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Reactions of an Osmium-Hexahydride Complex with Cytosine, Deoxycytidine, and Cytidine: The Importance of the Minor Tautomers

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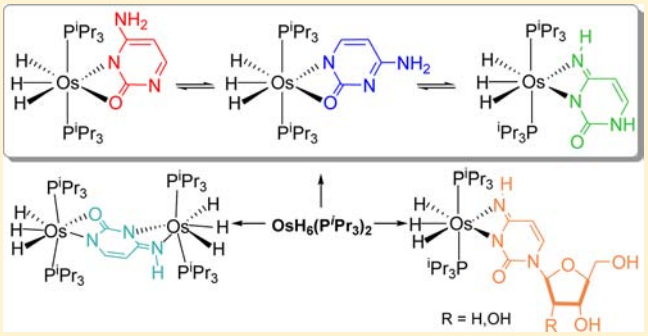
Supporting Information

ABSTRACT: Complex $OsH_6(P^iPr_3)_2$ (**1**) deprotonates cytosine to give molecular hydrogen and the d^4-trihydride derivative $OsH_3(cytosinate)(P^iPr_3)_2$ (**2**), which in solution exists as a mixture of isomers containing κ^2-N1,O (**2a**) and κ^2-N3,O (**2b**) amino-oxo and κ^2-N3,N4 (**2c**) imino-oxo tautomers. The major isomer **2b** associates with the minor one **2c** through N−H···N and N−H···O hydrogen bonds to form $[\mathbf{2b}\cdot\mathbf{2c}]_2$ dimers, which crystallize from saturated pentane solutions of **2**. Complex **1** is also able to perform the double deprotonation of cytosine (cytosinate′) to afford the dinuclear derivative $(P^iPr_3)_2H_3Os(cytosinate')OsH_3(P^iPr_3)_2$ (**3**), where the anion is coordinated κ^2-N1,O and κ^2-N3,N4 to two different $OsH_3(P^iPr_3)_2$ metal fragments. The deprotonation of deoxycytidine and cytidine leads to $OsH_3(deoxycytidinate)(P^iPr_3)_2$ (**4**) and $OsH_3(cytidinate)(P^iPr_3)_2$ (**5**), respectively, containing the anion κ^2-N3,N4 coordinated. Dimer $[\mathbf{2b}\cdot\mathbf{2c}]_2$ and dinuclear complex **3** have been characterized by X-ray diffraction analysis.



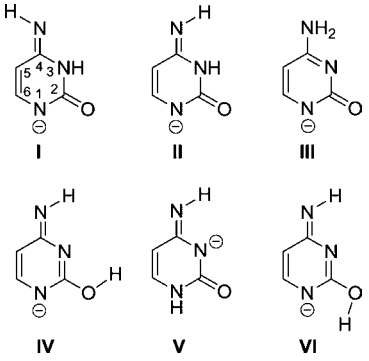
INTRODUCTION

Proton transfer in tautomeric systems is the key step in numerous important biological processes. For many transformations, the energetically less stable tautomer is often an active intermediate, which dictates the mechanism of the process.[1] A number of tautomers of the DNA bases can be stabilized by coordination to transition metals.[2] Where structure features are retained, biological activity is also kept.[3] Because of the close relationship between the structure and the biological function,[4] the control of the stability of the biological structures is challenging.

A group of six most stable tautomers with energies within 10 kcal mol^{-1} of each other has been identified by density functional theory (DFT) calculations for the monodeprotonated cytosine anion from 95 possible structures (Chart 1).[5] Tautomers **I** and **II** are imino-oxo rotamers that differ in the position of the imino hydrogen atom, **III** is an amino-oxo, **IV** and **VI** are imino-oxy rotamers that differ in the position of the O−H hydrogen atom, and **V** is an imino-oxo. In view of the wide range of coordination modes that are possible with the metals, a rich tautomeric chemistry should be expected for the monodeprotonated cytosine anion. However, the transition-metal complexes with this ligand are rare.[6] They involve N1- and/or N3-monodentated,[7] N3,N4-chelate,[8] and N1,N3- or N3,N4-bridging[9] coordination.

Some toxicological side-effects of cisplatin and the drug resistance developed by some tumors have stimulated research with transition metal different from platinum.[10] Thus, a few reports of anticancer active osmium complexes have recently appeared.[11] We have initiated a research program focused on the study of the behavior of osmium-polyhydride compounds with DNA bases, with the aim of investigating new models of anticancer drugs. Thus, some months ago, we reported the reactivity of the d^2-complex $OsH_6(P^iPr_3)_2$ toward 1-methylthymine, 1-methyluracil, thymidine, 5-methyluridine, deoxyuridine, and uridine.[12] Now, we have studied the behavior of this polyhydride with cytosine, deoxycytidine, and cytidine. In this

Chart 1. Most Stable Tautomers of Monodeprotonated Cytosine



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paper, we report the results of this study showing the stabilization of some cytosinato tautomers resulting from novel coordination modes of the anion.

RESULTS AND DISCUSSION

1. Cytosinate Tautomers and Their Coordinations. The saturated hexahydride d^2-complex $OsH_6(P^iPr_3)_2$ (**1**) activates C−H bonds of a broad number of organic molecules[13] and by protonation with weak Brønsted acids, releases molecular hydrogen to afford osmium-hydride d^4-species, which contain the corresponding conjugated Brønsted base as a ligand.[14] In agreement with this, the treatment of toluene solutions of **1** with 1.0 equiv of cytosine, for 3 h, under reflux produces the deprotonation of the nucleobase and the formation of the trihydride derivative $OsH_3(cytosinate)(P^iPr_3)_2$ (**2**), which is isolated as a white solid in 58% yield according to eq 1.

$$\underset{\mathbf{1}}{OsH_6(P^iPr_3)_2} + \text{cytosine} \rightarrow \underset{\mathbf{2}}{OsH_3(\text{cytosinate})(P^iPr_3)_2} + 2H_2 \quad (1)$$

Figure 1 shows the ^{1}H NMR spectrum of **2**, in benzene-d_6, at 343 K, between 8.1 and 7.4 ppm. According to it and the

