**Table I.** $^1H$ NMR Shift Data for $[ReO_2L_4]^+$ Complexes.

| complex | solvent | peak positions |
|---|---|---|
| $[ReO_2(4\text{-pyrrpy})_4]PF_6$ | $CD_2Cl_2$ | δ 8.31 d, 2 H, $J$ = 7 Hz |
| | | δ 6.34 d, 2 H, $J$ = 7 Hz |
| | | δ 3.36 m, 4 H |
| | | δ 2.00 m, 4 H |
| $[ReO_2(dmap)_4]PF_6$ | DMSO-$d_6$ | δ 8.24 d, 2 H, $J$ = 7 Hz |
| | | δ 6.68 d, 2 H, $J$ = 7 Hz |
| | | δ 3.30 s, 6 H |
| $[ReO_2(4\text{-MeOpy})_4]PF_6$ | $CDCl_3$ | δ 8.74 d, 2 H, $J$ = 7 Hz |
| | | δ 6.99 d, 2 H, $J$ = 7 Hz |
| | | δ 3.94 s, 3 H |
| $[ReO_2(3,5\text{-lut})_4]PF_6$ | $CD_3CN$ | δ 8.70 s, 2 H |
| | | δ 7.37 s, 1 H |
| | | δ 2.20 s, 6 H |
| $[ReO_2(4\text{-pic})_4]PF_6$ | acetone-$d_6$ | δ 8.95 d, 2 H, $J$ = 7 Hz |
| | | δ 7.42 d, 2 H, $J$ = 7 Hz |
| | | δ 2.58 s, 3 H |
| $[ReO_2(4\text{-Phpy})_4]I$ | $CDCl_3$ | δ 9.21 d, 2 H, $J$ = 7 Hz |
| | | δ 7.59 m, 7 H |
| $[ReO_2(py)_4]PF_6$ | $CD_3CN$ | δ 9.03 d, 2 H, $J$ = 7 Hz |
| | | δ 7.77 m, 1 H |
| | | δ 7.47 m, 2 H |

$^1H$ NMR data are set out in Table I. $^1H$ NMR spectroscopy has been found to be particularly useful in the characterization of $[ReO_2L_4]^+$ complexes; resonances due to the protons at the 2- and 6-positions of pyridines are sensitive to the coordination environment of the nitrogen. Incomplete product formation and decomposition reactions are indicated by the appearance of multiple signals in the region δ 8.2-9.2 of the proton NMR spectrum.

The complexes $[ReO_2L_4]^+$ show two prominent bands in their UV-visible absorption spectra. Band I, which has been assigned to a $^1A_{1g}[(b_{2g})^2] \rightarrow {}^1E_g[(b_{2g})^1(e_g)^1]$ LF transition, is found in the region 410-490 nm ($\epsilon \approx 1600$) and shifts to lower energy as the pyridine basicity increases. The absorption maximum of band II is located between 330 and 370 nm ($\epsilon \approx 25\,000$) and undergoes a slight blue shift as the pyridine basicity increases. This band has been attributed both to LMCT (oxo to Re)[4] and to MLCT (Re to $\pi^*$-pyridine)[13] transitions.

In summary, the complex $[ReO_2(PPh_3)_2I]$ rather than $K_2ReCl_6$ is the material of choice for high-yield syntheses of $[ReO_2L_4]X$ complexes. Reactions proceed quickly and give higher yields of product than former methods did. The new method also has the potential to accommodate a wide variety of ligands and reaction conditions.

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# Synthesis, Protonation Sequence, and NMR Studies of Polyazamacrocyclic Methylenephosphonates

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Macroscopic and microscopic protonation of a series of cyclic polyamino polyphosphonic acids (NOTP, DOTRP, and DOTP) was studied by using potentiometry and multinuclear magnetic resonance spectroscopy. The macroscopic protonation constants of these ligands were compared with those of the cyclic amines and corresponding acetate derivatives. Chemical shifts for the various protonated species derived from the $^{31}P$ and $^1H$ resonances are interpreted in terms of preferred conformational features due to intramolecular hydrogen bonding between protonated nitrogens and nonprotonated phosphonates and changes in phosphonate electronic structures with pH. Protonation sequences were obtained from the proton data by using published procedures. The data suggest that two nitrogens are protonated first in each compound followed by protonation of the phosphonate oxygens. In the triaza ligands, the third and fourth protonations occur at the phosphonate oxygens, and subsequent protons distribute between the remaining nitrogen and oxygens. This protonation scheme is quite similar to that previously observed for the analogous macrocycles containing acetate pendant groups.

## Introduction

Considerable interest has emerged regarding the properties of polyamino polyphosphonates as chelating agents for metal ions[1] and the comparison between these and the corresponding polyamino polycarboxylates. Various open-chain amino polyphosphonates, including iminobis(methylenephosphonic acid), nitrilotris(methylenephosphonic acid), ethylenediaminetetrakis(methylenephosphonic acid), and diethylenetriaminepentakis(methylenephosphonic acid), and various metal ion complexes of these ligands have been studied by potentiometry and NMR.[2-26] In the present study, protonation of three polyazamacrocyclic poly(methylenephosphonate) ligands, 1,4,7-triazacyclononane-*N*,*N*′,*N*″-tris(methylenephosphonic acid) (NOTP), 1,5,9-triazacyclododecane-*N*,*N*′,*N*″-tris(methylenephosphonic acid) (DOTRP) and 1,4,7,10-tetraazacyclododecane-*N*,*N*′,*N*″,*N*‴-tetrakis(methylenephosphonic acid) (DOTP) (see structures in Figures 1-3), has been investigated by means of potentiometry and $^{31}P$, $^1H$, and $^{13}C$ NMR spectroscopy. The results are compared with earlier

