reference measurements. In addition, our value for the chemical shift of N_2 could be influenced by liquid oxygen contamination which is claimed[5] to shift the $^{14}N_2$ resonance to lower field. The ^{15}N resonance is sharp (line width <0.5 ppm) and, because of rapid quadrupolar relaxation of the ^{14}N nucleus, it displays no evidence of ^{15}N–^{14}N scalar coupling.

Our value for the chemical shift in liquid nitrogen is consistent with the value found by Kent and Wagner[5] and casts further doubt on the earlier measurement by Holder and Klein.[4] Both the primary[9] and secondary isotope effects are likely to be small.

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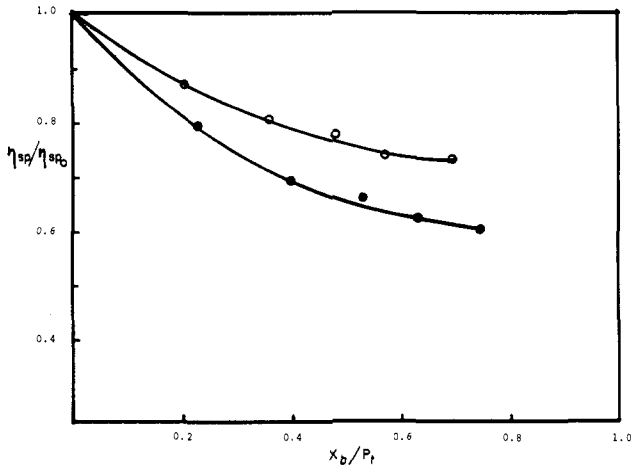

Figure 1. The effect of bound L-lys-L-pheA (●) and L-lys-D-pheA (○) on the relative specific viscosity of DNA (X_b represents the concentration of bound peptide and P_t the total DNA concentration in $P/1$). Viscosity measurements were carried out at near infinite dilution of salmon sperm DNA (0.26 mM in $P/1$) in 10 mM 2-(N-morpholino)ethane sulfonate (Mes) buffer pH 6.2 (5 mM in Na^+) using the low shear Zimm viscometer at 37.5°.

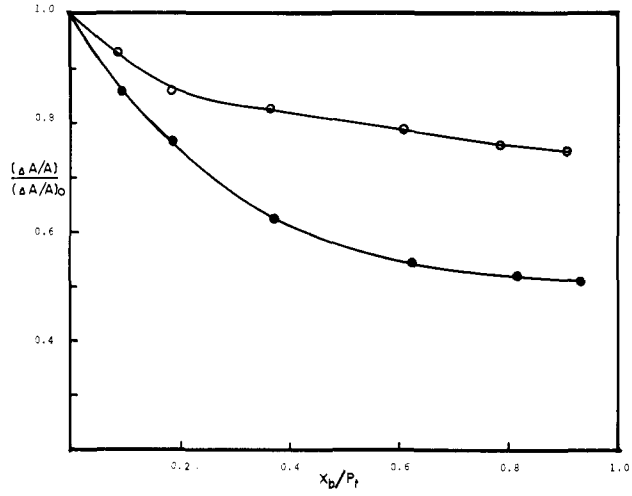

Figure 2. The effect of bound L-lys-L-pheA (●) and L-lys-D-pheA (○) on the relative reduced dichroism of DNA (X_b represents the concentration of bound peptide and P_t the total DNA concentration in $P/1$). Flow dichroism measurements were carried out at 25 ± 1° and at 260 nm using a Cary 15 spectrometer with a Glan-Taylor calcite polarizing prism. DNA (3 mM $P/1$) solution was flowed through a quartz capillary (0.415 mm radius) by means of a Sage syringe pump. The shear rate in all experiments was maintained constant at 2600 sec^{-1}. At the highest concentration used in these studies, the peptide contribution to the absorbance at 260 nm is found to be less than 1%. It should be noted that identical results are also obtained at lower DNA concentrations (0.5 mM $P/1$) which indicate that the effects are caused by a molecular conformational change rather than aggregation.

