

Table III. Test of Hypothesis a, $\Delta H_t^\circ([M^+222]) = \Delta H_t^\circ(222)$, and Hypothesis b, $\Delta H_t^\circ([M^+222]) = 0$

| transfer | $\Delta H_t^\circ([M^+222])/\text{kcal mol}^{-1}$ | | | |
|-----------------------|---|-----|----------------------|-----------------------|
| | calcd | | obsd ^a | |
| | (a) | (b) | [K ⁺ 222] | [Ag ⁺ 222] |
| water to | | | | |
| MeOH | 13.9 | 0.0 | 4.1 | 1.2 |
| DMF | 14.2 | 0.0 | 3.6 | 3.6 |
| Me ₂ SO | 14.4 | 0.0 | 3.1 | 2.9 |
| PC | 13.6 | 0.0 | 3.4 | 0.3 |
| MeCN | 10.7 | 0.0 | -1.0 | -2.7 |
| Me ₂ SO to | | | | |
| water | -14.4 | 0.0 | -3.1 | -2.9 |
| MeOH | -0.5 | 0.0 | 1.0 | -1.7 |
| DMF | -0.2 | 0.0 | 0.5 | 0.7 |
| PC | -0.8 | 0.0 | 0.3 | -2.6 |
| MeCN | -3.7 | 0.0 | -4.1 | -5.6 |

^a Using the single-ion Ph₄As⁺/Ph₄B⁻ assumption.

assumption a does not agree very well with the Ph₄As⁺/Ph₄B⁻ assumption. In Table III we also test assumption b that $\Delta H_t^\circ([M^+222]) = 0$. Without detailing the arguments again, it is evident that this assumption yields values that are also quite far from those calculated on the Ph₄As⁺/Ph₄B⁻ assumption.

In terms of enthalpies, it therefore seems that the cryptate assumptions (a) and (b) will yield single-ion values that are not the same as those obtained by using the Ph₄As⁺/Ph₄B⁻

assumption. This result by itself does not disprove assumptions a or b but merely indicates that these assumptions are not compatible with another extrathermodynamic assumption. However, if either assumption a or assumption b is applied to the determination of single-ion ΔH_t° values, unless the identity (2) is obeyed, different numerical values will be assigned depending on the actual metal cation used. Thus, as pointed out in the Introduction, if assumptions a and b are to be generally valid, $\Delta H_t^\circ([M_1^+222])$ must equal $\Delta H_t^\circ([M_2^+222])$. As can be seen from Tables II and III, we show that $\Delta H_t^\circ([K^+222])$ may or may not be the same as $\Delta H_t^\circ([Ag^+222])$, depending on the particular solvents studied. The possibility that for any two given cryptates $\Delta H_t^\circ([M_1^+222]) \neq \Delta H_t^\circ([M_2^+222])$ must surely be taken into account in any future application of cryptate assumptions to the assignment of single-ion enthalpies of transfer.

We think that our most important finding is that, generally, values of $\Delta H_t^\circ([M^+222])$ depend on the metal cation, M⁺, embedded in the cryptand. Thus the cryptand does not shield the cation from the solvent, and any cryptate hypothesis that depends on the explicit or implicit assumption that $\Delta H_t^\circ([M_1^+L]) = \Delta H_t^\circ([M_2^+L])$ is not likely to be generally valid. The same conclusions can be drawn in terms of free energy for the water to methanol transfer; at the moment we are investigating whether or not cryptate hypotheses may be valid for transfers between other solvents, in terms of free energy.

Registry No. Na⁺222, 32611-94-2; K⁺222, 32611-95-3; Ag⁺222, 57692-62-3; 222, 23978-09-8.

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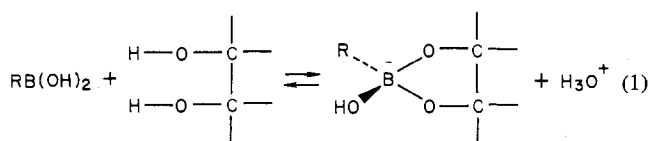
Dynamics of Boron Acid Complexation Reactions. Formation of 1:1 Boron Acid-Ligand Complexes

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Boron acids form 1:1 complexes with a variety of bidentate chelating ligands according to the equation $\text{RB(OH)}_2 + \text{H}_2\text{L} \rightleftharpoons \text{RB(OH)L}^- + \text{H}_3\text{O}^+$. Four boron acids (*m*-NO₂PhB(OH)₂, PhB(OH)₂, B(OH)₃, CH₃B(OH)₂) have been studied. Ten different ligands have been examined. Stability constants for the reactions were determined by pH titration methods, and the kinetics were done by temperature jump at $\mu = 0.1$ M (KNO₃) and 25 °C. The stability constants are affected by the acidities of both the boron acid and ligand. The stability constants increase as the ligand and boron acid become more acidic. Various kinetic pathways are possible. Trigonal boron acids, RB(OH)₂, can react with either fully protonated ligands or ligand anions. The pattern of reactivity is different for each case. The rate constants for the reactions of fully protonated ligands vary systematically with both ligand acidity and boron substituent. This is discussed in terms of a mechanism which involves proton transfer. The ligand anions do not display a simple correlation with any single ligand parameter, and their reactivities are discussed in terms of a number of ligand-specific effects. Borate anions, RB(OH)₃⁻, react with high rate constants with fully protonated ligands and with somewhat lower rate constants with ligand anions. Possible reasons for this are discussed.

