Investigating the reactivity of neutral water-soluble Ru(II)–PTA carbonyls towards the model imine ligands pyridine and 2,2′-bipyridine†

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As a continuation of our strategy for preparing new Ru(II) precursors to be exploited as building blocks in the construction of metal-mediated supramolecular assemblies with improved solubility in water, here we describe the reactivity of selected neutral Ru(II)–PTA carbonyls (PTA = 1,3,5-triazao-7-phosphaadamantane) towards the model imine ligands pyridine (py) and 2,2′-bipyridine (bpy) and the preparation and characterization of several neutral and cationic water-soluble derivatives: trans,trans,trans-[RuCl2(CO)(py)(PTA)]2 (7), cis,cis,trans-[RuCl2(CO)2(py)(PTA)] (9), cis,trans-[Ru(bpy)Cl(CO)(PTA)2]Cl (10), mer-[Ru(bpy)Cl2(CO)(PTA)2]Cl (12), cis,trans-[Ru(bpy)(CO)2Cl2(PTA)Cl] (13), cis,trans-[Ru(bpy)(CO)3(PTA)2]NO3 2H2O (14NO3). In addition, we found that light-induced isomerization in some bpy compounds could be induced. The following species, either side-products isolated in low yield or compounds obtained exclusively in solution, were also unambiguously identified: cis,cis,trans-[RuCl2(CO)2(py)(PTA)2] (8), trans-[RuCl2(bpy)(CO)(PTA)] (11), cis,cis-[Ru(bpy)Cl2(CO)(PTA)2]Cl (15) and cis,cis-[Ru(bpy)(CO)2Cl2(PTA)Cl] (16). The X-ray structures of 7, 11–H2O, and 12–7H2O are also reported. All compounds are new and – with few exceptions – show a good solubility in water.

Introduction

The cage-like monodentate phosphane 1,3,5-triazao-7-phosphaadamantane (PTA, Fig. 1)† is an amphiphilic, air-stable, neutral ligand that – besides dissolving in several organic solvents – is characterized by a high solubility in water (ca. 235 g L⁻¹) by virtue of H-bonding to the tertiary amine nitrogens. The coordination chemistry of PTA has been thoroughly addressed by Peruzzini and co-workers in a series of review papers.² PTA typically makes strong bonds with most transition metal ions through the free P atom (PTA-xP). P-bound PTA has moderate steric demand (cone angle 103°), good σ- and π-bonding abilities and, above all, it typically imparts excellent water solubility to its complexes. For this reason PTA metal compounds have been investigated as potential anticancer drugs,¹,⁷ and as homogeneous catalysts in aqueous solution or in biphasic aqueous–organic conditions.²,⁹−¹⁰

In addition, PTA-xP can bind also to other metal ions through the three hard N atoms, thus acting as a bridging ligand,²,¹¹ and undergo N-protonation at relatively mild pH (in Ru(II) complexes PTA-xP has a pKₐ value of ca. 3),¹²,¹³ thus altering the charge and solubility of its complexes.

In recent years we have actively investigated the chemistry of Ru(II)–PTA compounds, mainly with the aim of obtaining new precursors to be exploited as building blocks in the construction of metal-mediated conjugates and supramolecular assemblies with improved solubility in water. Ideally, such water-soluble fragments might contribute to the solubilization in aqueous media of neutral assemblies containing hydrophobic linkers (e.g. synthetic porphyrins). In particular, we focused on Ru–PTA–dmso and Ru–PTA–CO compounds, describing several new derivatives and finding systematic trends.¹⁴,¹⁵ Here we

![Fig. 1 Schematic structures of the chelating diimine linkers 4'-methyl-2,2'-bipyridine-4-carboxylic acid (bpyAc) and 2-(2'-pyridyl)pyrimidine-4-carboxylic acid (cppH) and 1,3,5-triazao-7-phosphaadamantane (PTA).](image-url)
report an explorative investigation on the reactivity of a series of Ru–PTA carbonyls towards the imine ligands pyridine (py) and 2,2′-bipyridine (bpy), used as models for monodentate pyridyl-linkers (e.g. 4,4′-bpy or pyridylporphyrins) and for chelating diimine linkers, such as 4,4′-methyl-2,2′-bipyridine-4-carboxylic acid (bpyAc) and 2-(2′-pyridyl)pyrimidine-4-carboxylic acid (cppH) (Fig. 1).6

In particular we investigated the six neutral and water-soluble Ru(II)–PTA–CO precursors shown in Fig. 2 that have at least one or two potentially labile ligands, i.e. H2O, dmso-S, Cl.15,17

We describe here the preparation and characterization of a series of new derivatives. The compounds trans,trans-[RuCl2(CO)(py)(PTA)2](7), cis,cis-trans-[RuCl2(CO)2(py)(PTA)] (9), cis,trans-[Ru(bpy)Cl(CO)(PTA)2]Cl (10), mer-[Ru(bpy)(CO)(PTA)]Cl2 (11), cis,trans-[Ru(bpy)(CO)2Cl(PTA)]Cl (13), cis,trans-[Ru(bpy)2(CO)2(PTA)]Cl (14), cis,trans-[RuCl2(CO)(OH2)(PTA)2](15), cis,cis-trans-[RuCl2(CO)(dmso-S)(PTA)] (2) with a slight excess of pyridine in water afforded mixtures of products, comprising 7, 8 (see below) and other unidentified minor species with coordinated py. However, when the reaction was performed in chloroform under microwave conditions, the isolated products were mixtures of cis and trans isomers, respectively. 

Finally, it is interesting to note that water-soluble Ru–PTA–CO complexes and their derivatives are potentially of interest as homogeneous catalysts in aqueous medium or in biphasic systems for reactions that involve CO or CO2,2,4,9,10,11,13,18–24 and as controlled CO-releasing and photo-releasing systems (CORMs and photolCORMs) for medicinal application.25–35

Results and discussion

Reactions with pyridine (py)

To the best of our knowledge, there are very few examples of Ru(II)–PTA coordination compounds with monodentate pyridine or azole ligands, i.e. not included in polydentate ligands.16,18–40 Only recently the group of Romerosa described a series of neutral Ru(II)–PTA half-sandwich compounds that bear a natural purine bound through the N7 or N9 of the imidazolic ring.41

When trans,trans-[RuCl2(CO)(OH2)(PTA)] (1) was treated with a slight excess of pyridine in water at room temperature, the yellow complex trans,trans-[RuCl2(CO)(py)(PTA)] (7) was selectively obtained upon evaporation of the solvent (Scheme 1) and fully characterized by ESI-MS, NMR, and IR spectroscopies (ESI†).

The geometry of complex 7 was confirmed by single crystal X-ray diffraction analysis (Fig. 3). In the structure, the trans CO/py ligands were found to be disordered by exchanging their mutual positions, with a major population of 74.7%.
assisted conditions (100 °C) it afforded a mixture of 7 (see above) and of a minor component (ca. 20%) that was identified as the stereoisomer cis,cis,trans-[RuCl₂(CO)(dmso-S)(PTA)₂] [8] (that formally derives from 2 upon replacement of the dmso without geometrical rearrangement) (Scheme 2). In fact, the main NMR resonances of 8 (i.e. the py signals in the proton spectrum and the singlet for the two PTAs in the phosphorous spectrum) are only slightly shifted compared to those of 7, and integration confirmed the stoichiometry (ESI†). The IR spectrum of the mixture shows a broad carbonyl stretching band at 1977 cm⁻¹.