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**Table I.** Comparison of Protonation Constants of the Polyazamacrocyclic Poly(methylenephosphonates)[a] with the Corresponding Macrocyclic Amines and Polyamino Polycarboxylates

| ligand | log $K_1$ | log $K_2$ | log $K_3$ | log $K_4$ | log $K_5$ | log $K_6$ | log $K_7$ | log $K_8$ |
|---|---|---|---|---|---|---|---|---|
| [9]-aneN$_3$[b] | 10.42 | 6.82 | <1 | | | | | |
| NOTP (NaCl) | 11.7 | 9.1 | 7.5 | 5.8 | 3.1 | 0.9 | *j* | |
| NOTP (N(CH$_3$)$_4$Cl) | 12.1 | 9.4 | 7.5 | 5.9 | 2.9 | *j* | | |
| NOTA[c,d] | 11.3 | 5.6 | 2.9 | *j* | | | | |
| [12]-aneN$_3$[e,f] | 12.6 | 7.57 | 2.41 | | | | | |
| DOTRP (NaCl) | >13[g] | 10.4 | 7.3 | 5.8 | 4.6 | 1.7 | *j* | |
| DOTRP (N(CH$_3$)$_4$Cl) | >13[g] | 10.4 | 7.4 | 6.0 | 4.9 | 1.9 | *j* | |
| DOTRA[h] | 12.8 | 7.6 | 3.7 | 2.1 | *j* | | | |
| [12]-aneN$_4$[i] | 10.7 | 9.7 | 1.73 | 0.94 | | | | |
| DOTP (NaCl) | 10.9 | 9.2 | 8.1 | 6.3 | 5.4 | 1.8 | 1.3 | *j* |
| DOTP (N(CH$_3$)$_4$Cl) | 12.6 | 9.3 | 8.0 | 6.0 | 5.2 | *j* | | |
| DOTA[i] | 11.08 | 9.23 | 4.24 | 4.18 | 1.88 | 1.71 | *j* | |

[a] Protonation constants are defined as stepwise proton association constants, i.e., $K_1$ = [HL]/[L][H], $K_2$ = [H$_2$L]/[HL][H], etc., and hence have units of M$^{-1}$. Values were determined by potentiometry at 25 °C in 0.1 M NaCl or N(CH$_3$)$_4$Cl, as indicated. [b] From ref 35 (0.1 M KNO$_3$). [c] From ref 29 (0.1 M NaClO$_4$). [d] Reference 39 gave 11.73, 5.74, and 3.16 for log $K_1$, log $K_2$, and log $K_3$, respectively (0.10 M NaNO$_3$). [e] From ref 36 (0.1 M KNO$_3$). [f] Reference 38 gave 13.15 and 7.97 for log $K_1$ and log $K_2$, respectively (0.5 M KNO$_3$). [g] Represents only a lower limit as this value could not be determined by potentiometry. [h] From ref 37 (0.1 M N(CH$_3$)$_4$Cl). [i] From ref 27 (1 M NaCl). [j] This value and those below were not obtained.

data for the analogous polyazamacrocyclic polycarboxylate ligands.[27-29]

## Experimental Section

**Synthesis and Characterization of the Ligands.** The cyclic amines, 1,4,7-triazacyclononane ([9]-aneN$_3$), 1,5,9-triazacyclododecane ([12]-aneN$_3$), and 1,4,7,10-tetraazacyclododecane ([12]-aneN$_4$), were synthesized and isolated as the trihydrobromide and tetrahydrobromide forms, respectively, according to the method of Richman and Atkins as described in the literature.[27,29,30,36] The ligands NOTP, DOTRP, and DOTP were prepared from the HBr salts of the corresponding cyclic amines via a Mannich-type reaction using published procedures.[8] In a typical synthesis of NOTP, 2 g of [9]-aneN$_3$·3HBr were added to a solution containing 8 mL of deionized water, 5 mL of concentrated HCl, and 3.4 g of solid phosphorous acid (2 equiv/amine equiv). After the solution was warmed to dissolve the amine salt, 2.5 g of formaldehyde (4 equiv/amine equiv) in 10 mL of water was added dropwise over a period of 1 h while the temperature was maintained near reflux. After an additional 1 h of reflux, the solution was brought to room temperature, and crystals of H$_6$NOTP were isolated by filtration after adding ethanol. The product was recrystallized from methanol–water (90:10) to yield 1.7 g (55% of theoretical yield). Elemental analysis of the product gave the molecular formula $C_9H_{24}N_3O_9P_3\cdot H_2O$ (Found: C, 25.52; H, 6.04; N, 9.80; O, 37.05 (by difference); P, 21.59. Calcd for $C_9H_{26}N_3O_{10}P_3$: C, 25.18; H, 6.11; N, 9.79; O, 37.28; P, 21.65). DOTRP was prepared and isolated similarly. Elemental analysis of the product gave the molecular formula $C_{12}H_{30}N_3O_9P_3\cdot HCl\cdot 2H_2O$ (Found: C, 27.20; H, 6.64; N, 7.75; O, 33.57 (by difference); P, 17.92; Cl, 6.92. Calcd for $C_{12}H_{35}N_3O_{11}P_3Cl$: C, 27.41; H, 6.71; N, 7.99; O, 33.47; P, 17.67; Cl, 6.74). The synthesis and characterization of DOTP have been reported elsewhere.[31]