Stereospecific Interaction of Dipeptide Amides with DNA. Evidence for Partial Intercalation and Bending of the Helix

Sir:

Recent studies from these laboratories have shown that small molecules may exert a pronounced effect on the tertiary structure of DNA.[1] This communication reports the studies on the interaction of the diastereomeric dipeptide amides, L-Lys-L-PheA (**1**) and L-Lys-D-PheA (**2**) with DNA. Figures 1 and 2 show the effect of bound peptide on the relative specific viscosity and reduced dichroism of DNA solution, respectively. Figure 3 shows the ^1H NMR signal of the phenyl protons of **1** and **2** in the presence and absence of DNA. Table I summarizes the ^1H NMR data obtained with these systems, i.e., the chemical shift, δ, and the spin-lattice relaxation time, T_1. (Experimental details are given in the legends of the table and figures.)

A number of interesting observations may be made. (1) The dipeptide amide, L-Lys-L-PheA (**1**), exhibits a larger decrease in the relative specific viscosity (η_{sp}/η_{sp0}, where η_{sp} and η_{sp0} are the specific viscosity in the presence and absence of peptide, respectively) of the DNA solution than the corresponding diastereomer, L-lys-D-pheA, **2** (Figure 1). (2) The value of the reduced dichroism ratio, $(\Delta A/A)/(\Delta A/A)_0$ (where $\Delta A = A_{\parallel} - A_{\perp}$ and A is the absorbance of a stationary DNA solution at 260 nm; $(\Delta A/A)$ and $(\Delta A/A)_0$ refer to the reduced dichroism of DNA complex and free DNA, respectively), is significantly diminished in the presence of the bound peptides. The decrease is more pronounced in the presence of L-lys-L-pheA than with the diastereomer L-lys-D-pheA (Figure 2). (3) In the presence of DNA (i.e., base-pair to peptide ratio of 7.2, 3.6, 2.4, and 0.5) large differences in the chemical shifts and line broadening of the ^1H NMR signals of the aromatic protons of **1** and **2** are observed (Figure 3 and Table I). For example, the L-lys-D-pheA, **2**, exhibits slight broadening and upfield

Table I. The Chemical Shift, δ, and the Spin–Lattice Relaxation Time, T_1, of the Aromatic Protons of L-Lys-L-PheA (1) and L-Lys-D-PheA (2) in the Presence and Absence of Salmon Sperm DNA.[a]

	Chemical shift, δ (Hz), and T_1 (sec)				
		Base pair/peptide			
System	Free	7.2	3.6	2.4	0.5
L-Lys-L-PheA	736.5 (2.02)	713.0 (0.57) 730.5 (0.77)	714.5 (0.62) 729.5 (0.80)	715.5 (0.61) 728.0 (0.79)	730.0
L-Lys-D-PheA	738.1 (2.02)	735.9 (0.66)	736.0 (0.71)	736.0 (0.72)	

[a] Sonicated low molecular weight salmon sperm DNA was used at 60–70 m*M* phosphate/l. in the presence of 1 m*M* EDTA in D_2O (pD 7.0). The concentration of 1 and 2 was varied from 4 to 15 m*M*. Spectra were recorded at 34° using a Varian XL-100-15 spectrometer equipped with a Nicolet Technology FT accessory. Chemical shifts (Hz) from the internal standard sodium 3-trimethylsilyl propionate-2,2,3,3-d_4 (TSP) are reported. It should be noted that the chemical shifts, δ, are accurate to ±0.2 Hz and T_1 values are accurate to ±10%. The T_1 value of the internal standard, TSP, is not affected by the presence of DNA (T_1 = 3.4 ± 0.2).