As previously observed by us, in aqueous solution the dinuclear species [RuCl₂(μ-Cl)(CO)₂(PTA)₂] (5) behaves as a monomer with a formally vacant position trans to PTA after the selective and rapid cleavage of the chloride bridges leading to the formation of the neutral aqua species cis,cis,trans-[RuCl₂(CO)₂(OH₂)(PTA)] [15]. Consistently, treatment of 5 with a slight excess of py in D₂O at ambient temperature afforded crystals of cis,cis,trans-[RuCl₂(CO)₂(py)(PTA)] (9). Even though the crystals were of low quality, the X-ray structure (ESI†) unambiguously confirmed the geometry of the complex, with the pyridine trans to PTA (first example in Ru(n) species), i.e. in the place of the cleaved bridging chloride (Scheme 3).

The ESI-MS and NMR spectra of 9 in CDCl₃ (ESI†; the solubility of this species was much higher in chloroform than in water) are fully consistent with this formulation. The IR spectrum presents two bands (2058 and 1994 cm⁻¹) at frequencies very similar to those found in the precursor 5,¹⁵ in agreement with the presence of two adjacent CO ligands that, in both compounds, are trans to chlorides. The ³¹P{¹H} NMR spectrum shows a singlet at −28.7 ppm.

Reactions with 2,2′-bipyridine (bpy)

Examples of neutral and cationic Ru(n)–PTA complexes, containing one (cis,cis- and cis,trans-[Ru(bpy)Cl₂(PTA)₂], fac- and mer-[Ru(bpy)Cl₂(PTA)₂][PF₆]₂) or two (cis- and trans-[Ru(bpy)₂(PTA)₂][PF₆]₂, and cis-[Ru(bpy)₂(OH₂)(PTA)][Cl₂(SO₄)₂] bpy ligands have been described by us and other groups.⁷,¹⁴,⁴₂ They were obtained either by treatment of Ru–PTA precursors with bpy, or through a complementary approach (i.e. by reaction of Ru–bpy complexes with PTA).

In this work, we found that trans,trans-[RuCl₂(CO)(OH₂)(PTA)₂] (1) reacts with bpy in refluxing water by replacing the water molecule and one of the adjacent chlorides affording the orange cationic complex cis,trans-[Ru(bpy)Cl₂(OH₂)(PTA)]Cl₂ (10) (Scheme 4).

Compound 10 was fully characterized by NMR spectroscopy and mass spectrometry. The ′H NMR spectrum in D₂O shows eight equally intense resonances in the aromatic region, consistent with the asymmetric environment of the bpy ligand (ESI†). In agreement with previous findings,⁴⁰,⁴¹ the highest frequency doublet was assigned to H₆, i.e. the proton with a partial positive charge that points towards the adjacent chloride (Scheme 4). The ³¹P{¹H} NMR spectrum presents a singlet in the region of mutually trans PTAs (δ = −50.6 ppm). The CO stretching frequency in the IR spectrum (1984 cm⁻¹) is shifted to higher wavenumbers compared to the precursor 1 (1941 cm⁻¹), in agreement with a lower π back-bonding contribution from ruthenium because of the positive charge. With time, a very small amount of colorless crystals grew spontaneously from the D₂O NMR solution of the raw product.⁴⁴ They were found to belong to the unexpected neutral Ru(n) complex trans-[RuCl₂(bpy)(CO)(PTA)] (11), whose formation implies replacement of one PTA. The full spectroscopic

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**Scheme 2** Reactivity of cis,cis,trans-[RuCl₂(CO)(dmso-S)(PTA)₂] (2) with bpy in chloroform under MW assisted conditions (100 °C) affording a mixture of the stereoisomers trans,trans,trans-[RuCl₂(CO)(py)(PTA)₂] (7) and cis,cis,trans-[RuCl₂(CO)(py)(PTA)₂] (8).

**Scheme 3** Reactivity of the dinuclear species [RuCl₂(μ-Cl)(CO)₂(PTA)₂] (5) with pyridine in water affording cis,cis,trans-[RuCl₂(CO)₂(py)(PTA)] (9).

**Scheme 4** Reactivity of trans,trans,trans-[RuCl₂(CO)(OH₂)(PTA)₂] (1) and cis,cis,trans-[RuCl₂(CO)(dmso-S)(PTA)₂] (2) with bpy in water affording cis,trans-[Ru(bpy)Cl₂(CO)(PTA)₂]Cl (10).
trans spectrum, were attributed to the two equivalent

\[ \text{[Ru(bpy)(CO)(PTA)₃]Cl}_2 \] 

This was obtained upon recrystallization of the raw product from water/acetone. Coordination distances (Å):

- Ru₁–C₁ = 1.8746(14), Ru₁–N₅₁ = 2.119(1), Ru₁–N₅₂ = 2.139(1), Ru₁–P₂ = 2.3650(4), Ru₁–P₃ = 2.3391(4), Ru₁–P₄ = 2.3631(4).

Fig. 4 X-ray molecular structure (50% probability ellipsoids) of mer-

\[ \text{[Ru(bpy)(CO)(PTA)₃]Cl}_2 \cdot 7\text{H}_2\text{O} \] (12) upon treatment of cis,mer-

\[ \text{[RuCl}_2\text{(CO)(PTA)₃]} \] with bpy in water at reflux.

The reaction of cis,mer-

\[ \text{[RuCl}_2\text{(CO)(PTA)₃]} \] with bpy in refluxing water led to the replacement of both chlorides by bpy, affording the orange dicaticonic complex mer-

\[ \text{[Ru(bpy)(CO)(PTA)₃]} \] (Scheme 5).

Compound 12 was fully characterized by NMR and IR spectroscopy, mass spectrometry, and its single-crystal X-ray structure was also determined (Fig. 4 and ES†). The PTA region of the \(^1\text{H}\) NMR spectrum in D₂O consists of two pairs of signals, in a 1 : 2 ratio. The two low-frequency multiplets (12H each) centered at 4.41 and 3.83 ppm and correlated in the H COSY spectrum, were attributed to the two equivalent trans PTA ligands whose protons fall in the shielding cone of the adjacent bpy. The other two signals (6H each), centered at 4.81 ppm (partially overlapped with the water signal) and 4.65 ppm, respectively, belonged to the PTA trans to N. The \(^1\text{H} \cdots ^{13}\text{C}\) HSQC spectrum established that, in each set, the high-frequency quartet belongs to the NCH₂N protons and the other signal to the NCH₂P protons. The downfield region of the spectrum (eight resonances, three of which overlapping in an unresolved multiplet centered at 8.42 ppm) is consistent with the asymmetric coordination environment of bpy. The aromatic protons were assigned through a 1D NOESY spectrum: saturation of the singlet of the NCH₂P protons of the PTA trans to bpy gave an NOE effect with the multiplet at 8.42 ppm thus implying that it contains the resonance of proton H₆‴, i.e. the one closest to the adjacent PTA. The other bpy resonances were then assigned through an H–H COSY spectrum. The \(^{31}\text{P}\{^1\text{H}\} \) NMR spectrum presents an AX₂ system. The triplet that belongs to the PTA trans to bpy (−49.6 ppm) is upfield shifted of ca. 10 ppm compared to most of the known monocationic and dicaticionic Ru(n) complexes featuring one or two PTAs trans to bpy, i.e. mer-

\[ \text{[Ru(bpy)Cl(PTA)₃]}(\text{PF}_6)^{2-}(30.2 \text{ ppm}), \text{fac-[Ru(bpy)Cl(PTA)₃]}(\text{PF}_6)^{2-}(43.5 \text{ ppm}), \text{cis-[Ru(bpy)₂(PTA)₂]}(\text{Cl}_2)^{2-}(38.8 \text{ ppm}) \] and cis-

\[ \text{[Ru(bpy)₂(PTA)₂]}(\text{H}_2\text{O})][\text{CF}_3\text{SO}_3]_2^{2-}(31.6 \text{ ppm}). \]

The difference might be attributed to the presence of the CO ligand in 12.