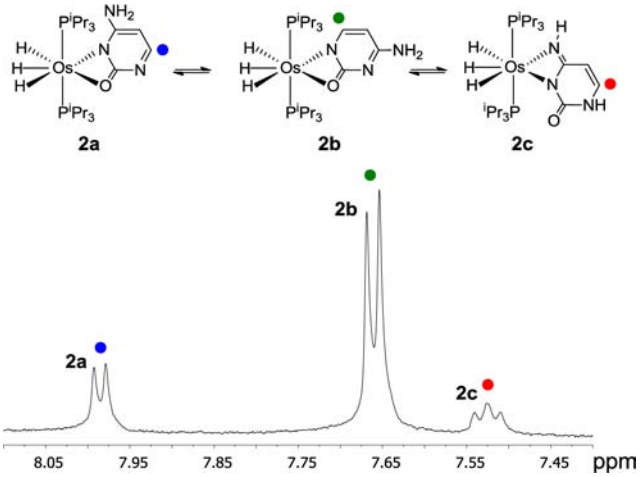

Figure 1. ^{1}H NMR spectrum (400 MHz, C_6D_6, 343 K) of **2** between 8.1 and 7.4 ppm.

$^{31}P\{^1H\}$ NMR spectrum, this compound exist as a 1.5:5:1 equilibrium mixture of the isomeric species **2a**, **2b**, and **2c**, in solution. Complexes **2a** and **2b** are coordination isomers of the amino-oxo tautomer **III**. The first of them results from the chelate coordination of the nitrogen atom at position 3 and the carbonyl group to the $OsH_3(P^iPr_3)_2$ metal fragment, whereas the second one is generated by coordination of the nitrogen atom at position 1 and the carbonyl group. Complex **2c** results from the chelate coordination of the endocyclic nitrogen atom at position 3 and the exocyclic NH-nitrogen atom of a C-NH rotamer of the imino-oxo tautomer **V**. As expected for the coordination modes of the deprotonated nucleobase in **2a** and **2b**, the resonances corresponding to the hydrogen atoms bonded to the carbon atoms at position 6 appear at 8.01 (**2a**) and 7.67 (**2b**) ppm as doublets with H−H coupling constants of 5.6 and 6.0 Hz, respectively, by spin-coupling with the neighboring hydrogen atom (5H). On the other hand, the resonance corresponding to this hydrogen atom of **2c** is observed at 7.47 ppm as a double doublet, with both H−H coupling constants of 6.1 Hz, by spin-coupling with the hydrogen atoms bonded to the carbon atom at position 5 and the nitrogen atom at position 1. In agreement with the presence of a free NH_2 group in both **2a** and **2b**, the spectrum also contains broad resonances at 4.11 (**2a**) and 5.03 (**2b**) ppm. In contrast to **2a** and **2b**, isomer **2c** displays two NH signals at 13.05 and 4.56 ppm; the first of them corresponding to the hydrogen atom bonded to the nitrogen atom at position 1 is observed as a doublet by spin-coupling with the hydrogen atom bonded to the carbon atom at position 6, while the second one due to the exocyclic NH group appears as a singlet. In the high field region, the spectrum shows three hydride resonances at −12.92 (**2b**), −12.88 (**2a**), and −11.91 (**2c**) ppm. The presence of only one signal per isomer is consistent with the operation of two thermally activated site exchange processes for each isomer, in agreement with the behavior of related OsH_3-derivatives.[12,14b,c,15] As expected for equivalent phosphine ligands the $^{31}P\{^1H\}$ NMR spectrum contains three singlets at 33.9 (**2b**), 30.2 (**2c**), and 29.8 (**2a**) ppm.

Isomer **2b** cocrystallizes with **2c** from saturated pentane solutions of **2**. Two molecules, one of each isomer, are associated through N−H···N and N−H···O hydrogen bonds to form [**2b**·**2c**] units, which dimerize (Figure 2). The N−H···N

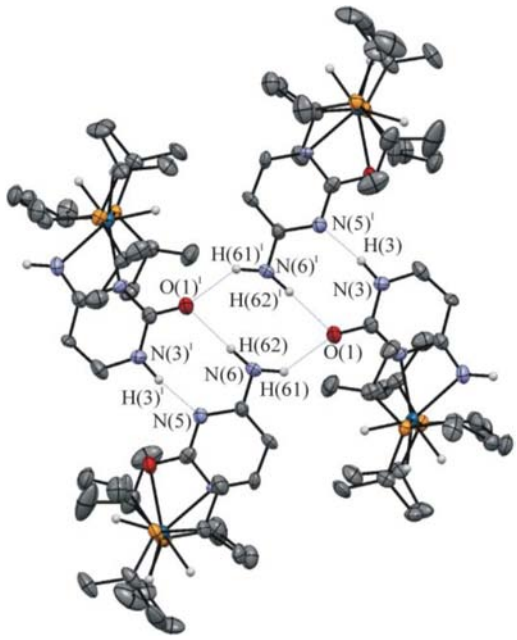

Figure 2. View of the interactions via hydrogen bonding in the structure of $[\mathbf{2b}\cdot\mathbf{2c}]_2$ (symmetry code: (I) $1-x, 1-y, -z$).

hydrogen bond involves the free nitrogen atom at position 3 of the heterocycle of **2b** (N(5)) and the hydrogen atom ($H(3)^I$) bonded to the nitrogen atom at position 1 of the heterocycle of **2c** ($N(3)^I$). According to this, the $N(5)\cdots H(3)^I$ distance of 1.81(4) Å is shorter than the sum of the van der Waals radii of the hydrogen and nitrogen ($r_{vdw}(H)$ = 1.20 Å, $r_{vdw}(N)$ = 1.55 Å),[16] the $N(3)^I-H(3)^I\cdots N(5)$ angle of 172(6) is almost linear, and the separation $N(3)^I\cdots N(5)$ is 2.81(1) Å. The N−H···O hydrogen bond implies one of the hydrogen atoms of the exocyclic NH_2 group (N(6)) of **2b** (H(62)) and the oxygen atom of the free carbonyl group of **2c** ($O(1)^I$). This hydrogen bond is strongly supported by the $O(1)^I\cdots H(62)$ distance of 2.02(3) Å, which is shorter than the sum of the van der Waals

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radii of the hydrogen and oxygen (r_{vdw}(O) = 1.52 Å),[12,16a,17] the almost linear N(6)−H(62)−O(1)^{I} angle of 178(5)°, and the N(6)···O(1)^{I} separation of 3.02(1) Å. The dimerization between the [**2b**·**2c**] units to form [**2b**·**2c**]$_2$ takes place by means of two N−H···O hydrogen bonds between the free hydrogen atom (H(61)) of the NH_2 group of an unit and the oxygen atom of the free carbonyl group of the another. The interaction gives rise to H(61)···O(1) and N(6)···O(1) separations of 2.03(5) Å and 2.86(1) Å, respectively, and a N(6)−H(61)−O(1) angle of 139(5)°.

