orcid.org/0000-0002-5141-0400

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.inorgchem.1c03831

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank Junta de Andalucía for funding the PAI Group FQM-317 and the Project PY20_00791, and the University of Almeria for the Project UAL2020-RNM-B2084 (both projects co-funded by the European Commission FEDER program). A.A. is thankful for Research Contract PY20_00791.

REFERENCES

(1) Li, C.-J. Organic Reactions in Aqueous Media with a Focus on Carbon-Carbon Bond Formations: A Decade Update. Chem. Rev. 2005, 105, 3095–3166.
(2) Joó, F. Aqueous Organometallic Catalysis; Catalysis by Metal Complexes; Springer: Dordrecht, The Netherlands, 2001; Vol. 23.
(3) Phillips, A. D.; Gonsalvi, L.; Romerosa, A.; Vizza, F.; Peruzzini, M. Coordination Chemistry of 1,3,5-Triaza-7-Phosphaadamantane (PTA): Transition Metal Complexes and Related Catalytic, Medicinal and Photochemical Properties. Coord. Chem. Rev. 2004, 248, 955–993.
(4) Verkade, J. G. Main Group Atranes: Chemical and Structural Features. Coord. Chem. Rev. 1994, 137, 233–295.
(5) Daigle, D. J.; Pepperman, A. B.; Vail, S. L. Synthesis of a Monophosphorus Analog of Hexamethylenetetramine. Journal of Heterocyclic Chemistry 1974, 11, 407–408.
(6) Bravo, J.; Bolaño, S.; Gonsalvi, L.; Peruzzini, M. Coordination Chemistry of 1,3,5-Triaza-7-Phosphaadamantane (PTA) and Derivatives. Part II. The Quest for Tailored Ligands, Complexes and Related Applications. Coord. Chem. Rev. 2010, 254, 555–607.
(7) Guerriero, A.; Peruzzini, M.; Gonsalvi, L. Coordination Chemistry of 1,3,5-Triaza-7-Phosphatricyclon[3,3,1]Decane (PTA) and Derivatives. Part III. Variations on a Theme: Novel Architectures, Materials and Applications. Coord. Chem. Rev. 2018, 355, 328–361.
(8) Bolaño, S.; Gonsalvi, L.; Zanobini, F.; Vizza, F.; Bertolasi, V.; Romerosa, A.; Peruzzini, M. Water Soluble Ruthenium Cyclopentadienyl and Aminocyclopentadienyl PTA Complexes as Catalysts for Selective Hydrogenation of α,β-Unsaturated Substrates (PTA = 1,3,5-Triaza-7-Phosphaadamantane). J. Mol. Catal. A: Chem. 2004, 224 (1–2), 61–70.
(9) Campos-Malpartida, T.; Fekete, M.; Joó, F.; Kathó, Á.; Romerosa, A.; Saoud, M.; Wojtków, W. Redox Isomerisation of Allylic Alcohols Catalysed by Water-Soluble Ruthenium Complexes in Aqueous Systems. J. Organomet. Chem. 2008, 693 (3), 468–474.
(10) González, B.; Lorenzo-Luis, P.; Serrano-Ruiz, M.; Papp, É.; Fekete, M.; Csépke, K.; Osz, K.; Kathó, Á.; Joó, F.; Romerosa, A. Catalysis of Redox Isomerisation of Allylic Alcohols by [RuClCp(DmoPTA)(PPh3)](OSO2CF3)2 and [RuClCp(MPTA)2(OH2-KO)](OSO2CF33(H2O)/CH1H10CO)S. Unusual Influence of the PF and Interaction of Phosphate with Catalyst on the Reaction Rate. J. Mol. Catal. A: Chem. 2010, 326 (1–2), 15–20.
(11) Serrano-Ruiz, M.; Lidrissi, C.; Mañas, S.; Peruzzini, M.; Romerosa, A. Synthesis, Reactivity and Catalytic Properties of the Allenyldiene [Ru(C = C=CH2)Cp(PTA)(PPh3)](CF3SO3) (PTA = 1,3,5-Triaza-7-Phosphaadamantane). J. Organomet. Chem. 2014, 751, 654–661.
(12) Mena-Cruz, A.; Serrano-Ruiz, M.; Lorenzo-Luis, P.; Romerosa, A.; Kathó, Á.; Joó, F.; Aguilera-Sáez, L. M. Evaluation of Catalytic Activity of [RuClCp(DmoPTA)(PPh3)](OSO2CF3) in the Isomerisation of Allylic Alcohols in Water (DmoPTA = 3,7-Dimethyl-1,3,7-Triaza-5-Phosphabicyclo[3.3.1]Nonane). J. Organomet. Chem. 2016, 474, 291–299.
(13) Servin, P.; Laurent, R.; Tristany, M.; Romerosa, A.; Peruzzini, M.; Garcia-Maroto, F.; Majoral, J. P.; Caminade, A. M. D. Dual Properties of Water-Soluble Ru-PTA Complexes of Dendrimers: Catalysis and Interaction with DNA. Inorg. Chim. Acta 2018, 470, 106–112.
(14) Scalambra, F.; Lorenzo-Luis, P.; de los Ríos, I.; Romerosa, A. New Findings in Metal Complexes with Antiproliferative Activity Containing 1,3,5-Triaza-7-Phosphaadamantane (PTA) and Derivative Ligands. Eur. J. Inorg. Chem. 2019, 2019 (11), 1529–1538.
(15) Murray, B. S.; Babak, M. v.; Hartinger, C. G.; Dyson, P. J. The Development of RAPTA Compounds for the Treatment of Tumors. Coord. Chem. Rev. 2016, 306 (P1), 86–114.
(16) Romerosa, A.; Campos-Malpartida, T.; Lidrissi, C.; Saoud, M.; Serrano-Ruiz, M.; Peruzzini, M.; Garrido-Cárdenas, J. A.; García-Maroto, F. Synthesis, Characterization, and DNA Binding of New Water-Soluble Cyclopentadienyl Ruthenium(II) Complexes Incorporating Phosphines. Inorg. Chem. 2006, 45 (3), 1289–1298.
(17) Romerosa, A.; Saoud, M.; Campos-Malpartida, T.; Lidrissi, C.; Serrano-Ruiz, M.; Peruzzini, M.; Garrido, J. A.; García-Maroto, F. DNA Interactions Mediated by Cyclopentadienidouruthenium(II) Complexes Containing Water-Soluble Phosphines. *Eur. J. Inorg. Chem.* 2007, 2007, 2803–2812.

