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Irreversible Insertion of Benzonitrile into Platinum(II)−Nitrogen Bonds of Nucleobase Complexes. Synthesis and Structural Characterization of Stable Azametallacycle Compounds

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Deprotonation of 1-methylcytosine (1-MeCy) and 9-methyladenine (9-MeAd) promoted by *cis*-$[L_2Pt(\mu\text{-}OH)]_2(NO_3)_2$ (L = PPh_3, $PMePh_2$, $^1/_2$dppe) in PhCN causes the irreversible insertion of a nitrile molecule into the Pt−N4 and Pt−N6 bonds of the cytosinate and adeninate ligands, respectively, to form the stable azametallacycle complexes *cis*-$[L_2PtNH{=}C(Ph)\{1\text{-}MeCy(-2H)\}]NO_3$ (L = PPh_3, **1**; $PMePh_2$, **2**; $^1/_2$dppe, **3**) and *cis*-$[L_2PtNH{=}C(Ph)\{9\text{-}MeAd(-2H)\}]NO_3$ (L = PPh_3, **4**; $PMePh_2$, **5**) containing the deprotonated form of the molecules (*Z*)-9-*N*-(1-methyl-2-oxo-2,3-dihydropyrimidin-4(1*H*)-ylidene)benzimidamide and (*Z*)-*N*-(9-methyl-1*H*-purin-6(9*H*)-ylidene)benzimidamide. Single-crystal X-ray analyses of **2** and **4** show the metal coordinated to the N3 cytosine site [Pt−N3 = 2.112(7) Å] and to the N1 site of adenine [Pt−N1 = 2.116(6) Å] and to the nitrogen atom of the inserted benzonitrile [Pt−N2 = 2.043(6) and 2.010(6) Å in **2** and **4**, respectively], with the exocyclic nucleobase amino nitrogen bound to the carbon atom of the CN group. Complex **2**, in solution, undergoes a dynamic process related to a partially restricted rotation around Pt−P bonds, arising from a steric interaction of the oxygen atom of the cytosine with one ring of the phosphine ligands. The reaction of **4** with acetylacetone (Hacac) causes the quantitative protonation of the anionic ligand, affording the acetylacetonate complex *cis*-$[(PPh_3)_2Pt(acac)]NO_3$ and the free benzimidamide NH=C(Ph){9-MeAd(−H)}. In the same experimental conditions, complex **3** reacts with Hacac only partially.

Introduction

The coordination of a nitrile (RC≡N) to a metal center [M] increases the rate of the nucleophilic attack to the carbon atom of the CN group.[1] When the nucleophile (Nu) is a protic species, the imino derivative [M]−NH=C(Nu)R is formed.[2] In this context, we have recently described the azametallacycles *cis*-$[L_2PtNH{=}C(Me)\{1\text{-}MeCy(-2H)\}]^+$ and *cis*-$[L_2PtNH{=}C(Me)\{9\text{-}MeAd(-2H)\}]^+$ (L = PPh_3, $PMePh_2$), where the anionic ligands are the deprotonated forms of the amidines shown in Chart 1.

These complexes are formed as the result of a formal insertion of an acetonitrile molecule into a Pt−N bond of the NH_2-deprotonated nucleobases 1-methylcytosine (1-MeCy) and 9-methyladenine (9-MeAd).[3] As an example, the trinuclear complex *cis*-$[(PMePh_2)_2Pt\{9\text{-}MeAd(-H),N^1N^6\}]_3^{3+}$, containing bridging 9-methyladeninate ligands,[4] dissolved in CH_3CN, gives the species *cis*-$[(PMePh_2)_2PtNH{=}C(Me)\{9\text{-}MeAd(-H)\}]^+$, as shown in Chart 2.

The reaction requires (i) the formation of a mononuclear species *cis*-$[L_2Pt(N{\equiv}C\text{-}Me)\{9\text{-}MeAd(-H)\}]^+$ containing a

Chart 1. Neutral Forms of the Anionic Ligands Found in Azametallacycle Complexes *cis*-$[L_2PtNH{=}C(Me)\{1\text{-}MeCy(-2H)\}]^+$ (Right) and *cis*-$[L_2PtNH{=}C(Me)\{9\text{-}MeAd(-2H)\}]^+$ (Left) (L = PPh_3, $PMePh_2$)

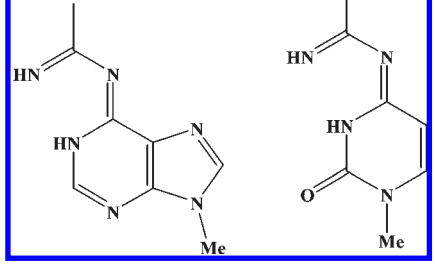

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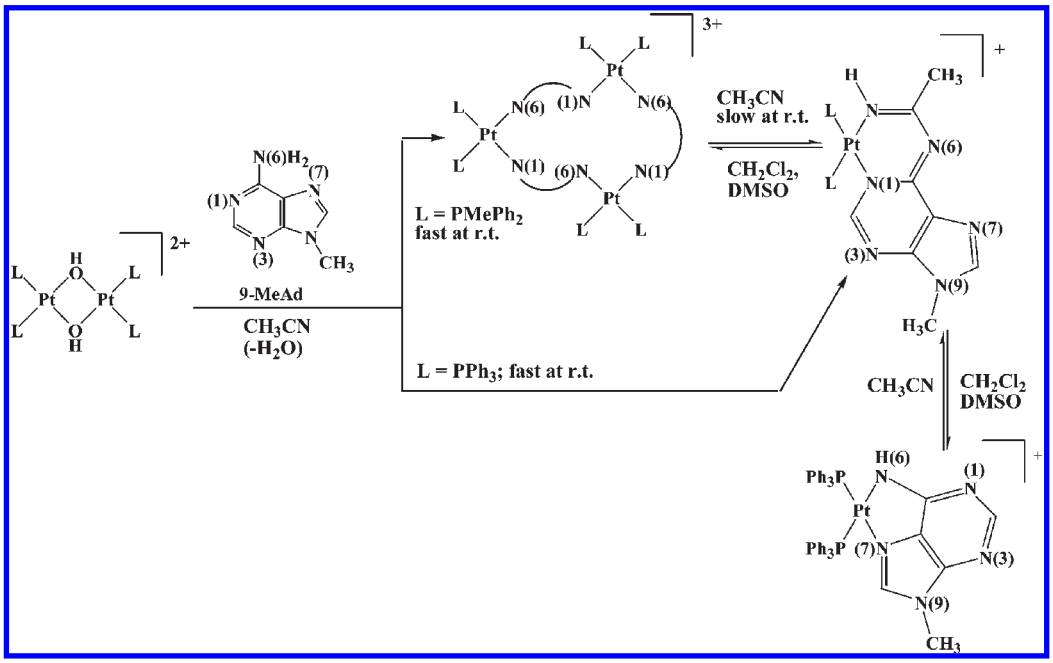
Chart 2



metal-coordinated solvent nitrile and the monodentate anionic 9-MeAd(−H), likely N^1-platinated, and (ii) the intramolecular nucleophilic attack at the carbon atom of the CH_3CN ligand by the N6 imino atom of the adeninate ion with concomitant migration of the N6*H* proton at the acetonitrile nitrogen atom to give the cyclic amidine complex. The trinuclear complex, in turn, was isolated by reacting the hydroxo complex *cis*-$[(PMePh_2)_2Pt(\mu\text{-}OH)]_2^{2+}$ with 9-MeAd, in a CH_3CN solution, in which the condensation reaction occurs quickly.[4] In the same experimental conditions, the hydroxo complex *cis*-$[(PPh_3)_2Pt(\mu\text{-}OH)]_2^{2+}$ leads directly to the insertion product *cis*-$[(PPh_3)_2PtNH{=}C(Me)\{9\text{-}MeAd(-2H)\}]^+$.

