

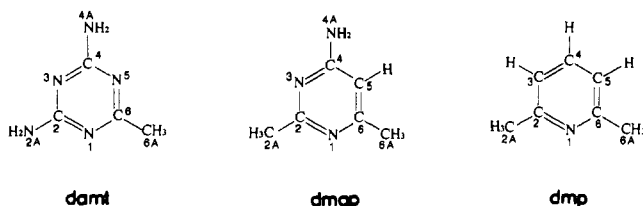
Interligand Interactions Affecting Site-Specific Metal Bonding. X-ray Crystal Structures of $[\text{Rh}_2(\text{acetato})_4(\text{L})_2]$, Where L = 2,4-Diamino-6-methyl-*s*-triazine, 2,6-Dimethyl-4-aminopyrimidine, and 2,6-Dimethylpyridine

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The importance of stereospecific interligand interactions as factors affecting the metal binding sites for nucleic acid bases has originally been demonstrated for the Cu^{II} and Co^{III} systems by Marzilli and Kistenmacher.² We have demonstrated³ the validity of this approach in which the adenine-specific reactivity of tetrakis(μ -carboxylato)dirhodium(II) (rhodium-carboxylate), an antitumor agent that functions by inhibiting DNA synthesis,⁴ could be rationalized by the formation of hydrogen bonding between the rhodium-carboxylate oxygens and the exocyclic amino group N(6) on the N(7)-metal-bonded adenine base. In order to obtain further insights into interligand interactions as factors determining the site(s) on the heteroaromatic ligand to which the metal ion(s) binds, we have now conducted a comparative study by changing the nature and the positioning of substituents adjacent to the donor nitrogen. Selected ligands are 2,4-diamino-6-methyl-*s*-triazine (damt), 2,6-dimethyl-4-ami-



nopyrimidine (dmap), and 2,6-dimethylpyridine (dmp): damt has three nitrogens in the ring to be attacked by metal ions, one being flanked by two amino substituents and the other two by an amino and a methyl group, dmap possesses two ring nitrogens with one interposed by an amino and a methyl group and the other by two methyl groups, and dmp bears two methyl groups adjacent to a ring nitrogen. We report here reaction properties of $[\text{Rh}_2(\text{OAc})_4]$ with damt, dmap, and dmp and crystal structures

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Table 1. Crystallographic Data

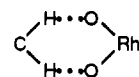
	1	2	3
composn	$\text{C}_{16}\text{H}_{26}\text{N}_{10}$ - O_8Rh_2	$\text{C}_{20}\text{H}_{30}\text{N}_6$ - O_8Rh_2	$\text{C}_{22}\text{H}_{30}\text{N}_2$ - O_8Rh_2
fw	692.256	288.304	656.298
space group	$C2/c$	$P2_1/c$	$P2_1/n$
<i>a</i> , Å	22.991(5)	10.644(3)	7.994(2)
<i>b</i> , Å	7.990(2)	16.260(6)	7.927(1)
<i>c</i> , Å	16.390(5)	7.984(2)	20.576(1)
β , deg	125.99(2)	108.63(2)	96.945(7)
<i>V</i> , Å ³	2436(1)	1309.4(7)	1294.3(3)
<i>Z</i>	4	2	2
<i>d</i> _{calc} , g cm ⁻³	1.887	1.746	1.684
<i>T</i> , K	293	293	293
$\lambda(\text{Mo K}\alpha)$, Å	0.710 73	0.710 73	0.710 73
μ , cm ⁻¹	13.943	12.926	13.034
rel trans cft ^a	0.983–1.020	0.972–1.030	0.978–1.028
no. of obsd rflns [$F_o > 3\sigma(F_o)$]	2163	1934	1573
<i>R</i> ^b	0.063	0.036	0.027
<i>R</i> _w ^c	0.047	0.043	0.032

^a Normalized to an average of unity. ^b $R = \sum |F_o - |F_c|| / \sum F_o$. ^c $R_w = [\sum w(F_o - |F_c|)^2 / \sum w F_o^2]^{1/2}$.

of the reaction products $[\text{Rh}_2(\text{OAc})_4(\text{L})_2]$ (1 for L = damt, 2 for L = dmap, and 3 for L = dmp).

