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The Dynamics of Boron Acid Complexation Reactions

by

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A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

1978

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Chairman of Examining Committee

20 July 1978
date

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Abstract

Boron acids react with hydroxyacids and polyols to give tetrahedral complexes in which the ligand is bidentate, and two of the four coordination sites on boron are occupied by ligand oxygen atoms. Boron, in these complexes, bears a charge of negative one. Since they are Lewis acids, boron acids decrease the pH of an aqueous solution by addition of a hydroxide ion. This results in an expansion of coordination number from three for the neutral acids to four for the tetrahedral anions. Both trigonal boron acids and their tetrahedral anions can react with ligands of the type mentioned above to give the same tetrahedral, anionic product. Formation of the complex from the trigonal form of the boron acid is both a substitution and an addition, while the reactions of the borate anions are substitution reactions, the coordination number of boron remaining constant. Complexation reactions of trigonal boron acids require some degree of ligand donor atom protonation. Both the fully protonated and the monoanionic forms of the ligand are reactive, but kinetic results indicate that complex formation in the case of ligand dianions is negligible. The studies herein were designed to investigate factors important in the following: (1) reactions of trigonal boron acids with fully protonated forms of the ligands, (2) reactions of trigonal boron acids with ligand anions, and (3) reactions of tetrahedral borate species. The various boron acids and ligands used spanned a

wide range of pK_as, allowing assessment of the effect of acidity of both the boron acid and the ligand upon the complexation reactions.

The reactions of trigonal boron acids with ligands in which both ligand donor atoms are protonated involve a rate determining proton transfer. The correlation between the pK_{a1} of the ligand and the log of the reverse rate constant is characteristic of reactions where the rate of proton transfer depends upon the magnitude of the difference in acidity between the donor and the acceptor. Because of variations in ligand flexibility and chelate ring size for the different ligands, the forward rate constants do not exhibit this precise correlation. In the complex, all ligands are constrained to the same geometry, and these factors are not of major importance in the reverse direction. For reactions of a single ligand with several boron acids, ligand related properties are held constant, and a precise correlation with pK_{a1} is observed for both the forward and reverse rate constants.

The ligand anion reactions are highly ligand dependent and represent the first study of reactions of this type. Properties such as ligand acidity, ligand flexibility, internal hydrogen bonding, and chelate ring size are all important in determining the complexation behavior of the ligand anions. As expected for ligand dependent processes, the reactions of various boron acids with a single ligand

anion show little variation in forward rate constant.

The tetrahedral borate anions undergo complexation via a reaction which can be viewed as a condensation between two hydroxyl groups of borate and two ligand hydroxyl groups. Similarly, the tetrahedral complexes of boric acid can undergo condensation with a second ligand molecule to form the 1:2 boric acid:ligand species. Reactions of the tetrahedral borate anions with fully protonated ligands seem to have relatively large rate constants. An important factor here may be the lengthening of the B-O bond relative to that of the trigonal form. For the reactions of borate anions with ligand anions, charge repulsion may also play a role. In the case of boric acid reactions with catechols, no appreciable amount of 1:2 complex is formed in solution. Since boric acid does form 1:2 complexes both with ligands which are more acidic and with ligands which are less acidic, this suggests that flexibility of an already bound ligand is important when subsequent chelation is possible.

The boron acid systems thus afford the opportunity to study (1) reactions involving rate determining proton transfer (2) dynamics of ligand dependent processes, and (3) the influence of a first bound ligand upon further complexation steps. These important processes are by no means unique to reactions of boron acids, and the results of these studies should find wide applicability in more general areas of complexation chemistry.

Acknowledgements

I would like to express my deepest gratitude to Professor Richard Pizer, the world champion mentor, from whom I have learned a great deal these past four years - some of it chemistry. I would also like to thank Professors Jack Morrow, Harry Gafney, and Ed Abbott, who have served on my thesis committee, for their interest in my project and for their many helpful suggestions. A special thanks goes to Professor Irwin Cohen whose enthusiasm convinced an undergraduate who never wanted to go to school again to become a graduate student.

My friends, Barbara, Barbara, Bob, Allen, Sene, Tony, Peter, and Sid have made the past four years most pleasant. Graduate school would have been a much less rewarding place without their friendship and generosity.

Finally, I wish to dedicate this thesis to my parents who have lovingly seen me through twenty years of schooling, and who never lost faith in me even when I spent most of my kindergarten year standing in the corner.

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CHAPTER ONE

Introduction to Boron Acid Chemistry

Historical Development of the Field

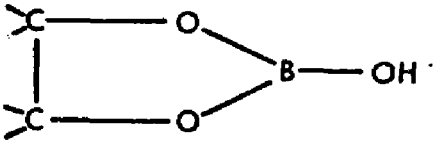
It has long been known that boric acid, a weak acid, can be titrated to a phenolphthalein endpoint in the presence of certain polyhydroxy "activators" such as glycerine and mannitol. In fact, it was first reported by Biot[1] in 1848 that a solution of boric acid turned litmus red upon addition of certain sugars. Several years prior to this, in 1835, Biot had also discovered that boric acid had the effect of altering the optical rotation of tartaric acid solutions. In addition, it was also discovered that solutions containing boric acid and one of the polyhydroxy compounds known to behave as an activator exhibited conductivities which were greater than the sum of the individual conductivities. van't Hoff,[2] in the late 1800's, attributed these phenomena (enhanced acidity, changes in optical rotation, and enhanced conductivity) to the formation of some sort of complex between boric acid and the polyols which produced these effects. It is well established, now, that boron acids and certain dihydroxy compounds do indeed form complexes in solution. In these complexation reactions, boron

is known to act as a Lewis acid and to undergo a change in coordination number from three to four, also gaining a formal negative charge of minus one. The boron atom is tetrahedrally coordinated to the two hydroxyl oxygens of the ligand as shown in the reaction sequence below:

The determination of the nature of the product of this complexation reaction spanned a time period of over one hundred years, and encompassed some very interesting chemistry. As late as 1955, Gould, in his book on inorganic reactions, wrote the following concerning the decrease in pH of a solution of boric acid upon addition of a polyol:

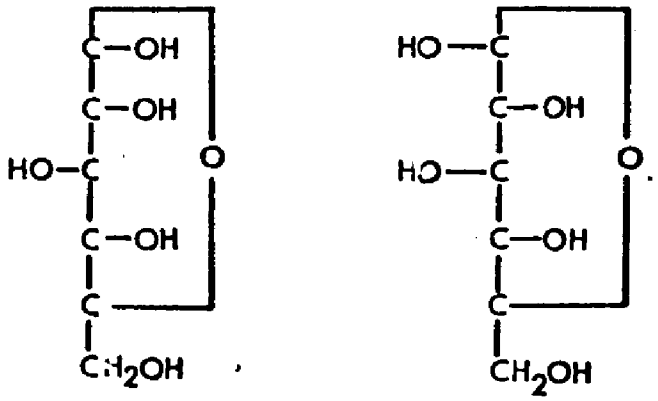
"A number of interesting explanations have been proposed to account for this increase in acidity, but none appear convincing.".[3]

Combining the fact that changes in optical rotation occur upon ring formation with the fact that three moles of boric acid are activated by one mole of mannitol (a polyhydroxy molecule with six -OH groups), van't Hoff[2] arrived at the conclusion that a ring structure involving one boric acid molecule and two hydroxyl groups was formed:



The proton of the complex thus formed was presumably more acidic than that of boric acid itself. In the early 1900's, Boeseken, Hermans, and Meulenhoff made an extensive study of the nature of the compounds which could produce enhanced acidity and conductivity effects in boric acid. Boeseken[4] studied the effects of catechol (1,2-dihydroxybenzene), pyrogallol (1,2,3-trihydroxybenzene), and resorcinol (1,3-dihydroxybenzene) on aqueous boric acid and found that while catechol and pyrogallol acted to produce an increase in conductivity, resorcinol did not. From these data, he determined that the two hydroxyl groups must be adjacent to one another for a particular molecule to act as an "activator". This was not the sole requirement, however, as shown by the inability of ethylene glycol (1,2-ethanediol) to activate solutions of boric acid. In addition to the condition that the diol be a 1,2-diol, it was apparent that these two hydroxy groups had also to be properly oriented, that is, cis to each other. Boeseken went on to use these two criteria to determine the structures of some polyhydroxy compounds, and to distinguish cis and trans isomers on the basis of the effect of the polyol on a boric acid solution. In this manner, he was able to determine the structures of α and β dextrose (α dextrose having the proper configuration

and orientation for conductivity and acidity enhancement).[5]



α-dextrose β-dextrose

Boeseken[6] also found that α-hydroxy carboxylic acids (tartaric acid, malic acid, and lactic acid) also cause a decrease in the pH when added to a solution of boric acid. The results of their work led Boeseken, Meulenhoff, and Hermans to restate the idea proposed by van't Hoff much earlier: that some sort of complex was formed between boric acid and both the polyols and α-hydroxy carboxylic acids which behaved as activators. They drew this conclusion on the basis of the following four phenomena known to occur for a solution of activator and boric acid:

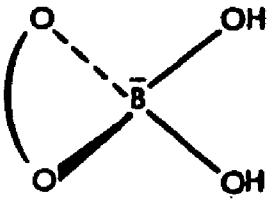
(1) the optical rotation of optically active polyols such as d,l-tartaric acid changed,

(2) the conductivity of such a solution was greater than the sum of the conductivities of boric acid and of the activator,

(3) the pH of the resulting solution was depressed (even though one would expect a decrease in the ionization of one

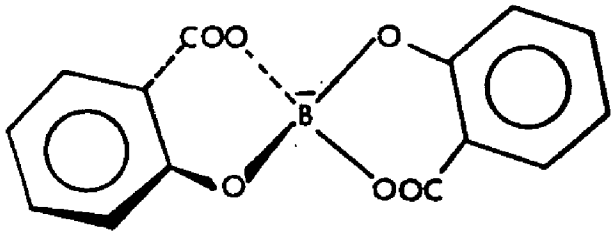
acid upon addition of another acid), and
(4) the molecules which could produce these effects had specific geometric requirements.

These extensive studies of boric acid activators led Boeseken, Meulenhoff, and Hermans to the same notion, that of complex formation, which van't Hoff had postulated[2] in the late 1800's However, a new piece of evidence caused Hermans,[7] in 1925, to propose a structure different from the tri-coordinate boron complex shown below. He found that certain diols could react with boric acid to give the trigonal boron structure and that the acidity of these compounds was not increased; therefore, the boric acid-activator complex could not have the trigonal structure. He was the first to suggest that the species responsible for the enhanced acidity involved a four coordinate, tetrahedral boron atom with a formal negative charge:

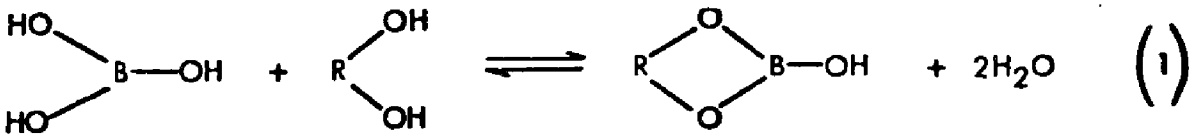


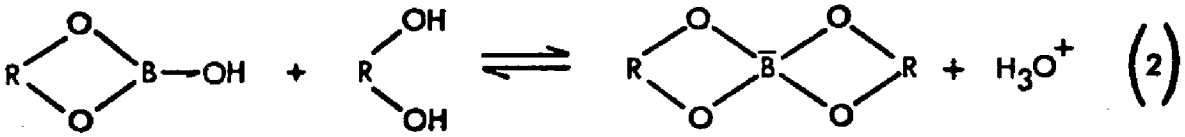
The acid thus produced would be stronger than boric acid itself, and the production of ions could nicely explain the enhanced conductivity. Meulenhoff also favored a tetrahedral structure in which the four coordinate boron was a chiral center and the complex could exhibit optical activity if bound to two molecules of activator. He mixed

boric acid and salicylic acid and, using an optically active base, isolated the 2:1 anion which he characterized as having the following structure:



Using this technique, Meulenhoff resolved several optical isomers of the type shown above. Boeseken and Vermaas[8] also reported the precipitation from solution of the 2:1 boric acid-salicylic acid complex by an optically active base. They, too, proposed a four coordinate, tetrahedral boron, and they postulated the following two step mechanism:





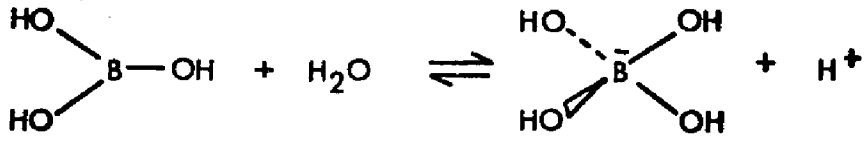
If a diol was "unfavorable" (did not produce increases in acidity and conductivity of boric acid solutions), it was presumed that the product of step one was the sole product, and that the second step could not occur. Despite the belief of Boeseken, Meulenhoff, and Hermans that a tetrahedral boron complex nicely explained their data, the concept was not immediately accepted. In fact, Bancroft and Davis[9] pub-

lished a lengthy and thorough paper in which they disputed the fact that a complex of any type was even formed. It was their hypothesis that the enhanced acidity and conductivity data could be explained on the basis of solvent effects; that is, boric acid exhibited increased dissociation in the water-, . solvent system due to changes in solvent association and dielectric constant. In 1943, Rippere and La Mer[10] attributed activation to complex formation, but stated that the structure had not clearly been determined. Based upon studies where the amount of water liberated by a boric acid-polyol reaction was measured, they concluded that the two step mechanism of Boeseken and Vermaas (cf. equations 1 and 2) was incorrect. They did not detect the water molecule which, according to Boeseken, should have been produced upon formation of the 2:1 boric acid-polyol species. Thus they came to the conclusion that the complex was trigonal as proposed by van't Hoff much earlier.

Structural Studies of Boron Acids and Their Complexes

The first related structural study done was a Raman study of the borate ion itself carried out by Edwards et al.[11] in 1955. From X-ray crystallographic data,[12] the teepleite crystal ($NaBO_2 \cdot NaCl \cdot 2H_2O$) is known to have a boron atom tetrahedrally coordinated to four oxygen atoms. Ed-

wards compared the IR spectrum of teepleite to the Raman spectrum of the aqueous borate ion and found good agreement among the various active vibrations. The Raman obtained also resembled that of the tetrahedral BF_4^- ion. In addition, he calculated the number of Raman active lines expected for the other two possible structures of the borate ion, BO_2^- and $H_2BO_3^-$. He found that the number of fundamental bands predicted for either of these structures (one for BO_2^- and six for $H_2BO_3^-$) was not compatible with the experimentally obtained spectrum containing four bands. These pieces of evidence led Edwards to conclude that boric acid is not an acid in the Bronsted-Lowry sense (with $H_2BO_3^-$ as the conjugate base), but rather is an acid in the Lewis sense,as shown below:



A study performed by Antikainen[13] on the formation of boric acid-mannitol complexes indicated the presence of more than one complex. Using the following expression:

$$HB + nM \rightleftharpoons BM_n^- + H^+$$

he found a dependence of the equilibrium constant upon [M] for n=2, but obtained good equilibrium constants using n=1.81. This confirmed the existence of not only a 2:1 mannitol-boric acid complex, but also of a 1:1 species.

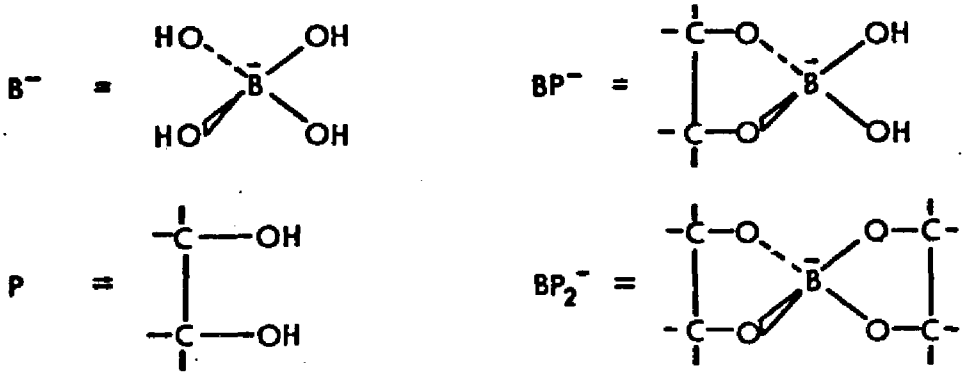
In an investigation of a series of polyol complexes of

borate, Edwards et al.[14] assumed the formation of a 1:1 species and a 2:1 species as well. They determined stability constants for the formation of both complexes in accordance with the following equilibria:

$$B^- + P \rightleftharpoons BP^- + H_2O \qquad K_1 = \frac{[BP^-]}{[B^-][P]}$$

$$B^- + 2P \rightleftharpoons BP_2^- + 2H_2O \qquad K_2 = \frac{[BP_2^-]}{[B^-][P]^2}$$

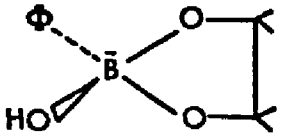
where:



It is important to note here the assumptions made by Edwards. First, he assumed that the reactive form of boric acid was the tetrahedral borate anion, a point which will be returned to later. And, second, he assumed that the structures of both the 1:1 and 2:1 complexes of polyol and borate were tetrahedral with four oxygen atoms coordinated to the boron atom. Had he maintained that either of these complexes were trigonal, he would have arrived at expressions for K_1 and/or K_2 which exhibited different dependences upon the hydrogen ion concentration. Edwards, however, obtained good values for both stability constants, K_1 and K_2, using

the equilibrium expressions involving the tetrahedral complexes. This thermodynamic evidence, as well as the knowledge that boron could coordinate to four different oxygen atoms (as in the borate anion), established quite well the tetrahedral nature of boric acid-polyol complexes, even though no direct structural study of the complex had yet been performed.

Phenylboronic acid, a substituted boron acid in which one of the hydroxyl groups has been replaced with a phenyl group, can form 1:1 complexes with polyols but cannot form 2:1 complexes since the phenyl group blocks the second chelation site. Lorand and Edwards[15] measured equilibrium constants for several phenylboronic acid-polyol complexes and concluded, on the basis of these measurements, that the phenylboronate-polyol complexes (like the borate-polyol complexes) must involve a tetrahedrally coordinated boron atom:



In a study in 1961, Edwards and Sederstrom[16] determined that the phenylboronate anion itself was tetrahedral. They performed a thermodynamic investigation of the ionization of phenylboronic acid, and discovered that the entropy of ionization, $\Delta S=-30.9$ cal/mol-deg, was more negative than the average entropy for the formation of an oxyanion from a neutral acid ($\Delta S=-22$ cal/mol-deg). This value of ΔS,

moreover, is close to that of boric acid, ΔS=-34.0 cal/mol-deg, which is known to be tetrahedral. The comparatively low value of ΔS, indicating an increase in coordination number upon ionization, and its similarity to the value for boric acid led Edwards and Sederstrom to conclude that borate and phenylboronate anions have similar structures.

Up to this point, all information regarding the structure of boron acid-polyol complexes had been indirect evidence: thermodynamic measurements such as formation constants, enthalpies, and entropies which indicated anionic complexes of increased coordination number; conductivity measurements which suggested the formation of ionic species; enhanced acidity which meant the formation of a more acidic proton than that of the boron acid; the separation of optically active species which presumably contained a tetrahedrally coordinated boron atom; and the knowledge (from Raman spectroscopy) that the borate ion in solution contained a four coordinate boron atom. From these data, a tetrahedral, anionic boron acid-polyol complex (with four oxygens coordinated to boron) had been inferred, but no structural study of the aqueous complex had been performed as yet.