The $^{31}P\{^{1}H\}$ NMR spectrum of the freshly prepared solutions of the crystals of [**2b**·**2c**]$_2$, in benzene-d_6, at room temperature is consistent with Figure 2, showing two singlets in 1:1 intensity ratio (Figure 3). This solution slowly reaches the

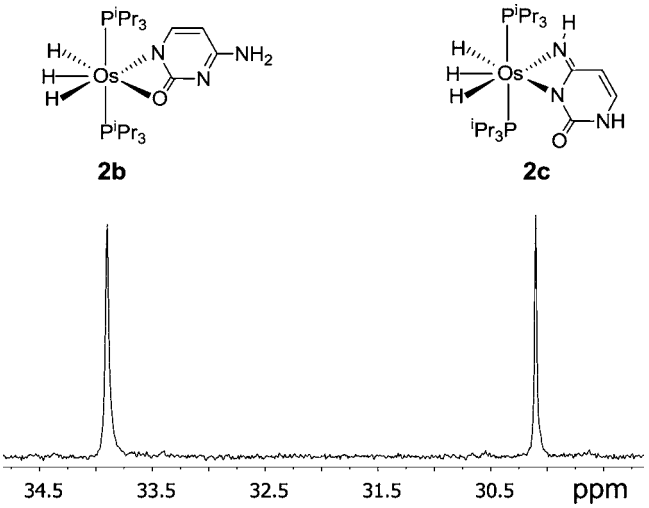

Figure 3. $^{31}P\{^{1}H\}$ NMR spectrum (202 MHz, C_6D_6, 298 K) of freshly prepared solutions of crystals of [**2b**·**2c**]$_2$.

equilibrium composition shown in Figure 1. This indicates that the composition of **2** depends upon its aggregation state, which has a marked influence on the hydrogen bonds between the isomers. Thus, since the difference in energy between them is small, the additional stability provided by the hydrogen bonds in the solid state shifts the equilibrium toward the formation of **2c**. Isomer **2a**, does not take part in the cocrystallization. In this context, it should be noted that the disposition of its free nitrogen atoms is not suitable for the formation of related hydrogen bonds.

Figure 4 shows a drawing of **2b**. The structure proves the chelate coordination of tautomer **III** by the nitrogen at position 1 of the heterocycle (N(4)) and the oxygen atom of the carbonyl group (O(2)). Thus, the geometry around the osmium atom can be rationalized as a distorted pentagonal bipyramid with the phosphine ligands occupying axial positions (P(3)−Os(2)−P(4) = 173.26(9)°). The metal coordination sphere is completed by the deprotonated nucleobase, which acts with a bite angle N(4)−Os(2)−O(2) of 60.0(2)°, and the hydride ligands. The Os(2)−N(4) and Os(2)−O(2) bond lengths are 2.182(6) and 2.221(6) Å, respectively.

Figure 5 shows a drawing of **2c**. In this case, the structure proves the chelate coordination of the deprotonated nucleobase by the nitrogen atom at position 3 of the heterocycle (N(1)) and the exocyclic nitrogen atom N(2). The geometry around the osmium atom is as that of **2b**; that is, a distorted pentagonal bipyramid with axial phosphines (P(1)−Os(1)−P(2) = 170.89(9)°) whereas the deprotonated nucleobase, which acts with a N(1)−Os(1)−N(2) bite angle of 59.1(3)°, and the hydride ligands lie in the perpendicular plane. The Os(1)−N(1) and Os(1)−N(2) distances are 2.166(7) and 2.235(7) Å, respectively.

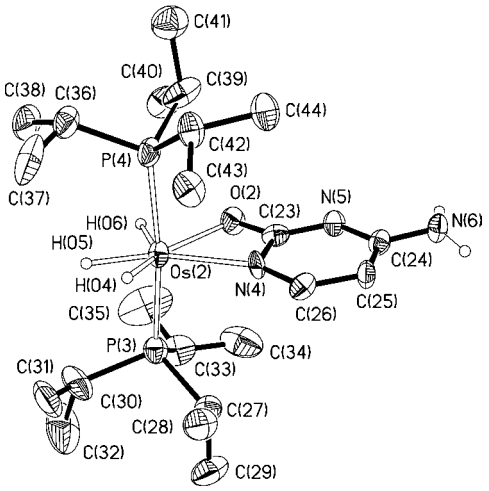

Figure 4. Molecular diagram of complex **2b**. Selected bond lengths (Å) and angles (deg): Os(2)−P(3) = 2.328(3), Os(2)−P(4) = 2.326(3), Os(2)−N(4) = 2.182(6), Os(2)−O(2) = 2.221(6), O(2)−C(23) = 1.278(10), C(23)−N(4) = 1.342(10), N(4)−C(26) = 1.357(9), C(25)−C(26) = 1.368(11), C(24)−C(25) = 1.377(11), C(24)−N(5) = 1.356(10), N(5)−C(23) = 1.352(10), C(24)−N(6) = 1.343(10); P(3)−Os(2)−P(4) = 173.26(9)°, N(4)−Os(2)−O(2) = 60.0(2)°.

