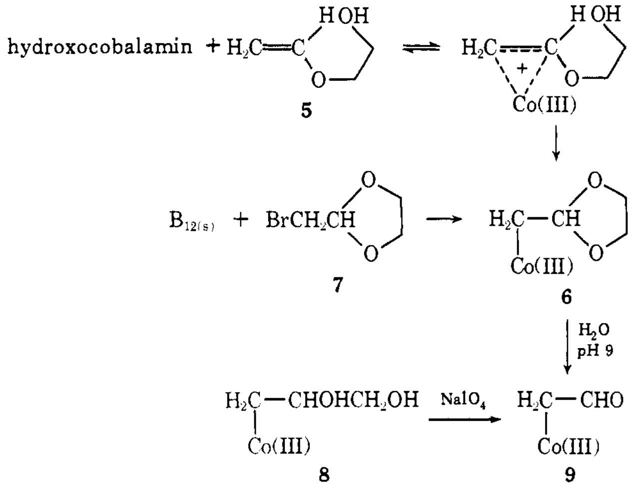

yield of cyclic acetal,[17] but this reaction was now slower ($t_{1/2}$ *ca.* 7 hr) than that with the cobalamin. Finally, the reaction between hydroxocobalamin and ethyl vinyl ether, in ethanol, gave a quantitative yield of the acetal, 2,2-diethoxyethylcobalamin, which was also prepared from B_{12s} and the corresponding bromoacetal.[18] Once again, as in the cobaloxime case, increasing amounts of water in this reaction gave increasing amounts of the aldehyde **9**.[18]

We have shown that the reactions of trivalent cobalt-containing cobalamins and cobaloximes with enol ethers can be formulated as proceeding *via* the formation of a Co(III) π complex, which can be quenched by ambient nucleophiles to give stable alkylcobalamins and cobaloximes. The observation of such reactions strengthens our hypothesis that the intermediacy of π complexes can explain the rearrangements controlled by coenzyme B_{12} dependent enzymes. These π complexes could be generated by the enzymatic removal of a group from a carbon atom β to the cobalt. This is a process which would clearly be assisted by the cobalt, for we have already seen that labilization of the "β groups" is greater with the cobalamins than with the cobaloximes. Thus, while the 2,2-diethoxyethylcobalamin is solvolyzed in water at pH 9, at room temperature, to the formylmethylcobalamin, solvolysis of the corresponding cobaloxime acetal requires 0.1 *M* acetic acid.

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Conformational Determination in Paramagnetic Metal Complexes

Sir:

When a labile complex is formed in solution between a diamagnetic ligand and a paramagnetic species, the nuclear magnetic resonance signals from those ligand nuclei closest to the site(s) of interaction are preferentially broadened. This effect has been widely employed in establishing paramagnetic metal binding sites.[1-4] However, the implied quantitative relationship between resonance line broadening and the electron-nucleus distances, r_i, has not been exploited.[5]

The conditions for which meaningful values of r_i can be obtained from paramagnetically broadened nuclear resonance lines are established herein. Experimental values for a variety of labile paramagnetic complexes are in excellent agreement with known structures.

The paramagnetic contribution to the spin-spin relaxation time, T_2, of a diamagnetic nucleus in a labile complex is given by[6] eq 1 when relaxation is modulated

$$\frac{1}{T_2} = \left(\frac{1}{15}\right)S(S+1)g^2\beta^2\gamma_I\left(\frac{N_sn}{N_I}\right)\left(\frac{1}{r_i^6}\right)\left[7\tau_c + \frac{13\tau_c}{1+\omega_s^2\tau_c^2}\right] + \left(\frac{1}{3}\right)S(S+1)\frac{A^2}{\hbar^2}\left(\frac{N_sn}{N_I}\right)\left[\tau_e + \frac{\tau_e}{1+\omega_s^2\tau_e^2}\right] \qquad (1)$$

by isotropic rotation of the complex. S is the effective electron spin quantum number, n is the number of identical nuclei coupled to the electron, and N_s and N_I are the total number of paramagnetic species and diamagnetic ligand molecules per cubic centimeter. A is the isotropic hyperfine coupling constant which is a complicated function of r_i. g, β, and γ_I have their usual meanings.

