

Effects of Sequential Replacement of $-\text{NH}_2$ by $-\text{OH}$ in the Tripodal Tetraamine Tren on Its Acidity and Metal Ion Coordinating Properties[†]

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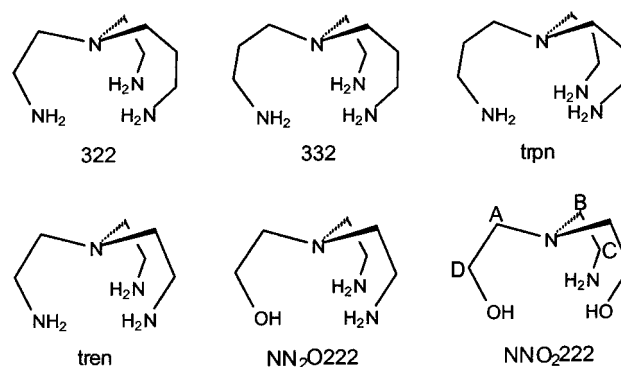
Received August 30, 2000

The preparation is described of two modified derivatives of the tripodal tetraamine tren, 2-hydroxy-*N,N*-bis(2-aminoethyl)ethylamine, $\text{NN}_2\text{O}222$, and 2-amino-*N,N*-bis(2-hydroxyethyl)ethylamine, NNO_2222 , in which one and two primary amines, respectively, have been replaced with hydroxyl groups. The aqueous acid–base and metal ion (Ni^{2+} , Cu^{2+} , Zn^{2+}) coordination properties of these two compounds were studied by potentiometric, spectrophotometric, and NMR titrations. Two and three acidity constants, respectively, were determined for NNO_2222 and $\text{NN}_2\text{O}222$ by potentiometry. NMR titrations proved that deprotonation of the two OH residues in NNO_2222 , and of the one in $\text{NN}_2\text{O}222$, corresponded to $\text{p}K_{\text{a}} > 14$. Acidity constants related to deprotonation of the terminal primary amine functions were similar in both NNO_2222 and $\text{NN}_2\text{O}222$ (and to those in the parent compound tren), whereas deprotonation of the tertiary ammonium N atom had a very different acidity constant in each of these three compounds. Charge repulsion, polar effects, and intramolecular hydrogen bond formation are responsible for the discrepancy. Chelated diamine metal complexes for each ligand studied depended only on the basicity of the corresponding two amines, suggesting that the hydroxyl group interacted with the metal ion very weakly in acidic or neutral solutions. The ML^{2+} species further deprotonated to form $\text{M}(\text{L} - \text{H})^+$ and $\text{M}(\text{L} - 2\text{H})$ complexes, in which the protons are released from the coordinated OH group. A pM vs pH correlation showed that replacing an NH_2 group with a OH group in tren or $\text{NN}_2\text{O}222$ makes the resulting metal complex less stable. Electronic spectra showed that the $\text{Cu}(\text{II})$ complexes of both NNO_2222 and $\text{NN}_2\text{O}222$ adopted a square pyramidal geometry rather than a trigonal bipyramidal geometry. The X-ray crystal structure analysis of the zinc complex $[\text{Zn}(\text{OH})(\mu\text{-NNO}_2222 - \text{H})\text{Zn}(\text{NNO}_2222)]^{2+}$, as its $[\text{BF}_4]^-$ salt, shows a dinuclear molecule containing two zinc ions, each coordinated in a distorted trigonal bipyramid. The coordination environment at one zinc atom is composed of the four donor groups of a mono-O-deprotonated ligand NNO_2222 and a hydroxyl ion with the central nitrogen atom of the ligand and the hydroxyl ion in equatorial positions. The oxygen atom of the deprotonated alkoxo group bridges to the second zinc atom, which is coordinated by this atom and one unde protonated ligand NNO_2222 .

Introduction

It has been found that the geometry adopted by the Cu^{2+} complexes of tren¹ (tren = tris(2-aminoethyl)amine, Chart 1) and analogous tripodal tetraamine ligands^{2–4} with varying arm lengths will vary between trigonal bipyramidal and square pyramidal. This fact has prompted us to embark on a larger

Chart 1



project to examine in detail new tripodal ligands with different arm lengths,^{2,3} substitution patterns,⁵ and donor atoms⁶ to deter-

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mine which factors influence the geometry and reactivity of not only copper complexes but also Ni^{2+} and Zn^{2+} complexes.

Cu^{2+} complexes of four symmetric and asymmetric tripodal N_4 ligands with different combinations of ethylene and propylene arms (tren, 322, 332, trpn, Chart 1) showed varying degrees of pH-dependent geometry intermediates between a mononuclear tetragonally distorted trigonal bipyramid (tren, 332, neutral pH) and binuclear square pyramids (all four ligands at basic pH).

$\text{Zn}(\text{II})$ complexes are also promiscuous, changing coordination geometries from octahedral to tetrahedral;⁷ this alteration renders the complexes more easily hydrolyzed than Zn^{2+} itself.⁸ $\text{Ni}(\text{II})$ complexes are well-known to take on a variety of geometries, such as octahedral, square pyramidal, tetrahedral, and square planar.⁹

It is, therefore, most interesting to see whether all three of these metal ions will undergo coordination geometry changes when complexed with tripodal ligands in which donor group and arm length alterations can be systematically undertaken. This takes on particular importance in light of the many important roles played by Ni^{2+} , Cu^{2+} , and Zn^{2+} in biological systems.¹⁰

Herein we report on the complexation in aqueous solution of Ni^{2+} , Cu^{2+} , and Zn^{2+} by two tren derivatives, NNO_222 and $\text{NN}_2\text{O}222$ (Chart 1), in which the arm lengths have been maintained but the donor atoms have been systematically varied from $-\text{NH}_2$ to $-\text{OH}$. We also report on the crystal structure of a binuclear Zn complex $[\text{Zn}(\text{OH})(\mu\text{-NNO}_222 - \text{H})\text{Zn}(\text{NNO}_222)]^{2+}$ as its $[\text{BF}_4]^-$ salt.

Experimental Section

Materials. Air-sensitive compounds were prepared and handled under Ar using Schlenk techniques. All solvents used in the syntheses were rigorously dried (typically, over Na, or Na/K and benzophenone) and freshly distilled prior to use. All starting materials used in the syntheses were commercially available (Aldrich) and were of reagent grade. Atomic absorption standard solutions of Ni^{2+} , Cu^{2+} , and Zn^{2+} were purchased from Sigma and used directly. The concentration of the titer (1 M NaOH, Fisher) was established with potassium biphthalate (Anachemia). Sodium chloride (for controlling solution ionic strength) and hydrochloric acid were also purchased from Fisher. Water was deionized (Barnstead D8902 and D8904 cartridges), distilled (Corning MP-1 Megapure still), and boiled under Ar for about 30 min to remove CO_2 . D_2O , NaOD, and DCl were purchased from Cambridge Isotope Laboratories.

Instrumentation. UV spectra were recorded with a HP 8453 UV-vis spectrophotometer. NMR spectra were obtained on a Bruker AC-200 (^1H 200 MHz), Bruker AM 250 (^1H 250 MHz, ^{13}C 62.9 MHz), or JEOL JNM-LA 400 (^1H 400 MHz, ^{13}C 100 MHz) instrument. Mass spectra (FAB or EI) were recorded on a Finnigan MAT 711 or Finnigan MAT 112 spectrometer, respectively. Elemental analyses were performed on a Vario EL elemental analyzer at the Freie Universität Berlin. Potentiometric measurements were made with an automatic titration system consisting of a Metrohm 713 pH meter equipped with a Metrohm 6.0233.100 electrode, a model 665 Metrohm Dosimat autoburet, and water-jacketed titration vessels connected to a Julabo UC circulating bath. Both the pH meter and the autoburet were controlled by an IBM-compatible PC, and the titration was controlled with a locally written QBasic program. The electrode was calibrated before each titration by titrating a known amount of aqueous HCl with

a known amount of NaOH. A plot of $\text{mV}(\text{calcd})$ vs pH gave a working slope and intercept so that pH could be read as $-\log [\text{H}^+]$ directly. The value of $\text{p}K_w$ used at $I = 0.16$ was 13.76.¹¹

Preparation of the Tripodal Amines (Schemes 1 and 2). **2-Hydroxy-*N*-(cyanomethyl)-*N*-(2-hydroxyethyl)ethylamine (1).** Diethanolamine (5.26 g, 0.05 mol) was treated at 0 °C with 5.70 g of HCl (32%). To this solution was added dropwise at 0 °C a solution of KCN (3.26 g, 0.05 mol) in 10 mL of water. Subsequently, an aqueous 37% formaldehyde solution (4.054 g, 0.05 mol) was added at such a rate that the temperature did not exceed 0 °C. The reaction mixture was then warmed to room temperature and stirred for an additional 2 h. The reaction solution was extracted with CH_2Cl_2 for 3 d, and the red organic phase was subsequently separated and dried with MgSO_4 . Removal of the solvent yielded 5.513 g (76.5%) of a pink oil. ^1H NMR (CDCl_3 , 400 MHz): δ 3.68 (s, 2 H, CH_2CN), 3.66 (t, 4 H, CH_2OH), 3.37 (s, 2 H, OH), 2.75 (t, 4 H, NCH_2CH_2). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz): δ 115.29 (CN), 59.12 (CH_2OH), 55.65 (NCH_2CH_2), 42.59 (CH_2CN).

