Synthesis and Structural Characterization of (Carbene)ruthenium Complexes Binding Nucleobases

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The new (carbene)ruthenium(II) nucleobase derivatives *fac,cis*-[(PNP)RuCl{C(NH$C_4H_3N_2O_2$)(CH_2Ph)}]Cl (**5**) and *fac,cis*-[(PNP)RuCl{C(NH$C_5H_3N_4$)(CH_2Ph)}]Cl (**6**) [PNP = $CH_3CH_2CH_2N(CH_2CH_2PPh_2)_2$] were synthesised by treating (vinylidene)ruthenium(II) complex *fac,cis*-[(PNP)RuCl_2{C=C(H)Ph}] (**1**) with 5-aminouracil or adenine, respectively. Both complexes were characterized by spectroscopic techniques (IR and NMR) and elemental analyses, which confirmed the formation of the aminocarbene moieties incorporating 1 equiv. of the nucleobase in the complex framework. Crystal and molecular structure determination by X-ray diffraction analysis of the uracil derivative **5** revealed a very unusual *O*-coordination of the exocyclic C=O group on the C(4) atom of the uracil ring to the ruthenium atom leading to an unprecedented six-membered aminocarbene metallacycle.

Introduction

The chemistry of organotransition metal complexes containing biologically important molecules as ligands constitutes a recent research field of general interest relevant to aspects such as DNA condensation,[1] heavy metal toxicity and mutagenicity,[2] and, in a broader sense, to topics related to the subject of supramolecular architectures where metal-to-ligand coordination bonds are intimately combined with H-bonding interactions. These supramolecular bio-organometallic aggregates have potential implications for the design of new metal-based drugs[3] as well as in material chemistry.[4]

The presence of metal ions in these systems introduces additional variables, whose effects remain largely to be explored in detail. These include inter alia the overall charge of the complex, the oxidation state of the metal atom, the electronic and steric properties of the coligands and also, in charged compounds, the nature of the counterion.[5] Among transition metal ions, ruthenium has unique properties making it particularly useful in drug design.[6] A ruthenium anticancer agent showing promising activity against otherwise resistant tumours and a low systemic toxicity has recently entered clinical trials.[7] Remarkably, bioorganometallic compounds conjugating nucleobases with typical metal−carbon multiple bond species such as carbenes and carbynes have not yet been described in spite of the enormous interest in this class of compounds[8] and the steadily increasing attention paid to the search of new routes to ruthenium species bio-conjugated with nucleobases.

Herein, we wish to report on our results in this area describing the first examples of transition metal carbenes incorporating nucleobases in their molecular structure. Noticeably, an unprecedented bonding mode of the uracil moiety to a transition metal ion has been ascertained by X-ray analysis.

Results and Discussion

Synthesis and Characterization of the (Carbene)ruthenium Nucleobase Derivatives *fac,cis*-[(PNP)RuCl{C(NH$C_4H_3N_2O_2$)-(CH_2Ph)}]Cl (5) and *fac,cis*-[(PNP)RuCl{C(NH$C_5H_3N_4$)(CH_2Ph)}]Cl (6)

In recent years, some of us reported that the reaction of the (vinylidene)ruthenium(II) complex *fac,cis*-[(PNP)-RuCl_2{C=C(H)Ph}] (**1**) [PNP = $CH_3CH_2CH_2N$-$(CH_2CH_2PPh_2)_2$] with a variety of primary amines is a simple general method to synthesising the neutral aminocarbene complexes *fac,cis*-[(PNP)RuCl_2{C(NHR)(CH_2Ph)}]

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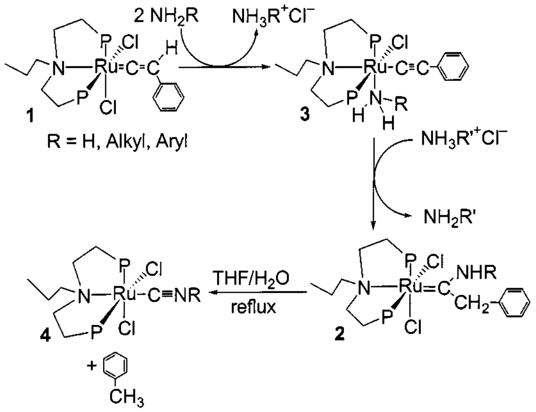
(**2**) in excellent yields via the intermediary aminoalkynyl compounds **3**.[9] The aminocarbene complexes are air- and thermally stable in the solid state but slowly decompose in boiling THF eliminating toluene and forming the corresponding isocyanide complexes *fac,cis*-[(PNP)RuCl$_2$(C≡NR)] (**4**) (Scheme 1).

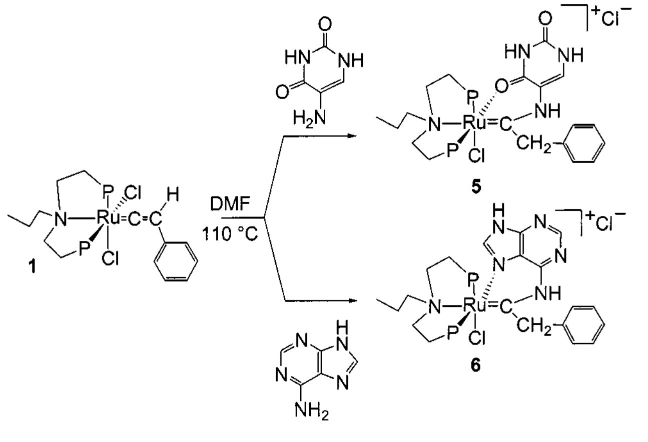


Scheme 1

We were intrigued by the generality of the reaction of **1** with primary amines, and so decided to investigate the possibility of introducing biologically relevant molecules such as 5-aminouracil and adenine into the skeleton of the ruthenium−carbene moiety. The incorporation of both 5-aminouracil and adenine in the ruthenium complex would lead to the building of bifunctional organometallic moieties that could exploit their potential to act as ligands capable of recognising complementary nucleobases trough hydrogen bond interactions.