The adenine derivatives *cis*-$[L_2PtNH{=}C(Me)\{9\text{-}MeAd(-2H)\}]^+$, in chlorinated solvents, release *reversibly* the inserted CH_3CN molecule to form the trinuclear cyclic species *cis*-$[L_2Pt\{9\text{-}MeAd(-H)\}]_3^{3+}$ when L is $PMePh_2$ or the mononuclear chelate adeninate complex *cis*-$[(PPh_3)_2Pt\{9\text{-}MeAd(-H),N^6N^7\}]^+$ when L is PPh_3.[5]

In spite of the large number of studies dealing with metal nucleobase complexes,[6] coupling reactions of nitriles with the exocyclic nitrogen atoms of 9-MeAd and 1-MeCy have only a precedent in the literature.[7]

In this paper, we report the coupling reactions of benzonitrile with 1-MeCy and 9-MeAd, occurring when the hydroxo complexes *cis*-$[L_2Pt(\mu\text{-}OH)]_2(NO_3)_2$ {L = PPh_3, $PMePh_2$, $^1/_2$dppe [dppe = 1,2-bis(diphenylphosphino)ethane]} react in a PhCN solution. The insertion products *cis*-$[L_2PtNH{=}C(Ph)\{1\text{-}MeCy(-2H)\}]NO_3$ (L = PPh_3, **1**; $PMePh_2$, **2**; $^1/_2$dppe, **3**) and *cis*-$[L_2PtNH{=}C(Ph)\{9\text{-}MeAd(-2H)\}]NO_3$ (L = PPh_3, **4**; $PMePh_2$, **5**) have been isolated as pure compounds and fully characterized by multinuclear NMR studies, and the molecular structures of **2** and **4** have been confirmed by single-crystal X-ray analyses. Unlike the CH_3CN analogues, these compounds are indefinitely stable in a solution of dimethyl sulfoxide (DMSO) or chlorinated solvents; i.e., the formal insertion of PhCN into the Pt−N bond of the nucleobase is irreversible. Moreover, the protonation of the anionic ligands in **3** and **4** has been examined. The reaction, carried out by dissolving **4** in acetylacetone (Hacac), causes the quantitative formation of the complex *cis*-$[(PPh_3)_2Pt(acac)]NO_3$, while the replacement of the benzimidamide ligand occurs only partially in the case of complex **3**.

Experimental Section

Instrumentation and Materials. The NMR spectra were obtained in a solution of various solvents at 300 K on a Bruker AVANCE 300 MHz for ^{1}H and ^{31}P NMR (ν_o 300.13 and 121.5 MHz, respectively) and on a Bruker 400 AMX-WB spectrometer for ^{15}N NMR (ν_o 40.6 MHz). δ are in parts per million and J in hertz. The ^{1}H, ^{31}P, and ^{15}N NMR chemical shift values were referenced to internal Me_4Si, external 85% aqueous H_3PO_4, and CH_3NO_2, respectively. The ^{15}N NMR parameters were obtained through HMBC experiments. The heteronuclear Overhauser enhancement spectroscopy (HOESY) experiments were obtained by using a Bruker QNP probe operating in the direct acquisition mode at 161.98 MHz for ^{31}P NMR and 400.13 MHz for ^{1}H NMR on a 9.4 T field. The ^{31}P NMR experiments carried out in nondeuterated solvents, Hacac and hexafluoroacetylacetonate (hfHacac), were recorded with an insert of D_2O for the instrumental lock. The labeling of the proton resonances follows the X-ray numbering scheme used for **2** and **4**.

cis-$[(PMePh_2)_2Pt(\mu\text{-}OH)]_2(NO_3)_2$,[4] *cis*-$[(dppe)Pt(\mu\text{-}OH)]_2(NO_3)_2$,[8] and 1-MeCy[9] were prepared as previously reported. 9-MeAd and all of the solvents were Aldrich products.

Synthetic Work. 1. *cis*-$[(PPh_3)_2PtNH{=}C(Ph)\{1\text{-}MeCy(-2H)\}]NO_3$ (1). A mixture of *cis*-$[(PPh_3)_2Pt(\mu\text{-}OH)]_2(NO_3)_2$ (410 mg, 2.57×10^{-1} mmol) and 1-MeCy (64.2 mg, 5.13×10^{-1} mmol) in PhCN (20 mL) was stirred at room temperature for ca. 4 h. The resulting yellow solution was filtered to remove trace amounts of a solid. The addition of Et_2O (100 mL) to the filtrate

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afforded **1**·Et_2O as a pale-yellow solid, which was isolated and dried under vacuum (yield 96%). Elem anal. Calcd for $C_{52}H_{51}N_5O_5P_2Pt$: C, 57.67; H, 4.76; N, 6.46. Found: C, 57.80; H, 4.85; N, 6.55. ^{1}H NMR in $CDCl_3$: δ 7.70−7.24 (c m, viz. complex multiplet, 35H, Ph−CN and PPh_3), 7.14 (d, $^3J_{HH}$ = 7.08, 1H, H6), 6.22 (dd, $^3J_{HH}$ = 7.08, $^5J_{HP}$ = 1.52, 1H, H5), 6.05 (br s, 1H, N2H), 2.76 (s, 3H, N1CH_3). ^{1}H NMR in DMSO-d_6: δ 7.84−7.22 (c m, 35H, Ph−CN and PPh_3), 7.21 (d, $^3J_{HH}$ = 7.75, 1H, H6), 6.12 (d, $^3J_{HH}$ = 7.75, 1H, H5), 6.60 (br s, 1H, N2H), 2.58 (s, 3H, N1CH_3). The presence of one molecule of Et_2O was confirmed by ^{1}H NMR.

The $^{31}P\{^1H\}$ NMR data of complexes **1**−**5** in different solvents are reported in Table 2.