2-Amino-*N,N*-bis(2-hydroxyethyl)ethylamine, NNO_222 (2). Lithium aluminum hydride (4.554 g (0.12 mol) was suspended under Ar in 150 mL of dry THF at -5 °C. To this suspension was added carefully 96% H_2SO_4 (6.13 g, 0.06 mol). The reaction mixture was warmed to 0 °C and stirred at this temperature for 1 h. After the reaction mixture achieved room temperature, **1** (5.513 g, 0.038 mol) dissolved in 30 mL of dry THF was added dropwise at such a rate that the solvent did not start to boil. The reaction mixture was then stirred at room temperature overnight. The residual lithium aluminum hydride was hydrolyzed with 10.2 mL of water, and the resulting suspension was filtered. The solid residue was washed several times with methanol, and the combined organic phases were concentrated to yield a yellow oil. This oil was dried by azeotropic distillation with cyclohexane, and finally the oily residue was distilled at 130–140 °C at 0.03 mbar, yielding 2.7 g (47.9%) of a colorless, strongly hygroscopic oil. Anal. Calcd (Found) for $\text{C}_6\text{H}_{16}\text{N}_2\text{O}_2$ (fw = 148.21): C, 48.63 (47.90); H, 10.88 (10.05); N, 18.90 (17.88). ^1H NMR (CDCl_3 , 400 MHz): δ 3.61 (s, br, 4 H, OH and NH_2), 3.41 (t, 4 H, CH_2OH), 2.59 (t, 2 H, $\text{NCH}_2\text{CH}_2\text{NH}_2$), 2.43 (t + t, 6 H, $\text{NCH}_2\text{CH}_2\text{OH}$ and CH_2NH_2). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz): δ 58.98 (CH_2OH), 57.77 ($\text{NCH}_2\text{CH}_2\text{OH}$), 56.42 ($\text{NCH}_2\text{CH}_2\text{NH}_2$), 39.13 (CH_2NH_2).

Synthesis of 2-Hydroxy-*N,N*-bis(2-aminoethyl)ethylamine, $\text{NN}_2\text{O}222$ (5), Method A. **2-Chloro-*N,N*-bis(cyanomethyl)ethylamine (3).** 2-Chloroethylamine hydrochloride (23.2 g, 0.2 mol) was dissolved in 20 mL of water, and KCN (13.03 g, 0.2 mol) in 25 mL of water was added at -5 °C. The resulting solution was stirred at -5 °C for 30 min, after which time an aqueous 37% formaldehyde solution (16.22 g, 0.2 mol) was added dropwise so that the temperature of the solution did not rise above 5 °C. This solution was stirred at -5 °C for 2 h, subsequently warmed to room temperature, and stirred for another 1 h. The reaction mixture was again cooled to -5 °C, and 32% aqueous HCl (22.78 g) was added. A clear solution was obtained to which KCN (13.03 g, 0.2 mol) in 25 mL of water and more aqueous 37% formaldehyde solution (16.22 g, 0.2 mol) were added, as described in the previous reaction step. The resulting reaction mixture was stirred at 0 °C for another 30 min and then at room temperature for 60 min. Upon cooling of the reaction mixture to 0 °C overnight, colorless crystals formed; recrystallization from ethanol yielded 16.39 g (52%) of these crystals. Anal. Calcd (Found) for $\text{C}_6\text{H}_8\text{N}_3\text{Cl}$ (fw = 157.60): C, 45.73 (45.76); H, 5.12 (5.23); N, 26.66 (26.17). ^1H NMR (CDCl_3 , 250 MHz): δ 3.68 (s, 4 H, CH_2CN), 3.57 (t, 2 H, CH_2Cl), 3.07 (t, 2 H, NCH_2). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 62.90 MHz): δ 113.88 (CN), 55.64 (CH_2N), 42.32 (CH_2CN), 40.61 (CH_2Cl).

2-Acetoxy-*N,N*-bis(cyanomethyl)ethylamine (4). Potassium acetate (1.22 g, 0.012 mol) and **3** (1.58 g, 0.01 mol) were dissolved in 30 mL of DMF, and the solution was heated to 80 °C for 4 h. The residual solvent was removed by distillation, and the oily residue was dissolved in CDCl_3 (25 mL) and filtered to remove KCl. The solvent was removed, leaving a yellow oil which crystallized at -30 °C to yield 1.8 g (99%). ^1H NMR (CDCl_3 , 250 MHz): δ 4.20 (t, 2 H, OCH_2),

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3.67 (s, 4 H, CH_2CN), 2.92 (t, 2 H, NCH_2), 2.06 (s, 3 H, CH_3). $^{13}\text{C}\{-^1\text{H}\}$ NMR (CDCl_3 , 62.90 MHz): δ 170.62 (COO), 114.27 (CN), 60.99 (OCH_2), 52.31 (CH_2N), 42.59 (CH_2CN), 20.84 (CH_3).

2-Hydroxy-*N,N*-bis(2-aminoethyl)ethylamine, $\text{NN}_2\text{O}222$ (5). Lithium aluminum hydride (6.90 g, 0.182 mol) was suspended in 200 mL of dry THF at -5°C under Ar. To this suspension was carefully added 96% H_2SO_4 (6.82 g, 66.9 mmol). The resulting AlH_3 suspension was stirred at -5°C for 30 min and then warmed to room temperature. A solution of **4** (3.64 g, 0.02 mol) in 20 mL of THF was added to the AlH_3 suspension at room temperature, at a rate such that the THF did not start to boil. The reaction mixture was stirred at room temperature overnight. The residual lithium aluminum hydride was carefully hydrolyzed with 10.7 mL of water, and the suspension was then filtered. The solid residue was extracted with methanol overnight, and the combined yellow organic phases were dried with MgSO_4 . After removal of the solvents in vacuo, the oily residue was distilled at 120°C and 10^{-2} mbar to yield 1.0 g (34%) of a colorless oil which crystallized at -30°C . ^1H NMR (CDCl_3 , 250 MHz): 3.62 (t, 2 H, CH_2OH), 2.79 (t, 4 H, $\text{NCH}_2\text{CH}_2\text{NH}_2$), 2.63 (m, 6 H, NCH_2), 2.19 (s, br, 5 H, NH_2 and OH). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 62.90 MHz): δ 60.05 (CH_2OH), 57.38 ($\text{NCH}_2\text{CH}_2\text{OH}$), 56.28 ($\text{NCH}_2\text{CH}_2\text{NH}_2$), 39.72 (CH_2NH_2). MS (EI, 70 eV): m/e (relative intensity, assignment) 148 (0.21, $[\text{M}]^+$), 130 (1.42 $[\text{M} - \text{H}_2\text{O}]^+$), 117 (75.71), 74 (57.61), 44 (100), 30 (21.8).

Synthesis of 2-Hydroxy-*N,N*-bis(2-aminoethyl)ethylamine, $\text{NN}_2\text{O}222$ (5), Method B. 2-Hydroxy-*N*-(cyanomethyl)ethylamine (6). Ethanolamine (3.05 g, 0.05 mol) was dissolved in 10 mL of water, and the solution was cooled to -5°C . To generate the hydrochloride salt, HCl (5.70 g, 0.05 mol) in water (32%) was added. A solution of KCN (3.26 g, 0.05 mol) in 10 mL of water was then added. To this reaction mixture was added dropwise a 37% formaldehyde solution (4.06 g, 0.05 mol) at 0°C , and the resulting mixture was stirred at 0°C for 60 min; it was allowed to warm to room temperature and was stirred at room temperature overnight. Subsequently the reaction solution was extracted with dichloromethane for 36 h, and the organic phase was then separated and dried with MgSO_4 . Removal of the solvent yielded a white residue which was recrystallized from diethyl ether/ethyl acetate to yield 4.0 g (80%) of a white powder. ^1H NMR (CDCl_3 , 250 MHz): δ 3.67 (t, 2 H, CH_2OH), 3.60 (s, 2 H, CH_2CN), 2.88 (t, 2 H, NCH_2), 2.05 (s, br, 2 H, NH and OH). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 62.90 MHz): δ 119.09 (CN), 60.77 (CH_2OH), 50.21 (CH_2N), 37.09 (CH_2CN).