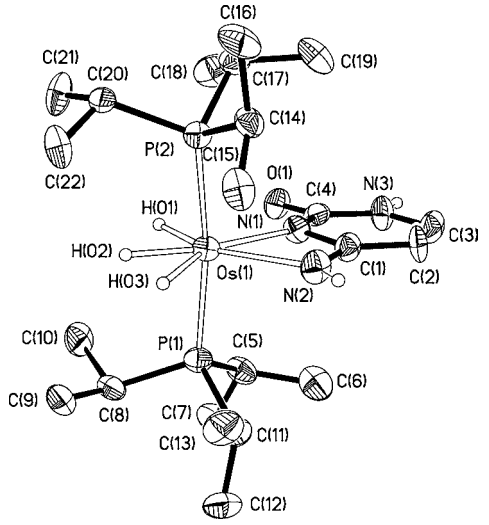

Figure 5. Molecular diagram of complex **2c**. Selected bond lengths (Å) and angles (deg): Os(1)−P(1) = 2.326(3), Os(1)−P(2) = 2.324(3), Os(1)−N(1) = 2.166(7), Os(1)−N(2) = 2.235(7), C(1)−N(2) = 1.290(10), C(1)−C(2) = 1.398(11), C(2)−C(3) = 1.381(12), C(3)−N(3) = 1.359(11), N(3)−C(4) = 1.386(10), C(4)−N(1) = 1.360(10), C(4)−O(1) = 1.267(9), N(1)−C(1) = 1.407(10); P(1)−Os(1)−P(2) = 170.89(9)°, N(1)−Os(1)−N(2) = 59.1(3)°.

2. Deprotonation of 2c. Isomer **2b** results from the deprotonation of the 2H-enol-amino and/or 1H-keto-amino tautomers of cytosine, which are within 0.96 kcal mol^{-1} of each other in gas phase.[6,18] Since the difference in stability between the isomers of **2** is small and **2c** contains a free carbonyl group and a hydrogen atom bonded to the nitrogen atom at position

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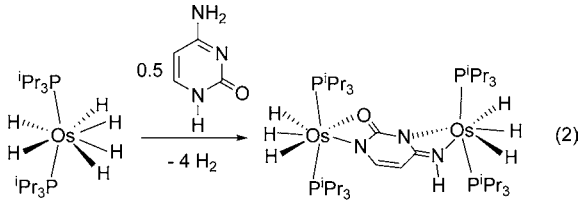
1 of the heterocycle, as the 1H-keto-amino tautomer of the cytosine, we reasoned that **2** could be deprotonated; that is, that under the appropriate conditions, the hexahydride complex **1** should perform the double deprotonation of cytosine. As expected, the treatment of toluene solutions of **1** with 0.5 equiv of the nucleobase, for 6 h, under reflux leads to the dinuclear complex **3** in 66% yield (eq 2), along with **2** (17%). In fact,



1 3 (2)

according to our initial hypothesis, its formation can be rationalized as the result from the deprotonation of a **2c** intermediate and the κ^2-N1,O-coordination of the resulting metal fragment to a new $OsH_3(P^iPr_3)_2$ unit.

Complex **3** was isolated as a pure white solid in 22% yield and characterized by X-ray diffraction analysis. Figure 6 shows a

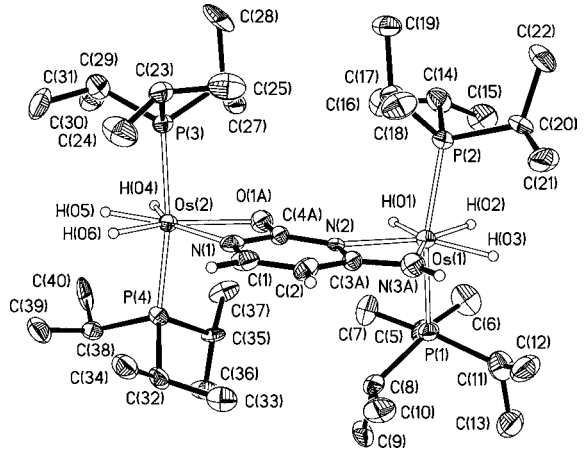


Figure 6. Molecular diagram of complex **3**. Selected bond lengths (Å) and angles (deg): Os(1)−N(2) = 2.199(8), Os(1)−N(3A) = 2.216(8), Os(2)−N(1) = 2.191(7), Os(2)−O(1A) = 2.235(7), O(1A)−C(4A) = 1.257(11), C(4A)−N(1) = 1.394(12), N(1)−C(1) = 1.344(11), C(1)−C(2) = 1.370(12), C(2)−C(3A) = 1.385(14), C(3A)−N(2) = 1.403(11), N(2)−C(4A) = 1.329(10), C(3A)−N(3A) = 1.312(10); P(1)−Os(1)−P(2) = 164.63(11)°, N(2)−Os(1)−N(3A) = 59.9(3)°, P(3)−Os(2)−P(4) = 168.71(9)°, N(1)−Os(2)−O(1A) = 59.5(3)°.

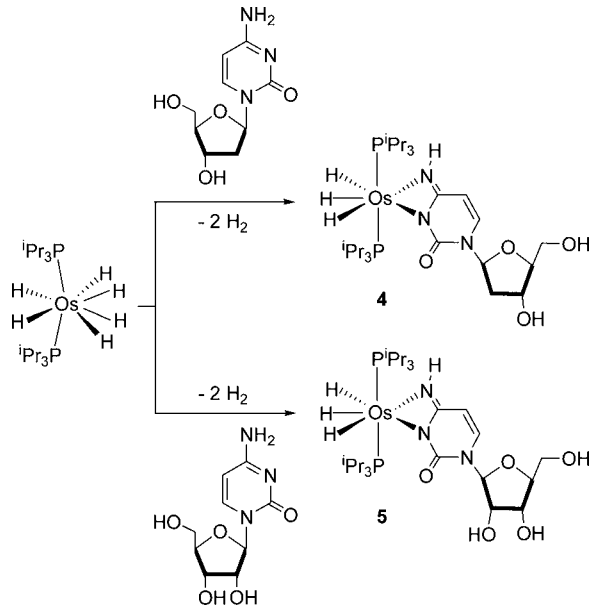
view of the molecule. The structure proves the double deprotonation of cytosine and the unprecedented coordination of the nucleobase skeleton as κ^2-N,N and κ^2-N,O to two different $OsH_3(P^iPr_3)_2$ metal fragments. Thus, the geometry around each osmium atom can be rationalized as a distorted pentagonal bipyramid with the phosphines occupying axial positions (P(1)−Os(1)−P(2) = 164.63(11)°, P(3)−Os(2)−P(4) = 168.71(9)°). The metal coordination spheres are completed by the donor atoms of the nucleobase skeleton, which act with bite angles N(2)−Os(1)−N(3A) and N(1)−Os(2)−O(1A) of 59.9(3)° and 59.5(3)°, and the hydride ligands. The Os(1)−N(2) and Os(1)−N(3A) bond lengths of 2.199(8) and 2.216(8) Å compare well with the respective Os−N distances in **2c**, whereas the Os(2)−N(1) and Os(2)−O(1A) bond lengths of 2.191(7) and 2.235(7) Å compare well with the respective Os−N and Os−O distances in **2b**.

