

characteristic of uncoordinated phosphate groups (Figure 1).⁹ Furthermore, on lowering the pD to 5.8 and to 4.7, the signal shifts upfield to -1.55 and to -2.77 ppm, respectively, characteristic of protonation. Heating the pD 6.8 solution produces a mixture of III and IV. The ³¹P signal for III is at +2.95 ppm—an unusually far downfield shift. Moreover, lowering the pD to 4.7 resulted in an upfield shift of less than 0.1 ppm. Second, addition of base (pH 7.9 in H₂O) converts IV immediately and III readily to *cis*-Pt(NH₂CH₃)₂(5'-IMP-N7)OH. Similarly, addition of Cl⁻ (100 mM) converts both I and II to the well-known *cis*-Pt(NH₃)₂(GMP-N7)Cl^{14,10} with *t*_{1/2} of ca. 1 and 8 h, respectively, as monitored by the H8 signals (25 °C, pH 7). Third, no similar complexes were observed when the 5'-NMP was replaced by 3'-GMP, inosine, or the methyl phosphate ester of 5'-GMP (Me-5'-GMP). Fourth, the chemical shift of H8 of III was nearly invariant (<0.03 ppm) between pH 4.5 and 7.5. Previous work^{2,10,11} has shown that H8 shifts upfield ca. 0.1–0.3 ppm on primary phosphate protonation both in 5'-NMP's² (pK_a ca. 6.7) and in complexes of the type *cis*-PtA₂(5'-NMP-N7)₂ and *cis*-PtA₂(5'-NMP-N7)X, where X = Cl⁻ or H₂O and 5'-NMP = 5'-GMP¹⁰ or where X = Br and 5'-NMP = 5'-AMP (pK_a ca. 5.7).¹¹ Fifth, addition of Cu²⁺ (0.01 Cu/NMP) to a solution of III and IV causes broadening of H8 of IV but no broadening of H8 of III. This result suggests that Pt is bound to both N7 and PO₄, blocking Cu²⁺ coordination. These five points are readily understood only if the 5'-phosphate group is bound to Pt. Sixth, there is no concentration dependence of the equilibrium III ⇌ IV but III is favored between pH 6 and 7; IV is favored at pH > 7 (~2:1 at pH 7.9). The equilibrium condition is established by the ready interconversion of III and IV as the pH is changed. These results rule out a dimer, particularly of the type proposed in the literature, since formation of such a dimer requires a concentration dependence. Seventh, the ¹H NMR spectrum obtained from addition of 2 equiv¹² of *cis*-Pt(NH₂CH₃)₂(OH)₂ to a mixture of 0.5 equiv each of 5'-GMP and 5'-IMP is essentially identical with the sum of the spectra obtained when similar reactions are carried out on the individual 5'-NMPs. Two new sets of resonances could be expected if species such as III were dimers. Finally, two CH₃ signals for III, each ca. 3 times the intensity of the H2 signal, indicate that two amine ligands in different environments and one nucleotide are connected to each Pt.

Several additional observations on III provide information on the relationship of the ribose and purine rings and suggest that the ribose sugar is in an unusual N-type conformation, ¹E or ¹T.¹³ First, the value of ³J_{1,2'} should be near zero due to an expected Cl⁻-H1' to C2'-H2' torsion angle of near 90° (we observe values of <0.2 Hz for all 5'-NMP's studied). Second, in the 5'-dNMP adducts we expected ³J_{1,2'} of 9.5–10.5 Hz for a pure N conformer.¹³ In fact, we observe a sharp doublet for H1', J = 6.9–7.4 Hz, depending on the complex.¹³ Third, an anisotropic downfield shift of H2' signals due to a positioning of this proton near N3 in the plane of the pyrimidine ring should be observed. Indeed, the H2' signal appears near 5.25 ppm (ribose) or near 3.25 ppm (deoxyribose), ca. 0.4 ppm downfield from the same signals in

the unreacted nucleotide or in II or IV. This signal for I was incorrectly assigned⁷ to an upfield-shifted H1'. Our assignment of H2' signals for the 5'-dNMP adducts is unambiguous since H2' is strongly coupled to H2'' (²J = 13.5 Hz) but not to H1' (supplementary material). Signals we assign to H1' are in the usual shift region. Fourth, it is likely that H5'' is shifted upfield slightly by the anisotropic five-membered ring (we observe a 0.2 ppm upfield shift). Molecular models reveal that coordination of the phosphate group and N7 to Pt would lead to the structural parameters consistent with these four points.