Trigonal boron acids, RB(OH)₂, form anionic four-coordinate complexes with bidentate chelating ligands according to eq 1. Ligands which participate in this type of reaction



include polyols,^{1,2} *o*-diphenols,¹⁻³ *o*-hydroxy acids,⁴ α -hy-

droxycarboxylic acids,⁵⁻⁷ and dicarboxylic acids.⁸⁻¹⁰ For a particular boron acid, the stability constants for reactions with a series of ligands show a general increase as the acidity ($\text{p}K_{\text{a}1}$) of the ligand increases. We recently reported³ in a study of

(1) G. L. Roy, A. L. Laferriere, and J. O. Edwards, *J. Inorg. Nucl. Chem.*, **4**, 106 (1957), and earlier references therein.

(2) J. P. Lorand and J. O. Edwards, *J. Org. Chem.*, **24**, 769 (1959).
 (3) R. Pizer and L. Babcock, *Inorg. Chem.*, **16**, 1677 (1977).
 (4) R. Larsson and G. Nunziata, *Acta Chem. Scand.*, **26**, 1503 (1972).
 (5) N. Vermaas, *Recl. Trav. Chim. Pays-Bas*, **51**, 955 (1932).
 (6) K. Kustin and R. Pizer, *J. Am. Chem. Soc.*, **91**, 317 (1969).
 (7) S. Friedman, B. Pace, and R. Pizer, *J. Am. Chem. Soc.*, **96**, 5381 (1974).
 (8) J. Boeseken, *Recl. Trav. Chim. Pays-Bas*, **61**, 82 (1942).
 (9) S. Friedman and R. Pizer, *J. Am. Chem. Soc.*, **97**, 6059 (1975).
 (10) G. Lorber and R. Pizer, *Inorg. Chem.*, **15**, 978 (1976).

Table I. Stability Constants of Boron Acid Complexes

| ligand | $pK_a(\text{ligand})$ | $m\text{-NO}_2\text{PhB}(\text{OH})_2$, $pK_a = 6.96$ | $\text{PhB}(\text{OH})_2$, $pK_a = 8.72$ | $\text{B}(\text{OH})_3$, $pK_a = 8.98$ | $\text{CH}_3\text{B}(\text{OH})_2$, $pK_a = 10.40$ |
|----------------------------|-----------------------|---|--|--|--|
| oxalic acid ^a | 1.04 | | 3.2 | | |
| malonic acid ¹⁰ | 2.59 | | 2.6×10^{-2} | | |
| salicylic acid | 2.83 | 1.1 | 6.8×10^{-2} | 1.1×10^{-2} ^a | 4.5×10^{-3} |
| tartaric acid ⁶ | 2.89 ^b | | | 1.8×10^{-2} ^c | |
| mandelic acid | 3.22 | 1.9×10^{-1} | 1.5×10^{-2} | | 2.1×10^{-3} |
| lactic acid ⁷ | 3.70 | | 3.7×10^{-3} | | |
| 4-nitrocatechol | 6.69 | 1.6×10^{-2} | 9.5×10^{-4} ^d | 1.5×10^{-4} ^d | 4.3×10^{-5} |
| catechol | 9.27 | | 4.7×10^{-5} ^d | 1.1×10^{-5} ^d | 1.6×10^{-6} |
| 4-methylcatechol | 9.39 | 5.5×10^{-4} | 3.0×10^{-5} ^d | 6.3×10^{-6} ^d | |
| mannitol | 13.5 ^e | | 5.3×10^{-6} ^d | | |

^a Reference 20. ^b V. Frei, *Collect. Czech. Chem. Commun.*, **30**, 1402 (1965). ^c L. I. Katzin and E. Gulyas, *J. Am. Chem. Soc.*, **88**, 5209 (1966); see also ref 6. ^d Reference 3. ^e J. Thamsen, *Acta Chem. Scand.*, **6**, 270 (1952).

the reaction kinetics that the variation in stability constant with ligand acidity is reflected in both the forward and reverse rate constants. As the ligand becomes more acidic, the forward rate constants display a general increase and the reverse rate constants decrease. This result is consistent with the idea that proton transfer is involved in the transition state.

Possible additional mechanistic pathways include the reactions of ligand anions with trigonal boron acids and the reactions of tetrahedral borate anions, $\text{RB}(\text{OH})_3^-$, with both fully protonated ligands and ligand anions. In all cases the same complex is formed as shown in eq 1. While we have previously discussed some aspects of the reactions of ligand anions, many mechanistic questions remain. With respect to the reactions of the borate anions, no kinetic results have yet been reported. This study addresses these questions.

An additional problem concerns the effect of the acidity of the boron acid on the reaction. While ligands of widely varying pK_a have been studied, the range of acidities of boron acids previously examined has been quite limited. This work greatly extends the range of boron acids which has been studied.

Our previous work has shown a striking similarity between the complexation reactions of boron acids and those of oxoanions such as molybdate and tungstate.¹¹ The understanding of the mechanism of the boron acid reactions will shed considerable light on the reaction mechanisms and patterns of reactivity displayed by metal oxoanions. Boron acids and their complexes have also found considerable recent application¹²⁻¹⁴ in various studies of enzyme reactions both as inhibitors in kinetic studies and as transition-state analogues.

Experimental Section

Three boron acids were used in this study: methylboronic acid (Alfa), phenylboronic acid (Alfa), and *m*-nitrophenylboronic acid (K&K). Several ligands were examined: salicylic acid (Fisher), mandelic acid (Fisher), 4-nitrocatechol (Aldrich), catechol (Fisher), and 4-methylcatechol (Aldrich). All of the reagents with the exception of 4-methylcatechol were used without further purification. That the reagents required no further purification was determined by titration with standard 0.1 N NaOH. Solid 4-methylcatechol was vacuum-distilled and the purity of the resultant white crystalline material checked by pH titration.

