

Ternary Alkaline Earth Metal Complex Ions in the M^{2+} /Borate/Tartrate System As Studied by ^{11}B NMR¹

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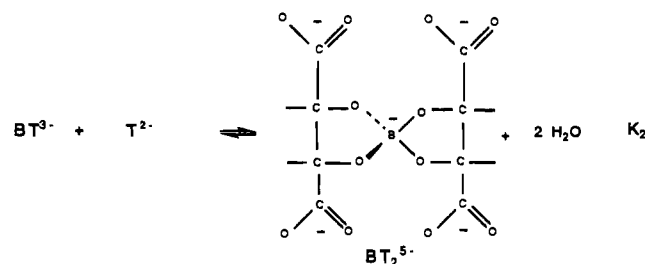
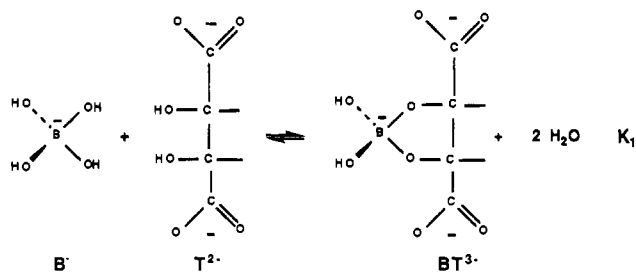
In aqueous alkaline solution, the borate ion ($\text{B}(\text{OH})_4^-$) is capable of forming both 1:1 and 1:2 complexes with polyhydroxy carboxylate ligands such as L-(2R,3R)-tartrate or *meso*-(2R,3S)-tartrate (T^{2-}). The mode of coordination is pH dependent and has been shown in base to be exclusively via the 2,3-diol linkage on the ligand. Equilibria in this system can be described by the following two equations: $\text{B}(\text{OH})_4^- + \text{T}^{2-} \leftrightarrow \text{BT}^{3-} + 2\text{H}_2\text{O}$ (K_1); $\text{BT}^{3-} + \text{T}^{2-} \leftrightarrow \text{BT}_2^{5-} + 2\text{H}_2\text{O}$ (K_2). ^{11}B NMR was used to study both these equilibria and the binding of alkaline earth metal ions by the several borotartrate complex ions. Metal ion specificity (Mg^{2+} , Ca^{2+} , Sr^{2+}) was studied in the $M^{2+}/\text{B}(\text{OH})_4^-/\text{L-tartrate}$ systems, while the effect of absolute ligand configuration (L-tartrate vs *meso*-tartrate) was studied in the $\text{Ca}^{2+}/\text{B}(\text{OH})_4^-/\text{tartrate}$ systems. The main conclusions of this work are (1) Mg^{2+} binds preferentially to free tartrate, T^{2-} , and shows little if any interaction with BT^{3-} and BT_2^{5-} , (2) Ca^{2+} and Sr^{2+} bind preferentially (by 3 orders of magnitude) to BT_2^{5-} (L-tartrate) with Ca^{2+} binding being selectively favored by a factor of 5, and (3) absolute ligand (tartrate) configuration has no significant effect on Ca^{2+} binding to BT_2^{5-} . Stability constants for the various complexation reactions are reported as well as a proposed Ca^{2+} and Sr^{2+} binding site in the MBT_2^{3-} complex ions.

The increased ability of polyhydroxy carboxylates to sequester Ca^{2+} in aqueous alkaline solution upon addition of borate has been recognized for over 50 years.² More recently, Environmental Protection Agency restrictions on the use of phosphates as builders in detergent formulations led to the application of mixtures of borate and polyhydroxy carboxylates as potential phosphate substitutes as disclosed in the patent literature.³ In this light, two excellent and comprehensive series of articles have been published by Peters and co-workers. One series⁴ is an extensive investigation by ^{11}B , ^{13}C , and ^1H NMR spectroscopy of borate complexes involving ligands ranging from diols to carbohydrates. Although stability constants for complex formation are reported in some of these studies,^{4a-e} the principal subjects of much of the work are questions of stereochemistry and the detailed determination of NMR coupling constants and chemical shifts for the various complexes.^{4a-d,f-h} The second series⁵ is one in which the "synergic" effect of borate on the metal ion sequestering ability of over 20 polyhydroxy carboxylates was studied using ^{11}B NMR and other experimental techniques. Although this outstanding contribution is unparalleled, no quantitative determination of stability constants for

metal cation binding by borate diesters of polyhydroxy carboxylates has yet been reported.

Our interest in boron acid complexation reactions has been primarily concerned with questions of equilibria, kinetics, and mechanism,⁶ but we recently extended our work to include quantitative thermodynamic studies⁷ using variable-temperature ^{11}B NMR spectroscopy. We present here an extension of our use of ^{11}B NMR to report the first determination of stability constants for ternary M^{2+} /borate/tartrate complexation reactions. Complexes of Mg^{2+} , Ca^{2+} , and Sr^{2+} were studied with L-tartrate in order to see whether the system displays any selectivity with respect to metal ion. The effect of ligand stereochemistry on the metal ion binding process was studied by using L-tartrate and *meso*-tartrate in the Ca^{2+} binding study.