Pt-OP bonds are known,¹⁴ and the inertness of the Pt II center allows identification of this novel chelate.¹⁵ However, the low stability of the chelate with a phosphate monoester suggests that such interactions will be at most transient with phosphodiester groups in DNA. Complexation to polynucleotides leads to ³¹P signals at ca. -3 ppm which have been attributed to N7,N7 chelates with no Pt-OP interactions.¹⁶ The absence of species III in studies with Me-5'-GMP supports this view.

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Supplementary Material Available: Figures illustrating ¹H NMR spectral studies of the mixed nucleotide reactions, selective ¹H decoupling experiments, and the pH and concentration dependence of the III ⇌ IV equilibrium (3 pages). Ordering information is given on any current masthead page.

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Macroscopically Oriented Copper(II) Chelates in Cast Multibilayer Films

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Bilayer membranes are two-dimensional arrays of molecules and constitute molecular systems useful for preparing ordered functional units.¹ This molecular ordering is readily transformable to macroscopic ordering, as regular multilayer films are obtainable by casting of aqueous bilayer dispersions onto solid supports.^{2–4} The cast films retain structural characteristics essentially analogous to those of the original aqueous dispersions, and the bilayers are aligned parallel to the substrate surface.

It occurred to us that the macroscopic ordering in cast films can be used for producing macroscopic orientations of electron spins. For this purpose, we prepared cast films of bilayer membranes in which the Cu(II) chelate moiety is either covalently⁵

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(12) In the preparation of IV from *cis*-Pt(NH₂CH₃)₂(OH)₂ and 5'-IMP, an excess of Pt is required to prevent formation of *cis*-Pt(NH₂CH₃)₂(5'-IMP-N7)₂.⁷ Five to ten minutes after the reactants were mixed and the pD adjusted to ~6.7, excess Pt was removed by addition of a slurry of CM-25 Sephadex. The complete removal of excess Pt was verified by the absence of the characteristic CH₃ ¹H NMR signal at 2.35 ppm.

(13) The furanose ring conformation cannot be fully deduced from the observation of ³J_{1,2'} alone. The observation of ³J_{1,2'} of ~7.0 Hz and ³J_{1,2'} of <0.5 Hz precludes a pure N conformer, which requires ³J_{1,2'} + ³J_{1,2''} = ³ΣJ₁ = 9.5–10.5 Hz. See Altona, C. *Recueil Travaux Chim. Pays-Bas.*, 1982, 101, 413. The situation is surprisingly similar to the case of Pt-d(GpG) where G(1)H1' exhibits a sharp doublet with ³J_{1,2'} (and thereby ³ΣJ₁) = 7.9 Hz. See: den Hartog, J. H. J.; Altona, C.; Chottard, J.-C.; Girault, J. P.; Lallemand, J.-Y.; deLeeuw, F. A. A. M.; Marcelis, A. T. M.; Reedijk, J. *Nucleic Acids Res.* 1976, 10, 4715.