Stability constants for complex formation and the acid dissociation constants of both the ligands and boron acids were determined by pH titration methods. Kinetic studies were all performed on the temperature-jump instrument described previously.⁷ The traces obtained experimentally were plotted semilogarithmically. In all cases simple exponentials were observed. Relaxation times obtained were averages of at least three traces, and the error is within $\pm 10\%$. Blank

solutions of the ligands and of the various boron acids were prepared and showed no effect at any pH over the entire time range accessible to the instrument. Depending upon the pH of the solution, either orange IV, bromophenol blue, or chlorophenol red was used to monitor the reaction.

All experiments were carried out at 25 °C and 0.1 M (KNO_3) ionic strength.

Stability Constants

The pK_a 's of salicylic acid, mandelic acid, methylboronic acid, and *m*-nitrophenylboronic acid were determined by titration with standard base. The results are salicylic acid $pK_a = 2.83$ (lit.¹⁵ 2.69), mandelic acid $pK_a = 3.22$ (lit.¹⁶ 3.41), *m*-nitrophenylboronic acid $pK_a = 6.96$ (lit.¹⁷ 7.23), and methylboronic acid¹⁸ $pK_a = 10.40$. pK_a 's for all of the other species studied have been reported previously and are included in Table I.

Stability constants for the various systems studied were determined by two independent pH titration methods. Solutions of boron acid and ligand were titrated with standard base in the usual way. Alternatively, solutions of one reactant at a particular pH were titrated with solutions of the other reactant also adjusted to the same initial pH. Equations for the calculation of stability constants from these data are found in a previous paper.^{9,19} Stability constants from this and other studies are collected in Table I.

For any particular boron acid, the stability constants increase as the ligands become more acidic. This is consistent with the trends previously observed for both $\text{PhB}(\text{OH})_2$ and $\text{B}(\text{OH})_3$. However, it is now clear that the acidity of the boron acid has a precisely similar effect on the stability constants. For any particular ligand, the stability constants increase as the boron acids become more acidic. In Table I as presented, the highest stability constants are in the upper left corner and

- (11) K. Gilbert and K. Kustin, *J. Am. Chem. Soc.*, **98**, 5502 (1976).
 (12) R. N. Lindquist and C. Terry, *Arch. Biochem. Biophys.*, **160**, 135 (1974).
 (13) G. P. Hess, D. Seybert, A. Lewis, J. Spoonhower, and R. Cookingham, *Science*, **189**, 384 (1975).
 (14) S. L. Johnson and K. W. Smith, *J. Org. Chem.*, **42**, 2580 (1977).

- (15) F. Secoo and M. Venturini, *Inorg. Chem.*, **14**, 1978 (1975); value reported at $\mu = 0.1$ M (NaClO_4). See also L. G. Bray, J. F. J. Dippy, S. R. C. Hughes, and L. W. Laxton, *J. Chem. Soc.*, 2405 (1957); $pK_a = 3.00$ at $\mu = 0$ and 25 °C.
 (16) W. H. Banks and C. W. Davies, *J. Chem. Soc.*, 73 (1938); value reported at $\mu = 0$.
 (17) J. Juillard and N. Gueguen, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **264**, 259 (1967); value reported at $\mu = 0$.
 (18) Alkylboronic acids are much less acidic than arylboronic acids: D. Y. Yabroff, G. E. K. Branch, and B. Bettmann, *J. Am. Chem. Soc.*, **56**, 1850 (1934).
 (19) The equations in ref 9 were slightly modified to take into account the $\text{RB}(\text{OH})_2/\text{RB}(\text{OH})_3^-$ equilibrium. This was necessary for *m*-nitrophenylboronic acid, the most acidic of the boron acids studied.
 (20) A. Queen, *Can. J. Chem.*, **55**, 3035 (1977). There is a discrepancy of about a factor of 3 between the thermodynamically determined stability constant and the kinetically determined (k_f/k_r) stability constant in this work (Tables I and II). The author attributes this to the presence of a complex in which only one ligand donor atom is bound to a four-coordinate boron. None of our work, either thermodynamic or kinetic, supports this conclusion. The results are, however, in general agreement with the trends in both stability constants and rate constants which are reported here.

Table II. Rate Constants for the Reactions of $\text{RB}(\text{OH})_2$ with Fully Protonated Ligands

