Lanthanide Porphyrin Complexes. Evaluation of Nuclear Magnetic Resonance Dipolar Probe and Shift Reagent Capabilities

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Abstract: Organic solvent soluble lanthanide complexes of tetraarylporphine (TAP) ligands with the general formulation $Ln^{III}TAP(\beta\text{-diketonate})$ have been prepared and characterized for the following elements: Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu. Paramagnetic NMR shifts (mostly downfield) are observed for the TAP protons of the Eu(III) and Yb(III) complexes. The β-diketonate proton resonances are shifted upfield. The aryl proton resonance shifts are consistent with a dominant dipolar interaction with the metal atom situated significantly out of the porphyrin plane by ~1.8 (Eu) and ~1.6 Å (Yb). From the magnitude of the observed shifts it is estimated that the Yb(III) complex has a dipolar field ~2.2 times as strong as that of the prosthetic group in metmyoglobin cyanide. The resonance shifts in the Yb(III) complex are linear in T^{-1} with a nonzero intercept at $T^{-1} = 0$. The Yb(III) complex serves as a downfield shift reagent toward heterocyclic amines and alcohols. The shift reagent action toward 4-picoline of the entire series of lanthanide complexes has been surveyed. Only very small resonance shifts are observed for the early elements (Pr, Nd, Sm, Eu); however, sizable upfield (Tb, Dy, Ho) and downfield (Er, Tm, Yb) shifts are observed for the elements at the end of the series. $Ln^{III}TAP$ complexes are somewhat less effective as shift reagents than their β-diketonate counterparts. The diamagnetic Lu(III) complexes represent a new class of upfield "ring current" shift reagent. An eight-coordinate model is proposed to account for the fact that the substrate resonance shifts are in the *same* direction as those of the TAP ligand.

The synthesis in our laboratory of the first lanthanide[1] and actinide[2] porphyrin complexes virtually completes the periodic table of metalloporphyrins.[3,4] This work opens up a new area of macrocyclic ligand chemistry of these elements. The resistance of complexes of this type to hydrolysis in neutral and basic solution allows the introduction of lanthanide complexes of naturally occurring porphyrin ligands into heme proteins via reconstitution reactions. The insertion in a highly specific manner of a lanthanide ion, with its characteristic spectroscopic and magnetic properties, into a heme protein provides a potentially powerful new class of metal-centered probe. We have recently demonstrated by a variety of physical techniques the successful introduction of ytterbium mesoporphyrin Ix into apomyoglobin.[5]

Our work provides a new means of introducing lanthanide ion probes into biological macromolecules. Insofar as it is applicable to a different class of biomolecules, the introduction of lanthanide porphyrins into heme proteins is complementary to the replacement of Ca(II) by trivalent lanthanide ions (Ln(III)) in calcium-dependent proteins,[6,7] an area in which we also have a strong interest.[8] Of particular importance in the present context are the large magnetic anisotropies generally associated with lanthanide complexes, which give rise to sizable nuclear magnetic resonance (NMR) paramagnetic shifts in solution.[9] Such shifts are dependent on the geometrical positioning of the resonating nuclei with respect to the metal ion and the principal magnetic axes of the complex. They are, in principle at least, capable of yielding information about geometry in solution. The β-diketonate variety of lanthanide shift reagent (LSR) has been exploited for NMR spectral simplification and structure assessment.[10,11] The results obtained in the latter application must, however, be accepted with some caution.[12,13] The present article is concerned with the NMR spectra and shift reagent capabilities of *meso*-tetraarylporphine complexes of the entire series of trivalent lanthanide complexes (Pr–Lu) in nonaqueous solution.

Experimental Section

Preparation and Purification of the Complexes. Owing to their extreme similarities it was found possible to synthesize and purify all the lanthanide tetraarylporphine complexes by the same procedure described below for the tetraphenylporphine (TPP) complexes. The tetraarylporphine free bases were prepared by a literature method.[14]

To a round-bottom flask (100 ml) equipped with a nitrogen inlet and reflux condenser were added H_2TPP (1.0 g, 1.63×10^{-3} mol), hydrated $Ln(acac)_3$[15] (2.0 g, $\sim 4.0 \times 10^{-3}$ mol, acac = $C_5H_7O_2^-$), and 1,2,4-trichlorobenzene (75 ml) to act as solvent. Lanthanide complexes of other β-diketonates such as 3-acetylcamphor and 2,2,6,6-tetramethylheptanedione (dpm) may be equally well employed as reactant. The solution was stirred magnetically and heated to reflux (~215 °C) while passing a slow flow of nitrogen which was allowed to exit through a bubbler. The course of the reaction was followed by examining the uv-visible absorption spectra of periodically withdrawn aliquots. Completion of the reaction, which generally occurs within 3-4 h, is indicated by the complete disappearance of the four visible absorptions of the free base at (relative intensities indicated) $510 > 550 > 590 > 645$ nm and the appearance of bands characteristic of the metalloporphyrin with relative intensities at the indicated wavelengths $510 \ll 550 > 590$ nm.[16] A shift in the Soret band may also be noted, that of H_2TPP being at ~415 nm and that of the metal derivatives at ~420 nm. Upon completion of the reaction the solvent was distilled away under reduced pressure (water aspirator) with the aid of a slow stream of dry nitrogen. Care was taken to ensure complete removal of solvent. Prolonged heating of the product should be avoided. The crude product was dried under vacuum.