The ^1H and $^{31}P\{^1H\}$ NMR spectra of **3** are consistent with the structure shown in Figure 6 and with those of **2b** and **2c**. As expected for the presence of two different $OsH_3(P^iPr_3)_2$ units, where the hydride ligands of each one undergo two site exchange processes in solution, the ^1H NMR spectrum in the high field region shows two resonances at −12.48 and −13.37 ppm, whereas the $^{31}P\{^1H\}$ NMR spectrum contains two singlets at 36.8 and 26.7 ppm in agreement with equivalent phosphine ligands within each $OsH_3(P^iPr_3)_2$ unit.

3. Deprotonation of Deoxycytidine and Cytidine. Since osmium-d^6 complexes are relatively inert toward substitution reactions because of the dependence of the crystal field activation energy on Δ_0,[19] the reactions shown in eqs 1 and 2 are a promising alternative to coordinate pyrimidinic nucleobases to osmium. They are a consequence of the fair acidity of the hydrogen atoms bonded to the heteroatoms of the nucleobases.[12] Nucleosides deoxycytidine and cytidine result from the formal replacement of the acidic hydrogen atom bonded to the nitrogen atom at position 1 of the 1H-keto-amino taoutomer of cytosine by deoxyribose and ribose, respectively. The position of the sugar in the nucleosides prevents the formation of species related to **2b**, containing a deprotonated nucleoside, while compounds related to **2c** should not be at the first glance discarded. This prompted us to perform the reactions of the hexahydride with nucleosides.

Treatment of toluene solutions of **1** with 3.0 equiv of deoxycytidine and cytidine, for 3.5 h, under reflux affords complexes **4** and **5**, as a result from the formal deprotonation of the amino group of the nucleosides and the κ^2-N,N-coordination of the nucleobase skeleton (Scheme 1). These

Scheme 1



compounds related to **2c** were isolated as yellow solids in 66% (**4**) and 63% (**5**) yield. Since the rather weak acidity of the amino group of the nucleosides,[20] the formation of **4** and **5** suggests that the commercially available amino-keto tautomers have spectroscopically undetected 3H-keto-imino tautomers that are able to protonate the hexahydride complex. In addition, it should be mentioned that in spite of the versatile reactivity of

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the osmium polyhydrides with alcohols, aldehydes, and ketones,[21] the reactions shown in Scheme 1 are selective, and side products resulting from the reactions of the sugars are not detected.

The ^{1}H and ^{31}P{^{1}H} NMR spectra of **4** and **5**, in toluene-d_8, at 353 K agree well with those of **2c**. The ^{1}H NMR spectra of both compounds contain only high field resonances at −12.16 ppm, in agreement with the operation of site exchange processes of the hydride ligands, whereas the ^{31}P{^{1}H} NMR spectra show at 30.5 (**4**) and 29.9 (**5**) ppm singlets due to equivalent phosphine ligands.

CONCLUDING REMARKS

This study has revealed that the d^2-hexahydride complex $OsH_6(P^iPr_3)_2$ is able to deprotonate cytosine. The coordination of the cytosinate anion to the resulting $OsH_3(P^iPr_3)_2$ metal fragment generates a d^4 OsH_3(cytosinate)$(P^iPr_3)_2$ species, which exists as an equilibrium mixture of three isomers in solutions. The behavior of the mixture is controlled by the minor isomer. The disposition of its free heteroatoms and the hydrogen atom bonded to them is suitable to form hydrogen bonds with the major isomer. The stability provided by the interactions is sufficient to shift the equilibrium. Thus, the major isomer selectively cocrystallizes with the minor one, to form a [major·minor]$_2$ dimer, from saturated pentane solutions of the mixture. The presence of an acidic hydrogen atom at the nitrogen at position 1 of the heterocycle of the minor isomer allows the deprotonation of the coordinated cytosinato group. As a consequence of this, the reaction of the hexahydride with 0.5 equiv of cytosine has given rise to the preparation of an unprecedented dimer with a double deprotonated cytosine that is coordinated κ^2-N4,N3 and κ^2-N1,O to two different $OsH_3(P^iPr_3)_2$ metal fragments. Minor, sprectroscopically undetected, 3H-keto-imino tautomers also appear to govern the reactions of the hexahydride complex with the commercially available keto-amino deoxycytidine and cytidine nucleosides, which yield the corresponding OsH_3(nucleosidate)$(P^iPr_3)_2$ compounds, related to the minor OsH_3(cytosinate)$(P^iPr_3)_2$ isomer, with κ^2-N3,N4-coordination of the anion.

In conclusion, the minor tautomers have a marked influence in the chemistry of cytosine and its nucleosides deoxycytidine and cytidine.