| ligand | $m\text{-NO}_2\text{PhB}(\text{OH})_2$ | | $\text{PhB}(\text{OH})_2$ | | $\text{B}(\text{OH})_3$ | | $\text{CH}_3\text{B}(\text{OH})_2$ | |
|----------------------------|--|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|
| | $k_f, \text{M}^{-1} \text{s}^{-1}$ | $k_r, \text{M}^{-1} \text{s}^{-1}$ | $k_f, \text{M}^{-1} \text{s}^{-1}$ | $k_r, \text{M}^{-1} \text{s}^{-1}$ | $k_f, \text{M}^{-1} \text{s}^{-1}$ | $k_r, \text{M}^{-1} \text{s}^{-1}$ | $k_f, \text{M}^{-1} \text{s}^{-1}$ | $k_r, \text{M}^{-1} \text{s}^{-1}$ |
| oxalic acid ⁹ | | | 2.0×10^3 | 6.2×10^2 | | | | |
| malonic acid ¹⁰ | | | 3.5×10^2 | 1.3×10^4 | | | | |
| salicylic acid | 6.5×10^2 | 5.9×10^2 | 2.3×10^2 | 3.3×10^3 | 1.4×10^2 ^a | 4.5×10^3 ^a | 5.5×10 | 1.2×10^4 |
| tartaric acid ⁶ | | | | | 4.8×10^2 | 2.6×10^4 | | |
| mandelic acid | 2.5×10^3 | 1.3×10^4 | 1.8×10^2 | 4.7×10^4 | | | | |
| lactic acid | | | 1.4×10^2 | 3.8×10^4 | | | | |
| 4-nitrocatechol | 2.0×10^3 | 1.3×10^5 | 6.5×10^2 ^b | 6.8×10^5 ^b | 2.5×10^2 ^b | 1.7×10^6 ^b | 4.5×10 | 1.0×10^6 |
| catechol | | | 1.1×10^2 ^b | 2.3×10^6 ^b | 6.0×10^2 ^b | 5.4×10^6 ^b | 7.6 | 4.8×10^6 |
| 4-methylcatechol | 1.5×10^3 | 2.7×10^6 | 1.2×10^2 ^b | 4.0×10^6 ^b | 5.4×10^2 ^b | 8.6×10^6 ^b | | |
| mannitol | | | ~ 50 ^b | $\sim 10^7$ ^b | | | | |

^a Reference 20. ^b Reference 3.Table III. Rate Constants for the Reactions of $\text{RB}(\text{OH})_2$ with Ligand Anions

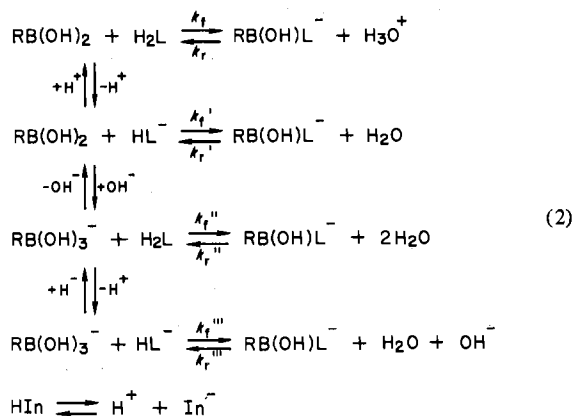
| ligand | $m\text{-NO}_2\text{PhB}(\text{OH})_2$ | | $\text{PhB}(\text{OH})_2$ | | $\text{B}(\text{OH})_3$ | | $\text{CH}_3\text{B}(\text{OH})_2$ | |
|--------------------------|--|-----------------------|-------------------------------------|--------------------------------|-------------------------------------|--------------------------------|-------------------------------------|-----------------------|
| | $k_f', \text{M}^{-1} \text{s}^{-1}$ | k_r', s^{-1} | $k_f', \text{M}^{-1} \text{s}^{-1}$ | k_r', s^{-1} | $k_f', \text{M}^{-1} \text{s}^{-1}$ | k_r', s^{-1} | $k_f', \text{M}^{-1} \text{s}^{-1}$ | k_r', s^{-1} |
| binoxalate ⁹ | | | 3.3×10^2 | 1.0×10 | | | | |
| bimalonate ¹⁰ | | | 1.5×10^2 | 1.5×10 | | | | |
| salicylate | 1.3×10^2 | 1.7×10^{-1} | 4.5×10 | 1.0 | 4.0×10^a | 4.0^a | 5.0×10 | 1.7×10 |
| tartrate ⁶ | | | | | 2.2×10^2 | 4.3×10 | | |
| mandelate | 1.5×10^4 | 4.8×10 | 1.3×10^3 | 5.2×10 | | | | |
| lactate ⁷ | | | 1.5×10^3 | 8.3×10 | | | | |
| 4-nitrocatecholate | | | 7.0×10^4 ^b | 1.5×10^5 ^b | 5.0×10^4 ^b | 6.8×10^5 ^b | 5.0×10^4 | 2.4×10^2 |

^a Reference 20. ^b Reference 3.

the lowest stability constants are in the lower right corner.

Kinetic Results and Treatment of Data

There are four possible reaction pathways which are indicated in eq 2.



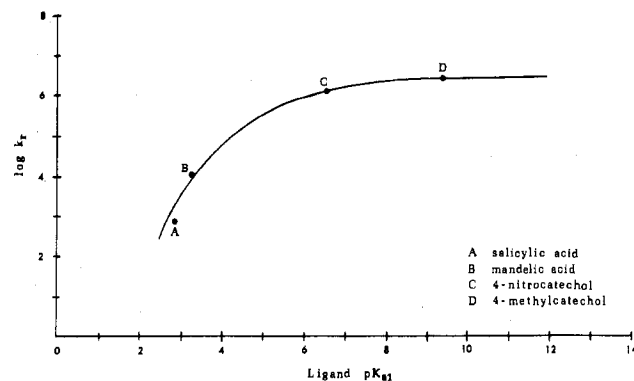
The protolytic reactions of indicator, boron acid, and ligand are all very much faster than the slower complexation reactions. Therefore, only one relaxation time is observed for this scheme, and it is characteristic of the boron acid complexation reactions. Assuming that the protolytic steps are in equilibrium with respect to the complexation pathways, we derived expression 3 the relaxation time. Here k_f , k_f' , k_f'' , and k_f''' refer