The IR spectrum shows a carbonyl stretching band at 1942 cm\(^{-1}\), i.e. at higher wavenumbers than in the precursor (1942 cm\(^{-1}\)), in agreement with the 2+ charge of 12. For comparison, the CO stretching band in the dicaticionic monocarbonyl Ru(n) complex fac-

\[ \text{[Ru(CO)(dmso-S)₃]}(\text{dmso-S})_2[\text{PF}_6]_2 \] falls at 2012 cm\(^{-1}\), suggesting that this parameter is not particularly affected by the nature of the ligands, but rather by the net charge of the complex.

X-ray quality crystals of 12 were obtained upon recrystallization of the raw product from water/acetone (Fig. 4). The coordination distances are in general agreement with the known trans influence of the ligands: thus, the Ru–P bond lengths of the two trans PTA ligands are longer than the Ru–P distance trans to N. Similarly, the Ru–N bond length trans to CO is longer than that trans to P, consistent with the previous finding that CO has a stronger trans influence than PTA.

The reaction of trans-

\[ \text{[RuCl}_2\text{(CO)(PTA)₃]} \] – a stereoisomer of 3 with bpy led to a mixture of compounds (Scheme 6), identified through the \(^{31}\text{P}\{^1\text{H}\} \) NMR spectrum as 10, 11, and mer-

\[ \text{[Ru(bpy)Cl(PTA)₃]} \] (previously described by us as PF₆ salt), in ca. 1 : 7.5 : 3 ratio. This finding suggests that, even though...
NMR spectrum in D2O presents a singlet at 3.62 ppm, and by a singlet at 3.93 ppm, is consistent with the stoichiometry of the complex. No hydroscopic evidence, typical of mutually stretching bands at 2085 and 2034 cm\(^{-1}\), was observed in re-lixing water a trans to CO, one bridging and the other terminal (Scheme 7). In fact, the \(^{31}\)P{\(^1\)H} NMR spectrum in D2O presents a singlet at \(-25.4\) ppm, i.e. in the typical region of PTA trans to Cl. The \(^1\)H NMR spectrum shows in the aromatic region four equally intense signals (2H each), in agreement with bpy coordinated in a symmetrical environment. The integration ratio of bpy and PTA resonances is consistent with the stoichiometry of the complex. No hydrolysis of the chloride was observed in D2O solution (i.e. no new set of proton resonances attributable to [Ru(bpy)\(_2\)(OH)\(_2\)\(\text{Cl}^{-}\)]\(^2+\)) grew with time), most likely because of the positive charge of the complex. The IR spectrum of 13 presents two CO stretching bands at 2085 and 2034 cm\(^{-1}\), in agreement with the presence of two cis carboxyls. For comparison, the CO stretching bands in the cationic dicarbonyl Ru(n) complex cis-fac-[Ru(CO)\(_2\)(dmso)]\(^2+\)([PF\(_6\)]\(_2\)) fall at 2092 and 2030 cm\(^{-1}\).

The reaction between cis,cis-trans-[RuCl\(_2\)(CO)\(_2\)](PTA)\(_2\) and bpy yielded a mixture of 13 with a new product 14 (in ca. 1/2 ratio) (Scheme 8). The new species is characterized by a set of four equally intense bpy signals in the aromatic region of the \(^1\)H NMR spectrum, and by a singlet at \(-50.9\) ppm in the \(^{31}\)P\(^{1\text{H/\text{H}}}\) NMR spectrum, typical of mutually trans PTAs. Based on this spectroscopic evidence, 14 was formulated as the dicaticonic complex with two mutually trans PTAs, cis,trans-[Ru(bpy)(CO)\(_2\)](PTA)\(_2\)Cl\(_2\) (14Cl), derived from 6 upon replacement of both chlorides. To be noted that the formation of 13 from 6 involves isomerization: Cl, that was trans to CO in the precursor, is trans to PTA in 13.

Compound 14 was selectively obtained, as the orange nitrate salt (14NO\(_3\)) when 6 was reacted with bpy in refluxing water after the addition of 2.1 eq. of AgNO\(_3\) (Scheme 9). The \(^1\)H, \(^{31}\)P \(^{1\text{H/H}}\) NMR, and ESI-MS spectra of 14NO\(_3\), are coincident with those of 14Cl (Scheme 8). Consistent with the cis geometry of the CO ligands, the complex has two CO stretching bands (2086 and 2038 cm\(^{-1}\)) in the IR spectrum. Compared with the precursor 6, the CO stretching frequencies of both 13 and 14 are shifted to higher wavenumbers, in accordance with the positive charge of the two products; nevertheless, it is remarkable that in 14 they are very similar to those found in 13, despite the higher positive charge. Compound 14 is the first dicaticonic dicarbonyl Ru(n) compound that we have isolated thus far; the previously prepared dicaticonic species have a single CO (e.g. [Ru(CO)(dmso)]\(_2\)\([\text{PF}_6]\)\(_2\)), whereas the dicarbonyl compounds were monocationic (e.g. 13).

**Light-induced rearrangements in Ru(n)-PTA-bpy carbonyls**

Both Ru(n)-PTA and RuX\(_2\)(CO)\(_n\)P\(_n\)-\(\text{Cl}^{-}\) (\(n = 1–3\)) complexes have shown to be photoreactive.\(^{16,17,24,46–49}\) The group of Romerosa has recently reported a study of the effects of visible light on a series of water-soluble Ru(n) complexes with PTA.\(^{24}\) For this reason we decided to perform a preliminary investigation of the effect of visible light on selected Ru(n)-PTA-bpy carbonyls, that are characterized by the presence of an absorption band in the range of 400–525 nm. In general, D\(_2\)O solutions of the complexes were directly irradiated in the NMR tube and the products were characterized spectroscopically, without being isolated.

We found that 24 h irradiation with blue light (\(\lambda = 470\) nm) of an orange D\(_2\)O solution of cis,trans-[Ru(bpy)Cl(CO)(PTA)]\(_2\)Cl\(_2\) (10) induces its clean and complete transformation to the new cis-isomer cis,cis-[Ru(bpy)Cl(CO)(PTA)]\(_2\)Cl\(_2\) (15) (Scheme 10). In fact, the \(^{31}\)P\(^{1\text{H/H}}\) NMR spectrum of the product (ESI\(^+\)) presents an AX system of two doublets, one in the region of PTA trans to Cl (\(-25.1\) ppm, \(J_{P-P} = 24.7\) Hz) and the second in that of PTA trans to bpy (ca. \(-42.3\) ppm). The PTA region of the \(^1\)H NMR spectrum shows a broad singlet at 3.93 ppm and three partially overlapping AB systems centered respectively at 4.31, 4.58, and 4.71 ppm (4H each), consistent with the non-equivalence of the two PTAs. The two most upfield signals, correlated in the \(^1\)H–\(^1\)H COSY spectrum (ESI\(^+\)), were attributed to the PTA trans to Cl that falls into the shielding cone of the adjacent bpy. As above
for 12, the aromatic protons were assigned through a 1D NOESY spectrum, followed by a 1H–1H COSY spectrum (ESI†). Finally, the IR spectrum of compound 15 shows a single carbonyl stretching band at 1992 cm\(^{-1}\), i.e. a frequency similar to that of the trans-isomer 10 (1984 cm\(^{-1}\)).