With these ideas in mind, we have examined the reactivity of the vinylidene complex **1** with a slight excess of 5-aminouracil or adenine. This was done by adapting our general preparation of the aminocarbene complexes **2** for both the insolubility of these nucleobases in common organic solvents and the reluctance of these weak bases to interact with the Ru=C=C fragment under less forceful conditions. A straightforward reaction was obtained by allowing **1** to react with an excess of either 5-aminouracil or adenine in distilled dimethylformamide at ca. 110 °C where both the nucleobases and the ruthenium precursors are soluble enough. Concentration of the hot solution to dryness under vacuum left a yellowish residue which was taken up with a mixture of dichloromethane/ethanol to yield, after workup, a crop of light-yellow microcrystals of *fac,cis*-[(PNP)RuCl{C(NHC$_4$H$_3$N$_2$O$_2$)(CH$_2$Ph)}]Cl (**5**) or orange platelets of *fac,cis*-[(PNP)RuCl{C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}]Cl (**6**), respectively (Scheme 2). The uracil derivative could be recrystallized in air as lemon-yellow needles suitable for an X-ray diffraction study from dichloromethane/petroleum ether mixtures. In contrast, several attempts to grow crystals of **6** (either as chloride or tetraphenylborate salt) were unsuccessful.

Apart from conventional spectroscopic techniques (IR and NMR spectroscopy) and elemental analysis (see Exp. Sect.), which confirmed the incorporation of one equiv. of nucleobase and the formation of the expected aminocarbene moiety in the complex framework of both **5** and **6**, precious information that shed light on their structures was inferred from chemical tests. A complete X-ray diffraction analysis was also obtained for **5** (see below).



Scheme 2

Unambiguous evidence for the presence of the aminocarbene ligands in **5** and **6** was provided by NMR spectroscopy ([D$_6$]DMSO) that showed the typical ^{13}C NMR absorptions of the aminocarbene carbon atom at δ = 257.9 (t, $^2J_{C,P}$ = 13.9 Hz) for **5** and δ = 284.5 (t, $^2J_{C,P}$ = 19.2 Hz) for **6**. The magnitude of the coupling constants, which are in the expected range for Fischer-type (carbene)ruthenium(II) complexes points to a *trans* disposition of the carbene ligand and the nitrogen donor atom of the PNP ligand. The IR spectra contained a broad absorption in the N−H stretching region (3500−3400 cm^{-1}), while the uracil derivative, in addition, exhibited medium-to-strong bands at 1720, 1643 and 1621 cm^{-1}, which were assigned to the stretching of the oxo groups in position 2 and 4 and to the C(5)−C(6) double bond in the uracil residue, respectively. In the ^{1}H NMR spectra, the hydrogen atoms of the benzyl substituents are diastereotopic and thus give rise to an AB multiplet, whereas the NH proton of the aminocarbene moiety appears as a very broad singlet at δ = 11.70 (**5**) and δ = 13.90 (**6**) due to the presence of the quadrupolar ^{14}N-nucleus.

In keeping with a *facial* arrangement of the PNP ligand and an inequivalent chemical environment of the two phosphane ends, the ^{31}P{^{1}H} NMR spectra in [D$_6$]DMSO showed slightly perturbed second-order AB splitting patterns with homonuclear geminal coupling constants $^2J_{P,P}$ equal to 32.5 and 27.5 Hz, respectively. The inequivalence of the two P-donor atoms in both **5** and **6** was quite unexpected in view of the *facial* geometry adopted by the aminodiphosphane ligand ($\delta_P > 39$)[10] and of the absence of any chiral element in the frame of the nucleobases incorporated in the complexes.[9] While a ^{31}P NMR singlet could be anticipated for a *fac,cis*-PNP(carbene)Ru complex, the occurrence of an AB system could not be simply explained. On the basis of the elemental analysis, confirming two chloride ligands for each ruthenium atom, a reasonable structural hypothesis suggested that one of the two chloride ligands was no longer coordinated to the metal centre, therefore acting as the counteranion in a charged complex. In agreement with this hypothesis, both **5** and **6** readily exchanged one of the two chloride ions with tetraphenylborate when their solutions in CH_2Cl_2/EtOH were treated with excess $NaBPh_4$. Elemental analysis, IR and NMR spectroscopy, as well as solution conductivities (1,2-dichloroethane) clearly indicated that the tetraphenylborate complexes *fac*,*cis*-[(PNP)RuCl{C($NHC_4H_3N_2O_2$)(CH_2Ph)}]BPh_4 (**5-BPh$_4$**) and *fac*,*cis*-[(PNP)RuCl{C($NHC_5H_3N_4$)(CH_2Ph)}]BPh_4 (**6-BPh$_4$**), were quantitatively produced by metathetical chloride substitution.

Crystal Structure of *fac*,*cis*-[(PNP)RuCl{C($NHC_4H_3N_2O_2$)(CH_2Ph)}]Cl·CH_3OH·H_2O (5·CH_3OH·H_2O)

The easy formation of the tetraphenylborate salts of **5** and **6** raised the question of which structure is attributed to carbenes **5** and **6** where a nucleobase is incorporated with a (carbene)ruthenium moiety. This makes it of paramount importance to attain single crystals suitable for an X-ray diffraction analysis. While for **6** we were unable to grow well-shaped crystals, the thermal and air robustness of the uracil derivative makes it feasible to grow crystals of **5** for the diffraction study from a saturated dichloromethane/methanol solution in air. Thus, in order to collect geometrical information on this class of aminocarbenes, an X-ray analysis was carried out on a single crystal of **5**. An ORTEP drawing of the complex is shown in Figure 1 with the adopted atomic numbering scheme. A list of selected bond lengths and angles is given in Table 1.