$$\begin{aligned}
 1/\tau = & k_f[S(\overline{\text{HB}}) + \overline{[\text{H}_2\text{L}]} + \\
 & (1/K)(R[\overline{\text{C}x^-}] + Q[\overline{\text{H}^+}]) + k_f'((Q-S)\overline{[\text{HB}]} + \overline{[\text{HL}^-}] + \\
 & K_{\text{H}_2\text{L}}Q/K) + k_f''S[\overline{\text{B}^-}] + (Q-1)\overline{[\text{H}_2\text{L}]} + K_{\text{HB}}Q/K + \\
 & k_f'''((Q-S)\overline{[\text{B}^-}] + (Q-1)\overline{[\text{HL}^-}] + \\
 & (K_{\text{H}_2\text{L}}K_{\text{HB}}/KK_w)(Q[\overline{\text{OH}^-}] - R[\overline{\text{OH}^-}][\overline{\text{C}x^-}]/[\overline{\text{H}^+}]) \quad (3)
 \end{aligned}$$

to the mechanistic pathways indicated in the reaction scheme, HB is trigonal $\text{RB}(\text{OH})_2$, B⁻ is tetrahedral $\text{RB}(\text{OH})_3^-$, Cx⁻ is the complex, $K_{\text{H}_2\text{L}}$ and K_{HB} are the acid dissociation constants for ligand and boron acid, and K is the stability constant for the reaction according to eq 1. The other terms in this

Table IV. Rate Constants for the Reactions of $m\text{-NO}_2\text{PhB}(\text{OH})_2$ and $m\text{-NO}_2\text{PhB}(\text{OH})_3^-$ with Salicylic Acid and Mandelic Acid

| ligand | $k_f, \text{M}^{-1} \text{s}^{-1}$ | $k_f', \text{M}^{-1} \text{s}^{-1}$ | $k_f'', \text{M}^{-1} \text{s}^{-1}$ | $k_f''', \text{M}^{-1} \text{s}^{-1}$ |
|----------------|------------------------------------|-------------------------------------|--------------------------------------|---------------------------------------|
| salicylic acid | 6.5×10^2 | 1.3×10^2 | 1.0×10^6 | $< 10^4$ |
| mandelic acid | 2.5×10^3 | 1.5×10^4 | 2.4×10^7 | 1.5×10^4 |

Figure 1. Reactions of $m\text{-NO}_2\text{PhB}(\text{OH})_2$ with H_2L .

expression are defined in the Appendix.

The pH dependence of the relaxation time permits the determination of the various rate constants in eq 3. For example, for ligands of relatively high pK_a (e.g., the catechols), only the first term in the expression is significant at low pH (~ 2). k_f can therefore be accurately determined under these experimental conditions. As the pH is increased, the relaxation data are fit to a two-term expression and k_f' is also evaluated. All of the various systems studied were analyzed in this way. Tables II and III contain the rate constants for the reactions of fully protonated ligands and for the reactions of ligand anions with trigonal boron acids.

Since all of the kinetic experiments were confined to pH ~ 6 and below, there was generally no contribution to the relaxation time from the terms k_f'' and k_f''' . However, the pK_a of m -nitrophenylboronic acid is sufficiently low that k_f'' and k_f''' could be evaluated in some cases. For mandelic acid, experiments were successfully carried out up to pH ~ 6 .

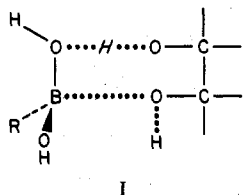
Therefore, both k_f'' and k_f''' could be determined. The relaxation times for the salicylic acid system were too long to be measured at this pH, and data were collected only up to pH ~ 4 . Consequently, it was not possible to obtain a precise value for k_f''' but an upper limit could be set. These results are presented in Table IV.

The error associated with all of the reported rate constants is $\pm 10\%$.

Discussion

Reactions of Fully Protonated Ligands. Inspection of the results in Table II demonstrates that the mechanism of the complexation process is ligand dependent. For any particular boron acid, the stability constants for complex formation increase with increasing ligand acidity and this is reflected in both the forward and reverse rate constants for the reactions. The significance of proton transfer in these reactions is immediately suggested by the correlation of the reverse rate constants with ligand pK_a . This is displayed in Figure 1 for the reactions of $m\text{-NO}_2\text{PhB(OH)}_2$. The fact that each of the four boron acids that have now been examined shows the same pattern of reactivity with a series of ligands strongly supports the idea that all of the reactions proceed via a common mechanism.

A plausible transition state for these reactions is I. The



proton which is transferred is italic. In the forward direction it is transferred from the fully protonated ligand to the leaving hydroxide on boron; in the reverse direction it is transferred from the entering water molecule to the leaving ligand. The observed curvature in Figure 1 is consistent with the proposed transition state and is an immediate consequence of the general mechanism for proton transfer advanced by Eigen.²¹ The fact that the forward rate constants do not display such a precise correlation may be due to stereochemical differences among the ligands. This point has been discussed more fully in a previous paper.³

All of the ligands examined lose two protons in the complexation process. One is displaced directly by boron, and the second is transferred to the leaving hydroxide in the closing of the chelate ring. Obviously the ligand can achieve this orientation in two ways. Either of the oxygen donor atoms can be thought of as attacking the boron atom with ring closure occurring via the second ligand donor atom. Since a precise correlation of rate constant with pK_{a1} of the ligand is observed and no dependence²² on pK_{a2} , we have assumed that direct displacement by boron of the less acidic proton in the ligand is a facile process with (rate-limiting) ring closure occurring via the more acidic ligand proton. If the two ligand protons are of nearly the same acidity, the two possible reaction pathways would become kinetically competitive.

Although each of the boron acids displays the same pattern of reactivity with the various ligands, the values of the reaction rate constants and stability constants are dependent upon the substituents on boron. For any particular ligand examined with a series of boron acids of increasing acidity, three consistent trends are observed: (1) The stability constants for

complex formation increase (Table I). (2) The forward rate constants increase (Table II). (3) The reverse rate constants generally²³ decrease (Table II).