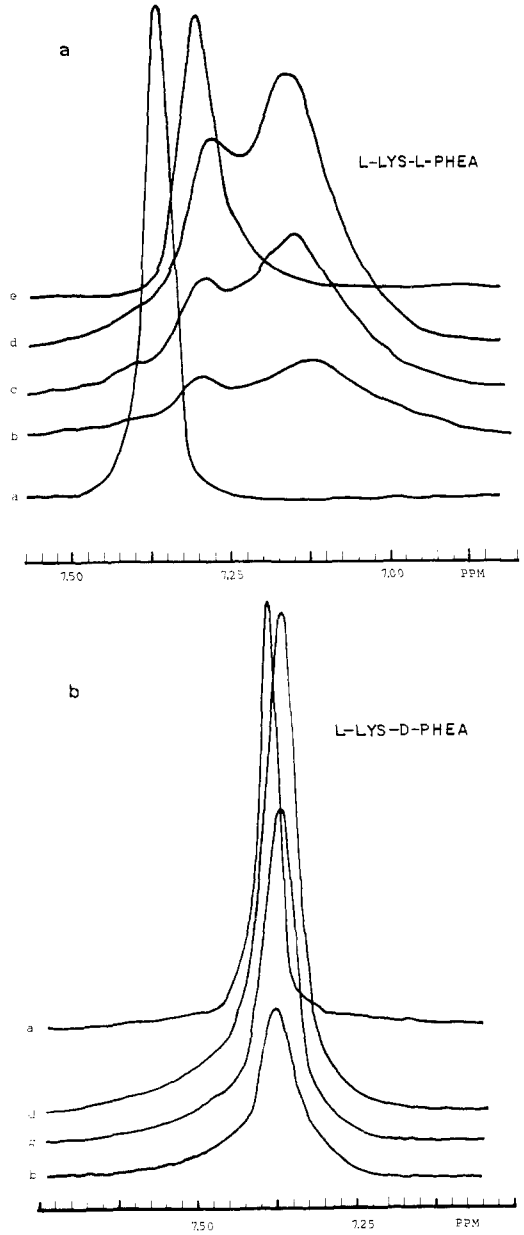

Figure 3. The proton magnetic resonance signal of the aromatic protons of L-lys-L-pheA and L-lys-D-pheA, (a) and (b), respectively; in the absence (a) and presence of DNA at a base-pair to peptide ratio of 7.2 (b), 3.6 (c), 2.4 (d), and 0.5 (e). See Table I for details.

chemical shift under conditions where the peptides are 100% bound to DNA.[2] On the other hand, the ^{1}H NMR signal of L-lys-L-pheA in the presence of DNA (base-pair to peptide ratio of 7.2) exhibits two broad resonance lines which are shifted upfield with respect to the free peptide by 6.0 and 23.5 Hz, respectively. At low base-pair to peptide ratio (e.g., 0.5), L-lys-L-pheA exhibits a single ^{1}H NMR resonance line for the aromatic protons which is indicative of fast exchange between the free and the various possible DNA binding sites of **1**. (4) The spin-lattice relaxation times, T_1,[3] for the aromatic protons of **1** and **2** are found to be identical for the free state, i.e., T_1 = 2.02 sec. In the presence of DNA (base-pair/peptide = 7.2), two T_1 values can be measured, e.g., T_1 = 0.57 and 0.77 sec for the high and low field signals, respectively (Figure 3, Table I). The T_1 value for the diastereomeric dipeptide amide, L-Lys-D-PheA, in the presence of DNA is also observed to be similar in magnitude, i.e., 0.66 sec.

The ^{1}H NMR relaxation data suggest that the phenyl rings of **1** and **2** in the DNA complex experience restriction in tumbling of equal magnitude. However, the differences in chemical shifts and line broadening suggest that the aromatic rings of **1** and **2** are in different chemical environments in the DNA complexes. A model which assumes that the aromatic ring of **1** points into the helix (i.e., partial insertion between base-pairs of DNA) and the aromatic ring of **2** points outward toward the solvent can best explain the data. For example, the observation of two ^{1}H NMR signals for the aromatic protons of **1** in the presence of excess DNA would result from the greater upfield chemical shift experienced by the meta and para protons than by the ortho protons as a consequence of ring current anistropy of neighboring base-pairs. The observed relative areas of the two aromatic signals of DNA-**1** (Figure 3) are consistent with the above interpretation.