2. *cis*-[(PMePh$_2$)$_2$PtNH=C(Ph){1-MeCy(−2H)}]NO$_3$ (2). A mixture of *cis*-[$(PMePh_2)_2Pt(\mu$-OH)$]_2(NO_3)_2$ (210 mg, 1.55 × 10^{-1} mmol) and 1-MeCy (38.9 mg, 3.1 × 10^{-1} mmol) in PhCN (15 mL) was stirred at room temperature for ca. 2 h. The addition of Et_2O (90 mL) to the resulting solution afforded a pale-yellow solid, which was isolated by filtration and dried under vacuum. Dissolution of the crude product in PhCN and vapor diffusion of Et_2O at room temperature afforded crystals of **2**·0.5Et_2O suitable for X-ray analyses (yield 79%). Elem anal. Calcd for $C_{40}H_{42}N_5O_{4.5}P_2Pt$: C, 52.12; H, 4.60; N, 7.59. Found: C, 52.35; H, 4.52; N, 7.66. ^{1}H NMR in CD_2Cl_2: δ 7.65−7.23 (c m, 25H, Ph−CN and PPh_2), 6.96 (d, $^3J_{HH}$ = 7.17, 1H, H6), 6.15 (d, $^3J_{HH}$ = 7.17, 1H, H5), 6.07 (br s, 1H, N2H), 2.68 (s, 3H, N1CH_3), 2.01 (br d, $^2J_{HP}$ 8.51, 3H, PMe), 1.86 (d, $^2J_{HP}$ 8.51, 3H, PMe). ^{1}H NMR in CD_2Cl_2 (−75 °C): δ 7.86−6.91 (c m, 52H, Ph−CN, H6, and PPh_2); the main conformer, δ 6.10 (d, $^3J_{HH}$ = 6.43, 1H, H5), 5.88 (br s, 1H, N2H), 2.63 (s, 3H, N1CH_3), 1.77 (d, $^2J_{HP}$ = 8.91, 3H, PMe), 1.30 (d, $^2J_{HP}$ = 7.65, 3H, PMe); the minor conformer, δ 6.17 (d, $^2J_{HP}$ = 6.58, 1H, H5), 5.97 (br s, 1H, N2H), 2.58 (s, 3H, N1CH_3), 2.70 (d, $^2J_{HP}$ = 9.70, 3H, PMe), 2.03 (d, $^2J_{HP}$ = 8.91, 3H, PMe). ^{1}H NMR in DMSO-d_6: δ 7.68−7.30 (c m, 25H, Ph−CN and PPh_2), 7.18 (d, $^3J_{HH}$ = 7.62, 1H, H6), 6.11 (d, $^3J_{HH}$ = 7.62, 1H, H5), 6.42 (br s, 1H, N2H), 2.61 (s, 3H, N1CH_3), 2.08 (br d, $^2J_{HP}$ = 10.92, 6H, PMe). The presence of Et_2O was confirmed by ^{1}H NMR.

3. *cis*-[(dppe)PtNH=C(Ph){1-MeCy(−2H)}]NO$_3$ (3). A mixture of *cis*-[(dppe)Pt$(\mu$-OH$)]_2(NO_3)_2$ (100 mg, 7.43 × 10^{-2} mmol) and 1-MeCy (18.6 mg, 1.49 × 10^{-1} mmol) in PhCN (8 mL) was stirred at room temperature for 1 day. The resulting yellow solution was filtered to eliminate trace amounts of a dark solid. The addition of Et_2O (70 mL) to the filtrate afforded a pale-yellow precipitate, which was isolated and dried under vacuum. The isolated solid corresponds to the formula *cis*-[(dppe)PtNH=C(Ph){1-MeCy(−2H)}]NO_3 (yield 65%). Elem anal. Calcd for $C_{38}H_{35}N_5O_4P_2Pt$: C, 51.70; H, 4.00; N, 7.93. Found: C, 51.92; H, 3.96; N, 7.98. ^{1}H NMR in CD_2Cl_2: δ 7.78−7.31 (c m, 25H, Ph−CN and PPh_2), 7.19 (d, $^3J_{HH}$ = 7.08, 1H, H6), 6.21 (d, $^3J_{HH}$ = 7.08, 1H, H5), 7.01 (br s, 1H, N2H), 2.78 (s, 3H, N1CH_3), 2.53−2.23 (c m, 4H, P$(CH_2)_2$). ^{1}H NMR in DMSO-d_6: δ 7.71−7.25 (c m, 25H, Ph−CN and PPh_2), 7.01 (d, $^3J_{HH}$ = 7.48, 1H, H6), 6.42 (d, $^3J_{HH}$ = 7.48, 1H, H5), 6.53 (br s, 1H, N2H), 2.98 (s, 3H, N1CH_3), 2.65−2.31 (c m, 4H, P$(CH_2)_2$).

4. *cis*-[L$_2$PtNH=C(Ph){9-MeAd(−2H)}]NO$_3$ (L = PPh$_3$, 4; PMePh$_2$, 5). A mixture of *cis*-[$(PPh_3)_2Pt(\mu$-OH$)]_2(NO_3)_2$ (92.1 mg, 5.7 × 10^{-2} mmol) and 9-MeAd (17 mg, 1.2 × 10^{-1} mmol) in PhCN (5 mL) was stirred at room temperature for ca. 48 h. The addition of Et_2O (20 mL) to the resulting solution afforded a pale-yellow solid, which was isolated by filtration and dried under vacuum. Dissolution of the crude product in PhCN, followed by precipitation with Et_2O at room temperature, afforded microcrystals of **4** having the composition *cis*-[$(PPh_3)_2$-PtNH=C(Ph){9-MeAd(−2H)}]NO_3·H_2O (yield 83%). Elem anal. Calcd for $C_{49}H_{43}N_7O_4P_2Pt$: C, 56.00; H, 4.13; N, 9.32. Found: C, 55.88; H, 4.20; N, 9.38. The presence of water in the isolated solid was confirmed by ^{1}H NMR, although the crystals, obtained by vapor diffusion of Et_2O into a PhCN solution used for single-crystal X-ray analyses, appear to be an anhydrous product. ^{1}H NMR in $CDCl_3$: δ 7.57−7.20 (c m, 35H, Ph−CN and PPh_3), 8.28 (s, 1H, H2), 7.95 (s, 1H, H8), 6.32 (br dd, 1H, N2H), 3.60 (s, 3H, N1CH_3). ^{1}H NMR in DMSO-d_6: δ 7.71−7.19 (c m, 35H, Ph−CN and PPh_3), 8.26 (s, 1H, H2), 8.15 (s, 1H, H8), 6.29 (br s, 1H, N2H), 3.50 (s, 3H, N1CH_3).

With a similar procedure, complex **5** was prepared by reacting *cis*-[$(PMePh_2)_2Pt(\mu$-OH$)]_2(NO_3)_2$ (20 mg, 1.4 × 10^{-2} mmol) and 9-MeAd (4.3 mg, 2.8 × 10^{-2} mmol) in PhCN (2 mL). The ^{31}P NMR of the reacting mixture indicated an almost quantitative formation of **5**. The ^{31}P NMR in PhCN is an AB multiplet at δP_A = −2.80 ($^1J_{PPt}$ = 3242) and δP_B = −3.30 ($^1J_{PPt}$ = 3222). The addition of Et_2O formed a yellow solid, which was isolated and further analyzed by ^{1}H and ^{31}P NMR in $CDCl_3$. ^{1}H NMR in $CDCl_3$: δ 7.68−7.24 (c m, 25H, Ph−CN and PPh_2), 8.22 (s, 1H, H2), 7.94 (s, 1H, H8), 6.12 (br s, 1H, N2H), 3.66 (s, 3H, N1CH_3), 2.16 (d, $^2J_{HP}$ = 9.00, 3H, PMe), 1.85 (d, $^2J_{HP}$ = 9.00, 3H, PMe).