The borate complexation reactions are



where $K_1 = [\text{BT}^{3-}]/[\text{B}^-][\text{T}^{2-}]$ and $K_2 = [\text{BT}_2^{5-}]/[\text{BT}^{3-}][\text{T}^{2-}]$. The complexation reactions of M^{2+} with each of the four anions in this reaction sequence are considered.

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Experimental Section

Boric acid, phenylboronic acid, L-tartaric acid, potassium nitrate, potassium hydroxide, tetramethylammonium chloride, tetramethylammonium hydroxide, calmagite, and deuterium oxide, as well as Certified solutions (0.1000 ± 0.0005 M) of calcium chloride, magnesium chloride, strontium chloride, and barium chloride (Aldrich), were all used as received. *meso*-Tartaric acid (Sigma) was also used as received.

All solutions were purged with dry $N_2(g)$ to remove any dissolved $CO_2(g)$ prior to experimentation. Since this study was conducted exclusively in basic media (pH = 11.5), the results presented here are limited to those reactions which are important at high pH. At this pH, boric acid (HB) as well as the two diastereomers of tartaric acid (L- H_2T and *meso*- H_2T) are completely ionized to B^- and T^{2-} , respectively. Under these conditions, reactant and product concentrations are independent of pH^{6d} and, furthermore, the concentration of hydrogen ion is not needed in any of the calculations. Because of this, a precise calibration of the pH electrode for 20% D_2O/H_2O is not necessary, and we report the measured pH to only one significant figure. The measurement of pH in pure D_2O using glass electrodes has been discussed⁸ as well as the effect of solvent composition (D_2O/H_2O) on measured pK_a values.^{9,10}

Stability Constant Determination via ^{11}B NMR. Stability constants (K_1 and K_2) for the 1:1 and 1:2 borate complexation reactions in both the L-tartrate and *meso*-tartrate systems were determined using the ^{11}B NMR spectroscopic technique described in detail elsewhere.⁷ Stability constants for divalent metal ion binding (Mg^{2+} , Ca^{2+} , Sr^{2+}) to the various borotartrate complexes were determined in the presence of the appropriate divalent metal ion using the same ^{11}B NMR technique. All solutions were prepared using 20% D_2O in H_2O as the solvent mixture. Boric acid concentrations in various experiments ranged from 0.03 to 0.15 M, tartrate concentrations ranged from 0.20 to 0.50 M, Ca^{2+} and Sr^{2+} ion concentrations ranged from 4.0 to 25.0 mM, and Mg^{2+} concentrations ranged from 4.0 to 82.0 mM. In the case of Ba^{2+} , precipitation even at low concentrations made quantitative study of this system impossible. Ionic strength was maintained at $\mu = 1.5$ M by the addition of the requisite amount of KNO_3 . The relatively high reactant concentrations (and, therefore, ionic strength) are necessary so that complex concentrations are sufficiently high to allow accurate ^{11}B NMR peak integration for all boron-containing species. Final solution pH measurements were made directly in the NMR sample tube using a Fisher Ag/AgCl microprobe combination pH electrode. Samples were thermostated at 298 K during the ^{11}B NMR experiments using a Bruker BVT-1000 variable-temperature unit.

Stability Constant Determination for Simple Metal Ion/Tartrate Complex Formation. Although stability constants for Mg^{2+} , Ca^{2+} , and Sr^{2+} binding to both L-tartrate and *meso*-tartrate have been published,¹¹ no measurement consistent with our experimental conditions has been reported. To determine these stability constants, a spectrophotometric technique which we have used previously in studies of lanthanide^{12a} and alkaline earth metal^{12b,c} cryptate formation was chosen rather than a potentiometric technique in order to circumvent typical interferences associated with potentiometric techniques at high

ionic strength. Calmagite was used as the metal ion indicator because reasonable conditions for competitive binding could be established under our experimental conditions for Ca^{2+} and Sr^{2+} with both tartrate diastereomers. These spectrophotometric experiments were conducted under experimental conditions of pH, ionic strength, and temperature similar to those used in the ^{11}B NMR studies described above. The only exception is that tetramethylammonium compounds were used instead of potassium compounds to avoid possible problems associated with the complexation of potassium ion and calmagite. In each experiment the analytical concentration of the chromophore ($(calmagite)_0 = 6.64 \times 10^{-5}$ M) was held constant while the concentration of the divalent metal cation ($(M^{2+})_0$) was varied from zero ($\lambda_{max} = 602$ nm) to an excess ($(M^{2+})_0$) value at which all the calmagite is in a bound state ($\lambda_{max} = 525$ nm). All spectra were recorded with a Perkin-Elmer Lambda 3B UV/vis spectrophotometer using a matched set of quartz cells.