The results of the flow dichroism and viscometric studies provide added evidence in support of the "partial intercalation" model. For example, the *selective* lowering of the relative specific viscosity and reduced dichroism of DNA solution upon binding the dipeptide amide, **1**, suggests that the effective length of the DNA helix is smaller in the DNA-**1** than in the DNA-**2** complex. Tilting (or bending) of the helix at the point of insertion of the aromatic ring of the dipeptide amide, **1**, between base-pairs would adequately account for the observed data.

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(2) The binding constants of **1** and **2** to DNA were determined by equilibrium dialysis and found to be 8000 and 6000, respectively. Under the conditions of the ^{1}H NMR experiments shown in Figure 3, the dipeptide amides are totally bound to DNA at base-pair to peptide ratio greater than 1.0.

(3) Values of T_1 were measured by the inversion recovery method on a Varian XL-100-15 spectrometer with a Nicolet Technology Corporation FT accessory. Pulse widths of 49 (180°) and 24.5 μsec (90°) were used, and 50 scans were accumulated for each delay time. Twenty seconds

was taken as the infinite delay time and a 4K transform was used. The probe temperature was approximately 34°.
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Hexakis(methyl isocyanide)dipalladium(I). Preparation, Structure, and Fluxional Behavior

Sir:

Although palladium(I) complexes have been proposed as intermediates in a number of palladium-catalyzed organic reactions,[1] only a few compounds of this type have been isolated.[2-6] With the possible exception of the ill-defined solid $[Pd(C_6H_6)(H_2O)(ClO_4)]_n$,[3] all of these complexes are diamagnetic, ligand-bridged dimers. The presence of direct Pd-Pd bonding in these systems has been inferred from the absence of paramagnetism and, in the two cases where X-ray structures are available,[2,5] from the proximity of the Pd atoms. We now report the first example of a cationic Pd(I) dimer containing only terminal isocyanide ligands.

The colorless solution formed by adding excess methyl isocyanide to an aqueous solution of $Na_2(PdCl_4)$ becomes pale yellow during 18 hr at room temperature. Following precipitation with ammonium hexafluorophosphate complex **1** having the empirical formula $[Pd(CNCH_3)_3(PF_6)]$ is obtained in 80% yield. Complex **1** is an electrolyte in nitromethane solution and the dimeric formulation $[Pd_2(CNCH_3)_6][PF_6]_2$ follows unambiguously from measurements of the equivalent conductance over a range of concentrations for **1** and for a series of related PF_6^- salts of known composition. The infrared spectrum of **1** (fluorocarbon mull) shows only absorptions typical of terminal isocyanide ligands: ν(C—H) 3040, 2975, 2928; ν(C≡N) 2260, 2252, 2240, 2234; δ(C—H) 1452, 1410. The low-temperature ^{1}H NMR spectrum (acetone-d_6, −30 to −90°) consists of resonances at τ 6.22 (singlet, relative intensity 2) and 6.31 (s, 1).

Complex **1** crystallizes from acetone-2-propanol as its acetone solvate in the triclinic space group $P\bar{1}$. Crystal data: a = 12.281 (2), b = 12.544 (3), c = 10.388 (2) Å; α = 111.03 (1), β = 111.12 (1), γ = 75.95 (1)°; V = 1381.6 Å^3; ρ_{exptl} = 1.87 (1), ρ_{calcd} = 1.87 g/cm^3 for Z = 2; μ_{mo} = 14.96 cm^{-1}. Intensity data were collected on a Picker FACS-1 diffractometer, and the structure was solved by the usual heavy atom methods using 3249 independent, absorption-corrected reflections with $F_o^2 > 3\sigma(F_o^2)$. In the final refinements all nonhydrogen atoms except those of the solvent were allowed to vibrate according to an anisotropic thermal model and the conventional discrepancy indices R and R' converged to values of 0.045 and 0.057, respectively.