5. *cis*-[(dppe)Pt(acac)]NO$_3$. *cis*-[(dppe)Pt$(\mu$-OH$)]_2(NO_3)_2$ (50 mg, 3.7 × 10^{-2} mmol) was dissolved in 1 mL of Hacac. The addition of Et_2O to the resulting solution afforded a white solid, which was recovered by filtration, washed several times with Et_2O, and dried under vacuum for 24 h (yield 88%). Elem anal. Calcd for $C_{31}H_{31}NO_5P_2Pt$: C, 49.34; H, 4.15; N, 1.86. Found: C, 49.28; H, 4.03; N, 1.90. ^{1}H NMR in $CDCl_3$: δ 7.83−7.50 (c m, 20H, PPh_2), 5.67 (s, 1H, CH(acac)), 2.86 (d, $^2J_{HP}$ = 11.30, 4H, P$(CH_2)_2$), 1.98 (s, 6H, CH_3 (acac)). $^{31}P\{^1H\}$ NMR in $CDCl_3$: singlet at δ 30.26 ($^1J_{PPt}$ = 3711). $^{31}P\{^1H\}$ NMR in Hacac: singlet at δ 31.41 ($^1J_{PPt}$ = 3879).

6. *cis*-[(PPh$_3$)$_2$Pt(acac)]NO$_3$. *cis*-[$(PPh_3)_2Pt(\mu$-OH$)]_2(NO_3)_2$ (42.4 mg, 2.65 × 10^{-2} mmol) was suspended in 3 mL of Hacac. In few minutes, a pale-yellow solution was obtained, which was further stirred for 2 h at room temperature. The addition of Et_2O (30 mL) afforded a white solid, which was recovered by filtration, washed several times with Et_2O, and dried under vacuum (yield 82%). Elem anal. Calcd for $C_{41}H_{37}NO_5P_2Pt$: C, 55.91; H, 4.24; N, 1.59. Found: C, 55.93; H, 4.30; N, 1.56. ^{1}H NMR in $CDCl_3$: δ 7.50−7.26 (c m, 30H, PPh_3), 5.59 (s, 1H, CH(acac)), 1.51 (s, 6H, CH_3 (acac)). $^{31}P\{^1H\}$ NMR in $CDCl_3$: singlet at δ 8.65 ($^1J_{PPt}$ = 3850). $^{31}P\{^1H\}$ NMR in Hacac: singlet at δ 9.09 ($^1J_{PPt}$ = 3868).

X-ray Structure Determinations. Diffraction data for compounds **2** and **4** were collected at room temperature on a Nonius DIP-1030H system with Mo Kα radiation (λ = 0.710 73 Å). Cell refinement, indexing, and scaling of the data set were carried out using programs *Denzo*[10] and *Scalepack*.[10] The structures were solved by direct methods and subsequent Fourier analyses[11] and refined by the full-matrix least-squares method based on F^2 with all observed reflections.[11] The ΔF map of **2** revealed a molecule of diethyl ether located on a 2-fold axis (isotropically refined atoms, 0.5 occupancy, hydrogen atoms not assigned), while the nitrate anion in **4** was found to be disordered over two positions (0.5 occupancy each, isotropically refined atoms with restraints on N−O bond distances and angles). All the calculations were performed using *WinGX*, version 1.80.05.[12] Crystal data and details of refinement are collected in Table 1.

Results and Discussion

Synthesis of the Complexes *cis*-[L$_2$PtNH=C(Ph){1-MeCy(−2H)}]NO$_3$ (L = PPh$_3$, 1; PMePh$_2$, 2; $^1/_2$dppe, 3) and *cis*-[L$_2$PtNH=C(Ph){9-MeAd(−2H)}]NO$_3$ (L = PPh$_3$, 4; PMePh$_2$, 5). We have recently shown that the hydroxo complex *cis*-[$(PPh_3)_2Pt(\mu$-OH$)]_2(NO_3)_2$ reacts with

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Table 1. Crystallographic Data and Details of Structural Refinement Parameters for **2** and **4**

	2·0.5OEt$_2$	**4**
formula	$C_{40}H_{42}N_5O_{4.50}P_2Pt$	$C_{49}H_{41}N_7O_3P_2Pt$
fw	921.82	1032.92
cryst syst	monoclinic	triclinic
space group	$C2/c$	$P\bar{1}$
a, Å	29.932(5)	10.332(3)
b, Å	9.882(2)	13.470(3)
c, Å	28.250(4)	16.910(4)
α, deg		92.32(2)
β, deg	107.45(3)	99.71(2)
γ, deg		109.18(3)
V, Å^3	7971(2)	2179.2(9)
Z	8	2
D_{calcd}, g cm^{-3}	1.536	1.574
μ, mm^{-1}	3.648	3.345
$F(000)$	3688	1032
θ range, deg	2.18−25.68	1.61−24.71
reflns collected	17 652	30 566
reflns unique	6571	6647
reflns [$I > 2\sigma(I)$]	3089	3559
no. of param	432	556
R(int)	0.0867	0.0560
GOF on F^2	0.787	0.765
R1[a]	0.0421	0.0389
wR2[a]	0.0833	0.0724
residuals	0.916, −0.601	0.803, −0.625

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$, $wR2 = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$.

1-MeCy, in chlorinated solvents, to give the complex *cis*-[(PPh$_3$)$_2$Pt{1-MeCy(−H),N^4}(1-MeCy,N^3)]NO$_3$ containing a NH$_2$-deprotonated and a neutral cytosine acting as monodentate ligands through the N4 and N3 atoms, respectively.[13] When the same reaction is carried out in CH$_3$CN, however, the complex *cis*-[(PPh$_3$)$_2$PtNH=C(Me){1-MeCy(−2H)}]NO$_3$ is obtained in quantitative yield.[3] The anionic ligand is the deprotonated form of the *N*-(9-methyl-2-oxo-2,3-dihydro-1*H*-pyrimidin-4-ylidene)-acetamidine molecule shown in Chart 1 and can be described as the result of the coupling of the metal-activated CH$_3$CN molecule with the N4 exocyclic atom of the N3 coordinated cytosine. Analogous reactions, depicted in Chart 3, occur in benzonitrile, and the new metallacycles **1**−**5** have been isolated as pure compounds.

The reaction of *cis*-[(PPh$_3$)$_2$Pt(μ-OH)]$_2$(NO$_3$)$_2$ with 1-MeCy is fast at room temperature, being complete upon dissolution of the reagents in PhCN, as shown by monitoring of the reaction mixture by ^{31}P NMR. The yield of **1** was quantitative, and no intermediates were detectable. A similar behavior was observed with the hydroxo complexes stabilized by PMePh$_2$ and dppe. Compounds **2** and **3** have been isolated in good yield, and no intermediates were identified when the condensation reaction in benzonitrile was monitored by ^{31}P NMR.