**Potentiometric Measurements.** pH titrations were performed by using an Orion Research Model 701A pH meter. The glass electrode was calibrated by measuring the emf of a series of standard buffers (Anderson Laboratories), which measure hydrogen ion activity at zero ionic strength over a range of pH values from 2.00 to 12.72. The chelates were dissolved in 0.1 M NaCl and titrated with standard 0.100 M NaOH or dissolved in 0.1 M tetramethylammonium chloride, made basic with tetramethylammonium hydroxide, and titrated with standard 0.100 M HCl. The hydrogen ion activity coefficient (0.782) and the value of $K_w$ ($1.64 \times 10^{-14}$) was determined separately in these same salt solutions. Protonation constants were obtained from the potentiometric data by using a simplex nonlinear regression algorithm[33] run on an IBM PC.

**NMR Measurements.** Solutions of the ligands (0.01 M) for NMR pH titrations were made up in D$_2$O (99.8% from Sigma), and the pD was adjusted with DCl or CO$_2$-free NaOD (Sigma). The final pH was corrected for a deuterium isotope effect by using the equation pD = pH + 0.4.[34] The hydrogen electrode used in this work allows a reliable and accurate determination of the proton activity over an extended pH range. Solutions of the free ligands were titrated to the basic form in a NMR tube with use of CO$_2$-free NaOD or tetramethylammonium hydroxide solutions (Sigma). Some of the titrations were also carried out at constant ionic strength by using 0.5 M tetramethylammonium perchlorate (Sigma).

$^1$H and broad-band proton-decoupled $^{13}$C and $^{31}$P NMR spectra were obtained, respectively, at 200, 50.1, and 82.7 MHz on a JEOL FX-200 FT spectrometer. Proton and $^{13}$C shifts were referenced to TMS with use of *tert*-butyl alcohol and dioxane, respectively, as internal standards. The $^{31}$P shifts were referenced to external 85% H$_3$PO$_4$.

## Results and Discussion

**Protonation Constants.** Table I summarizes the protonation constants of the polyazamacrocyclic poly(methylenephosphonate) ligands NOTP, DOTRP, and DOTP obtained by potentiometry at 25 °C. These are compared with values reported previously for the corresponding macrocyclic amines, [9]-aneN$_3$,[35] [12]-aneN$_3$,[36-38] and [12]-aneN$_4$[36] and polyamino polycarboxylates, 1,4,7-triazacyclononane-*N*,*N*′,*N*″-triacetic acid (NOTA),[29,39] 1,5,9-triazacyclododecane-*N*,*N*′,*N*″-triacetic acid (DOTRA),[37] and 1,4,7,10-tetraazacyclododecane-*N*,*N*′,*N*″,*N*‴-tetraacetic acid (DOTA).[27,28] A comparison of protonation constants measured in 0.1 M NaCl and 0.1 M N(CH$_3$)$_4$Cl shows that the replacement


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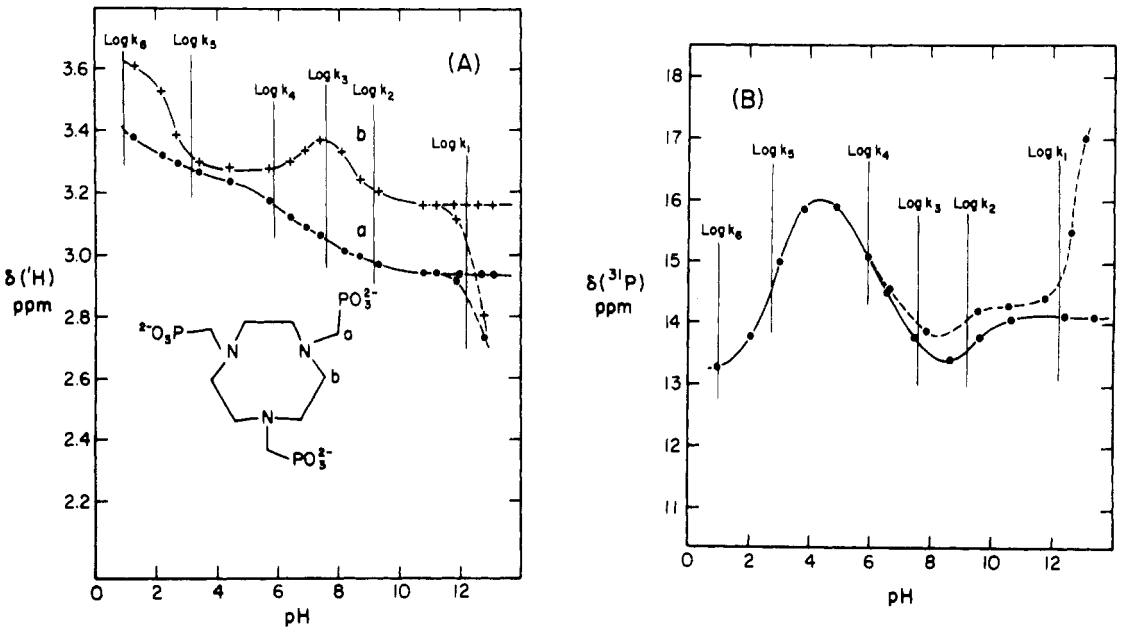