A similar light-induced isomerization was observed with cis,trans-[Ru(bpy)(CO)\(_2\)Cl(PTA)]Cl (13) (Scheme 11). In this case the process was slower (and less selective) and complete transformation required the irradiation of an aqueous solution of 13 with blue light for 3 days. The major product of this reaction, 16, shows a singlet in the region of PTA to bpy (ca. 39.6 ppm) in the \(^{31}\)P\(^{1}H\) NMR spectrum, and eight resonances in the aromatic region of the \(^{1}\)H NMR spectrum for an asymmetrically bound bpy (with two multiplets of overlapping resonances). Consistent with these spectroscopic evidence, the new compound 16 was formulated as cis,cis-[Ru(bpy)(CO)\(_2\)Cl(PTA)]Cl. The IR spectrum presents two carbonyl stretching bands at 2006 and 1979 cm\(^{-1}\) in agreement with the presence of two cis CO ligands. Compared to the starting trans isomer 13 (2085 and 2034 cm\(^{-1}\)), the two bands of 16 are shifted to lower wavenumbers, possibly because one CO is trans to the good \(\pi\)-donor Cl.

To our surprise, the \(^{31}\)P\(^{1}H\) NMR spectrum showed that formation of 16 is accompanied by that of 15 (ca. 6/1 ratio), in addition to other uncharacterized minor species (ESI†). Since there is no external source of PTA, the formation of 15 from 13 implies the occurrence of a decarbonylation process followed by disproportionation.

Conversely, compound cis,trans-[Ru(bpy)(CO)\(_2\)Cl(PTA)\(_2\)](NO\(_3\))\(_2\) (14NO\(_3\)) was light-stable. The \(^{31}\)P NMR spectrum of a D\(_2\)O solution of 14NO\(_3\) remained unchanged even after one week of irradiation either with blue or white light.
Table 3  Typical $^{31}$P($^1$H) NMR chemical shift intervals ($\Delta$) and Ru–P distances for PTA bound to octahedral Ru(n) complexes as a function of the nature of the trans ligand

| Ligand trans to PTA | $\Delta$ $^{31}$P($^1$H) ($\delta$ ppm) | $\Delta$ Ru–P distance (Å) | Ref. |<sup>a</sup> |
|---------------------|--------------------------------------|---------------------------|------|---------|
| OH$_2$/OH           | $-5 \pm -16$                         | —                         | 14, 15, 24 and 50 |
| Cl                  | $-14 \pm -30$                        | $2.232 \pm 2.283$         | p.w. and 88, 14 and 15 |
| N(azole)            | $-17 \pm -49$                        | $2.2605 \pm 2.2971$       | 36–40 |
| Br                  | $-24 \pm -27$                        | $2.266 \pm 2.281$         | 51 |
| H                   | $-26.6^c$                            | $2.299 \pm 2.300$         | 48 |
| N(py)$^b$            | $-28.8$                              | —                         | p.w. |
| S$^b$               | $-30 \pm -45$                        | $2.280 \pm 2.318$         | 12, 16b and 43 |
| N(bpy, phen)        | $-30 \pm -50^f$                      | $2.2849 \pm 2.3391^f$     | p.w. and 7, 14 and 42b |
| P(PTA)              | $-42 \pm -60$                        | $2.290 \pm 2.400$         | p.w. and 7, 8b, 15–24, 24, 42, 48, 50 and 52–54 |
| CO                  | $-55 \pm -70$                        | $2.3821 \pm 2.3828$       | 15 |
| C$^b$               | $-68.4$                              | $2.395(1)$                | 55 |

For comparison, the singlet of free PTA falls at $\delta = -98.2$ ppm in $D_2$O and at $-102.3$ ppm in CDCl$_3$.  

<sup>a</sup>  Single hit. 
<sup>b</sup>  From [9]. 
<sup>c</sup>  Concerns bpy complexes exclusively. In the single phen complex, $mer$-[Ru(pHEN)Cl(PTA)$_3$]Cl (two independent cations in the asymmetric unit), the Ru–P distances are slightly shorter, 2.269(3) and 2.279(3) Å, see below.  
<sup>f</sup>  Single hit, from cycloammoniated 2-phenylpyridine. 

Conclusions

We have investigated the reactivity of selected neutral Ru(n)—PTA carbonyls with potentially labile ligands (i.e. H$_2$O, dmso and/or Cl) towards the model imine ligands pyridine (py) and 2,2'-bipyridine (bpy). The results are graphically summarized in Tables 1 and 2 that collect the main products with their respective precursors. To be noted that the only precursor that affords derivatives with a single PTA bound to ruthenium. Whereas the monodentate pyridine replaces exclusively neutral ligands, i.e. H$_2$O or dmso-S, bpy is capable of replacing also the chlorides, thus affording mono- and dicaticionic products. PTA and supporting CO ligands are typically not replaced. Consistent with the expected lability order, the aqua ligand is easily replaced by pyridine at room temperature (e.g. 7), whereas replacement of dmso-S required more forcing conditions (refluxing chloroform or ethanol) that induced partial isomerization. Replacement of chlorides by bpy was typically performed in refluxing water, and was occasionally silver-assisted. Most of the complexes are well soluble in water and alcohols (methanol and ethanol). Exceptions are the neutral carbonyls 9 and 11, both containing a single PTA ligand.

Coordination of bpy is often accompanied by stereochemical changes. We notice that bpy does not like being bound trans to two PTA ligands. In fact, in all the Ru(n)—PTA—bpy complexes described in the literature that feature two or three PTA ligands, the coplanar [Ru(bpy)Cl(PTA)$_2$] fragment is found only in fac-[Ru(bpy)Cl(PTA)$_2$][PF$_6$], that however is a kinetic product that thermally isomerizes to the thermodynamic meridional stereoisomer. We believe that this is due to both steric and electronic factors (π back-bonding competition).

We found that in some bpy compounds light-induced isomerization could be induced. Thus, irradiation with blue light selectively transformed cis,trans-[Ru(bpy)Cl(CO)(PTA)$_2$]Cl (10) into cis,cis-[Ru(bpy)Cl(CO)Cl(PTA)$_2$]Cl (15) (Scheme 10), whereas the isomerization of cis,trans-[Ru(bpy)(CO)Cl]Cl (13) to cis,cis-[Ru(bpy)(CO)Cl(PTA)]Cl (16) was accompanied by formation of 15 (Scheme 11).

We have already observed that it is possible to use $^{31}$P($^1$H) NMR chemical shifts as a diagnostic tool for establishing the geometry of octahedral Ru–PTA complexes. We report here an updated list of the typical $^{31}$P($^1$H) NMR chemical shift intervals ($\Delta$) for PTA bound to Ru(n) as a function of the nature of the trans ligand, that contains the data from the new py and bpy derivatives (Table 3). We observe that when PTA is trans to an imine nitrogen (i.e. py, bpy), the $^{31}$P($^1$H) NMR chemical shift is remarkably affected by the nature of the ligand: when trans to py it falls at $-28$ ppm (we have only one example: complex 9), whereas when trans to bpy it falls in a rather broad range which is shifted to lower frequencies compared to py: $-30 \pm -50$ ppm (but most often between $-30 a -40$ ppm, see below). Pyridine is known to be a weaker field ligand compared to bpy, being both a worse σ-donor and π-acceptor. In addition, the orientation of the pyridyl rings are different: for bpy they are in the plane containing PTA, whereas pyridine is typically canted with respect to such plane, implying a different involvement of their π orbitals. Indeed, in the complex trans-[RuCl$_2$(R,R)-Pr-pybox](PTA) where pyridine is part of a tridentate chelating ligand, and is forced to lay in the equatorial plane that contains the trans PTA, the $^{31}$P chemical shift falls at $-41.5$ ppm, i.e. in the range typical for bpy.  