(18) Hajji, L.; Saraíba-Bello, C.; Romerosa, A.; Segovia-Torrente, G.; Serrano-Ruiz, M.; Bergamini, P.; Canella, A. Water-Soluble Cp Ruthenium Complex Containing 1,3,5-Triaza-7-Phosphaadamantane and 8-Thiotheophylline Derivatives: Synthesis, Characterization, and Antiproliferative Activity. *Inorg. Chem.* 2011, 50 (3), 873–882.

(19) Rios-Luci, C.; León, L. G.; Mena-Cruz, A.; Pérez-Roth, E.; Lorenzo-Luis, P.; Romerosa, A.; Padron, J. M. Antiproliferative Activity of DmoPTA-Ru(II) Complexes against Human Solid Tumor Cells. *Bioorg. Med. Chem. Lett.* 2011, 21 (15), 4568–4571.

(20) Allardछया, C. S.; Dyson, P. J.; Ellis, D. J.; Heath, S. L. [Ru(H6-p-Cymene)Cl2(PTA)] (PTA = 1,3,5-Triaza-7-Phosphatricyclcoc-[3.3.1]-Decane): A Water Soluble Compound That Exhibits PH Dependent DNA Binding Providing Selectivity for Diseased Cells. *Chem. Commun.* 2001, 15, 1396–1397.

(21) Vock, C. A.; Renfrew, A. K.; Scopelliti, R.; Jullerat-Janneret, L.; Dyson, P. J. Influence of the Diketonato Ligand on the Cytotoxicities of [Ru(H6-p-Cymene)-(R2acac)(PTA)]+ Complexes (PTA = 1,3,5-Triaza-7-Phosphaadamantane). *Eur. J. Inorg. Chem.* 2008, (10), 1661–1671.

(22) Chatterjee, S.; Kundu, S.; Bhattacharyya, A.; Hartinger, C. G.; Dyson, P. J. The Ruthenium(II)-Arene Compound RAPTA-C Induces Apoptosis in EAC Cells through Mitochondrial and P53-JNK Pathways. *Journal of Biological Inorganic Chemistry* 2018, 23 (7), 1149–1155.