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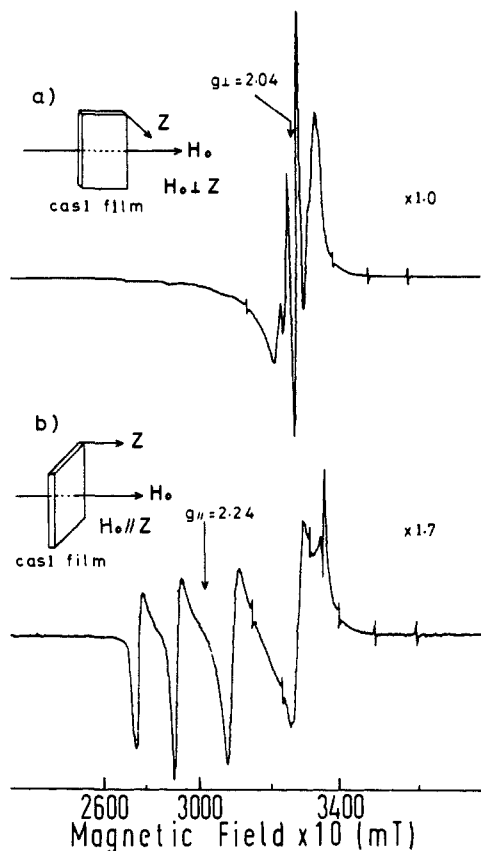
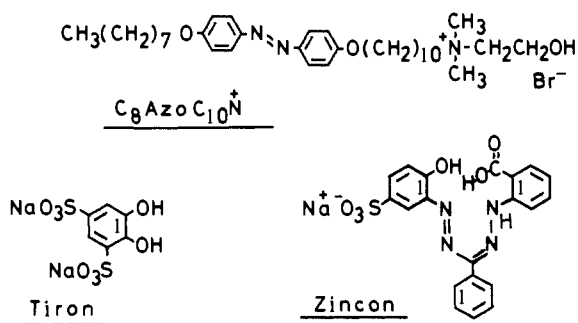


Figure 1. ESR spectra of $\text{Cu}(\text{Tiron})_2$ bound to a cast multilayer film: $[\text{C}_8\text{AzoC}_{10}\text{N}^+]/[\text{Tiron}]/[\text{CuSO}_4] = 27.4/2/1$; room temperature; modulation amplitude, 12.5 G; microwave frequency, 9.444 GHz. The film is placed parallel (a) and perpendicular (b) to the magnetic field.

Chart I



or noncovalently bound. This paper describes the ESR behavior of the latter.

Tiron (4 mM) (Chart I) and CuSO_4 (2 mM) were dissolved in deionized water and the pH was adjusted to 8.1 (at 20 °C) by adding 1 N NaOH. Powdery $\text{C}_8\text{AzoC}_{10}\text{N}^+$ was added and sonicated to give yellow dispersions. Transparent films were obtained by spreading the dispersion on Teflon plates and allowing them to stand at 20–25 °C for a few days. ESR spectra were measured with a JEOL JESME 3 X-band spectrometer with 100-KHz magnetic field modulation. The magnetic field was calibrated by the splitting of Mn(II) in MgO.

When the ESR spectrum was measured for a rapidly quenched sample of the aqueous dispersion, it was typical of a randomly oriented square planar Cu(II) complex. The observed ESR parameters ($g_{\parallel} = 2.27$, $g_{\perp} = 2.06$, $|A_{\parallel}| = 172 \times 10^{-4} \text{ cm}^{-1}$, $|A_{\perp}| = 22 \times 10^{-4} \text{ cm}^{-1}$) coincide with the published values.⁶ In contrast, a cast film showed peculiar ESR patterns. The spectra shown