2-Hydroxy-*N,N*-bis(cyanomethyl)ethylamine (7). Aqueous 32% HCl (2.28 g, 0.02 mol) was added at -5°C to **6** (2.0 g, 0.02 mol), and to the resulting solution were added at -5°C KCN (1.30 g, 0.02 mol) in 10 mL of water and then an aqueous 37% formaldehyde solution (1.623 g, 0.02 mol). The reaction mixture was stirred at 0°C for 60 min and then at room temperature overnight. The yellow reaction mixture was extracted with dichloromethane for 12 h, and the organic phase was dried with MgSO_4 . The solvent was removed to yield 2.51 g (90.2%) of a colorless oil. ^1H NMR (CDCl_3 , 400 MHz): δ 3.72 (s + t, 6 H, CH_2OH and CH_2CN), 2.82 (t, 2 H, NCH_2CH_2), 2.54 (s, 1 H, OH). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz): δ 114.68 (CN), 59.55 (CH_2OH), 55.23 (NCH_2), 42.69 (CH_2CN).

2-Hydroxy-*N,N*-bis(2-aminoethyl)ethylamine, $\text{NN}_2\text{O}222$ (5). The reduction of the nitrile groups in **7** was achieved as described for the reduction of **4**. For the reduction of **4** (4.18 g, 0.03 mol), AlH_3 was generated from lithium aluminum hydride (6.83 g, 0.18 mol) and 96% H_2SO_4 (6.75 g, 66.2 mmol) to yield 3.02 g of **5** (68.5%). The analytical data of **5** obtained this way are identical to those of **5** obtained by method A.

Determination of Acidity Constants. The titrations for determining the acidity constants of NNO_222 or $\text{NN}_2\text{O}222$ were carried out by adding standardized NaOH solution (0.11 M) to 2.6 mM HCl (50 mL) and NaCl ($I = 0.16$ M, 25°C) in the presence of 0.4–0.6 mM $\text{H}_2(\text{NNO}_222)^{2+}$ or $\text{H}_3(\text{NN}_2\text{O}222)^{3+}$ under N_2 . The constants were calculated using an IBM-compatible computer with a Pentium II processor by a curve-fit procedure using a Newton–Gauss nonlinear least-squares program similar to that used in other studies.¹² For NNO_222 , the calculation pH range was $3.3 \leq \text{pH} \leq 10.6$, corresponding to

about 2% neutralization for the equilibrium between $\text{H}_2(\text{NNO}_222)^{2+}$ and $\text{H}(\text{NNO}_222)^+$, and about 96% neutralization for the equilibrium between $\text{H}(\text{NNO}_222)^+$ and NNO_222 . For $\text{NN}_2\text{O}222$, the calculation pH range was $2.0 \leq \text{pH} \leq 10.6$, corresponding to about 35% neutralization for the equilibrium between $\text{H}_3(\text{NN}_2\text{O}222)^{3+}$ and $\text{H}_2(\text{NN}_2\text{O}222)^{2+}$, and about 83% neutralization for the equilibrium between $\text{H}(\text{NN}_2\text{O}222)^+$ and $\text{NN}_2\text{O}222$. More than 50 data points were recorded in each titration and used in the fit. The final results for the acidity constants given in Table 1 are from the average of more than 10 independent titrations in each case (throughout this work, the error limits are 3 times the standard error of the mean value, 3σ).

To prove that deprotonation of the OH group occurs at very high pH, ^1H NMR titrations were undertaken (Table 2). A series of samples of identical ionic strengths (total 0.16 M, in some combination of NaOD and NaCl) but different pH values ($3.1 \leq \text{pH}^* \leq 13.4$) were prepared; the pH^* (pH meter reading value of the D_2O solutions) was measured with the same pH meter and electrode. The pD values were obtained by adding 0.4 to pH^* .¹³ The ^1H NMR spectrum of each sample was recorded, and the acidity constants were evaluated by fitting the chemical shifts of a given signal with the appropriate pD values using a program similar to that described for treating the potentiometric data.

Determination of Stability Constants. The stability constants of Ni^{2+} , Cu^{2+} , and Zn^{2+} with the two ligands NNO_222 and $\text{NN}_2\text{O}222$ were determined under the same conditions outlined above, except that Na^+ in the supporting electrolyte was partly replaced by the appropriate M^{2+} ($I = 0.16$ M, 25°C). To prevent the hydrolysis of the metal ions, $[\text{L}]_{\text{tot}} > [\text{M}^{2+}]_{\text{tot}}$ in all experiments ($[\text{L}]_{\text{tot}}$ and $[\text{M}^{2+}]_{\text{tot}}$ are the total ligand and total metal ion concentrations in solution, respectively). To evaluate the importance of ML_2 complexes, in some experiments $[\text{L}]_{\text{tot}}/[\text{M}^{2+}]_{\text{tot}} = 2$ was employed. The stability constants were calculated by using a Newton–Gauss nonlinear least-squares program, as previously mentioned. All the stability constant determinations were from an average of at least eight independent titrations (Tables 3 and 4). In the $\text{Ni}^{2+}/\text{NN}_2\text{O}222$ system, the kinetics were so slow that about 20 min was required after each addition of NaOH until equilibrium was attained; for all the other reactions studied, this was not a problem.

Preparation of Zn Complexes. $[\text{Zn}(\text{OH})(\mu\text{-NNO}_222 - \text{H})\text{Zn}(\text{NNO}_222)](\text{BF}_4)_2$, **8.** To a solution of $\text{Zn}(\text{BF}_4)_2 \cdot \text{H}_2\text{O}$ ($x = 6-7$) (382 mg, 1.6 mmol) in 20 mL of methanol was added **2** (238 mg, 1.61 mmol). The reaction mixture was stirred for 30 min at room temperature. Addition of diethyl ether gave slightly yellow crystals which were recrystallized from methanol/diethyl ether to yield 534 mg (54%) of colorless crystals. Anal. Calcd (Found) for $\text{C}_{12}\text{H}_{32}\text{B}_2\text{F}_8\text{N}_4\text{O}_5\text{Zn}_2$ (fw = 616.79): C, 23.37 (23.55); H, 5.23 (5.38); N, 9.08 (9.14). MS (FAB, positive ions): m/e (relative intensity, assignment) 423 (12.5, $[\text{M} - \text{H}_2\text{O}]^+$), 211 (29.50 $[\text{Zn}(2)]^+$). IR (KBr, cm^{-1}): $\nu = 3349, 3335, 3300$ (w, $\nu(\text{O}-\text{H})$ and $\nu(\text{N}-\text{H}_2)$), 2967, 2921, 2889 (m, $\nu(\text{C}-\text{H})$), 1484 (m, $\delta(\text{N}-\text{H}_2)$), 1262 (m, $\nu(\text{C}-\text{N})$), 1059 (s, $\nu(\text{C}-\text{O})$).

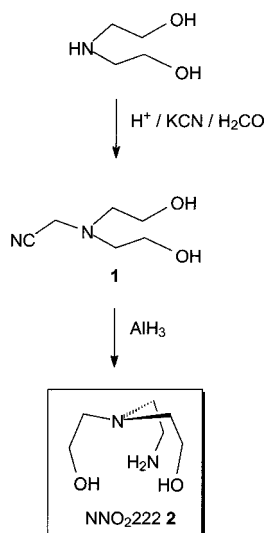
$[\text{Zn}(\text{NNO}_222)(\text{H}_2\text{O}) - \text{H}]\text{BF}_4$ (9). A solution of **5** (256 mg, 1.74 mmol) in 10 mL of methanol was added dropwise to a solution of $\text{Zn}(\text{BF}_4)_2 \cdot \text{H}_2\text{O}$ ($x = 6-7$) (1.74 mmol) in 10 mL of methanol at room temperature. The solution was stirred at room temperature for 30 min, over which time the color changed to yellow. Slow diffusion of diethyl ether into the reaction solution yielded colorless crystals which were recrystallized from methanol/diethyl ether to yield 266 mg (48.3%) of colorless crystals of complex **9**. Anal. Calcd (Found) for $\text{C}_6\text{H}_{18}\text{BF}_4\text{N}_3\text{O}_2\text{Zn}$ (fw = 316.41): C, 22.78 (22.70); H, 5.73 (5.81); N, 13.28 (12.95). MS (FAB, positive ions): m/e (relative intensity, assignment) 210 (100, $[\text{Zn}(5)]^+$), no further fragments were detected. IR (KBr, cm^{-1}): $\nu = 3293$ (w, $\nu(\text{O}-\text{H})$ and $\nu(\text{N}-\text{H}_2)$), 2961, 2926, 2881 (m, $\nu(\text{C}-\text{H})$), 1473 (m, $\delta(\text{N}-\text{H}_2)$), 1277 (m, $\nu(\text{C}-\text{N})$), 1064 (s, $\nu(\text{C}-\text{O})$). The formulation of the complex monocation in **9** $[\text{Zn}(\text{NNO}_222)(\text{H}_2\text{O})-\text{H}]$ is arbitrary since it could not be confirmed which one of the ligand or the coordinated water molecule was deprotonated; this, however, influences neither the elemental analysis nor the FAB MS data.