Ca^{2+} /Calmagite: (Ca^{2+})₀ was varied over a range from 5.0×10^{-5} to 4.0×10^{-4} M with the excess Ca^{2+} experiment being conducted at (Ca^{2+})₀ = 8.0×10^{-3} M. **Sr^{2+} /Calmagite:** (Sr^{2+})₀ was varied over a range from 4.5×10^{-3} to 5.0×10^{-2} M with the excess Sr^{2+} experiment being conducted at (Sr^{2+})₀ = 0.20 M. **Ca^{2+} /Calmagite/L- or *meso*-Tartrate:** (Ca^{2+})₀ was varied over a range from 5.0×10^{-5} to 4.0×10^{-4} M and either L- or *meso*-tartrate concentration was varied over a range from 1.2×10^{-2} to 0.10 M. **Sr^{2+} /Calmagite/L-Tartrate:** (Sr^{2+})₀ was varied over a range from 4.5×10^{-3} to 5.0×10^{-2} M while L-tartrate concentration was varied over a range from 0.10 to 0.32 M.

Results and Treatment of Data

Determination of Stability Constants for Borotartrate Complex Formation (K_1 and K_2) by ^{11}B NMR. At high pH (11.5) and in the absence of any divalent cation, it is possible to keep the concentrations of borate (~ 0.10 M) and tartrate (~ 0.10 M) sufficiently low that only the 1:1 complex (BT^{3-} , -12.6 ppm) and the free borate (B^- , -17.6 ppm) resonances are observed.^{7b} Under these conditions, direct integration of the spectrum along with mass balance affords the calculation of K_1 values (eq 1) for the L-tartrate and *meso*-tartrate systems (Table 1). Extending the technique to measure K_2 is simply a matter of decreasing the concentration of borate (~ 0.05 M) and increasing the tartrate concentration (~ 0.40 M) under the same experimental conditions of pH and ionic strength.^{7a} Under these conditions, ^{11}B NMR spectra (Figure 1a) are well resolved and can be easily integrated for B^- , BT^{3-} , and BT_2^{5-} (-8.5 ppm). The stability constant, K_2 , for the L-tartrate and *meso*-tartrate systems (eq 2) can therefore be calculated from the ^{11}B integration as described in detail elsewhere.^{7a}

The ratio of stability constants, K_2/K_1 , is equal to $[BT_2^{5-}][B^-]/[BT^{3-}]^2$. This ratio is independent of tartrate concentration and can be calculated using ^{11}B NMR integration alone. Calculated in this manner, K_2/K_1 values for both systems studied agree with the ratio of K_2 to K_1 calculated independently as described above. This agreement is a critical validation of the accuracy of the K_1 and K_2 values.

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Table 1. Stability Constants for the M²⁺/Borate/x-Tartrate System (pH = 11.5, 298 K, $\mu = 1.5$ M)

ligand	M ²⁺ (ionic radius (Å) ^a)			
	Mg ²⁺ (0.78)	Ca ²⁺ (1.06)		Sr ²⁺ (1.27)
L-tartrate	L-tartrate	L-tartrate	<i>meso</i> -tartrate	L-tartrate
K_1 (M ⁻¹)	5.0 (± 0.29) ^b	5.0 (± 0.29)	1.4 (± 0.10)	5.0 (± 0.29)
K_2 (M ⁻¹)	0.12 (± 0.01)	0.12 (± 0.01)	0.11 (± 0.02)	0.12 (± 0.01)
K_{MT} (M ⁻¹)	~ 11 ^c	37 (± 2)	53 (± 2)	18 (± 3)
K_{MBT_2} (M ⁻¹)	<11	$3.7 (\pm 0.3) \times 10^4$	$4.5 (\pm 0.3) \times 10^4$	$8.0 (\pm 0.4) \times 10^3$
K_{ex} ^d	<1	$1.0 (\pm 0.08) \times 10^3$	$8.5 (\pm 0.6) \times 10^2$	$4.5 (\pm 0.2) \times 10^2$

^a Emsley, J. *The Elements*; Clarendon Press: Oxford, U.K., 1989. ^b The numbers in parentheses are the standard deviations. These values were estimated using at least eight independent determinations over the reported concentration range. ^c Extrapolated from the value given at $\mu = 0.2$ M, 25 °C: Martell, A. E.; Smith, R. E. *Critical Stability Constants*; Plenum: New York, 1977; Vol. 3, p 127. ^d Although $K_{ex} = K_{MBT_2} / K_{MT}$, the values of K_{ex} presented here were calculated directly from experimental data and standard deviations were calculated as described in footnote b.