The two terms in eq 1 represent dipolar and scalar relaxation components with motional correlation times,[6] τ_c and τ_e, respectively. In cases where dynamic scalar coupling is relatively inefficient[7,8] (*e.g.*, between protons and labile paramagnetic metal ions other than lanthanide and actinide ions), r_i can be estimated (assuming $A = 0$) from a plot of T_2^{-1} *vs.* N_s, provided that τ_c and n are known for each proton.

The very sensitive distance dependence (r_i^{-6}) of dipolar relaxation actually enables meaningful values of r_i to be obtained even when some scalar relaxation occurs. Furthermore, only small errors result if it is assumed[9] that τ_c is the same for all protons in the complex. Thus, relative r_i values can be obtained directly from the relative slopes of $[nT_2]^{-1}$ *vs.* N_s plots.

Measurements of T_2 for individual peaks in a high resolution nmr spectrum are usually accomplished by measuring resonance line widths, $\Delta\nu_{1/2}$ $(=[\pi T_2]^{-1})$.[10] However, many useful resonance lines exhibit multiplet

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Table I. Proton to Metal Distances

	Hydroxyproline					
	H_3	H_1	H_2	H_4	H_5	H_6
Mn^{II}, pH 10.1	3.5 (3.5)	4.3 (4.3)	5.2 (4.9)	3.1 (2.8)	3.6 (3.7)	3.6 (3.5)
Cu^{II}, pH 10.1	3.5 (3.5)	4.3 (4.3)	5.1 (4.9)	3.0 (2.8)	3.6 (3.7)	3.4 (3.5)

	$CH_3(CH_2)_nCH(NH_2)COO^-$			
	H_α	H_β	H_γ	H_δ
n = 0, Cu^{II}, pH 10.0	3.6 (3.6)	5.0 (4.7)		
n = 1, Cu^{II}, pH 10.0	3.6 (3.6)	4.5 (4.5)	5.5 (5.5)	
n = 2, Cu^{II}, pH 10.0	3.6 (3.6)	4.5 (4.5)	5.7 (5.5)	6.7 (6.7)

structures whose individual component line widths can, at best, be measured only in the presence of small amounts of paramagnetic species. Multiplet structures can be collapsed by applying double irradiation techniques, however, a simpler procedure is to plot the composite multiplet width at half-height *vs.* N_s. The curve thus obtained tends asymptotically to a straight line of slope parallel to that of the decoupled multiplet as the broadening of individual components becomes greater than their separation.

The following results are all based on multiplet "line width" measurements. Identical results were obtained where multiplets were decoupled.

Complexes investigated were those between the paramagnetic metal ions Mn^{II}, Cu^{II}, Co^{II}, Ni^{II}, Fe^{III}, Cr^{III} and the ligands α-alanine, α-aminobutyric acid, norvaline, asparagine, glutamine, aspartic acid, itaconic acid, acetylmercaptoic acid, glycine methyl ester, *N*-acetylglycine, tyrosine, L-proline, L-hydroxyproline, adenosine 5′-monophosphate (AMP), and histidine at the appropriate pH(s) in aqueous solution. Of these, only AMP, histidine, proline, and hydroxyproline form rigid complexes suitable for comparing experimental values of r_i with those measured from molecular (Dreiding) models. Nonrigid complexes were assumed to be in their least hindered conformation. Spectra for L-hydroxyproline are shown in Figure 1.

With the exception of the Cu^{II}–histidine complex, all calculated r_i values agree (within 10%) with those measured from models. Representative results are presented in Table I with measured distances (Å) in parentheses. The first value quoted for each complex is assumed in order to convert r_i ratios to absolute distances.