Table 1. Selected bond lengths [Å] and angles [°] for *fac*-[(PNP)RuCl{C($NHC_4H_3N_2O_2$)(CH_2Ph)}]Cl·CH_3OH·H_2O (**5**·CH_3OH·H_2O)

Ru(1)−C(12)	1.956(6)	C(12)−Ru(1)−O(1)	91.99(19)
Ru(1)−O(1)	2.126(4)	C(12)−Ru(1)−P(2)	100.27(17)
Ru(1)−P(2)	2.2792(17)	O(1)−Ru(1)−P(2)	165.25(11)
Ru(1)−P(1)	2.2847(17)	C(12)−Ru(1)−P(1)	98.58(17)
Ru(1)−N(1)	2.352(5)	O(1)−Ru(1)−P(1)	85.37(11)
Ru(1)−Cl(1)	2.4631(17)	P(2)−Ru(1)−P(1)	100.71(6)
O(1)−C(11)	1.240(6)	C(12)−Ru(1)−N(1)	176.0(2)
O(2)−C(10)	1.203(7)	O(1)−Ru(1)−N(1)	84.19(15)
N(2)−C(12)	1.349(7)	P(2)−Ru(1)−N(1)	83.33(12)
N(2)−C(8)	1.415(7)	P(1)−Ru(1)−N(1)	82.42(12)
N(3)−C(10)	1.368(8)	C(12)−Ru(1)−Cl(1)	86.94(17)
N(3)−C(9)	1.372(7)	O(1)−Ru(1)−Cl(1)	81.15(11)
N(4)−C(11)	1.371(7)	P(2)−Ru(1)−Cl(1)	91.28(6)
N(4)−C(10)	1.386(7)	P(1)−Ru(1)−Cl(1)	165.61(6)
C(8)−C(9)	1.352(7)	N(1)−Ru(1)−Cl(1)	91.20(12)
C(8)−C(11)	1.430(8)	C(11)−O(1)−Ru(1)	124.2(4)
C(12)−C(13)	1.528(8)	C(12)−N(2)−C(8)	128.6(5)
C(13)−C(1*5)	1.518(6)	C(10)−N(3)−C(9)	123.9(5)
		C(11)−N(4)−C(10)	127.5(5)
		C(9)−C(8)−N(2)	118.0(5)
		C(9)−C(8)−C(11)	118.3(5)
		N(2)−C(8)−C(11)	123.7(5)
		C(8)−C(9)−N(3)	121.7(5)
		O(2)−C(10)−N(3)	124.3(6)
		O(2)−C(10)−N(4)	123.0(6)
		N(3)−C(10)−N(4)	112.6(5)
		O(1)−C(11)−N(4)	117.5(5)
		O(1)−C(11)−C(8)	126.6(5)
		N(4)−C(11)−C(8)	115.9(5)
		N(2)−C(12)−C(13)	107.5(5)
		N(2)−C(12)−Ru(1)	123.1(4)
		C(13)−C(12)−Ru(1)	128.8(4)
		C(1*5)−C(13)−C(12)	118.6(5)

In the structure of *fac*,*cis*-[(PNP)RuCl{C($NHC_4H_3N_2O_2$)(CH_2Ph)}]Cl·CH_3OH·H_2O (**5·CH_3OH·H_2O**), formed by *fac*,*cis*-[(PNP)RuCl{C($NHC_4H_3N_2O_2$)(CH_2Ph)}]$^+$ cations, chloride anions and interspersed solvate molecules of methanol and water in a 1:1:1:1 ratio, the arrangement of the non-hydrogen atoms about the metal atom in the cation is approximately octahedral with the aminodiphosphane ligand occupying three facial coordination sites. A chloride ligand and one aminocarbene group incorporating the 5-aminouracil fragment and located *trans* to the PNP nitrogen donor, are also coordinated to the metal centre. The coordination polyhedron about the ruthenium atom is completed by O-coordination from the exocyclic C=O group on the C(4) atom of the uracil ring. The arrangement found in **5** does not significantly differ from that established in the related aminocarbene derivative *fac*,*cis*-[(PNP)RuCl$_2${C[NH(*S*)-(−)-CH(Me)(1-naphthyl)]-(CH_2Ph)}], which was also authenticated by X-ray methods,[9] as well as in other PNPruthenium(II) complexes.[10,11] Bond lengths and angles match well with the data reported for other (aminocarbene)ruthenium complexes.[9,12] Cocrystallised molecules of methanol and water, the latter likely taken from the air, contribute to the stability of the crystal lattice. As a matter of fact, a net of hydrogen bonding interactions involves the uracil N(4), the methanol O(3) and the water O(4) atoms, the most important contacts being N(4)···O(3) 2.79 Å and O(3)···O(4) 2.72 Å. Additionally, the O(4) water atom shows weak interactions