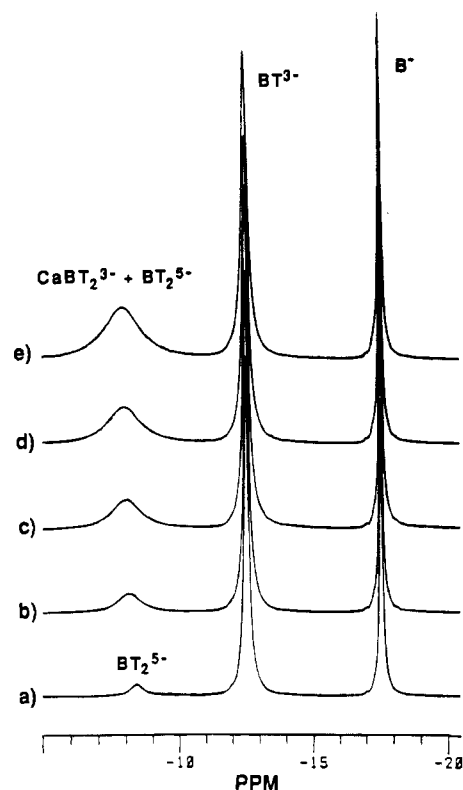
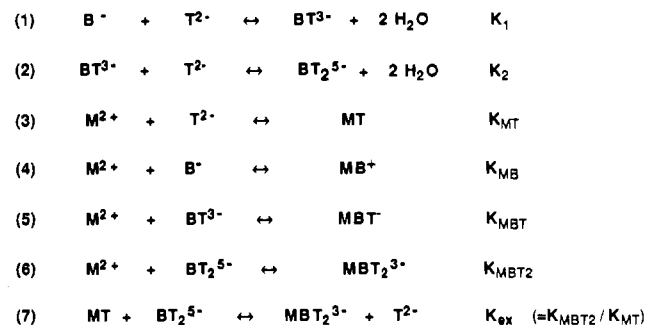


Figure 1. ¹¹B NMR spectra for the Ca²⁺/borate ($(B^-)_0 = 0.050$ M)/L-tartrate ($(T^{2-})_0 = 0.40$ M) system as a function of total Ca²⁺ concentration: (a) $(Ca^{2+})_0 = 0.0$; (b) $(Ca^{2+})_0 = 5.0$ mM; (c) $(Ca^{2+})_0 = 10.0$ mM; (d) $(Ca^{2+})_0 = 15.0$ mM; (e) $(Ca^{2+})_0 = 20.0$ mM. All solutions were prepared in 20% D₂O/H₂O (v/v); pH = 11.5; T = 298 K; $\mu = 1.5$ M (KNO₃). Chemical shifts are relative to external 0.15 M boric acid in 20% D₂O/H₂O (v/v) at pH(D) = 2.0.

Metal Tartrate Complex Formation. The conditional indicator constants as defined in the literature¹³ for the M²⁺/calmagite systems were determined over the range of concentrations described in the Experimental Section. K_{In} was calculated for each equilibrium experiment at two independent wavelengths (525 and 615 nm). Identical results were obtained at each wavelength. K_{In} values for Ca²⁺ and Sr²⁺ binding to calmagite are $9.9 (\pm 0.6) \times 10^3$ M⁻¹ and $1.02 (\pm 0.05) \times 10^2$ M⁻¹, respectively. Ca²⁺ and Sr²⁺ binding to L-tartrate and Ca²⁺ binding to *meso*-tartrate were determined via competitive binding with calmagite, and K_{MT} values (Scheme 1, eq 3) for these systems are given in Table 1.¹⁴ All spectra for either binary systems (M²⁺/calmagite) or ternary systems (M²⁺/

Scheme 1



calmagite/tartrate) have a common isosbestic point at 555 nm. Competitive binding conditions could not be established for the Mg²⁺/calmagite/tartrate system at high pH due to the very large conditional indicator constant (K_{In}) compared with Mg²⁺ binding by tartrate.

Metal Ion Binding by Borotartrate Complex Ions As Determined by ¹¹B NMR. The addition of millimolar quantities of Ca²⁺ or Sr²⁺ to solutions of borate with L- or *meso*-tartrate causes a dramatic increase in the relative integration of the 1:2 peak with respect to the 1:1 peak (BT³⁻) and the free borate peak (B⁻). The 1:2 peak also shows a substantial metal ion induced shift^{5e} from -8.5 ppm in the blank spectrum (Figure 1a) to -7.9 ppm in the $(Ca^{2+})_0 = 20$ mM spectrum (Figure 1e) as well as increased broadening with increased concentrations of Ca²⁺ or Sr²⁺. Neither the 1:1 peak (BT³⁻) nor the free borate peak (B⁻) shows appreciable changes in relative integration, chemical shift, or line width as a function of M²⁺ concentration. Metal ion exchange between the various borotartrate complexes and the corresponding ternary M²⁺/borotartrate complexes is fast on the ¹¹B NMR time scale, as no separate ¹¹B signals are observed for the ternary complexes. The 1:2 peak, which is dramatically affected by the addition of Ca²⁺ or Sr²⁺, is therefore assigned to be the composite of the MBT₂³⁻ and BT₂⁵⁻ resonances exchanging rapidly on the ¹¹B NMR time scale as described by previous workers.^{5e}

The Ca²⁺/borate/L-tartrate, Sr²⁺/borate/L-tartrate, and Ca²⁺/borate/*meso*-tartrate systems have been quantitatively modeled by considering the set of coupled equilibria given in Scheme 1. K_1 , K_2 , and K_{MT} (eqs 1–3) have been determined as described above. Equation 4, which represents M²⁺ coordination to borate (B⁻) can be ignored because of the low stability constants for CaB⁺ and SrB⁺ complex formation. The fact that added Ca²⁺ or Sr²⁺ has no effect (Figure 1) on the chemical shift or line

(13) $K_{In} = [MIn^-]/[M^{2+}][In^-]$ where $[In^-] = [H_3In] + [H_2In^-] + [HIn^{2-}] + [In^{3-}]$. pH = 11.50; $\mu = 1.5$ M ((CH₃)₄NCl); Laitinen, H.; Harris, W. *Chemical Analysis*, 2nd ed.; McGraw-Hill: New York, 1975; p 201.