EXPERIMENTAL SECTION

General Information. All reactions were carried out with rigorous exclusion of air using Schlenk-tube techniques. Solvents (except methanol that was dried over magnesium and distilled under argon) were obtained oxygen- and water-free from an MBraun solvent purification apparatus. ^{1}H, ^{31}P{^{1}H}, and ^{13}C{^{1}H} NMR spectra were recorded on Bruker 300 ARX, Bruker Avance 300 MHz, Bruker Avance 400 MHz, and Bruker Avance 500 MHz instruments. Chemical shifts (expressed in parts per million) are referenced to residual solvent peaks (^{1}H, ^{13}C{^{1}H}) or to external 85% H_3PO_4 (^{31}P{^{1}H}). Coupling constants J and N are given in hertz. The ^{13}C{^{1}H} NMR spectra and some ^{1}H and ^{31}P{^{1}H} NMR spectra had to be recorded at high temperatures because of the low solubility of the complexes at room temperature. Attenuated total reflection infrared spectra (ATR-IR) of solid samples were run on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. C, H, and N analyses were carried out in a Perkin-Elmer 2400 CHNS/O analyzer. High-resolution electrospray mass spectra were acquired using a MicroTOF-Q hybrid quadrupole time-of-flight spectrometer (Bruker Daltonics, Bremen, Germany). $OsH_6(P^iPr_3)_2$ was prepared by published methods.[22]

Reaction of $OsH_6(P^iPr_3)_2$ with Cytosine: Preparation of 2a, 2b, and 2c. A colorless solution of **1** (100 mg, 0.193 mmol) in toluene (10 mL) was treated with 1.0 equiv of cytosine (21.5 mg, 0.193 mmol) and heated under reflux during 3 h. During this time the solution changed from colorless to pale yellow. The resulting solution was filtered through Celite, and the solvent was removed in vacuo. Addition of pentane to the residue afforded a white solid that was washed with pentane (2 × 1 mL) and dried in vacuo. ^{1}H and ^{31}P{^{1}H} NMR spectroscopies show a mixture of complexes **2a**, **2b**, and **2c** in a 1.5:5:1 ratio. Anal. Calcd for $C_{22}H_{49}N_3OOsP_2$: C, 42.36; H, 7.92; N, 6.74. Found: C, 42.69; H, 8.14; N, 6.52.

*Spectroscopic Data for **2a**.* ^{1}H NMR (400 MHz, benzene-d_6, 343 K): δ 8.01 (d, J_{H-H} = 5.6, 1H, =C(6)*H*), 5.51 (d, J_{H-H} = 5.6, 1H, =C(5)*H*), 4.11 (br, 2H, NH_2), 1.89 (m, 6H, PC*H*$(CH_3)_2$), 1.15 (dvt, J_{H-H} = 7.1, N = 13.6, 18H, PCH$(CH_3)_2$), 1.13 (dvt, J_{H-H} = 7.1, N = 13.6, 18H, PCH$(CH_3)_2$), −12.88 (br, 3H, OsH). ^{31}P{^{1}H} NMR (161.9 MHz, benzene-d_6, 293 K): δ 29.8 (s). ^{13}C{^{1}H} NMR plus HMBC (101 MHz, benzene-d_6, 343 K): δ 169.7 (s, *C*O, C2), 160.7 (s, *C*NH_2, C4), 157.2 (s, =CH, C6), 93.0 (s, =CH, C5), 26.9 (vt, N = 31, PCH$(CH_3)_2$), 20.4, 20.1 (both s, PCH$(CH_3)_2$).

*Spectroscopic Data for **2b**.* ^{1}H NMR (400 MHz, benzene-d_6, 343 K): δ 7.67 (d, J_{H-H} = 6.0, 1H, =C(6)*H*), 5.36 (d, J_{H-H} = 6.0, 1H, =C(5)*H*), 5.03 (br, 2H, NH_2), 1.89 (m, 6H, PC*H*$(CH_3)_2$), 1.15 (dvt, J_{H-H} = 7.1, N = 13.6, 18H, PCH$(CH_3)_2$), 1.13 (dvt, J_{H-H} = 7.1, N = 13.6, 18H, PCH$(CH_3)_2$), −12.92 (br, 3H, OsH). ^{31}P{^{1}H} NMR (161.9 MHz, benzene-d_6, 343 K): δ 33.9 (s). ^{13}C{^{1}H} NMR plus HMBC (101 MHz, benzene-d_6, 343 K): δ 168.2 (s, *C*O, C2), 163.8 (s, *C*NH_2, C4), 155.0 (s, =CH, C6), 94.4 (s, =CH, C5), 26.9 (vt, N = 31, PCH$(CH_3)_2$), 20.5, 20.2 (both s, PCH$(CH_3)_2$).

*Spectroscopic Data for **2c**.* ^{1}H NMR (400 MHz, benzene-d_6, 343 K): δ 13.05 (d, J_{H-H} = 6.1, 1H, N(1)*H*), 7.47 (dd, J_{H-H} = 6.1, J_{H-H} = 6.1, 1H, =C(6)*H*), 4.60 (d, J_{H-H} = 6.1, 1H, =C(5)*H*), 4.56 (s, 1H, NH-Os), 1.89 (m, 6H, PC*H*$(CH_3)_2$), 1.05 (dvt, J_{H-H} = 6.6, N = 12.5, 36H, PCH(C*H*$_3)_2$), −11.91 (t, J_{H-P} = 12.8, Os−H). ^{31}P{^{1}H} NMR (161.9 MHz, benzene-d_6, 343 K): δ 30.2 (s). Because of its low concentration and the low solubility of the mixture suitable ^{13}C{^{1}H} NMR data could not be recorded.