As already observed by us, Table 3 provides also a trans-influence ranking for the ligands trans to PTA; in fact there is a rough correlation between the Ru–P bond length and the chemical shift of the $^{31}$P($^1$H) NMR resonance: as the Ru–P distance increases, the phosphorus resonance shifts progressively to lower frequencies (i.e. closer to that of free PTA). To this regard we notice that there are only two examples of PTA trans to bpy in which the $^{31}$P chemical shift falls at frequencies lower than $-40$ ppm: fac-[Ru(bpy)Cl(PTA)$_3$][PF$_6$] (−43.5 ppm) and mer-[Ru(bpy)(CO)(PTA)$_3$]Cl$_2$ (12, −49.6 ppm). In both complexes, due to the overall charge and competing ligands, the π-back...
donation to such PTAs is expected to be lower than for the other cases, leading to weaker and longer Ru–P bonds.

**Experimental section**

**Materials**

All chemicals were purchased from Sigma-Aldrich and used as received. Solvents were of reagent grade. The Ru(n)-PTA carbonyls 1–6 were synthesized and purified as previously reported by us.15

**Instrumental methods**

Mono- and bi-dimensional $\{^1\text{H}-^1\text{H COSY}, ^1\text{H}-^1\text{C} \text{ HSQC}\}$ NMR spectra were recorded at room temperature on a Varian 400 or 500 spectrometer ($^1\text{H}: 400$ or 500 MHz, $^{13}\text{C}(^1\text{H}): 100.5$ or 125.7 MHz, $^{31}\text{P}(^1\text{H}): 161$ or 202 MHz). $^1\text{H}$ and $^{13}\text{C}(^1\text{H})$ chemical shifts were referenced to the peak of residual non-deuterated solvent ($\delta = 7.26$ and 77.16 for CDCl$_3$, 2.50 and 39.52 for DMSO-$d_6$) or were measured relative to the internal standard DSS ($\delta = 0.00$) for D$_2$O. Carbon resonances were assigned through the HSQC spectra. $^{31}\text{P}$ chemical shifts were referenced to external 85% H$_3$PO$_4$ at 0.00 ppm. ESI mass spectra were collected in the positive and negative mode on a PerkinElmer API spectrometer at 5600 eV. The UV-vis spectra were obtained on an Agilent Cary 60 spectrophotometer, using 1.0 cm path-length quartz cuvettes (3.0 mL). Solid state infrared spectra were obtained as Nujol mulls between NaCl plates and recorded on a PerkinElmer Fourier-transform IR/Raman 2000 instrument in the transmission mode. Solution IR spectra (in chloroform, ethanol or methanol) in the CO stretching region were recorded between CaF$_2$ windows (0.5 mm spacer). A thermostatted Berghof stainless steel vessel (autoclave), equipped with a 100 mL Teflon liner, was used for the reactions with CO under pressure. A CEM Discover microwave reactor was used for the microwave-assisted reactions performed in 10 mL vessels. Elemental analyses were performed in the Department of Chemistry of the University of Bologna (Italy). A homemade LED apparatus, described in detail elsewhere,26 was used for performing the photochemical reactions in NMR tubes.

**X-ray diffraction**

Data collections were performed at the X-ray diffraction beamline (XRD1) of the Elettra Synchrotron of Trieste (Italy) equipped with a Pilatus 2 M image plate detector.

Collection temperature was 100 K (nitrogen stream supplied through an Oxford Cryostream 700); the wavelength of the monochromatic X-ray beam was 0.700 Å and the diffractograms were obtained with the rotating crystal method. The crystals were dipped in N-paratone and mounted on the goniometer head with a nylon loop. The diffraction data were indexed, integrated and scaled using the XDS code.57 The structures were solved by the dual space algorithm implemented in the SHELXT code.24 Fourier analysis and refinement were performed by the full-matrix least-squares methods based on F2 implemented in SHELXL.29 The Coot program was used for modeling.60 Anisotropic thermal motion was allowed for all non-hydrogen atoms. Hydrogen atoms were placed at calculated positions with isotropic factors $U = 1.2 \times U_{eq}$, $U_{eq}$ being the equivalent isotropic thermal factor of the bonded non hydrogen crystal. Data crystal and details of refinements are in the ESL.†

**Synthesis of the complexes**

All the synthetic procedures with Ru–PTA carbonyls precursors were performed under dimmed light and in light-protected glassware.

$\text{trans,trans,trans-}[\text{RuCl}_2(\text{CO})_2(\text{PTA})_2]$ (7). $\text{trans,trans,trans-}[\text{RuCl}_2(\text{CO})(\text{OH})_2(\text{PTA})_2] \cdot 3\text{H}_2\text{O}$ (1, 30 mg, 0.051 mmol) was dissolved in 3 mL of water obtaining a yellow solution; 1.4 equivalents of pyridine (13.1 µL, 0.07 mmol) were added and the solution was stirred at room temperature for three days. Removal of the water by rotary evaporation afforded a yellow precipitate that was treated with acetone (2 × 2 mL). The resulting yellow powder was collected on a glass filter, washed with acetone and diethyl ether, and dried in vacuo (yield: 19.2 mg, 63%). The solid was pure 7 according to $^1\text{H}$ and $^{31}\text{P}(^1\text{H})$ NMR spectra. Elemental analysis calcd for [C$_{13}$H$_{17}$Cl$_2$N$_4$O$_2$PRu] (MW: 593.0): C 36.43; H 4.93; N 16.52. Found: C 36.53; H 4.89; N 16.59. $^1\text{H}$ NMR (D$_2$O) $\delta$ (ppm): 9.08 (d, 2H, H$_2$, 6), 8.11 (t, 1H, H4), 7.66 (t, 2H, H3, 5), 4.35 (m, 12H, NC$_{12}$H$_{22}$N$_{2}$), 3.90 (br s, 12H, NCH$_2$P). $^{13}\text{C}$ NMR from the HSQC spectrum (D$_2$O), $\delta$ (ppm): 151.0 (C2, 6), 139.6 (C4), 125.8 (C3, 5), 73.1 (NCH$_2$N). $^{31}\text{P}(^1\text{H})$ NMR (D$_2$O), $\delta$ (ppm): −50.0 (s, 2P, mutually trans PTAs). Selected IR absorption (Nujol, cm$^{-1}$): 1946 ($\nu_{CO}$). ESI mass spectrum: 594.3 m/z [M + H]$^+$ (calcd 594.0).

