11230 *J. Am. Chem. Soc.* **1995,** *117,* 11230−11238

# Potentiometric, Calorimetric, and Solution NMR Studies of a Tridentate Ligand Which Has a Marked Preference for Formation of Bis(ligand) versus Mono(ligand) Lanthanide Complexes and Which Exhibits High Selectivity for Heavier Lanthanides

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*Received April 19, 1995*[⊗]

**Abstract:** A new water-soluble $N_4O_3$ tripodal amine phenol ligand, tris(((2-hydroxy-5-sulfobenzyl)amino)ethyl)amine ($H_3TRNS$) has been synthesized, and its complexation properties with six lanthanide(III) ions (La, Nd, Gd, Ho, Yb, Lu) have been probed. In water, the ligand coordinates in a tridentate fashion through the three phenolato oxygen atoms to give mono- and bis(ligand) complexes. The bis complexes are proposed to be 7-coordinate containing one bound water as evinced by $^{17}O$ NMR experiments on the $Dy^{3+}$ complex, while the mono complexes are proposed to have a coordination number of eight or nine. The stepwise formation constants for the 1:1 and 2:1 (L:M) complexes have been measured at 25 °C ($\mu$ = 0.16 M NaCl) for $Nd^{3+}$ ($\log K_1 = 6.41$, $\log K_2 = 6.34$), $Gd^{3+}$ ($\log K_1 = 6.67$, $\log K_2 = 7.69$), $Ho^{3+}$ ($\log K_1 = 7.67$, $\log K_2 = 8.75$), and $Yb^{3+}$ ($\log K_1 = 8.53$, $\log K_2 = 9.73$). The formation constants show an increasing affinity and an unprecedented selectivity for the heavier lanthanides ($\beta_{2(\mathrm{Yb})} - \beta_{2(\mathrm{Nd})} = 10^{5.5}$). Furthermore, the stepwise stability constant for the 2:1 complex is increasingly greater than that for the 1:1 complexes of $Gd^{3+}$, $Ho^{3+}$, and $Yb^{3+}$, while $K_1$ and $K_2$ for the 1:1 and 2:1 complexes of $Nd^{3+}$ are approximately the same. Solution calorimetry shows that the selectivity for the heavier lanthanides is an enthalpic effect ($\Delta H_{\beta 2} = -45.11$ (Yb) and $-13.71$ kJ·mol$^{-1}$ (Nd)), while the anomalous behavior in formation constants ($K_2 > K_1$) is predominantly entropic ($\Delta S_2 > \Delta S_1$) and is rationalized in terms of solvation of the complexes. Lanthanum(III) forms only the 1:1 complex ($\log K = 5.65$) which precipitates from solution.

## Introduction

There has been a proliferation in the chemistry of multidentate ligands with lanthanide(III) ions (Ln(III)) in the past decade. Much of this has been spurred by the application of Gd-DTPA[2] (DTPA = diethylenetriaminepentaacetic acid) and Gd-DOTA[3] (DOTA = 1,4,7,10-tetraazacyclododecane-*N,N′,N″,N‴*-tetraacetic acid) and their derivatives as magnetic resonance imaging (MRI) contrast agents.[4] The similarity in size of Ln(III) and Ca(II) has led to various lanthanides being substituted for Ca in biological systems with the physical properties of the lanthanide being used as a probe,[5−7] *e.g.* Eu(III) luminescence,[8,9] Gd(III) as an EPR probe,[10] and various paramagnetic lanthanides as NMR shift probes.[11−13] This flurry of activity has been a boon to those interested in studying lanthanide coordination chemistry. The work done on multidentate ligand complexation of lanthanides for MRI has greatly increased the knowledge base in the kinetic and thermodynamic stability of multidentate metal complexes, and the exploitation of the physical properties of the lanthanides as probes has expanded the arsenal of techniques with which to study metal complexes.

The aqueous chemistry of Ln(III) ions is dominated by their oxophilicity,[14,15] with most ligands studied containing carboxylato or phosphonato oxygen donors. Amines alone are poor donors for lanthanides in water; however, incorporated into aminocarboxylates or aminophosphonates, they form quite stable Ln(III) complexes, much more stable than the analogous oxo acids. This can be ascribed to the initial coordination of the anionic oxygen which disrupts the hydration sphere and serves to anchor the ligand while the amine moiety coordinates secondarily.[14] Excluding catecholato derivatives,[16,17] there has been little attention paid to the phenolato group as an anionic oxygen donor for lanthanides. Ligands such as bis(2-hydroxybenzyl)ethylenediaminediacetic acid (HBED)[18] and 5-sulfosali-

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[⊗] Abstract published in *Advance ACS Abstracts,* October 15, 1995.

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(2) Watson, A. D. *J. Alloys Compd.* **1994**, *207/208*, 14.

(3) Kumar, K.; Jin, T.; Wang, X.; Desreux, J. F.; Tweedle, M. F. *Inorg. Chem.* **1994**, *33*, 3823.

(4) Lauffer, R. B. *Chem. Rev.* **1987**, *87*, 901.

(5) Martin, R. B.; Richardson, F. S. *Q. Rev. Biophys.* **1979**, *12*, 181.

(6) Meares, C. F.; Wensel, T. G. *Acc. Chem. Res.* **1984**, *17*, 202.

(7) Bünzli, J.-C. G.; Choppin, G. R. *Lanthanide Probes in Life, Chemical, and Earth Sciences*; Bünzli, J.-C. G., Choppin, G. R., Eds.; Elsevier: Amsterdam, 1989.

(8) Bünzli, J.-C. G. *Inorg. Chim. Acta* **1987**, *139*, 219.

(9) Horrocks, W. D. J.; Albin, M. *Prog. Inorg. Chem.* **1984**, *31*, 1.

(10) Stephens, E. M. In ref 7.

(11) Gupta, R. K.; Gupta, P. *J. Magn. Reson.* **1982**, *47*, 344.

(12) Pike, M. M.; Springer, C. S. *J. Magn. Reson.* **1982**, *46*, 348.

(13) Sherry, A. D.; Geraldes, C. F. G. C.; Cacheris, W. P. *Inorg. Chim. Acta* **1987**, *139*, 137.

(14) Choppin, G. R. *Pure Appl. Chem.* **1971**, *27*, 23.

(15) Moeller, T. *The Lanthanides*; Moeller, T., Ed.; Pergamon: Oxford, 1973; Vol. 4, p 1.

(16) Zhu, D.-H.; Kappel, M. J.; Raymond, K. N. *Inorg. Chim. Acta* **1988**, *147*, 115.

(17) Freeman, G. E.; Raymond, K. N. *Inorg. Chem.* **1985**, *24*, 1410.

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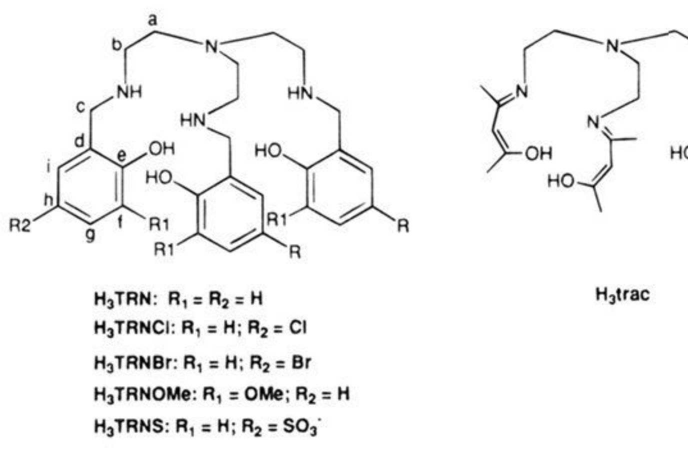
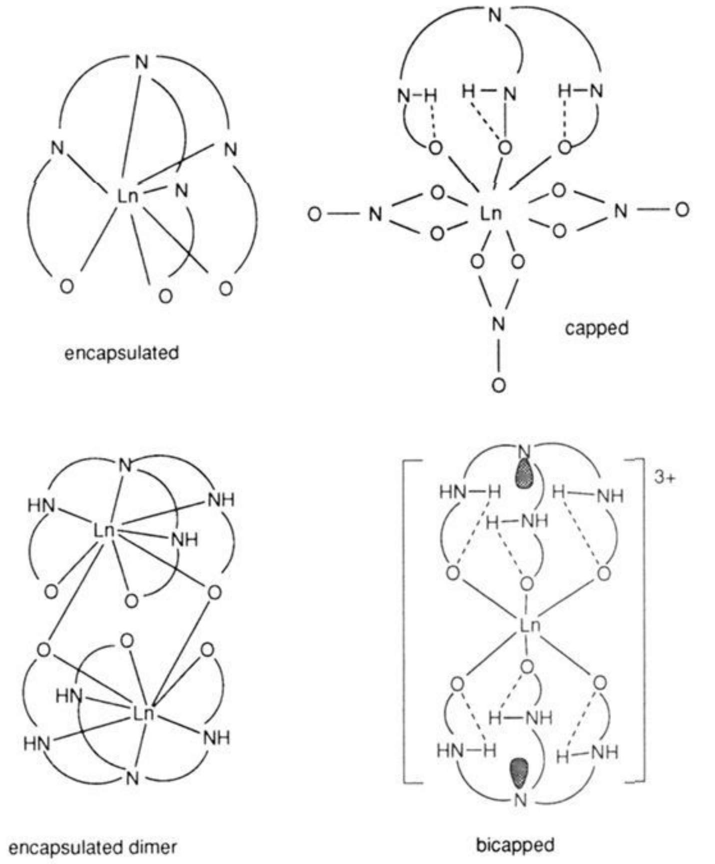
**Scheme 1**