Infrared spectroscopic investigations of boric acid and lactic acid as well as boric acid and salicylic acid systems were carried out in 1970 and 1971 by Larsson and Nunzia-

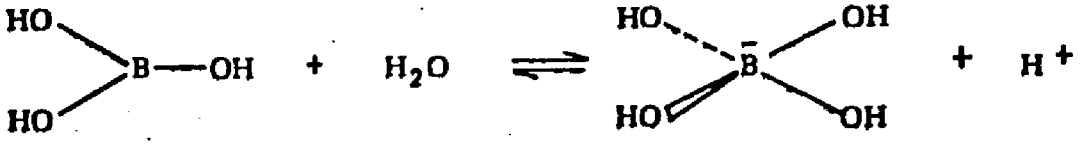
ta.[17,18] They determined the coordination number of boron by observing the B-O bond stretching frequency. The trigonal B-O stretch of $B(OH)_3$ appears at $\nu = 1410\ cm^{-1}$ and the B-O stretch of $B(OH)_4^-$ appears at $\nu = 945\ cm^{-1}$; this decrease in stretching frequency is indicative of the decrease in bond order upon conversion from the trigonal boric acid to the tetrahedrally coordinated complex. Examination of the IR spectra of the boric acid complexes of both lactic acid and salicylic acid showed not only that both the 1:1 and 2:1 complexes were present, but also that both were tetrahedral. In 1972, Oertel[19] published a Raman study of the structures of boric acid complexes of several 1,2- and 1,3-diols. His data established that the structures originally proposed by Hermans were indeed the correct ones. The 1:1 and 1:2 complexes contain five or six membered chelate rings and a boron atom which is tetrahedrally coordinated to four oxygen atoms.

General Characteristics of Boron Acids

Boric acid, then, acts as a Lewis acid, using a vacant p orbital to accept electrons and form a covalent bond. The trigonal planar boric acid is of sp^2 hybridization with a formal charge of zero on the boron atom; the tetrahedral anion is of sp^3 hybridization, and the boron atom here bears a

charge of negative one. Variation of the substituents bonded to the boron can increase or decrease the Lewis acidity of the boron acid, and this has been attributed in part to backbonding. Several experimental factors have lent credence to the existence of backbonding in boron compounds. First, these compounds can exist in monomeric states, whereas compounds of aluminum and gallium use the vacant p orbitals in forming dimers, and do not exist in a monomeric form.[20] This indicates that backbonding stabilizes the trigonal boron compounds, since dimerization would necessarily cause a loss of backbonding. Second, force constant calculations from trigonal boron frequencies suggest significant backbonding.[21] And, finally, NMR data show that trigonal boron compounds exhibit hindered rotation about the boron-ligand single bond.[22] It is important to note that the degree of backbonding may affect the acidity of a particular boron compound, since the loss of this backbonding interaction may oppose the formation of the tetrahedral anion.

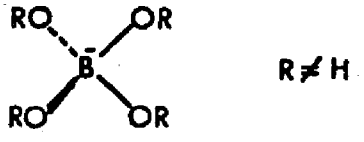
The trigonal-tetrahedral equilibrium, shown below, is rapidly established, as shown by Eyring et al.[23]



The pK_a of boric acid has been established by many techniques; studies carried out by Ingri[24] show it to have a

value of 9.0. Edwards attributed the fact that boric acid is a weak acid to entropic rather than enthalpic effects since the change in entropy of boric acid upon ionization is -34 cal/mol-deg.[16]

In its complexation reactions with polyols and α-hydroxycarboxylic acids, boric acid also acts as a Lewis acid, accepting electrons with the formation of a covalent bond. These reactions proceed with a rehybridization of boron from sp^2 to sp^3. Species of the type shown below are unstable, and are rapidly hydrolyzed back to boric acid.[25]

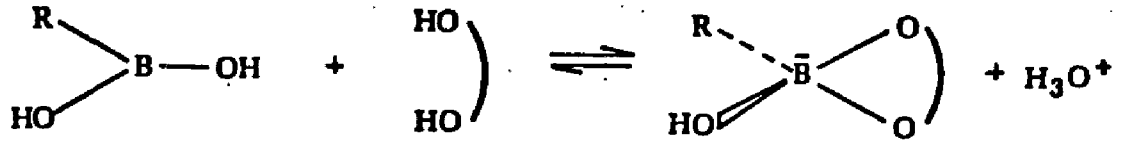


The chelate effect, however, stabilizes complexes of bidentate ligands. Complexation in the case of boron-halide compounds is accompanied by an increase in B-X bond distance and a decreased B-X bond angle.[26] This agrees with the IR and Raman data obtained by Edwards,[11] Larsson and Nunziata,[17,18] and Oertel,[19] and also establishes the tetrahedral structure of the complex. Finally, it has been shown, with the use of optically active ligands, that it is the B-O bond rather than the C-O bond which is cleaved upon coordination.[27,28] Substituted boron acids (such as phenylboronic acid) behave similarly, but do not afford the possibility of 2:1 complex formation since the second chelation site is blocked.

In summary, the following statements can be made:
(1) boron acids are Lewis acids, and exhibit a change in formal charge as well as coordination number upon ionization and complexation,
(2) there is evidence for the existence of backbonding in the trigonal forms of boron acids, and this may affect relative acidities,
(3) the acid ionization equilibria are rapidly established; the ionization constants show these acids to be weak, and
(4) these acids form 1:1 (and 2:1 in the case of boric acid) complexes with fission of the B-O bond; these complexes are stabilized by the chelate effect.

Introduction to Boron Acid Kinetics

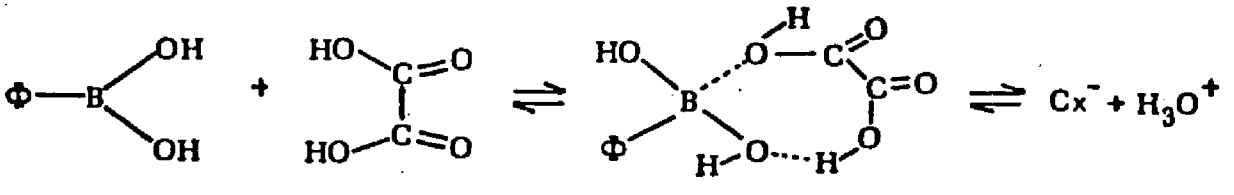
It is not surprising that an interest in the kinetics of these boron acid complexation reactions should appear with the intent of elucidating the reaction mechanism. The reaction proceeds to give a tetrahedral, anionic product in which both ligand protons have been displaced, and one of the boron acid hydroxy groups has been replaced by a ligand donor atom.



An equilibrium situation is rapidly arrived at in the reac-

tions of boron acids with α-hydroxycarboxylic acids and polyols, thereby necessitating the use of fast kinetic techniques.

The first kinetic investigation of this type, carried out by Kustin and Pizer,[29] was a temperature-jump study of the complexation reaction of boric acid and tartaric acid. They looked at the reactions of both tartaric acid and the tartrate anion. Because the ligand anion reacted more slowly with boric acid than did the fully protonated form of the ligand, they concluded that ligand acidity was an important factor affecting relative reaction rates, and that ligand donor atom protonation also played an important role. The mechanism that they proposed involved attack by the hydroxyl oxygen on the boron atom followed by ring closure via loss of a water molecule. A subsequent study of the reaction of phenylboronic acid with the dicarboxylic acid oxalic acid [30] also suggested that this mechanism was in operation; the protonated ligand reacted with a rate constant greater than the binoxalate anion, indicating that hydrogen bonding from the ligand carboxyl group to the leaving hydroxyl on boron may be important.



Pizer et al. also investigated the complexation of phenyl-

boronic acid with lactic acid[31] and with malonic acid,[32] and found that the rate constants for the fully protonated forms of the ligands were in agreement with the mechanism pictured above. That is, one would expect the more acidic ligands to react faster, and the rate constants for the reactions of phenylboronic acid with oxalic acid (pK_a=1.04), malonic acid (pK_a=2.59), and lactic acid (pK_a=3.70) reflect this.

A comparison of the rate constants of the fully protonated form of the ligand with that of the ligand anion for oxalate, malonate, and tartrate showed that for each of these, the anion reacted more slowly (an observation consistent with a mechanism in which proton transfer aids in the leaving of the hydroxyl). In its reactions with phenylboronic acid, however, the lactate anion reacted with a rate constant greater than that of lactic acid by more than an order of magnitude.[31] The authors postulated that this phenomenon could be the result of an interaction between the carboxylate group of the lactate anion and the phenyl ring of the phenylboronic acid. This interaction becomes apparent in an increased rate of reaction over that which would be normally expected.

The kinetic study of these four systems (boric acid/tartaric acid, phenylboronic acid/lactic acid, phenylboronic acid/oxalic acid, and phenylboronic acid/malonic acid) led to the following conclusions:

(1) complexation may occur by ligand hydroxyl attack on the

empty boron p orbital, followed by ring closure via loss of a water molecule,

(2) ligand acidity plays an important role in the rate of complexation,

(3) ring closure must occur immediately upon loss of the hydroxyl group to avoid hydrolysis as a result of the rapid trigonal-tetrahedral interconversion,

(4) some degree of ligand protonation is required, as evidenced by the failure of ligand dianions to react,[30,32]

(5) as in metal ion chemistry, any interaction which increases reactant association or properly orients the reactants will increase the rate constant, and

(6) chelate ring size is another factor which affects relative rate constants.[32]

Comparison with Other Kinetic Systems

Although no parallel between metal oxyanion reactions and the reactions of metal cations can be drawn, there are several marked similarities between the boron acid complexation processes and those of oxyanions. Metal cation substitution chemistry is dominated by ion pairing constants and water exchange rates,[33] and shows little ligand discrimination. Oxyanions, on the other hand, may undergo structural changes upon complexation, and are sensitive to the nature

of the ligand. Studies of the molybdate and tungstate oxyanions[34] indicate that some degree of protonation of either the ligand or the oxyanion is required. Furthermore, reactions of unprotonated ligand with unprotonated oxyanion and of fully protonated ligand with fully protonated oxyanion do not occur, indicating that no reaction can take place without proton transfer. This is similar, to some extent, to the requirement of ligand donor atom protonation in boron acid complexation reactions, and to the idea of a rate determining proton transfer. There is a dependence of the rates of both the protonated and unprotonated forms of molybdate and tungstate upon ligand basicity; this was explained by the authors[34] on the basis of the ligand's ability to participate in hydrogen bonding to aid the leaving hydroxyl.

The molybdate, MoO_4^{2-}, and tungstate, WO_4^{2-}, oxyanions have a tetrahedral structure.[35] Upon complexation, they undergo an expansion of coordination number to form octahedral complexes. In their protonated forms, these oxyanions are most likely octahedral, as indicated by the fact that the addition of a proton is not diffusion controlled, and may point to a change in coordination number upon protonation.[36,37] Thus, reactions involving the unprotonated MoO_4^{2-} and WO_4^{2-} ions are addition reactions, while the reactions of the protonated octahedral ions are substitution reactions. Complexation of trigonal boron acids involves

addition and substitution; the coordination number of boron is increased from three to four, and one of the boron hydroxyl groups is displaced by a ligand donor atom. In addition, reactions of the tetrahedral boronate anions (like the reactions of protonated oxyanions) are substitution reactions.

To summarize, the following mechanistic similarities are observed:

(1) both boron acids and oxyanions, unlike metal cations, show ligand discrimination on the basis of specific ligand geometry and ligand basicity,

(2) both require some degree of protonation of binding sites,

(3) both have a reactive form which undergoes expansion of coordination number upon complexation, and

(4) both emphasize proton transfer as important in the transition state.

For these reasons, the study of boron acid reactions is of value not only in determining the details of boron acid complexation, but also in probing the more general class of reactions which are dependent upon ligand properties such as basicity, geometry, and degree of binding site protonation.

Studies of the effect of substituted boron acids, $RB(OH)_2$, on enzymes and coenzymes have shown that the Lewis acidity of the boron as well as the particular alkyl or aryl group, R, are important. There is much information which

can be gained from an investigation of boron acid-enzyme systems; a knowledge of boron acid reactions indicates that protonation will play an important role. When enzymes react with a particular substrate, high energy metastable substrates are formed which then continue on to eventually give products. In order to study enzyme mechanisms and structures, it is desirable to find analogues of these metastable states which resemble the enzyme-substrate species in structure and charge, but which are stable enough to allow investigation. Some substituted boron acids act as specific enzyme inhibitors for subtilisin Carlsberg[38] and α-chymotrypsin,[39] and are thought to be transition state analogues in these cases. Phenylboronic acid and 2-phenylethaneboronic acid were found to inhibit subtilisin-catalyzed hydrolyses, and it was postulated[38] that proton transfer to and from the active site may be involved. Methylboronic acid, $CH_3B(OH)_2$, was not an effective inhibitor, indicating that the aromatic group is necessary. Examination of the effect of 2-phenylethaneboronic acid on α-chymotrypsin by laser-Raman[39] showed the boron acid to be an inhibitor, and also indicated that both the trigonal and tetrahedral forms were involved in the reactions (in a pH-dependent manner). Johnson and Smith[40,41] looked at the effect of boric acid and phenylboronic acid on the coenzyme nicotinamide dinucleotide, NAD^+; this coenzyme undergoes boration at a ribose adjacent to a pyridinium ring. The

complexation of NAD^+ with boric acid results in a three- to seven-fold decrease in the equilibrium constant for nucleophilic substitution on the ring.

A knowledge of boron acid reactions in general would be invaluable when applied to specific boron acid-enzyme systems in an attempt to study the mechanisms by which enzymes operate.

Experimental Objective

The series of experiments undertaken here have three main objectives. First is an investigation of the reactions of fully protonated ligands with boron acids. This includes a study over the complete range of ligand pK's in order to assess the effect of ligand acidity on reaction rate. In addition, variations in ligand structure and ligand substituents allows an evaluation of a number of effects due to ligand geometry or orientation. Second, it was intended to look at the reactions of ligand anions with boron acids. Such a study permits determination of factors important in ligand anion reactions. Third, the investigation of a series of boron acids with a particular ligand (either in the fully protonated or in the anionic form) demonstrates the effect of boron acid acidity upon the complexation reactions.

These studies are the first of their kind, and elucidate several facts concerning the nature of ligand dependent processes. Many ligand specific effects not previously seen can be examined through the investigation of the boron acid systems. For the reactions of trigonal boron acids with fully protonated ligands, proton transfer plays a vital role. These reactions thus afford the possibility for examining factors which are important for systems in which proton transfer occurs in the rate determining step. The reactions of ligand anions with trigonal boron acids do not involve proton transfer in the rate determining step, and the forward rate constants for these reactions are strongly ligand dependent, exhibiting little discrimination among the different boron acids. Finally, the reactions of boric acid where the formation of 1:2 complexes is possible provide insight into the influence of a first bound ligand upon subsequent chelation steps. Ligand flexibility seems to be a major factor in these reactions. Generally, metal ions are constrained to particular geometries and, therefore, are not sensitive to the flexibility of an already bound ligand, the boric acid systems undergo geometric changes upon complexation, and this flexibility during reaction makes them ideal for an investigation of the effect of a first bound ligand.

There are many unanswered questions concerning the factors which influence ligand dependent processes, and the boron acid systems lend themselves very nicely to the eluci-

dation and evaluation of such factors. The ligand specific effects which are important in these reactions are not unique to boron acid chemistry, and the results of these studies have wider applicability to the more general class of reaction which is sensitive to ligand properties.

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CHAPTER TWO

The Experimental Methods and Analysis of Data

The Relaxation Technique

For chemical systems which quickly attain equilibrium, conventional kinetic techniques and even rapid-mixing techniques are not suitable for rate studies. These reactions are conveniently investigated using one of a group of chemical relaxation methods introduced by Eigen in the 1950's.[1] A single principle forms the basis of chemical relaxation: if a system which is initially in equilibrium is perturbed by a change in some variable of state (for example, temperature or pressure), the system will readjust to a new equilibrium under the altered conditions. The process by which the concentrations return to an equilibrium state following the perturbation is termed relaxation, and this relaxation occurs in accordance with the rate laws governing the system. Thus, a measure of the time-dependence characteristic of the system's return to equilibrium, the relaxation time, is a direct measurement of the kinetic behavior of the system.

According to the van't Hoff equation:

$$\left(\frac{\partial \ln K}{\partial T}\right)_P = \frac{\Delta H}{RT^2}$$

a system having a finite enthalpy of reaction will experience a shift in equilibrium upon a change in temperature. When the temperature is the state parameter used to perturb an equilibrium system, the technique is referred to as the temperature-jump method.

As the perturbed system approaches a new state of equilibrium, the deviations from equilibrium concentrations tend to vanish. If the initial deviations are small, then the expression can be linearized and the rate of disappearance of this differential concentration is proportional to the difference itself. The reciprocal of the probability factor has units of time and is termed the relaxation time. That is, for a species, x, whose concentration at time t can be expressed as:

$$x(t) = \overline{x} + \delta x(t)$$

where:

$\overline{x}$ = the equilibrium value at the new temperature

δx = the deviation from the equilibrium concentration at time t

The approach to equilibrium is given by the rate of disappearance of the deviation from equilibrium, δx, and is proportional to δx:

$$-\frac{d\delta x}{dt} = k\delta x$$

where:

$k = (\tau)^{-1}$

τ = the relaxation time

It can be seen, then, that for small perturbations (where the rate expression can be linearized) the approach to equilibrium is a first order process, and the relaxation time, τ , is the inverse of the observed first order rate constant, k. Tau is also the time at which the time dependent concentration, δx, is equal to 1/e of the initial concentration, δx_o, as shown below and illustrated in Figure II-1:

$$\frac{d\delta x}{dt} = -k\delta x$$

$$\delta x = ce^{-kt}$$

$$\text{at } t=0,\ \delta x = \delta x_o$$

$$\therefore c = \delta x_o$$

$$\delta x = \delta x_o e^{-t/\tau}$$

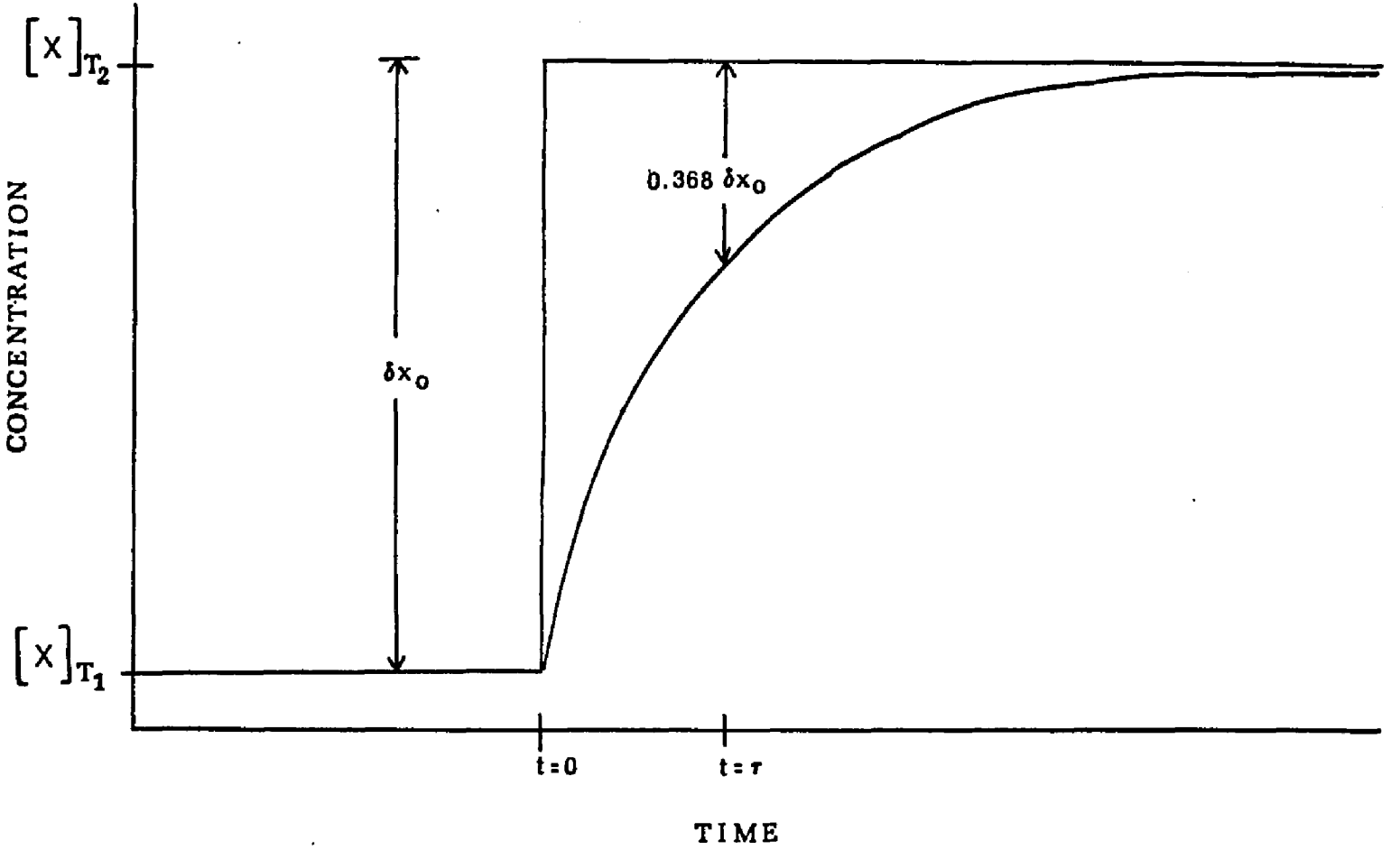
if $t = \tau$:

$$\delta x = e^{-1}\delta x_o$$

$$\delta x = \frac{1}{e}\delta x_o$$

The characterstic relaxation time is related to the overall mechanism of the reaction, and is a function of all of the rate constants as well as the concentrations of the species present. Because the system is close to equilibrium, both forward and reverse rate constants will contribute in a positive way to the relaxation time, making τ independent of the sign of the perturbation. In addition, the expression for the relaxation time will depend upon concentrations and rate constants in a way which differs for each mechanism.