(14) Under our experimental conditions of high ionic strength, values of K_{MT} are lower than those reported in the literature at lower ionic strength.¹¹

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width of the B^- peak also supports this point. In our mathematical analysis, K_{MBT} (eq 5) was set equal to K_{MT} in each system. This assumes that M^{2+} coordination by BT^{3-} is essentially the same as M^{2+} coordination by T^{2-} (eq 3). Experimentally this approximation is supported by the following observations: (1) almost no change in the relative integration, chemical shift, or line width is observed for the BT^{3-} peak in the ^{11}B NMR spectrum with added Ca^{2+} or Sr^{2+} , (2) ^{11}B NMR spectra of the phenylborate/L-tartrate system (which can form only the 1:1 borate complex $PhBT^{3-}$) are virtually identical in the absence and presence of Ca^{2+} , and (3) calcium ion specific electrode experiments¹⁶ conducted in this laboratory¹⁷ for the Ca^{2+} /phenylborate/L-tartrate system are identical with those conducted for the Ca^{2+} /L-tartrate system showing that formation of $PhBT^{3-}$ does not significantly increase or decrease the concentration of free Ca^{2+} in the solution. The approximation that K_{MBT} is about equal to K_{MT} has also been made by Peters and co-workers.^{5e}

Stability constants for eqs 1–5, along with ^{11}B NMR integration and mass balance, allow the calculation of the stability constant for eq 6 (K_{MBT_2}) in each system. The only approximation used in these calculations is that $[BT^{3-}] \gg [MBT^-]$. Therefore the integration of the 1:1 peak determines $[BT^{3-}]$ directly. The concentration of BT_2^{5-} can then be calculated from the equation $[BT_2^{5-}] = (K_2/K_1)[BT^{3-}]^2/[B^-]$. Finally, the concentration MBT_2^{3-} can be determined from the difference of the integration of the 1:2 peak and the above result. The approximation is validated by the final results of the calculation which show $[MBT^-]$ to be <1% of $[BT^{3-}]$ in all cases. This result is consistent with the observed independence of the 1:1 peak as a function of $(M^{2+})_0$.

All results are presented in Table 1. Experiments were carried out over a wide range of reactant concentrations in order to establish the reaction stoichiometry of the ternary complex. Only one metal ion is bound per bis(borotartrate) complex ion under our experimental conditions. The distribution of species of the $Ca^{2+}/B(OH)_4^-/L$ -tartrate system as a function of total calcium ion concentrations is shown in Figure 2.

The stability constant K_{MBT_2} (eq 6) represents metal ion binding by the bis(borotartrate) ionophore, and K_{ex} (eq 7) is a measure of the synergic effect observed in this chemistry. A large K_{ex} value represents the enhanced binding of M^{2+} to BT_2^{5-} rather than T^{2-} . K_{ex} is as large as 10^3 in the $Ca^{2+}/B(OH)_4^-/L$ -tartrate system.

The ^{11}B NMR results for the addition of Mg^{2+} to the borate/L-tartrate system are dramatically different compared with those for addition of Ca^{2+} and Sr^{2+} . Instead of the 1:2 peak (BT_2^{5-}) growing relative to the other two peaks in the spectrum with increased Mg^{2+} concentration, both complex peaks, 1:1 (BT^{3-}) and 1:2 (BT_2^{5-}), shrink relative to the free borate peak (B^-). Additionally, there is no metal ion induced shift or line broadening caused by Mg^{2+} addition. These results can be interpreted by assuming that Mg^{2+} preferentially coordinates to T^{2-} over BT^{3-} and BT_2^{5-} . Therefore, K_{MBT_2} and K_{MBT} must be less than K_{MT} , and K_{ex} must be less than 1. Since no synergic effect was observed, no further analysis of this system was undertaken.