**Figure 1.** NMR pH titrations of NOTP: (A) proton shifts; (B) $^{31}P$ shifts. Broken (- - -) lines indicate titration with NaOD; solid (—) lines indicate titration with $N(CH_3)_4OH$. The potentiometric log $K_i$ values are also shown.

of $Na^+$ by tetramethylammonium cations in the titration medium sharply increases the first protonation constant of the ligands NOTP and DOTP, whereas the other protonation constants are not significantly affected. This likely reflects complex formation between $Na^+$ ions and these two macrocyclic ligands at high pH. The first protonation constant of DOTRP could not be determined by potentiometry in either 0.1 M NaCl or $N(CH_3)_4Cl$, so possible interaction between $Na^+$ ions and this chelate are effectively masked.

Substitution of methylenephosphonate groups on each nitrogen atom of the parent cyclic amine results in an increase in the first protonation constant of the macrocyclic phosphonate ligands, similar to that observed for the linear methylenephosphonate chelates.[7,9,11,17] As shown by the $^{31}P$ NMR shifts (see below), protonation first occurs at one of the ring nitrogens, whose basicity is increased by the double negative charge on the neighboring fully ionized phosphonic acid group. This electrostatic effect prevails over the inductive electron-withdrawal effects of the phosphonate group. Appending acetate groups onto each nitrogen of [9]ane$N_3$, [12]ane$N_3$, and [12]ane$N_4$, to form NOTA, DOTRA, and DOTA, respectively, similarly increases the first protonation constant in these chelates. This trend is also observed in EDTA versus ethylenediamine but not with EDDA versus ethylenediamine, where a small decrease was noted.[11]

The effect of the methylenephosphonate or acetate functionality on the second protonation constant (Table I) varies depending upon the possibility of formation of internal hydrogen bonds in the monoprotonated forms of the ligands as well as on the way monoprotonation changes the electrostatic and inductive effects of those substituent groups. The $^{31}P$ NMR data indicates that the second protonation also occurs at a ring nitrogen and these increase sharply in NOTP and DOTRP but not in DOTP versus their respective cyclic amines. The next three or four protonations occur at the phosphonate ligands, and these decrease regularly from a high of 8.1 to 4.6 or below depending upon the protonation state of the remaining methylenephosphonate groups within the same chelate. These values are in general agreement with similar protonation constants measured for the linear polyamino poly(methylenephosphonates).[6,7,11,13,17]

**NMR Studies of Ligand Protonation.** The proton-decoupled $^{13}C$ NMR spectra of NOTP and DOTP show two resonances with relative intensities of 2:1 corresponding to the ethylenediamino and methylenephosphonate carbons. The spectrum of DOTRP shows an additional resonance corresponding to the central carbon in the propylenediamine bridges. The methylenephosphonate $^{13}C$ resonances are split into a doublet by spin coupling to the adjacent phosphorus ($^1J_{PC}$ = 141.6 Hz for NOTP and 143.7 Hz for DOTP, at pH 6.8). Although the pH dependence of the $^{13}C$ spectra of these ligands was not investigated in detail, we observed a 10% increase in $^1J_{PC}$ for both compounds between pH 11.7 and 1.8 and shifts of about 1.3 ppm to higher frequency for the ethylenediamino $^{13}C$ resonances of NOTP and DOTP as a result of ligand protonation. The methylenephosphonate carbons shifted first to lower and then to higher frequency as the nitrogens and phosphonate groups were protonated.

The proton NMR spectra of NOTP and DOTP consist of two resonances with intensities of 2:1 corresponding to a singlet from the ethylenediamino (b) and a doublet from the methylenephosphonate (a) protons (see structures in Figures 1 and 3). The spectrum of DOTRP (see structure in Figure 2) consists of three resonances with intensities of 3:1:1 corresponding to a triplet from the $CH_2$ protons $\alpha$ to the ring nitrogens (b), a quintet from the bridging $CH_2$ protons (c), and a doublet from the methylenephosphonate protons (a). $^2J_{PH}$ was observed to be 10.8 Hz for all three chelates at pH 6.8.

Figures 1–3 illustrate the pH dependence of the proton and $^{31}P$ chemical shifts of the phosphonate ligands in the presence and absence of $Na^+$ ions. All spectra showed single resonances for each magnetically equivalent group of nuclei over the entire pH range, indicating rapid exchange between all protonated species, $H_nL$. The resonances were generally sharp, except for the $^{31}P$ signal of DOTP, which broadens considerably below pH 9 from a line width of 8 Hz at pH 12 to 190 Hz at pH 5. This indicates that proton exchange involving the phosphonate groups in this chelate is slower than in the two triazamacrocycles.