Unreacted H_2TPP and $Ln(acac)_3$ were removed by column chromatography. A neutral aluminum oxide column (2.5 × 15 cm) was prepared and saturated with toluene. The crude product was dissolved in a minimum volume of toluene and applied to the column and H_2TPP was eluted with toluene. The column was then eluted with acetone to remove all remaining H_2TPP and a trace of metalloporphyrin. Finally, dimethyl sulfoxide (Me_2SO) was used to elute the majority of the metalloporphyrin, with the unreacted $Ln(acac)_3$ apparently remaining at the top of the column. The Me_2SO fractions were treated with equal volumes of freshly distilled chloroform (previously treated with a 0.1 M NaOH solution) and extracted three times with equal volumes of water. The metalloporphyrin was recovered from the chloroform solution by rotary evaporation. The product was further purified by dissolution in base-treated chloroform, followed by precipitation with distilled methanol or by cooling. The product so obtained was dried under vacuum.

Characterization of the Complexes. Representative samples were submitted for elemental analysis (Galbraith Laboratories, Knoxville, Tenn.). $Yb(p\text{-}CH_3)TPPacac$: Anal. Calcd for $YbC_{53}H_{43}N_4O_2$: C,

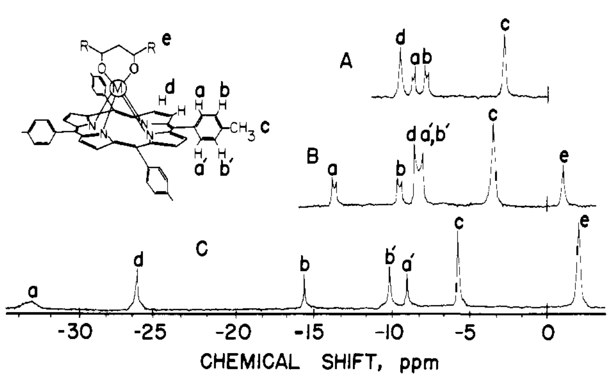

Figure 1. Proton NMR spectra of $H_2(p\text{-}CH_3)TPP$, (A); $Eu(p\text{-}CH_3)TPP(acac)$, (B); and $Yb(p\text{-}CH_3)TPP(dpm)$, (C); taken in deuteriochloroform at −21 °C. Chemical shifts in parts per million from Me_4Si as an internal standard.

67.66; H, 4.57; N, 5.96. Found: C, 67.56; H, 4.70; N, 5.80. $Yb(p\text{-}CH_3)TPPdpm$: Anal. Calcd for $YbC_{59}H_{55}N_4O_2$: C, 69.14; H, 5.37; N, 5.48. Found: C, 69.70; H, 5.74; N, 4.89. Products were routinely analyzed spectrophotometrically by quantitative conversion to the dication[17] of the free base H_4TPP^{2+} by bubbling hydrogen chloride gas through solutions of the metalloporphyrin complexes in organic solvents. On the basis of the spectrophotometric diacid cation analysis, extinction coefficients were determined for the Soret band at ~420 nm and the three visible bands at ~510, ~550, and ~590 nm. The molar extinction coefficients (ϵ (M^{-1} cm^{-1}) × 10^{-3}) are given for the four bands in order of increasing wavelength: Sm (381, 2.8, 15.2, 4.6); Eu (365, 2.8, 13.2, 4.8); Tb (491, 3.0, 18.4, 5.3); Dy (401, 2.7, 16.8, 4.3); Ho (348, 2.4, 16.8, 3.9); Er (397, 3.3, 17.3, 5.5); Tm (365, 2.3, 18.0, 3.7); Yb (346, 3.3, 15.8, 6.6); Lu (380, 3.7, 18.9, 4.1).

Mass spectra data were obtained using a MS 902 instrument operating at 70 eV with a chamber temperature of 350-400 °C, employing perfluorokerosene or tris(perfluoroheptyl)-*s*-triazine as a fragment reference. In all cases molecular parent ions with satellite peaks consistent with the known isotopic abundance for each metal were observed as well as a peak corresponding to the loss of the β-diketonate anion. Often a minor peak corresponding to the parent ion of an acetate complex was observed, perhaps formed by pyrolysis in the high-temperature probe with loss of a C_3H_4 fragment.