There are two arguments which can be advanced to account for these observations. One argument emphasizes the electronegativity of the substituent, and the other centers upon the extent to which the substituent is able to interact with the vacant p_z orbital in the trigonal RB(OH)_2 species.

The effect of an electronegative substituent is to stabilize the reaction product and, to a lesser extent, the transition state by delocalizing the negative charge on boron. In the transition state I there is a nucleophilic attack on boron which results in the boron atom developing a partial negative charge. The formal charge on boron in the complex is minus one. The effect of an electron-withdrawing substituent on boron is to stabilize both the transition state and the complex by delocalizing the negative charge. Since the formal charge on boron is greater in the complex than in the transition state, the complex is stabilized to the greater extent. That is, $\Delta\Delta G^\circ > \Delta\Delta G^\ddagger$.

Although this argument accounts qualitatively for the variation in stability and rate constants for the boron acids with organic substituents (CH_3 , C_6H_5 , and $m\text{-NO}_2\text{C}_6\text{H}_5$), it does not account for all of the observed results. The stability constants are not entirely parallel to the group electronegativities of the substituents (e.g., OH is probably more electronegative²⁴ than C_6H_5). An additional factor to be considered is the interaction of a substituent with the vacant p_z orbital on boron. This interaction stabilizes the trigonal reactant and has no effect on the four-coordinate (sp^3 -hybrid boron) product. This partial multiple-bond character is partly lost in the transition state and does not exist at all in the products. While OH is more electronegative than C_6H_5 , it may also interact more strongly with the boron p_z orbital. This interaction tends to lower the complex stability constants. Since the multiple-bond character is partly lost on going to the transition state, the forward rate constant should also be decreased. These conclusions are consistent with the experimental results for B(OH)_3 and PhB(OH)_2 .

Both of these effects are undoubtedly displayed by each substituent to a different extent.²⁵ The ways in which they modify the potential energy surfaces for the reactions are consistent with the observed kinetic and thermodynamic parameters.

Reactions of Ligand Anions. The common transition state for the reactions of fully protonated ligands is characterized by proton transfer as its most significant and distinctive feature. This proton is not present in the ligand anions, and they display a considerably different pattern of reactivity (Table III).

Most striking is the fact that the reverse rate constants for the reactions of PhB(OH)_2 vary by less than 2 orders of magnitude, and they do not vary in an obvious systematic way. The incoming nucleophile in these reactions is not water but hydroxide. The transition state is similar to I, but the transferred proton is absent. The fact that the reverse rate constants for the anionic reactions are so similar suggests that the boron-oxygen bonds that are being formed and broken in the transition state are of comparable strength in the various systems studied.

The forward rate constants show a general increase as the ligand becomes more basic, but, again, this is not entirely

(21) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964).

(22) pK_{a2} varies by more than 10 units among the ligands, and the variation in the values of pK_{a1} does not parallel the pK_{a2} values.

(23) The only minor exceptions to this trend are for reactions of 4-nitrocatechol and catechol. In these cases the reverse rate constants are $\sim 10^6 \text{ M}^{-1} \text{ s}^{-1}$. The rate constants are close to the maximum values observed for these reactions and are in the region where the curve of $\log k_r$ vs. ligand pK_a is leveling off.

(24) A. F. Clifford, *J. Phys. Chem.*, **63**, 1227 (1959).

(25) This kind of argument has been advanced to account for the variation in boron acid pK_a . See ref 18.

systematic. The general increase in forward rate constant with ligand basicity may be due to the fact that very basic ligands (such as 4-nitrocatecholate) orient solvent about them in such a way as to diminish electrostatic repulsion between the entering anionic donor atom and the leaving OH^- . The leaving OH^- on boron is protonated by an intervening water molecule with an OH^- being injected into solution at a point removed from the reaction site.²⁶

Ring closure via the anionic donor atom is made difficult by the electrostatic repulsion generated by the leaving OH^- . An alternative pathway involving attack on boron by the anionic donor atom with ring closure proceeding via the protonated donor atom is possible, but the high $\text{p}K_{\text{a}2}$ values of some of the ligands would render this a very slow pathway. Since binoxalate and bimalonate are themselves reasonably acidic, it is possible that they do react in this way. ($\text{p}K_{\text{a}2}$ for oxalic acid (3.78) is close to $\text{p}K_{\text{a}1}$ for lactic acid (3.70), and the forward rate constants for the reactions of binoxalate and lactic acid with $\text{PhB}(\text{OH})_2$ differ by only a factor of about 2.) However, this cannot be the general pathway for all of the ligands since a correlation with $\text{p}K_{\text{a}2}$ is not observed.

More detailed discussions of the reactivity of the dicarboxylic acid anions^{9,10} and catecholate anions³ are to be found in our previous work. Three additional mechanistic considerations will be discussed here: the effect of intramolecular hydrogen bonding on the reaction rate, the dependence of reaction rate constants on the acidity of the boron acids, and stacked interactions.

Intramolecular Hydrogen Bonding. Salicylate anion displays the lowest forward rate constants of all of the ligands examined. One reason which can be advanced to account for this is the strong intramolecular hydrogen bond in the ligand. The dicarboxylic acids are other ligands where such effects might be expected to be of importance. In these cases there are four potential oxygen donor atoms, and the complexation reaction may proceed by the nucleophilic attack on boron of one of the oxygens not involved in the hydrogen bond.⁹ In the case of salicylate, nucleophilic attack on boron by the hydroxyl oxygen directly involves the hydrogen bond. This is reflected in the low rate of complex formation.