Under conditions of fast proton exchange among the various protonated species, $H_nL$, the observed averaged chemical shift of nucleus $i$ is given by

$$\delta^i_{obs} = \sum \delta^i_n X_{H_nL} \qquad (1)$$

where $\delta^i_n$ values are the intrinsic chemical shifts of the protonated or unprotonated species, and $X_{H_nL}$ is the mole fraction of each species. Using the protonation constants, $K_n$, obtained by potentiometry (Table I), it was possible to calculate the intrinsic chemical shifts, $\delta^i_n$, by using a computer program that minimizes the sum of the squares of the deviations between the observed and calculated $\delta^i_{obs}$ values. A series of fits were attempted on each set of shift data (Figures 1–3), first by fixing the protonation constants to values obtained by potentiometry in NaCl and in $N(CH_3)_4Cl$ and then by also allowing optimization of the log $K_1$ values. Generally better fits were obtained with the potentiometric log $K_i$ values obtained in $N(CH_3)_4Cl$ than in NaCl. This was most

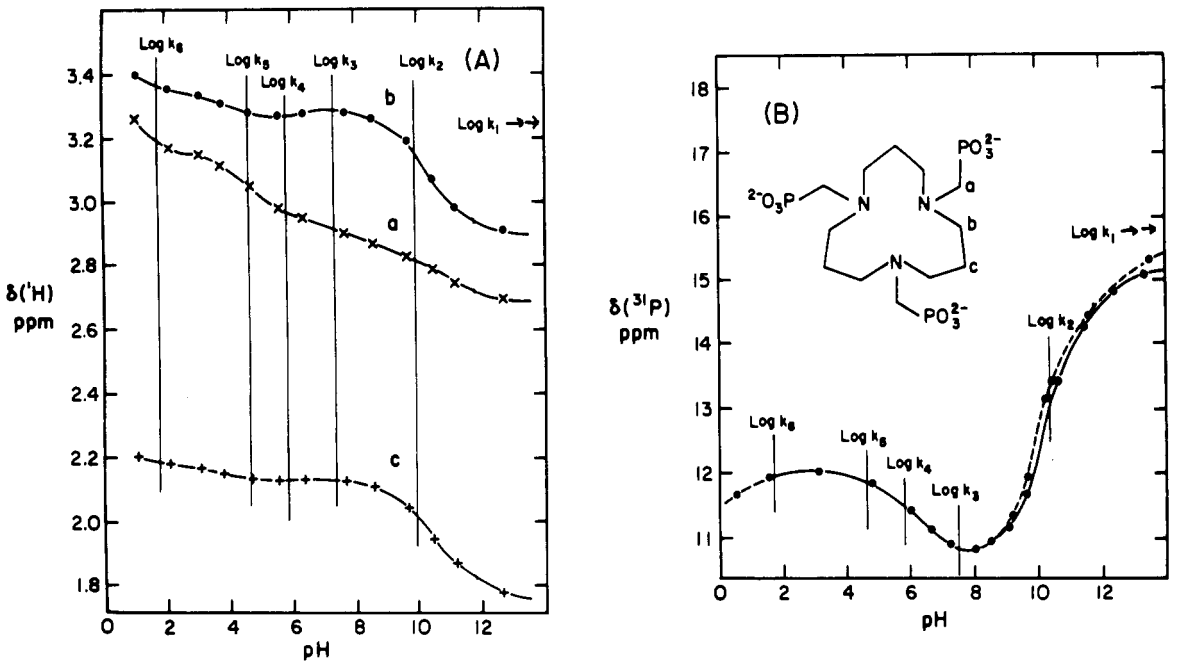


**Figure 2.** NMR pH titrations of DOTRP: (A) proton shifts; (B) $^{31}P$ shifts.

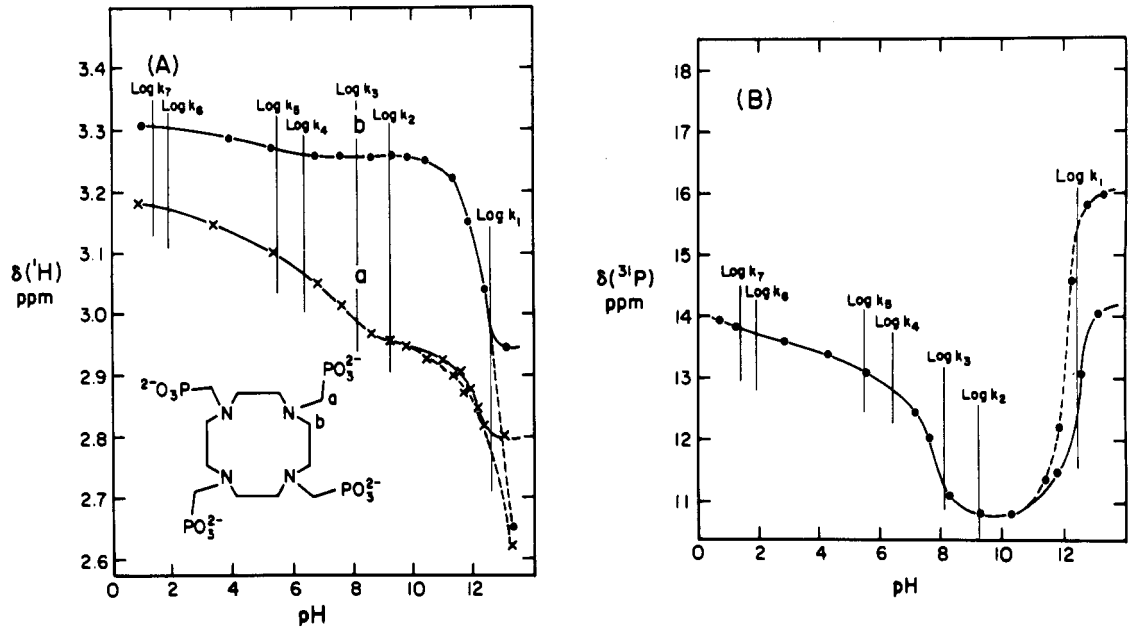


**Figure 3.** NMR pH titrations of DOTP: (A) proton shifts; (B) $^{31}P$ shifts.

**Table II.** Proton and $^{31}P$ NMR Intrinsic Shifts ($\delta_n^i$, ppm) for the Macrocyclic Phosphonates as a Function of the Number of Protons ($n_h$) Bound to the Ligand ($H_nL$)