In contrast, the suspension of 9-MeAd and *cis*-[(PPh$_3$)$_2$Pt(μ-OH)]$_2$(NO$_3$)$_2$ in PhCN, in ca. 1 h, forms a pale-yellow solution containing, as the main product, the intermediate species *cis*-[(PPh$_3$)$_2$Pt{9-MeAd(−H),N^6N^7}]$^+$, previously characterized.[5] This compound, in several hours at room temperature, reacts quantitatively with the solvent, affording **4**. These transformations are clearly evidenced in the ^{31}P NMR spectra of the reaction mixture obtained immediately after dissolution of the reagents (Figure 1a) and after 48 h (Figure 1b).

The AB multiplets at δ 9.2 ($^1J_{PPt}$ = 3870) and 6.0 ($^1J_{PPt}$ = 3104) are attributable to the adeninato complex *cis*-[(PPh$_3$)$_2$Pt{9-MeAd(−H),N^6N^7}]$^+$ formed by deprotonation of the exocyclic NH$_2$ group of the nucleobase. This complex, in fact, is the only product formed when the condensation reaction is carried out in chlorinated solvents.[5] Its dissolution in PhCN causes the appearance of new AB multiplets at δ 10.9 ($^1J_{PPt}$ = 3308) and 9.9 ($^1J_{PPt}$ = 3425), due to the product **4**, and the reaction appears complete in several hours at 27 °C.

Complex **4** has been isolated as a pure compound and further characterized by multinuclear NMR in a CDCl$_3$ solution. Attribution of the adenine H2 and H8 resonances is supported by ^{1}H−^{15}N heteronuclear multiple-bond correlation (HMBC) experiments (see Figure S1 in the Supporting Information). The H2 resonance, at δ 8.28, correlates with the ^{15}N resonances at δ −202 and −143, whereas the H8 proton (at δ 7.95) correlates with the ^{15}N resonances at δ −136 and −224. The latter resonance, in turn, correlates with the N9 methyl protons. The proton resonance at δ 6.32 appears as a poorly resolved triplet (or a doublet of doublets) due to coupling with the ^{31}P nuclei and is attributed to the N2H proton of the inserted PhCN molecule. In fact, it correlates with the ^{15}N resonance at δ −243, with a $^1J_{NH}$ value of ca. 80 Hz. Moreover, in the ^{1}H−^{31}P HMBC experiment, the adenine H2 signal exhibits correlations with the ^{31}P resonances, in line with the metalation of the nucleobase at the N1 position. A broad resonance for the N2H proton, in the range of δ 6.05−7.01, is observed also in the ^{1}H NMR spectra of the 1-MeCy derivatives **1**−**3**. In these complexes, coordination of cytosine at the N3 atom causes a weak interaction of the pyrimidinic H5 proton with the phosphine in the trans position, leading to the appearance of this resonance as a well-resolved doublet of doublets in **1** ($^3J_{H5H6}$ = 7.08 and $^5J_{HP}$ = 1.52).

It is interesting to note that the reaction with PhCN (Chart 3) does not occur when the phosphine is PMe$_2$Ph. Thus, the trinuclear complex *cis*-[(PMe$_2$Ph)$_2$Pt{9-MeAd(-H)}]$_3$(NO$_3$)$_3$ can be quantitatively prepared by reacting *cis*-[(PMe$_2$Ph)$_2$Pt(μ-OH)]$_2$(NO$_3$)$_2$ and 9-MeAd in CH$_3$CN,[14] and it remains unchanged upon dissolution in PhCN even after 12 h at 50 °C. This lack of reactivity can be interpreted by assuming a high thermodynamic stability of the trinuclear species *cis*-[(PMe$_2$Ph)$_2$Pt{nucleobase(−H)}]$_3^{3+}$, which prevents the formation of the key intermediate *cis*-[(PMe$_2$Ph)$_2$Pt(N≡CR){nucleobase(−H)}]$^+$, susceptible to nucleophilic attack of the N4 cytosine or N6 adenine to the metal-activated nitrile molecule.

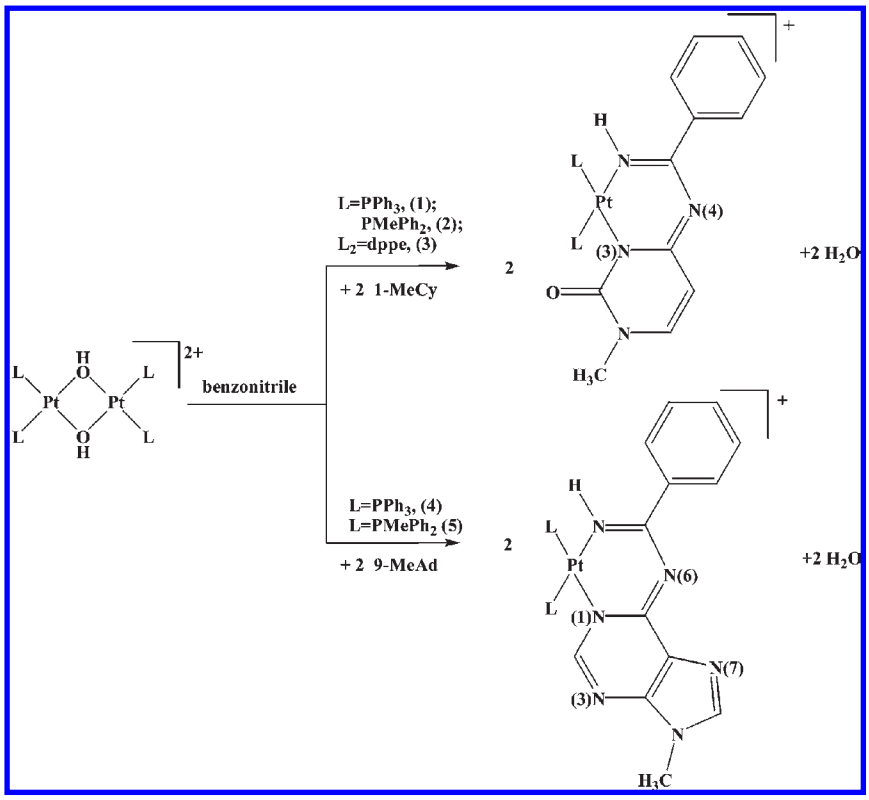
Unlike the MeCN analogues (Chart 2), complexes **1**−**5** are indefinitely stable in a solution of chlorinated solvents or DMSO (at least 24 h at 50 °C).

NMR Behavior of Complex 2. As anticipated for **4** (Figure 1b), the ^{31}P NMR spectra of these insertion products exhibit sharp AB multiplets with well-resolved ^{195}Pt satellites (Table 2 and Figure S2 in the Supporting Information). Only in the case of the PMePh$_2$ complex **2** is

(13) Longato, B.; Montagner, D.; Zangrando, E. *Inorg. Chem.* **2006**, *45*, 8179–8187.

(14) Longato., B.; Pasquato, L.; Mucci, A.; Schenetti, L. *Eur. J. Inorg. Chem.* **2003**, 128–137.