**Scheme 2**



cylic acid[19] have been studied, but these contain carboxylate groups which greatly facilitate phenol complexation. Coordination of lone phenols is hindered by the weak acidity of the hydroxyl group (p$K_a$ of phenol ~10),[20] and since the aqueous lanthanide ions are themselves weak Lewis acids which precipitate as hydroxides above pH 8, they generally cannot compete with the hydrogen ion for complexation of phenols in water. Hence a ligand consisting of only amines and phenols would not be expected to be a particularly good ligand for aqueous lanthanide chelation as it should simply be too basic.

We have, however, recently prepared a number of lanthanide complexes of tren based amine phenols (Scheme 1) and have discovered three different coordination geometries (Scheme 2) with coordination numbers of 9, 8, and 6, which have been described as capped,[21] encapsulated dimer,[22] and bicapped,[23] respectively. We had previously shown that a tripodal Schiff tribase ligand trac$^{3-}$ forms a 1:1 seven-coordinate encapsulated complex with Yb.[24] Although all preparations were in nonaqueous solvents, the capped and bicapped complexes were stable (at least kinetically) in weakly acidic, neutral, and weakly basic aqueous solutions (the encapsulated Schiff base complex hydrolyzed, and the encapsulated dimer was insoluble). As the capped complexes were prepared by stoichiometric metathesis of lanthanide nitrate with the neutral form of the ligand (no added base), it appeared that the nitrogen atoms were acting as an internal base source. The encapsulated dimer was prepared by adding an excess of hydroxide. Based on these results we were interested in which complexes, if any, were present in aqueous solution, and if the coordination geometry was pH dependent. We were curious to see if phenolato coordination could provide an anchoring effect which would enable the amino nitrogen atoms to coordinate in water.

It has been recognized that the stability trends for lanthanides with various ligands fall into two categories:[25] (1) one in which the stability increases with increasing charge to ionic radius ratio, as with EDTA, and (2) the other in which the stability increases across the series, reaches a plateau, and then declines, as with DTPA. The enthalpies and entropies of formation show no apparent trends. A plot of $\Delta H$ or $\Delta S$ of complex formation versus atomic number may be S-shaped ($\Delta S$, HEDTA), U-shaped ($\Delta S$, DTPA), or linear ($\Delta S$, DCTA).[14,26,27] Often, a change in coordination number (either the degree of inner sphere hydration or a change in the ligand binding mode) has been suggested for the inflections in the curves; however, recent NMR studies have cast doubts on this assumption.[28,29]

Since the parent amine phenol was insoluble in the pH range 7–11, the sulfonic acid derivative tris(((2-hydroxy-5-sulfobenzyl)amino)ethyl)amine ($H_3TRNS$) was synthesized. In this paper the stability constants of this ligand with a variety of lanthanides are determined potentiometrically, the enthalpic and entropic contributions to these stability constants are obtained via calorimetry, and the variable pH solution NMR spectra of these complexes ($^1H$, $^{17}O$) are reported. What emerges is an unexpected picture of a ligand which has an unprecedented selectivity for heavier lanthanides over lighter rare earths and which has an increasing tendency to favor bicapped complexation with the heavier lanthanides, so much so that $K_2 > K_1$. These results and the overall trends will be discussed with respect to ionic radius and solvation.

## Experimental Section

**Materials.** Sodium borohydride, tris(2-aminoethyl)amine (tren), salicylaldehyde, aniline, sodium deuteroxide (NaOD, 40%), deuterium chloride (DCl, 12 M), and the lanthanide atomic absorption standards were obtained from Aldrich. Hydrated lanthanide nitrates were obtained from Alfa. Deuterium oxide ($D_2O$) was purchased from Isotec. Anhydrous sodium carbonate was obtained from BDH. All were used without further purification.

**Instrumentation.** $^1H$ NMR spectra (200 and 300 MHz) were referenced to TMS and recorded on Bruker AC-200E and Varian XL 300 spectrometers, respectively. $^{17}O$ NMR spectra (natural abundance) were recorded at 40.67 MHz on the latter instrument. Mass spectra were obtained with a Kratos Concept II H32Q ($Cs^+$, LSIMS) instrument. UV–vis spectra were recorded on a Shimadzu UV–2100. Infrared spectra were obtained as KBr disks in the range 4000–400 cm$^{-1}$ on a Perkin-Elmer PE 783 or a Bomem MB-100 spectrophotometer, and were referenced to polystyrene. Analyses of C, H, and N were performed by Mr. Peter Borda in this department. Melting points were measured on a Mel-Temp apparatus and are uncorrected.

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(18) Ma, R.; Motekaitis, R. J.; Martell, A. E. *Inorg. Chim. Acta* **1994**, *224*, 151.

(19) Lajunen, L. H. J. *Finn. Chem. Lett.* **1976**, 36.

(20) Martell, A. E.; Smith, R. M. *Critical Stability Constants*; Plenum: New York, 1974–1989; Vols. 1–6.

(21) Smith, A.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1988**, *27*, 3929.

(22) Liu, S.; Gelmini, L.; Rettig, S. J.; Thompson, R. C.; Orvig, C. *J. Am. Chem. Soc.* **1992**, *114*, 6081.

(23) Liu, S.; Yang, L.-W.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1993**, *32*, 2773.

(24) Berg, D. J.; Rettig, S. J.; Orvig, C. *J. Am. Chem. Soc.* **1991**, *113*, 2528.

(25) Tse, P.-K.; Powell, J. E. *Inorg. Chem.* **1985**, *24*, 2727.

(26) Anderegg, G., Anderegg, G., Eds.; Van Nostrand, Reinhold: New York, 1971; Vol. 1, 427.

(27) Ashcroft, S. J.; Mortimer, C. T. *Thermochemistry of Transition Metal Complexes*; Academic Press: London, 1970.

(28) Peters, J. A. *Inorg. Chem.* **1988**, *27*, 4686.

(29) Huskens, J.; Peters, J. A.; van Bekkum, H.; Choppin, G. R. *Inorg. Chem.* **1995**, *34*, 1756.