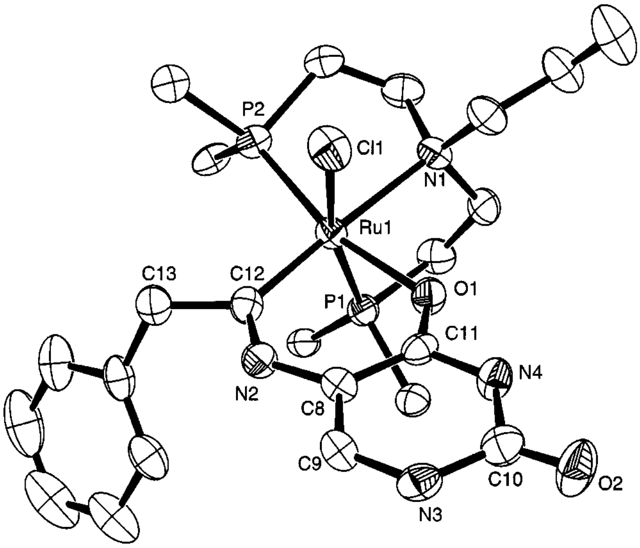
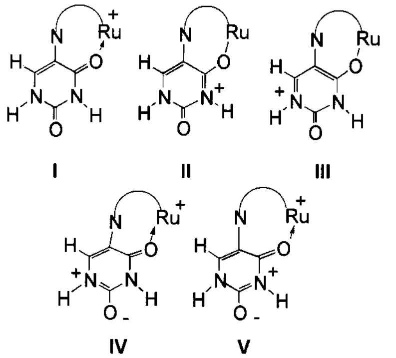


Figure 1. ORTEP drawing of the complex cation *fac*,*cis*-[(PNP)RuCl{C($NHC_4H_3N_2O_2$)(CH_2Ph)}]$^+$; only the *ipso*-carbon atoms of the PNP phenyl substituents are shown for the sake of clarity

with both chlorine atoms [3.24 Å with Cl(1), 3.31 Å with Cl(2)].

The most notable feature of the crystal structure of **5** is the unexpected metallation of the C=O group at the 4-position of the uracil moiety, that, therefore, behaves as an η^1-monodentate ligand through the exocyclic oxygen atom. The complexation of one of the carbonyl groups of the uracil ligand to the ruthenium centre was quite surprising and has no precedents in this series of PNP(carbene)Ru derivatives. In this regard, it is remarkable to underline that the reaction of **1** with several α,ω-diamines parallels that established for simple monoamines and resulted in the synthesis of (aminocarbene)ruthenium complexes with a pendant, noncoordinated, amino arm.[13]

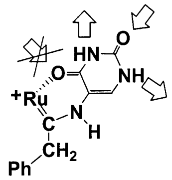
Although few examples of transition metal complexes containing uracil residues have been described so far,[5a,14a] the arrangement found in **5**, where the nucleobase metallates through one carbonyl group, is unprecedented.[14] The C(11)−O(1) bond length [1.240(6) Å] of the carbonyl group involved in the intramolecular interaction with the ruthenium atom [the O(1)−Ru separation is 2.126(4) Å], even if longer than in free uracil [1.227(2) Å],[15] does not significantly differ from that observed in the known uracil derivatives containing metal complexes.[5a,14a] This points to a weak interaction between the uracil moiety and the ruthenium centre. The two rings deriving from the adopted geometry of the (aminocarbene)ruthenium complex with 5-aminouracil are virtually planar. In order to analyse the influence of the coordination of one uracil carbonyl group to the ruthenium centre, the bond lengths of the uracil ring in **5** have been compared with those determined for the free ligand.[15] Five different valence isomers may be drawn in which the positive charge is moved from the metal atom to the nitrogen atoms N(3) and N(4) (Scheme 3).



Scheme 3. Structure of the possible valence isomers for the metal modified uracil ring in **5**

A perusal of the bond lengths listed in Table 1, suggests that both **IV** and **V**, in which the oxygen atom O(2) bears a negative charge, do not provide a major contribution to the representation of **5**, and, in keeping with this hypothesis, the "distal" C(10)−O(2) separation (1.203 Å), which is typical of a C=O double bond, is shorter in **5** than in the free uracil molecule [1.218(2) Å].[15] In contrast, the C(10)−N(4) bond length is definitely longer than all the other C−N distances pertaining to the uracil residue in **5**, which rules out the occurrence of a ketoimine equilibrium involving N(4) and O(2). The closeness of two positive charges in **V** also agrees with this observation. In accordance with a significant contribution from the structures **II** and **III**, both C(9)−N(3) and C(11)−N(4) bond lengths are slightly shorter in **5** than in the free uracil while the separations C(9)−C(8) and C(8)−C(11) are longer and shorter, respectively, with respect to the free nucleobase. On the basis of all these findings, it is conceivable that form **I** corresponds to the closest representation of the cationic complex **5**.

Although one of the two carbonyl groups of the uracil moiety is blocked by coordination to the ruthenium centre, preventing H-bonding, **5** still presents a potential hydrogen bond donor/hydrogen bond acceptor/hydrogen bond donor arrangement (DAD),[16] capable of forming hydrogen bonds with molecules containing complementary ADA or AD ends (Scheme 4).



Scheme 4

The formation of centrosymmetric [2+2] "dimer pairs" by association of N−H···O hydrogen bonds between an amide N−H group of one molecule of **5** with the "free" carbonyl oxygen atom of a second molecule of **5** and vice versa could be expected. Actually, the analysis of the crystal packing of **5** does not permit us to detect any links via hydrogen bonds between independent molecules, even if geometrical complementarity is unaltered.