Infrared spectra were taken on a Perkin-Elmer 621 instrument using the KBr disk technique. Bands at ~1510 and ~1595 cm^{-1} characteristic[18] of metalloporphyrin-acetylacetonate complexes were observed in most cases. Further infrared and mass spectral data on these complexes can be found in a thesis.[19]

NMR spectra were obtained using a Varian A-60-A instrument equipped with variable temperature accessory and employing Me_4Si as an internal standard.

Results and Discussion

Dipolar Probe Characteristics. Porphyrin Proton Resonance Shifts. Lanthanide complexes of tetra-*p*-tolylporphine (($p\text{-}CH_3$)TPP) were synthesized in order to obtain cleanly assignable resonances for the porphyrin ligand and to simplify the diamagnetic reference spectrum in the aromatic region. The proton NMR spectra of the free base $H_2(p\text{-}CH_3)TPP$ and the Eu(III) and Yb(III) complexes taken at −21 °C are shown in Figure 1. Signal assignments, made on the basis of relative areas, temperature dependencies, and agreement with calculated dipolar shift ratios (vide infra), are as indicated in the insert. The results for the Yb(III) complex will be discussed first. All of the porphyrin proton resonances of $Yb(p\text{-}CH_3)TPPdpm$ are shifted downfield. The ortho and meta aryl proton resonances, equivalent in the free base, become nonequivalent in the complex owing to the out-of-plane position of the metal ion. This nonequivalence is amplified in the present case by the paramagnetic shift effect to the extent that the two ortho proton resonances a and a′ are separated by 22.5 ppm. On the basis of the work of others,[20-23] aryl group rotation is expected to be slow on the NMR time scale at this temperature, even for much smaller chemical-shift differences. The *tert*-butyl proton resonances of the apical dpm ligand are shifted upfield.

For $Eu(p\text{-}CH_3)TPPacac$ the shift magnitudes are much smaller with the endo-ortho proton resonance (a) being shifted only one-fifth as far as the corresponding resonance in the Yb(III) complex. In the Eu(III) complex the pyrrole proton resonance (d) and the exo-ortho resonance (a′) appear to be upfield shifted as is the methyl proton resonance of the apical acac ligand.

It is well known[9] that for an axially symmetric system, dipolar shifts are determined by the product of a magnetic anisotropy factor and a geometric factor of the form $(3\cos^2\theta - 1)r^{-3}$, where r is the length of a radius vector from the metal to the resonating nucleus and θ is the angle made by this vector with the principal axis. In order to achieve a more quantitative analysis of the shifts and to estimate the out-of-plane displacement of the metal ion, the following calculations were carried out. Assuming axial symmetry with the principal axis normal to the porphyrin plane[24] and adopting structural parameters for the TPP ligand as determined by Collins et al.[25] with the aryl ring planes normal to the porphyrin plane, geometric factors and ratios thereof were calculated as a function of R, the distance of the metal from the porphyrin plane. The calculated dipolar shift ratios are compared with the observed shift ratios in Table I. It should be emphasized that the model is a crude one, with no account being taken of phenyl ring oscillation[26] or porphyrin skeletal doming. Ignoring, for the moment, the small shifts of the exo-ortho and -meta protons (a′, b′) and the pyrrole proton shifts (d), quite satisfactory agreement between the calculated and observed shift ratios is obtained for out-of-plane displacements (R) of 1.80 Å for the Eu(III) complex and 1.60 Å for the Yb(III) complex. These rough estimates lead to Eu-N and Yb-N distances of 2.69 and 2.56 Å, respectively, which are, respectively, 0.04 and 0.07 Å greater than the pyridine or picoline to Eu(III) or Yb(III) distances measured or estimated from x-ray crystallographic results[27,28] on β-diketonate adducts. This trend in distances is consistent with the different ionic radii for the two metals, with that of Yb(III) 0.09 Å smaller.

For R = 1.60 Å in the Yb(III) complex the calculated and observed shift ratios for the pyrrole protons are in reasonably good agreement, implying that any Fermi contact contribution to this shift is fairly small. On the other hand, for the Eu(III) complex, a sizable downfield shift is predicted, while a small upfield shift is actually observed. This suggests a sizable upfield contact contribution to the pyrrole proton resonance shift. These findings are consistent with theoretical work[29] that suggests that Eu(III) complexes should exhibit far larger contact shifts than Yb(III) complexes. They are also in agreement with results on low-spin $Fe^{III}TPP$ complexes, where the aryl proton shifts were found to be purely dipolar in origin while the pyrrole protons show large contact contributions to the total shifts.[26]