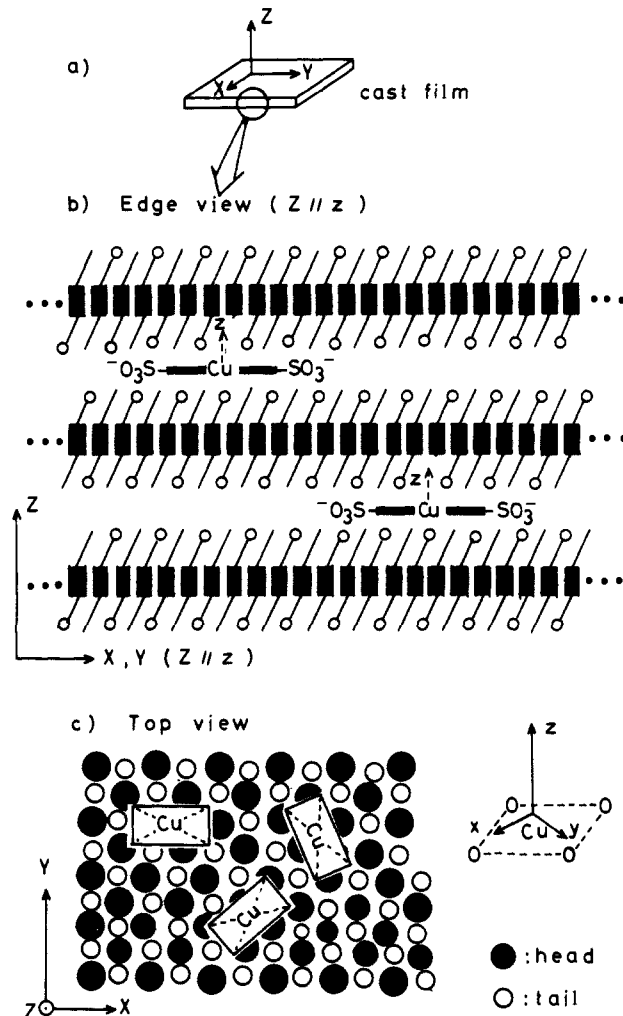


Figure 2. Schematic illustration of $\text{Cu}(\text{Tiron})_2$ in a cast film of $\text{C}_8\text{AzoC}_{10}\text{N}^+$.

in parts a and b of Figure 1 were obtained for a cast $\text{C}_8\text{AzoC}_{10}\text{N}^+/\text{Cu}(\text{Tiron})_2$ film which was placed parallel and perpendicular to the magnetic field, respectively. The signals are made solely of the perpendicular component (g_{\perp} and A_{\perp}) in Figure 1a and solely of the parallel component (g_{\parallel} and A_{\parallel}) in Figure 1b. In-plane rotation of the film did not change either spectrum. Therefore, the ESR pattern depends only on the angle between the film Z-axis and the magnetic field, and the Z-axis of the film and the z-axis of $\text{Cu}(\text{Tiron})_2$ complex must be parallel. This situation is schematically illustrated in Figure 2. The planar Cu(II) complex is placed flat on the membrane surface (the edge view), but the in-plane arrangement is random (the top view). It is noted in Figure 1b that the shapes of the four peaks due to hyperfine splitting are not symmetrical. This suggests that the z-axis of individual complexes fluctuates around the film Z-axis according to a certain distribution function, although the averaged orientation is perpendicular to the film plane. Similar fluctuations have been reported for Cu(II) chelates and a nitroxide spin probe oriented in nematic liquid crystals.^{7–9}

In the second series of experiment, $\text{Cu}(\text{Zincon})$ complex was used in place of $\text{Cu}(\text{Tiron})_2$. The dependence of the spectral pattern on the film position was totally different. When the cast film is placed perpendicular to the magnetic field, the ESR spectrum is composed only of the g_{\perp} component. Out-of-plane rotation of the film by 90° (the film plane is now parallel to the

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magnetic field) gives the g_{\parallel} component and the intensities of the g_{\perp} component are lessened to one-half. Therefore, the averaged z-axis of Cu(Zincon) molecules is situated parallel to the film plane: that is, Cu(Zincon) molecule is inserted vertically into the bilayer. The number of the negative charge in Cu(Zincon) is only one, in contrast to the six negative charges in Cu(Tiron)₂. This structural difference might be the cause of the different arrangement of these Cu(II) chelates in the bilayer membrane.

Cast multilayer films of double-chain, ammonium amphiphiles are similarly useful as matrices. A mixed cast film containing a covalently bound Cu(II) chelate gave also anisotropic ESR spectra.⁵ Thus, magnetically anisotropic thin films are obtainable from Cu(II) chelates that are either covalently or noncovalently bound to multilayer matrices. We are looking at further examples to establish how general this phenomenon might be.