FIGURE II-1. INSTANTANEOUS TEMPERATURE DISPLACEMENT FOLLOWED BY CHEMICAL RELAXATION



The kinetic derivation given below for the reaction:

$$A + B \rightleftharpoons C$$

illustrates the linearization process, the additive contributions from both k_f and k_r, and the dependence of the expression for τ upon the overall reaction mechanism. The rate law is given by:

$$-\frac{dA}{dt} = k_f[A][B] - k_r[C] \qquad (1)$$

At any time, t, the concentration is given by the time independent equilibrium concentration plus some time dependent deviation from equilibrium:

$$A = \bar{A} + \delta A \qquad (2)$$
$$B = \bar{B} + \delta B \qquad (3)$$
$$C = \bar{C} + \delta C \qquad (4)$$

where:

$\bar{A}$, $\bar{B}$, and $\bar{C}$ are equilibrium concentrations

δA, δB, and δC are concentration changes

Substitution of the equations above into the rate law yields the following expression:

$$-\frac{d(\bar{A}+\delta A)}{dt} = k_f[\bar{A}+\delta A][\bar{B}+\delta B] - k_r[\bar{C}+\delta C]$$

$$-\frac{d(\bar{A})}{dt} - \frac{d\delta A}{dt} = k_f\{[\bar{A}][\bar{B}] + [\bar{B}]\delta A + [\bar{A}]\delta B + \delta A\delta B\} - k_r[\bar{C}] - k_r\delta C$$

However, since $\bar{A}$ is time independent, the following is true:

$$\frac{d\bar{A}}{dt} = 0$$

and when the relationship $k_f[\bar{A}][\bar{B}]-k_r[\bar{C}]=0$ is used, the rate

law reduces to:

$$-\frac{d\delta A}{dt} = k_f \left\{ \left[\bar{B}\right]\delta A + \left[\bar{A}\right]\delta B + \delta A \delta B \right\} - k_r \delta C$$

Since the deviation from equilibrium is small, i.e. $\delta A \ll A$, the cross terms can be neglected:

$$\delta A \, \delta B = 0$$

Thus, the rate expression is linearized, and:

$$-\frac{d\delta A}{dt} = k_f \left[\bar{A}\right]\delta B + k_f \left[\bar{B}\right]\delta A - k_r \delta C$$

From the stoichiometry, it can be seen that $\delta A = \delta B = -\delta C$.

$$-\frac{d\delta A}{dt} = \left\{ k_f \left(\left[\bar{A}\right] + \left[\bar{B}\right] \right) + k_r \right\} \delta A$$

This has the form of the first order expression with:

$$k = \left\{ k_f \left(\left[\bar{A}\right] + \left[\bar{B}\right] \right) + k_r \right\}$$

or

$$\tau = \left\{ k_f \left(\left[\bar{A}\right] + \left[\bar{B}\right] \right) + k_r \right\}^{-1}$$

Thus, the relaxation process is seen to be first order and τ is a function of all of the rate constants, both forward and reverse.

For mechanisms with multiple equilibria, two possibilities exist. First, all the steps except one may involve

equilibria which are rapidly established with respect to the time scale of temperature-jump (for example, protolytic reactions). These are considered to be in equilibrium throughout the chemical relaxation process. And, second, a multistep reaction may contain more than one equilibrium which exhibits a relaxation which is within the time range of the technique. For such a reaction, a number of relaxation times are expected, that number being determined by the following expression:[2]

$$t = n - (m + r)$$

where:

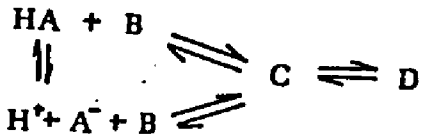
t = the number of τ's to be expected

n = the number of variables in the equations

m = the number of conservation relations

r = the number of rapid (e.g. protolytic) equilibria

In the following reaction scheme:



one would expect 6-(3+1)=2 relaxation times. These reactions, however, are all coupled, and so the relaxation times obtained are not, in general, associated with particular steps, but are functions of all the rate constants. In a manner analogous to the coupling of normal modes of vibration, the τ's of a coupled reaction system are functions of the normal mode coordinates of the system. These normal

modes of reaction are linear combinations of the concentrations of all of the species pesent, and the t relaxation times are the eigenvalues obtained by diagonalization of the txt matrix.[1]

There are reasons, however, why all of the expected relaxation times may not be seen. First, if the amplitude of a relaxation time is too small, it may not be observed. In fact Strehlow and Jehn have determined that separation of superimposible relaxation times of very different amplitudes is difficult even if the s differ by a factor of four.[3] Second, if two reactions have the same time constant, only a single exponential will appear;[4] and third, if a steady state exists for a particular species, no relaxation time for that process will be seen.[5] It is important to point out that, for a series of coupled equilibria, the system can be perturbed even if only one step has a finite enthalpy of reaction. The superposition of more than one first order process to give a non-linear plot of the log of the concentration as a function of time is a situation often encountered in radioactive decay processes. Methods for obtaining first order rate constants from these data are well known and are documented in many texts concerning nuclear and radiochemistry.[6]

The Temperature-Jump Method

As mentioned previously, the perturbation of the equilibrium in temperature-jump is produced by a rapid increase in the temperature of the solution under study. The most common way of effecting this temperature rise is Joule heating; a capacitor is charged with a certain voltage and this is then discharged through the solution, putting into the system an amount of energy given by:

$$E = \tfrac{1}{2}CU^2$$

where:

C = capacitance, farads

U = charging voltage, volts

The mathematical description of the temperature rise is called the forcing function, and it is characterized by a finite rise time which is given by RC/2, where R is the resistance in ohms, and C is the capacitance, as mentioned before. If the relaxation time is much larger than the rise time, $\tau > RC/2$, the change in temperature can be considered a step function, and the system can be described using conventional rate expressions after the perturbation is completed.[1]

Since the time constant for the temperature rise is given by RC/2, the smaller the resistance, the closer the temperature perturbation is to a step function. Addition of an inert electrolyte (such as KNO_3) keeps the resistance

small (a typical solution and cell resistance is 100 ohms), and the current is carried from one electrode of the cell to the other by the ions of the inert electrolyte. In this manner, the increase in temperature is effected by use of the electrical properties of the system (not by adiabatic compression and dilation). The addition of inert electrolyte also serves another important function - it maintains a constant ionic strength within the reacting system. If ionic species are involved in the equilibria, and, as a result, the ionic strength varies during the course of the relaxation, the expression for the relaxation time must be modified to include ion activities.[1] Thus, addition of bulk electrolyte is two-fold in purpose: one, it makes the electric properties of the system under study suitable for temperature-jump by maintaining a small resistance (which leads to a fast rise time), and two, it maintains a constant ionic strength throughout the course of the reaction.

To produce a fast, homogeneous rise in temperature, an energy distribution within the system must take place. Translational and rotational energy distribution within liquids takes place in about 10^{-12} seconds,[1] and generally, in liquids, vibrational energy can be partitioned well within the time of the temperature rise (which typically is on the order of microseconds). Because the thermal equilibration is rapid, expansion which occurs as a result of heating may lag behind. The propagation of this thermal ex-

pansion takes place with approximately the velocity of sound, and expansion times are on the order of 10^{-5} to 10^{-6} seconds.[1] Because the volume change lags behind the change in temperature, the pressure increase is propagated through the solution as a shock wave, with pressure increases of up to fifty atmospheres. If the pressure wave is reflected by the cell walls, a phase reversal may occur; the rise and collapse of the shock wave is known as cavitation.[1] This effect is important only if the heating process occurs in less than 10^{-5} seconds, and can be avoided by working at lower temperatures, as is apparent from the following relationship:

$$\left(\frac{\partial P}{\partial T}\right)_V = \frac{\alpha_p}{\kappa_T} \quad \text{and} \quad \alpha_{p_{H_2O}} = 0 \quad \text{at} \quad 4^\circ C$$

Relaxation methods in general and the experimental measurement of characteristic relaxation times have been discussed in many places.[1,4,7,8]

The principles of the temperature-jump technique, then, can be summarized as follows:

(1) perturbation of the equilibrium is brought about by a sudden increase in temperature; in cases where the rise time is small compared to the relaxation times being studied, the increase in temperature may be considered a step function;

(2) the system's approach to an equilibrium at the new temperature is in accordance with the rate laws governing the system, and is first order;

(3) the time constant characteristic of this first order approach to equilibrium is the relaxation time, τ , and it is directly related to the concentrations and rate constants (both forward and reverse) of the system involved;

(4) the expression for τ in terms of concentrations and rate constants is dependent upon the overall mechanism, and quasi-stationary species do not appear;

(5) a system may be characterized by more than one relaxation time, depending upon the number of independent steps (interrelationships between paths leading to the same state reduce the number of τs expected);

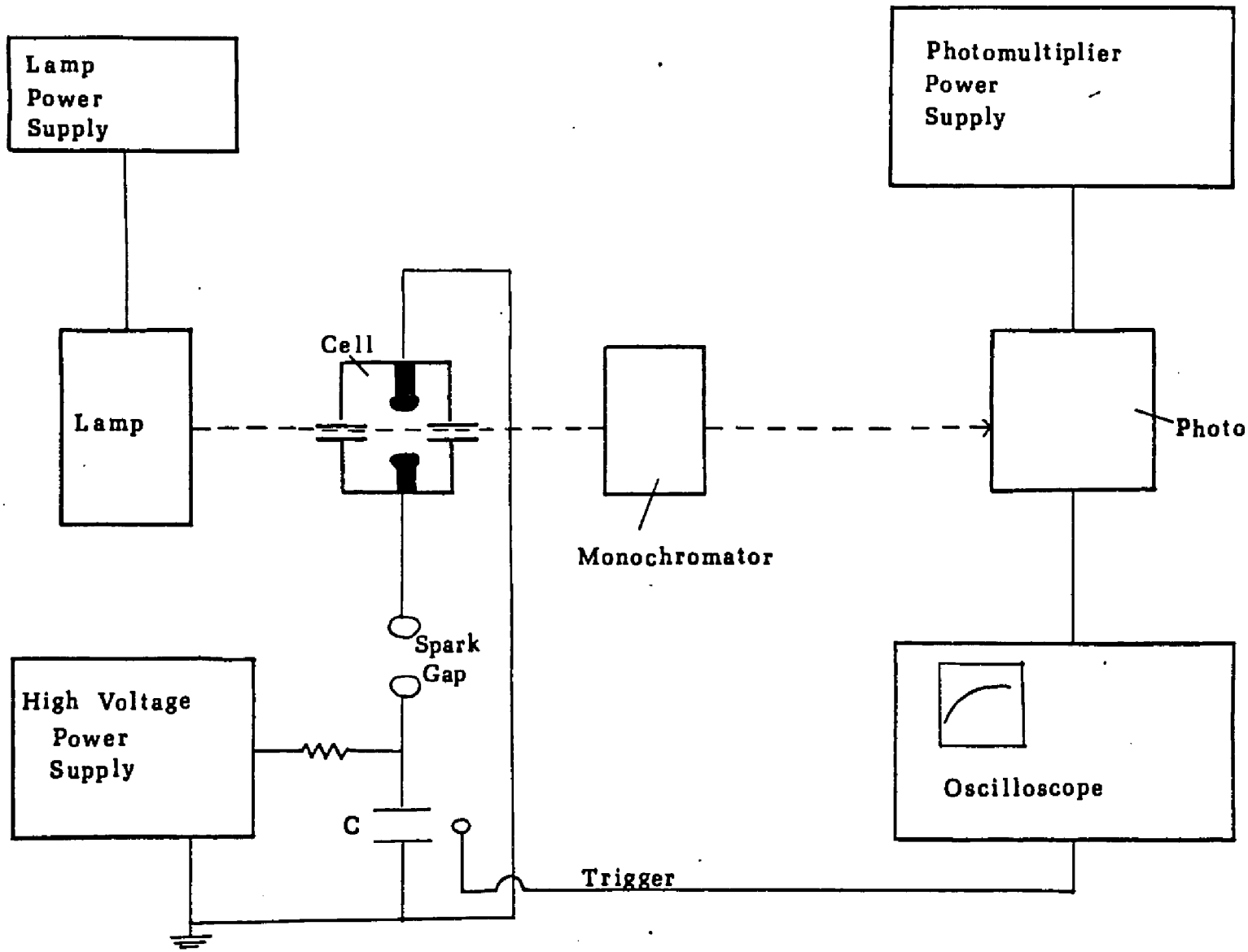
(6) for a change in temperature to produce a perturbation of the system, at least one step must have a finite enthalpy of reaction;

(7) the equilibria must be reasonably reversible so that measurable changes are produced;

(8) the time range of τ must be 5 μsec $< \tau <$ 1 sec, where the upper limit is set by the onset of convective cooling, and the lower limit is set by the rise time of the perturbation.

The temperature-jump instrument itself must be designed to bring about a rapid increase in the temperature of the system and must have a sensitive (since the perturbations are small) and quickly responding means of detection. A schematic of the temperature-jump apparatus used in these studies is shown in Figure II-2. This instrument uses Joule

FIGURE II-2. SCHEMATIC OF THE TEMPERATURE-JUMP APPARATUS



heating to effect an increase in temperature of 10°C (from 15°C to 25°C). A 0.1 μfarad capacitor is charged to 30,000 volts using a high voltage power supply. When the capacitor is discharged through the solution, the energy delivered to the system is 45 Joules, as calculated by the equation above. Upon a signal from an external trigger a variable spark gap completes the circuit, and the capacitor discharges through the solution; this discharge occurs in about 10^{-5} to 10^{-6} sec. The sample cell is constructed such that the total volume is approximately 25 ml, but the volume between the electrodes is 1 ml. The discharge of 45 Joules of energy through this 1 ml volume brings about a ten degree increase in temperature within the electrode region. The solution outside of this region acts as a heat sink, and the onset of convective cooling after approximately 1 sec provides an upper limit to the range of times accessible to temperature-jump. The lower limit is set by the rise time which is given by:

$$t = RC/2$$

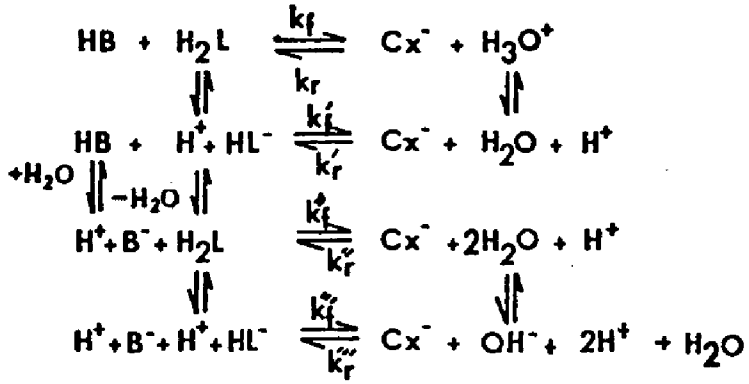
The total resistance of the cell and a solution with an ionic strength of 0.1M is 100 ohms, and as mentioned before, the capacitance is 0.1 μf. This leads to a rise time of 5 μsec, well out of the range of any of the relaxation times studied. By addition of KNO_3, the ionic strength of all solutions is maintained at $\mu = 0.1$ M, insuring a resistance of 100 ohms as well as maintaining a constant ionic strength

throughout the course of the reaction. Experimentally, the 10^{o} degree temperature rise is confirmed by comparison of the output voltages of an indicator at 15°C and 25°C with the change in voltage which occurs when the capacitor is discharged through a solution of the indicator.

For transient methods such as temperature-jump, the chemical changes as a function of time can be directly measured by observing any quantity which is related to concentration and which undergoes a transformation. This instrument uses a spectrophotometric detection system, but conductimetric, fluorimetric, and polarimetric properties are examples of other parameters which can be used to follow the kinetic processes. The systems studied here are coupled to acid-base indicators, and the change in absorbance of the indicator is monitored at a suitable wavelength (λ = 580 nm for orange IV, bromophenol blue, and chlorphenol red, and λ = 540 nm for phenolphthalein). The equilibria of these acid-base indicators are protolytic and, as such, are rapidly established (τ for the indicator << τ for the reaction of interest). Therefore, the coupled reactions can be considered constantly in equilibrium with the system whose relaxation time is being studied. In this way, the change in concentration of one of the reacting species, the hydrogen ion, is monitored as the system approaches equilibrium at 25°C.

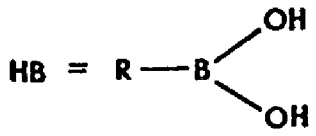
Temperature-Jump Kinetics for Boron Acid Systems

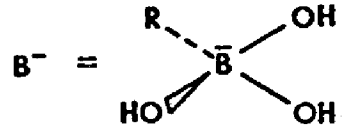
The particular expression which relates the experimentally obtained relaxation time to the specific rate constants is dependent upon the overall reaction mechanism. For the reactions of boron acids with polyols, α-hydroxycarboxylic acids, and dicarboxylic acids, the kinetic data were evaluated using the following reaction scheme:

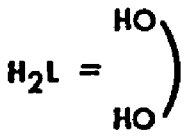


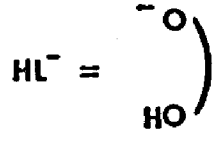
$$HIn \rightleftharpoons H^+ + In^-$$

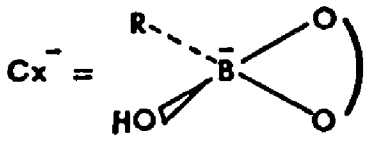
where the vertical equilibria involve protonation reactions and are fast, and where:











The derivation for the relaxation time is given here.