It is of interest to compare the potency, as a dipolar NMR shift probe, of the $Yb^{III}TPP$ complex with analogous low-spin Fe(III) systems. From the NMR work of La Mar and Walker,[26] correcting for the temperature difference and the difference in magnitude of the geometric factors (low-spin Fe(III) lies in the porphyrin plane), we find that the magnetic anisotropy of YbTPPdpm is ~3.1 times that of the bisimidazole complex of $Fe^{III}TPPCl$ and is in the opposite sense. For low-spin Fe(III) systems the resonances of nuclei in the equatorial region (prophyrin plane) are upfield shifted by the dipolar mechanism, while the opposite is true for the Yb(III) systems studied here. On the basis of our detailed comparison[30] of the magnetic anisotropies of various low-spin Fe(III) heme proteins, we estimate that the present Yb(III) porphyrin complex has ~2.2 times the dipolar shifting ability of the prosthetic

Table I. Comparison of the Observed Relative Shifts for the Aryl Proton of Eu^{III}- and $Yb^{III}(p\text{-}CH_3)TPP$ Complexes with Those Calculated[a] as a Function of the Out-of-Plane Displacement of the Metal, *R*[b]

	Calcd relative shifts						Obsd relative shifts	
R, Å	1.5	1.6	1.7	1.8	1.9	2.0	Eu(III)	Yb(III)
H_a	10.0	10.0	10.0	10.0	10.0	10.0	10.0[c]	10.0[d]
H_b	3.21	3.17	3.14	3.12	3.11	3.09	3.14	3.19
CH_3	1.42	1.37	1.33	1.29	1.26	1.23	1.28	1.36
$H_{a'}$	0.07	−0.14	−0.33	−0.49	−0.65	−0.80	−0.61	0.25
$H_{b'}$	1.10	1.00	0.91	0.83	0.75	0.68	0.68	0.92
Pyrrole(d)	6.90	6.41	5.96	5.55	5.14	4.77	−1.89	6.95
$(3\cos^2\theta - 1)r^{-3}$ [e]	−6.82	−6.96	−7.07	−7.15	−7.23	−7.28		

[a] See text. [b] See Figure 1 for proton labeling system. [c] Observed shift: −4.88 ppm at −21 °C. [d] Observed shift: −24.13 ppm at −21 °C. [e] Calculated geometric factor × 10^3 Å^{-3} for H_a.

group in metmyoglobin cyanide, the most effective of the low-spin Fe(III) dipolar probes.[30]

Temperature Dependencies of the Resonance Shifts. The temperature dependencies to be expected for dipolar NMR shifts in lanthanide complexes have been the subject of some discussion since the publication of a theoretical treatment by Bleaney.[31] Bleaney's theory accounts reasonably well for the variations of the signs and magnitudes of the magnetic anisotropies (and hence of dipolar shifts) of axially symmetric complexes as one proceeds across the Ln(III) series. His theory predicts (with the exceptions of Sm(III) and Eu(III) complexes) that the anisotropies should vary linearly with T^{-2}; however, owing to certain approximations employed in Bleaney's approach, this prediction is not strictly correct, as discussed in detail elsewhere.[32] We have presented[12] an alternative, more exact theoretical approach to this problem, which involves a more general expansion of the ligand field potential and employs the entire Russell-Saunders ground term as a basis, including both the ground- and excited-state *J* multiplets. Our calculations show that the temperature dependencies of magnetic anisotropies will not, in general, be simple, but will vary from case to case. A linear dependence on T^{-1} in the temperature range of interest for NMR, with a nonzero intercept at $T^{-1} = 0\ \mathrm{deg}^{-1}$ frequently occurs. Experimentally it is clear that several exceptions to Bleaney's theory exist. The magnetic anisotropies ($\Delta\chi$) of single crystals of the axially symmetric complexes $Yb(C_2H_5SO_4)_3 \cdot 9H_2O$[33] and $Yb(antipyrene)_6I_3$[34] have been measured as a function of temperature in the range ~100–300 K. In neither case is the product $\Delta\chi \cdot T^2$ even approximately independent of temperature,[32] as predicted by Bleaney's theory.[31] Anisotropy measurements of our own[12,32,35,36] on single crystals of the nonaxially symmetric shift reagent adducts $Ln(dpm)_3(4\text{-pic})_2$ (Ln = Pr, Nd, Eu, Yb; 4-pic = 4-picoline) reveal temperature dependencies which are either linear in T^{-1} or more complex, depending on the metal ion and the orientation of the crystal.