Reaction of $OsH_6(P^iPr_3)_2$ with 0.5 Equiv of Cytosine: Preparation of 3. A colorless solution of **1** (100 mg, 0.193 mmol) in toluene (10 mL) was treated with 0.5 equiv of cytosine (10.7 mg, 0.096 mmol) and heated under reflux during 6 h. During this time the solution changed from colorless to pale yellow. The resulting solution was filtered through Celite, and the solvent was removed in vacuo. The ^{31}P{^{1}H} NMR spectrum of the residue thus obtained showed the presence of complexes **1**, **2**, and **3** in a ratio 17:17:66, respectively. The residue was washed with methanol, affording complex **3** as a white solid in pure form. Yield: 45 mg (22%). Anal. Calcd for $C_{40}H_{93}N_3OOs_2P_4$: C, 42.27; H, 8.25; N, 3.70. Found: C, 42.56; H, 7.98; N, 3.43. IR (cm^{-1}): ν(N−H) 3410 (w); ν(Os−H) 2144 (w), 2117 (w); ν(C=C) 1580 (s). ^{1}H NMR (300 MHz, benzene-d_6, 333 K): δ 7.30 (d, J_{H-H} = 6.3, 1H, =C(6)*H*), 4.89 (d, J_{H-H} = 6.3, 1H, =C(5)*H*), 3.92 (br, 1H, NH), 2.00 (m, 6H, PC*H*$(CH_3)_2$), 1.96 (m, 6H, PC*H*$(CH_3)_2$), 1.31 (dvt, J_{H-H} = 6, N = 11.7, 18H, PCH(C*H*$_3)_2$), 1.23 (dvt, J_{H-H} = 6.9, N = 12.9, 36H, PCH(C*H*$_3)_2$), 1.12 (dvt, J_{H-H} = 7.5, N = 12, 18H, PCH(C*H*$_3)_2$), −12.48 (br, 3H, OsH), −13.37 (br, 3H, OsH). ^{31}P{^{1}H} NMR (161.9 MHz, benzene-d_6, 333 K): δ 36.8 (s), 26.7 (s). ^{13}C{^{1}H} NMR plus HMBC (75 MHz, benzene-d_6, 343 K): δ 170.2 (s, *C*O, C2), 166.8 (s, *C*NH-Os, C4), 151.2 (s, =CH, C6), 96.1 (s, =CH, C5), 28.3 (vt, N = 22.5, PCH$(CH_3)_2$), 27.3 (vt, N = 22.7, PCH$(CH_3)_2$), 21.5, 20.7, 20.3 (all s, PCH(C*H*$_3)_2$).

Reaction of $OsH_6(P^iPr_3)_2$ (1) with Deoxycytidine: Preparation of 4. A colorless solution of **1** (100 mg, 0.193 mmol) in toluene (10 mL) was treated with 3.0 equiv of deoxycytidine (131.9 mg, 0.579 mmol) and heated under reflux during 3.5 h. During this time the solution changed from colorless to pale yellow. The resulting solution was filtered through Celite and the solvent was removed in vacuo. The subsequent addition of cold pentane to the residue afforded a yellow solid. Yield: 93.8 mg (66%). Anal. Calcd for $C_{27}H_{57}N_3O_4OsP_2$: C, 43.83; H, 7.76; N, 5.68. Found: C, 44.26; H, 8.04; N, 5.92. ESI-HRMS (m/z); calcd for $C_{27}H_{58}N_3O_4OsP_2$ [M + H]$^+$ 742.3513; found: 742.3512. IR (cm^{-1}): ν(OH) 3330 (br), ν(Os−H); 2114 (m), ν(C=O) 1631 (s), ν(C=C) 1551. ^{1}H NMR (400 MHz, toluene-d_8, 298 K):

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δ 7.55 (d, J_{H-H} = 7.2, 1H, =C(6)*H*), 6.48 (dd, J_{H-H} = 6.5 1H, NC*H*), 5.33 (very br, 1H, OH), 4.85 (s, 1H, NH), 4.77 (d, 1H, J_{H-H} = 7.2, =C(5)*H*), 4.75 (m, 1H, C*H*OH), 4.22 (m, 1H, C*H*CH_2OH), 3.97 (d, J_{H-H} = 10.4, 1H, CH_2OH), 3.91 (d, J_{H-H} = 10.4, 1H, CH_2OH), 2.47 (m, 1H, CH_2), 2.38 (m, 1H, CH_2), 2.30 (very br, 1H, OH), 2.03 (m, 6H, PCH(CH_3)$_2$), 1.22 (dvt, J_{H-H} = 6.9, *N* = 13.7, 18H, PCH(CH_3)$_2$), 1.20 (dvt, 18H, J_{H-H} = 6.6, *N* = 12.8, PCH(CH_3)$_2$), −12.16 (t, J_{P-H} = 12.0, 3H, OsH). $^{31}P\{^1H\}$ NMR (121.4 MHz, toluene-d_8, 353 K): δ 30.5 (s). $^{13}C\{^1H\}$ NMR plus HMBC (75 MHz, toluene-d_8, 353 K): δ 168.1 (t, J_{C-P} = 2.3, *C*NH-Os, C4), 154.1 (s, *C*O, C2), 139.4 (s, =*C*H, C6), 97.0 (s, =*C*H, C5), 89.6 (s, N*C*H), 88.4 (s, *C*HCH$_2$), 72.8 (s, *C*HOH), 63.7 (s, *C*H$_2$OH), 41.5 (s, *C*H$_2$), 27.9 (vt, *N* = 23.2, PCH(CH_3)$_2$), 21.0 (d, J_{C-P} = 3.2, PCH(CH_3)$_2$), 20.7 (s, PCH(CH_3)$_2$).