| | NOTP | | | DOTRP | | | | DOTP | | |
|---|---|---|---|---|---|---|---|---|---|---|
| $n_H$ | $H_a$ | $H_b$ | $^{31}P$ | $H_a$ | $H_b$ | $H_c$ | $^{31}P$ | $H_a$ | $H_b$ | $^{31}P$ |
| 0 | 2.94 | 3.16 | 14.1[a] | 2.66 | 2.88 | 1.74 | 15.2[a] | 2.80 | 2.95 | 14.6[a] |
| 1 | 3.00 | 3.25 | 13.78 | 2.76 | 3.06 | 1.92 | 13.75 | 2.90 | 3.13 | 11.65 |
| 2 | 3.05 | 3.37 | 13.41 | 2.88 | 3.28 | 2.13 | 10.73 | 2.97 | 3.27 | 11.30 |
| 3 | 3.10 | 3.32 | 14.32 | 2.93 | 3.28 | 2.13 | 11.09 | 3.04 | 3.27 | 12.40 |
| 4 | 3.23 | 3.27 | 16.11 | 2.98 | 3.27 | 2.13 | 11.47 | 3.09 | 3.26 | 13.60 |
| 5 | 3.32 | 3.53 | 13.53 | 3.16 | 3.35 | 2.17 | 12.09 | 3.15 | 3.29 | 13.94 |
| 6 | 3.48 | 3.67 | 13.0[a] | 3.34 | 3.48 | 2.25 | 10.9[a] | 3.17 | 3.30 | 14.30 |
| 7 | *b* | *b* | *b* | *b* | *b* | *b* | *b* | 3.19 | 3.32 | 14.5[a] |

[a] The $^{31}P$ shifts for the $H_nL$ species with the largest and smallest $n$ were least accurate. [b] This value and those below this one were not obtained.

apparent in the fit involving log $K_1$. It must be noted, however, that the NMR pH titrations were carried out by using NaOD or $N(CH_3)_4OH$, and the ionic strength was not strictly constant. Therefore, the best overall fits were obtained by allowing optimization of the log $K_i$ values, especially of log $K_1$ and log $K_2$.

The $\delta_n^i$ thus obtained for the proton and $^{31}P$ resonances of the three phosphonate ligands are listed in Table II. The calculated proton intrinsic shifts for the various $H_nL$ forms can be used to calculate the percent protonation of the nitrogen and oxygen sites[23] using the method of Sudmeier and Reilley.[40] According to this

**Table III.** Percent Protonation of the Various Basic Sites of Polyazamacrocyclic Poly(methylenephosphonates)

| | NOTP[a] | | | DOTRP[b] | | | DOTP[c] | | |
|---|---|---|---|---|---|---|---|---|---|
| $n_H$ | pH | $f_P$ | $f_N$ | pH | $f_P$ | $f_N$ | pH | $f_P$ | $f_N$ |
| 0 | 12.0 | | | 13.8 | | | 14.0 | | |
| 1 | 8.9 | 2 ± 3 | 30 ± 3 | 11.0 | 1 ± 1 | 31 ± 2 | 12.1 | −2 ± 2 | 27 ± 4 |
| 2 | 7.6 | −2 ± 3 | 70 ± 3 | 8.0 | 0 ± 1 | 68 ± 2 | 8.7 | 0 ± 1 | 50 ± 1 |
| 3 | 6.7 | 21 ± 4 | 57 ± 4 | 6.8 | 16 ± 1 | 68 ± 2 | 7.1 | 12 ± 1 | 50 ± 1 |
| 4 | 4.3 | 44 ± 6 | 45 ± 9 | 5.8 | 33 ± 1 | 68 ± 3 | 5.6 | 25 ± 1 | 49 ± 1 |
| 5 | 2.2 | 50 ± 7 | 67 ± 14 | 3.0 | 45 ± 1 | 77 ± 3 | 3.3 | 37 ± 2 | 52 ± 2 |
| 6 | 0 | 54 ± 10 | 93 ± 20 | 0 | 53 ± 4 | 95 ± 8 | 1.5 | 49 ± 2 | 53 ± 2 |
| 7 | *d* | *d* | *d* | *d* | *d* | *d* | 0 | 60 ± 2 | 55 ± 3 |
| 8 | | | | | | | *d* | *d* | *d* |

[a] $C_N$ = 0.18 ppm, $C_N'$ = 0.12 ppm, $C_P$ = 0.30 ppm ($n_H$ = 1–4); $C_N$ = 0.43 ppm, $C_N'$ = 0.12 ppm, $C_P$ = 0.23 ppm ($n_H$ = 5, 6). [b] $C_N$ = 0.58 ppm, $C_N'$ = 0.29 ppm ($C_P$ varied with pH, e.g. 0.24 ppm for $n_H$ = 6). [c] $C_N$ = 0.38 ppm, $C_N'$ = 0.26 ppm ($n_H$ = 1–7); $C_P$ = 0.40 ppm ($n_H$ = 1–5); $C_P$ = 0.34 ppm ($n_H$ = 6, 7). [d] Not calculated.