Only fragmentary data exist in the literature regarding the temperature dependencies of lanthanide-induced NMR shifts. The interpretation of such results is complicated by the presence of other potentially temperature-dependent processes which may affect the shift magnitudes, e.g., ligand exchange and equilibrium between complexes of different stoichiometries and/or conformations. In the cases of the $Pr(fod)_3$[37]-$C_2H_4(OCH_3)_2$[38] and $Yb(fod)_3\text{-}(CH_3)_2C{=}O$[39] systems a linear dependence of the shifts upon T^{-2} was observed, while a more complex behavior ($T^{-1/2}$?) was observed for the resonances of some ketones in the presence of $Yb(dpm)_3$.[40] In lanthanide porphyrin complexes the prophyrin moiety is exchange inert,[41] which eliminates at least one of the factors which can complicate the interpretation of the temperature dependencies of NMR shifts. The temperature dependencies of the porphyrin and dpm proton resonances of $Yb(p\text{-}CH_3)$TPPdpm in the range −38 to 36 °C are shown as a plot of chemical shift vs. T^{-1} in Figure 2. The plots are quite linear in T^{-1} and, with the exception of the pyrrole proton resonance, all signals extrapolate to their diamagnetic positions at $T^{-1} \simeq 0.7 \times 10^{-3}\ \mathrm{deg}^{-1}$. The pyrrole proton resonance extrapolates to its diamagnetic position at $T^{-1} \simeq 0.0\ \mathrm{deg}^{-1}$, perhaps owing to a small contact contribution which will in general have a temperature dependence different from that of dipolar shifts. A plot of the shifts of the endo-ortho proton vs. T^{-2} (not shown) is slightly convex upward with the best straight line through the points extrapolating to nowhere near the diamagnetic position at $T^{-2} = 0.0\ \mathrm{deg}^{-2}$.

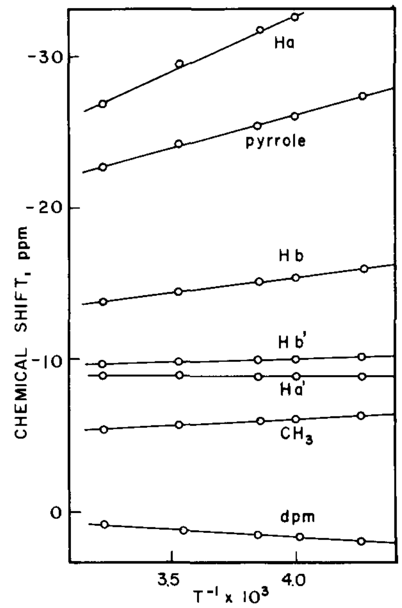

Figure 2. Plot of chemical shift (ppm from Me_4Si) vs. T^{-1} for proton resonances of $Yb(p\text{-}CH_3)TPP(dpm)$ in deuteriochloroform.

Action as Shift Reagents. $Yb(p\text{-}CH_3)$TPPacac. LnTPPacac and related complexes are soluble in noncoordinating solvents such as chloroform. In such a solvent, in the absence of self-association, they are formally six-coordinate with four nitrogen and two oxygen donor atoms. Six coordination is rare in lanthanide chemistry, with seven-, eight-, and nine-coordinate complexes being more common. Examples of each of these coordination numbers have been found in β-diketonate LSR's. It is not unreasonable, then, to expect that LnTPPacac complexes would be capable of accommodating additional ligands in the primary coordination sphere of the lanthanide ion and that they might act as shift reagents toward molecules with donor atoms. This expectation has been fulfilled for the ligands that we have surveyed. Yb(III) systems were chosen for our

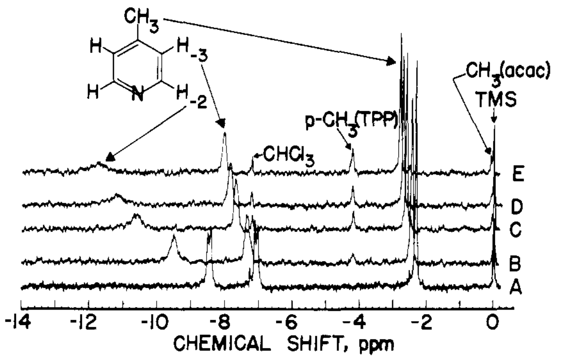

Figure 3. Effect of increasing concentrations of Yb(p-CH_3)TPPacac on the proton NMR spectrum of 4-picoline in deuteriochloroform at 36 °C; A, $R_p = 0.0$; B, $R_p = 0.021$; C, $R_p = 0.043$; D, $R_p = 0.053$; E, $R_p = 0.064$.

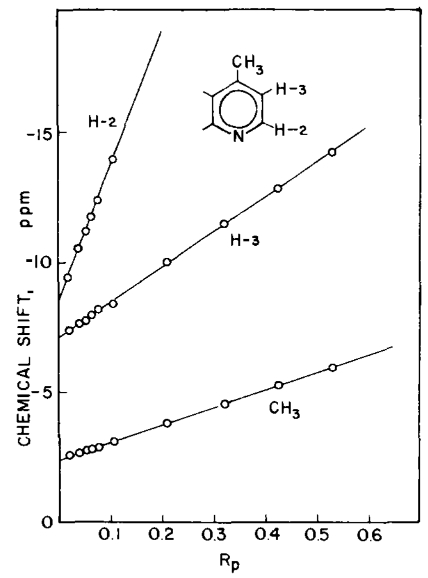

Figure 4. Plot of chemical shift (ppm from Me_4Si) of proton resonances of 4-picoline (0.225 M) in the presence of Yb(p-CH_3)TPPacac vs. R_p in deuteriochloroform at 36 °C.