Calculated r_i values indicate that the imidazole ring protons in the 1:2 Cu^{II}–histidine complex are equidistant from the copper. This is inconsistent with any structural model. However, the complex is thought to exist as an equilibrium between two structures[3] whose averaged conformation could have apparently equal r_i values for the ring protons. Alternatively, the established π bonding[11] between the imidazole ring and Cu^{II} undoubtedly facilitates electron–nucleus scalar coupling thereby rendering the assumption of purely dipolar relaxation invalid.

The exactness with which electron–nucleus distances can be obtained by this simple procedure leaves little room for compromise in establishing metal binding sites and molecular conformations. Thus, for AMP the calculated distances strongly indicate metal chelation between the phosphate and amino groups above pH 3.9 as suggested by Li, *et al.*[12,13] Chelation between the phosphate group and the imidazole nitrogen, as suggested by a number of other workers,[2,4,14,15] cannot be accommodated even with the assumption of π bonding.

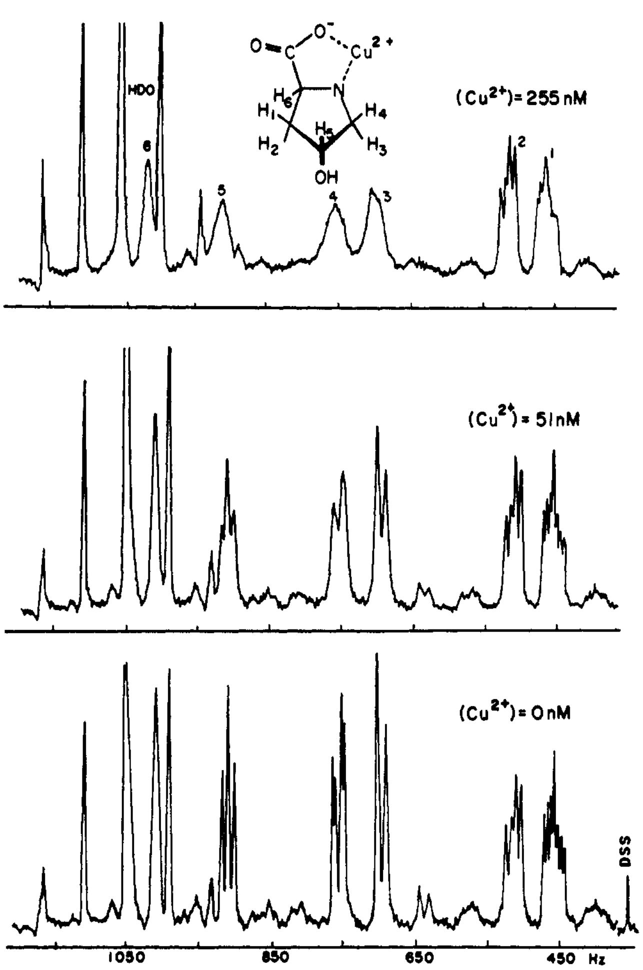

Figure 1. Proton spectra (220 MHz) of 0.1 *M* L-hydroxyproline in D_2O (pD 10.0) in the presence of $CuCl_2$.

Although the above procedure has been cast in terms of T_2 and line width measurements in order to illustrate its simplicity, electron–nucleus distances can also be obtained in an analogous manner from T_1 measurements.[6] More paramagnetic material is required, however, to establish T_1^{-1} *vs.* N_s plots for *S* state ions since $T_1/T_2 > 1$.

The procedure is also applicable to paramagnetic

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species other than metal ions, provided that a labile complex is formed and that scalar coupling is effectively negligible. Thus, the possibility of determining molecular conformation with respect to spin labels and rare earth shift reagents is indicated.[16] The method is thus complementary to that of conformational determination from rare earth shift measurements.[17] Applications to large molecular complexes are limited only by the ability to resolve and assign proton resonance lines.