The boron acids are labile species and bear comparison with labile metal-ion complexation reactions. In this regard, it is interesting to note that the reactions of binoxalate with Ni^{2+} are normal²⁷ whereas those of salicylate are often slow with labile ions. This latter conclusion is one result of the extensive and detailed work of Perlmutter-Hayman and co-workers²⁸ concerning the effects of intramolecular hydrogen bonding on reaction rates.

The Effect of Boron Acid on $\text{p}K_{\text{a}}$. Both salicylate and 4-nitrocatecholate display similar behavior. As the boron acid becomes more acidic, the forward rate constant remains almost unchanged and the reverse rate constant decreases. That the forward rate constant does not vary reflects the fact that the central mechanistic problem is the closure of a chelate ring in the presence of considerable electrostatic repulsion from the leaving OH^- . As this repulsion is independent of the substituent on boron, each ligand undergoes reaction at a rate characteristic of it. Salicylate is slow due to intramolecular hydrogen bonding, and 4-nitrocatecholate is faster for the reasons presented earlier.

The variation in reverse rate constant is similar to that observed for the reactions of the fully protonated ligands discussed previously. In this case, however, the variation in rate constant is quantitatively more precise. From $\text{PhB}(\text{OH})_2$

to $\text{CH}_3\text{B}(\text{OH})_2$, k_r increases by a factor of 17 for salicylate and by a factor of 16 for 4-nitrocatecholate.

Stacked Interactions. Both forward and reverse rate constants for the reactions of lactate with $\text{PhB}(\text{OH})_2$ are somewhat higher than might otherwise be expected. k_r' is the highest value for reactions of $\text{PhB}(\text{OH})_2$. k_r' is high when compared with the reaction of tartrate with $\text{B}(\text{OH})_3$. This observation led us to propose⁷ that an interaction between the delocalized π system in the carboxylate and the phenyl substituent in $\text{PhB}(\text{OH})_2$ is an attractive interaction which stabilizes the transition state. Since this stacked interaction occurs only in the transition state, not in the reactants or products, its effect is felt only in enhanced forward and reverse rate constants, not in stability constants.²⁹ The reactivity of mandelate is similar to that of lactate, and similar considerations apply.

What is at issue here is the reaction of mandelate with $m\text{-NO}_2\text{PhB}(\text{OH})_2$. Both forward and reverse rate constants seem high when compared with other systems. It was noted above that the variation in reverse rate constants for salicylate and 4-nitrocatecholate is quantitatively precise. If this is general for the reactions of ligand anions, predictions can be made about the relative rate constants to be expected for reactions of particular ligands with $m\text{-NO}_2\text{PhB}(\text{OH})_2$ and $\text{PhB}(\text{OH})_2$. The forward rate constant for salicylate on going from $\text{PhB}(\text{OH})_2$ to $m\text{-NO}_2\text{PhB}(\text{OH})_2$ increases by a factor of 3; the reverse rate constant decreases by a factor of 5. The mandelate forward rate constant increases by slightly more than 1 order of magnitude, and the reverse rate constant is almost unchanged. Both the mandelate forward and reverse rate constants are larger by a factor of about 4 than those which might be expected if the relative rate behavior were parallel to that of salicylate.

This analysis suggests that the stacked interaction between the carboxylate and the aromatic substituent on boron is enhanced in $m\text{-NO}_2\text{PhB}(\text{OH})_2$ compared with the interaction in $\text{PhB}(\text{OH})_2$. This is consistent with the fact that the nitro substituent is electron withdrawing. The phenyl ring in $m\text{-NO}_2\text{PhB}(\text{OH})_2$ bears a slight positive charge. Interaction with the negative carboxylate in the transition state results in greater stabilization of the transition state and larger forward and reverse rate constants.

This argument offers an explanation for the observed trends in mandelate rate constants compared with the other systems studied. While dramatic increases in rate constants are not observed, the result does support the contention that stacked interactions may be kinetically significant in this case. In some reactions of transition metal ion complexes, more extended π systems in the reactants have been found to produce²⁹ considerably greater rate enhancements than observed here.

Reactions of Tetrahedral Borate Anions. Rate constants for the reactions of salicylic acid and mandelic acid with tetrahedral $m\text{-NO}_2\text{PhB}(\text{OH})_3^-$ have been determined, and they are presented in Table IV. Fully protonated mandelic acid reacts faster than does salicylic acid (k_r'') by more than 1 order of magnitude. Mandelic acid also reacts faster than salicylic acid with trigonal $m\text{-NO}_2\text{PhB}(\text{OH})_2$ (k_r). Of greater significance is the fact that the reactions with the borate anion are 3–4 orders of magnitude faster than the reactions of trigonal $m\text{-NO}_2\text{PhB}(\text{OH})_2$.

These are the first reported rate constants for complexation reactions of tetrahedral borate anions, and it is not yet possible to make general mechanistic conclusions. One point, however, can be made. The boron–oxygen bond length in tetrahedral borate anions is greater than the boron–oxygen bond length in trigonal boron acids.³⁰ The hydroxide may be a better

(26) See ref 11 for a more complete discussion of this point.

(27) E. G. Moorhead and N. Sutin, *Inorg. Chem.*, **5**, 1866 (1966).

(28) B. Perlmutter-Hayman and E. Tapuhi, *Inorg. Chem.*, **18**, 875 (1979), and earlier references therein.