cis,cis,cis-[RuCl$_2$(CO)$_2$(py)(PTA)$_2]$ (9). [RuCl$_2$(μ-Cl)(CO)$_2$(PTA)$_2$] (5, 30 mg, 0.038 mmol) was partially dissolved in 3 mL of water obtaining a colorless solution; 1.2 equivalents of pyridine (16.0 µL, 0.091 mmol) were added and the solution was stirred at room temperature for three days. Removal of the water by rotary evaporation afforded a precipitate that was dissolved in chloroform (a small amount of undissolved solid was removed by filtration over Celite). Removal of the chloroform by rotary evaporation afforded a solid that was pure 9 according to $^1\text{H}$ and $^{31}\text{P}(^1\text{H})$ NMR spectra (yield: 7.3 mg, 55%). X-ray quality crystals of 9 formed spontaneously from a concentrated D$_2$O solution. Elemental analysis calcd for [C$_{23}$H$_{32}$Cl$_2$N$_8$O$_2$PRu] (MW: 463.9): C 32.63; H 3.69; N 12.07. Found: C 32.54; H 3.59; N 11.95. $^1\text{H}$ NMR (CDCl$_3$) $\delta$ (ppm): 8.91 (d, 2H, H2, 6), 7.87 (t, 1H, H4), 7.45 (t, 2H, H3, 5), 4.60 (br s, 6H, NCH$_2$N$_2$), 4.53 (br s, 6H, NCH$_2$P). $^{13}\text{C}$ NMR from the HSQC spectrum (CDCl$_3$), $\delta$ (ppm): 154.2 (C2, 6), 138.8 (C4) 125.8 (C3, 5), 73.1 (NCH$_2$N), 53.5 (NCH$_2$P). $^{31}\text{P}(^1\text{H})$ NMR (CDCl$_3$), $\delta$ (ppm): −28.8 (s, 1P, PTAs trans to py). Selected IR absorption (chloroform solution, cm$^{-1}$): 2058 ($\nu_{CO}$), 1994 ($\nu_{CO}$). ESI mass spectrum: 464.5 m/z [M + H]$^+$ (calcd 464.9).

cis,cis-[Ru(bpy)Cl(μ-Cl)(CO)(PTA)$_2$]Cl (10). cis,cis,cis-[RuCl$_3$(CO)(PTA)$_2$]Cl$_2$·3H$_2$O (1, 20 mg, 0.034 mmol) was dissolved in 5 mL of water. One eq. of bpy (5.3 mg, 0.034 mmol) was added and the mixture was refluxed for 2 h. The yellow solution turned rapidly orange. The solvent was removed by rotary evaporation affording an orange solid. The solid was pure 10, according to $^1\text{H}$ and $^{31}\text{P}(^1\text{H})$ NMR spectra (yield 22.3 mg, 98%). Elemental analysis calcd for [C$_{32}$H$_{32}$Cl$_4$N$_8$OP$_2$Ru] (MW: 670.5): C 41.20; H 3.58; N 16.65; Cl 23.65; P 3.60; Ru 14.37.
4.81; N 16.71. Found: C 41.12; H 4.86; N 16.77. 1H-NMR (D2O) δ (ppm): 9.27 (d, 1H, H6), 8.93 (d, 1H, H6*), 8.66 (d, 1H, H3), 8.55 (d, 1H, H3*), 8.42 (t, 1H, H4), 8.23 (t, 1H, H4*), 7.96 (t, 1H, H5), 7.60 (d, 1H, H5*), 4.41, 4.31 (ABq, 12H, NCH3), 3.82, 3.76 (ABq, 12H, NCH3). 13C NMR from the HSQC spectrum (D2O), δ (ppm): 155.7 (C6*), 149.0 (C6), 141.0 (C4), 139.4 (C4*), 128.1 (C5), 127.9 (C5), 125.0 (C3*), 124.8 (C3), 70.3 (NCH3), 46.3 (NCH3). 31P{1H} NMR (D2O), δ (ppm): −50.6 (s, 2P, mutually trans PTAs). Selected IR absorption (ethanol solution, cm−1): 1984 (ν(CO)). ESI mass spectrum: 635.6 m/z [M' − CO] (calcd 635.9). UV-vis (H2O): λmax = 401 nm.

Compound 10 was also obtained, in lower yield, by treatment of an aqueous solution of cis,cis-trans-[RuCl2(CO)(dmso-S)](PTA)2] (2) (40.0 mg, 0.067 mmol) with bpy (10.5 mg, 0.067 mmol) for 16 h at reflux or in a microwave reactor at 150 °C for 30 min. The solvent was removed by rotary evaporation affording an orange solid that was crushed with acetone (2 × 2 mL), then washed with diethyl ether, and dried in vacuo (yield 25.6 mg, 57%). Complex 14NO3, according to 1H and 31P{1H} NMR spectra (yield 30.0 mg, 57%). Complex cis,cis-trans-[RuCl2(CO)(PTA)2]Cl (15) (23.5 mg, 7 μmol) was dissolved in 0.6 mL of D2O, and the orange solution was irradiated with blue light (λ = 470 nm, 40 mW) for 24 h. Even though no evident color change was observed during the reaction, the final 1H and 31P{1H} NMR spectra indicated complete formation of 15. 1H-NMR (D2O) δ (ppm): 9.09 (d, 1H, H6), 8.75 (d, 1H, H6*), 8.65 (d, 1H, H3), 8.58 (d, 1H, H3*), 8.41 (t, 1H, H4), 8.32 (t, 1H, H4*), 7.87 (t, 1H, H5), 7.81 (d, 1H, H5*), 4.61 (br s, 6H, NCH3), 4.45 (m, 6H, NCH3) 31P{1H} NMR (D2O), δ (ppm): −25.0 (1P, 2P, mutually trans PTAs). Selected IR absorption (methanol solution, cm−1): 2086 (ν(CO)), 2038 (ν(CO)-). UV-vis (H2O): λmax = 523 nm.

cis,cis-[Ru(bpy)(CO)2Cl(PTA)]Cl (13). [RuCl([μ-Cl])(CO)2·PTA]2 (5, 30 mg, 0.038 mmol) was dissolved in 5 mL of water. One eq. of bpy (5.9 mg, 0.038 mmol) was added and the colorless solution was refluxed for 1 h, during which time it turned rapidly to orange-red. The solvent was removed by rotary evaporation affording an orange solid that was treated with acetone (2 × 2 mL), washed with diethyl ether, and dried in vacuo. The solid was pure 13, according to 1H and 31P{1H} NMR spectra (yield 13.4 mg, 65%). Elemental analysis calcd for [C26H18Cl2N2O2PRu] (Mw: 541.3): C 39.94; H 3.72; N 12.94. Found: C 39.84; H 3.66; N 12.85. 1H-NMR (D2O) δ (ppm): 9.08 (d, 2H, H6, H6*), 8.67 (d, 2H, H3, H3*), 8.44 (t, 2H, H4, H4*), 7.91 (t, H2, H5, H5*), 4.46 (m, 6H, NCH3), 4.09 (br s, 6H, NCH3). 13C NMR from the HSQC spectrum (D2O), δ (ppm): 153.5 (C6, C6*), 142.0 (C4, C4*), 129.0 (C5, C5*), 125.5 (C3, C3*), 70.3 (NCH3), 50.6 (NCH3). 31P{1H} NMR (D2O), δ (ppm): −25.5 (s, 1P, PTA trans to Cl). Selected IR absorption (methanol solution, cm−1): 2085 (ν(CO)), 2034 (ν(CO)-). ESI mass spectrum: 478.6 m/z [M − CO] (calcd 478.7). UV-vis (H2O): λmax = 526 nm.

cis,cis-trans-[Ru(bpy)2(PTA)2(NO3)2 (14NO3)] (7) (40.0 mg, 0.074 mmol) was dissolved in 8 mL of water. 2.1 eq. of AgNO3 (26.4 mg, 0.155 mmol) and 1 eq. of bpy (11.6 mg, 0.074 mmol) were added and the mixture was heated to reflux for 1 h. Upon heating the colorless solution turned rapidly orange-red, and a grey AgCl precipitate formed. At the end of reaction, the precipitate was removed by filtration on a Celite pad. The solution was rotary evaporated to dryness affording a red solid that was treated with acetone (3 × 2 mL), washed with diethyl ether, and dried in vacuo. The solid was pure 14NO3, according to 1H and 31P{1H} NMR spectra (yield 30.0 mg, 57%). Complex cis,cis-trans-[RuCl2(bpy)(PTA)2]Cl (12). cis,mer-[RuCl2(bpy)2Cl2] (12). 1H-NMR (D2O) δ (ppm): 9.02 (d, 2H, H6, H6*), 8.82 (d, 2H, H3, H3*), 8.57 (2H, H4, H4*), 8.02 (2H, H5, H5*), 4.47, 4.43 (ABq, 12H, NCH3), 4.04 (br s, 12H, NCH3). 13C NMR from the HSQC spectrum (D2O), δ (ppm): 153.9 (C6*, C6), 142.7 (C4, C4*), 129.1 (C5*, C5), 126.7 (C3, C3*), 70.4 (NCH3), 47.8 (NCH3). 31P{1H} NMR (D2O), δ (ppm): −50.9 (s, 2P, mutually trans PTAs). Selected IR absorption (methanol solution, cm−1): 2086 (ν(CO)), 2038 (ν(CO)-). UV-vis (H2O): λmax = 523 nm.
Conflicts of interest

There are no conflicts to declare.