Results

$[\text{Rh}_2(\text{OAc})_4]$ reacted with damt, dmap, and dmp to give $[\text{Rh}_2(\text{OAc})_4(\text{L})_2]$, stoichiometrically for L = damt and dmap and in a good yield for L = dmp (see Experimental Section), whose crystal structures were determined by X-ray diffraction with crystallographic parameters listed in Table 1. Figure 1a shows the molecular structure of $[\text{Rh}_2(\text{OAc})_4(\text{damt})_2]$, 1, in which the molecule resides on a crystallographic center of inversion at the midpoint of the Rh–Rh bond with the damt ligand coordinated to the two axial positions of the dirhodium-tetraacetate cage through the N(3) site. The structure is stabilized by two interligand hydrogen bonds between the two amino substituents and the acetato oxygens (distances N(2A)···O(14) = 3.04(1) Å and N(4A)···O(12) = 3.00(1) Å). Figure 1b depicts the molecular structure of $[\text{Rh}_2(\text{OAc})_4(\text{dmap})_2]$, 2, where the metal binds to N(3) of dmap. Both the amino and the methyl substituents adjacent to the donor N(3) participate in hydrogen bonding with the acetate oxygens, with an N–H···O hydrogen bond (N(4A)···O(13) = 2.886(8) Å) and



(bifunctional C–H···O–Rh hydrogen bonds;⁵ C(2A)···O(11) = 3.205(7) Å and C(2A)···O(14') = 3.022(9) Å). Figure 1c shows the molecular structure of $[\text{Rh}_2(\text{OAc})_4(\text{dmp})_2]$, 3, in which the Rh atom binds to dmp with the formation of two sets of bifunctional C–H···O–Rh hydrogen bonds (C(2A)···O(11') = 3.082(8) Å, C(2A)···O(13') = 3.118(7) Å, C(6A)···O(12) = 3.073(7) Å, and C(6A)···O(14) = 3.091(8) Å).

Table 2 gives the selected interatomic distances and angles within the $[\text{Rh}_2(\text{OAc})_4(\text{L})_2]$ framework, together with those⁶ for L = pyridine. The Rh–N bond length becomes longer in the following sequence of the ligand (L): pyridine < damt < dmap < dmp. This may be due to a steric effect caused by the substituents adjacent to the nitrogen donor, in agreement with the bulkiness of C–NH₂ < C–CH₃. The Rh–Rh bond distance

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Table 2. Relevant Interatomic Distances and Angles in the $[\text{Rh}_2(\text{OAc})_4(\text{L})_2]$ Framework, Where L = damt, dmap, dmp, or Pyridine

L	metal binding site	Rh–Rh, Å	Rh–N, Å	C(2)–N(1)–C(6), deg	C(2)–N(3)–C(4), deg	ref
damt	N(3)	2.401(1)	2.315(9)	114.4(7) 113.1(8) ^a	114.1(9)	this work
dmap	N(3)	2.4121(5)	2.370(6)	115.6(5)	116.7(5)	this work
dmp	N(1)	2.4137(5)	2.403(4)	117.8(5)		this work
pyridine ^b	N(1)	2.3994(5)	2.234(3)	118.6(3)		6
			2.225(3)	118.2(3)		

^a This value is that of the C(4)–N(5)–C(6) angle, which is chemically equivalent to the C(2)–N(1)–C(6) angle. ^b This complex involves two crystallographically independent pyridine ligands.