(29) G. R. Cayley and D. W. Margerum, *J. Chem. Soc., Chem. Commun.*, 1002 (1974).

leaving group in this case and the ring closure process via the proton-transfer mechanism may be more facile. It is not necessary that prior dissociation of an OH⁻ on boron precede the initial attack of the ligand. Five-coordinate boron has been proposed³¹ in the hydrolysis of BH₄⁻, and calculations have been done³² on the possible geometries of such species.

With respect to the reactions of the ligand anions (k_f'''), the rate constants are again in accord with those obtained for their reactions with trigonal *m*-NO₂PhB(OH)₂. Mandelate reacts faster than salicylate in both cases. The reactions of these anions with *m*-NO₂PhB(OH)₃⁻ are slower than the reactions of the fully protonated ligands with *m*-NO₂PhB(OH)₃. This may simply be a reflection of the electrostatic repulsion between the anionic reactants.

The surprisingly large rate constants for the reactions of borates with fully protonated ligands indicate that this could be a facile reaction pathway for the formation of complexes with ligands such as polyols, which bear no acidic protons.

Conclusions

The reactions of trigonal boron acids with fully protonated ligands are characterized by a mechanism that involves proton transfer in a rate-limiting ring-closure step. Correlations of rate constants with the acidities of the boron acid and ligand are direct consequences of this mechanism. Some relatively minor ligand-specific effects are observed. Catechols seem to have somewhat higher forward rate constants than would be predicted from their p*K*_a's, and six-membered chelate rings seem to form with slightly low rate constants. These points are discussed in detail elsewhere.^{3,10}

In contrast, the reactions of ligand anions with trigonal boron acids display no simple correlations with ligand parameters. Ligand basicity, intramolecular hydrogen bonding, and stacked interactions are some ligand-specific effects which are kinetically significant. The central mechanistic problem in the formation of complexes with ligand anions is the electrostatic repulsion between the negatively charged ligand donor atom and the leaving hydroxide.

The tetrahedral borate anions display relatively large forward rate constants for reaction with fully protonated ligands,

(30) In B(OH)₃ the boron-oxygen bond length is 1.37 Å; in B(OH)₄ the boron-oxygen bond length is 1.48 Å (C. L. Christ, J. R. Clark, and H. T. Evans, *Acta Crystallogr.*, **11**, 761 (1958)).

(31) M. M. Kreevoy and J. E. C. Hutchins, *J. Am. Chem. Soc.*, **94**, 6371 (1972).

(32) I. M. Pepperberg, T. A. Halgren, and W. N. Lipscomb, *J. Am. Chem. Soc.*, **98**, 3442 (1976).

reflecting the fact that the hydroxide may be a better leaving group in this case. The analogous reactions with ligand anions are somewhat slower.

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Appendix

The terms appearing in the expression for the relaxation time are defined as

$$\gamma = \alpha + \frac{[\text{OH}^-]}{[\text{H}^+]}$$

$$\alpha = \frac{K_{\text{HIn}} + [\text{H}^+] + [\text{In}^-]}{K_{\text{HIn}} + [\text{H}^+]}$$

$$A = \gamma(K_{\text{H}_2\text{L}} + [\text{H}^+]) + [\text{HL}^-]$$

$$Q = \frac{(A/[\text{B}^-])(K_{\text{HB}} + [\text{H}^+]) + K_{\text{H}_2\text{L}} + [\text{H}^+]}{A[\text{H}^+]/[\text{B}^-] + K_{\text{H}_2\text{L}}}$$

$$R = \frac{[\text{H}^+] - K_{\text{H}_2\text{L}}K_{\text{HB}}/[\text{H}^+]}{K_{\text{H}_2\text{L}}[\text{B}^-]/[\text{H}^+] + A}$$

$$S = \frac{\left[\frac{\gamma[\text{H}^+] + [\text{HL}^-]}{\gamma[\text{H}^+] + [\text{B}^-]} \right] K_{\text{HB}} + [\text{H}^+]}{\left[\frac{\gamma[\text{H}^+] + [\text{HL}^-]}{\gamma[\text{H}^+] + [\text{B}^-]} \right] [\text{H}^+] + K_{\text{H}_2\text{L}}}$$

Registry No. *m*-NO₂PhB(OH)₂, 13331-27-6; PhB(OH)₂, 98-80-6; B(OH)₃, 10043-35-3; CH₃B(OH)₂, 13061-96-6; *m*-NO₂PhB(OH)₃⁻, 71749-74-1; salicylic acid, 69-72-7; mandelic acid, 90-64-2; oxalic acid, 144-62-7; malonic acid, 141-82-2; tartaric acid, 526-83-0; lactic acid, 50-21-5; 4-nitrocatechol, 3316-09-4; catechol, 120-80-9; 4-methylcatechol, 452-86-8; PhB(OH)(oxalate)⁻, 71749-75-2; PhB(OH)(malonate)⁻, 57473-97-9; *m*-NO₂PhB(OH)(salicylate)⁻, 71749-76-3; PhB(OH)(salicylate)⁻, 71749-77-4; CH₃B(OH)(salicylate)⁻, 71749-78-5; *m*-NO₂PhB(OH)(mandelate)⁻, 71749-79-6; PhB(OH)(mandelate)⁻, 71749-80-9; CH₃B(OH)(mandelate)⁻, 71749-81-0; PhB(OH)(lactate)⁻, 53360-58-0; *m*-NO₂PhB(OH)(4-nitrocatecholate)⁻, 71749-82-1; CH₃B(OH)(4-nitrocatecholate)⁻, 71749-83-2; CH₃B(OH)(catecholate)⁻, 71749-84-3; *m*-NO₂PhB(OH)(4-methylcatecholate)⁻, 71749-85-4.