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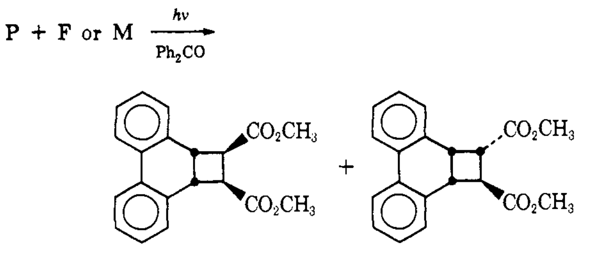
Intermediates and Stereochemistry in the Triplet-State Photocycloaddition of Phenanthrene to Electron-Poor Olefins

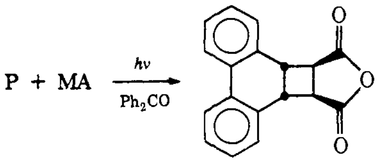
Sir:

The intermediacy of singlet excited-state complexes (exciplexes) in singlet-state [2 + 2] photocycloadditions is well documented;[1] it is common, if not universal. By contrast, triplet exciplexes in sensitized photocycloadditions stand on less firm ground. Evidence in their support has been largely inferential.[2] The extreme difficulty of observing exciplex phosphorescence,[3] and the expectation that triplet exciplexes will show substantially less binding energy than singlet exciplexes,[4] make their importance a moot point. Our recent[5] indirect demonstration of a triplet exciplex in the Paterno–Buchi reaction of diaryl ketones led us to examine other systems. A recent report[6] of the reaction of phenanthrene (P) with dimethyl fumarate (F) prompts us to report the results of our own study of this and related reactions. We have observed patterns of reactivity and stereoselectivity that suggest a triplet exciplex intermediate.

The benzophenone-photosensitized cycloaddition of phenanthrene to F, dimethyl maleate (M), and maleic anhydride (MA) leads to the photocycloadducts C, T, and CA of eq 1 and 2. The structures of these adducts follow from their satisfactory analyses, their nmr spectra, the conversion of C to T with sodium methoxide in dry methanol, the conversion of CA to C with acidic methanol, and the ozonolysis of C (acetic acid solvent, hydrogen peroxide work-up, and diazomethane esterification) to the known[7] *cis,trans,cis*-cyclobutane-1,2,3,4-tetracarboxylic acid tetramethyl ester. In the reaction with MA,[8] less than 5% of an endo anhydride isomer was formed as evidenced by the nmr of reaction mixtures. In the reaction with F or M, the unknown cis,endo isomer was absent (<3%), as evidenced by the nmr spectra and glpc analysis of reaction mixtures; ozonolysis of reaction mixtures revealed none (<2%) of the all-cis cyclobutane tetraester.[7] Material balance (±3%) was maintained throughout, by comparison of P + C + T with P(initial) and F + M + C + T with M or F(initial). This was true even in prolonged irradiation (eight times the time necessary for 90% conversion).



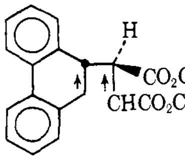
C T (1)



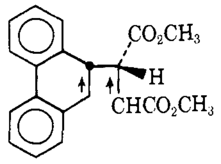
(2)

CA

The ratio of T to C was 1.8 ± 0.05, independent of reaction time and of whether F or M was the reactant.[9] Although concomitant F to M and M to F isomerization occurred, we were able to observe this same T:C ratio in experiments in which isomerization of F to M was as low as 0.9% or M to F as low as 1.2%. The intermediacy of a triplet 1,4-biradical intermediate, analogous to those proposed in other triplet-state photocycloadditions,[1b,2,5,10] is thus indicated. Quantum yield studies confirmed that P^3 and not F^3 is the reactive species and that its probability of ultimate conversion to C + T is 0.11 (Figure 1).



SR



SS

Two stereoisomeric biradicals, *SR* and *SS*, are possible. Both C and T can be formed from *SR*, but *SS* would give the isomeric cis,endo diester in addition to T. If a biradical is precursor to CA, it must also have the *SR* stereochemistry. Our product ratios in-

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