(23) Sclaro; C.; Hartinger, C. G.; Allardछया, C. S.; Keppler, B. K.; Dyson, P. J. Hydrolysis Study of the Biofunctional Antitumour Compound RAPTA-C, [Ru(H6-p-Cymene)Cl2(PTA)]. *Inorganic Biochemistry* 2008, 102 (9), 1743–1748.

(24) Ang, W. H.; Casini, A.; Sava, G.; Dyson, P. J. Organometallic Ruthenium-Based Antitumor Compounds with Novel Modes of Action. *J. Organomet. Chem.* 2001, 696, 989–998.

(25) Süss-Fink, G. Arene Ruthenium Complexes as Anticancer Agents. *Dalton Transactions* 2010, 39 (7), 1673–1688.

(26) Vergara, E.; Cerrada, E.; Casini, A.; Zava, O.; Laguna, M.; Dyson, P. J. Antiproliferative Activity of Gold(I) Alkyne Complexes Containing Water-Soluble Phosphine Ligands. *Organometallics* 2010, 29 (11), 2596–2603.

(27) Scalambra, F.; Serrano-Ruiz, M.; Nahim-Granados, S.; Romerosa, A. Ruthenium Complex Containing 2,2′-Bipyridine and 1,3,5-Triaza-7-Phosphaadamantane. *Eur. J. Inorg. Chem.* 2016, 2016 (10), 1528–1540.

(28) Scalambra, F.; Serrano-Ruiz, M.; Romerosa, A. First Water-Soluble Backbone Ru-Ru-Ni Heterometal Organometallic Polymer. *Macromol. Rapid Commun.* 2015, 36 (7), 689–693.

(29) Scalambra, F.; Serrano-Ruiz, M.; Romerosa, A. Water Driven Formation of Channels: Unusual Solid-State Structural Transformation of a Heterometallic Polymer. *Dalton Transactions* 2018, 47 (10), 3588–3595.

(30) Sierra-Martín, B.; Serrano-Ruiz, M.; García-Sakai, V.; Scalambra, F.; Romerosa, A.; Fernandez-Barbero, A. Self-Organization and Swelling of Ruthenium-Metal Coordination Polymers with PTA (Metal = Ag, Au, Co). *Polymers* 2018, Vol. 10, Page 528 2018, 10 (5), 528.

(31) Sierra-Martín, B.; Serrano-Ruiz, M.; Scalambra, F.; Fernandez-Barbero, A.; Romerosa, A. Novel Ruthenium-Silver PTA-Based Polymers and Their Behavior in Water. *Polymers* 2019, 11, 1249.

(32) Scalambra, F.; Rudić, S.; Romerosa, A. Molecular Insights into Bulk and Porous κ2 P,N-PNTA Metal-Organic Polymers by Simultaneous Raman Spectroscopy and Inelastic Neutron Scattering. *Eur. J. Inorg. Chem.* 2019, 2019 (8), 1155–1161.

(33) Scalambra, F.; Sierra-Martín, B.; Serrano-Ruiz, M.; Fernandez-Barbero, A.; Romerosa, A. First Exfoliated Ru-Ru-Au Organometallic Polymer with Layered Structure. *Chem. Commun.* 2020, 56 (66), 9441–9444.
Phosphabicyclo[3.3.1]Nonane. Inorg. Chem. 2016, 55 (16), 7820–7822.

(49) Mendoza, Z.; Lorenzo-Luis, P.; Scalambra, F.; Padrón, J. M.; Romerosa, A. One Step Up in Antiproliferative Activity: The Ru-N Complex [RuCp(PPh3)2-µ-μ-DimetaPTA-l:K-2x2N,N'-ZnCl2]- (CF3SO3). Eur. J. Inorg. Chem. 2018, 2018 (43), 4684–4688.

(50) Scalambra, F.; Serrano-Ruiz, M.; Gudat, D.; Romerosa, A. Amorphization of a Ru-Ru-Cd-Coordination Polymer at Low Pressure. ChemSelect 2016, 1 (5), 901–905.

(51) Mohr, F.; Falvello, L. R.; Laguna, M. A Silver(I) Coordination Polymer Containing Tridentate N- and P-Coordinating 1,3,5-Triaza-Phosphaadamantane (PTA) Ligands. Eur. J. Inorg. Chem. 2006, 2006 (16), 3152–3154.