**Synthesis of Tris(((2-hydroxy-5-sulfobenzyl)amino)ethyl)amine Monohydrate ($H_3$TRNS·$H_2O$).** This was prepared by the sodium borohydride reduction of the corresponding Schiff base, saltrens (tris(((5-sulfosalicylidene)amino)ethyl)amine), which was itself prepared via the method of Evans.[30] Sodium borohydride (1.6 g, 4 mmol) was added to a suspension of saltrens (7.65 g, 1.0 mmol) in MeOH over a period of 30 min. After the addition was complete, the solvent was removed to give a white solid. MeOH (60 mL) was added and removed under reduced pressure. This was repeated twice more. The resultant solid was dissolved in a minimal amount of water (15 mL) and the pH adjusted to about 2 with concentrated HCl; a white solid precipitated and was collected on a Buchner funnel. It was purified by redissolving the precipitate in a mildly basic solution (pH ~8), filtering the solution, and acidifying the filtrate to give a white precipitate as the zwitterion. This was filtered and dried overnight *in vacuo* at 95 °C to yield 5.0 g (71%); mp >250 °C. Anal. Calcd (found) for $C_{27}H_{36}N_4O_{12}S_3 \cdot H_2O$: C, 44.87 (44.86); H, 5.30 (5.46); N, 7.75 (7.59). Potentiometric analysis was consistent with this molecular weight. $^1$H NMR (200 MHz, $D_2O$, pD = 7.1): 2.80 (t, 6H, ethylenic $CH_2$, $^3J = 6$ Hz), 3.08 (t, 6H, ethylenic $CH_2$, $^3J = 6$ Hz), 4.18 (s, 6H, benzylic $CH_2$), 6.70 (d, 3H, H(3), $^3J = 9$ Hz), 7.61 (d of d, 3H, H(4), $^3J = 9$ Hz, $^4J = 1$ Hz), 7.63 (d, 3H, H(6), $^4J = 1$ Hz). Mass spectrum (LSIMS): $m/z = 705$ ($[M + 1]^+$, $[C_{27}H_{36}N_4O_{12}S_3]^+$). IR (cm$^{-1}$, KBr disk): 3500–2600 (b s, $\nu_{N-H,O-H}$), 1730 (m, $\delta_{N-H}$), 1604 (s, $\nu_{N-H}$), 1502, 1442, 1375 (s, $\nu_{C=C}$), 1200 (vs, $\nu_{S=O}$). UV ($\lambda_{max}$ nm, ($\epsilon$ M$^{-1}$ cm$^{-1}$)): pH = 2, 276 (4800), 232 (26000), 203 (72000); pH = 12, 290 (11000), 256 (47000). It is slightly soluble in acid and soluble in neutral to basic pH.

**Preparation of Metal Complexes.** Metal complexes were prepared *in situ* by mixing stoichiometric amounts of ligand, metal, and hydroxide solutions. Lu(TRNS)$_2^{3-}$: $^1$H NMR (200 MHz, $D_2O$) 2.40, 2.70 (AA′BB′ coupling pattern, 24H, ethylenic $CH_2$); 3.88, 4.44 (AB doublet of doublets, 12H, benzylic $CH_2$, $^2J = 14$ Hz); 5.98 (d, 6H, H(3), $^3J = 8$ Hz); 7.62 (d of d, 6H, H(4), $^3J = 8$ Hz, $^4J = 1$ Hz); 7.70 (d, 6H, H(6), $^4J = 1$ Hz).

La(TRNS): $^1$H NMR (200 MHz, $D_2O$) 2.8 (broad, 12H, ethylenic $CH_2$), 4.2 (broad, 6H, benzylic $CH_2$), 6.81 (d, 3H, H(3)), 7.70 (m, 6H, H(4) and H(6)). Long needles were obtained by allowing the solution to stand; however none proved suitable for X-ray diffraction. Anal. Calcd (found) for $C_{27}H_{36}LaN_4O_{12}S_3 \cdot 11.5H_2O$: C, 30.95 (30.92); H, 5.39 (5.34); N, 5.35 (5.36). IR (cm$^{-1}$, KBr disk): 3500–2600 (b s, $\nu_{N-H,O-H}$), 1595, 1480, 1290 (s, $\nu_{C=C}$), 1160 (vs, $\nu_{S=O}$).

**NMR Measurements.** The variable pH $^1$H NMR spectra of the ligand and the complexes were run in $D_2O$ with the pD values being measured by a Fisher Accumet 950 pH meter employing an Accumet Ag/AgCl combination microelectrode. The pD values were converted to pH by adding 0.40 to the observed reading.[31] The variable pH $^{17}$O NMR spectra were run in $H_2O$ and were referenced to 0.16 M NaCl. The Dy(III) experiments were recorded at 21 °C while the spectra for the Gd(III) titration were run at 25.0 ± 0.3 °C. With the $^{17}$O NMR, a spectral window of 1000 Hz, with a 90° pulse width of 18 $\mu$s, and an acquisition time of 0.256 s was usually employed which gave 512 data points. Two thousand transients were collected per spectrum. The $^{17}$O line widths for $H_2O$ were about 60 Hz. Concentrations employed ranged from 1 to 40 mM. The dysprosium induced shifts (DIS) were obtained from the observed shift by making a correction for the bulk magnetic susceptibility of the solution.[32] Stock solutions were prepared from metal nitrates in $D_2O$ ($H_2O$) and the metal–ligand solutions were prepared by pipeting the required amounts of stock solution and adjusting the pH with acid or base. Dy(TRNS)$_2^{3-}$ was prepared by adding a 5-fold excess of $Na_3$TRNS to Dy($NO_3$)$_3$. In the case of equilibrium measurements, the ionic strength was controlled by addition of NaCl.

**Potentiometric Equilibrium Measurements.** Potentiometric measurements of the ligands in the absence, and presence, of lanthanide ions were performed with a Fisher Acumet 950 pH equipped with an Orion Ross glass and calomel reference electrodes. The electrode was calibrated before each titration, and often afterwards, by titrating a known amount of aqueous HCl with a known concentration of NaOH. A plot of mV (measured) vs pH (calculated) gave a working slope and intercept so that the pH could be read as $-\log [H^+]$ directly. A Metrohm automatic buret (Dosimat 665) was used for the NaOH additions and the buret and pH meter were interfaced to a PC such that each titration was automated. The temperature of the solutions in covered, water-jacketed beakers was kept constant at 25.0 ± 0.1 °C by a Julabo circulating bath. The ionic strength was fixed at 0.16 M NaCl. Argon, which had been passed through 10% NaOH, was bubbled through the solutions to exclude $CO_2$.

The ligand was checked for purity by NMR and elemental analysis before titration. Titrations were also employed to ensure that the molecular weight obtained by elemental analysis was the same as that determined by titration. Fresh ligand solutions were used as the ligand slowly oxidizes in aerated solutions, especially in the presence of base. The lanthanide solutions were prepared by dilution of the appropriate atomic absorption standards. Since the lanthanides do not hydrolyze below pH 6, the excess acid in the solutions could be obtained by titrating with standard NaOH and analyzing for the strong acid by the method of Gran.[33] NaOH solutions (0.1M) were prepared from dilution of 50% NaOH with freshly boiled distilled, deionized water and standardized potentiometrically against potassium hydrogen phthalate.

The ratio of ligand to metal used was $1{:}2 < L{:}M < 4{:}1$. Concentrations were in the range 0.5–2.5 mM. A minimum of five titrations were performed for each metal. The ligand was titrated over the range $2 < pH < 11$, while the metal–ligand solutions were titrated to just beyond 3 equiv of NaOH/ligand (about pH 7) as the complexes were found to undergo slow hydrolysis beyond this point (*vide infra*). In the case of La$^{3+}$ where the 1:1 complex precipitates, data points corresponding to $\bar{n} \leq 0.8$ ($\bar{n}$ = moles of bound L/moles of M) were used. Although complexation was rapid (1–3 min per point to give a stable pH reading), care was taken to ensure that no trace hydrolysis or precipitation was occurring by monitoring up to 30 min for pH drift.

**Calorimetry.** The automated titration calorimeter used was essentially the same as described previously[34,35] with some of the instrumentation modernized so that it is controlled by a PC. The gold reaction vessel had a volume of 104 mL and the volume was kept constant during the titrations by removing 1 mL of solution and then adding 1 mL of titrant via automatic burets (Metrohm Dosimat and Hamilton, respectively). The initial solutions typically consisted of 2 mM ligand, 1–2 mM Ln$^{3+}$, and 3 mM H$^+$ in an ionic medium of 0.16 M NaCl. The solutions were titrated with a standardized carbonate free NaOH solution, with each titration consisting of 18 data points. The calorimeter was calibrated twice for each titration, once before any base was added and again after the final addition of base. The calibration consisted of supplying a known quantity of electrical heat and recording the thermocouple reading in the solution. Eleven calibration points were measured, which spanned the heat range produced during the actual titration, and a linear calibration was obtained. The ligand titrations in the presence, and absence, of Ln(III) ions were repeated two or three times, and in some cases the L:M ratios were varied.