Discussion

MBT_2^{3-} : Metal Ion Specificity. The order of stability constants (K_{MT}) for the M^{2+}/L -tartrate reaction is $Mg^{2+} < Ca^{2+} > Sr^{2+}$. This order is common for α -hydroxy carboxylates,

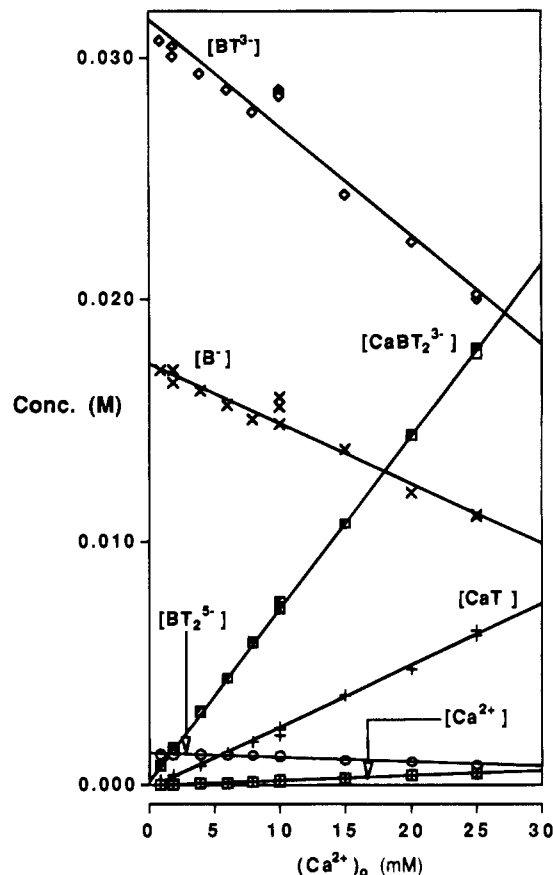


Figure 2. Distribution of species at equilibrium for the Ca^{2+} /borate (0.050 M)/L-tartrate (0.40 M) system as a function of total calcium concentration $(Ca^{2+})_0$. pH = 11.5; $\mu = 1.5$ M (KNO_3); $T = 298$ K. $[T^{2-}]$ and $[CaBT^-]$ are omitted for clarity.

and a thermodynamic explanation has been given for the result.¹⁸ In the presence of borate, the order of stability constants is qualitatively the same but quantitatively very different: $Mg^{2+} \ll Ca^{2+} > Sr^{2+}$. While $K_{MBT_2} < K_{MT}$ for Mg^{2+} , both Ca^{2+} and Sr^{2+} have greatly enhanced binding to BT_2^{5-} relative to T^{2-} . This synergic effect is reflected in K_{ex} , which reaches a value of 1.0×10^3 in the case of Ca^{2+} . These results differ from the qualitative conclusions of Peters and co-workers in just two respects: (1) While we agree that Ca^{2+} and Sr^{2+} behave very similarly to one another, we find that Mg^{2+} behaves quite differently with tartrate and cannot be grouped in the same class^{5d,19} as Ca^{2+} and Sr^{2+} . (2) Tartrate clearly displays a synergic effect^{5e} as do other polyhydroxy carboxylates.

The magnitude of K_{MBT_2} for Ca^{2+} can be compared with the binding of Ca^{2+} to other ligands. With macrobicyclic ligands such as cryptands, Ca^{2+} binds with exceptionally high stability constants when there is a best fit of Ca^{2+} to the ligand cavity. For Ca^{2+} , this occurs with the [221] cryptand, and the equilibrium constant for $Ca^{2+}/221$ cryptate formation is slightly less²⁰ than 10^7 . Stability constants are often much less with multidentate, but not macrocyclic, ligands.²¹ The Ca^{2+} /citrate stability constant,²² for example, is 4.3×10^3 , and this is 1 order of magnitude less than K_{CaBT_2} . The binding of Ca^{2+} with the BT_2^{5-} complex is, in fact, only slightly less strong than the

(18) Aruga, R. *Inorg. Chem.* **1980**, *18*, 2895.

(19) Reference 5d deals with glucarate, not tartrate. In that paper, Mg^{2+} , Ca^{2+} , and Sr^{2+} are grouped in the same class. That is clearly not the case here.

(20) Lehn, J. M.; Sauvage, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 6700.

(21) Of course, multidentate ligands such as EDTA have quite high stability constants with Ca^{2+} (see ref 13, p 194).

(22) Pearce, K. N. *Aust. J. Chem.* **1980**, *33*, 1511.

(16) Kereichuk, A. S.; Mokhnatova, N. V. *Russ. J. Inorg. Chem. (Engl. Transl.)* **1976**, *21*, 651.

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recently reported "unusually strong binding of Ca^{2+} ions by the novel antibiotic squalastatin-1".²³

The binding of Ca^{2+} (and Sr^{2+}) to BT_2^{5-} is exceptional, and one other aspect of the chemistry should be mentioned. Since BT_2^{5-} complex formation is pH dependent, metal ion binding is clearly a strong function of pH. BT_2^{5-} is formed in alkaline media. As the pH is lowered, dissociation of BT_2^{5-} occurs and synergic metal ion binding is no longer possible. We have previously discussed the pH dependence of borate complex ion formation,^{6d,7a} and an extensive discussion of the coordination chemistry of polyhydroxy carboxylates has been presented by Peters and coworkers.²⁴ This latter work explicitly discusses the linkage isomerism of polyhydroxy carboxylates with borate ion. Coordination in base occurs only via the diol functionality, but in acidic solution coordination to boron occurs via one carboxylate oxygen and one hydroxyl oxygen.