Chart 3



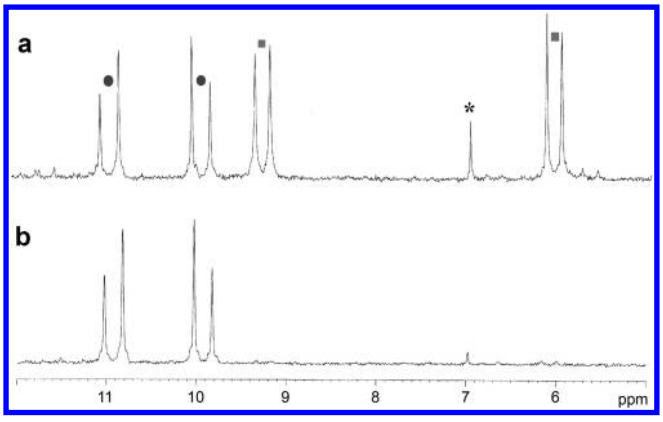


Figure 1. $^{31}P\{^1H\}$ NMR spectra (central part) of the reaction between *cis*-$[(PPh_3)_2Pt(\mu\text{-}OH)]_2(NO_3)_2$ (*) and 9-MeAd in benzonitrile (D_2O as the inset) at 27 °C: (a) after 2 h; (b) after 48 h at room temperature. (■) Intermediate complex *cis*-$[(PPh_3)_2Pt\{9\text{-}MeAd(-H),N^6N^7\}]NO_3$. (●) Insertion product **4**.

the high-field component observed as a broad signal at ambient temperature, whereas the low-field resonances are sharp, as shown in Figure 2a.

At −75 °C, two sharp AB spin systems are detected (Figure 2b) whose spectroscopic parameters are collected in Table 2. Similarly, the ^1H NMR spectrum of **2** at room temperature exhibits a sharp doublet for the methyl protons of one phosphine (at δ 1.86, $^2J_{HP}$ = 8.51) flanked by ^{195}Pt satellites ($^3J_{HPt}$ = ca. 30) and a broader one (at δ 2.01, $^2J_{HP}$ = 8.51). At low temperature (−75 °C), two sets of resonances of comparable relative intensities for each phosphine ligand are detected, as reported in the Experimental Section. A very similar behavior was also observed for the pyrimidinic resonances.

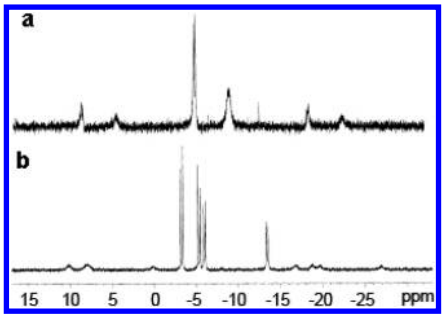


Figure 2. $^{31}P\{^1H\}$ NMR spectra of **2** in CD_2Cl_2: (a) at room temperature; (b) at −75 °C.

Table 2. ^{31}P NMR Value of Complexes **1**−**5** in Different Solvents and at Different Temperatures (δ in ppm and J in Hz)

compound	solvent (K)	P_A ($^1J_{PPt}$)	P_B ($^1J_{PPt}$)	$^2J_{PP}$
1	$CDCl_3$ (298)	9.03 (3486)	7.77 (3417)	24.9
1	DMSO-d_6 (298)	8.22 (3509)	7.85 (3443)	25.2
2	CD_2Cl_2 (298)	−5.14 (3306)	−9.27 (3340)	27.8
2	CD_2Cl_2 (223)	−3.27 (3283)	−5.32 (3277)	28.8 [56%]
		−5.95 (3364)	−13.41 (3291)	25.9 [44%]
2	DMSO-d_6 (298)	−4.38 (3354)	−8.66 (3301)	26.1
3	CD_2Cl_2 (298)	39.89 (3358)	35.57 (3408)	11.5
3	DMSO-d_6 (298)	38.45 (3384)	37.26 (3308)	7.17
4	$CDCl_3$ (298)	10.95 (3263)	10.70 (3370)	24.5
4	DMSO-d_6 (298)	9.96 (3347)	9.28 (3436)	25.5
5	$CDCl_3$ (298)	−2.97 (3240)	−3.45 (3149)	27.3

These spectral changes are consistent with the occurrence of an equilibrium between preferred conformational arrangements related to a partially restricted rotation around the Pt−P bonds. These two conformations arise from the position of the phosphine substituents with respect to the two sides of the coordination plane of

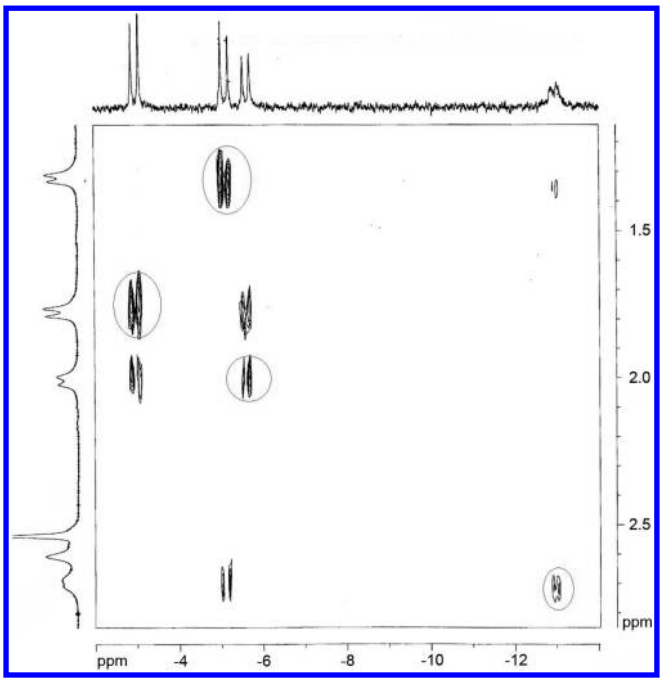


Figure 3. $^{1}H-^{31}P$ NMR HOESY spectrum of **2** at −70 °C in CD_2Cl_2. The circles indicate pure dipolar correlations, with the other cross-peaks being heteronuclear COSY scalar correlations.

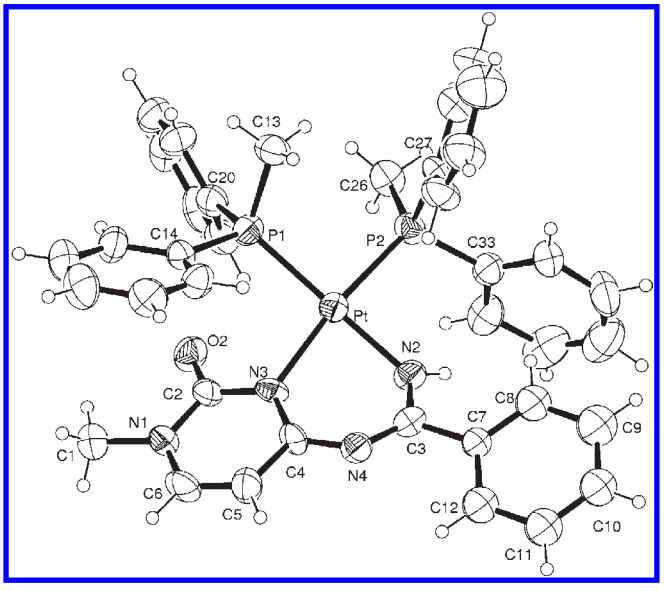


Figure 4. ORTEP drawing (40% ellipsoid probability) of the complex cation of **2**.

the complex: i.e., one presents two phenyls on one side and the methyl on the other, and the second one would have a phenyl and a methyl on the same side, leaving a phenyl on the other. At −75 °C, the molar ratio between the two conformers is measured to be 56/44. The difference likely arises from a steric interaction of the oxygen atom of 1-MeCy with the ipso carbon of one phenyl ring of the phosphine located in trans to the inserted PhCN molecule and with the phosphorus atom of the same phosphine (see the structure discussion below).