NMR Spectroscopic Studies of the H-Binding Properties of the (Aminocarbene)ruthenium Complexes 5 and 6

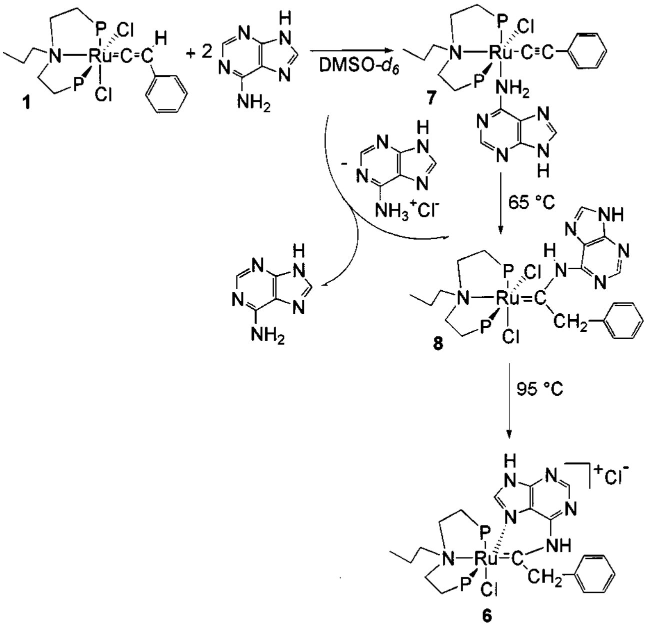
Because of coordination to the metal centre in **5** (and **6**), it is evident that the "usual" H bonding at the uracil (or adenine) fragment is not possible. Nevertheless, the new aminocarbenes **5** and **6** bear appropriate hydrogen bonding molecular recognition sites, which could, in principle, still form non-covalent host-guest assemblies with suitable substrates.[5a,17] Therefore, in order to assess this property, we decided to study how the ^{1}H NMR chemical shift of the N−H protons of **5** and **6** change as a function of the sample concentration and of the presence of substrates with complementary hydrogen-bonding recognition sites.[18] At first, we noticed that, independently from the solvent used, (CD_2Cl_2 or CD_3CN), the N−H chemical shift of both **5** and **6** is not concentration-dependent. Whereas this fact is quite intriguing and suggests that dimerisation of these nucleobase aminocarbenes does not occur through hydrogen bonding, it can be related with the information derived from the X-ray study of **5**. This behaviour does not have a clear explanation as electrostatic repulsions between cationic organometallic species, steric hindrance due to the presence of bulky ancillary ligands,[19] or even changes in the electronic distribution in the metal-bounded nucleobases,[20] could be responsible. In order to understand better this piece of evidence, we unsuccessfully attempted to detect by ^{1}H NMR spectroscopy the formation of hydrogen bonding adducts of **5** in the presence of adenine. The latter could indeed act as a neutral sterically nondemanding molecule with a DA (DA = donor/acceptor)[16] motif capable of utilising only one hydrogen bond acceptor and donor motif of the uracil derivative **5** in a Watson−Crick manner.[16,17] This negative result could suggest that either electrostatic repulsions or steric hindrance at the approaching of a complementary motif to the metal-modified uracil are not decisive. In any case, it can be anticipated that O-binding of the uracil ring to a metal ion significantly disturbs its electronic complementarity with the adenine partner.

Mechanism of the Formation of the Nucleobase Carbene Complexes

The mechanism accounting for the formation of the vast family of PNP aminocarbene derivatives by nucleophilic attack of primary amines to the (vinylidene)ruthenium complex **1** encompasses a well-established pathway requiring 2 equiv. of amine.[9,10] In summary, the first amine equivalent deprotonates the vinylidene C_β carbon atom, while the second one coordinates the metal centre prior to be transferred, by an intramolecular nucleophilic attack, on the C_α carbon atom of the alkynyl intermediate (Scheme 1).

The synthetic route to both **5** and **6** most likely goes through a related pathway with the obvious changes expected by the formation of the metallated aminocarbenes. In the case of **6**, the N(7) atom of the adenine is responsible for chelation at the ruthenium centre affording the unprecedented cyclic adeninylcarbene **6**. Remarkably, once formed, **5** is much more robust than **6** indicating that the Ru−O=C interaction involving the uracil system is much more stable than the Ru−N(7) interaction of the aminocarbene deriving from adenine.

Monitoring the reaction between **1** and adenine in an NMR tube via ^{1}H and ^{31}P NMR spectroscopy is a straightforward method to providing experimental evidence for the proposed mechanism as well as confirming that for **6,** the final reaction product is an N(7)-metallated adeninylcarbene (Scheme 5). In the case at hand, when 2 equiv. of adenine are dissolved in a 5-mm NMR tube containing a solution of **1** in [D$_6$]DMSO and the solution is monitored by ^{31}P NMR spectroscopy, a neat reaction takes place at room temperature affording a single compound displaying a well-resolved AB spin system at δ = 53.90 and 52.01 with $J_{P,P}$ = 35.2 Hz. The latter derives from the chemical inequivalence of the two PPh$_2$ groups in the adenine complex *fac,cis*-[(PNP)RuCl(C≡CPh)(NH$_2$C$_5$H$_3$N$_4$)}] (**7**) that forms after the substitution of one chloride ligand by an amine. Attempts to isolate **7** by stripping off DMSO at room temperature leave a yellowish residue whose ^{31}P NMR spectrum denies a simple analysis owing to the accompanying presence of several unidentified products. Nevertheless, the IR spectrum of this solid species exhibits a sharp IR absorption at 2050 cm^{-1} assigned to the phenylethynyl ligand in **7**. Heating the [D$_6$]DMSO solution of **7** at 65 °C turns the light yellow colour to greenish yellow as **7** transforms into a new compound still exhibiting an AB spin system in the phosphorus NMR spectrum. The formation of this latter species, assigned to the nonmetallated neutral (aminocarbene)ruthenium complex *fac,cis*-[(PNP)RuCl$_2${C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}] (**8**), is accompanied by the appearance of the final metallated derivative **6**. In keeping with the accepted mechanistic hypothesis, on transforming **7** into **8** (and then into **6**), the informative AB system of the diastereotopic benzylic CH$_2$ protons and the featureless NH signal of the aminocarbene (δ = 11.91) rises in the ^{1}H NMR spectrum indicating that the intramolecular ruthenium-mediated attack of the adenine-NH$_2$ end has just occurred along the C=C moiety of the vinylidene ligand. The conversion of **8** into **6** is not completed at 65 °C in 1 d and goes to completion only after prolonged heating at 95 °C. A perusal of the collected pieces of evidence makes it reasonable to assign **6** to a structure similar to that ascertained in **5** by X-ray methods.