X-ray Structure Analysis. $[\text{Zn}(\text{OH})(\mu\text{-NNO}_222 - \text{H})\text{Zn}(\text{NNO}_222)](\text{BF}_4)_2$ (**8**) was crystallized from methanol/diethyl ether at room

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Scheme 1



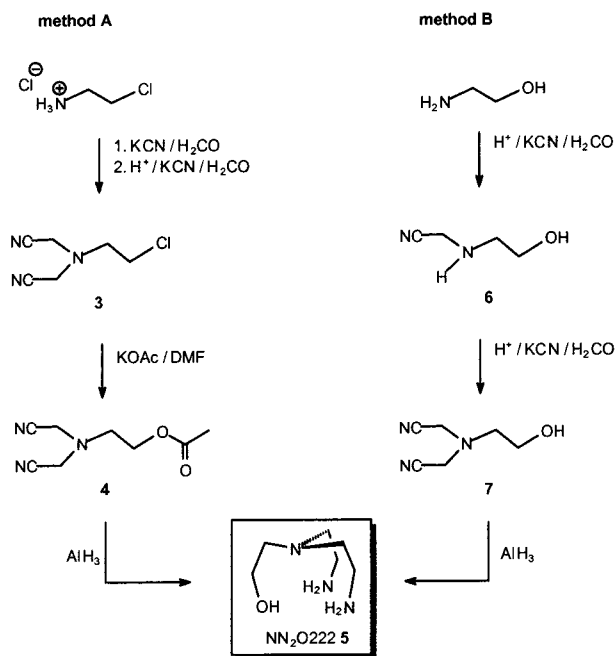
temperature. A suitable specimen with approximate dimensions $0.42 \times 0.14 \times 0.14$ mm was selected in air and mounted onto a Enraf-Nonius CAD-4 diffractometer at room temperature. **8** crystallizes with one independent molecule in the asymmetric unit, empirical formula $C_{12}H_{32}B_2F_8N_5O_5Zn_2$, $M = 616.78$, $a = 7.234(3)$ Å, $b = 10.990(3)$ Å, $c = 15.411(5)$ Å, $\alpha = 99.87(2)^\circ$, $\beta = 92.10(3)^\circ$, $\gamma = 105.58(3)^\circ$, $V = 1158.3(7)$ Å³, $\rho_{\text{calcd}} = 1.768$ g·cm⁻³, $\mu(\text{Mo K}\alpha) = 2.166$ mm⁻¹, $Z = 2$, triclinic, space group $P\bar{1}$ (no. 2), Mo K α radiation, $\lambda = 0.71073$ Å, $T = 293(2)$ K, ω -scans, reflections $h, \pm k, \pm l$ collected, 2θ range 4.5 – 50.0° , 4072 independent and 2352 observed reflections [$I > 2\sigma(I)$], 299 refined parameters (refinement on F^2), $R1 = 0.067$, $wR2 = 0.168$, maximum residual electron density 1.08 (-0.97) e Å⁻³, hydrogen atoms placed on calculated positions and unrefined. No hydrogen positions were calculated or identified for hydroxyl groups. The programs used were Siemens SHELX-93¹⁴ for structure refinement and MolEN¹⁵ for data reduction. Molecular structure plots were generated with ORTEP.¹⁶

X-ray data were also collected for complex **9** in a rhombohedral space group with $a = 15.060(2)$ Å and $\alpha = 114.564(8)^\circ$; however, owing to the site symmetry 3 of the complex cation in the unit cell, a disorder must exist between the three ligand arms. Multiple data sets did not lead to a satisfactory refinement.

Results and Discussion

Ligand Synthesis. Our strategy for the synthesis of tripods **2** and **5** is depicted in Schemes 1 and 2, respectively. A preparation of ligand **2** has been reported by Peck et al.¹⁷ Their synthesis involved monoacylation of ethylenediamine, followed by dialkylation of the remaining amine function with ethylene oxide, and subsequent reduction of the amide into an amine. The number of reaction steps, the difficult purification of the reaction products, and the poor yield prompted us to develop an easier synthesis of **2**, one which in particular avoided the use of ethylene oxide. We chose to proceed via a one-pot cyanomethylation of diethanolamine, which we have used previously for the preparation of unsymmetrical tripodal tetraamines.^{2,3} The cyanomethylation of primary or secondary amines was developed in 1955 by Schwarzenbach et al.¹⁸ and

Scheme 2



is best carried out according to the modifications of Knoevenagel and Bucherer in dilute hydrochloric acid.¹⁹ Reduction of the cyanomethyl group in **1** is difficult and in our hands gave acceptable yields only when freshly prepared AlH_3 was used as the reducing agent.²⁰ Under these conditions, the formation of side products was suppressed and **2** could be isolated in a satisfactory yield. It is notable that the NH and OH protons give rise to only one resonance in the ¹H NMR spectrum (in $CDCl_3$), most likely due to the formation of intramolecular hydrogen bonds.

A multistep low-yield preparation for **5**, again making use of ethylene oxide, was published by Vasil'eva et al.²¹ This synthesis is similar to another synthesis reported by the same authors for the preparation of an unsymmetrical tripodal tetraamine.²² We were unable to repeat either of these two preparations and therefore employed a new strategy for the preparation of **5**. Two pathways for the synthesis of **5** are conceivable, and both were investigated (Scheme 2). Method A starts with the *extremely toxic*²³ (facile formation of aziridine) 2-chloroethylamine hydrochloride, which is doubly cyanomethylated in a one-pot synthesis with KCN and formaldehyde under acidic conditions to give **3** in moderate yield.²⁰ The chlorine atom in **3** is then substituted with acetate to give **4**; reduction of the ester and cyano functions in **4** is best achieved by freshly prepared AlH_3 .²⁰ The moderate yields of ligand **5** obtained by method A prompted us to investigate another synthetic route (method B) to **5**. Method B has two significant advantages over method A: 2-chloroethylamine hydrochloride is avoided, and the yield and purity of **5** obtained by method B are improved over those in method A. It is, however, impossible to cyanomethylate 2-aminoethanol twice in a one-pot synthesis. The two cyanomethyl groups must be introduced in two

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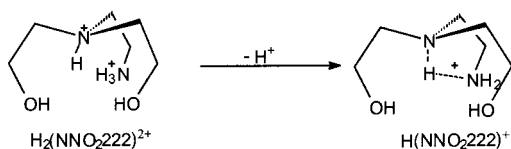
Table 1. Acidity Constants of NNO_2222 and $\text{NN}_2\text{O}222$ Measured by Potentiometry and Values³ for Tren and 322 (25 °C, $I = 0.16 \text{ M NaCl}$)

	NNO_2222	$\text{NN}_2\text{O}222$	tren	322
$\text{p}K_{\text{H}_1\text{L}}^{\text{H}} (\text{HL}^+ = \text{H}^+ + \text{L})$	9.78 ± 0.05	9.92 ± 0.04	10.14	10.14 ± 0.09
$\text{p}K_{\text{H}_2\text{L}}^{\text{H}} (\text{H}_2\text{L}^{2+} = \text{H}^+ + \text{L}^+)$	5.04 ± 0.02	9.19 ± 0.01	9.43	9.72 ± 0.06
$\text{p}K_{\text{H}_3\text{L}}^{\text{H}} (\text{H}_3\text{L}^{3+} = \text{H}_2\text{L}^{2+} + \text{H}^+)$		2.26 ± 0.05	8.41	8.40 ± 0.04
$\text{p}K_{\text{H}_4\text{L}}^{\text{H}} (\text{H}_4\text{L}^{4+} = \text{H}_3\text{L}^{3+} + \text{H}^+)$			<2	2.1 ± 0.3

Table 2. Chemical Shift Changes ($\Delta\delta$, ppm) for the ^1H NMR Signals in NNO_2222^a

signal	$\Delta\delta$, $7.3 \leq \text{pD} \leq 13.85$		$\Delta\delta$, $3.5 \leq \text{pD} \leq 7.3$	
	$\Delta\delta$, $7.3 \leq \text{pD} \leq 13.85$	$\Delta\delta$, $3.5 \leq \text{pD} \leq 7.3$	signal	$\Delta\delta$, $7.3 \leq \text{pD} \leq 13.85$
A	0.24	0.78	C	0.43
B	0.21	0.69	D	0.05

^a See Chart 1 for assignments.

Scheme 3

independent reactions to give the desired dinitrile **7** via compound **6**. Dinitrile **7** can then be reduced to the diamine with AlH_3 as described for method A. Again, the OH and NH protons show only one resonance in the ^1H NMR spectrum, apparently due to formation of intermolecular or intramolecular hydrogen bonds.