The structure of the cationic dimer is illustrated in Figure 1. A metal-metal bond of length 2.5310 (9) Å joins the two Pd atoms, each of which possesses an essentially square-planar coordination geometry with the Pd-Pd bond occupying one of the coordination sites. The dihedral angle between the two coordination planes is 86.2° and the overall complex symmetry is nearly D_{2d}. The four "equatorial" Pd-C bonds are structurally equivalent, and their average length is significantly shorter than that of the two "axial" Pd-C bonds, 1.963 (5) vs. 2.049 (6) Å. An additional structural feature, which may bear on mechanisms formulated to account for the fluxional behavior of the complex in solution (vide infra), is the average Pd-Pd-cis C bond angle of 85.0 (9)° indicating displacement of the equatorial isocyanide ligands toward the neighboring Pd atom. A complete table of distances and angles may be found in the microfilm edition of this journal.

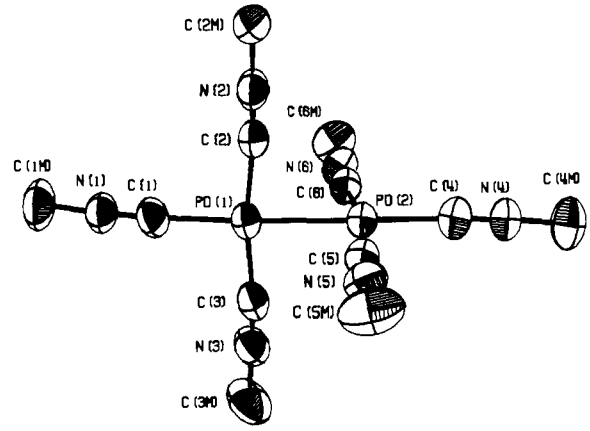

Figure 1. A perspective drawing of $[Pd_2(CNCH_3)_6]^{2+}$ showing the numbering scheme used. Bond distances and angles follow this article in the microfilm edition.

Complex **1** is the first Pd(I) dimer which does not contain bridging ligands in the solid state. A similar geometry has been reported for the Ni(I) complex $[Ni_2(CN)_6]^{4-}$,[7] and the vibrational spectra described for the dimeric Pt(I) complex $[Pt_2(CO)_2(Cl)_4]^{2-}$ [8] can be interpreted in terms of the present structural arrangement. The Pd-Pd distance in **1** is the shortest recorded for this bond. For comparison, values of 2.58 (1) and 2.686 (7) Å are reported respectively for the ligand-bridged dimers $[Pd(Al_2Cl_7)(C_6H_6)]_2$[2] and $[Pd_2(C_3H_5)(PPh_3)_2(I)]$.[5]

While the ^{1}H NMR spectrum of **1** is acetone-d_6 solution at or below −30° is consistent with the solid state geometry, warming the solution causes the two methyl resonances to broaden and eventually coalesce. At 35° the spectrum of **1** consists of a single resonance at τ 6.35. The dynamic process (or processes) responsible for the temperature dependence of the ^{1}H NMR spectrum appear to be intraionic in nature. The temperature dependence of the ^{1}H NMR spectrum was not altered by changing the dimer concentration or by adding palladium chloride which should scavenge free methyl isocyanide[9] that might catalyze exchange through an associative process. Several intraionic pathways seem plausible. Since $[Pd_2(CNCH_3)_6]^{2+}$ may be viewed as the result of the bonding of two d^9 $Pd(CNCH_3)_3^+$ fragments, the only vacant molecular orbital composed mainly of metal d functions is the σ^* orbital of the metal-metal bond. This means that deformations at the metal center may be facile because of limited ligand field stabilization effects. One pathway which appears to follow the normal modes of vibration involves the formation of a symmetric D_{3d} "staggered ethane" type structure. A second equilibration mechanism invokes a mixed Pd(II)-Pd(0) intermediate or transition state with square-planar and tetrahedral geometry about the respective metal centers. A third pathway involves exchange through bridging isocyanide ligands. The operation of this last process has been demonstrated in the case of $(\eta^5\text{-}C_5H_5)_2Fe_2(CO)_3(CNC(CH_3)_3)$.[10]

The complex reaction sequence which leads to the formation of **1** from $[PdCl_4]^{2-}$ and methyl isocyanide has not been fully elucidated. The initial steps are known to involve formation of $[Pd(CNCH_3)_4]^{2+}$ [11] and this is probably followed by nucleophilic attack by water or hydroxide ion at a metal-bound isocyanide carbon. Further investigations con-