Reaction of $OsH_6(P^iPr_3)_2$ (1) with Cytidine: Preparation of 5. A colorless solution of **1** (100 mg, 0.193 mmol) in toluene (10 mL) was treated with 3.0 equiv of cytidine (141.0 mg, 0.579 mmol) and heated under reflux during 3.5 h. During this time the solution changed from colorless to pale yellow. The resulting solution was filtered through Celite, and the solvent was removed in vacuo. The subsequent addition of cold pentane to the residue afforded a yellow solid. Yield: 91.0 mg (63%). Anal. Calcd for $C_{27}H_{57}N_3O_5OsP_2$: C, 42.90; H, 7.60; N, 5.56. Found: C, 42.63; H, 7.97; N, 5.34. ESI-HRMS (electrospray, *m*/*z*): calcd for $C_{27}H_{57}N_3O_5OsP_2$ $[M]^+$ 758.3374; found: 758.3462. IR (cm^{-1}): ν(OH) 3277 (br); ν(OsH) 2123 (w); ν(C=O) 1636 (s), ν(C=C) 1550. ^1H NMR (300 MHz, toluene-d_8, 353 K): δ 6.88 (d, J_{H-H} = 7.3, 1H, =C(6)*H*), 6.40 (very br, 1H, OH), 5.61 (d, J_{H-H} = 3.4, 1H, NC*H*), 5.31 (very br, 1H, OH), 4.76 (s, 1H, NH), 4.72 (dd, J_{H-H} = 5.6, J_{H-H} = 5.1, 1H, C*H*OH), 4.62 (dd, J_{H-H} = 3.4, J_{H-H} = 5.1, 1H, C*H*OH), 4.46 (d, J_{H-H} = 7.3, 1H, =C(5)*H*), 4.21 (m, 1H, C*H*CH$_2$OH), 3.80 (d, J_{H-H} = 11.9, 1H, CH_2OH), 3.65 (d, J_{H-H} = 11.3, 1H, CH_2OH), 3.11 (s, 1H, OH), 1.97 (m, 6H, PC*H*(CH_3)$_2$), 1.18 (dvt, J_{H-H} = 6.0, *N* = 12.0, 18H, PCH(CH_3)$_2$), 1.14 (dvt, J_{H-H} = 6.0, *N* = 12.0, 18H, PCH(CH_3)$_2$), −12.16 (t, J_{P-H} = 11.9, 3H, OsH). $^{31}P\{^1H\}$ NMR (121.4 MHz, toluene-d_8, 353 K): δ 29.9 (s). $^{13}C\{^1H\}$ NMR plus HMBC (75 MHz, toluene-d_8, 353 K): δ 168.1 (t, J_{C-P} = 2.6, *C*NH-Os, C4), 155.0 (s, *C*O, C2), 139.0 (s, =*C*H, C6), 96.6 (s, =*C*H C5), 95.8 (s, NCH), 87.00 (s, *C*HCH$_2$), 76.9 (s, *C*HOH), 71.9 (s, *C*HOH), 63.3 (s, *C*H$_2$OH), 27.9 (vt, *N* = 22.4, PCH(CH_3)$_2$), 20.9 and 20.7 (both s, PCH(CH_3)$_2$).

Structural Analysis of Complexes [2b·2c] and 3. Crystals suitable for the X-ray diffraction were obtained by cooling a solution of the mixture of derivatives **2a**, **2b**, and **2c** in pentane ([**2b·2c**]) or by cooling a solution of **3** in pentane. X-ray data were collected on a Bruker Smart APEX CCD ([**2b·2c**]) and on an Oxford Diffraction Xcalibur TS (**3**) using graphite monochromated Mo Kα radiation (λ = 0.71073 Å). Data were collected over the complete sphere and were corrected for absorption by using a multiscan method applied with the CrisAlys RED package[23] for complex **3**, and with the SADABS program[24] for complexes [**2b·2c**]. The structures of all compounds were solved by the Patterson method. Refinement, by full-matrix least-squares on F^2 with SHELXL97,[25] was similar for all complexes, including isotropic and subsequently anisotropic displacement parameters. The atoms O(1), N(3), C(3), and C(4) of the cytosinato ligand of complex **3** were found to be disordered. These atoms were defined with two moieties (50, 50), complementary occupancy factors, isotropic atoms, and restrained geometry. The hydrogen atoms (except hydride ligands and those of the cytosinato ligands) were calculated and refined using a restricted riding model. Hydride ligands were observed in the difference Fourier maps and refined with restrained Os−H bond length (1.59(1) Å, CSD). In the last cycles of refinement of dimer [**2b·2c**] residual electronic peaks as possible hydrogen atoms bonded to O(1) and N(3) were observed in the difference Fourier maps. The refinement of one of these residual electronic peaks as a hydrogen atom bonded to O(1) was not appropriate (imino-oxyl tautomer). However, the refinement of the other residual density peak as a hydrogen bonded to N(3) was appropriate. This, in addition to the C−C, C−O, and C−N bond distances in the cytositato ligand, as well as the hydrogen bonds observed, strongly supports that in the solid state this isomer is as in solution, that is, an imino-oxo tautomer. In the checkCIF of both structures there are alerts of level A that are due to a relatively large residual density on the osmium atoms. These residual density peaks are ghost peaks residing less than 1 Å from the metal and are chemically meaningless. The absorption correction did not improve the refinement.

Crystal Data for [2b·2c]. $C_{44}H_{98}N_6O_2Os_2P_4·0.5(C_5H_{12})$, M_r 1283.64, colorless, prism (0.08 × 0.07 × 0.03), triclinic, space group $P\bar{1}$, *a* = 11.9800(11) Å, *b* = 16.5360(15) Å, *c* = 16.9391(16) Å, α = 93.0220(10)°, β = 98.4770(10)°, γ = 111.0880(10)°, *V* = 3076.3(5) Å^3, *Z* = 2, D_{calc} = 1.386 g cm^{-3}, *F*(000) = 1306, *T* = 100(2) K, μ 4.266 mm^{-1}. 37406 measured reflections (2θ: 3−58°, ω scans 0.3°), 14297 unique (R_{int} = 0.0827); minimum/maximum transmission factors 0.717/0.827. Final agreement factors were R^1 = 0.0499 (7102 observed reflections, $I > 2\sigma(I)$) and wR^2 = 0.1025; data/restraints/parameters 14297/9/599; GoF = 0.825. Largest peak and hole 3.744 and −2.173 e/Å^3.

Crystal Data for 3. $C_{40}H_{93}N_3OOs_2P_4$, M_r 1136.45, colorless, block (0.10 × 0.09 × 0.04), monoclinic, space group *P*2(1)/*n*, *a* = 14.1939(9) Å, *b* = 15.7893(11) Å, *c* = 21.4859(13) Å, β = 96.021(6)°, *V* = 4788.7(5) Å^3, *Z* = 4, D_{calc} = 1.576 g cm^{-3}, *F*(000) = 2296, *T* = 100(2) K, μ 5.467 mm^{-1}. 21958 measured reflections (2θ: 4−58°, ω scans 0.3°), 10920 unique (R_{int} = 0.0927); minimum/maximum transmission factors 0.966/1.000. Final agreement factors were R^1 = 0.0715 (6256 observed reflections, $I > 2\sigma(I)$) and wR^2 = 0.1051; data/restraints/parameters 10920/6/477; GoF = 0.984. Largest peak and hole 1.546 and −1.356 e/ Å^3.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

CIF files giving positional and displacement parameters, crystallographic data, and bond lengths and angles of compounds **2b·2c** and **3**. NMR and IR spectra of compounds **2**, **3**, **4**, and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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