Variables: HB, B^-, H_2L, HL^-, H^+, OH^-, Cx^-, HIn, In^-

Conservation relationships:

$$0 = \delta HB + \delta B^- + \delta Cx^- \qquad \text{II.A.1}$$

$$0 = \delta H_2L + \delta HL^- + \delta Cx^- \qquad \text{II.A.2}$$

$$0 = \delta HIn + \delta In^- \qquad \text{II.A.3}$$

$$0 = \delta HB + \delta H_2L + \delta Cx^- + \delta H^+ + \delta HIn - \delta OH^- \qquad \text{II.A.4}$$

Rapid equilibria:

$$K_{H_2L} = \frac{[H^+][HL^-]}{[H_2L]} \qquad K_W = [H^+][OH^-]$$

$$K_{HB} = \frac{[H^+][B^-]}{[HB]}$$

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

The number of relaxation times expected for this system (see page 34) is n-(m+r)=9-(4+4)=1. Therefore, a single relaxation time should be seen, and the rate expression should take the form:

$$-\frac{d\delta x}{dt} = \frac{1}{\tau}\delta x$$

Expressing the concentrations as time independent equilibrium concentrations plus small deviation terms, one can rewrite the equilibrium constants.

$$K_{H_2L}[\overline{H_2L}] + K_{H_2L}\delta H_2L = [\overline{HL^-}][\overline{H^+}] + [\overline{H^+}]\delta HL^- + [\overline{HL^-}]\delta H^+ + \delta H^+\delta HL^-$$

The use of

$$K_{H_2L}\,[\overline{H_2L}] = [\overline{HL^-}][\overline{H^+}]$$

and

$$\delta H^+ \delta HL^- = 0$$

gives the following equilibrium expression:

$$K_{H_2L}\,\delta H_2L = [\overline{HL^-}]\,\delta H^+ + [\overline{H^+}]\delta HL^- \qquad \text{II.A.5}$$

Similarly:

$$K_{HB}\,\delta HB = [\overline{H^+}]\delta B^- + [\overline{B^-}]\,\delta H^+ \qquad \text{II.A.6}$$

and

$$K_{HIn}\,\delta HIn = [\overline{H^+}]\,\delta In^- + [\overline{In^-}]\delta H^+ \qquad \text{II.A.7}$$

and, from K_w:

$$0 = [\overline{OH^-}]\delta H^+ + [\overline{H^+}]\delta OH^- \qquad \text{II.A.8}$$

Since the desired form of the rate law is in terms of a single variable, δx, equations II.A.1 through II.A.8 are used to eliminate all but one of the nine concentration variables.

From equation II.A.3

$$\delta HIn = -\delta In^-$$

Substituting this into II.A.7 and solving for δHIn yields:

$$\delta HIn = \frac{[\overline{In^-}]}{[\overline{H^+}] + K_{HIn}} \qquad \text{II.A.9}$$

To solve for δOH^-, equation II.A.8 is rearranged:

$$\delta OH^- = \frac{[\overline{OH^-}]}{[\overline{H^+}]}\delta H^+ \qquad \text{II.A.10}$$

By substitution of II.A.9 and II.A.10 into equation II.A.4, and collection of terms in δH^+, one arrives at the following form of the proton balance equation:

$$0 = \delta HB + \delta H_2L + \delta Cx^- + \gamma\delta H^+ \qquad \text{II.A.4a}$$

where:

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

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

(α is the indicator coupling term.) The equilibrium expressions II.A.5 and II.A.6 can be used to solve for δHL^- and δB^-:

$$\delta HL^- = \frac{K_{H_2L}}{[\overline{H^+}]}\delta H_2L - \frac{[\overline{HL^-}]}{[\overline{H^+}]}\delta H^+ \qquad \text{II.A.5a}$$

$$\delta B^- = \frac{K_{HB}}{[\overline{H^+}]}\delta HB - \frac{[\overline{B^-}]}{[\overline{H^+}]}\delta H^+ \qquad \text{II.A.6a}$$

Using II.A.5a and II.A.6a in equations II.A.1 and II.A.2 allows reduction of the system to a set of three equations in four unknowns:

$$0 = \left(K_{HB} + [\overline{H^+}]\right)\delta HB - [\overline{B^-}]\delta H^+ + [\overline{H^+}]\delta Cx^- \qquad \text{II.A.11}$$

$$0 = \left(K_{H_2L} + [\overline{H^+}]\right)\delta H_2L - [\overline{HL^-}]\delta H^+ + [\overline{H^+}]\delta Cx^- \qquad \text{II.A.12}$$

$$0 = \delta HB + \delta H_2L + \gamma\delta H^+ + \delta Cx^- \qquad \text{II.A.13}$$

Multiplying II.A.13 by $(K_{H_2L} + [\overline{H^+}])$ and subtracting II.A.12

eliminates the term in δH_2L to give:

$$(K_{H_2L} + [\overline{H^+}])\delta HB + A\delta H^+ + K_{H_2L}\delta Cx^- = 0 \qquad \text{II.A.14}$$

where:

$$A = \gamma(K_{H_2L} + [\overline{H^+}]) + [\overline{HL^-}]$$

One can solve for δCx^- by multiplication of II.A.11 by $A/([\overline{B^-}])$ and addition of this to II.A.14 to eliminate δH^+:

$$\left\{\frac{A}{[\overline{B^-}]}\left(K_{HB} + [\overline{H^+}]\right) + K_{H_2L} + [\overline{H^+}]\right\}\delta HB + \left\{\frac{A}{[\overline{B^-}]}[\overline{H^+}] + K_{H_2L}\right\}\delta Cx^- = 0$$

and

$$\delta Cx^- = -Q\delta HB \qquad \text{II.A.15}$$

where:

$$Q = \left\{\frac{\frac{A}{[\overline{B^-}]}(K_{HB} + [\overline{H^+}]) + K_{H_2L} + [\overline{H^+}]}{\frac{A}{[\overline{B^-}]}[\overline{H^+}] + K_{H_2L}}\right\}$$

An expression for δH^+ in terms of δHB is arrived at by multiplying II.A.11 by

$$\frac{K_{H_2L}}{[\overline{H^+}]}$$

and subtracting II.A.14:

$$\delta H^+ = -R\delta HB \qquad \text{II.A.16}$$

where:

$$R = \left\{\frac{\frac{-K_{H_2L}K_{HB}}{[\overline{H^+}]} + [\overline{H^+}]}{\frac{K_{H_2L}[\overline{B^-}]}{[\overline{H^+}]} + A}\right\}$$

Multiplying II.A.13 by $[\overline{H^+}]$ and subtracting II.A.11 yields:

$$-K_{HB}\,\delta HB + \left[\overline{H^+}\right]\delta H_2L + \left(\gamma\left[\overline{H^+}\right]+\left[\overline{B^-}\right]\right)\delta H^+ = 0 \qquad \text{II.A.13a}$$

Multiplication of II.A.13 by ($[\overline{H^+}]$) followed by subtraction of II.A.12 results in:

$$\left[\overline{H^+}\right]\delta HB - K_{H_2L}\,\delta H_2L - \left(\gamma\left[\overline{H^+}\right]+\left[\overline{HL^-}\right]\right)\delta H^+ = 0 \qquad \text{II.A.13b}$$

If II.A.13a is multiplied by

$$\frac{\gamma\left[\overline{H^+}\right]+\left[\overline{HL^-}\right]}{\gamma\left[\overline{H^+}\right]+\left[\overline{B^-}\right]}$$

and II.A.13b is subtracted from this product, one can eliminate δH^+ and solve for δH_2L in terms of δHB:

$$\delta H_2L = S\delta HB \qquad \text{II.A.17}$$

where:

$$S = \left\{ \frac{\left(\dfrac{\gamma\left[\overline{H^+}\right]+\left[\overline{HL^-}\right]}{\gamma\left[\overline{H^+}\right]+\left[\overline{B^-}\right]}\right)K_{HB}+\left[\overline{H^+}\right]}{\left(\dfrac{\gamma\left[\overline{H^+}\right]+\left[\overline{HL^-}\right]}{\gamma\left[\overline{H^+}\right]+\left[\overline{B^-}\right]}\right)\left[\overline{H^+}\right]+K_{H_2L}} \right\}$$

The following expressions have now been obtained:

$$\delta Cx^- = -Q\delta HB \qquad \text{II.A.15}$$

$$\delta H^+ = -R\delta HB \qquad \text{II.A.16}$$

$$\delta H_2L = S\delta HB \qquad \text{IIA.17}$$

From equations II.A.1 and II.A.15:

$$\delta B^- = (Q-1)\,\delta HB \qquad \text{II.A.18}$$

From equations II.A.2, II.A19, and II.A.15:

$$\delta HL^- = (Q - S)\,\delta HB \qquad \text{II.A.19}$$

From equations II.A.10 and II.A.16: $\delta OH^- = \dfrac{[\overline{OH^-}]}{[\overline{H^+}]} R\,\delta HB$ II.A.20

Equations II.A.15 through II.A.20 now express all of the concentration changes in terms of δHB.

The rate law for the disappearance of HB is given by:

$$\begin{aligned} -\frac{d\,HB}{dt} &= k_f [HB][H_2L] - k_r [Cx^-][H^+] \\ &+ k_f' [HB][HL^-] - k_r' [Cx^-] \\ &+ k_f'' [B^-][H_2L] - k_r'' [Cx^-] \\ &+ k_f''' [B^-][HL^-] - k_r''' [Cx^-][OH^-] \end{aligned}$$

Using:

$$\begin{aligned} [HB] &= [\overline{HB}] + \delta HB \\ [B^-] &= [\overline{B^-}] + \delta B^- \\ [H_2L] &= [\overline{H_2L}] + \delta H_2L \\ [HL^-] &= [\overline{HL^-}] + \delta HL^- \\ [Cx^-] &= [\overline{Cx^-}] + \delta Cx^- \\ [H^+] &= [\overline{H^+}] + \delta H^+ \\ [OH^-] &= [\overline{OH^-}] + \delta OH^- \end{aligned}$$

and linearizing the rate expression (neglecting any $\delta x\,\delta y$ terms), one obtains:

$$\begin{aligned} -\frac{d\,\delta HB}{dt} = {} & k_f\left([\overline{HB}]\,\delta H_2L + [\overline{H_2L}]\,\delta HB\right) - k_r\left([\overline{Cx^-}]\,\delta H^+ + [\overline{H^+}]\,\delta Cx^-\right) \\ & + k_f'\left([\overline{HB}]\,\delta HL^- + [\overline{HL^-}]\,\delta HB\right) - k_r'\left(\delta Cx^-\right) \\ & + k_f''\left([\overline{B^-}]\,\delta H_2L + [\overline{H_2L}]\,\delta B^-\right) - k_r''\left(\delta Cx^-\right) \\ & + k_f'''\left([\overline{B^-}]\,\delta HL^- + [\overline{HL^-}]\,\delta B^-\right) - k_r'''\left([\overline{Cx^-}]\,\delta OH^- [\overline{OH^-}]\,\delta Cx^-\right) \end{aligned}$$

Putting equations II.A.15 through II.A.20 into this rate expression and making use of the fact that $K_{stab} = k_f/k_r$, the following is arrived at:

$$
\begin{aligned}
-\frac{d\,\delta HB}{dt} = {} & k_f \left\{ S\left[\overline{HB}\right] + \left[\overline{H_2L}\right] + \frac{1}{K}\left(R\left[\overline{Cx^-}\right] + Q\left[\overline{H^+}\right]\right)\right\} \delta HB \\
& + k_f' \left\{ (Q-S)\left[\overline{HB}\right] + \left[\overline{HL^-}\right] + \frac{K_{H_2L}}{K} Q \right\} \delta HB \\
& + k_f'' \left\{ S\left[\overline{B^-}\right] + (Q-1)\left[\overline{H_2L}\right] + \frac{K_{HB}}{K} Q \right\} \delta HB \\
& + k_f''' \left\{ (Q-S)\left[\overline{B^-}\right] + (Q-1)\left[\overline{HL^-}\right] + \frac{K_{HL} K_{HB}}{K K_w}\left(Q\left[\overline{OH^-}\right] - R\frac{\left[\overline{OH^-}\right]\left[\overline{Cx^-}\right]}{\left[\overline{H^+}\right]}\right)\right\} \delta HB
\end{aligned}
\qquad \text{II.A.22}
$$

This is of the form:

$$-\frac{d\delta HB}{dt} = \frac{1}{\tau}\,\delta HB$$

for:

$$\frac{1}{\tau} = k_f\{W\} + k_f'\{X\} + k_f''\{Y\} + k_f'''\{Z\} \qquad \text{II.A.23}$$

with the expressions for W, X, Y and Z given by equation II.A.22.

The stability constant, K, is defined as follows:

$$K = \frac{\left[Cx^-\right]\left[H^+\right]}{\left[HB\right]\left[H_2L\right]}$$

For each boron acid-ligand system, a number of relaxation times were measured for varying concentrations of boron acid and ligand at different pH's. The coefficients of equation II.A.23 were evaluated for each solution and best fit values of the forward rate constants were determined. Reverse rate

constants were calculated using the stability constants and the appropriate forward rate constants. It should be noted that by adjustment of the pH of the particular solution, different terms in expression II.A.22 can become dominant, and the relaxation times may be fit to a rate expression of fewer than four terms. For example, at pH=2, for a boron acid such as $\phi B(OH)_2$ (pK_a=9.25) and a ligand such as 4-nitrocatechol (pK_a=6.69), the boron acid exists mainly as HB and the ligand as H_2L, and the rate constant, k_f can be calculated from the single term expression:

$$\frac{1}{\tau} = k_f \{W\}$$

Relaxation times are obtained from semilogarithmic plots of ln δHB as a function of time. The traces are recorded on a storage oscilloscope, and the amplitudes taken from pictures of the reaction curves. The intercept, δHB_o, is graphically determined and τ is taken as the value of t at 0.368 ($=e^{-1}$) times δHB_o. This is illustrated in Figure II-3. When the rate constants for a particular system have been determined, these values can then be used to calculate an expected relaxation time, again by the use of equation II.A.23. Table II-1 shows a comparison of experimentally measured relaxation times and relaxation times calculated using appropriate values for the rate constants for the $\phi B(OH)_2$- 4-nitrocatechol system.

In principle, if all the equilibrium constants of a

FIGURE II-3. GRAPHICAL DETERMINATION OF RELAXATION TIME

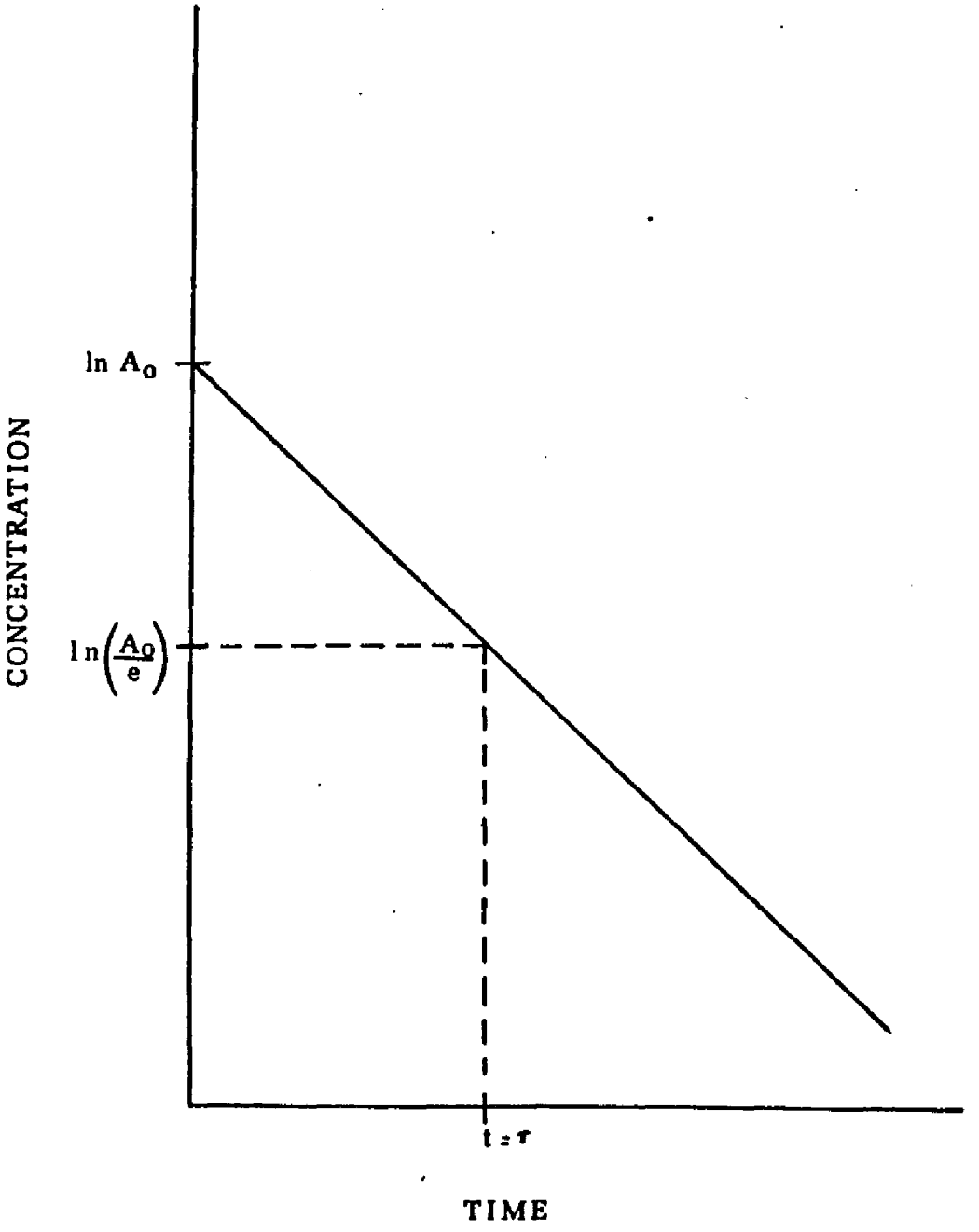


Table II-1. Relaxation Spectra of $\phi B(OH)_2$/4-nitrocatechol Solutions

$[\phi B(OH)_2]$,M	[4-nitrocatechol],M	pH[a]	tau_{exp},msec	tau_{calc},msec
0.0396	0.0364	4.33	0.20	0.20
0.0396	0.0364	3.91	0.22	0.27
0.0396	0.0364	6.48	0.41	0.41
0.0163	0.0439	3.90	0.49	0.43
0.0163	0.0439	3.42	0.77	0.80
0.0407	0.0228	4.43	0.25	0.27
0.0407	0.0228	3.97	0.30	0.33
0.0407	0.0228	3.49	0.69	0.64
0.0407[b]	0.0510	4.48	0.25	0.26
0.0407[b]	0.0510	4.05	0.18	0.19
0.0407[b]	0.0510	3.60	0.33	0.28
0.0407[b]	0.0459	6.02	1.97	1.99
0.0407[b]	0.0459	5.59	1.45	1.31

[a] The indicator in all solutions between pH4.48 and pH 3.42 was bromophenol blue (2.52×10^{-5} M); above pH 5.59, chlorphenol red (2.02×10^{-5} M) was used. All reactions were monitored at λ=580nm.

[b] These solutions contain 0.01 M sodium bisulfite.

reaction scheme are known, all the equilibrium concentrations can be determined. This is essential for a correct interpretation of the kinetic properties of the system. Acid dissociation constants of the species involved (HB and H_2L) can be determined by titration with standard base. In addition, determination of the stability constants for the complexation reactions, as defined below, must be carried out.

$$HB + H_2L \rightleftharpoons Cx^- + H^+ \qquad K = \frac{[Cx^-][H^+]}{[HB][H_2L]}$$

This is important not only in the calculation of equilibrium concentrations of the species involved in the reacting system, but also in relating the forward and reverse rate constants as given by the law of mass action:[9]

$$K = \frac{[R]^r [S]^s}{[P]^p [Q]^q} = \frac{k_f}{k_r}$$

for:

$$pP + qQ \rightleftharpoons rR + sS$$

This permits calculation of the reverse rate constants from a knowledge of K and k_f, and allows the rate law to be expressed in terms of the forward rate constants alone, as in the relaxation expression given previously. Various methods for the calculation of both acid dissociation constants[10] and complex stability constants[11] are well docu-

mented.

Stability Constant Determination

In these cases, the K's were obtained by either or both of two methods: (1) the titration of a boron acid-ligand solution with standard base, or (2) the titration of ligand with boron acid (and vice versa). Derivations of the expressions used to calculate the stability constants by each of these methods follow.

In the titration with standard NaOH, the pH of a solution of known initial boron acid and ligand concentration is measured at several incremental additions of base. A stability constant is then calculated for each point on the titration curve.