most extensive studies, since these produce sizable shifts with the least objectionable signal broadening. Figure 3 shows the results of adding successive quantities of Yb(p-CH_3)TPPacac to chloroform solutions of 4-picoline. Downfield shifts are observed for all proton resonances and, as in β-diketonate LSR systems, a labile exchange of coordinated and noncoordinated ligand is evident. It is significant that the direction of the substrate resonance shifts is the *same* as those of the porphyrin resonances, indicating that the picoline ligand *also* occupies, on the average, the equatorial region where $(3 \cos^2 \theta - 1) < 0$. This finding is consistent only with a significantly out-of-plane positioning of the metal. Plots of the observed chemical shifts vs. the Yb(p-CH_3)TPPacac to substrate ratio (R_p) for 4-picoline are shown in Figure 4. The shifts are quite linear in R_p, although the 2-H resonance is so severely broadened as to be undetectable at R_p values $> \sim 0.15$. As expected, the shifts extrapolate back to very close to their diamagnetic positions at $R_p = 0$. Downfield shifts are also observed for the proton resonances of the aliphatic alcohol 1-pentanol in the presence of Yb(p-CH_3)TPPacac, although some curvature in the plots (not shown) of chemical shifts vs. R_p is observed. The present results indicate that the lanthanide ion in these porphyrin complexes can accommodate additional nitrogen or oxygen donor ligands in the first coordination sphere, thereby serving as shift reagents.

Diamagnetic LuTPPacac as a "Ring Current" Shift Reagent. Before surveying the behavior of other paramagnetic lanthanide porphyrin complexes as shift reagents and comparing them quantitatively with the β-diketonate variety, it is worthwhile to assess the action of a diamagnetic analogue. The proton resonances of 4-picoline are all shifted upfield in the presence of LuTPPacac. The slopes of plots of chemical shift vs. R_p (not shown) for the 2-H, 3-H, and 4-CH_3 resonances are respectively, 3.0, 0.68, and 0.30 ppm. Thus, for the readily obtainable R_p value of 0.5, shifts of up to ~1.5 ppm can be obtained. LuTPPacac represents a new class of diamagnetic, "ring current" shift reagent. Its behavior contrasts with "ring current" shift reagents based on silicon, germanium,[42] and low-spin Fe(II)[43,44] phthalocyanine (Pc) complexes particularly in that a labile equilibrium between coordinated and uncoordinated ligand is observed in the LuTPPacac case. In this regard LuTPPacac is more like ruthenium(II) carbonyl porphyrin complexes,[20] which are known to bind nitrogen heterocyclic compounds and, depending on the substrate, to display a labile exchange at or above room temperature.[45-47] For silicon and germanium phthalocyanine reagents the "substrate" is covalently bound to the complex, while for low-spin adducts of $Fe^{II}Pc$, exchange of coordinated and uncoordinated substrate is slow on the NMR time scale. This latter reagent, while involving a coordinate bond as in the present LuTPPacac case, is apparently limited in use to unhindered amines.[44] While the observed shifts are somewhat larger for the nonlabile "ring current" shift reagents (the methyl resonance of methyl amine coordinated to $Fe^{II}Pc$ is shifted upfield by 5.18 ppm[44]), the LuTPPacac reagent is perhaps more versatile in that shifts may be observed simply upon mixing a solution of the substrate with the reagent. Another advantage is that no paramagnetic species are involved at any stage ($Fe^{II}Pc$ is itself paramagnetic, although its amine adducts are not[44]). The "ring current" shift effect will, of course, be present in the paramagnetic LnTPPacac reagents, augmenting the shifts of upfield reagents and decreasing the shifts of downfield reagents. The "ring current" shift is, however, considerably smaller than the paramagnetic effect in the latter half of the lanthanide series (Tb-Yb), vide infra.

Shifting Abilities Across the Series. Very small or vanishing upfield shifts were observed for 4-picoline proton resonances in shift reagent studies involving TPP complexes of Pr(III), Nd(III), Sm(III), and Eu(III). Of these, the largest shifts were observed for PrTPPacac with the slope of a plot of the 2-H chemical shift vs. R_p of 2.5 ppm, which is smaller than the 3.0 value for the diamagnetic Lu(III) reagent. No picoline proton resonance shifts whatsoever were observed in the EuTPPacac system. On the other hand, sizable upfield or downfield shifts were observed for the six paramagnetic complexes in the second half of the series as is shown by the data in Table II. Corresponding data[36,48] for the β-diketonate shift reagents involving the same metal-substrate combinations are also shown for comparison. Several features are apparent. The induced shifts are of the same sign as in the corresponding β-diketonate shift reagent systems, upfield for the Tb, Dy, Ho triad, and downfield for the Er, Tm, Yb triad. This finding agrees with the theoretically predicted[12,31,49] variation of magnetic anisotropy with f-electron configuration across the series and provides evidence for a dominant dipolar shift mechanism. For a given value of R_p, the shift magnitudes are smaller in the LnTPPacac series, with the Ln(dpm)$_3$ reagents producing shifts greater by factors ranging from 1.6 in the Yb(III) case to 3.5 in the Dy(III) system. Another significant difference is in the shift ratios for the two series. In the Ln(dpm)$_3$ series the shift ratios are relatively constant and are reasonably close to those predicted for an axial model, with the Ln-N bond defining the axis. In contrast, the shift ratios in the LnTPPacac series are