The different line-width values observed at room temperature (Figure 2a) are related to the different $\Delta\delta$ values exhibited by the two AB multiplets (Figure 2b).

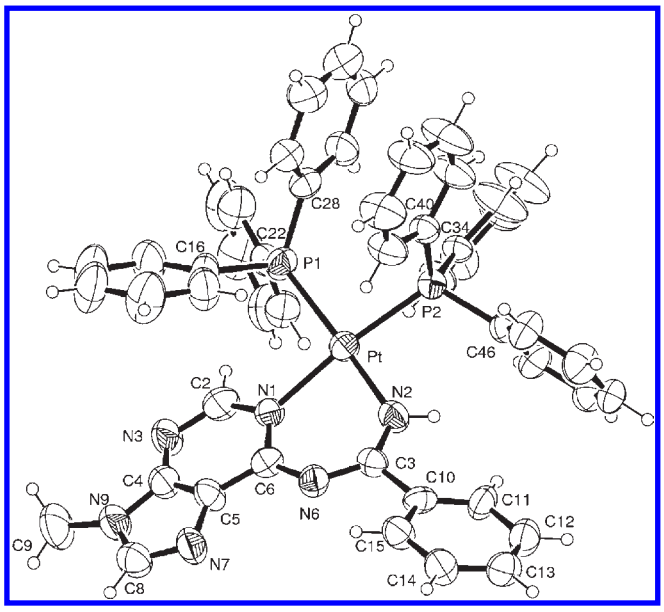


Figure 5. ORTEP drawing (40% ellipsoid probability) of the complex cation of **4**.

Table 3. Selected Bond Lengths (Å) and Angles (deg) for **2** and **4**

2		**4**	
Pt−N3	2.112(7)	Pt−N1	2.116(6)
Pt−N2	2.043(6)	Pt−N2	2.010(6)
Pt−P1	2.281(2)	Pt−P1	2.313(2)
Pt−P2	2.271(2)	Pt−P2	2.280(2)
N3−C4	1.339(10)	N1−C6	1.388(9)
C4−N4	1.342(10)	C6−N6	1.341(9)
N4−C3	1.302(10)	N6−C3	1.308(9)
C3−N2	1.327(10)	C3−N2	1.295(8)
N3−Pt−N2	83.2(3)	N1−Pt−N2	84.5(3)
N3−Pt−P1	94.73(19)	N1−Pt−P1	93.80(19)
N3−Pt−P2	172.38(18)	N1−Pt−P2	172.7(2)
N2−Pt−P1	169.2(2)	N2−Pt−P1	172.55(19)
N2−Pt−P2	90.0(2)	N2−Pt−P2	88.23(18)
P1−Pt−P2	92.58(9)	P1−Pt−P2	93.33(8)
N3−C4−N4	127.5(9)	N1−C6−N6	127.2(8)
C4−N4−C3	122.8(8)	C6−N6−C3	124.0(7)
N4−C3−N2	126.7(8)	N6−C3−N2	126.5(8)

Moreover, the interconversion between the conformers is confirmed by the presence of pure dipolar correlations in the $^{31}P-^{1}H$ NMR HOESY spectrum shown in Figure 3, together with the expected heteronuclear $^{31}P-^{1}H$ NMR scalar correlations (Figure S3 in the Supporting Information).

It is interesting to note that the previously reported acetonitrile analogue showed identical NMR behavior.[3]

Crystal and Molecular Structures of 2 and 4. The X-ray structural determinations of **2** and **4** show that the insertion of a PhCN molecule into the cytosine Pt−N4 and adenine Pt−N6 bonds had occurred with the formation of a six-membered ring, as depicted in Figures 4 and 5, respectively. Selected bond distances and angles are collected in Table 3.

In the two adducts, the Pt is bound to the nucleobase N donor site, the inserted benzonitrile nitrogen N2, completing the square-planar coordination through P donors. The Pt−N(nucleobase) bond lengths are 2.112(7) and

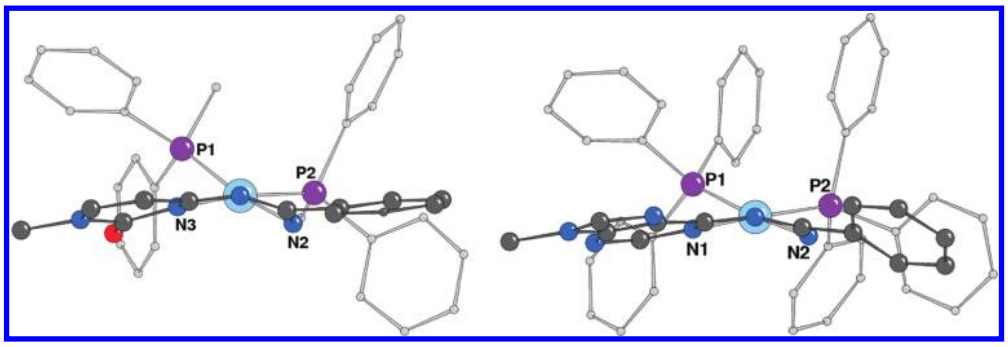


Figure 6. Side views of **2** (left) and **4** (right) showing the conformation of the nucleobase benzimidamide with respect to the coordination plane.