Acidity Constants. The two acidity constants determined potentiometrically for NNO_2222 in the range $3.3 \leq \text{pH} \leq 10.6$ are listed in Table 1. The two deprotonation reactions can be assigned to the primary ($\text{R}-\text{NH}_3^+$) and tertiary (R_3-NH^+) ammonium groups.

To confirm these assignments, and to estimate $\text{p}K_a$ values of any potential further deprotonations (such as from the two hydroxyl groups), ^1H NMR titrations were undertaken. The NMR spectra showed four triplets corresponding to the methylene protons A, B, C, and D (see Chart 1 for assignments). The chemical shifts of each signal vary ($\Delta\delta$) with solution pD, and a larger chemical shift change indicates that the corresponding methylene group is closer to the deprotonation center (Table 2). Over the entire pD range studied, methylene D had the smallest $\Delta\delta$, indicating that it and the hydroxyl group were furthest from a deprotonation in the range $3.5 \leq \text{pD} \leq 13.85$. Deprotonation from the OH group did not occur in this pD range; therefore, it can be concluded that the deprotonation of the OH group must take place at $\text{pD} > 13.85$. Hence, it is reasonable to estimate that the $\text{p}K_a$ value for the alcohols must be higher than 14.

Also noteworthy in Table 2 is the slight difference in the $\Delta\delta$ values of signals A, B, and C in the range $3.5 \leq \text{pD} \leq 7.3$; signal C has the highest $\Delta\delta$ value when $7.3 \leq \text{pD} \leq 13.85$. These observations verify the formation of an intramolecular hydrogen bond in the monoprotonated cation $\text{H}(\text{NNO}_2222)^+$ (Scheme 3). In the $3.5 \leq \text{pD} \leq 7.3$ deprotonation of $\text{H}_2(\text{NNO}_2222)^{2+}$, both the reactant and product ammonium N atoms are almost identical (the only difference being whether the primary (RNH_2) or the tertiary (R_3N) amine N is the donor or the acceptor of the hydrogen bond). Hence, the $\Delta\delta$ values resulting from this deprotonation step for signals A, B, and C are so close. In the second deprotonation step, however, signal C has a significantly larger $\Delta\delta$ value than do signals A and B. It is most likely, therefore, that the hydrogen bond donor is the primary amine N atom (RNH_2) and that the acceptor is the tertiary (R_3N)

amine N atom. This means that, as the first step, deprotonation of the central ammonium is favored.

The three acidity constants measured potentiometrically for $\text{NN}_2\text{O}222$ in the range $2.0 \leq \text{pH} \leq 11$ are listed in Table 1. As per the above discussion, the deprotonation steps occurred at the three ammonium N atoms, and the deprotonation step with the low $\text{p}K_a = 2.26$ represents the deprotonation of the tertiary ammonium N atom. The other two acidity constants for this tripod differ by $10^{0.73}$ ($9.92 - 9.19 = 0.73$). That this value is close to, but slightly larger than, the statistical estimation $10^{0.6}$ indicates that the two deprotonation positions are almost identical and that there is only a weak interaction between these two residues. This result proves that the deprotonation steps correspond to releasing protons from the two terminal ammonium N atoms (RNH_3^+).

On close inspection of the acidity constants in Table 1, one can see that the values for deprotonation of the terminal ammonium N atoms are close to each other ($8.4 \leq \text{p}K_a \leq 10.2$) for different ligands. Deprotonation of the central tertiary ammonium N atom has very different values ($5 < \text{p}K_a < 2 > \text{p}K_a$) for the ligands listed; i.e., replacing an $-\text{NH}_3^+$ group by a $-\text{OH}$ group makes the R_3N group more basic.

Three factors, polar and charge effects and intramolecular hydrogen bonding, contribute to this observation. When a terminal $-\text{NH}_3^+$ exists, the tertiary ammonium group (R_3NH^+) encounters both charge repulsion and polar effects, and these combine to make the R_3N group more acidic. A third effect is the formation of an intramolecular hydrogen bond between the tertiary amine group R_3NH^+ and the terminal $-\text{NH}_3^+$ group after the former deprotonates (as shown by NMR titration, vide supra). In this hydrogen bond, the donor is $-\text{NH}_3^+$ and the acceptor is R_3N , making the R_3N group more acidic because the product of the deprotonation is more stable. On the other hand, in arms with only a terminal OH group, the central ammonium only experiences the polar effect, which also makes the R_3N group more acidic; however, the OH group can also form an intramolecular hydrogen bond with R_3NH^+ in which R_3NH^+ is the donor and OH is the acceptor.¹² (The fact that signal D had a larger chemical shift change in the range $3.5 \leq \text{pD} \leq 7.3$ (0.31, Table 2) than in the range $7.3 \leq \text{pD} \leq 13.85$ (0.05, Table 2) supports this suggestion.) This effect makes the R_3NH^+ proton more stable or, in other words, the R_3N group more basic. Therefore, when a primary ammonium group $-\text{NH}_3^+$ is replaced by an OH group, the R_3N group should be more basic.

This discussion qualitatively explains why the $\text{p}K_a$ values of the central amine have the sequence $\text{NNO}_2222 > \text{NN}_2\text{O}222 > \text{tren}$; however, this result can also be analyzed quantitatively. The $\text{p}K_a$ values of protonated ethylamine, protonated 2-aminoethanol, and diprotonated H_2en^{2+} ($\text{en} = 1,2$ -diaminoethane) are 10.66,²⁴ 9.64,²⁵ and 7.19,²⁶ respectively. Comparing these three values, we can calculate that adding a OH group at the β carbon of ethylamine lowers the $\text{p}K_a$ of the ammonium $-\text{NH}_3^+$ by 1.02

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Table 3. Logarithms of the Stability Constants of NNO₂222 with Ni²⁺, Cu²⁺, and Zn²⁺ (25 °C, *I* = 0.16 M NaCl)

reaction	log <i>K</i>		
	Ni ²⁺	Cu ²⁺	Zn ²⁺
M ²⁺ + HL ⁺ ⇌ M(HL) ³⁺	<2	<2	<2
M ²⁺ + L ⇌ ML ²⁺	6.89 ± 0.05	10.09 ± 0.05	5.42 ± 0.11
ML ²⁺ ⇌ M(L - H) ⁺ + H ⁺	-9.7 ± 0.2	-6.91 ± 0.05	-7.61 ± 0.09
M(L - H) ⁺ ⇌ M(L - 2H) + H ⁺	-10.9 ± 0.2	-9.59 ± 0.12	-8.88 ± 0.07
M(L - 2H) ⇌ M(L - 3H) ⁻ + H ⁺			-10.8 ± 0.2

log units (from 10.66 to 9.64), and that adding a second ammonium group at the β carbon lowers the p*K*_a of the ammonium by 3.47 log units (from 10.66 to 7.19). These values reflect all the effects discussed above. For the central ammonium of NNO₂222, there are two β-OH groups and one β-NH₃⁺ group. The total effect should be the sum of the three groups; that is, the p*K*_a value of the tertiary R₃NH⁺ group should be 10.66 - (2 × 1.02) - 3.47 = 5.15. This estimated value is very close indeed to our experimental value of 5.04 (Table 1). In NN₂-O222, the corresponding p*K*_a value should be 10.66 - (2 × 3.47) - 1.02 = 2.70, somewhat higher than the experimental result of 2.26 (Table 1), possibly because there is a weak interaction between the two terminal ammonium groups. For tren, the calculated value is 10.66 - (3 × 3.47) = 0.25, the experimental estimation being < 2. Although these estimations are quite rough, they at least verify that the experimental results in Table 1 are reasonable.

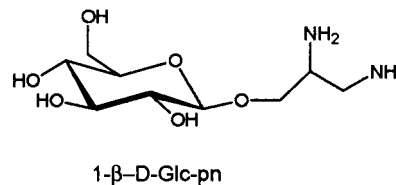
Stability Constants of NNO₂222 with Ni²⁺, Cu²⁺, and Zn²⁺. These are summarized in Table 3. Only 1:1 complexes were found for all three metal ions studied. Although it should be possible to form M²⁺:L = 1:2 complexes, especially for Ni²⁺ and Cu²⁺ when [L]_{tot}/[M²⁺]_{tot} ≥ 2, these complexes were not detected in the experiments, clearly because the two CH₂CH₂-OH arms surrounding the central amine group inhibit the approach of a second ligand to the ML²⁺ species. Hydrolysis of the metal ion itself, i.e., formation of M_x(OH)_y (*x* = 1, 2; *y* = 1-4), was not important for any of the three metal ions although hydrolysis reactions, with the known constants,²⁷ were included in the data evaluation.