(52) Frost, B. J.; Bautista, C. M.; Huang, R.; Shearer, J. Manganese Complexes of 1,3,5-Triaza-7-Phosphaadamantane (PTA): The First Nitrogen-Bound Transition-Metal Complex of PTA. Inorg. Chem. 2006, 45 (9), 3481–3483.

(53) Jaros, S. W.; Guedes Da Silva, M. F. C.; Kôl, J.; Conceição Oliveira, M.; Smoleński, P.; Pombeiro, A. J. L.; Kirillov, A. M. Bioactive Silver-Organic Networks Assembled from 1,3,5-Triaza-7-Phosphaadamantane and Flexible Cyclohexanecarboxylate Blocks. Inorg. Chem. 2016, 55 (4), 1486–1496.

(54) Armstrong, D.; Kirk, S. M.; Murphy, C.; Guerriero, A.; Peruzzi, M.; Consolvi, L.; Phillips, A. D. Water-Soluble Silver(I) Complexes Featuring the Hemilabile 3,7-Dimethyl-1,3,5-Triaza-7-Phosphaadamantane (PTA) (28). J. Org. Chem. 2016, 81 (21), 10653–10657.

(55) Pelmenschikov, V.; Gonnelli, L.; Felli, I. C.; Kaupp, M.; Emsley, L.; Scalambra, F.; Romerosa, A. Study of the Interaction of Water with兜(μ-CN)2Ru-H2 RuCp(PPh3)2, and of the Hybrid Organic Inorganic Complex with 1,3,5-Triaza-7-Phosphaadamantane (PTA), [ZnCl2-(PTA)2], and of the Hybrid Organic-Inorganic Salts of N-Methyl-1,3,5-Triaza-7-Phosphaadamantane with Tetralobalocizine [PTA=Me]-[Zn2l2 × 2] (X = I, Cl). Eur. J. Inorg. Chem. 2009, 2009 (9), 1181–1186.

(56) Niedzielska, D.; Pawlak, T.; Wojtczak, A.; Pazderski, L.; Szyk, E. Structural and 1H, 13C, 15N NMR Spectroscopic Studies of Pd(II) Chloride Organometallcs with 2-Phenylpyridine and Ammonia, Pyridine or Its Methyl Derivatives. Polyhedron 2015, 92, 41–51.

(57) Ross, A.; Choi, J. J.; Hunter, T. M.; Pannecoque, C.; Moggach, S. A.; Parsons, S.; de Clercq, E.; Sadler, P. J. Zinc(I) Complexes of Constrained Antiviral Macrocycles. Dalton Transactions 2012, 41 (21), 6408–6418.

(58) Ruhayel, R. A.; Zgani, I.; Berners-Price, S. J.; Farrell, N. P. Solution Studies of Dinuclear Polymanganese-Linked Platinum-Based Antitumour Complexes. Dalton Transactions 2011, 40 (16), 4147–4154.

(59) Davies, M. S.; Hall, M. D.; Berners-Price, S. J.; Hambley, T. W. [1H, 15N] Heteronuclear Single Quantum Coherence NMR Study of the Mechanism of Aquation of Platinum(IV) Ammine Complexes. Inorg. Chem. 2008, 47 (17), 7673–7680.

(60) Bruch, Q. J.; Lindley, B. M.; Askevold, B.; Schneider, S.; Miller, A. J. M. A Ruthenium Hydrid Dinitrogen Core Conserved across Multielectron/Multiproton Changes to the Pincer Ligand Backbone. Inorg. Chem. 2018, 57 (4), 1964–1975.

(61) Paprocka, R.; Modzelewska-Banachiewicz, B.; Pazderski, L.; Mazur, L.; Kutkowska, J.; Niedzielska, D.; Psurski, M.; Wietrzyk, J.; Szczechowski, J. Synthesis, Characterization, and Antimicrobial Activity. Inorg. Chem. 2018, 57 (11), 6309–6323.

(62) Pazderski, L. 15N NMR Coordination Shifts in Transition Metal Complexes and Organometallics with Heterocycles Containing Nitrogen—Update for 2012–20. Annu. Rep. NMR Spectros. 2020, 101, 151–284.