Table II. Comparison of Shift Reagent Capabilities of LnTPPacac and $Ln(dpm)_3$ Complexes toward 4-Picoline in Deuteriochloroform Solution at 36 °C

	LnTPPacac				$Ln(dpm)_3$		
Ln	Observed slope[a] 2-H resonance, ppm	Corrected slope[b] 2-H resonance, ppm	Slope ratios[b] 3-H/2-H	Slope ratios[b] $4-CH_3/2-H$	Obsd[c] slope[a] 2-H resonance, ppm	Slope ratios 3-H/2-H	Slope ratios $4-CH_3/2-H$
Tb	98	95	0.39	0.20	249	0.37	0.19
Dy	101	98	0.32	0.23	339	0.36	0.19
Ho	84	81	0.22	0.10	187	0.38	0.19
Er	−36	−39	0.13	0.03	−82	0.35	0.21
Tm	−88	−91	0.15	0.07	−173	0.37	0.20
Yb	−51	−54	0.26	0.12	−86	0.36	0.17
Lu	3	0					
Axial model[d]						0.43	0.24

[a] Slope of plot of chemical shift vs. R_p, i.e., shift in parts per million extrapolated to $R_p = 1.0$. [b] Corrected for diamagnetic "ring current" shift taken to be that of Lu(III) complex. [c] Taken from ref 36, corrected to 36 °C. [d] Axis defined by picoline nitrogen to lanthanide bond.

quite variable and only in the cases of Tb(III) and Dy(III) do they agree at all well with those observed for the $Ln(dpm)_3$ systems.

Perhaps the most remarkable and, at first sight, surprising feature of the results is that the observed shifts for the substrate are in the *same* direction as those of the porphyrin protons. Since the aryl groups are all equivalent, as judged from the NMR spectra of the Eu(III) and Yb(III) derivatives (Figure 1), it is clear that there is effective axial symmetry on the NMR time scale. Furthermore, the aryl proton resonance shifts are fit satisfactorily by an axial model with the principal axis normal to the prophyrin plane (Table I). One must conclude, therefore, that the protons of the substrate, on the average, occupy the equatorial region where $(3 \cos^2 \theta - 1) < 0$. The tentative structure for a LnTPPacac complex sketched in Figure 1 does not, of course, possess C_4 symmetry; however the stereochemical nonrigidity of lanthanide ion coordination spheres will lead to rapid interconversion of structures in which the acac ligand is rotated by $\pi/2$ about the porphyrin C_4 axis. Direct evidence for considerable mobility in the present systems comes from the fact the apical acac or dpm ligand exchanges rapidly (on the NMR time scale) with the β-diketonate ligands of $Ln(acac)_3$ or $Ln(dpm)_3$ when these are added to the solution. As noted above, coordinated monodentate substrates are also in labile equilibrium with those outside the first coordination sphere. The upfield shifts observed (Figure 1) for the methyl or *tert*-butyl resonances of the apical β-diketonate ligands in the Eu(III) and Yb(III) systems are consistent with the positioning of these ligands along the "C_4" axis where $(3 \cos^2 \theta - 1) > 0$. Inspection of models reveals that there remains considerable room in the primary coordination sphere for the coordination of additional ligands, leading to coordination numbers greater than six. For instance, for the YbTPPacac complex a Yb-O (of acac) distance of 2.22 Å and a O-Yb-O angle of 73.4° may be estimated from crystallographic results on lanthanide β-diketonate complexes.[27,28,36] Positioning the apical acac ligand such that its methyne proton lies on the "C_4" axis and the acac plane bisects two N-Yb-N angles of the Yb-TPP moiety, with the Yb atom 1.6 Å above the porphyrin plane, results in a coordination sphere which can easily accommodate two additional ligands. Fixing the YbN_4O_2 coordination geometry as described above, calculations show that the nitrogen atoms of two picoline molecules can readily approach the Yb atom to a bonding distance of ~2.5 Å (estimated for lanthanide β-diketonate picoline adduct structures[27,28,36]). In order for the picoline nitrogen atoms to be equidistant (at ~2.9 Å) from two porphyrin nitrogen atoms and the two acac oxygen atoms, they must lie in a plane perpendicular to that of the acac ligand, with the picoline nitrogen to Yb bond axis making an angle θ of 70-75° with the "C_4" axis. This finding is significant, since it requires that $(3 \cos^2 \theta - 1) < 0$ for the picoline protons, as is required by the NMR results! This postulated eight-coordinate structure is by no means the only possibility. The actual situation in solution may be a complex one involving other coordination geometries, species of different stoichiometry, and possibly self-associated species. Any such structures, if present, will be rapidly interconverting; indeed, it is the rapid interconversion of an ensemble of fluctional forms that has been postulated[13] to account for the apparent axial symmetry observed in NMR experiments with β-diketonate shift reagents.