The coordination of the central amine only, to form MHL³⁺, with any of the three metal ions is very weak, with a stability constant below 10². The low stability/predominance may have several causes. First, the surrounding arms might inhibit the metal ion from reaching the central nitrogen, especially when the terminal amine is protonated. Second, to form MHL³⁺ would take energy to break the intramolecular hydrogen bond between two amines. Third, the diamine chelate of the metal ion should be much more stable; hence, it is very easy for MHL³⁺ to form ML²⁺ species.

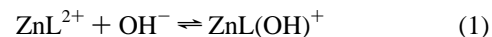
The species distribution diagram (not shown, available in the Supporting Information) shows that the ML²⁺ species for Ni²⁺ and Cu²⁺ each predominate in a characteristic pH range, but that ZnL²⁺ is only >20% in the range 7.5 ≤ pH ≤ 8.5; this can be attributed to the lower affinity of Zn²⁺ for nitrogen donor ligands than that of Ni²⁺ or Cu²⁺.

In the ML²⁺ species, the metal ion must be coordinated to both amines, forming a chelate; however, are the hydroxyl groups in NNO₂222 also coordinated? Straight line correlations have been established between stability constants log *K* and ligand acidity constants p*K*_{a1} + p*K*_{a2} for Ni²⁺, Cu²⁺, and Zn²⁺ complexes of a series of simple bidentate diamine ligands.¹² If the log *K* vs p*K*_{a1} + p*K*_{a2} data point for a similar ligand lies on the straight reference line, there are only two amine groups

coordinated to the metal ion in the ML²⁺ complex. Any additional coordination from the other groups in the same ligand (such as the hydroxyl arms) would increase the stability constant, and the corresponding data point would lie above the corresponding reference line. The plot (not shown, available in the Supporting Information) showed that the data points for the Ni²⁺ and Zn²⁺ complexes of NNO₂222 lie on the reference lines, and for Cu²⁺ the point is only slightly above the reference line. We can, therefore, conclude that the hydroxyl groups in NNO₂-222 bind the metal ion in ML²⁺ very weakly, or not at all (different from the solid-state result, *vide infra*); the coordination ability of the OH groups in NNO₂222 is on par with the coordination ability of water at acidic or neutral pH.



When the pH is sufficiently high, however, the ML²⁺ complexes deprotonate to M(L - H)⁺ species, which predominate over significant pH ranges and can themselves further deprotonate. The deprotonation to form M(L - H)⁺ could possibly occur at an OH arm of the ligand, or possibly at a coordinated water molecule. To decide, we have compared our results with those of the literature for tren, for similar ligands (e.g., 1-β-D-Glc-pn), and for en.^{3,12,28,29} For the Cu²⁺-tren system, a p*K*_a value of 9.09 was obtained for deprotonation of a coordinated H₂O.³ For 1-β-D-Glc-pn, M(L - H)⁺ species were observed for neither Ni²⁺ nor Cu²⁺ at pH < 7, and with Zn²⁺, a stability constant of 4.2 ± 0.2 for the complex ZnL(OH)⁺ was determined.¹² This constant corresponds to the reaction



It can be easily converted into the comparable log *K* value (related to deprotonation of a coordinated H₂O) by subtracting the p*K*_a value of water (under our conditions 15.5); i.e., log *K* = 4.2 - 15.5 = -11.3. Although there are many en studies available,²⁸ for few of them have stability constants with OH⁻ been determined; for example, Jonassen et al.²⁹ measured a constant for the reaction



(log *K* = 0.73, 25 °C, *I* = 0.50 M KNO₃), and the comparable value is log *K* = 0.73 - 15.5 = -14.8. (The value is so low since it is a bis(ethylenediamine)-N₄ system and the coordinated water molecule is on the apical position. We will discuss this effect later.) These are much smaller than the values given in

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Table 4. Logarithms of the Stability Constants of $\text{NN}_2\text{O}222$ with Ni^{2+} , Cu^{2+} , and Zn^{2+} (25 °C, $I = 0.16 \text{ M NaCl}$)

reaction	log K		
	Ni^{2+}	Cu^{2+}	Zn^{2+}
$\text{M}^{2+} + \text{H}_2\text{L}^{2+} \rightleftharpoons \text{M}(\text{H}_2\text{L})^{4+}$	<2	<2	<2
$\text{M}^{2+} + \text{HL}^+ \rightleftharpoons \text{M}(\text{HL})^{3+}$	6.27 ± 0.15	<8.5	<5
$\text{M}^{2+} + \text{L} \rightleftharpoons \text{ML}^{2+}$	10.65 ± 0.06	15.28 ± 0.06	9.55 ± 0.06
$\text{ML}^{2+} \rightleftharpoons \text{M}(\text{L} - \text{H})^+ + \text{H}^+$	-9.03 ± 0.18	-8.70 ± 0.06	-8.19 ± 0.08
$\text{M}(\text{L} - \text{H})^+ \rightleftharpoons \text{M}(\text{L} - 2\text{H}) + \text{H}^+$		-10.64 ± 0.19	-11.0 ± 0.2

Table 3 for $\text{Zn}(\text{L} - \text{H})^+$, -7.61 ± 0.09 , and for $\text{Cu}(\text{L} - \text{H})^+$, -6.91 ± 0.05 . This comparison suggests that the deprotonation of $\text{M}(\text{NNO}_222)^{2+}$ complexes may not occur at a coordinated water molecule, but at the OH group of the ligand (in the solid-state structure of $[\text{Zn}(\text{OH})(\mu\text{-NNO}_222 - \text{H})\text{Zn}(\text{NNO}_222)]^{2+}$ both deprotonations are seen, vide infra). Even the further deprotonation to form $\text{M}(\text{L} - 2\text{H})$ is unlikely to be the deprotonation of a coordinated H_2O because the corresponding log K value = -8.88 ± 0.07 for Zn^{2+} is still much higher than the previously mentioned value for $\text{Zn}(1\text{-}\beta\text{-D-Glc-pn})(\text{OH})^+$. Only the last deprotonation step for $\text{Zn}(\text{NNO}_222)^{2+}$, to $\text{Zn}(\text{L} - 3\text{H})^-$ with log $K = -10.8 \pm 0.2$, is quite close to the value of $\text{Zn}(1\text{-}\beta\text{-D-Glc-pn})(\text{OH})^+$; this final step is likely to be from a coordinated H_2O molecule. In the case of Cu^{2+} , however, deprotonation from $\text{Cu}(\text{NNO}_222 - \text{H})^+$ has log $K = -9.59 \pm 0.12$, which is lower than the corresponding value in tren, log $K = -9.09$, so the proton may be, at least partly, from the coordinated water molecule, i.e., there may be a mixture of $\text{M}(\text{L} - \text{H})$ where one species has a deprotonated coordinated water molecule (hydroxo complex) and another with an alkoxide donor after the deprotonation.

Another notable result is obtained from the stability constants in Table 3 by comparing the two constants related to deprotonation from species ML^{2+} and $\text{M}(\text{L} - \text{H})^+$ for each metal ion. The differences between these two constants for Ni^{2+} , Cu^{2+} , and Zn^{2+} are 1.2 ± 0.3 , 2.68 ± 0.13 , and 1.27 ± 0.11 , respectively. Despite the larger error limits, it is clear that the values for Ni^{2+} and Zn^{2+} are quite similar, but that for Cu^{2+} differs significantly. These results actually shed some light on the aqueous coordination geometries of the complexes. Because of the tripodal structure of NNO_222 , only two of its three arms can coordinate in the equatorial plane in an octahedral complex, and the final arm, if coordinated, must be apical. For Ni^{2+} and Zn^{2+} , the apical and equatorial bond lengths should be similar; therefore, the acidity imparted by coordination of the metal ion on the OH coordinated from either direction should be the same. The difference between the first deprotonation, from ML^{2+} , and the second deprotonation, from $\text{M}(\text{L} - \text{H})^+$, reflects the statistical effect and the charge effect (2+ in ML^{2+} and only 1+ in $\text{M}(\text{L} - \text{H})^+$). For Cu^{2+} , however, the well-known Jahn–Teller distortion means that the equatorial and apical bond lengths are different; hence, with an axial elongation, the OH group, coordinated in the equatorial plane, might more easily deprotonate than that coordinated from the apical direction. This additional factor makes the difference between the two constants greater than in the case of Ni^{2+} and Zn^{2+} . The result agrees with the previous assertion that further deprotonation of $\text{Cu}(\text{NNO}_222 - \text{H})^+$ is at the coordinated water molecule, with that water molecule in an equatorial position, and the second OH group in an apical position. Taken together, these results suggest that the Cu^{2+} coordination geometry in this case is square pyramidal rather than trigonal bipyramidal.

Stability Constants of $\text{NN}_2\text{O}222$ with Ni^{2+} , Cu^{2+} , and Zn^{2+} . These are listed in Table 4. $\text{L}:\text{M}^{2+} = 2:1$ complexes also were not observed, even when $[\text{L}]_{\text{tot}}/[\text{M}^{2+}]_{\text{tot}} \geq 2$.