(63) Bertarelli, A.; Benda, L.; Sanders, K. J.; Pell, A. J.; Knight, M. J.; Pelmenschikov, V.; Gonnelli, L.; Felli, I. C.; Kaupp, M.; Emsley, L.; Pierattelli, R.; Pintacuda, G. Picrometer Structure of the Coordination Sphere in the Metal-Binding Site in a Metalloprotein by NMR. J. Am. Chem. Soc. 2020, 142 (39), 16757–16765.

(64) Kock, M.; Junker, J.; Lindel, T. Impact of the 1H,15N-HMB-Experiment on the Constitutional Analysis of Alkaldoids. Org. Lett. 1999, 1 (13), 2041–2044.

(65) Fukushima, E. Advanced NMR Approaches for a Detailed Structure Analysis of Natural Products. Biosci., Biotechnol., Biochem. 2006, 70, 1803–1812.

(66) Pérez-Trujillo, M.; Nolis, P.; Parella, T. CN-HMBC: A Powerful NMR Technique for the Simultaneous Detection of Long-Range 1H,13C and 1H,15N Connectivities. Org. Lett. 2007, 9 (1), 29–32.

(67) Kang, U.; Carleen, K. L.; Wang, D.; Kim, C. K.; Thomas, C. L.; Woldemichael, G. M.; Gudat, D.; Schubert, W.; Schirru, M.; Khan, J.; Castello-Branco, C.; Sheer, E. C.; Wang, X.; Regaldo, E. L.; Gustafson, K. R.; Denigris and Dactylypyrroles, Arylpyrrole Alkaloids from a Dactylia Sp. Marine Sponge. J. Nat. Prod. 2020, 83 (11), 3464–3470.

(68) Tsuichi, S.; Sakai, K.; Iwano, K.; Nakane, Y.; Tsuchiya, K.; Akutagawa, T. Color Changes of a Full-Color Emisive ESIPT Fluorophore in Response to Recognition of Certain Acdins and Their Conjugate Base Anions. Chem. - Eur. J. 2018, 24 (22), 5868–5875.

(69) Afonin, A. V.; Vashchenko, A. V.; Albanov, A. I.; Nosyreva, V. V.; Mal’kina, A. G.; Trofimov, B. A. Study of Spontaneous E/Z Isomerization of Bis[(Z)-Cyamethylenedi-]Diazapentacyclodienecarboxylates by 1H, 13C, and 15N NMR Spectroscopy, X-Ray, and Quantum Chemical Calculation Data. Magn. Reson. Chem. 2017, 55 (6), 563–569.

(70) Ho, E. N. M.; Lin, Z.; Wang, W.-T. Ruthenium-cobalt mixed-metal nitrido and nitrene carbonyl clusters: Structure, reactivity, and 15N NMR spectroscopy. Eur. J. Inorg. Chem. 2001, 2001, 1321–1338.

(71) Sandoval, C. A.; Yamaguchi, Y.; Okhuma, T.; Kato, K.; Noyori, R. Solution Structures and Behavior of Trans-Ru(H)(H-BH2)4 (Binap)(1,2-Diamine) Complexes. Magn. Reson. Chem. 2006, 44 (1), 66–75.

https://doi.org/10.1021/acs.inorgchem.1c03831
tane) by Neutron and X-Ray Diffraction in Solution. Chem. Commun. 2014, 50 (78), 11587−11590.

(80) Frost, B. J.; Mebi, C. A. Aqueous Organometallic Chemistry: Synthesis, Structure, and Reactivity of the Water-Soluble Metal Hydride CpRu(PTA)2H. Organometallics 2004, 23 (22), 5317−5323.

(81) Serrano-Ruiz, M.; Lorenzo-Luis, P.; Romerosa, A. Easy Synthesis and Water Solubility of Ruthenium Complexes Containing PPh3, MTPPMS, PTA and MPTA, (MTPPMS = Meta-Triphenylphosphine Monosulfonate, PTA = 1,3,5-Triaza-7-Phosphaadamantane, MPTA = N-Methyl-1,3,5-Triaza-7-Phosphaadamantane). Inorg. Chem. Acta 2017, 455, 528−534.

(82) Girotti, R.; Romerosa, A.; Mañas, S.; Serrano-Ruiz, M.; Perutz, R. N. Visible-Light Photoisomerization and Photoaquation of Trans-[Ru(1,3,7-Triaza-5-Phosphabicyclo[3.3.1]Nonane)]2+ in Organic Solvent and Water. Inorg. Chem. 2009, 48 (8), 3692−3698.