**Computations. (a) Potentiometry.** The protonation constants for the ligand and the lanthanide–ligand stability constants were determined by using the program BEST.[36] This program sets up simultaneous mass-balance equations for all the components present at each addition of base and calculates the pH at each data point according to the current set of stability constants and total concentrations of each component. The stability constants are iteratively varied to minimize the sum of the square of the difference between observed and calculated pH. An indication of the fit is given by $\sigma$, where $\sigma$ is

$$\sigma = \sum (\mathrm{pH}_{\mathrm{calc}} - \mathrm{pH}_{\mathrm{obs}})^2/(N - 1)$$

where $N$ is the total number of data points. In all the titrations considered, $\sigma < 0.01$. TRNS can be considered a hexaprotic acid and its 6 p$K_a$s were determined directly by potentiometry; however, in the case of the lanthanide complexes, the ligand coordinated in a tridentate fashion and was treated as a triprotic acid in the computations. This

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(30) Evans, D. F.; Jakubovic, D. A. *Polyhedron* **1988**, *7*, 1881.

(31) Glasoe, P. K.; Long, F. A. *J. Phys. Chem.* **1960**, *64*, 188.

(32) Bertini, I.; Luchinat, C. *NMR of Paramagnetic Molecules in Biological Systems*; Benjamin/Cummings: Menlo Park, 1986; Vol. 3.

(33) Gran, G. *Acta Chem. Scand.* **1950**, *4*, 559.

(34) Ginstrup, O. *Chem. Scr.* **1973**, *3*, 97.

(35) Danielsson, D.; Ginstrup, O.; Ingri, N. *Chem. Scr.* **1973**, *3*, 81.

(36) Motekaitis, R. J.; Martell, A. E. *Can. J. Chem.* **1982**, *60*, 2403.

is because the lanthanide titrations never reached a pH that was high enough for ammonium deprotonation. The validity of this assumption was tested by including L(OH) and $ML_2(OH)$ species in the calculation. These did not improve the fit of the data. The $Ln(OH)^{2+}$ species[37] were also included in the calculation, but these do not form in any appreciable amount. The best fit of the data consisted simply of the two metal–ligand species LnL and $LnL_2$. Protonated metal complexes were tried but these did not improve the fit. Typically 100 data points were collected with about 80–90% of the points being in the buffer region of metal–ligand complexation, with the remainder in the strong acid region being used as a check of excess acid concentration.

**(b) Calorimetry.** A version of the program SOLGASWATER[38] was used to calculate the molar amounts of each species present at each data point based on the equilibrium constants, the initial concentrations of metal, ligand, and acid, the base concentration, and the volumes added and removed. The following equilibria comprised the observed heat change:

$$H^+ + OH^- \rightleftharpoons H_2O \tag{1}$$

$$L^{3-} + H^+ \rightleftharpoons HL^{2-} \tag{2}$$

$$HL^{2-} + H^+ \rightleftharpoons H_2L^- \tag{3}$$

$$H_2L^- + H^+ \rightleftharpoons H_3L \tag{4}$$

$$L^{3-} + Ln^{3+} \rightleftharpoons LnL \tag{5}$$

$$L^{3-} + LnL \rightleftharpoons LnL_2^{\ 3-} \tag{6}$$

As the titrations began in an acidic medium, the heat measured for the first few data points was solely because of eq 1 and the heat of dilution of the NaOH titrant. Correcting for the heat of dilution[39] and using only these initial points, the heat of neutralization at $I = 0.16$ M NaCl was obtained. This value of $-55.92$ kJ·mol$^{-1}$, which was in agreement with the data of Grenthe and co-workers,[40] was then fixed for the other calculations. In the case of the ligand-only titrations, eqs 1–4 defined the system. The observed heat, $Q_{obs}$, can be expressed as the sum of the contributions from each equilibrium,

$$Q_{obs} = \Delta n_1 \Delta H_1 + \Delta n_2 \Delta H_2 + \Delta n_3 \Delta H_3 + \Delta n_4 \Delta H_4 \tag{7}$$

where $\Delta n$ is the change in the number of moles of a given species after an addition of base. Since $\Delta n$ can be calculated, and $\Delta H_1$ is known, the other three molar heats can be solved by linear algebra. Similarly for the metal–ligand titrations, $\Delta H$ for the ligand protonations was fixed, and $\Delta H$ calculated for the metal complexes. The unknowns were solved using matrices with the aid of the Matlab suite of programs.[41] The largest source of error would arise from an error in concentration or in the stability constants used to calculate the relative amounts of species. To estimate the error, the heats were calculated using concentrations that were purposefully incorrect by 5% and stability constants incorrect by 0.2 log units; however, since the calculation involves changes in species concentrations, in the buffer region this will not differ greatly. The error was estimated to be ±0.3 kJ·mol$^{-1}$.

## Results

**Protonation Constants.** The six p$K_a$s obtained for the ligand are listed in Table 1, along with those of tren for comparison. Although there are ten potentially ionizable groups on the ligand, three are sulfonic acid moieties which have p$K_a$s <1. One of the four amines is exceedingly acidic (p$K_a$ < 2), while the other three have p$K_a$s in the normal range for aliphatic amines (9–11). This is analogous to tren itself which has three measurable p$K_a$s and a fourth which is strongly acidic. In a related tripodal aminocarboxylate based on tren, Sherry and co-workers[42] ascertained that it is the apical nitrogen atom which is the most acidic and this appears to be true of TRNS. A plot of chemical shift difference ($\Delta\delta$) versus pH for the hydrogen atoms on the carbon atoms adjacent to the amines (Figure 1) shows an inflection between pH 10 and 11 for hydrogen atoms on carbon atoms c and d; yet the hydrogen atom on carbon atom a shifts only slightly, demonstrating that the three secondary amines, not the tertiary nitrogen atom, are protonated. The phenolic hydrogen atoms are removed in the pH range 6–9. This is clearly shown by variable pH UV spectroscopy where, between pH 6 and 9, there is a bathochromic shift in the absorption maxima typical of phenols. It can also be deduced by monitoring the change in chemical shift of the hydrogen α to the hydroxyl group which shifts in this pH region (Figure 1).

**Table 1.** p$K$ Values for $H_6$TRNS and tren

| | TRNS | $\Delta H$ (kJ·mol$^{-1}$) | $\Delta S$ (J·K$^{-)}$·mol$^{-1}$) | tren[20] |
|---|---|---|---|---|
| p$K_{a1}$ | 11.2(1) | | | 10.13 |
| p$K_{a2}$ | 10.6(1) | | | 9.43 |
| p$K_{a3}$ | 9.59(3) | | | 8.41 |
| p$K_{a4}$[a] | 8.07(3) | 27.6(3) | 62(3) | |
| p$K_{a5}$ | 7.29(3) | 30.7(3) | 36(3) | |
| p$K_{a6}$ | 6.17(3) | 24.8(3) | 35(3) | |

[a] p$K_a$s 4–6 and corresponding $\Delta H$ and $\Delta S$ values refer to eqs 2–4.

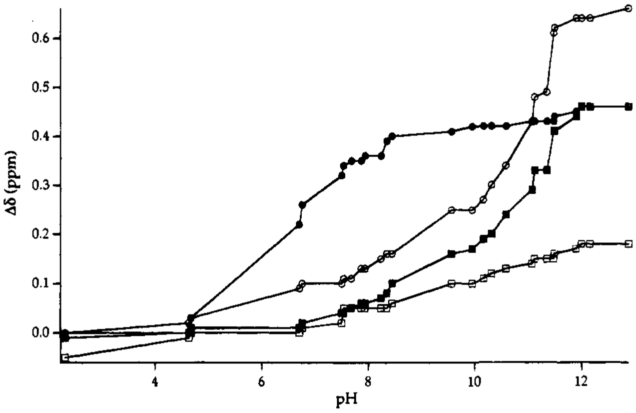

**Figure 1.** Plot of chemical shift difference ($\Delta\delta$) versus pH for the hydrogen atoms on the carbon atoms adjacent to the amino nitrogen atoms and for those on the aromatic ring (labeling as in Scheme 1): a (□), b (■), c (○), and f (●).

The p$K_a$s of the three amino groups are all higher than those of the amines in tren, while the phenol p$K_a$s are all lower than that of 4-sulfophenol (p$K_a$ = 8.6).[20] This can be ascribed to a strong ion–hydrogen bond between a hydrogen on a protonated amine and the deprotonated phenolato group. This is not an uncommon effect; it has been observed in other aminophenols where there is a six-membered ring containing the N–H–O hydrogen bond.[43] A well-known example is salicylic acid in which the p$K_a$ of the phenolic hydrogen is 13.4. If the intramolecular H-bonding is removed, as in 4-hydroxybenzoic acid, the phenol p$K_a$ drops to 8.95.[20]

**Metal Complexes.** Figure 2a shows the experimental titration curves for the lanthanides studied at a ratio of 2 $H_3$TRNS:1 Ln. The flatness of the curves (except for La) is indicative of a predominant 2:1 complex. This is also shown by an $\bar{n}$ plot

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(37) Baes, C. F.; Mesmer, R. E. *Hydrolysis of Cations*; Wiley-Interscience: New York, 1976.