The behavior of Mg^{2+} with BT_2^{5-} is similar to its behavior with the [221] cryptand. The stability constant for $Mg^{2+}/221$ cryptate formation is at least 5 orders of magnitude less than those for Ca^{2+} and Sr^{2+} complex formation with 221.²⁰ Since metal ion cryptate chemistry is generally so clearly related to the complementarity of cation radius with cryptand cavity size, a molecular mechanics study of BT_2^{5-} was carried out to gain some understanding of the metal ion binding site.

Metal Ion Binding Site in MBT_2^{3-} . Molecular mechanics (MM2)²⁵ calculations were performed on BT_2^{5-} (L-tartrate) in order to understand possible reasons for the metal ion specificity. The energy-minimized structure is shown in Figure 3a. The two carboxylate groups in each tartrate moiety are necessarily oriented on opposite sides of each borate ester ring. Simply placing a metal ion in this structure in such a way as to give the largest number of oxygen donor atoms with acceptable metal-oxygen distances provides the structure shown in Figure 3b for $CaBT_2^{3-}$. BT_2^{5-} functions as a terdentate ligand with Ca^{2+} being bound to two carboxylate oxygens and one borate oxygen. The Ca^{2+} -carboxylate oxygen distances are each 2.55 Å, and the Ca^{2+} -borate oxygen distance is 2.43 Å. Additional coordination sites on Ca^{2+} are occupied by water molecules (not shown). All other potential oxygen donor atoms are much too far away for effective coordination to Ca^{2+} .

The binding of Ca^{2+} to carboxylate groups is a subject of continuing structural investigation, and several types of coordination have been described.²⁶ The Ca^{2+} /tartrate structure²⁷ shows an eight-coordinate Ca^{2+} and an average Ca^{2+} -oxygen distance of 2.47 Å. Ca^{2+} -oxygen distances in the structure range from 2.39 to 2.54 Å. The proposed $CaBT_2^{3-}$ structure (Figure 3b) is entirely consistent with these results. The participation of borate oxygens in metal ion coordination has been shown in the crystal structure of a K^+ /boromaleate complex.²⁸ A similar structure has been previously proposed for Na^+ /borotartrate by Peters and co-workers.^{5f} The $SrBT_2^{3-}$ complex has essentially the same structure as $CaBT_2^{3-}$, but Sr^{2+}

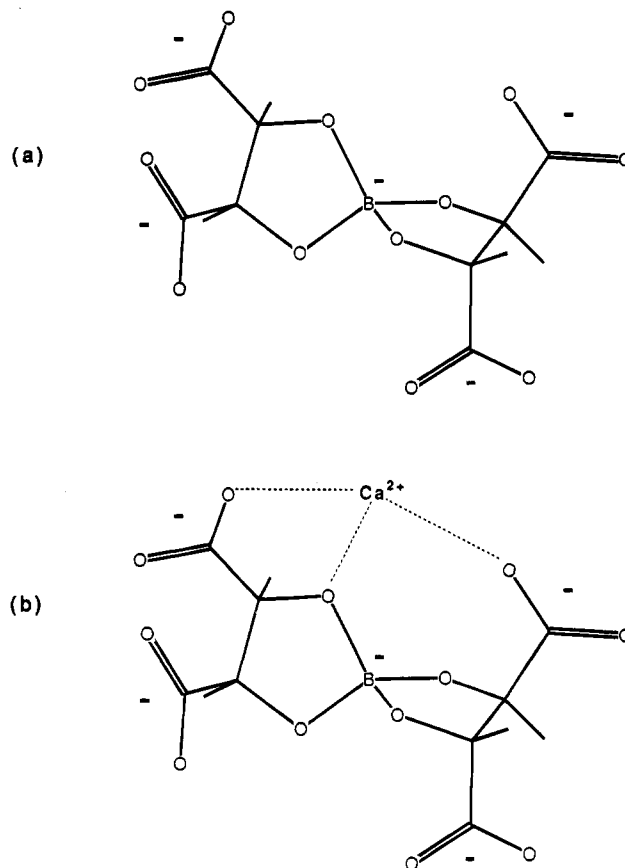


Figure 3. (a) MM2 energy-minimized structure for the BT_2^{5-} (L-tartrate) ionophore. (b) Proposed terdentate Ca^{2+} -binding site of BT_2^{5-} (L-tartrate).

must be moved away slightly to accommodate its larger radius²⁹ compared with that of Ca^{2+} . The decreased electrostatic interaction may account in part for the slight preference for Ca^{2+} over Sr^{2+} shown by BT_2^{5-} .

Given the structure of BT_2^{5-} (Figure 3a), there is no way to accommodate the much smaller Mg^{2+} ion and maintain coordination to three oxygen donor atoms in BT_2^{5-} . While Ca^{2+} -oxygen distances in various carboxylate complexes show a substantial range^{26b} with many examples between 2.3 and 2.6 Å, the great majority of Mg^{2+} -oxygen distances fall in a much narrower range^{26b} between 2.0 and 2.1 Å. At these distances, Mg^{2+} coordination can occur with at most two oxygen donor atoms in BT_2^{5-} , and as a result, $MgBT_2^{3-}$ is much less stable than its Ca^{2+} and Sr^{2+} analogs. Similarly, since BT^{3-} provides only one carboxylate oxygen donor atom which is available for metal ion coordination, the various MBT^- complex ions are much less stable than the MBT_2^{3-} ternary complexes.