The equilibria involved are:

$$K_{a1} = \frac{[H^+][HL^-]}{[H_2L]} \qquad \text{II.B.1}$$

$$K_{a2} = \frac{[H^+][L^{2-}]}{[HL^-]} \qquad \text{II.B.2}$$

$$K_{HB} = \frac{[H^+][B^-]}{[HB]} \qquad \text{II.B.3}$$

$$K_W = [H^+][OH^-] \qquad \text{II.B.4}$$

Conservation of mass and conservation of charge yield the following equations:

$$L_o = [H_2L] + [HL^-] + [L^{2-}] + [Cx^-] \qquad \text{II.B.5}$$

$$B_o = [HB] + [B^-] + [Cx^-] \qquad \text{II.B.6}$$

$$[Na^+] + [H^+] = [B^-] + [HL^-] + 2[L^{2-}] + [OH^-] + [Cx^-] \qquad \text{II.B.7}$$

From II.B.1:

$$[H_2L] = \frac{[H^+]}{K_{a1}} [HL^-]$$

From II.B.2:

$$[L^{2-}] = \frac{K_{a2}}{[H^+]} [HL^-]$$

Putting these expressions into II.B.5, one obtains:

$$L_o = \alpha[HL^-] + [Cx^-]$$

$$[HL^-] = \frac{L_o - [Cx^-]}{\alpha} \qquad \text{II.B.5a}$$

where:

$$\alpha = 1 + \frac{[H^+]}{K_{a1}} + \frac{K_{a2}}{[H^+]}$$

From II.B.3:

$$HB = \frac{[H^+]}{K_{HB}} [B^-]$$

Substitution for [HB] in II.B.6 gives:

$$B_o = \beta[B^-] + [Cx^-]$$

$$[B^-] = \frac{B_o - [Cx^-]}{\beta} \qquad \text{II.B.6a}$$

where:

$$\beta = 1 + \frac{[H^+]}{K_{HB}}$$

Using $[OH^-] = K_w/[H^+]$, and $[Na^+] = Na_o$, and putting II.B.5a and II.B.6a into equation II.B.7 gives:

$$Na_o + [H^+] - \frac{B_o}{\beta} - \frac{K_w}{[H^+]} - \frac{\gamma}{\alpha} L_o = [Cx^-]\left(1 - \frac{\gamma}{\alpha} - \frac{1}{\beta}\right) \qquad \text{II.B.8}$$

where:

$$\gamma = 1 + \frac{2K_{a2}}{[H^+]}$$

Equation II.B.8 can now be solved for $[Cx^-]$:

$$[Cx^-] = \left\{ \frac{\left(Na_o + [H^+] - \frac{B_o}{\beta} - \frac{\gamma}{\alpha} L_o - \frac{K_w}{[H^+]}\right)}{\left(1 - \frac{\gamma}{\alpha} - \frac{1}{\beta}\right)} \right\} \qquad \text{II.B.9}$$

Using II.B.5a, the HL^- concentration can be calculated, and this result inserted into equation II.B.1 gives $[H_2L]$. Equation II.B.6a can be solved for $[B^-]$ knowing $[Cx^-]$, and this is used in II.B.3 to obtain [HB]. The value of the equilibrium constant, K, can now be calculated according to:

$$K = \frac{[H^+][Cx^-]}{[HB][H_2L]} \qquad \text{II.B.10}$$

It is important to point out here that these calculations can be done at low pH's, and yield good values of the stability constant.

Recall that Edwards[12] determined K values assuming that it was the tetrahedral anion which reacted:

$$B^- + H_2L \rightleftharpoons Cx^- + H_2O$$

$$K' = \frac{[Cx^-]}{[B^-][H_2L]} \qquad \text{II.B.11}$$

Because he worked with buffered solutions of boric acid and phenylboronic acid, this assumption holds true. However, examination of equations II.B.10 and II.B.1 shows that the two expressions for the stability constant are related:

$$K = K' K_{HB}$$

This would seem to indicate that, while at high pHs it is predominantly the tetrahedral form which reacts, at low pHs the trigonal form also reacts to give a tetrahedral product. Kinetic data also indicate that trigonal as well as tetrahedral boron acids will undergo complexation, and that only the tetrahedral form reacts[12] was an idea which developed from thermodynamic work done at high pHs and from the knowledge that the complex was tetrahedral.

The pH mixing technique makes use of the fact that the complexation reaction causes readjustment of the equilibria involved, and consequently a change in pH. Solutions of ligand and boron acid are adjusted to the same initial pH,

and the change in pH of one is measured upon addition of known volumes of the other. The overall complexation can be viewed as:

$$HB + HL^- \rightleftharpoons Cx^- + H_2O \qquad K' = K/K_{a1} \qquad \text{II.C.1}$$

The equilibria which readjust following reaction II.C.1 are:

$$HB \rightleftharpoons H^+ + B^- \qquad \text{II.C.2}$$

$$H_2L \rightleftharpoons H^+ + HL^- \qquad \text{II.C.3}$$

$$HL^- \rightleftharpoons H^+ + L^{2-} \qquad \text{II.C.4}$$

The changes in H^+ concentration due to the shift of reactions II.C.2 through II.C.4 are given by:

ΔH_1=change due to dissociation of $H_2L \rightleftharpoons H^+ + HL^-$

ΔH_2=change due to association of $L^{2-} + H^+ \rightleftharpoons HL^-$

ΔH_3=change due to association of $B^- + H^+ \rightleftharpoons HB$

The conservation relationships can be written as:

$$[HL^-] = [HL_o^-] - [Cx^-] + \Delta H_1 + \Delta H_2 \qquad \text{II.C.5}$$

$$[H_2L] = [H_2L_o] - \Delta H_1 \qquad \text{II.C.6}$$

$$[L^{2-}] = [L_o^{2-}] - \Delta H_2 \qquad \text{II.C.7}$$

$$[HB] = [HB_o] - [Cx^-] + \Delta H_3 \qquad \text{II.C.8}$$

$$[B^-] = [B_o^-] - \Delta H_3 \qquad \text{II.C.9}$$

$$\Delta H = \Delta H_1 - \Delta H_2 - \Delta H_3 \qquad \text{II.C.10}$$

where the subscript zero indicates the initial concentration before the shift in equilibrium due to complexation, and ΔH

represents the measured change in pH ($H^+_f - H^+_i$); ΔH_1 tends to increase the H^+ concentration, while ΔH_2 and ΔH_3 tend to decrease it. From II.C.2, II.C.8, and II.C.9:

$$K_{HB} = \frac{[H^+_f][B^-]}{[HB]}$$

$$= \frac{[H^+_f]\left([B^-_o] - \Delta H_3\right)}{\left([HB_o] - [Cx^-] + \Delta H_3\right)} \qquad \text{II.C.11}$$

This can be solved for ΔH_3:

$$\Delta H_3 = \alpha + \beta[Cx^-] \qquad \text{II.C.12}$$

where:

$$\alpha = \frac{[H^+_f][B^-_o] - K_{HB}[HB_o]}{K_{HB} + [H^+_f]}$$

and

$$\beta = \frac{K_{HB}}{K_{HB} + [H^+_f]}$$

Now, from II.C.10 and II.C.12:

$$\Delta H_1 = \Delta H + \Delta H_2 + \alpha + \beta[Cx^-] \qquad \text{II.C.13}$$

And from II.C.3, using II.C.5, II.C.6, and II.C.13, solving for ΔH_2 yields:

$$\Delta H_2 = \frac{K_{a1}\left\{[H_2L_o] - \Delta H - \alpha\right\} - [H^+_f]\left\{[HL^-_o] + \Delta H + \alpha\right\} - \left\{K_{a1}\beta + [H^+_f](\beta - 1)\right\}[Cx^-]}{2[H^+_f] + K_{a1}}$$

II.C.14

From equation II.C.4, using II.C.5, II.C.7, and II.C.13, a second expression for ΔH_2 is obtained:

$$\Delta H_2 = \frac{[H_f^+][L_o^{2-}] - K_{a2}\left([HL_o^-] + \Delta H + \alpha\right)\left[Cx^-\right]\left(K_{a2} - \beta K_{a2}\right)}{2K_{a2} + [H_f^+]} \qquad \text{II.C.15}$$

Equating II.C.14 and II.C.15 and solving for $[Cx^-]$ yields:

$$Cx^- = \frac{\left\{\frac{K_{a1}\left\{[H_2L_o] - \Delta H - \alpha\right\} - [H_f^+]\left\{[HL_o^-] + \Delta H + \alpha\right\}}{2[H_f^+] + K_{a1}}\right\} - \left\{\frac{[H_f^+][L_o^{2-}] - K_{a2}\left\{[HL_o^-] + \Delta H + \alpha\right\}}{2K_{a2} + [H_f^+]}\right\}}{\left\{\frac{K_{a2} - \beta K_{a2}}{2K_{a2} + [H_f^+]}\right\} + \left\{\frac{K_{a1}\beta + H_f^+\left\{\beta - 1\right\}}{2[H_f^+] + K_{a1}}\right\}}$$

From the equation above, the concentration of complex can be calculated, and from this, using II.C.14, II.C.12, and II.C.5 through II.C.10, all the equilibrium concentrations can be calculated. As in the NaOH titration, the stability constant is then determined using the equation:

$$K = \frac{[H^+][Cx^-]}{[HB][H_2L]}$$

The determination of stability constants of the complexation reactions allows calculation of the equilibrium concentrations which appear in equation II.A.22.

The titrations performed to determine both acid dissociation constants and stability constants were done at constant temperature under a nitrogen atmosphere. A circulating constant temperature bath maintained all solutions at 25°C . The ionic strength was maintained at μ=0.1 M by ad-

dition of KNO_3, and the hydrogen ion activity correction was made using the Davies equation:[13]

$$\log \gamma_{\pm} = -0.5 \left| z_+ z_- \right| \left(\frac{\sqrt{\mu}}{1+\sqrt{\mu}} - 0.3\sqrt{\mu} \right)$$

pH measurements were done on a Corning Model 12 research pH meter.

Introduction to the Specific Systems Investigated

The total reaction scheme for the reactions of boron acids with the bidentate ligands studied is given by:

$$\begin{array}{ccc} HB + H_2L & \rightleftharpoons & Cx^- + H_3O^+ \\ \rightleftharpoons & & \rightleftharpoons \\ HB + H + HL & \rightleftharpoons & Cx^- + H_2O + H^+ \\ {}^{+H_2O}\rightleftharpoons{}^{-H_2O} & & \\ H^+ + B^- + H_2L & \rightleftharpoons & Cx^- + 2H_2O + H^+ \\ \rightleftharpoons & & \rightleftharpoons \\ H^+ + B^- + H^+ + HL^- & \rightleftharpoons & Cx^- + OH^- + 2H^+ + H_2O \end{array}$$

A single relaxation time which is characteristic of the formation of the complex, Cx^-, is measured, and it contains contributions from all four pathways. By suitable adjustment of the solution pH, different species can be made to predominate, and the measurement of the relaxation times obtained at varying reactant concentrations and initial pHs permits evaluation of the different rate constants. A

series of experiments thus yields the various forward rate constants (k_r' can then be calculated from these and the appropriate stability constant, K.) The results of these studies will be presented and discussed in a somewhat different format. Rather than examining each system in toto, the reactions will be looked at in terms of the following: (1) the reactions of fully protonated ligands with boron acids, (2) the reactions of ligand anions with boron acids, (3) the reactions of tetrahedral boron, and (4) the 1:2 complexes of boric acid.

A study was made of the reactions of four boron acids with several ligands which span a pK_{a1} range of 1.04 to 13.5; the boron acids had pK_as which varied from 6.96 to 10.4. Stability constants of a series of ligands with one boron acid increase as the ligand pK_{a1} decreases and, for a single ligand, the stability constants increase as the acidity of the boron acid increases. The thermodynamic and kinetic results indicate a mechanism in which proton transfer plays an important role. Effects due to ligand geometry are also observed.

The boron acids used were methylboronic acid ($CH_3B(OH)_2$), boric acid ($B(OH)_3$), phenylboronic acid ($\phi B(OH)_2$), and m-nitrophenylboronic acid ($m\text{-}NO_2\phi B(OH)_2$). Acid dissociation constants were determined by titration with 0.1N NaOH, and found to be as follows: methylboronic acid, pK_a=10.4, boric acid, pK_a=9.0,[14] phenylboronic acid,

pK_a=8.7,[15] and m-nitrophenylboronic acid, pK_a=6.96, (lit. 7.3[16]). The ligands investigated were mannitol, pK_{a1}=13.5;[17] catechol (1,2-dihydroxybenzene), pK_{a1}=9.27 (lit. 9.25[18]); the substituted catechols 4-nitrocatechol, pK_{a1}=6.69 (lit. 6.78[19]) and 4-methylcatechol, pK_{a1}=9.39; mandelic acid, pK_{a1}=3.22, and salicylic acid, pK_{a1}=2.83 (lit. 2.69[20]). Structures of these ligands and boron acids are found in Appendix A.

All ligands and boron acids were reagent grade and were used as received unless otherwise specified. Solid 4-methylcatechol was further purified by vacuum distillation and the purity of the resultant white crystalline material was checked by pH titration. Methylboronic acid is stabilized by the addition of water, and titration as well as NMR data revealed this amount of water to be less than one per cent by weight.

The catechols undergo oxidation by molecular oxygen in neutral and basic solution to form their various quinones.[21] Therefore, kinetic studies involving catechol, 4-nitrocatechol, and 4-methylcatechol were carried out in the presence of sodium bisulfite to inhibit this oxidation. At pHs of about six, the addition of bisulfite was found to be necessary; oxidation of the catechols interfered with the complexation reactions, and the relaxation times for the complexation reactions at these pHs were reproducible only in the presence of bisulfite. At pHs of about four, the re-

laxation times obtained with and without bisulfite were virtually identical, indicating that oxidation at these pHs is not a serious problem.

Stability constants for the boron acid/ligand systems were determined both by the pH mixing method and by the titration with standard sodium hydroxide. The calculations were carried out using equations II.B.1 through II.B.9 and II.C.1 through II.C.15. Kinetic data were fit according to the equation for the relaxation time derived in section II.A. For studies at low pHs, the relaxation times could be fit to one or two term rate expressions. At higher pHs, the number of terms necessary to obtain a good fit for the experimentally obtained τ's was dependent upon the pK_{a1} of the ligand and the pK_a of the boron acid involved. The error associated with all of the reported rate constants is ±10 per cent. The values of the stability constants have associated errors of ±5 per cent.

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CHAPTER THREE

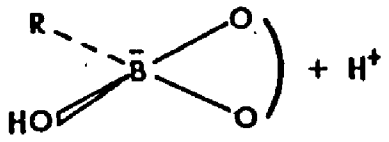
Reactions of Fully Protonated Ligands with Trigonal Boron Acids

General

The reaction of boron acids with fully protonated ligands is represented by the first equation presented in section II.A:

$$H_2L + RB(OH)_2 \rightleftharpoons Cx^- + H_3O^+$$

The complex is formed via a reaction which is both an addition and a substitution; one ligand donor atom occupies a previously vacant site on the boron, and the other displaces a hydroxyl group from the boron. Some ligands which form complexes of this type are polyols,[1,2] α-hydroxycarboxylic acids,[3,4] and dicarboxylic acids.[5,6] The ligand donor atoms are oxygen atoms in these cases, and both ligand protons are displaced upon reaction. Five and six membered chelate rings are formed:[7,8,9]



The stability constants of the various ligands with methylboronic acid, boric acid, phenylboronic acid, and m-nitrophenylboronic acid are presented in Tables III-1 through III-4. It can be seen that for each boron acid, the stability constant increases as the acidity of the ligand increases. The variation in stability constant as a function of boron acid pK_a is presented in Table III-5 for the 4-nitrocatechol ligand. In general, the value increases from m-nitrophenylboronic acid to methylboronic acid. This trend, an increase in stability constant as the acidity of the boron acid or of the ligand increases, will be seen shortly to be reflected kinetically in both an increase in the forward rate constant and a decrease in the reverse rate constant. The proposed mechanism of complexation emphasizes proton transfer as an important factor.

It is interesting and surprising to note that no thermodynamic evidence was found for the formation of any 1:2 complexes of boric acid with catechol and the substituted catechols. Calculations for both pH mixing and sodium hydroxide titrations gave good values of K_{stab} for the 1:1 complexes under the experimental conditions. This is consistent with the recent studies of E.J. Hakoila et al.[11] and of M. Bartusek[12] in which stability constants of some boric acid systems were determined. It is easy to visualize the formation of a 1:2 complex via the condensation between the hydroxyl groups of the second ligand and the hydroxyl groups

Table III-1. Stability Constants of $\phi B(OH)_2$/Ligand Complexes

Ligand	pK_{a1}	pK_{a2}	K_{stab}
Oxalic Acid[5]	1.04	3.78	3.2
Malonic Acid[6]	2.59	5.25	2.6×10^{-2}
Salicylic Acid	2.83	-	6.8×10^{-2}
Mandelic Acid	3.22	-	1.5×10^{-2}
Lactic Acid[4]	3.70	-	3.7×10^{-3}
4-nitrocatechol	6.69	10.57	9.5×10^{-4}
Catechol	9.27	11.49	4.7×10^{-5}
4-methylcatechol	9.39	11.59	3.0×10^{-5}
Mannitol	13.5	-	5.3×10^{-6}

Table III-2. Stability Constants of $B(OH)_3$/Ligand Complexes

Ligand	pK_{a1}	pK_{a2}	K_{stab}
Salicylic Acid[10]	2.83	-	1.1×10^{-2}
Tartaric Acid[3]	2.89	4.52	1.85×10^{-2}
4-nitrocatechol	6.69	10.57	1.5×10^{-4}
Catechol	9.27	11.49	1.1×10^{-5}
4-methylcatechol	9.39	11.59	6.3×10^{-6}

Table III-3. Stability Constants of $CH_3B(OH)_2$/Ligand Complexes

Ligand	pK_{a1}	pK_{a2}	K_{stab}
Salicylic Acid	2.83	-	4.5×10^{-3}
Mandelic Acid	3.22	-	2.1×10^{-3}
4-nitrocatechol	6.69	10.57	4.3×10^{-5}
Catechol	9.27	11.49	1.6×10^{-6}

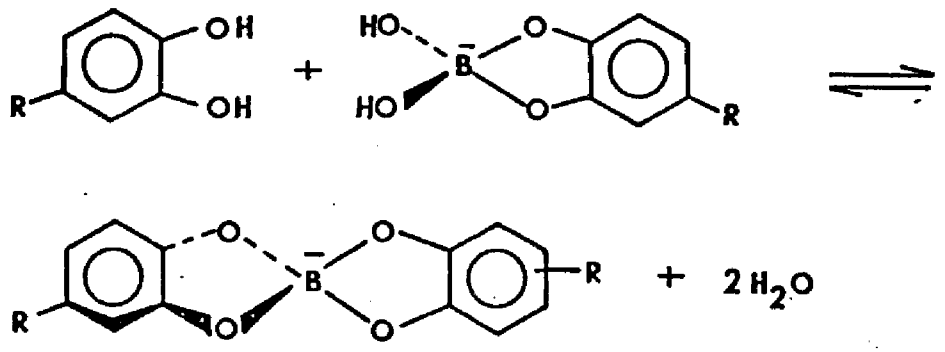
Table III-4. Stability Constants of m-$NO_2\phi B(OH)_2$/Ligand Complexes

Ligand	pK_{a1}	pK_{a2}	K_{stab}
Salicylic Acid	2.83	-	1.1
Mandelic Acid	3.22	-	1.9×10^{-1}
4-nitrocatechol	6.69	10.57	1.6×10^{-2}
4-methylcatechol	9.39	11.59	5.5×10^{-4}

Table III-5. Stability Constants of $RB(OH)_2$/4-nitrocatechol Complexes

Boron Acid	pK_a	k_{stab}
m-nitrophenylboronic Acid	6.96	1.6×10^{-2}
Phenylboronic Acid	8.7	9.5×10^{-4}
Boric Acid	9.0	1.5×10^{-4}
Methylboronic Acid	10.4	4.3×10^{-5}

of the 1:1 complex:



In fact, 1:2 complexes of boric acid do exist for ligands which are less acidic than catechol and also for ligands which are more acidic than catechol. Ligand geometry and rigidity are factors to consider in discussing the absence of the 1:2 complexes. The rigidity of the catechol ligands seems to favor complex formation in the 1:1 case, but this rigidity may hinder the formation of the 1:2 species for which the geometric requirement is certainly different. That these reactions in general are sensitive to ligand stereochemistry is seen in the failure of ethylene glycol[2] and the 1,2-cyclohexanediols[13] to form detectable amounts of either 1:1 or 1:2 complexes with boron acids.