(38) Eriksson, G. *Anal. Chim. Acta* **1979**, *112*, 375.

(39) Rossini, F. D. National Bureau of Standards Circular No. 500; U.S. Government Printing Office: Washington, 1952.

(40) Grenthe, I.; Heikki, O.; Ginstrup, O. *Acta Chem. Scand.* **1979**, *A24*, 1067.

(41) *MATLAB*; ver. 4.0; The MathWorks Inc., 1993.

(42) Geraldes, C. F. G. C.; Brücher, E.; Cortes, S.; Koenig, S. H.; Sherry, A. D. *J. Chem. Soc., Dalton Trans.* **1992**, 2517.

(43) Wong, E.; Caravan, P.; Liu, S.; Rettig, S. J.; Orvig, C. Submitted for publication.

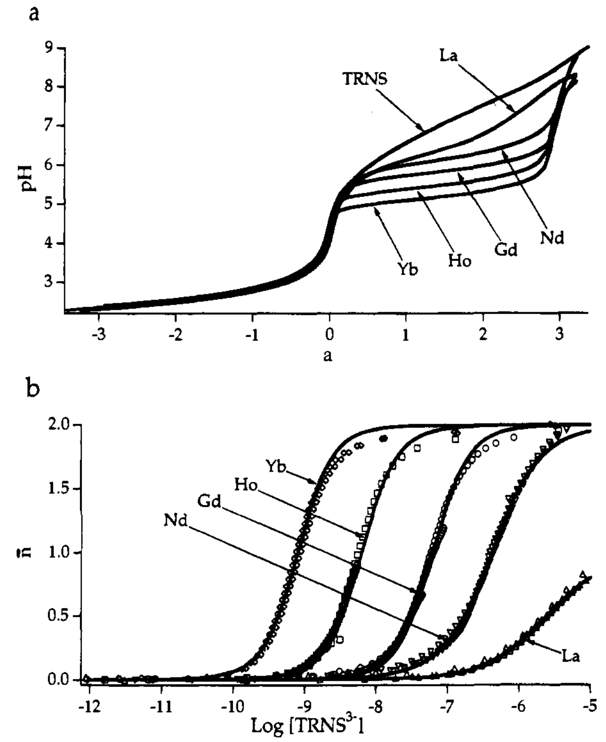

**Figure 2.** (a) Experimental lanthanide titration curves at 2 mM $H_3$-TRNS:1 mM Ln(III). (b) Experimental plots of $\bar{n}$ vs log [TRNS] (symbols) and curves generated from the calculated stability constants (solid lines).

**Table 2.** Thermodynamic Parameters for the Complexation Equilibria[a,b]

| $Ln^{3+}$ | $\log K_1$ | $\log K_2$ | $\log \beta_2$ | $\Delta H_1$ | $\Delta H_2$ | $\Delta H_{\beta 2}$ | $\Delta S_1$ | $\Delta S_2$ | $\Delta S_{\beta 2}$ |
|---|---|---|---|---|---|---|---|---|---|
| La | 5.65 | | | | | | | | |
| Nd | 6.41 | 6.34 | 12.75 | −20.34 | +6.63 | −13.71 | 54 | 143 | 197 |
| Gd | 6.67 | 7.69 | 14.36 | −12.11 | −15.15 | −27.26 | 88 | 97 | 185 |
| Ho | 7.67 | 8.75 | 16.42 | −21.33 | −14.06 | −35.39 | 74 | 121 | 195 |
| Yb | 8.53 | 9.73 | 18.26 | −23.30 | −21.81 | −45.11 | 85 | 113 | 198 |

[a] Estimated errors: $\log K_1$, $\log K_2 \pm 0.1$; $\log \beta_2 \pm 0.03$; $\Delta H_n \pm 0.3$; $\Delta S_n \pm 3$. [b] Units: $\Delta H$ (kJ·mol$^{-1}$); $\Delta S$ (J·K$^{-1}$·mol$^{-1}$).

(Figure 2b), a typical stepwise equilibrium in which $K_1 \gg K_2$ would show a plateau at $\bar{n} = 1$, whereas in this system, $\bar{n}$ rises directly to 2. In the plot of $\bar{n}$ vs log [TRNS] (Figure 2b), all the data for a given lanthanide ion coincide to a single curve independent of the ligand or metal concentrations or ratios proving that only mononuclear complexes are formed.[44] If the curves curled back upon themselves, or if at different ratios the curves did not overlap, polynuclear complex formation or protonated metal complex formation, respectively, would be indicated. Furthermore, at ratios less than 2:1, there was rapid hydrolysis after $a = 3$ ($a$ = moles of OH$^-$/moles of ligand), whereas with a ratio of 2:1 or greater, hydrolysis was quite slow, which suggests a stable 2:1 complex. Analysis of the potentiometric data gave the formation constants listed in Table 2. Figure 2b shows the agreement of the calculated constants with the experimental data in the $\bar{n}$ plot. It was found that the second formation constant was greater than the first ($K_2 > K_1$) for the heavier lanthanides, with the crossover point coming at neodymium. Because there is only a small amount of 1:1 complex formed, the error associated with $K_1$ and hence $K_2$ is larger than that for $\beta_2$. For lanthanum, only the 1:1 constant could be determined because the 1:1 complex precipitated. With Nd, if the ratio of $H_3$TRNS:Nd was less than 1.3, a hydrolysis/polymerization took place at a ~1.5, most likely to a slightly soluble 1:1 complex.

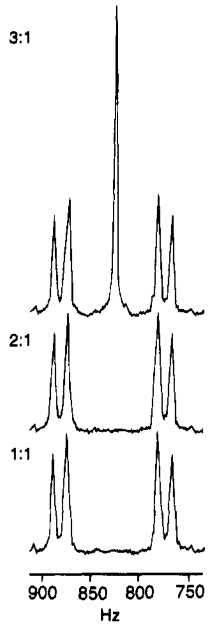

**Figure 3.** $^1H$ NMR of the benzylic region for various TRNS:Lu(III) ratios at $a = 3$.

**Calorimetry.** The calorimetric results for the free ligand showed values consistent with those measured for other phenols.[20] The thermodynamic measurements are summarized in Table 2. The heats of formation were all exothermic, except that for the Nd(TRNS)$_2^{3-}$ complex, which was slightly endothermic. The heats of formation of the 1:1 complexes were more exothermic than those of the 2:1 complexes, except for gadolinium. The entropies for the second equilibrium ($\Delta S_2$) were greater than those of the first ($\Delta S_1$), but this difference decreased across the series. Overall (*i.e.* in terms of $\beta_2$), the entropy term was fairly static at about 195 J·K$^{-1}$·mol$^{-1}$, while the enthalpic term became more and more exothermic.

**$^1$H NMR.** The $^1$H NMR spectrum of the free ligand was typical of that of the other amine phenols based on tren.[45,23] The 3-fold symmetry of the ligand yields only six of a possible eighteen $^1$H resonances. Upon complexation to Lu, this 3-fold symmetry is retained and the molecule becomes rigid. The rigidity is apparent in that the benzylic resonance splits from a singlet in the free ligand to an AB quartet in the complex (Figure 3, 1:1 and 2:1 spectra). Likewise, the two triplets representing the ethylenic backbone hydrogen atoms split upon complexation to give an AA'BB' system. The three ring hydrogen atoms (assigned by the magnitude of their coupling constants, $J_{\text{ortho}} > J_{\text{meta}} > J_{\text{para}}$ also shift upon coordination; however, the hydrogen ortho to the phenolate oxy group undergoes the greatest coordination induced shift. In the $^1$H NMR of the Lu complex as a function of ligand added (at $a = 3$), the spectrum was unchanged up to TRNS:Lu = 2 after which free ligand peaks appeared (Figure 3), corroborating the 2:1 stoichiometry determined by potentiometry. The La complex also had $C_3$ symmetry but was not as rigid, the hydrogen atoms in the backbone displaying fluxionality. The 1:1 complex precipitated, obviating quantitative study of this fluxionality. As predicted from the potentiometric data, free ligand peaks appear in the Lu−TRNS $^1$H NMR spectra at TRNS:La ratios <1. The $^1$H NMR spectra of the Yb, Ho, Gd, and Nd complexes all showed broad unassignable resonances; however, the spectra in all cases showed evidence of 2:1 complex formation. At ratios greater than 2:1, free ligand resonances appeared. The spectra also showed rigid species which did not change upon heating to 70 °C.