procedure, the observed shifts of the $H_a$, $H_b$, and $H_c$ protons ($\delta^i_{obs}$) are a function of the intrinsic shifts of the fully deprotonated form of the ligand ($\delta^i_0$), the fraction of protonation of the nitrogen and of the phosphonate sites at each pH ($f_N$ and $f_P$), the change in proton chemical shift due to phosphonate protonation ($C_P$), and protonation of a N atom in the $\alpha$ position ($C_N$) or in the $\beta$ position $C_N'$) relative to the $CH_2$ group under study. For example, in the case of DOTRP, four equations may be written:

$$\delta^a = \delta^a_0 + f_N C_N + f_P C_P \quad (2)$$

$$\delta^b = \delta^b_0 + f_N C_N \quad (3)$$

$$\delta^c = \delta^c_0 + 2f_N C_N' \quad (4)$$

$$n_H = 3f_N + 6f_P \quad (5)$$

where $n_H$ is the average number of ligand-bound protons. However, due to inadequate additivity of the protonation shifts associated with the various basic sites described by the substituent shielding constants $C_P$, $C_N$, and $C_N'$,[40] a given set of protonation fractions, $f_N$ and $f_P$, does not lead to perfect agreement between observed and calculated protonation shifts. An optimal set of $f_i$ parameters was therefore obtained by least-squares methods[40] and the results of such an analysis are summarized in Table III. The best values obtained for $C_N$ and $C_N'$ are different for each phosphonate ligand and also differ from values reported for EDTMP[23] and for the corresponding aminopolycarboxylate analogues.[27-29,40] These values were obtained in the calculation by assuming that the first two protons are associated exclusively with the macrocyclic nitrogen sites, as indicated by the $^{31}P$ shifts for these ligands and as observed previously for the carboxylate analogues.[27-29] It was found that $C_P$ was pH dependent[23] for all three phosphonate chelates, perhaps due to formation of intramolecular hydrogen bonds between the phosphonate oxygens and the protonated amino groups. The $f_i$ values of Table III indicate that after the first two protons add to the ring nitrogens, subsequent stepwise protonation of the phosphonate oxygens occurs to different degrees before further N protonation occurs. In the case of DOTP, the next five protons add to the phosphonates, whereas for NOTP and DOTRP, only the next two protons add exclusively to the phosphonates. Further protonation is divided between the $O^-$ and N sites in each chelate. This different behavior probably results from the better capacity of DOTP to form internal $NH^+\cdots N$ hydrogen bonds in the ring, leaving the phosphonate groups free of hydrogen bonding interactions with neighboring $NH^+$ groups and therefore more basic than in the triazamacrocyclic phosphonate ligands.

The data in Figures 1–3 (summarized in Table II) show that the first two protonations result in $^{31}P$ shifts to low frequency totaling −0.7 ppm for NOTP, −4.6 ppm for DOTRP, and −2.9 ppm for DOTP. This is only consistent with the first two protonations occurring at ring nitrogens. These shifts are relatively small compared to the $^{31}P$ shift of −12 ppm found for nitrilotris(methylenephosphonate) upon protonation of its single nitrogen.[17] Thus, protonation of N can dramatically affect the electronic configuration of the phosphorous atom. It has been argued[17] that this reflects a through-bond ($P-(C)_xN$) electronic effect based upon experimental observations[41] that the first protonation shift of $NH_2(CH_2)_xPO_3^{2-}$ decreases as the number of methylene groups increases. However, these and our own observations can also be interpreted by assuming formation of an intramolecular hydrogen bond between $NH^+$ and the phosphonate $O^-$. This type of interaction has been observed in N-protonated polyamino polycarboxylates.[27,29,42,43] When $x$ = 1, the resulting formation of a stable five-membered ring leads to a strong hydrogen bond, and the $^{31}P$ shift is affected both by the electric field created by the $NH^+$ groups and by the perturbations of the phosphonate structures caused by the hydrogen bond itself. When $x$ increases, the larger ring formed decreases the stability of the hydrogen bond, thus decreasing the protonation shift.

Figures 1–3 (and Table II) also show the change in the $^{31}P$ shift when the phosphonate oxygens are protonated. These shifts are to high frequency for the first two oxygen protonations in NOTP, three oxygen protonations in DOTRP, and five oxygen protonations in DOTP. The shifts reverse sign upon further protonation of the phosphonate groups only in the two triazamacrocycles. These observations could result from breaking or weakening of $NH^+\cdots O^-$ hydrogen bonds after each of the phosphonate groups become singly protonated, as has been observed with carboxylates.[27,29] However, the multiplicity of possible electronic effects with potential opposite signs contributing to the $^{31}P$ shifts[44,45] precludes a definitive conclusion.

Figures 1–3 also show that the presence of $Na^+$ ions causes large shifts of opposite signs in the proton and $^{31}P$ resonances of NOTP and DOTP at basic pH. This indicates that $Na^+$ binds within the cavity of these two chelates, interacting with both the nitrogen and the phosphonate oxygen donor atoms. This is contrary to the results of Kabachnik et al.[46] where no interaction between $Na^+$ and NOTP was detected by potentiometry. However, the $Na^+$-induced shifts on DOTRP at high pH are almost negligible, indicating that $Na^+$ does not bind within the macrocyclic cavity, possibly due to increased flexibility of the propylene versus ethylene groups that bridge the nitrogen donors.