For all three metal ions, the fraction of the $\text{M}(\text{H}_2\text{L})^{4+}$ species, in which only the central nitrogen coordinated, is always very low over the whole pH range and only resolvable at low pH; therefore, only an upper limit of the corresponding stability constants is given. Except for $\text{Ni}(\text{HL})^{3+}$, $\text{M}(\text{HL})^{3+}$ species, in which two nitrogen atoms chelate the metal ion, also have very low predominance; thus, only the Ni stability constant log $\langle \text{abv} \rangle K_{\text{Ni}(\text{HL})}^{\text{Ni}} \langle \text{blw} \rangle$ was obtained with a reasonable error limit (Table 4). Factors similar to those discussed above for NNO_222 are likely to be operational with $\text{NN}_2\text{O}222$. In ML^{2+} , the three amine groups coordinate the metal ion with two five-membered chelate rings. As per the discussion for NNO_222 , it can be concluded that, in ML^{2+} species, the $\text{CH}_2\text{CH}_2\text{OH}$ arm plays only a minor role in the coordination.

Further deprotonation from $\text{M}(\text{NN}_2\text{O}222)^{2+}$ is observed in all three metal ion systems. On the basis of the previous discussion for the NNO_222 system and on the constants listed in Table 4, it is clear that, for Zn^{2+} , deprotonation occurred at the coordinated OH group. The species $\text{Zn}(\text{NN}_2\text{O}222 - \text{H})^+$ can be further deprotonated to form $\text{Zn}(\text{NN}_2\text{O}222 - 2\text{H})$, and the corresponding constant -11.0 ± 0.2 is close to the value of -11.3 obtained for deprotonation from a coordinated water molecule in the $\text{Zn}^{2+}\text{-}1\text{-}\beta\text{-D-Glc-pn}$ system.¹² This result indicates that in $\text{Zn}(\text{NN}_2\text{O}222 - \text{H})^+$ the proton was also released from the coordinated water molecule. In a poor crystal structure (vide infra), a trigonal bipyramidal $[\text{Zn}(\text{NN}_2\text{O}222)(\text{H}_2\text{O}) - \text{H}]^+$ cation (**9**) was found as its ClO_4^- salt, wherein one of the ligand hydroxyl groups or an axial coordinated water molecule is deprotonated.

For Cu^{2+} , the situation is less clear; deprotonation from $\text{Cu}(\text{NN}_2\text{O}222)^{2+}$ has a slightly larger constant (log $K = -8.70 \pm 0.06$) compared to that for tren (-9.09),³ whereas releasing a proton from $\text{Cu}(\text{NN}_2\text{O}222 - \text{H})^+$ is more difficult, log $K = -10.64 \pm 0.19$. This result suggests that the first proton released from $\text{Cu}(\text{NN}_2\text{O}222)^{2+}$ is from an equatorial coordinated water molecule and the second proton from the apical coordinated hydroxyl group (vide supra).

Comparison across the Series Triethanolamine, NNO_222 , $\text{NN}_2\text{O}222$, and Tren. When an $-\text{NH}_3^+$ moiety in tren is replaced by a $-\text{OH}$ group, the central amine group becomes more basic, but how are the stability constants affected by this functional group alteration?

We have already established that a decrease in the pK_a values will decrease the analogous stability constants, and that there is a linear relationship between log K and $\text{pK}_{a1} + \text{pK}_{a2}$ for a given metal ion and a series of structurally similar bidentate ligands.¹² It has already been shown that, for the Ni^{2+} , Cu^{2+} , and $\text{Zn}^{2+}\text{-NNO}_222$ systems, the results for the stability constants ML^{2+} lie on the log K vs $\text{pK}_{a1} + \text{pK}_{a2}$ reference lines (Ni^{2+} , Zn^{2+}) or slightly above the reference line (Cu^{2+}). In the case of $\text{NN}_2\text{O}222$, the corresponding stability constant for MHL^{3+} should be on the same line. For $\text{Ni}(\text{HNN}_2\text{O}222)^{3+}$, log $K = 6.27 \pm 0.15$ (Table 4) vs the value $\text{pK}_{\text{H}_{31}}^{\text{H}} + \text{pK}_{\text{H}_{21}}^{\text{H}} = 9.19 + 2.26 = 11.45$ (Table 1, $\text{NN}_2\text{O}222$) lies on the Ni^{2+} reference line. If we suppose that this relationship holds also for Cu^{2+}

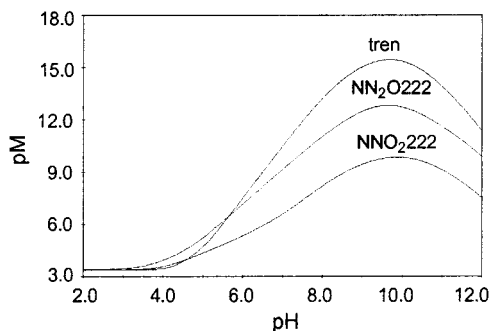


Figure 1. pM versus pH for Cu^{2+} -tren, $-\text{NN}_2\text{O}222$, and $-\text{NNO}_2222$ systems (see the text).

and Zn^{2+} , the estimated values according to the appropriate straight lines are 8.58 and 4.89, respectively, quite close to the estimations (according to the experimental data fitting) in Table 4. We can conclude, therefore, that, for diamine coordination, the stability of the complex only depends on the sum of the basicity of the two coordinated amine groups. On the basis of this conclusion, we can estimate for $\text{Cu}(\text{H}_2\text{tren})^{4+}$ the stability constant, which cannot be measured experimentally. Using the pK_a values in Table 1 ($8.41 + 2 = 10.41$) and the Cu^{2+} reference line, a stability constant of $\log K = 8.2$ can be estimated.

It is not possible to compare directly the metal ion coordination strength of the three ligands in Table 1 (excluding 332) by comparing their stability constants, because the definitions of the constants are not consistent (the protonation behaviors varying considerably). Rather, this problem can be solved by comparing pM values (where $\text{pM} = -\log [\text{M}]$) at consistent pH and concentration conditions; stronger binding will give a larger pM value. Hence, we have examined $\text{pM} (= -\log([\text{M}] + [\text{M}(\text{OH})_y]), y = 1-4)$ vs pH (Figure 1). Instead of just the free metal ion concentration $[\text{M}]$, $[\text{M}] + [\text{M}(\text{OH})_y]$ was used because this sum reflects the total unligated metal ion concentration, including that which has hydrolyzed.

For Cu^{2+} , the pM/pH plot is given in Figure 1; clearly, replacing an NH_2 group with a OH group lowers the ligand's coordination affinity for Cu^{2+} . This also obtains for Ni^{2+} and Zn^{2+} (similar plots are not shown). This result is quite different from the conclusion drawn above for diamine coordination where, because of the repulsion of the protonated ammonium residue, the stability of the complex increases with the number of OH groups in the ligand. The result is not surprising, however, because when the ammonium residue deprotonates, the repulsion between positive charges no longer exists, and concomitantly the stability of the complex increases. This concurs with the observation that the NH_2 group has a higher affinity for Cu^{2+} than does OH .

To be comprehensive, we found constants for triethanolamine ($\text{N}(\text{CH}_2\text{CH}_2\text{OH})_3$) with H^+ (central ammonium N, $\text{pK}_a = 7.80$),³⁰ Ni^{2+} ($\log K_1 = 2.76$),³¹ Cu^{2+} ($\log K_1 = 4.07$),³¹ and Zn^{2+} ($\log K_1 = 2.05$).³¹ It is clear that the acidity constant is consistent with the pK_a values discussed above; i.e., when an NH moiety is replaced by a OH group, the central amine group becomes more basic. However, when all three arms are $\text{CH}_2\text{-CH}_2\text{OH}$, the coordination ability of the ligand for all three metal ions becomes very weak indeed.