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(44) Rossotti, H. *The Study of Ionic Equilibria*; Longman: London, 1978.

(45) Liu, S.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1992**, *31*, 5400.

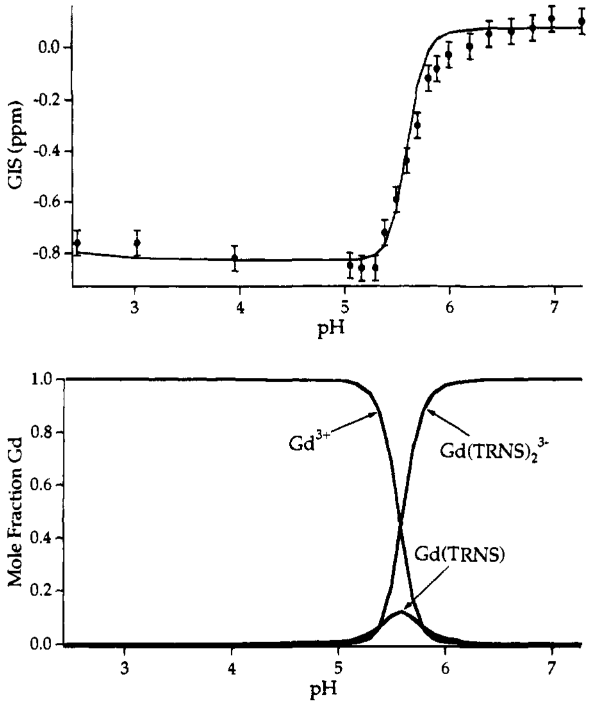

**Figure 4.** Plot of GIS versus pH for 4 mM TRNS:2 mM Gd(III) (top) and the relevant speciation diagram calculated from the constants shown in Table 2 (bottom).

The $^{1}$H NMR spectra of the soluble lanthanide complexes run at $a > 3$ showed the resonances from the complex being slowly replaced by those of the free ligand. There was no indication of different complexes being formed (involving amine coordination, for instance), although one instance of a possible different $N_4O_3$ isomer was observed. The spectrum of a pH 12, 2 TRNS:1 Lu showed about 95% free ligand, but there was also a $C_3$ symmetric species present. In the capped and bicapped complexes, the hydrogen atom ortho to the phenolate was shifted upfield. The minor species has this resonance shifted downfield, which is analogous to the In(III) complex which has the metal encapsulated.[45] This minor isomer is a kinetic product which eventually gives way to lutetium hydroxide and was not further apprehended.

**$^{17}$O NMR.** The natural abundance $^{17}$O NMR of water in the presence of a lanthanide ion and ligand gives a qualitative picture of complexation. A plot of lanthanide induced shift (LIS) versus pH shows complexation occurring as the ligand becomes deprotonated. As the number of metal sites for water exchange decreases with complexation, so does the LIS. Figure 4 (top) shows a plot of the $^{17}$O shift versus pH in a titration of 4 mM TRNS:2 mM Gd(III), roughly the same conditions employed in the potentiometric titrations. The bottom half of Figure 4 is the speciation of Gd(III) under these conditions, calculated based on the stability constants determined in this work.

Peters and co-workers have exploited the dysprosium induced shift of water (DIS) to estimate quantitatively the number of bound water molecules associated with various lanthanide complexes.[46,47,29] The DIS of water is measured at varying dysprosium concentrations. The plot of DIS versus [Dy(III)] is linear with a slope of −358 ppm/M. It has been previously established that the contact contribution of a paramagnetic Ln(III)-induced shift of a Ln(III)-bound $^{17}$O nucleus is almost independent of the nature of the probed O-containing ligand in question and of other co-ligands coordinated to the lanthanide.[47,48] Since the $^{17}$O shift is predominantly contact in nature, the slope of a plot of DIS versus [Dy(III)] should be proportional to the number of bound water molecules associated with the complex. If the hydration number of Dy(III) is given as eight,[49] then a slope of $-358/8 = -45$ would be indicative of one bound water and each multiple of 45 corresponds to one water. Figure 5 shows the DIS versus [Dy(III)] for the aquo ion and for the $Dy(TRNS)_2{}^{3-}$ complex. The slope of −358 ppm/M is in excellent agreement with that obtained by Alpoim *et al.*[46] (−357 ppm/M) and by Reuben and Fiat[50] (−360 ppm/M). The error bars show the line widths at half height (60 Hz); however, the precision was ±5 Hz. Both plots were linear with correlation coefficients of greater than 0.999. The slope of the plot for $Dy(TRNS)_2{}^{3-}$ was −50 ppm/M, or 1.1 $H_2O$, very close to the value reported for $Dy(dtpa)^{2-}$, −52 ppm/M, under the same conditions.[46]

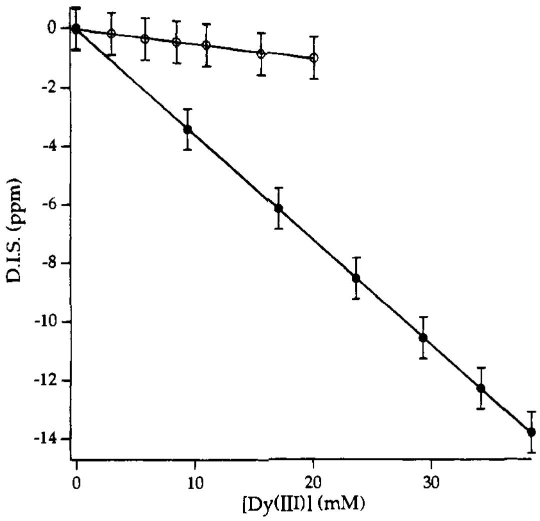

**Figure 5.** Plot of DIS versus [Dy(III)] (mM): (○) $[Dy(TRNS)_2]^{3-}$; (●) $Dy^{3+}{}_{(aq)}$. Error bars represent line widths at half-height.

The low concentration of the 1:1 complex made a confident estimation of the number of bound waters associated with it impossible. The 1:1 species will always exist with large amounts of either the 2:1 species or the aquo ion and will be pH dependent. Since the majority of aqueous lanthanide complexes are 9 coordinate in solution,[9,46] and since a crystal structure of an analogous 1:1 complex has been reported,[21] it is likely that the coordination number of the 1:1 complex reported here is 9 with 6 associated water molecules.

Studies with TRNS:Dy ratios as high as 25 showed the same DIS: [Dy(III)] ratio, indicating that the maximum number of ligands bound is two.

## Discussion

In previous studies on tripodal $N_4O_3$ ligands with lanthanide(III) ions, the ease of formation of the monocapped complexes was noticed.[22] Simply mixing the free base form of the ligand with a lanthanide salt yielded the 1:1 capped complex. With the tren based amine phenol, addition of base gave a 2:2 encapsulated dimer. This dimerization can be prevented by employing the same ligand with methoxy substituents in the 3 positions; however, reaction of this ligand with lanthanide salts

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(46) Alpoim, M. C.; Urbano, A. M.; Geraldes, C. F. G. C.; Peters, J. A. *J. Chem. Soc., Dalton Trans.* **1992**, 463.

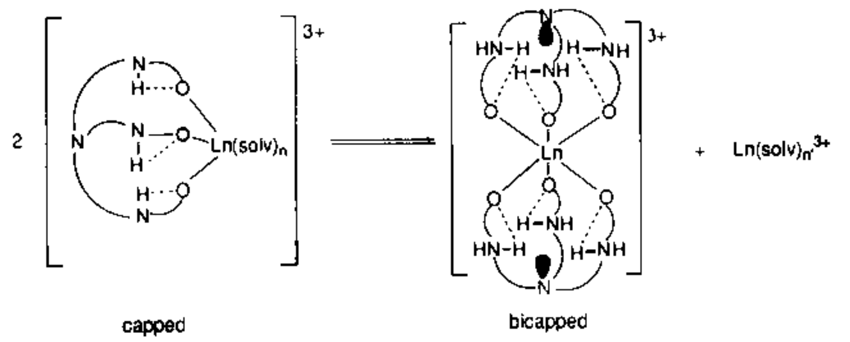
(47) Huskens, J.; Kennedy, A. D.; van Bekkum, H.; Peters, J. *J. Am. Chem. Soc.* **1995**, *117*, 375.