2.116(6) Å in **2** and **4**, respectively, while Pt−N2 bond lengths, of 2.043(6) and 2.010(6) Å, are slightly shorter. The Pt−P bond distances fall in the range from 2.271(2) to 2.313(2) Å. These values are comparable to those measured in the acetonitrile derivatives.[3] The N_2P_2 donors show a slight tetrahedral distortion in **2**, with deviations of ±0.125 Å from their mean plane, while milder deformations (±0.056 Å) are measured in **4**. Figure 6 displays a side view of the complexes, showing the conformation assumed by the nucleobase benzimidamide moiety with respect to the coordination plane. The dihedral angle formed by the nucleobase ring with the N_2P_2 coordination plane is of 36.5(2)° and 27.3(2)° in **2** and **4**, respectively. The phenyl from benzonitrile is almost coplanar with the cytosine ring in **2**, while it is tilted with respect to the adenine in **4**. Inside the six-membered-ring fragment, the geometrical parameters are comparable in the two cases and indicate an electron delocalization. The more apparent difference is observed for the C3−N2 bond distance, which is 1.327(10) and 1.295(8) Å in **2** and **4**, respectively. Making allowance for the estimated standard deviations, the value measured in **2** is also longer than the distances measured in the crystal structures with acetonitrile, viz., 1.279(11)−1.295(7) Å.[3]

In complex **2**, the short distance measured between the 1-MeCy oxygen atom with phosphorus P1 and with the ipso carbon C14 of the phosphine (2.88 and 2.92 Å, respectively) is an indication of a weak intramolecular bonding interaction, and it gives support to the observed behavior in solution (see the NMR results) for this species. The corresponding values in the acetonitrile derivative were found to be 3.08 and 3.00 Å, respectively. On the other hand, complex **4** shows an intramolecular stacking between the phenyl rings C28 and C40 of PPh_3 [distance between centroids of 3.731(6) Å; dihedral angle 6.4(5)°], while the stacking between the six-membered adenine ring and phenyl C16 appears marginal [3.924(6) Å; 37.5(5)°]. Finally, an edge-to-face C*H*···π interaction is observed between the hydrogen atom C11−H and ring C46 (H−phenyl centroid distance = 2.87 Å). This kind of stabilizing interaction, the so-called π-hydrogen bond, was sometimes observed in organometallic complexes[15] and could support the observed stability of the benzonitrile with respect to the acetonitrile derivatives. In principle, this interaction (although not observed in the solid state likely for the packing requirement) is also feasible in complex **2** (distance between C8−H and centroid C33 ring = 3.06 Å).

The difference Fourier maps allow one, in both structural determinations, to prudently fix the proton on the benzonitrile nitrogen N2 as determined through NMR.

Reaction of *cis*-[$(PPh_3)_2$PtNH=C(R){9-MeAd(−2H)}]$^+$ (R = Ph, Me) and *cis*-[(dppe)PtNH=C(Ph){1-MeCy-(−2H)}]$^+$ with Hacac. In order to characterize the benzimidamide ligands, the reactivity of the new complexes toward Hacac has been investigated. This weakly acidic molecule (pK_a = 8.95)[16] has well-established chelating properties in its deprotonated form ($acac^-$),[17] and it is expected to replace the anionic ligand in **1**−**5**. In fact, complex **4** dissolves in pure Hacac in a few minutes at room temperature to give a pale-yellow solution. Its ^{31}P NMR spectrum exhibits two signals at δ 11.58 and 9.09, flanked by ^{195}Pt satellites. The lower field signal, observed as an apparent singlet having a relative intensity of 60% with a rather large line width, is attributable to the unreacted complex **4**. The sharp singlet at δ 9.09 is due to the reaction product, namely, the complex *cis*-[$(PPh_3)_2$Pt(acac)]NO_3, which contains the chelating acetylacetonate ligand. After 2 days at room temperature, this is the only detectable signal, indicating that the anionic ligand in **4** has been quantitatively replaced by $acac^-$. The compound *cis*-[$(PPh_3)_2$Pt(acac)]NO_3, previously characterized as a BPh_4 salt,[18] can be quantitatively prepared by dissolving the hydroxo complex *cis*-[$(PPh_3)_2$Pt(μ-OH)]$_2$$(NO_3)_2$ in Hacac, where it reacts immediately (see the Experimental Section). The complete characterization of the organic moiety NH=C(Ph){9-MeAd(−H)} resulting from the ligand exchange will be reported elsewhere.[19] It can be anticipated that ^1H NMR analysis of the solid-state residue and of the liquid components of the reaction mixture, separated under vacuum and dissolved in DMSO-d_6 and $CDCl_3$, respectively, rules out the presence of free 9-MeAd and benzonitrile. Similarly, the acetonitrile analogue of **4**, *cis*-[$(PPh_3)_2$PtNH=C(Me){9-MeAd-(−2H)}]NO_3,[3] reacts easily in pure Hacac to give quantitatively *cis*-[$(PPh_3)_2$Pt(acac)]NO_3, as shown by the

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^{31}P NMR spectrum recorded immediately after dissolution of the complex.

A different behavior was observed for complex **3**. Even though it dissolves easily in Hacac, protonation of the coordinated ligand NH=C(Ph){1-MeCy(−2H)} occurs only to a minor extent. In fact, the ^{31}P NMR spectrum of the resulting solution shows AB multiplets of **3** [at δ 40.7 ($^1J_{PPt}$ = 3347) and 36.35 ($^1J_{PPt}$ = 3386)] and a singlet at δ 31.41 flanked by ^{195}Pt satellites ($^1J_{PPt}$ = 3879 Hz), having a relative intensity ratio of 4:1. This latter signal is clearly attributable to *cis*-[(dppe)Pt(acac)]NO_3 (see the Experimental Section). The spectrum does not change after several days, indicating that the reaction mixture is at equilibrium. If Hacac is replaced by the more acidic hexafluoroacetylacet one (pK_a = 4.35),[16] the equilibrium appears strongly shifted toward protonation of **3**. In this case, the relative abundance of **3** and *cis*-[(dppe)Pt(hfacac)]NO_3 was 1:1.5. The latter species, observed in the ^{31}P NMR spectrum as a singlet at δ 37.12 with $^1J_{PPt}$ = 3860 Hz, is quantitatively formed when *cis*-[(dppe)Pt(μ-OH)]$_2$-$(NO_3)_2$ is dissolved in hfHacac.

Conclusions

The first examples of azametallacycles resulting on the formal insertion of benzonitrile into Pt^{II}−N bonds of nucleobase complexes are described. The compounds *cis*-[L_2-PtNH=C(Ph){9-MeAd(−2H)}]$^+$ and *cis*-[L_2PtNH=C(Ph)-{1-MeCy(−2H)}]$^+$ have been obtained when the neutral ligands L are PPh_3, $PMePh_2$, and dppe but not with the more basic phosphine PMe_2Ph.

Unlike the acetonitrile analogues, which release CH_3CN in DMSO or chlorinated solvents,[3] the benzonitrile derivatives here reported are indefinitely stable in solution. The higher thermodynamic stability of these substituted benzamidine complexes could be ascribed (i) to a more extended π-electron delocalization in the organic ligand due to the presence of the phenyl group and (ii) to an edge-to-face C$H\cdots\pi$ interaction between a *Ph*CN phenyl hydrogen with one PPh_3 phenyl ring, clearly evidenced in the X-ray structure of **4**.

The anionic ligands in *cis*-[$(PPh_3)_2$PtNH=C(R){9-MeAd-(−2H)}]NO_3 (R = Me, Ph) can be quantitatively protonated by Hacac, leading to formation of the free amidines NH=C-(R){9-MeAd(−H)} and the acetylacetonate complex *cis*-[-$(PPh_3)_2$Pt(acac)]NO_3. The incomplete protonation of the anionic ligand in **3** by Hacac or hfHacac is likely due to electronic effects related to the presence of dppe, which is more basic in comparison with the PPh_3 ligand.

Supporting Information Available: Crystallographic data for the structures reported in this paper. This material is available free of charge via the Internet at http://pubs.acs.org.