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References

1 (a) D. J. Daigle, A. B. Pepperman Jr and S. L. Vail, J. Heterocycl. Chem., 1974, 11, 407–408; (b) D. J. Daigle, T. J. Decuir, J. B. Robertson and D. J. Darenbourg, Inorg. Synth., 1998, 32, 40–45.
2 (a) A. D. Phillips, L. Gonsalvi, A. Romerosa, F. Vizza and M. Peruzzini, Coord. Chem. Rev., 2004, 248, 955–993; (b) J. Bravo, S. Bolaño, L. Gonsalvi and M. Peruzzini, Coord. Chem. Rev., 2010, 254, 555–607; (c) A. Guerriero, M. Peruzzini and L. Gonsalvi, Coord. Chem. Rev., 2018, 355, 328–361.
3 D. N. Akbayeva, L. Gonsalvi, W. Oberhauser, M. Peruzzini, F. Vizza, P. Brueggeller, A. Romerosa, G. Sava and A. Bergamo, Chem. Commun., 2003, 264–265.
4 (a) C. S. Allardyce, P. J. Dyson, D. J. Ellis and S. L. Heath, Chem. Commun., 2001, 1396–1397; (b) C. Sciarolo, A. Bergamo, L. Brescacin, R. Delfino, M. Cocchietto, G. Laurenczy, T. J. Geldbach, G. Sava and P. J. Dyson, J. Med. Chem., 2005, 48, 4161–4171; (c) P. J. Dyson and G. Sava, Dalton Trans., 2006, 1929–1933; (d) P. J. Dyson, Chimia, 2007, 61, 698–703; (e) A. Bergamo, A. Masi, P. J. Dyson and G. Sava, Internet J. Oncol., 2008, 33, 1281–1289; (f) W. H. Ang, A. Casini, G. Sava and P. J. Dyson, J. Organomet. Chem., 2011, 696, 989–998; (g) C. M. Clavel, E. Paunescu, P. Nowak-Sliwinska, A. W. Griiffoen, R. Scopelliti and P. J. Dyson, J. Med. Chem., 2015, 58, 3356–3365; (h) M. V. Babak, S. M. Meier, K. V. M. Huber, J. Reynisson, A. A. Legin, M. A. Jakupec, A. Roller, A. Stukalov, M. Gridling, K. L. Bennett, J. Colinge, W. Berger, P. J. Dyson, G. Superti-Furga, B. K. Keppler and C. G. Hartinger, Chem. Sci., 2015, 6, 2449–2456; (i) A. Weiss, X. Ding, J. R. van Beijnum, I. Wong, T. J. Wong, R. H. Berndsen, O. Dormond, M. Dallinga, L. Shen, R. O. Schlingemann, R. Pili, C.-M. Ho, P. J. Dyson, H. van den Bergh, A. W. Griiffoen and P. Nowak-Sliwinska, Angiogenesis, 2015, 18, 233–244; (j) B. S. Murray, M. V. Babak, C. G. Hartinger and P. J. Dyson, Coord. Chem. Rev., 2016, 306, 86–114.
5 (a) A. García-Fernández, J. Diez, Á. Manteca, J. Sánchez, R. García-Nava, B. G. Sierra, F. Mollinedo, M. Pilar Gamasa and E. Lastra, Dalton Trans., 2010, 39, 10186–10196; (b) E. Menéndez-Pedregal, J. Diez, Á. Manteca, J. Sánchez, A. C. Bento, R. García-Nava, F. Mollinedo, M. Pilar Gamasa and E. Lastra, Dalton Trans., 2013, 42, 13955–13967.
6 R. Pettinari, F. Marchetti, F. Condello, P. Pettinari, G. Lupidi, R. Scopelliti, S. Mukhopadhyay, T. Riedel and P. J. Dyson, Organometallics, 2014, 33, 3709–3715.
7 A. Woloszyn, R. Pettinari, R. Pettinari, G. V. Badillo Patzmay, A. Kwiecień, G. Lupidi, M. Nabissi, G. Santoni and P. Smoleński, Dalton Trans., 2017, 46, 10073–10081.
8 (a) D. J. Darenbourg, F. Joó, M. Kannisto, Á. Kathó and J. H. Reibenspies, Organometallics, 1992, 11, 1990–1993; (b) D. J. Darenbourg, F. Joó, M. Kannisto, A. Kath, J. H. Reibenspies and D. J. Daigle, Inorg. Chem., 1994, 13, 200–208; (c) F. Joó, L. Nadasí, J. Elek and G. Laurenczy, Chem. Commun., 1999, 971–972; (d) G. Laurenczy, F. Joó and L. Nádasí, Inorg. Chem., 2000, 39, 5083–5088; (e) G. Laurenczy, F. Joó and L. Nádasí, High Pressure Res., 2000, 18, 251–255; (f) G. Kovács, L. Nádasí, G. Laurenczy and F. Joó, Green Chem., 2003, 5, 213–217.
9 Aqueous-phase Organometallic Catalysis: Concepts and Applications, ed. B. Cornils and W. A. Hermann, Wiley-VCH, Weinheim, 2nd edn, 2004.
10 W.-C. Lee and B. J. Frost, Green Chem., 2012, 14, 62–66.
11 F. Battistin, A. Vidal, P. Cavigli, G. Balducci, E. Iengo and E. Alessio, Inorg. Chem., 2020, 59, 4068–4079 and references therein.
12 B. Serli, E. Zangrando, T. Gianferrara, C. Sciarolo, P. J. Dyson, A. Bergamo and E. Alessio, Eur. J. Inorg. Chem., 2005, 3423–3434.
13 A. Udvardy, A. C. Bényei and A. Kathó, J. Organomet. Chem., 2012, 717, 116–122.
14 F. Battistin, G. Balducci, E. Iengo, N. Demitri and E. Alessio, Eur. J. Inorg. Chem., 2016, 2850–2860.
15 F. Battistin, G. Balducci, B. Milani and E. Alessio, Inorg. Chem., 2018, 57, 6991–7005.
16 (a) F. Battistin, G. Balducci, N. Demitri, E. Iengo, B. Milani and E. Alessio, Dalton Trans., 2015, 44, 15671–15682; (b) F. Battistin, D. Siegmund, G. Balducci, E. Alessio and N. Metzler-Nolte, Dalton Trans., 2019, 48, 400–414.
17 In all the Ru(II) compounds described in this paper PTA is always bonded exclusively through the P atom, thus kP is omitted in the formulas.
18 G. Laurenczy, S. Jedner, E. Alessio and P. J. Dyson, Inorg. Chem. Commun., 2007, 10, 558–562.
19 P. Crochet and V. Cadierno, Dalton Trans., 2014, 43, 12447–12462.
20 S. Moret, P. J. Dyson and G. Laurenczy, Nat. Commun., 2014, 5, 4017–4024.
21 A. Guerriero, H. Bricout, K. Sordakis, M. Peruzzini, E. Monflièr, F. Hapiot, G. Laurenczy and L. Gonsalvi, ACS Catal., 2014, 4, 3002–3012.
22 A. Guerriero, H. Bricout, M. Peruzzini, P. J. Dyson, E. Monflier, F. Haplot, L. Gonsalvi and G. Laurenczy, *Inorg. Chim. Acta*, 2015, 431, 132–138.