(48) Peters, J. A.; Kieboom, A. P. G. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 381.

(49) Helm, L.; Foglia, F.; Kowall, T.; Merbach, A. E. *J. Phys.: Condens. Matter* **1994**, *6*, A137.

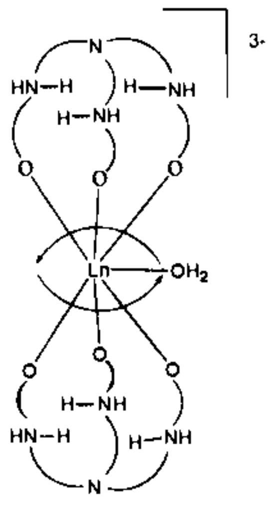
(50) Reuben, J.; Fiat, D. *J. Chem. Phys.* **1969**, *51*, 4909.

**Scheme 3**



in the presence of excess NaOH resulted in the formation of bicapped 6-coordinate complexes.[23] In light of the current solution chemistry results, this reaction can be explained by the relative inertness of the bicapped complex, coupled with its high formation constant. The 1:1 capped complex disproportionated in the presence of base to give Ln(OH)$_3$, which was filtered out, and the bicapped 2:1 complex, which was isolated (Scheme 3).

The work described here supports a solution structure for the 2:1 bicapped complex that is similar to that determined by X-ray crystallography in the 3′-methoxy-substituted Gd(III) complex.[23] From the proton stoichiometry, only three donor atoms were deprotonated, and these donors were shown by variable pH $^{1}$H NMR and UV spectroscopies to be all phenolato oxygen donors. The $^{1}$H NMR of the Lu(III) complex shows a rigid complex possessing $C_3$ symmetry, which rules out a non-apical N/O$_3$ donor set per ligand. The $^{17}$O NMR studies on the Dy(III) 2:1 complex showed it to contain one inner-sphere coordinated water molecule, hence a coordination number of 7 obtained in solution. The Gd(TRNOMe)$_2^{3+}$ complex was obtained from a nonaqueous solvent and contained methoxy substituents ortho to the phenolate oxygen atoms which probably contributed to its low coordination number (6). The $^{17}$O NMR study of the bicapped dysprosium complex indicated one bound water (the slope of the DIS plot being the same as that of the dtpa complex which had been established to have one inner-sphere water molecule based on Tb[51] and Eu[52] fluorescence), but the $^{1}$H NMR of the Lu complex is consistent with a bicapped structure owing to the 3-fold symmetry. To account for the $^{1}$H and $^{17}$O results, a seven-coordinate solution structure similar to the bicapped crystal structure is proposed in which there is one water molecule in the equatorial plane. Since the rate of water exchange in Ln complexes is very fast,[53-55] the water molecule will be averaged about the equatorial plane on the NMR time scale, thus preserving the 3-fold symmetry seen in the Lu complex.



Less can be said about the 1:1 complex, since it was formed in such small amounts. Variable pH and variable M:L ratio $^{1}$H NMR studies on the Lu(III) system showed only one set of resonances for the complex, suggesting that the 1:1 complex had the same structure as the 2:1 complex, and that removal of one capping ligand did not effect the chemical shift of the remaining bound ligand, or that the bound ligand in the 1:1 complex is in fast exchange with the free ligand. The coordination number could not be determined for the 1:1 complex. The small percentage relative to either the aquo ion or the 2:1 complex coupled with its pH dependence made an accurate determination of the hydration number of the capped complex by $^{17}$O NMR impossible. A variable pH luminescence study on the europium or terbium system may prove sensitive enough to ascertain the coordination number of the capped complex. However, the proton stoichiometry places the ligand denticity at 3 and the likely coordination number is 9 (6 bound waters) in accord with the crystal structure of the related Gd(H$_3$trac)(NO$_3$)$_3$.[21]

The high formation constant of the 2:1 complex relative to that for the 1:1 complex was surprising, and no examples could be found in the lanthanide literature. It is a well-known fact of coordination chemistry that the formation constants for stepwise equilibria generally decrease with increasing substitution due to statistical, electrostatic, and steric effects, but exceptions to this general rule have been known for a long time. Most notable perhaps is Bjerrum's work on silver ammine complexes where $K_2 > K_1$.[56,57] Other instances include $K_4 > K_3$ in the Hg(II)–Cl equilibria[20] and $K_3 > K_2$ in the Fe(II)–phenanthroline equilibria.[28] The Fe(II)–phen anomaly is attributed to the gain in free energy from the change in electronic configuration on going from Fe(phen)$_2^{2+}$ (high spin) to Fe(phen)$_3^{2+}$ (low spin), which should be an enthalpic effect. The other anomalies can also be attributed to enthalpy changes from reduction of hydration number associated with the formation of highly stable linear (Ag(I), Hg(II)) complexes. For instance, HgCl$_2$ is a linear species, whereas [HgCl$_3$(H$_2$O)]$^-$ and HgCl$_4^{2-}$ are both tetrahedral. Thus, on going from HgCl$_2$ to [HgCl$_3$(H$_2$O)]$^-$ a molecule of solvent is required, while the fourth addition of chloride to give HgCl$_4^{2-}$ displaces this bound water. In the Ag(I)–ammine system, the first equivalent of ammonia displaces one water from a tetrahedral Ag$^+$ ion, while the second displaces three waters to give the linear [Ag(NH$_3$)$_2$]$^+$. Presumably, the change in hybridization from sp$^3$ to sp results in the anomalous order observed.[58] With a lowering of coordination number (more bound H$_2$O liberated), a positive entropy change should accompany complex formation; however, in these instances the entropy term is static or negative, and the increase in stability can be traced to the enthalpy term. This low, or negative, entropy change which occurs despite the net increase in the number of molecules in the reaction

$$[Ag(NH_3)(H_2O)_3]^+ + NH_3 \rightleftharpoons [Ag(NH_3)_2]^+ + 3H_2O \qquad (8)$$

emphasizes the fact that thermodynamic quantities are measured globally and cannot always be rationalized locally.

In the TRNS:Ln(III) system, the anomaly is likely to be predominantly entropic. It is well-known that lanthanide(III)

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(51) Chang, C. A.; Brittain, H. G.; Telser, J.; Tweedle, M. F. *Inorg. Chem.* **1990**, *29*, 4468.

(52) Bryden, C. C.; Reilley, C. N. *Anal. Chem.* **1982**, *54*, 610.

(53) Cossy, C.; Helm, L.; Merbach, A. E. *Inorg. Chem.* **1988**, *27*, 1973.

(54) Micskei, K.; Helm, L.; Brücher, E.; Merbach, A. E. *Inorg. Chem.* **1993**, *32*, 3844.

(55) Powell, D. H.; González, G.; Tissières, V.; Micskei, K.; Brücher, E.; Helm, L.; Merbach, A. E. *J. Alloys Compd.* **1994**, *207/208*, 20.

(56) Bjerrum, J. *Metal Ammine Formation in Aqueous Solution*; P. Haase and Son: Copenhagen, 1957.

(57) Maeda, M.; Arnek, R.; Biedermann, G. *J. Inorg. Nucl. Chem.* **1979**, *41*, 343.

(58) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 4th ed.; Wiley: New York, 1980.