(83) Kovács, J.; Jóó, F.; Bényei, A. C.; Laurenczy, G. Reactions of [Ru(H2O)6]2+ with Water-Soluble Tertiary Phosphines. Dalton Transactions 2004, 4 (15), 2336−2340.

(84) Maeda, M.; Ito, T.; Hori, M.; Johansson, G. The Structure of Zinc Chloride Complexes in Aqueous Solution. Zeitschrift fur Naturforschung - Section A Journal of Physical Sciences 1996, 51 (1−2), 63−70.

(85) Ninmermark, A.; Öhrström, L.; Reedijk, J. Metal-Ligand Bond Lengths and Strengths: Are They Correlated? A Detailed CSD Analysis. Z. Kristallogr. 2013, 228 (7), 311−317.

(86) Serrano-Ruiz, M.; Aguilara-Sáez, L. M.; Lorenzo-Luis, P.; Padrón, J. M.; Romerosa, A. Synthesis and Antiproliferative Activity of the Heterobimetallic Complexes [RuClCp(PPh3)-μ-DMoPTA]1P2=2N′N=MC12 (M = Co, Ni, Zn; DmoPTA = 3,7-Dimethyl-1,3,7-Triaza-5-Phosphacyclo[3,3.1]Nonane). Dalton Transactions 2013, 42 (31), 11212−11219.

(87) Serrano-Ruiz, M.; Lorenzo-Luis, P.; Romerosa, A.; Mena-Cruz, A. Catalytic Isomerization of Allylic Alcohols in Water by [RuClCp(PPh3)-μ-DMoPTA]1P2=2N′N=MC12 (M = Co, Ni, Zn; DmoPTA = 3,7-Dimethyl-1,3,7-Triaza-5-Phosphacyclo[3,3.1]Nonane). Inorganic Chemistry 2014, 53 (6), 433−441.

(88) Sapunov, V. N.; Mereriter, K.; Schmid, R.; Kirchner, K. Structure and Bonding in a Series of Cyano Complexes: RuCp(PPh3)2CN, [RuCp2(PPh3)2(CNH)CF3SO3] and H-Bridged (Ru2(Cp2)2(PPh3)4CNHNC)CF3SO3. J. Organomet. Chem. 1997, 530 (1−2), 105−115.

(89) Serrano-Ruiz, M.; Lorenzo-Luis, P.; Passarelli, V.; Romerosa, A.; Serrano-Ruiz, M. Comparative Study of [RuClCp(HdmoPTA-KP)-PPPh3][CF3SO3] and the Heterobimetallic Complexes [RuClCp(PPh3)-μ-DMoPTA]1P2=2N′N=MC12 = M = Co, Ni, Zn; DmoPTA = 3,7-Dimethyl-1,3,7-Triaza-5-Phosphaadamantane. Dalton Transactions 2011, 40 (13), 3237−3244.

(90) Tolman, C. A. Phosphorus Ligand Exchange Equilibria on Zerovalent Nickel. A Dominant Role for Steric Effects. J. Am. Chem. Soc. 1970, 92 (10), 2956−2965.

(91) Tolman, C. A.; Seidel, W. C.; Gossler, L. W. Formation of Three-Coordinate Nickel(0) Complexes by Phosphorus Ligand Dissociation from NiL2. J. Am. Chem. Soc. 1974, 96, 53−60.

(92) Tolman, C. A. Steric Effects of Phosphorus Ligands in Organometallic Chemistry and Homogeneous Catalysis. Chem. Rev. 1977, 77 (3), 313−348.

(93) Mena-Cruz, A.; Lorenzo-Luis, P.; Romerosa, A.; Serrano-Ruiz, M. Water-Soluble 3,7-Dimethyl-1,3,7-Triaza-5-Phosphaadamantane as a Polydentate Ligand: Synthesis of [RuClCp(PPh3)-μ-DMoPTA-1K2K2N′-NC(Ph)-K2O-O-2′]2+. H2O. Inorg. Chem. 2008, 47, 2246−2248.

(94) Duthaler, R. O.; Roberts, J. D. Steric and Electronic Effects on 15N Chemical Shifts of Piperidine and Decahydroquinoline Hydrochlorides. J. Am. Chem. Soc. 1978, 100 (12), 3882−3889.