23 F. Scalambra, M. Serrano-Ruiz and A. Romerosa, *Dalton Trans.*, 2017, 46, 5864–5871.

24 A. Udvardy, M. Serrano-Ruiz, V. Passarelli, E. Bolyog-Nagy, F. Joó, A. Kathó and A. Romerosa, *Inorg. Chim. Acta*, 2018, 470, 82–92.

25 T. R. Johnson, B. E. Mann, J. E. Clark, R. Foresti, C. J. Green and R. Motterlini, *Angew. Chem., Int. Ed.*, 2003, 42, 3722–3729.

26 R. Motterlini and L. E. Otterbein, *Nat. Rev. Drug Discovery*, 2010, 9, 728–743.

27 B. E. Mann, *Organometallics*, 2012, 31, 5728–5735.

28 C. C. Romao, W. A. Blättler, J. D. Seixas and G. J. L. Bernardes, *Chem. Soc. Rev.*, 2012, 41, 3571–3583.

29 S. H. Heinemann, T. Hoshi, M. Westerhausen and A. Schiller, *Chem. Commun.*, 2014, 50, 3644–3660.

30 S. Garcia-Gallego and G. J. L. Bernardes, *Angew. Chem., Int. Ed.*, 2014, 53, 9712–9721.

31 I. Chakraborty, S. J. Carrington and P. K. Mascharak, *Acc. Chem. Res.*, 2014, 47, 2603–2611.

32 U. Schatzschneider, *Br. J. Pharmacol.*, 2015, 172, 1638–1650.

33 J. Marhenke, L. Trevino and C. Works, *Coord. Chem. Rev.*, 2016, 306, 533–543.

34 M. A. Wright and J. A. Wright, *Dalton Trans.*, 2016, 45, 6801–6811.

35 M. Kubeil, R. R. Vernooij, C. Kubeil, B. R. Wood, B. Graham, H. Stephan and L. Spiccia, *Inorg. Chem.*, 2017, 56, 5941–5952.

36 S. Bolaño, J. Bravo, J. Castro, M. M. Rodríguez-Rocha, M. F. C. Guedes da Silva, A. J. L. Pombeiro, L. Gonsalvi and M. Peruzzini, *Eur. J. Inorg. Chem.*, 2007, 5523–5532.

37 A. García-Fernández, J. Diez, A. Manteca, J. Sánchez, M. P. Gamasa and E. Lastra, *Polyhedron*, 2008, 27, 1214–1228.

38 S. Bolaño, M. M. Rodríguez-Rocha, J. Bravo, J. Castro, E. Óñate and M. Peruzzini, *Organometallics*, 2009, 28, 6020–6030.

39 S. Miguel, J. Diez, M. P. Gamasa and M. E. Lastra, *Eur. J. Inorg. Chem.*, 2011, 951, 4745–4755.

40 A. García-Fernández, J. Diez, M. Pilar Gamasa and E. Lastra, *Eur. J. Inorg. Chem.*, 2014, 5, 917–924.

41 L. Hajji, C. Saraiba-Bello, G. Segovia-Torrente, F. Scalambra and A. Romerosa, *Eur. J. Inorg. Chem.*, 2019, 4078–4086.

42 (a) F. Scalambra, M. Serrano-Ruiz, S. Nahim-Granados and A. Romerosa, *Eur. J. Inorg. Chem.*, 2016, 1528–1540; (b) F. Scalambra, N. Holzmann, L. Bernasconi, S. Imberti and A. Romerosa, *Eur. J. Inorg. Chem.*, 2019, 1162–1170.

43 E. Iengo, N. Demitri, G. Balducci and E. Alessio, *Dalton Trans.*, 2014, 43, 12160–12163.

44 In the proton NMR spectrum of raw 10 a set of very small resonances, partially overlapped with those of 11, presumably belonging to 11 (or perhaps to the corresponding complex with protonated PTA and thus more soluble) is barely visible. 11 could also be the product of a slow transformation of 10 (perhaps light mediated), since it forms in few weeks ESI.†

45 I. Bratsos, S. Calmo, E. Zangrando, G. Balducci and E. Alessio, *Inorg. Chem.*, 2013, 52, 12120–12130.

46 C. F. J. Barnard, J. A. Daniels, J. Jeffery and R. J. Mawby, *Dalton Trans.*, 1976, 953–961.

47 (a) L. M. Wilkes, J. H. Nelson, J. P. Mitchener, M. W. Babich, W. C. Riley, B. J. Helland, R. A. Jacobson, M. Y. Cheng, L. Seff and L. B. McCusker, *Inorg. Chem.*, 1982, 21, 1376–1382; (b) D. W. Krassowski, J. H. Nelson, K. R. Brower, D. Hauenstein and R. A. Jacobson, *Inorg. Chem.*, 1988, 27, 4294–4301.

48 C. A. Mibi and B. J. Frost, *Inorg. Chem.*, 2007, 46, 7115–7120.

49 R. Girotti, A. Romerosa, S. Mañas, M. Serrano-Ruí and R. N. Perutz, *Inorg. Chem.*, 2009, 48, 3692–3698.

50 J. Kovács, F. Jóó, A. Bényei and G. Laurenzy, *Dalton Trans.*, 2004, 2336–2340.

51 F. Battistin, F. Scaletti, G. Balducci, S. Pilozzi, A. Arcangeli, L. Messori and E. Alessio, *J. Inorg. Biochem.*, 2016, 160, 180–188.

52 D. N. Akbayeva, S. Moneti, M. Peruzzini, L. Gonsalvi, A. Ienco and F. Vizza, *C. R. Chim.*, 2005, 8, 1491–1496.

53 S. Grgoric-Sipka, C. R. Kowol, S-M. Valiahdi, R. Eichinger, M. A. Jakupec, A. Roller, S. Shova, V. B. Arion and B. K. Kepller, *Eur. J. Inorg. Chem.*, 2007, 2870–2878.

54 S. Yazdani, B. E. Silva, T. C. Cao, A. L. Rheingold and D. B. Grotjahn, *Polyhedron*, 2018, 161, 63–70.

55 L. Leyva, C. Sirlin, L. Rubio, C. Franco, R. Le Lagadec, J. Spencer, P. Bischoff, C. Gaiddon, J.-P. Loe and R. J. Mawby, *Eur. J. Inorg. Chem.*, 2007, 3055–3066.

56 F. Battistin, G. Balducci, J. Wei, A. K. Renfrew and E. Alessio, *Eur. J. Inorg. Chem.*, 2018, 2018, 1469–1480.

57 W. Kabsch, *Acta Crystallogr., Sect. D: Biol. Crystallogr.*, 2010, 66, 125–132.

58 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv.*, 2015, 72, 3–8.

59 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, 64, 112–122.

60 P. Emsley and K. Cowtan, *Acta Crystallogr., Sect. D: Biol. Crystallogr.*, 2004, 60, 2126–2132.