Implications of the present results are as follows: (1) Macroscopic orientations of electron spins can be achieved by using anionic Cu(II) chelates embedded into cast films of ammonium bilayers. (2) Doping with the Cu(II) chelates is a very good means to probe the macroscopic and microscopic orders of multilayered cast films. The ESR technique is more flexible and convenient than the X-ray diffraction method we used previously.⁴ (3) Conversely, the mode of binding of metal chelates at the bilayer surface is readily inferred from ESR spectra. It does correlate with the molecular structure of bound chelates. (4) ESR spectroscopy of the cast film is a new, powerful methodology for studying the electronic structure of metal complexes. The magnetic anisotropy of metal complexes has been investigated by doping of single crystals⁷ and liquid crystals.⁸ These techniques possess, however, serious limitations such as the structural matching in the former and limited orientations in the latter. The present method is superior in both aspects.

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Aza- and Oxaphosphands, a New Class of Hard/Soft Binucleating Phosphine Macrocycles

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In recent years considerable effort has been devoted to the design and synthesis of binucleating macrocyclic ligands capable of binding two metals in close proximity.¹ Various bimetallic complexes have been synthesized by using ligands that contain two chelating subunits, such as aza, thia, phospho,² Schiff base,³

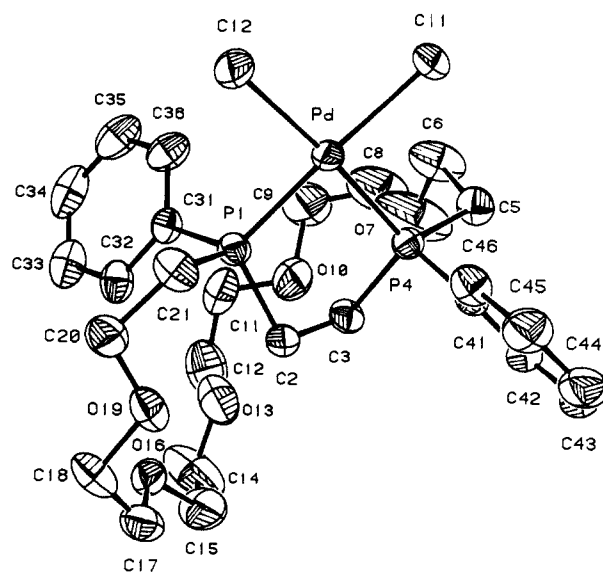
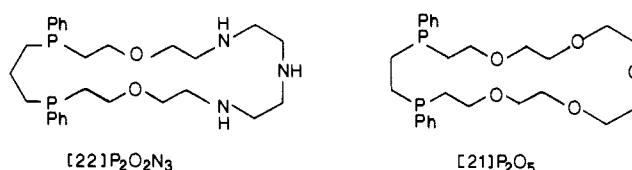


Figure 1. Structure of *anti*-(P₂PdCl₂O₅) showing the 40% probability thermal ellipsoids and atom labeling scheme and omitting hydrogen atoms. Selected interatomic distances (Å) and angles (deg) are as follows: Pd-P1 2.237 (1); Pd-P4 2.232 (1); Pd-C11 2.352 (1); Pd-C12 2.357 (2); P1-C2 1.824 (5); C2-C3 1.535 (7); C3-P4 1.825 (5); P4-Pd-C12 175.12 (5); C11-Pd-C12 93.62 (5); Pd-P1-C2 108.3 (2); P1-C2-C3 108.3 (3); C2-C3-P4 107.2 (3); C3-P4-Pd 107.5 (2). The deviations for P1 and P4 from the PdCl₂ plane are -0.11 and +0.10 Å, respectively.

or tetrapyrrole⁴ macrocycles or compartmentalized ligands.⁵ Previous studies in our laboratory have focused on the chemistry of dicopper(I), dicopper(II), and dirhodium(I) tropocoronand complexes⁶ and the coordination properties of homobinucleating hexaamine macrocycles.⁷ We have now developed a convenient, practical synthesis for two new, heterobinucleating azaphospho and oxaphospho macrocycles, [22]P₂O₂N₃ and [21]P₂O₅, re-



spectively, designated as "phosphands".⁸ Here we report details of the ligand syntheses, the high-yield separation of ligand diastereoisomers, the preparation and X-ray structural characterization of metal complexes *anti*-(P₂PdCl₂O₅) and *rac,anti*-(P₂Ni(NCS)₂[H₂N₃](NCS)₂), and the optical resolution of the latter by the method of Pasteur.⁹

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