Solution Geometry of the Cu(II) Complexes. A series of visible spectra of the $\text{Cu}(\text{II})$ - NNO_2222 and $\text{Cu}(\text{II})$ - $\text{NN}_2\text{O}222$ systems were recorded in the range $3 \leq \text{pH} \leq 10$. In the

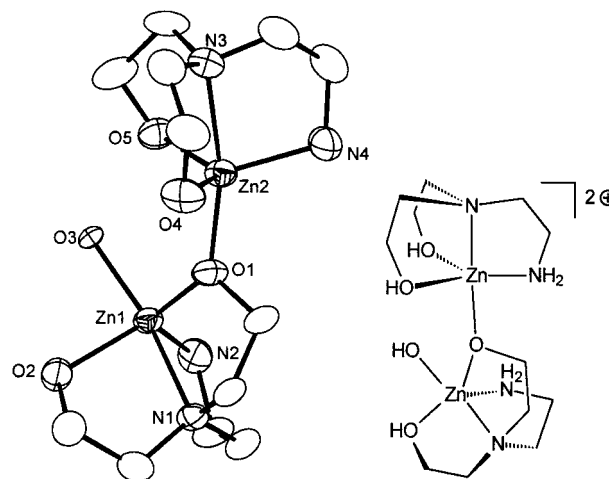


Figure 2. ORTEP plot and schematic representation of the $[\text{Zn}(\text{OH})(\mu\text{-NNO}_2222 - \text{H})\text{Zn}(\text{NNO}_2222)]^{2+}$ dication in **8**. Hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and bond angles (deg): Zn1-O1 1.976(6), Zn1-O2 2.072(7), Zn-O3 1.968(5), Zn1-N1 2.178(7), Zn1-N2 2.051(9), Zn2-O2 1.933(6), Zn2-O4 2.113(7), Zn2-O5 2.039(7), Zn2-N3 2.189(8), Zn2-N4 2.033(9); O1-Zn1-O2 121.6(3), O1-Zn1-O3 98.3(3), O1-Zn1-N1 83.5(3), O1-Zn1-N2 117.5(3), O2-Zn1-O3 90.3(2), O2-Zn1-N1 78.9(3), O2-Zn1-N2 115.4(3), O3-Zn1-N1 168.1(3), O3-Zn1-N2 105.3(3), N1-Zn1-N2 84.0(3), O1-Zn2-O4 91.8(3), O1-Zn2-O5 94.8(3), O1-Zn2-N3 166.2(3), O1-Zn2-N4 110.5(3), O4-Zn2-O5 122.3(3), O4-Zn2-N3 80.3(3), O4-Zn2-N4 113.5(4), O5-Zn2-N3 80.1(3), O5-Zn2-N4 117.2(4), N3-Zn2-N4 83.1(3), Zn1-O1-Zn2 132.9(3).

wavelength range 450–900 nm, only a broad peak at $\lambda_{\text{max}} = 660$ nm was found, and the spectra were almost invariant with pH, suggesting square pyramidal coordination and that the geometry was invariant for the diverse protonated species. This is quite different from the situation observed with the tetraamine ligands of varying arm lengths where the coordination geometry changed with increasing pH toward a more trigonal bipyramidal structure.³ In tren, the four amine groups, providing they are not protonated to ammonium moieties, all have similar affinities for Cu^{2+} . Trigonal bipyramidal geometry would allow all four Cu-N bonds to have similar lengths, but in a square pyramidal geometry, one of these four bonds must be apical. This bond would be longer than the others, because of the Jahn-Teller effect. Because OH is a poorer ligand than NH_2 , it is likely to be energetically favorable for complexes of mixed OH/NH_2 ligands to take on a square pyramidal geometry with OH on the apical position; hence, both the $\text{Cu}(\text{II})$ - NNO_2222 and $\text{Cu}(\text{II})$ - $\text{NN}_2\text{O}222$ complexes may be square pyramidal structures.

Changes in the absorption spectra as a function of pH were also used to calculate the stability constants for the Cu^{2+} - $\text{NN}_2\text{O}222$ system, and the results (not shown) agreed well with those obtained from the potentiometric titrations.

Molecular Structures of Complexes 8 and 9. The zinc complexes **8** ($[\text{Zn}(\text{OH})(\mu\text{-NNO}_2222 - \text{H})\text{Zn}(\text{NNO}_2222)](\text{BF}_4)_2$) and **9** ($[\text{Zn}(\text{NNO}_2222)(\text{H}_2\text{O}) - \text{H}](\text{BF}_4)_2$) were crystallized; the X-ray structure analysis of **8** revealed a dicationic binuclear complex with two trigonal bipyramidal coordinated zinc atoms (Figure 2). The charges at the ligand atoms were assigned on the basis of the following considerations. The dinuclear complex is a dication based on the two $[\text{BF}_4]^-$ anions in the asymmetric unit. Oxygen atoms O1 and O3 show short O-Zn distances (1.976(6) and 1.968(5) Å, respectively) and were assigned as anionic, while the other O-Zn separations fall in the range well above 2.0 Å, which under these conditions indicates them to be neutral OH . That oxygen atom O1 is definitely in the

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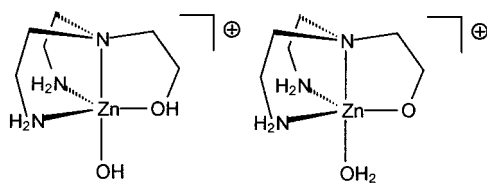


Figure 3. Schematic representation of the two possible complex cations in **9**.

deprotonated/anionic state is witnessed by the distances $\text{Zn1}-\text{O1}$, $\text{Zn2}-\text{O1}$, and $\text{Zn1}-\text{O3}$, all of which are close in length.

Zinc complexes with an N,O coordination environment made up by triethanolamine and monodentate coligands have been described.³² They show zinc in the center of a trigonal bipyramid, with the central nitrogen atom of the triethanolamine and a monodentate coligand in axial positions. Complexes with unsymmetrical tripodal N,O ligands have, to our knowledge, not yet been described. As found in these triethanolamine complexes of zinc, **2**, which shows the same topology but not the same donor set as triethanolamine, also forms trigonal bipyramidal complexes with zinc. The dication $[\text{Zn}(\text{OH})(\mu\text{-NNO}_2\text{222}-\text{H})\text{Zn}(\text{NNO}_2\text{222})]^{2+}$ contains two zinc atoms in a trigonal bipyramidal coordination environment ($\tau = 0.77$ for Zn1 and $\tau = 0.73$ for Zn2).³³ The two zinc atoms are bridged by atom O1, which occupies an equatorial position at Zn1 and an axial one at Zn2 . The central nitrogen atoms of the tripod always reside in axial positions, and for Zn2 the second axial position is occupied by the hydroxyl group O3. The angles among the central nitrogen atom, the zinc atom, and the equatorial ligands of a given trigonal bipyramid are always $<90^\circ$. This behavior has been noted previously in trigonal bipyramidal complexes of $\text{Cu}(\text{II})$ with symmetric and unsymmetric tripodal tetraamine ligands.^{2,3}

The molecular structure of complex **9** could not be unequivocally established. The determination of the crystal structure failed, even after collection of multiple data sets, owing to a severe disorder. Crystallographic, as well as microanalytical,

data showed the formation of complex $[\text{Zn}(\text{NNO}_2\text{222})(\text{H}_2\text{O})-\text{H}](\text{BF}_4)$ (**9**). Zn and the central nitrogen atom of the ligand reside on a 3-fold axis in the rhombohedral unit cell, leading to a disorder of the three ligand arms. While it was established that the zinc complex is a monocation, the site of deprotonation (axial water or equatorial OH) could not be established; therefore, the complex cation in **9** can be formulated in two ways, as depicted in Figure 3.

Conclusions

Deprotonation of $\text{H}_2(\text{NNO}_2\text{222})^{2+}$ was in the order of tertiary amine first and primary amine second, and there was an intramolecular hydrogen bond in the species $\text{H}(\text{NNO}_2\text{222})^+$. Releasing a proton from the OH group in the ligand has a very high $\text{p}K_a$ value (>14). The first proton released from $\text{H}_2(\text{NN}_2\text{-O222})^{2+}$ was also from the tertiary amine group, and there was only a weak interaction between the other two terminal amine groups. Replacing an $-\text{NH}_3^+$ group by a $-\text{OH}$ group in tren makes the R_3N group more basic because of the decreasing charge repulsion and polar effects, and intramolecular hydrogen bonding. In $\text{M}(\text{NNO}_2\text{222})^{2+}$ or $\text{M}(\text{NN}_2\text{O222})^{2+}$ at acidic or neutral pH, the hydroxyl group in the ligand coordinated the metal ions very weakly, whereas at basic pH, $\text{M}(\text{L}-\text{H})^+$ and $\text{M}(\text{L}-2\text{H})$ formed for both ligands and deprotonation occurred mainly at the coordinated OH. Replacing an NH_2 group with a OH group in tren or $\text{NN}_2\text{O222}$ makes the metal ion complex less stable. The Cu^{2+} complexes maintain a square pyramidal geometry rather than a trigonal bipyramidal geometry when an NH_2 group is replaced with a OH group in tren.

Acknowledgment. This work was financially supported by the Natural Sciences and Engineering Research Council (NSERC) of Canada, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie. C.O. acknowledges the Alexander von Humboldt Foundation for a Research Award.

Supporting Information Available: An X-ray crystallographic file in CIF format for the structure determination of **8**, the species distribution diagrams for the two studied ligands and three metal ions (i.e., Ni^{2+} , Zn^{2+} , and Cu^{2+}), and a plot of $\log K_{\text{ML}}$ vs $\text{p}K_{a1} + \text{p}K_{a2}$ for 1,2-diamine ligand systems. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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