Scheme 5

Conclusions

In this paper we have described the first examples of transition metal carbenes incorporating nucleobases such as adenine and 5-aminouracil. Surprisingly these novel bio-organometallic derivatives exploit a new coordination mode towards a ruthenium centre. Thus, in the 5-aminouracil derivative a six-membered ring is closed by metallation of the oxo group on C(4) while in the adenine complex the aminocarbene uses the nitrogen atom N(7) to coordinate the ruthenium atom. This behaviour is quite surprising and has no precedents either in the series of PNP(carbene)Ru derivatives, or, to the best of our knowledge, in the coordination chemistry of these nucleobases. As a final consideration, it can be stressed that the present coordination mode of the two nucleobases has an important influence on their hydrogen-bonding pattern.

Experimental Section

General Procedures: Dimethylformamide (DMF), *n*-hexane and dichloromethane were purified by distillation under nitrogen over molecular sieves, sodium and P_2O_5, respectively. Adenine and 5-aminouracil were purchased from Aldrich and used as received. All the other reagents and chemicals were reagent grade and, unless otherwise stated, were used as received from commercial suppliers. All reactions and manipulations were routinely performed under dry nitrogen by using standard Schlenk-tube techniques. The solid complexes were collected on sintered glass-frits and washed with light petroleum ether (b.p. 40−60 °C) before being dried in a stream of nitrogen. The ligand $CH_3CH_2CH_2N(CH_2CH_2PPh_2)_2$ (PNP)[21] and the vinylidene complex *fac*,*cis*-[(PNP)RuCl$_2${C=C(H)Ph}] (**1**),[10b] were prepared as described in the literature. [D$_6$]DMSO for NMR measurements (Aldrich) was dried with molecular sieves (0.4 nm). ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded with Varian VXR 300 or Bruker AC200 spectrometers operating at 299.94 or 200.13 MHz (^{1}H) and 75.42 or 50.32 MHz (^{13}C), respectively. Peak positions are relative to tetramethylsilane and were calibrated against the residual solvent resonance (^{1}H) or the deuterated solvent multiplet (^{13}C). ^{13}C-DEPT-135 experiments were run with the Bruker AC200 spectrometer. ^{31}P{^{1}H} NMR spectra were recorded with the same instruments operating at 121.42 and 81.01 MHz, respectively. Chemical shifts were measured relative to external 85% H_3PO_4 with downfield values taken as positive. Infrared spectra were recorded as Nujol mulls with a Perkin−Elmer 1600 series FT-IR spectrometer between KBr plates. The molar conductivities were measured with an AMEL model 134 conductance cell connected with a model 101 conductivity meter. The conductivity data were obtained at sample concentration of 10^{-3} M in 1,2-dichloroethane solution at room temperature (22 °C). Elemental analyses (C,H,N) were performed using a Carlo Erba model 1106 elemental analyser.

Synthesis of *fac*,*cis*-[(PNP)RuCl{C(NHC$_4$H$_3$N$_2$O$_2$)(CH$_2$Ph)}]Cl (5): A fourfold excess of 5-aminouracil (0.27 g, 2.12 mmol) was added in small portions at room temperature to a stirred suspension of the vinylidene complex **1** (0.40 g, 0.53 mmol) in 30 mL of dichloromethane. The reaction mixture was stirred for 30 min and then DMF (15 mL) was added and the temperature gently raised to evaporate all the dichloromethane and then to about 110 °C. Heating was continued for 30 min to afford a light yellow solution, which was concentrated to dryness under vacuum. The crude yellowish material was taken with two portions (10 mL each) of a 1:2 mixture of ethanol and dichloromethane and the excess of unchanged 5-aminouracil was separated by filtration of the hot solutions. The filtered yellow solutions were collected in an Erlenmeyer flask and concentrated to ca. 5 mL. Addition of petroleum ether (3 mL) and slow concentration in air gave lemon-yellow crystals of the aminocarbene complex **5** that were recrystallised from dichloromethane and methanol in air to yield the solvate salt **5·CH$_3$OH·H$_2$O**. Yield ca. 82%. $C_{44}H_{49}Cl_2N_4O_4P_2Ru$ (931.16): calcd. C 56.72, H 6.01, N 5.30; found C 56.39, H 5.89, N 6.10. IR: $\tilde{\nu}$ = 3400 (br, m, ν_{NH}), 1720 (s, $\nu_{C=O}$), 1643 (s, $\nu_{C=O-Ru}$), 1621 (sh, $\nu_{C=C}$) cm^{-1}. ^{31}P{^{1}H} NMR (22 °C, [D$_6$]DMSO, 121.42 MHz): AB system: δ_A = 55.24, δ_B = 50.14, $^2J(P_A,P_B)$ = 32.5 Hz. ^{1}H NMR (22 °C, [D$_6$]DMSO, 299.94 MHz): δ = 12.4 [br, 2 H, NH(uracil)], 11.70 [s, 1 H, NH(aminocarbene)], 8.04 [s, 6-H, 1 H, CH(uracil)], 5.13 (CH$_2$Ph), 4.75 [AB system, $^3J_{H,H}$ = 16.9 Hz, 2 H]. ^{13}C{^{1}H} NMR (22 °C, [D$_6$]DMSO, 75.42 MHz): δ = 257.9 [t, $^2J_{C,P}$ = 13.9 Hz, Ru=*C*], 161.3 [*C*=O(uracil)], 149.1 (s, C-2 and C-4), 118.0 [s, C-6, C=*C*H(uracil)], 66.0 [br d, $^3J_{C,P}$ = 2.2 Hz, *C*H$_2$Ph].