**Conclusions.** A comparison of the acid–base behavior of various macrocyclic amines and their derivatives containing methylenephosphonate and acetate pendant groups has allowed a better understanding of the proton equilibria in these polyfunctional ligands, both at the macroscopic and microscopic levels. Substitution of methylenephosphonate groups on each nitrogen atom sharply increases the first protonation constant at a ring nitrogen. This results from an electrostatic effect of the double negative charge on the neighboring phosphonate group. Acetate substi-

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tution has a similar but smaller effect upon nitrogen protonation.

A computer fit of the NMR chemical shift vs pH curves allowed the intrinsic shifts of the various ligand protonated species, $H_nL$, to be obtained. The $^{31}P$ shifts for the various $H_nL$ species are dependent upon protonation of the nitrogen and the phosphonate oxygen atoms, and also on the possible formation of intramolecular hydrogen bonds between $NH^+$ and $O^-$ neighboring groups. Those effects are reflected in the $^{31}P$ chemical shifts in a complex way through $\sigma$ and $\pi$ contributions to the electronic structure of the phosphonate moiety.[44] The protonation shifts of the phosphonate ligands were used to obtain microscopic protonation fractions at various pH values. Although a quantitative fit of the experimental data was difficult due to pH-dependent conformational effects, the general picture of microscopic protonation of the macrocyclic phosphonate ligands is not very different from that found for the acetate couterparts.[27-29] The most basic sites are two ring nitrogens, followed by the phosphonate oxygens, which are protonated to different degrees depending on the ring structure. In the tetraaza ligand, the protonation of the pendant phosphonate oxygens is more extensive than in the triaza ligand before further protonation of the ring nitrogens occurs.

Finally, the magnitude and sign of the $Na^+$-induced shift on the $^1H$ and $^{31}P$ signals of the phosphonate chelates indicate that this ion binds within the macrocyclic cavities of NOTP and DOTP but not DOTRP, at least below pH 13. This may be due to an unusually high first protonation constant for DOTRP or to unique conformational features of the bridging propylenes in this chelate that precludes $Na^+$ binding in its cavity.

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# Evidence for the Donor Capacity of Nitrogen in Acyclic Aminophosphines: A Multinuclear NMR Study

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The reactions of $R_2PNMe_2$, $Me_2PNR'_2$, and $(Me_2N)_nPMe_{3-n}$, where R = Me, Et, Ph, and Cl, R' = Me, Et, $Pr^n$, $Pr^i$, and $SiMe_3$, and $n$ = 1–3, with varying mole ratios of $BH_3$·THF have been carried out and studied by using multinuclear NMR spectroscopy. Although P–B-bonded monoadducts were always obtained, B–P–N–B-bonded bisadducts were also obtained for $Me_2PNMe_2$, $Me_2PNEt_2$, and $Et_2PNMe_2$. These are the first reported examples where the nitrogen atom in acyclic aminophosphines demonstrates reactivity toward $BH_3$. The extent of bisadduct formation decreases dramatically in going from $Me_2PNMe_2$ to $Me_2PNEt_2$. $K_{eq}$, $\Delta H$, and $\Delta S$ values were obtained for the $Me_2\overline{PNMe_2}\cdot BH_3/H_3BP(\overline{NMe_2}\cdot BH_3)Me_2$ and $Et_2\overline{PNMe_2}\cdot BH_3/H_3BP(\overline{NMe_2}\cdot BH_3)Et_2$ equilibrium systems. The results are compared with those reported previously for analogous aminoarsines. A competition study involving the $Me_3N$, $Me_3P$, $Me_3As$, $Me_2PNMe_2$, $Me_2AsNMe_2$, and $BH_3$·THF systems is discussed relative to the nature of P–N and As–N bonding.

## Introduction

The borane coordination chemistry and Lewis basicity of the phosphorus and nitrogen atoms in aminophosphines have been studied extensively,[1-19] with experimental results suggesting that the phosphorus atom is the more basic site. For example, in the reactions of $B_2H_6$ with acyclic aminophosphines of the type $(Me_2N)_nPMe_{3-n}$,[14-17,19] $Me_2NPF_2$,[9] $(Me_2N)_2PF$,[9] $Me_2NPBu_2$,[18] and $(Me_2N)_2PBu$,[18] the $BH_3$ moiety binds only to the phosphorus atom. The prevailing view is that in these phosphines the nitrogen atom assumes a planar configuration and through $d\pi$–$p\pi$ multiple bonding it experiences diminished basicity, and the phosphorus atom, enhanced basicity.[20-24] Only in some constrained cyclic aminophosphines is there evidence for the binding of $BH_3$ to the nitrogen atom.[5,20,21,24] With $P(NMeCH_2)_3CMe$,[5] coordination to the nitrogen occurs after $BH_3$ binds to the phosphorus. Similarly, the constrained bicyclic $P(OCMe_2CH_2)_2N$ forms a bis(borane) adduct.[21,24]

In a recent communication,[25] we demonstrated conclusively[19] the synthesis and characterization of the first known bis(borane) adduct, $H_3BP(NMe_2\cdot BH_3)Me_2$, of an acyclic aminophosphine. Previously, the possibility of the nitrogen atom serving as a donor site in this compound was dismissed.[6,15,17] We have now extended this work to establish the generality of N–B bonding and those factors influencing P–B and N–B bonding in acyclic aminophosphine/$BH_3$ reaction systems. In this paper, we describe a systematic study of the reaction of $BH_3$·THF in varying reactant mole ratios with three series of aminophosphines: series A,

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