It may be seen from the data in Table II that the 4-picoline proton shift ratios are relatively constant across the $Ln(dpm)_3$ series and in reasonable agreement with those predicted for axial symmetry. In contrast, there are significant changes in these ratios across the LnTPPacac series. Owing to the integrity of the Ln-TPP moiety, it can be argued that the number of possible fluctional forms for complexes of this type might be limited, particularly for complexes of the smaller ions toward the end of the series. In the absence of free rotation[13,50] about the metal-substrate bond axis, this is expected to lead to deviations from axiality (from the point of view of the substrate) and therefore to divergence from the shift ratios observed in the $Ln(dpm)_3$ series. A geometric factor calculation[51] based on the bispicoline adduct described above predicts 3-H/2-H and $4-CH_3/2-H$ shift ratios of 0.16 and 0.05, respectively, somewhat more in accord with the shift ratios observed for the later members of the series (Table II).

The reasons for the lack of significant shift reagent action by the TPP complexes of the early lanthanides Pr-Eu are not entirely clear. As judged from the $(p-CH_3)$TPP proton resonances, the magnetic anisotropy of the Eu(III) complex is about one-fifth that of the Yb(III) complex and, everything being equal, a small downfield shift should be observed for the 4-picoline proton resonances, even when the counteracting upfield "ring current" contribution is considered. No shifts were detected, however. Consistent with these observations, the data in Table II reveal a trend wherein the ratio of resonance shifts produced by LnTPPacac to those produced by the corresponding $Ln(dpm)_3$ shift reagent decrease from right to left across the series. Part of the reason for this may be that as the size of the Ln(III) ion increases, the picoline ligand may tend fortuitously to lie, on the average, in a region where $(3 \cos^2 \theta - 1)$ is near zero. Other explanations are possible. A definitive answer to this question must await further work.

Acknowledgment. This research was supported by the National Science Foundation through Grant MPS73-08550. We wish to thank Dr. R. F. Venteicher for helpful discussions concerning many aspects of this work.

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Limitations of Lanthanide Shift Reagents for Determination of Conformation of Nonrigid Molecules[1]

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Received April 5, 1976

Abstract: Studies on the correlation of observed lanthanide-induced shifts (LIS) in the ^1H, ^{13}C, and ^{19}F NMR spectra with those calculated by application of the McConnell equation in order to determine configuration and conformation in solution have been made on two sets of diastereomeric compounds: **1**, **2**, **3** and **4**, **5**. This correlation method was applied to diastereomers **1** and **3** using LIS from all hydrogen and ^{13}C atoms in the molecule. These diastereomers differ in exo vs. endo configuration in the rigid portion of the molecule. No significant difference in calculated LIS for the correct vs. incorrect diastereomeric structures was noted when unit weights were used in determining the R values (a measure of the degree of correlation). However, when LIS values were weighted according to the inverse of the magnitude of the shift, a significant correlation with the correct configuration was found. Even then the magnitude of the difference was small considering the major stereochemical difference in the structures of **1** and **3**. Diastereomers **1** and **2** as well as **4** and **5**, which differ in configuration at the nonrigid portion of the molecule, showed no significant correlation of observed and simulated LIS with the correct diastereomer even when using inverse weights in determining the R values. These results indicate that extreme caution should be used in assigning configurations to nonrigid molecules based on this method and that, with the possible exception of very carefully selected examples, solution conformations derived from such studies are of dubious value at this time.

In 1969, Hinckley[3] demonstrated that the addition of the dipyridine adduct of tris(2,2,6,6-tetramethyl-3,5-heptanedionate)europium(III), $Eu(dpm)_3$, resulted in downfield shifts of the proton signals of cholesterol, which were proximal to the OH function. Following Hinckley's discovery, the literature flourished with reports further delineating this phenomenon and the application of it to chemical problems.

The lanthanide-induced shifts (LIS) arising from the presence of a paramagnetic complex have been expressed as a sum of terms for contact and dipolar (or pseudocontact) interactions. The contact term is the result of the Fermi contact interaction.[4] This is a "through-bond" interaction which takes place only if there is a finite probability of finding an unpaired electronic spin on the atomic s orbital of the nucleus being observed. The LIS resulting from dipolar interaction was first described in detail by McConnell and Robertson.[5] Assuming