Studies of a Single Boron Acid with a Variety of Ligands

The results of the kinetic studies of the $RB(OH)_2/H_2L$ reactions are given in Tables III-6 through III-9. Within a particular $RB(OH)_2$ series, the rate constants, both forward

Table III-6. Rate Constants for $\phi B(OH)_2/H_2L$ Reactions (pK_{aHB}=8.7)

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	log k_f	log k_r
Oxalic Acid[5]	1.04	$2x10^3$	$6.2x10^2$	3.3	2.8
Malonic Acid[6]	2.59	350	$1.3x10^4$	2.5	4.1
Salicylic Acid	2.83	225	$3.3x10^3$	2.4	3.5
Mandelic Acid	3.22	175	$4.7x10^4$	2.2	4.7
Lactic Acid[4]	3.70	140	$3.8x10^4$	2.2	4.6
4-nitrocatechol	6.69	650	$6.8x10^5$	2.8	5.8
Catechol	9.27	110	$2.3x10^6$	2.0	6.4
4-methylcatechol	9.39	120	$4x10^6$	2.1	6.6
Mannitol	13.5	50	10^7	1.7	7

Table III-7. Rate Constants for $B(OH)_3/H_2L$ Reactions (pK_{HB}=9.0)

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	log $_f$	log k_r
Salicylic Acid[10]	2.83	135	$4.5x10^3$	2.1	3.7
Tartaric Acid[3]	2.89	475	$2.6x10^4$	2.7	4.4
4-nitrocatechol	6.69	250	$1.7x10^6$	2.4	6.2
Catechol	9.27	60	$5.4x10^6$	1.8	6.7
4-methylcatechol	9.39	54	$8.6x10^6$	1.7	6.9

Table III-8. Rate Constants for $CH_3B(OH)_2/H_2L$ Reactions (pK_{HB}=10.4)

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	log k_f	log k_r
Salicylic Acid	2.83	55	1.2×10^4	1.7	4.1
4-nitrocatechol	6.69	45	1.0×10^6	1.7	6.0
Catechol	9.27	7.6	4.8×10^6	0.9	6.7

Table III-9. Rate Constants for $m\text{-}NO_2\phi B(OH)_2/H_2L$ Reactions (pK_{HB}=6.96)

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	log k_f	log k_r
Salicylic Acid	2.83	650	590	2.8	2.8
Mandelic Acid	3.22	2.5×10^3	1.3×10^4	3.4	4.1
4-nitrocatechol	6.69	2×10^3	1.3×10^5	3.3	5.1
4-methylcatechol	9.39	1.5×10^3	2.7×10^6	3.2	6.4

and reverse, depend upon ligand acidity. As mentioned previously, the general increase in stability constant with an increase in ligand acidity is seen kinetically as an increased forward rate constant and a decreased reverse rate constant as well. This is evident from the tabulated results. The studies carried out with phenylboronic acid (Table III-6) are the most comprehensive, the range of pK_{a1}s spanned by the ligands being from pK_{a1}=1.04 to pK_{a1}=13.5. Investigations of the other boron acids (boric acid, methylboronic acid, and m-nitrophenylboronic acid) indicate that the conclusions which can be made on the basis of the reactions of phenylboronic acid can be extended to include other boron acids as well. The variation in rate constants for reactions of different boron acids with fully protonated ligands can be attributed to differences in acidity among these acids, and will be discussed subsequently.

From Table III-6, the reactions of phenylboronic acid with H_2L, it is seen that as ligand pK_{a1} decreases, k_f increases and k_r decreases. The correlation of k_f with pK_{a1} is not precise, although a general trend exists. In the reverse direction, however, the log of the rate constant can be precisely correlated with the acid dissociation constants of the ligands studied as shown in Figure III-1. The correlation of the log of the reverse rate constant with the pK_{a1} of the ligand is shown in Figure III-2 for the reactions of m-nitrophenylboronic acid, and indicates that the same

FIGURE III-1. REACTIONS OF PHENYLBORONIC ACID WITH H_2L

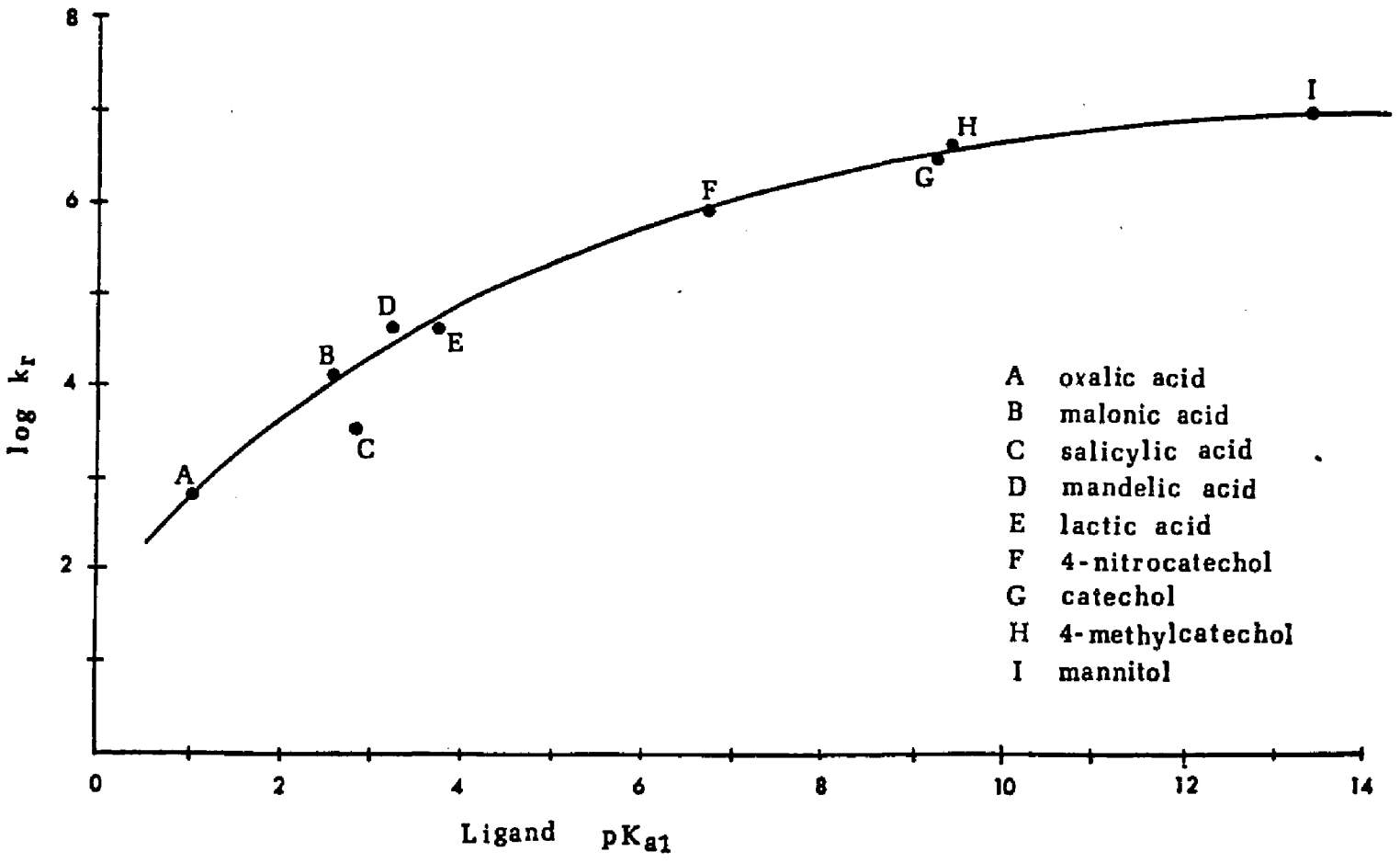
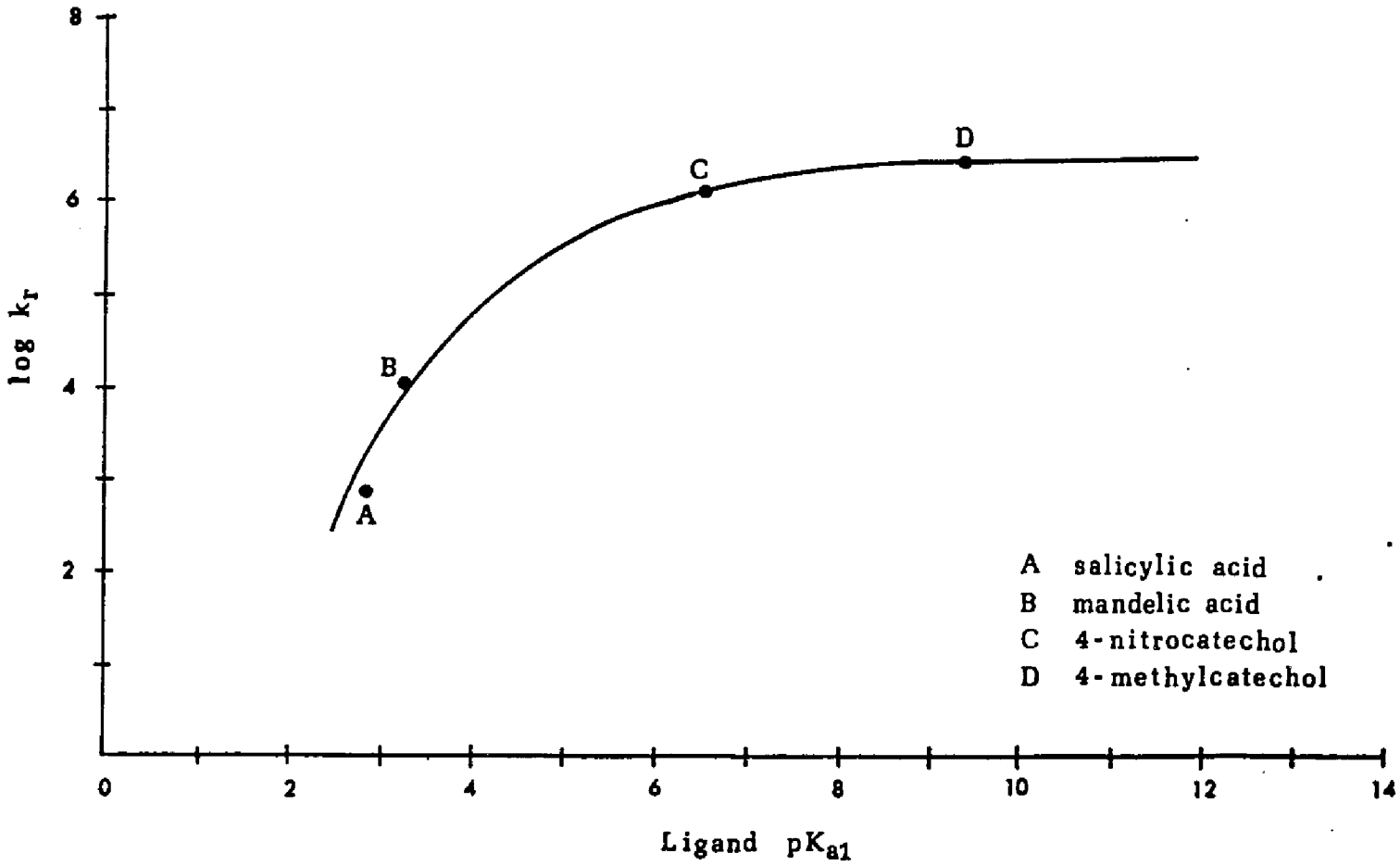
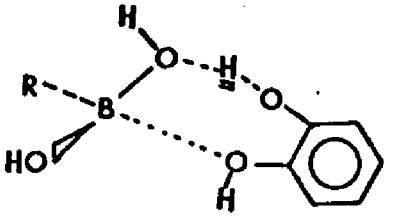


FIGURE III-2. REACTIONS OF m-NITROPHENYLBORONIC ACID WITH H_2L

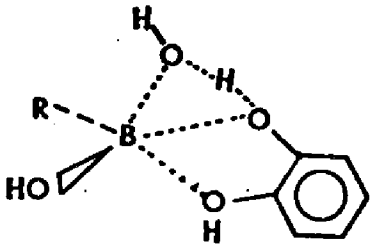


mechanism is applicable to the reactions of other boron acids as well. This correlation suggests a mechanism in which proton transfer in the transition state plays an important role. The transition state can be pictured as follows, where the ligand depicted is catechol, but could be any one of the complexing ligands:



The proton being transferred is underlined. In the forward direction, the proton is transferred from the oxygen donor atom of the ligand to the leaving hydroxyl group on the boron. The leaving of the water molecule is then followed by chelate ring closure. In the reverse direction, a proton is transferred from an incoming water molecule to the leaving catecholate ligand. The correlation of rate with pK_{a1} and not with pK_{a2} indicates that the displacement of the second ligand proton in the forward direction and the protonation of the second donor atom in the reverse direction are relatively facile processes. The reaction results in a complex which contains a four coordinate boron atom. It is possible that the transition state pictured above contains a boron atom which is five coordinate. That is, the transition state may involve partial bonding of boron to both ligand donor atoms and also to the leaving hydroxyl, as

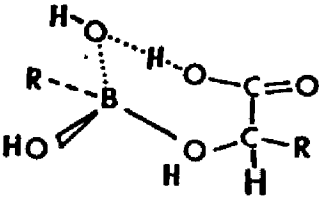
shown below:



A five coordinate boron has been proposed in the hydrolysis of BH_4^-,[14] and recently calculations concerning the geometries of such species have been carried out.[15]

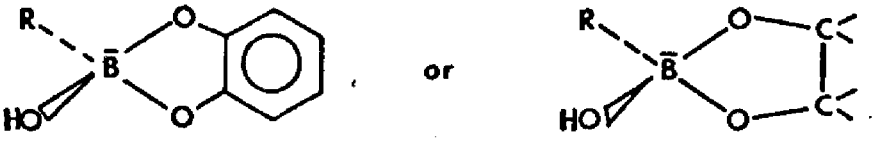
The correlation of log k_r with pK_{a1}, shown in Figures III-1 and III-2, agrees with the theory of proton transfer advanced by Eigen.[16] The rate of proton transfer depends upon the difference in acidity between the proton donor and the proton acceptor. As the acceptor becomes more basic with respect to the donor, the rate of proton transfer increases to a maximum value where it levels off. The correlation in Figure III-1 is similar to the graphs presented by Eigen in which log k is plotted as a function of ΔpK, where $\Delta pK = pK_{acceptor} - pK_{donor}$. In the case of the boron acid complexation reactions, the donor atom in the reverse direction is the incoming water molecule and the acceptor is the leaving ligand. Thus, the pK_a of the donor is constant, and pK_{a1} rather than ΔpK is the abcissa, even though the ligand is partially coordinated to the boron atom so that the exact pK_a is not known. That the correlation is with pK_{a1} and not with pK_{a2} suggests that the proton transferred in the rate determining step is the one associated with the less basic

oxygen donor atom. The proton associated with pK_{a2} is displaced directly by boron, and this displacement must be a facile process. In the case of hydroxy acids, this means that the major kinetic pathway involves attack on boron by the hydroxyl oxygen and direct displacement of this proton (pK_{a2}). This is then followed by ring closure via transfer of the carboxyl group proton (pK_{a1}) to the leaving hydroxyl, as shown below:



The absence of a precise correlation between the forward rate constants, k_f, and the pK_{a1} of the ligands can be attributed, at least in part, to two phenomena. First, a statistical adjustment must be made to account for those ligands which have different numbers of potential donor atoms. And, second, ligand geometry must be considered. There is a general tendency for the forward rate constant to decrease as the ligand acidity decreases. The catechols, as a class, however, seem to exhibit rate constants larger than those which would be predicted on the basis of ligand acidity. This is true even after statistical factors have been taken into account. For example, the forward rate constant for the reaction of 4-nitrocatechol with phenylboronic acid is larger than that for the reaction of lactic acid with

phenylboronic acid even though the pK_{a1} of lactic acid is smaller than that of 4-nitrocatechol by a factor of almost two. Table III-6 shows that, in general, the k_{fs} for the catechol reactions are larger than expected on the basis of acidity, but are internally consistent, the forward rate constant for the reaction of 4-nitrocatechol (pK_{a1}=6.69) being greater than that of 4-methylcatechol (pK_{a1}=9.37). This effect could be due to the rigidity of the catechol ligands which may properly orient them for chelation. If this is the case, then these molecules will suffer fewer geometric constraints upon entering the transition state than will the less rigid ligands which must lose rotational and configurational entropy in order to become properly oriented for complex formation. In the reverse direction, all of the ligands are constrained to the same particular geometry shown below:



and the entropic factors which favor the catechols over the more flexible ligands in the forward direction are not present in the reverse direction.

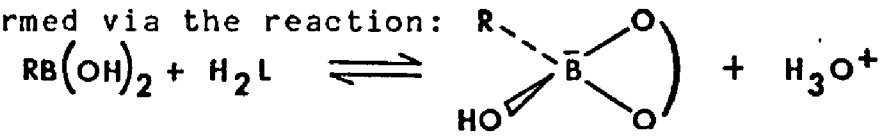
The studies performed with phenylboronic acid and mannitol indicate that boron acids can form complexes with polyols (whose pK_as are in the range 13-14). From the graph presented in Figure III-1, it is evident that, under the in-

terpretation of the proposed mechanism, all polyols should react with approximately the same reverse rate constant. Because of the relatively high pK_as characteristic of the polyols, the reverse rate constants are predicted to lie in that region of the curve which is levelling off at a maximum value. Thus, any differences in boron acid/polyol stabilities should be due to differences in the forward rate constants which will reflect any statistical or stereochemical differences among the ligands. The thermodynamic determination of the stability constant by the pH depression method described in section II.C was carried out in acidic medium, and the equations derived assuming that the trigonal form of the boron acids reacts. The stability constants obtained in this way are in good agreement with the results obtained from work carried out at the pK_a of the boron acid where it was assumed that the tetrahedral form reacted.[2] Kinetic data as well indicate that the trigonal form of the boron acid can react with polyols. As mentioned previously, many authors[2,17] had come to the conclusion that only the tetrahedral borate anion was reactive. While it may be true that the tetrahedral form of a given boron acid reacts more rapidly with polyols, the thermodynamic and kinetic evidence obtained from these studies indicate that trigonal boron acids react, although slowly, with polyols.

Studies of a Single Ligand with Several Boron Acids

By examining the reactions of a variety of boron acids with a single ligand, it is possible to investigate kinetic effects which are due to the nature of the boron acid. Substituted boron acids, $RB(OH)_2$, exhibit a variation in acidity which is dependent upon the particular -R group which is present. Table III-10 displays the stability constants, K, and the forward and reverse rate constants, k_f and k_r, as a function of boron acid pK_a for several fully protonated ligands.

The first thing to note is that the stability of the complex formed via the reaction:



increases as the acidity of the boron acid increases. That is, for any ligand H_2L, the stability constant for complexation with m-nitrophenylboronic acid (pK_a6.96) is greater than that for complexation with methylboronic acid (pK_a=10.4). The second point to be made is that the increase in K as the boron acid pK_a decreases is seen kinetically as both an increase in the forward rate constant, k_f, and a decrease in the reverse rate constant, k_r.