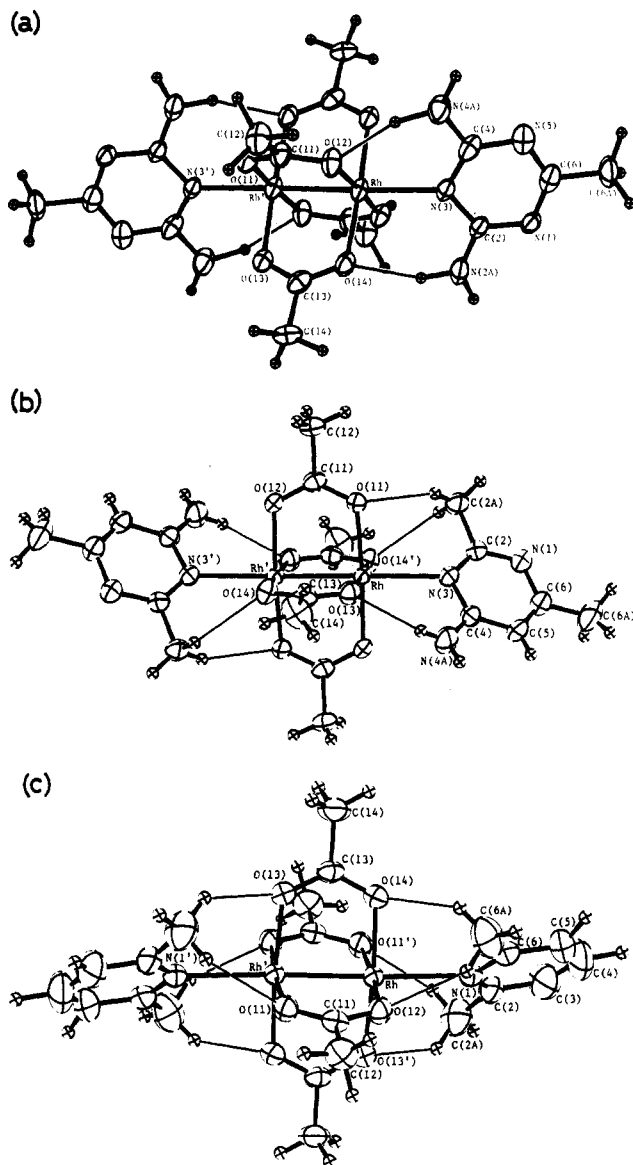


Figure 1. Molecular structures of $[\text{Rh}_2(\text{acetato})_4(\text{L})_2]$, where (a) L = damt (**1**), (b) L = dmap (**2**), and (c) L = dmp (**3**), noting the metal binding site on the heterocyclic ring and interligand hydrogen bonds (depicted by thin lines). A crystallographic center of symmetry passes through the midpoint of the Rh–Rh' bond.

also increases in the same order but is less affected. The bond angle C(2)–N(3)–C(4) does not essentially deviate from the C(2)–N(1)–C(6) angle for **1** and **2**, thereby ruling out the ligand strain upon complex formation; this is a rather common structural aspect observed in the metal–nucleic acid derivative structures.⁷

Discussion

We discuss here factors that affect the site-specific metal bonding. In **1** the damt ligand coordinates to the rhodium atom

through the N(3) site with the formation of interligand N–H...O hydrogen bonds but not through N(1) (or N(5)), and in **2** the dmap ligand coordinates through N(3) with the formation of interligand N–H...O and C–H...O hydrogen bonds but not through N(1). The quantitative formation of **2** in which dmap does bind to the metal through N(3) indicates that the steric hindrance between the methyl group and the acetato oxygens, caused by the octahedral environment about the metal center, may be of little significance. Thus the absence of the metal bonding to N(1) (or N(5)) of damt in **1**, the site being sterically equivalent to N(3) of dmap in **2**, is possibly not due to steric hindrance. Accordingly, we can expect any factor, other than a steric factor, which affects the stoichiometric formation of **1** in which the metal binds to N(3) despite the statistical advantage of N(1) over N(3) by two times; we suggest this to be the formation of interligand N–H...O hydrogen bonds. A question arises here again why there is no metal bonding to N(1) but there is to N(3) for dmap in **2**. It is of interest to note here that the $[\text{PtCl}_4]^{2-}$ or $[\text{PdCl}_4]^{2-}$ ion is bound to dmap at N(1) but not at N(3), there being no interligand hydrogen bonding.⁸ Since in this case, however, the steric requirements of the square-planar Pt or the Pd fragments are less demanding than that of the octahedral Rh core, the following possibility still should be considered: (i) The Rh bonding to N(3) may be induced by the formation of interligand hydrogen bonds and/or (ii) the coordination to N(1) may be impossible due to steric constraint around the Rh atom. It was then examined whether the octahedral Rh atom could bind to dmp or not, which is believed⁹ to possess only limited coordination power and is thus used⁹ as a “noncoordinating” buffer compound. As shown in Figure 1c, the Rh atom does bind to dmp with the formation of interligand C–H...O hydrogen bonds. The nonquantitative yield of **3** even under a large excess of dmp presumably reflects some interligand steric constraint. It should be emphasized here, however, that the structural rigidity of the RhO_4 core is rather of benefit for the formation of such bifunctional hydrogen bonds since, otherwise, the C–H...O hydrogen bonding may be weak.

From these observations, we suggest that the site to which the Rh atom binds to damt or dmap is affected largely by interligand hydrogen bonds, in accordance with their relative extent, N–H...O > C–H...O, and may be partly influenced by the bulkiness of the substituent, amino group < methyl group,^{10,11} although we realize that to strictly prove this argument we must show N(1)–metal bonding without hydrogen bonding and N(3)–metal bonding with hydrogen bonding in the system involving the same steric environments about the metal centers.¹² The significance of the

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(10) MO calculations by using a MINDO method¹¹ show that an electronic factor may also in part affect the metal binding site in agreement with the basicity of the ring nitrogen, N(3) > N(1), but this is not, at least, a major factor since electron charges are only slightly larger on N(3) (–0.425 e) than on N(1) (–0.401 e) (or N(5) (–0.406 e)) for damt and on N(3) (–0.361 e) than N(1) (–0.345 e) for dmap (supplementary material) and, hence, such a small charge difference seems not enough to rationalize the quantitative formation of the complexes for **1** and **2**. In the MO calculations, the molecular dimensions of damt, dmap, and dmp were taken from the present work but these were not optimized.

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methyl group as a hydrogen-bonding donor should be emphasized, at least for that attached to the π -ring system in which the methyl group may assume partial double-bond character with the concomitant acidic nature of the methyl protons (C(ring)-C(methyl) bond = 1.50(2) Å for 1, 1.506(9) Å and 1.519(11) Å for 2, and 1.478(9) Å and 1.475(10) Å for 3, while 1.541 ± 0.003^{13} Å for the C-C single bond) and especially when it meets stereochemically desirable environments, such as the present octahedral MO_4 rigid core.