Synthesis of *fac*,*cis*-[(PNP)RuCl{C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}]Cl (6): A threefold excess of adenine (0.22 g, 1.63 mmol) was added at room temperature to a stirred suspension of the vinylidene complex **1** (0.40 g, 0.53 mmol) in 20 mL of DMF. The reaction mixture was stirred for 10 min and then gently heated to about 110 °C. Heating was continued for 30 min to afford a light orange solution, which was concentrated to dryness under vacuum. The crude orange material was combined with two portions (10 mL each) of hot dichloromethane and the excess of unchanged adenine was separated by filtration through a cotton plug. Addition of *n*-hexane (8 mL) and concentration of the orange solution under nitrogen gave orange yellowish crystals of the aminocarbene complex **6** that were recrystallised from dichloromethane/*n*-hexane (2:1). Yield ca. 74%. $C_{44}H_{46}Cl_2N_6P_2Ru$ (892.81): calcd. C 59.19, H 5.19, N 9.41; found C 58.87, H 5.20, N 9.22. IR: $\tilde{\nu}$ = 3480−3350 cm^{-1} (br, ν_{NH}). ^{31}P{^{1}H} NMR (22 °C, [D$_6$]DMSO, 81.01 MHz): AB system: δ_A 47.74, δ_B 39.21, $^2J(P_A,P_B)$ = 27.5 Hz. ^{1}H NMR (22 °C, [D$_6$]DMSO, 299.94 MHz): δ = 13.9 [br. d, $J_{H,P}$ = 12.4 Hz, 1 H, NH(aminocarbene)], 8.75 [s, 1 H, NH(adenine)], 8.62 [CH(adenine)], 7.90 (s, 2 H, 2-H + 8-H), 5.88 (CH$_2$Ph), 5.25 [AB system, $^3J_{H,H}$ = 16.8 Hz, 2 H]. ^{13}C{^{1}H} NMR (22 °C, [D$_6$]DMSO, 75.42 MHz): δ = 284.5 [t, $^2J_{C,P}$ = 19.2 Hz, Ru=*C*], 154.7 [s, C-5(adenine)], 152.6 [s, C-2(adenine)], 146.8 [s, C-4(adenine)], C-8(adenine) not observed, likely masked by aromatic resonances, 56.3 (s, *C*H$_2$Ph).

Synthesis of *fac*,*cis*-[(PNP)RuCl{C(NHC$_4$H$_3$N$_2$O$_2$)(CH$_2$Ph)}](BPh$_4$) (5-BPh$_4$) and *fac*,*cis*-[(PNP)RuCl{C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}](BPh$_4$) (6-BPh$_4$): Metathetical reaction of **5** or **6** with NaBPh$_4$ (2 equiv.) in CH$_2$Cl$_2$/EtOH (2:1) yielded the tetraphenylborate salts *fac*,*cis*-[(PNP)RuCl{C(NHC$_4$H$_3$N$_2$O$_2$)(CH$_2$Ph)}](BPh$_4$) **(5-BPh$_4$)** and *fac*,*cis*-[(PNP)RuCl{C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}](BPh$_4$) **(6-BPh$_4$)** in almost quantitative yields. **5-BPh$_4$:** $C_{67}H_{63}BClN_4O_2P_2Ru$ (1165.54): calcd. C 69.04, H 5.45, N 4.81; found C 69.67, H 5.65, N 4.59. **6-BPh$_4$:** $C_{68}H_{66}BClN_6P_2Ru$ (1176.59): calcd. C 69.42, H 5.65, N 7.14; found C 69.56, H 5.42, N 6.84. $\Lambda_{M(\mathbf{5\text{-}BPh4})}$ = 26 Ω^{-1} cm^2 mol^{-1} (295 K, in 1,2-dichloroethane). $\Lambda_{M(\mathbf{6\text{-}BPh4})}$ = 24 Ω^{-1} cm^2 mol^{-1} (295 K, in 1,2-dichloroethane).[22] IR: $\tilde{\nu}$ = 612 cm^{-1} (m, ν_{BC}).

In situ NMR Spectroscopic Study of the Reaction of 1 and Adenine: A 5-mm NMR tube was filled under nitrogen with **1** (20 mg, 0.026 mmol), adenine (7 mg, 0.052 mmol) and [D$_6$]DMSO (0.8 mL). ^{31}P{^{1}H} NMR monitoring of the reaction showed the fast and complete conversion of **1** into *fac*,*cis*-[(PNP)RuCl(C≡CPh)(NH$_2$C$_5$H$_3$N$_4$)}] (**7**). After 2 h, when **7** was the only ruthenium complex, the temperature of the probehead was raised to 65 °C and the NMR analysis showed a slow conversion of **7** into a mixture of *fac*,*cis*-[(PNP)RuCl$_2${C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}] (**8**) and **6** {after 12 h: **8** (68%), **6** (30%), *mer*,*trans*-[(PNP)RuCl$_2$(CO)] (2%)}. Heating to 95 °C completed the transformation of **8** into **6** in 24 h, but caused the formation of several unidentified compounds {after 24 h at 95 °C: **6** (81%), **8** (5%), *mer*,*trans*-[(PNP)RuCl$_2$(CO)] (3%), *fac*,*cis*-[(PNP)RuCl$_2$(CO)] (2%), unidentified compounds (9%, δ = 46.9, 36.5, 34.9 all singlets)}.