The variation of the boron acid is an interesting way to approach an investigation of the reactions of boron acids in general; it is the usual case to vary the ligand substituents in such a study. This approach, however, affords the

Table III-10. Reactions of Several Boron Acids with a Single Ligand

Reactions with 4-nitrocatechol

Boron acid	pK_a	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	log k_f	log k_r
m-nitrophenylboronic Acid	6.96	$2x10^3$	$1.3x10^5$	3.3	5.1
Phenylboronic Acid	8.7	650	$6.8x10^5$	2.8	5.8
Boric Acid	9.0	250	$1.7x10^6$	2.4	6.2
Methylboronic Acid	10.4	45	$1.0x10^6$	1.7	6.0

Reactions with Salicylic Acid

Boron acid	pK_a	$k_f, M^{-1}s^{-1}$	$k_r, M^{1-}s^{-1}$	log k_f	log k_r
4-nitrophenylboronic Acid	6.96	650	590	2.8	2.8
Phenylboronic Acid	8.7	225	$3.3x10^3$	2.4	3.5
Boric Acid[21]	9.0	135	$4.5x10^3$	2.1	3.7
Methylboronic Acid	10.4	55	$1.2x10^4$	1.7	4.1

Reactions with 4-methylcatechol

Boron Acid	pK_a	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	log k_f	log k_r
m-nitrophenylboronic Acid	6.96	$1.5x10^3$	$2.7x10^6$	3.2	6.4
Phenylboronic Acid	8.7	120	$4x10^6$	2.1	6.6
Boric Acid	9.0	54	$8.6x10^6$	1.7	6.9

opportunity to look at the reactions without effects such as chelate ring size and the differences in configurational entropy among the ligands playing a role in the determination of the relative forward rate constants. For a given ligand, these factors will be held constant as the boron acid substituent is varied. The major role of the substituent on boron is the determination of the electron density on the boron atom. By using an electron withdrawing group, such as $-NO_2$, the Lewis acidity of the boron acid may be increased, while an electron releasing group, such as $-CH_3$, will bring about a decrease in Lewis acidity. Other than this electron withdrawing or releasing effect, the -R group plays no direct part in the formation of the chelate ring. None of the substituents are particularly bulky, and as such do not sterically hinder the trigonal-tetrahedral rehybridization which occurs upon complexation.

Recall that for complexation reactions involving different ligands and the same boron acid, there was a precise correlation of log k_r with ligand acidity, but that this correlation was not observed for k_f, the forward rate constant. This was attributed to the fact that, in the forward direction, ligand specific factors such as flexibility, geometry, and chelate ring size were important; because of the geometry of the complex, these factors were minimal in the reverse direction, and a precise correlation was observed. If the mechanism which emphasizes proton transfer

is correct, and if the interpretation of the importance of ligand dependent properties in the forward direction is correct, then for the reactions of a single ligand with a variety of boron acids, one should observe a precise correlation of the type predicted by Eigen[16] for both the forward and the reverse rate constants. This correlation of log k_f with pK_a is now seen because the ligand dependent properties affecting complexation are held constant. Figures III-3 through III-5 show that this is indeed true, and that the correlation is present for both k_f and k_r as expected. No attempt was made to draw curves rather than straight lines through these points. On the basis of the studies done with phenylboronic acid and with m-nitrophenylboronic acid, one expects a levelling off of the rate constants at values of 10^5 or 10^6 for k_r. Thus, the relatively small variation in k_r from boron acid to boron acid is not surprising, since the rate constants are sufficiently large that the points lie in that region of the curve which is levelling off at a maximum value.

To discuss possible reasons for the increase in k_f and the concomitant decrease in k_r for complexation formation as the acidity of the boron acid increases, one must first consider the acidity patterns of the boron acids themselves. These acids behave as acids in the Lewis sense; the boron atom expands its coordination number to four by addition of a hydroxyl group, thereby releasing a proton into solution.

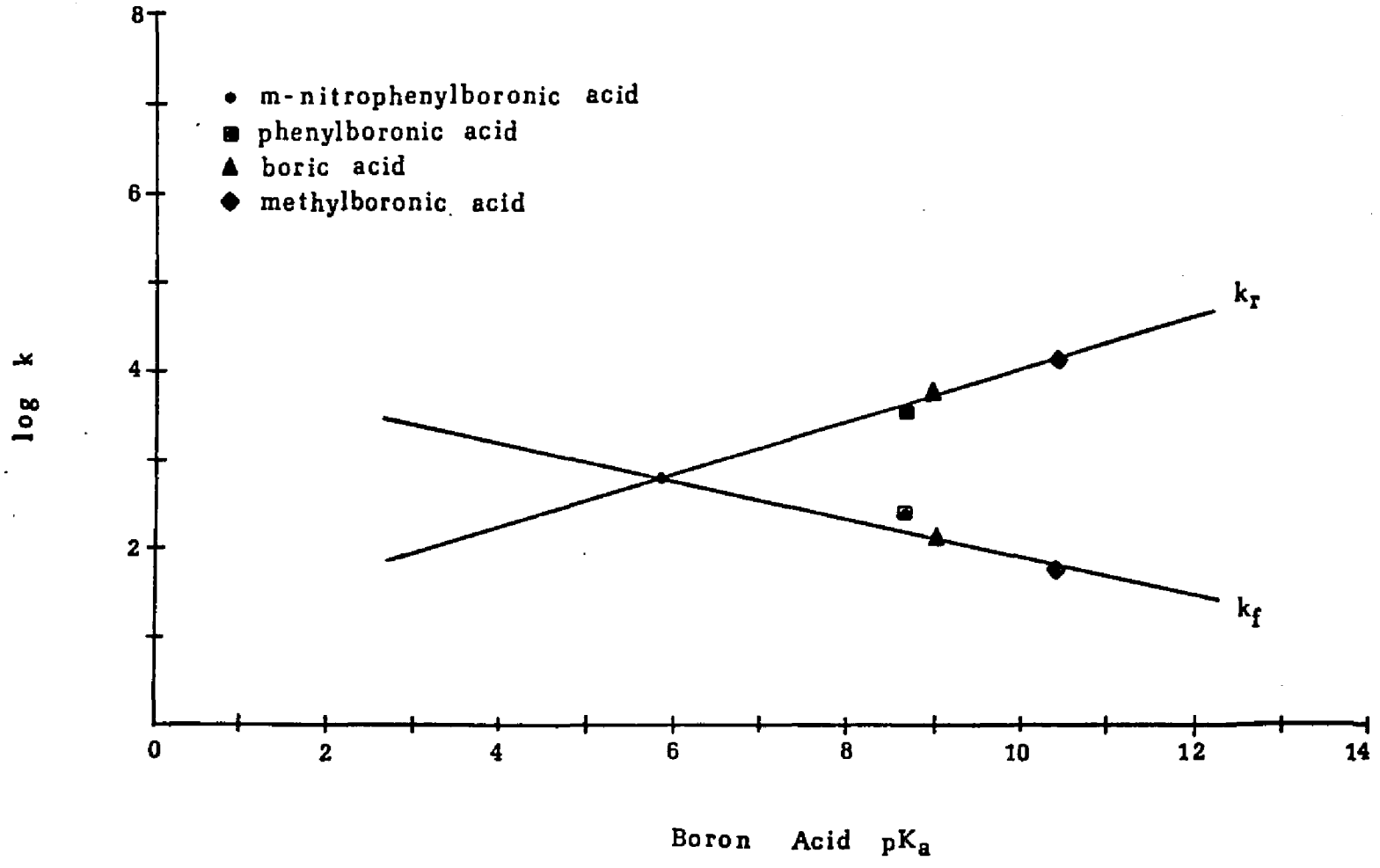


FIGURE III-3. REACTIONS OF $RB(OH)_2$ WITH SALICYLIC ACID

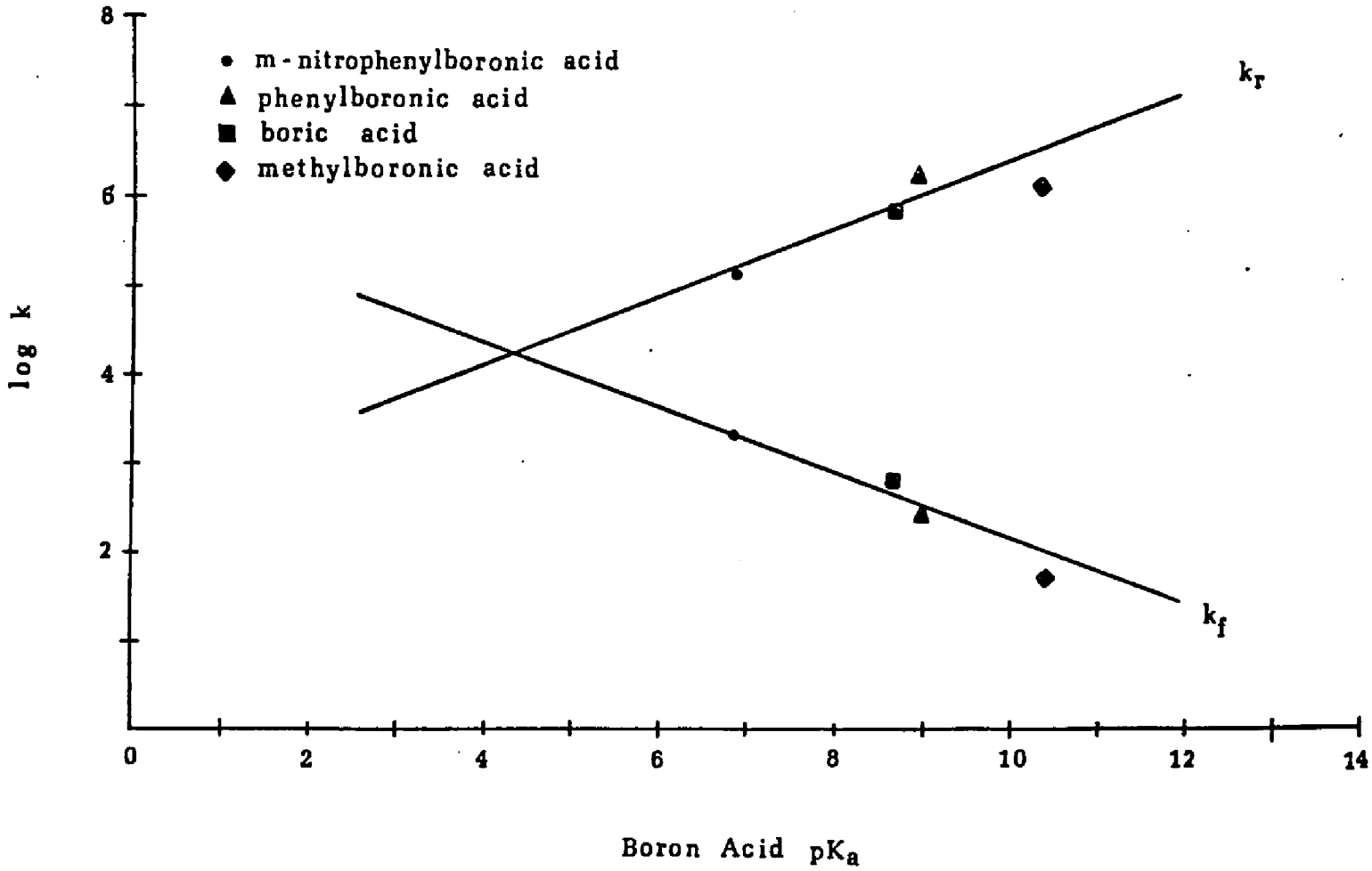
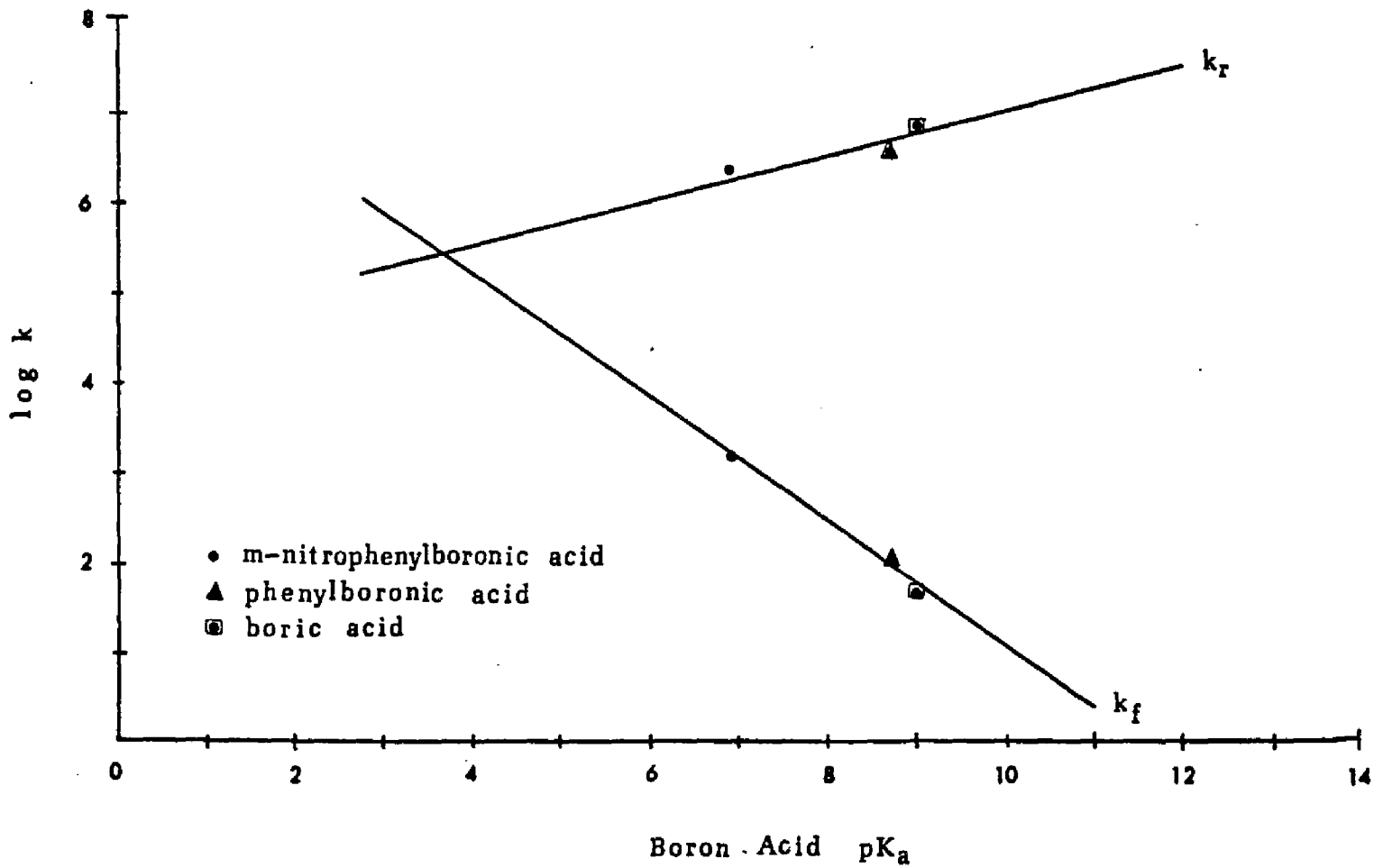
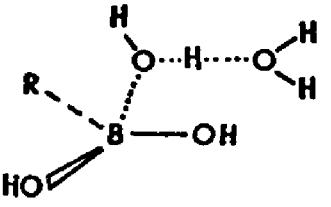


FIGURE III-4. REACTIONS OF $RB(OH)_2$ WITH 4-NITROCATECHOL

FIGURE III-5. REACTIONS OF $RB(OH)_2$ WITH 4-METHYLCATECHOL



This transition state can be pictured as below, where the oxygen on an incoming water molecule attacks the vacant p orbital of boron and the proton is transferred to bulk solvent:



As boron acid acidity increases, the decrease in pK_a may be due kinetically to an increase in the forward rate constant, a decrease in reverse rate constant, or a combination of the two, as seen in the following relationship:

$$K = \frac{k_f}{k_r}$$

Although no definitive NMR studies have been done to determine which of these three kinetic possibilities is responsible for the differences in acidity, the studies done here may shed some light on this.

Since the reactions of boron acids with ligands containing protonated oxygen donor atoms seem to indicate an important proton transfer, it seems reasonable to assume that the acid-base reactions of boron acids similarly involve proton transfer to and from the oxygen atoms of the solvent, water. If acidity differences are due to differences in forward rates, then the more acidic boron acids will be the ones for which proton transfer from the incoming water molecule to a solvent molecule is more facile. If the

reverse rates are responsible for differences in acidity, then the less facile the leaving of the hydroxyl group, the more acidic the boron acid. If variations in K_a are due to variations in both k_f and k_r, then the two situations above exist simultaneously. If a particular -R group is electron withdrawing, thereby increasing the Lewis acidity of the boron, then the donor oxygen atom on the incoming water molecule will also experience a greater degree of electron withdrawal, and the bound hydrogen atom, as a result of the decreased electron density on the partially bonded oxygen atom, will be more easily abstracted. This, then, will lead to more facile transfer of that proton to a solvent molecule, resulting in an increase in k_f. In the reverse direction, the hydroxyl might also be more tightly bound as a result of the electron withdrawing group, and this will make it less effective in abstracting a proton to form a leaving water molecule, with the subsequent return of the boron acid to its trigonal form. This would be reflected in a decreased reverse rate constant. Thus, if one argues that the more acidic boron acids, by means of their electron withdrawing substituents, are involved in transition states with a greater degree of bond formation to the fourth oxygen donor atom, then the increase in acid dissociation constant is due both to an increase in ease of proton transfer in the forward direction and to a decreased rate of proton transfer in the reverse direction. The results of studies of boron

acid reactions with the ligands examined in these studies support this idea; stability constant differences in these cases are seen in both the forward and reverse rate constants (as discussed below).

Tables III-1 through III-4 present the stability constant data for the reactions of the four boron acids with a variety of ligands, H_2L. It can be seen that these stability constants follow a trend with the change in boron acid pK_a: as the pK_a increases, K becomes smaller. This is seen kinetically as an increase in k_r and a decrease in k_f as demonstrated in Table III-10. Following the argument presented above concerning the effect of electron withdrawing and electron donating groups on the fourth B-O bond, the more acidic boron acids should experience a greater degree of bond formation in the transition state than should those which are less acidic. Kinetically, this would mean that the transfer of a proton in the forward direction becomes more facile as the pK_a of the boron acid decreases. This is exactly the trend in rate constants which is seen: the forward rate constant increases and the reverse rate constant decreases for the reactions of a series of boron acids with one particular ligand. This is also illustrated in Figures III-3 through III-5. These results, then, seem to indicate that if the same mechanism which involves a rate determining proton transfer operates in the acid-base reactions of boron acids, the differences in K_a values should be seen in varia-

tions in both k_f and k_r for the reactions. The possible explanation, which is consistent with the acid-base processes and with the complexation processes, is the variation in degree of bond formation in the transition state; this variation could be due to the electron withdrawing or electron donating properties of the particular -R group involved.

In the reactions of fully protonated ligands with trigonal boron acids, $RB(OH)_2$, one more result should be noted. The complexation reactions of salicylic acid exhibit lower forward and reverse rate constants than expected on the basis of ligand pK_a. Figure III-3, however, shows the reactions to be internally consistent when the ligand is held constant and the boron acid is varied. This points to the conclusion that the lowered forward and reverse rate constants are a consequence of the nature of the ligand. Complexation reactions involving salicylic acid result in the formation of six membered chelate rings, while all the other ligands (with the exception of malonic acid) form five membered chelate rings. A previous study of the effect of chelate ring size on the substitution reactions of boron acids indicated that slower rates of complexation are observed in the case of the larger six membered rings.[6]

In summary, the reactions of fully protonated ligands with boron acids can be represented by the following:

$$HB + H_2L \rightleftharpoons Cx^- + H^+$$

The transition state is one in which the importance of proton transfer is emphasized, and there is a precise correlation between the pK_{a1} of the ligand and the reverse rate constant for the complexation reaction. The proposed mechanism is one in which the hydroxy group of an α- hydroxycarboxylic acid or a hydroxy group of a diol or polyol attacks the vacant p orbital of boron. A proton is transferred from the second oxygen donor atom to the leaving hydroxyl group, and a water molecule leaves with concomitant ring closure. The specific rate constants depend upon the facility of proton transfer which is a function of the differences in basicity between the ligand and the boron hydroxyl group. A five coordinate boron atom in which both ligand oxygen atoms as well as the hydroxyl oxygen are partially bonded may be involved. The correlation of k_r with pK_{a1} is precise due to the constrained geometry of the complex, but this is not so with the forward rate constant which is sensitive to ligand properties such as geometry, orientation, configurational entropy, and chelate ring size as well as ligand acidity. For a series of boron acids with the same ligand, these ligand dependent processes are constant and there is a precise correlation of both k_f and k_r with pK_{a1} which is consistent with the proposed mechanism involving a rate determining proton transfer.