In conclusion, the present study shows that when a metal atom is presented with a choice between several similar heterocyclic N atoms, the hydrogen-bonding ability of the exocyclic substituents could play a crucial role. Thus we *reemphasize* the validity of an approach in which metal ion-ligand interactions could be better understood in terms of interligand interactions, which may be still overlooked.

Experimental Section

Preparation of $[\text{Rh}_2(\text{OAc})_4(\text{L})_2]$ (L = 2,4-Diamino-6-methyl-s-triazine (damt) (1), 2,6-Dimethyl-4-aminopyrimidine (dmap) (2), and 2,6-Dimethylpyridine (dmp) (3)). damt, dmap, and dmp were purchased from Aldrich and were used without further purification. $[\text{Rh}_2(\text{OAc})_4] \cdot 2\text{MeOH}^{14}$ (51 mg, 0.1 mM) dissolved in 10 mL of hot (80 °C) water was added to damt (22 mg, 0.2 mM) in 10 mL of water for 1, to dmap (25 mg, 0.2 mM) in 10 mL of water for 2, and to dmp (1.16 mL, 10.0 mM) for 3. After the violet solutions (pH about 5) were allowed to stand for 1 day at room temperature, purple crystals formed stoichiometrically for 1 and 2 and purple crystals formed in an 85%¹⁵ yield (on the basis of $[\text{Rh}_2(\text{OAc})_4] \cdot 2\text{MeOH}$) for 3. Anal. Calcd for 1, $\text{C}_8\text{H}_{13}\text{N}_5\text{O}_4\text{Rh}$: C, 27.76; H, 3.79; N, 20.23. Found: C, 27.25; H, 3.68; N, 20.35. Calcd for 2, $\text{C}_{10}\text{H}_{15}\text{N}_5\text{O}_4\text{Rh}$: C, 34.90; H, 4.39; N, 12.21. Found: C, 34.67; H, 4.36; N, 12.28. Calcd for 3, $\text{C}_{11}\text{H}_{15}\text{NO}_4\text{Rh}$: C, 40.26; H, 4.61; N, 4.27. Found: C, 39.80; H, 4.53; N, 4.33.

X-ray Crystal Structure Determination. X-ray crystallographic data were collected on a Rigaku AFC5 diffractometer, using graphite-

monochromated Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å). A summary of relevant crystal data is given in Table 1, and a full table including particulars of data collection and refinement is given in the supplementary material. No absorption corrections were made because of a maximum variation in intensity of the axial reflections (ψ scans) less than 3% from the mean for 2. The structures were solved by heavy-atom methods and refined by block-diagonal least-squares methods.¹⁶ All non-hydrogen atoms were refined anisotropically. All hydrogens atoms were located from difference Fourier maps, and their positional and isotropic thermal parameters were refined for 1-3. The final positional and thermal parameters are given in the supplementary material. All calculations were performed with a UNICSIII program system¹⁸ on a FACOM 780 computer at the Institute of Physical and Chemical Research, incorporating atomic scattering factors with Rh corrected for anomalous dispersion.¹⁹

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Supplementary Material Available: Text describing X-ray experimental details, tables of crystal data and data collection and refinement parameters, positional parameters, anisotropic thermal parameters, and bond distances and angles for 1-3, and a table of MO-calculated electron charges on the damt, dmap, and dmp ligands (14 pages). Ordering information is given on any current masthead page.

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- (15) This value varied depending on the concentration of starting dmp and $[\text{Rh}_2(\text{OAc})_4]$: 72% after 1 day for the dmp: $[\text{Rh}_2(\text{OAc})_4]$ ratio of 20:1, whereas no detection of 3 for 2:1. The direct dissolution of $[\text{Rh}_2(\text{OAc})_4] \cdot 2\text{MeOH}$ (51 mg, 0.1 mM) (without water) into a dmp solution (5 mL, 43 mM) on warming at 60 °C brought immediate precipitation of 3 in a 20% yield, and after complete evaporation of the dmp solvent had occurred, $[\text{Rh}_2(\text{OAc})_4(\text{dmp})_2]$ was quantitatively isolated with two crystalline forms, one being purple columns consistent with 3 and the other being brown plates (poor crystallinity).
 (16) The assignment of the C or N atoms of the damt or the dmap ligands was unambiguously made on the basis of the exocyclic C(ring)-C(methyl) and C(ring)-N(amino) bond distances of 1.49(1)¹⁷ and 1.325(9)¹⁷ Å; hydrogen atoms attached to the corresponding atoms could, indeed, be located from difference Fourier maps.
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