***fac*,*cis*-[(PNP)RuCl(C≡CPh)(NH$_2$C$_5$H$_3$N$_4$)}] (7):** ^{31}P{^{1}H} NMR (22 °C, [D$_6$]DMSO, 121.42 MHz): AB system: δ_A 53.90, δ_B 52.01,

$^2J(P_A,P_B)$ = 35.2 Hz. ^{1}H NMR (22 °C, [D$_6$]DMSO, 299.94 MHz): δ = 3.21 (br. s, 2 H, NH$_2$, superimposed to aliphatic resonances of PNP ligand), , 8.60 [NH(adenine) and CH(adenine)], 8.52, 7.85 (all s, NH, 2-H, 8-H, 3 H).

***fac*,*cis*-[(PNP)RuCl$_2${C(NHC$_5$H$_3$N$_4$)(CH$_2$Ph)}] (8):** ^{31}P{^{1}H} NMR (22 °C, [D$_6$]DMSO, 121.42 MHz): AB system: δ_A 49.69, δ_B 37.99, $^2J(P_A,P_B)$ = 28.0 Hz. ^{1}H NMR (22 °C, [D$_6$]DMSO, 299.94 MHz): 11.91 [br. s, 1 H, NH(aminocarbene)], , 8.88 [NH(adenine) + CH(adenine)], 8.56, 8.21 (all s, NH, 2-H, 8-H, 3 H), 5.04 (CH$_2$Ph), 4.87 [AB system, $^3J_{H,H}$ = 17.1 Hz, 2 H]. ^{13}C{^{1}H} NMR (22 °C, [D$_6$]DMSO, 75.42 MHz): 279.9 [t, $^2J_{C,P}$ = 13.6 Hz, Ru=*C*], 163.7 [s, C-5(adenine)], 156.1 [s, C-2(adenine)], 141.3 [s, C-4(adenine)], C-6(adenine) and C-8(adenine) not observed, likely masked by aromatic resonances, 62.6 [t, $^3J_{C,P}$ = 1.9 Hz, *C*H$_2$Ph].

X-ray Diffraction Study of *fac*,*cis*-[(PNP)RuCl{C(NHC$_4$H$_3$N$_2$O$_2$)(CH$_2$Ph)}]Cl·CH$_3$OH·H$_2$O (5·CH$_3$OH·H$_2$O): A lemon-yellow crystal of **5·CH$_3$OH·H$_2$O** was chosen for an X-ray analysis. A summary of crystal and intensity data for the compound is presented in Table 2. Experimental data were recorded at room temperature with an ENRAF-NONIUS CAD4 diffractometer using graphite-monochromated Mo-K_α radiation. A set of 25 carefully centred reflections in the range 7.5° ≤ θ ≤ 9° was used for determining the lattice constants. As a general procedure, the intensity of three standard reflections was measured periodically every 2 h for orientation and intensity control. This procedure did not reveal any decay of intensities. The data were corrected for Lorentz and polarisation effects. Atomic scattering factors were those tabulated by Cromer and Waber[23] with anomalous dispersion corrections taken from ref.[24] An empirical absorption correction was applied via Ψ scan with transmission factors in the range 1.0−0.9. All the calculations were performed using the WINGX package[25] SIR97,[26] SHELX97[27] and ORTEP-III.[28] Final atomic coordinates with equivalent isotropic thermal parameters of all atoms and structure factors are available as supplementary material. All the non-hydrogen atoms were found through a series of F_0 Fourier maps. Refinement was done by full-matrix least-squares calculations, initially with isotropic thermal parameters, and then, in the last least-squares cycle, with anisotropic thermal parameters for all atoms, except the solvents ones. All of the phenyl rings were treated as rigid bodies with D_{6h} symmetry and C−C distances fixed at 1.39 Å. Hydrogen atoms of the PNP ligand were introduced in calculated positions, but not refined. At an advanced stage of the refinement, two solvent molecules, one of methanol and the other of water, were located in the Fourier map and successfully refined. CCDC-172155 (**5·CH$_3$OH·H$_2$O**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Table 2. Crystal data and structure refinement for *fac*-[(PNP)RuCl{C(NHC$_4$H$_3$N$_2$O$_2$)(CH$_2$Ph)}]Cl·CH$_3$OH·H$_2$O (**5**·CH$_3$OH·H$_2$O)

Empirical formula	C$_{44}$H$_{49}$Cl$_2$N$_4$O$_4$P$_2$Ru
Formula mass	931.16
Temperature	293(2) K
Wavelength	0.71069 Å
Crystal system, space group	monoclinic, $P2_1/n$
Unit cell dimensions	a = 15.682(9) Å b = 14.273(5) Å, β = 102.79(3) ° c = 19.748(2) Å
Volume	4311(3) Å^3
Z, calculated density	4, 1.447 Mg/m^3
Absorption coefficient	0.609 mm^{-1}
F(000)	1952
Crystal size	0.30 × 0.25 × 0.55 mm
θ range for data collection	1.51−22.48 °
Limiting indices	$-16 \le h \le 16$, $0 \le k \le 15$, $0 \le l \le 21$
Reflections collected/unique	5788/5596 [R(int) = 0.0401]
Completeness to θ	22.48 99.6%
Refinement method	Full-matrix least squares on F^2
Data/restraints/parameters	5596/0/443
Goodness-of-fit on F^2	1.016
Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.0455, $wR2$ = 0.1012
R indices (all data)	$R1$ = 0.0962, $wR2$ = 0.1167
Largest diff. peak and hole	0.893 and −0.484 eÅ^{-3}

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