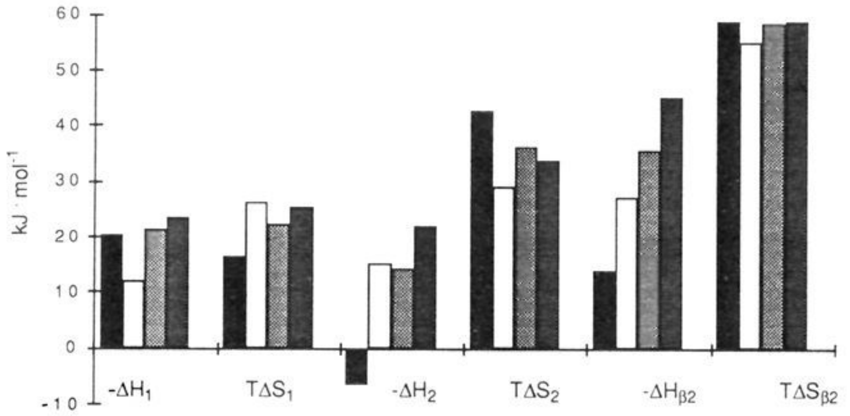

**Figure 6.** Enthalpies and entropies for the Ln(III)−TRNS equilibria (from left to right within each grouping): Nd, Gd, Ho, Yb.

bonding is primarily electrostatic in nature. In the TRNS:Ln(III) system, a tripositive lanthanide reacts with a trinegative ligand to give a neutral 1:1 complex, which then reacts with a second trinegative ligand to give a trinegative complex. There should be no favorable enthalpy associated with $K_2$ based on electrostatic arguments, and even less so if the coordination number decreases. The coordination number of lanthanide(III) aquo ions has been the subject of numerous investigations, with eight or nine being the generally accepted number.[49,53] Based on a crystal structure of an analogous compound[21] and the preponderance of nine-coordinate lanthanide complexes in solution and the solid state, the 1:1 complex should have a coordination number of 9. The 2:1 dysprosium complex has a coordination number of 7, based on $^{17}O$ NMR shifts of water. A similar bicapped complex had been obtained which was six coordinate; however, it contained methoxy groups ortho to the phenolate donors which may have forced such a low coordination number on the lanthanides. It appears a change in coordination number is occurring as the equilibrium shifts from monocapped to bicapped. For the equilibria considered here, the first equivalent of $TRNS^{3-}$ displaces 3 waters, while the second equivalent should displace 5 waters. This second equilibrium should increase the translational entropy of the system more than the first, and this will be seen in the large $K_2$. This is most likely a steric effect which arises from placing six phenolato groups about the metal and crowding out any further coordination sites.

The argument is supported by the calorimetric measurements, which show $\Delta S_2 > \Delta S_1$ for each Ln(III) under consideration (Figure 6). The difference $(\Delta S_2 - \Delta S_1)$ decreases across the series, consistent with the fact that the first equilibrium involves two triply charged species coming together to give a neutral 1:1 complex which should result in a positive entropic contribution. The second equilibrium involves no such net change in charge; therefore, one would expect $\Delta S_1$ to increase across the series as the effective nuclear charge increases. The overall entropic effect, $\Delta S_{\beta 2}$, is fairly static across the series studied (Figure 6), which is to be expected if the degree of solvation of the 2:1 complex is constant across the lanthanide series.

The second surprising phenomenon was the high selectivity that TRNS displayed for the heavier lanthanides, clearly evident in Figure 2 which shows the Yb complex forming at a pH unit lower than that of the Nd complex. A change in the overall stability constant $\beta$ of $10^{5.5}$ was observed on going from Nd(III) to Yb(III). This compares with $10^{2.9}$ for EDTA, $10^{1.9}$ for NTA, or $10^{1.0}$ for DTPA.[20] The calorimetric data for $\Delta H_{\beta 2}$ showed an increasing exothermicity on traversing the lanthanide series (Figure 6), while $\Delta S_{\beta 2}$ was fairly static. This result is in accord with an electrostatic bonding model, in which the formation constants should increase with effective nuclear charge (or $1/r$)[59] as they do here (Figure 7). This selectivity may prove useful in the separation of lanthanides by chelation ion chromatography.[60]

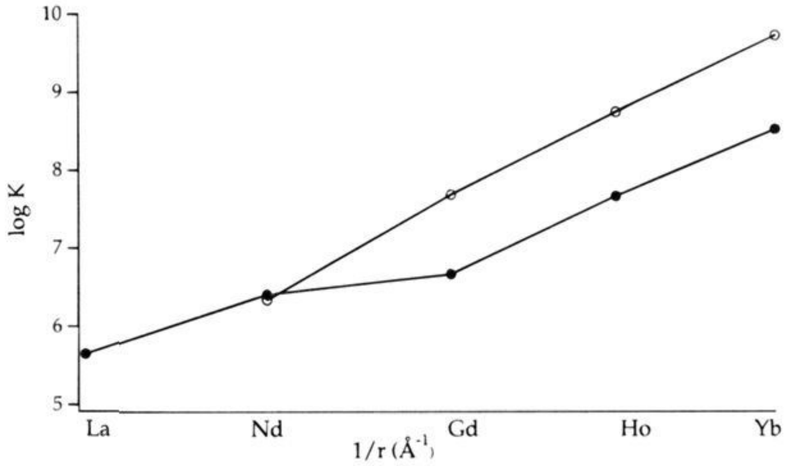

**Figure 7.** log $K_n$ versus $1/r$ (ionic radii for CN = 6, ref 59): (●) $K_1$; (○) $K_2$.

When $TRNS^{3-}$ binds to a lanthanide(III) in a tridentate fashion, three 16-membered chelate rings are formed. There should be no chelate effect on forming such large rings; however, the three protonated amine functionalities in this ligand make it different from a tris(phenol) linked by nine carbon chains. The elevated $pK_a$s of the amines coupled with the depressed $pK_a$s of the phenols (relative to their molecular substituents) implies that an intrastrand hydrogen ion bond exists between the protonated N atom of the amine, its acidic H atom, and the deprotonated phenolato oxygen atom. Interstrand H bonding may also be postulated if only because of coordination to the metal. In aqueous media interstrand H bonding is unlikely; however, given the relatively high stability of these capped 16-membered ring complexes, there must be an effect which predisposes the ligand to a binding posture. In a related ligand crystal structure interstrand H bonding, as well as intrastrand H bonding, was noted.[61] This interstrand H bonding, if present, is certainly not expected to be strong (the ligand $^1H$ NMR spectra show $C_3$ symmetry). The flexibility imparted by a loose H-bond network coupled with the large chelate ring size results in a tridentate ligand which should have little or no strain energy created in accommodating different Ln(III) ions; thus the increase in stability is purely electrostatic and increases with the inverse ionic radius of the lanthanide considered (Figure 7).

Although the results obtained for overall formation (*i.e.* $\beta_2$) of the 2:1 complex can be explained in terms of a 7-coordinated species, the $\Delta S_1$ and $\Delta H_1$ (and hence the $\Delta S_2$ and $\Delta H_2$) data show no apparent trends (Figure 6). If there is a change in coordination number in the 1:1 complex because of the steric requirements of the ligand (*e.g.* five bound $H_2O$ for the late lanthanides, six for the early lanthanides), then one would expect to see two trends in $\Delta S_1$ (and $\Delta H_1$) as the Ln(III) series is traversed. Figure 6 shows a linear relationship between log $K_2$ and $1/r$ ($r^2 = 0.999$), whereas there appears to be a discontinuity in the log $K_1$ vs $1/r$ data at Gd. The lack of smooth trends in the enthalpic and entropic data is consistent with the aqueous calorimetric literature on the lanthanides.[14,26,27] Whether this can be interpreted as a change in inner-sphere coordination appears dubious, since a recent calorimetric and multinuclear NMR study demonstrated that a series of Ln complexes with constant geometry and constant coordination number can also give rise to this phenomenon of a discontinuation in the enthalpic and entropic terms.[29]

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(59) Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751.
(60) Kumar, M. *Analyst* **1994**, *119*, 2013.
(61) Liu, S.; Wong, E.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1993**, *32*, 4268.

Current work is focusing on the preparation of other tripodal amine phenols to glean information on the effect of this large chelate ring size. We are also preparing analogues which contain no secondary amines, in order to evaluate possible interstrand H-bonding effects in the complexes.

## Conclusion

We have demonstrated that the tripodal aminophenol ligand $H_3TRNS$ acts as a tridentate ligand toward lanthanide ions in aqueous solution, binding through the phenolato oxygen atoms to form large 16-membered chelate rings. The formation constant for the 2:1 complex ($K_2$) is larger than that of the 1:1 complex ($K_1$), and this is believed to be an entropic effect based on the desolvation of the 1:1 complex because of steric crowding. The ligand is highly selective for the heavier lanthanides, and this has been determined to be an enthalpic effect which agrees well with the electrostatic nature of Ln(III) bonding.

**Acknowledgment** is made to the Natural Sciences and Engineering Research Council (NSERC) for a postgraduate schlorship (1992–96, P.C.), a postdoctoral fellowship (1991–93, S.L.), and an operating grant (C.O.) and to the Swedish Natural Science Research Council for support (S.S.). We would like to acknowledge the referees for suggesting the Dy experiment. P.C. and C.O. would also like to thank Dr. Tom McMurry for a copy of the software which ran the autotitrator.

JA9512384