MM2 calculations²⁵ were also done on BT_2^{5-} (*meso*-tartrate). The major structural difference is that both carboxylates in each tartrate are necessarily oriented on the same side of each borate ester ring. This does not change the metal ion binding site in any substantial way, nor does it bring the pendant (uncoordinated) carboxylate groups appreciably closer to the metal ion. As a result there is not much difference in K_{CaBT_2} for the two tartrate isomers.

Borotartrate Equilibrium Constants. Although the K_{CaBT_2} values are almost the same for L-tartrate and *meso*-tartrate, there is a measurable difference in K_1 values, with L-tartrate being favored by a factor of 3 over *meso*-tartrate. An explanation

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(28) Mariezcurrena, R. A.; Rasmussen, S. E. *Acta Crystallogr., Sect. B* **1973**, 29, 1035.

(29) In the Sr^{2+} /tartrate crystal structure²² the average Sr^{2+} -oxygen distance is 2.65 Å.

for this kind of result has been presented^{4d} in which the difference is attributed to the greater repulsion experienced by pendant carboxylate groups which are in a *gauche* conformation (*meso*-tartrate) as opposed to an *anti* conformation (L-tartrate).

On the other hand, models show that interligand repulsions in BT_2^{5-} are greater in the bis(L-tartrate) complex than they are in the bis(*meso*-tartrate) complex. This is because the pendant carboxylates on the two tartrate ligands are necessarily quite far from one another in BT_2^{5-} (*meso*-tartrate), but there is at least one close approach of carboxylate groups on different tartrates in BT_2^{5-} (L-tartrate). The greater interligand repulsion in BT_2^{5-} (L-tartrate) may account for the fact that K_2 values for L-tartrate and *meso*-tartrate are quite similar.

Complex Stoichiometry. Over the range of concentrations we have used, only one metal ion is bound per BT_2^{5-} complex ion. This is supported directly by the results for Ca^{2+} presented in Figure 2. The solid lines are calculated on the basis of the stability constants determined in this study (Table 1). The various points shown are experimental results. $[\text{B}^-]$, $[\text{BT}^{3-}]$, $[\text{BT}_2^{5-}]$, and $[\text{CaBT}_2^{3-}]$ are determined from the ^{11}B NMR integration and mass balance as described above. K_{MT} and mass balance are used to determine $[\text{CaT}]$ and $[\text{Ca}^{2+}]$. The excellent agreement between calculation and experiment validates the reaction scheme and the stability constants.

NMR Chemical Shifts. At low pH (~ 2) the borotartrate complex ion has tartrate ligands which are coordinated to the boron center via one carboxylate oxygen and one α -hydroxyl oxygen.^{6i,24} This complex ion has a chemical shift of -9.4 ppm.³⁰ In this species the boron nucleus experiences a more shielded environment (upfield shift) compared with the BT_2^{5-} complex in base, which is coordinated exclusively via the 2,3-diol linkage (-8.5 ppm). This shows that the ^{11}B NMR chemical shift of the 1:2 (BT_2^{5-}) complex is sensitive to changes

in the electronic environment of the boron nucleus. The observed downfield metal ion induced shift found in Figure 1 is in accord with these ideas. Coordination of M^{2+} by BT_2^{5-} removes electron density from the boron center, leaving it more deshielded in MBT_2^{3-} relative to BT_2^{5-} . In general the ^{11}B NMR chemical shift gives an accurate picture of the electronic environment of the boron center in these systems, with upfield shifts corresponding to a more shielded environment. An experimental correlation between ^{11}B NMR chemical shift and apparent charge density at the boron center has been documented.³¹

Conclusion

In this work, the first quantitative analysis of metal ion binding by borotartrate complexes is presented. The conclusions of this study are as follows: (1) Mg^{2+} binds preferentially to free tartrate, T^{2-} , and shows little if any interaction with the borotartrate complex ions (BT^{3-} and BT_2^{5-}). (2) Both Ca^{2+} and Sr^{2+} bind preferentially to BT_2^{5-} with Ca^{2+} binding slightly better than Sr^{2+} . (3) The proposed Ca^{2+} and Sr^{2+} binding site on BT_2^{5-} is one in which M^{2+} is coordinated to two carboxylate oxygens (one from each of the tartrate ligands) and one borate ester ring oxygen. (4) The observed metal ion specificity of the BT_2^{5-} complex ($\text{Mg}^{2+} \ll \text{Ca}^{2+} > \text{Sr}^{2+}$) is consistent with such a binding site. (5) The absolute configuration of the ligand (L-tartrate vs *meso*-tartrate) does not significantly alter the binding properties of BT_2^{5-} .

Acknowledgment. The support of the PSC/CUNY Faculty Research Award Program is gratefully acknowledged.

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