The idea of proton transfer in the rate determining step is not unique to the reactions of boron acids. This

concept seems to be important in work done in the field of oxyanion chemistry.[18] However, the oxyanion systems present several experimental difficulties (for example, polymerization at high pHs) and in many cases allow the determination of only maximum rate constants. The boron acid systems permit evaluation of actual rate constants, not just upper limits, and substituted boron acids do not polymerize even at high pHs. For this reason, elucidation of the mechanism of complexation of boron acids is important to studies of the more general class of ligand dependent processes which involve proton transfer.

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There is a discrepancy between the thermodynamically determined stability constant and the kinetically determined stability constant in Queen's work. The author attributed this to the presence of a species in which only one arm of the ligand is chelated to a four coordinate boron. None of our work, either thermodynamic or kinetic, supports this conclusion. Queen's data are, however,

sufficiently accurate to indicate agreement with the general trends which we observe in our own studies.

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CHAPTER FOUR

Reactions of Ligand Anions with Trigonal Boron Acids

General

The reactions of ligand anions, HL^-, with boron acids, $RB(OH)_2$, is given below (see equation 2 of the total reaction scheme, Chapter Two):

$$HB + HL^- \rightleftharpoons Cx^- + H_2O$$

Recall that the derived relaxation time contains contributions from all pathways which lead to the formation of Cx^-, and has the general form:

$$\frac{1}{\tau} = k\{W\} + k'\{X\} + k''\{Y\} + k'''\{Z\}$$

where k_f' is the forward rate constant characteristic of the HB/HL^- reaction pathway, and [X] represents the concentration dependent coefficient which contains terms in [HB] and $[HL^-]$. $k_f[W]$, $k_f''[Y]$, and $k_f'''[Z]$ represent contributions from pathways involving HB/H_2L, B^-/H_2L, and B^-/HL^- respectively. By suitable adjustment of the pH of the solutions of boron acid and ligand, the concentrations of [HB] and $[HL^-]$ can be made large enough so that the $k_f'[X]$ term is a major contributor to the experimentally determined relaxation time. Variation of the initial concentrations of boron

acid and ligand as well as pH then allows the calculation of the various forward rate constants. With the exception of the reactions of m-nitrophenylboronic acid with salicylic acid and of m-nitrophenylboronic acid with mandelic acid, the relaxation times were fit to a maximum of two terms even at pHs as high as pH~6.

Reactions of a Single Boron Acid with Several Ligand Anions

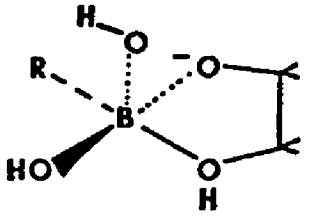
Table IV-1 displays both the forward and reverse rate constants, k_f' and k_r', for the reactions of phenylboronic acid with a variety of ligand anions whose pK_{a1} values range from 1.04 for binoxalate to 6.69 for 4-nitrocatecholate. As the acidity of the ligand decreases, one observes a general increase in the forward rate constant. However, there is no exact correlation of k_f' with the ligand pK_{a1}. This is certainly different from the case of the reactions of the fully protonated ligands, H_2L, where k_f increased as ligand pK_{a1} decreased, and where log k_r and pK_{a1} exhibited a precise correlation.

In discussing the mechanism for the reactions of boron acids with these ligand anions, it is clear that two mechanistic pathways can be envisioned. The first involves attack on the boron atom by the protonated oxygen donor atom. This is then followed by ring closure via the nega-

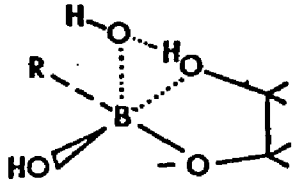
Table IV-1. Reactions of $\phi B(OH)_2$ with HL^-

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	log k_f	k_r, s^{-1}	log k_r	$K'=K/K_{a1}$
binoxalate[2]	1.04	3.3×10^2	2.5	10	1	3.3×10^1
Bimalonate[6]	2.59	1.5×10^2	2.2	15	1.2	1.0×10^1
Salicylate	2.83	45	1.7	1	0	4.6×10^1
Mandelate	3.22	1.3×10^3	3.1	52	1.7	2.5×10^1
Lactate[3]	3.70	1.5×10^3	3.2	83	1.9	1.8×10^1
4-nitrocatecholate	6.69	7.0×10^4	4.8	15	1.2	4.6×10^3

tive arm of the ligand, with loss of a hydroxyl group from boron:



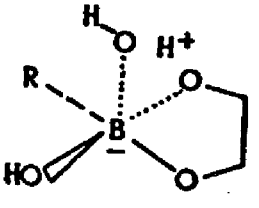
The second mode of reaction available is one in which the attack on the vacant boron p orbital is by the anionic ligand donor atom, and the chelation occurs by means of the protonated oxygen atom with simultaneous loss of the H_2O group:



While these two alternatives represent competing mechanistic pathways, there is evidence which points to the first path as being the more effective one. First, if the second path were the predominant route to complex formation, one would expect a rather strong dependence of the forward and reverse rate constants upon the acidity of the ligand. In this event, the reaction would somewhat resemble the reactions of the fully protonated ligands in that a rate determining proton transfer would be involved, and similar trends of k_f' and k_r' with changes in ligand pK would not be unreasonable to expect. This is not the case. In fact, the rate data

show the opposite trend in the forward direction - for the reactions of HL^- with HB, k_f' increases as ligand acidity decreases. In the reverse direction, rather than the precise correlation seen for transition states in which proton transfer is involved, one observes that k_r' does not depend greatly upon ligand acidity at all. For the reactions of oxalic acid (pK_{a1}=1.04) and 4-nitrocatechol (pK_{a1}=6.69) the k_f' values differ by a factor of 10^3, while the k_r' values characteristic of the reactions of the corresponding ligand anions differ only by a factor of 1.5. These results would seem to indicate that proton transfer in the rate determining step does not represent the major mechanistic pathway. Second, the previous studies carried out with boron acids indicate that direct displacement by boron of the proton associated with the pK_{a2} of the ligand is quite facile.[1,2,3] This process, which would occur in the first of the mechanistic pathways presented, competes with removal of this proton either by transfer to the leaving hydroxyl on boron or by transfer to bulk solvent (as would be required by the second of the mechanistic schemes). It is obvious that the first process, direct displacement by boron, should be the more effective of the two, since the proton associated with the pK_{a2} of the ligand is not very acidic ($pK_{a2} > 10$ for all but the dicarboxylic acids) and this proton transfer is not facile when the acceptor is the leaving hydroxyl or bulk solvent. While it may be argued that ring closure via

the protonated oxygen results in the leaving of a water molecule, a much better leaving group than hydroxide, and should therefore be the favored process, there are two possibilities which may serve to ease the leaving of the hydroxide in the case of ring closure via the negative arm of the ligand anion. The first involves catalysis by the proton which has been directly displaced by the boron atom; reports of catalyses similar to this appear in the literature. Higginson[4,5] studied ring closure in EDTA complexes of Co^{+3}; a Cl^- is displaced upon complexation. In the case where the EDTA ligand is anionic and ring closure occurs via the negative carbolylate group, the process is catalyzed by metal ions in solution. The analogous reactions of protonated EDTA show no such catalysis. Presumably, the metal ions minimize the charge repulsion between the entering anionic arm of the ligand and the leaving chloride ion, thereby catalyzing the ring closure process. This direct displacement is a facile process. The geometry of the complex is such that this proton could easily be transferred to the site of the leavihg hydroxide, thus minimizing the charge repulsion and aiding in the exit of the hydroxyl group:



A second possibility is intimately related to the basicity

of the negatively charged ligand anion. The more basic this anion is, the more easily it will be able to orient water molecules about itself. These intervening water molecules will then be able to hydrogen bond to the leaving hydroxyl group to form a leaving water molecule and injecting a hydroxide ion into solution at a site remote from the complexation site. This concept will be discussed in greater detail later in this section. In view of these considerations, although the two pathways available for complexation represent competing mechanistic routes, it would seem that the more effective pathway for the complexation reaction between HB and HL^- is the one involving initial attack on boron by the protonated ligand donor site. The kinetic data are interpreted in terms of this as the major mechanism of complex formation.

Because the rate determining step does not involve proton transfer, it is not surprising, then, that neither k_f' nor k_r' correlates exactly with either pK_{a1} or pK_{a2}. Instead, what is observed is a forward rate constant which is very dependent upon ligand properties such as basicity and a reverse rate which is relatively constant. This is observed for all of the boron acids studied as shown in Tables IV-2 through IV-4 as well as in Table IV-1.

Table IV-2. Reactions of $B(OH)_3$ with HL^-

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	log k_f	k_r, s^{-1}	log k_r	$K'=K/K_{a1}$
Salicylate[20]	2.83	40	1.6	4	0.6	6.8
Tartrate[1]	2.89	215	2.3	43	1.6	5
4-nitrocatecholate	6.69	5×10^4	4.7	68	1.8	7.3×10^2

Table IV-3. Reactions of $m\text{-}NO_2\phi B(OH)_2$ with HL^-

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	log k_f	k_r, s^{-1}	log k_r	$K'=K/K_{a1}$
Salicylate	2.83	125	2.1	.17	-.8	7.4×10^2
Mandelate	3.22	1.5×10^4	4.2	48	1.7	3.1×10^2

Table IV-4. Reactions of $CH_3B(OH)_2$ with HL^-

Ligand	pK_{a1}	$k_f.M^{-1}s^{-1}$	log k_f	k_r, s^{-1}	log k_r	$K'=K/K_{a1}$
Salicylate	2.83	50	1.7	16.6	1.2	3.0
4-nitrocatecholate	6.69	5×10^4	4.7	2.4×10^2	2.4	2.1×10^2

The Effect of Internal Hydrogen Bonding

Before the general mechanism is discussed, the specific case of the reactions of the salicylate anion should be considered. Table IV-1 shows that k_f' for this anion is abnormally small. It has been clearly demonstrated that chelate ring size plays a role in determining the rate of complexation, reactions in which five membered rings are formed being kinetically favored over those in which six membered rings are formed.[6] It is also true that k_f' tends to increase as ligand pK_{a1} increases. Therefore, if chelate ring size were the only factor responsible for the lower k_f' value for salicylate, then the trend with pK_{a1} predicts that k_f' for the salicylate anion should be greater than that for the bimalonate anion. Yet, this is not the case, and there must be additional factor(s) which also act to bring about a decreased forward rate constant for the reaction of the salicylate anion. This is consistent with the results of studies of the complexation reactions of some labile metal cations with ligands in which the reactive site is blocked due to internal hydrogen bonding.[7,8]

Most di- and tri-valent metal ions undergo complexation reactions in accordance with the Eigen mechanism.[9] This mechanism involves a rapid, reversible association between reactants, followed by the rate determining loss of water from the inner coordination sphere of the metal ion. The

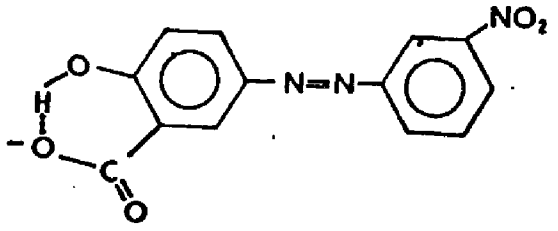
ligand donor atom then enters the vacant site in the coordination sphere of the metal, and, in the case of bidentate ligands, rapid ring closure occurs.

$$M + H_2L \rightleftharpoons M,H_2L \rightleftharpoons ML H_2 \rightleftharpoons \text{etc.}$$

The observed rate constant is the product of an ion pairing constant and the water exchange rate of the particular cation involved:

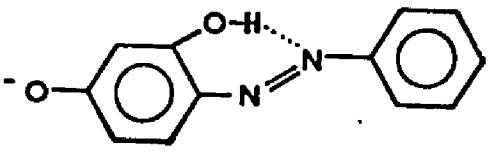
$$k_{obs} = K_{ip}\, k_{\text{water exchange}}$$

It is unusual for rates of complexation of metal cations to show a dependence upon the nature of the ligand, other than the charge dependence which appears in K_{ip}. Rates of complexation for the reactions of Ni^{2+} and Mg^{2+} with the internally hydrogen bonded ligand Alizarin Yellow G (shown below) were carried out.[10,11]



Assuming an Eigen mechanism, the authors calculated rate constants for the reactions of Ni^{2+} and Mg^{2+} with HL^- and L^{2-}. The calculated and experimentally measured rates for the M^{2+}/L^{2-} reactions were in good agreement. However, the experimentally determined and the predicted values of k_{HL^-} differed for both Ni(II) and Mg(II), the measured rates being smaller in both cases than the theoretical value. Two

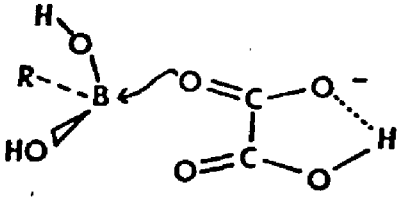
possibilities exist which could be responsible for the lowered rates observed: (1) reaction occurs via attack on the blocked binding site, and (2) reaction occurs via an Eigen type mechanism, but only that fraction of ligand which is not hydrogen bonded reacts. For the reaction of Mg^{2+} with the Alizarin Yellow G anion, the forward rate constant was lower than the predicted value by a factor of 30-100. This is characteristic of reactions where the reaction site is blocked by a proton, and the authors concluded that Mg^{2+} complexation with this ligand anion proceeds with attack on the hydrogen bonded moiety. In the case of Ni^{2+}, however, the predicted forward rate constant for reaction with HL^- was $\sim 4 \times 10^4$ $M^{-1}s^{-1}$, while the observed rate constant was 22 $M^{-1}s^{-1}$. This is much lower than the factor of 30-100 expected for attack on a blocked binding site. Calculations had been done[12] which indicated that the fraction of non-hydrogen bonded ligand in solution was about 1/300 of the total anion concentration. The authors concluded that Ni^{2+} reacts with Alizarin Yellow G by complexing with that small fraction which is not internally hydrogen bonded. B. Perlmutter-Hayman[7] also investigated the effect of ligand basicity on the rates of reaction of Ni^{2+} with a series of phenylazo ligands; the common structural unit for these ligands is shown here:



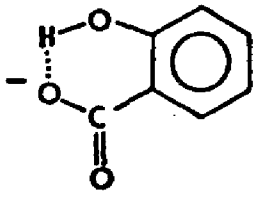
The authors have determined that the reactions of Ni^{2+} with these particular ligands proceed by attack of the metal ion on the O-H·····N bond (although the proton is not displaced upon complexation). For the reactions of Ni^{2+} with HL^-, an increase in the forward rate constant as the pK_{a1} of the ligand decreases is observed. That is, the weaker the internal hydrogen bond, the larger the forward rate constant for the Ni^{2+}/HL^- reaction. The reactions of magnesium (II) with Eriochrome Black T,[8] another ligand whose anion is internally hygrogen bonded, also demonstrate a dependence of k upon the ligand. It is interesting to note that this influence of a blocked binding site upon k_{HL^-} has been observed only in the reactions of the more labile metal cations, Mg^{2+} ($k_{water\ exchange} > 10^4\ s^{-1}$)[13] and Ni^{2+} ($k_{water\ exchange} \sim 3\times10^4\ s^{-1}$).[14] Investigation of Al(III)/salicylate,[15] Al(III)/sulfosalicylate,[16] and Ga(III)/salicylate[17] systems show that the reactions of these less labile metal cations are not affected by internal hydrogen bonds; $k_{water\ exchange}$[18] for Ga^{3+} is $1.8\times10^3\ s^{-1}$ and that for Al^{3+} is $.13\ s^{-1}$.[18]

It is seen, then, that the effect of internal hydrogen bonding in ligands similar to salicylate (Alizarin Yellow G) and in ligands containing the O-H·····N hydrogen bond (the phenylazo ligands) is well documented.[7,8,10,11] For ligands such as this, a decrease in the forward rate constants for labile processes is observed. The lowered rate constant for

the reactions of the salicylate anion with phenylboronic acid is consistent with this observation, and can be explained on the basis of an attack on the site which is blocked as a result of internal hydrogen bonding. It is important to point out a possible reason that the effect of internal hydrogen bonding is not felt in the reactions of the monoanions of the dicarboxylic acids, oxalic acid and malonic acid. Because of the closeness of pK_{a1} and pK_{a2}, one might expect hydrogen bonding in the binoxalate and bimalonate anions to be important. While this may be true, it is possible to envision a complexation pathway which does not involve direct attack on the hydrogen bonded site. Instead, initial attack on the vacant p orbital of boron may occur through one of the carbonyl oxygens, with displacement of the proton from the other side of the molecule:



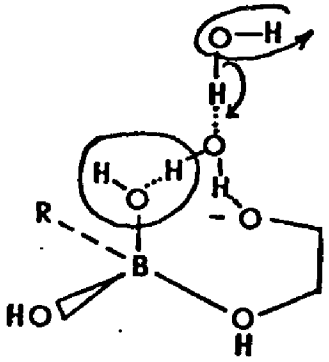
This option is not open to the salicylate anion, and here complexation must proceed by attack at the blocked binding site, with breakage of the internal hydrogen bond:



The Effect of Ligand Basicity

The effect of chelate ring size (in bimalonate and salicylate) having been pointed out, and the effect of internal hydrogen bonding having been examined, the rest of this discussion will focus on the trend in ligand anion rate constants as a function of ligand acidity. Table IV-1, the reactions of phenylboronic acid with HL^-, and Tables IV-2 through IV-4, the reactions of HL^- with boric acid, m-nitrophenylboronic acid, and methylboronic acid, show that as ligand anion basicity increases, the forward rate constant for the reaction of HB with HL^- also increases. This is similar to the pattern observed for the reactions of the protonated molybdate, $HMoO_4^-$, and tungstate, HWO_4^-, oxyanions.[19] These complexation reactions are substitution reactions in which at least one of the leaving groups is a hydroxyl group. Ligand basicity seems to control the rates of the substitution processes, with the forward rate constant increasing as pK_{a1} for the ligand decreases. The authors have attributed this to the increased ability of the more basic ligand anions to orient water molecules about the anionic site. Thus, through hydrogen bonding of these intervening water molecules, the solvent acts to produce a better leaving group, a water molecule, and the injection of the

hydroxide into solution takes place at a site removed from the reaction site. In this manner, the more basic ligands aid in the elimination of the hydroxyl group. The results of the boron acid studies with ligand anions are consistent with such a mechanism, and the transition site may be pictured as:



The less basic the ligand anion, the less able it is to orient water molecules to aid in the leaving of the hydroxyl from boron, and, as a result, the forward rate constant is lower, as observed. It is also possible that the reason for this increase in k_f' with an increase in ligand pK_{a1} is of an entropic nature as well as one of aiding in the leaving of the -OH. The solvent molecules present around the anionic binding site may afford greater flexibility with regard to the geometry required by the transition state. In the case where several water molecules intervene, there may be an increased number of ligand orientations which can result in successful chelation . For the less basic ligand anions where there are not as many intervening water molecules, the ligand geometry required by the transition state may be more restrictive.

These data demonstrate the ligand dependent nature of the complexation reactions of a particular boron acid with a series of ligand anions. The dominant factor in the determination of the relative rates seems to be ligand basicity, but factors such as ring size and internal hydrogen bonding also affect the magnitude of k_f'. In view of the ligand dependent nature of the postulated mechanism of the reactions of HB with HL^-, it would be very interesting to examine the results of a study which determined the rates of reactions for a series of boron acids with a single ligand anion.

Reactions of Several Boron Acids with a Single Ligand Anion

Table IV-5 presents the kinetic results of an investigation of a variety of boron acids (spanning a range in pK_a from 6.96 to 10.4) with the salicylate anion and with the 4-nitrocatecholate anion. A study of this type allows the ligand specific effects such as basicity, ring size and internal hydrogen bonding to be held constant. In this manner, the influence of the acidity of the boron acid can be assessed. The most striking characteristic of these reactions is the relative independence of the forward rate constant from the pK_a of the boron acid. For either of the given ligands, the value of k_f is fairly constant, regard-

Table IV-5. Reactions of Several Boron Acids with a Single Ligand Anion

Reactions of Salicylate

Boron Acid	pK_a	$k_f, M^{-1}s^{-1}$	log k_f	k_r, s^{-1}	log k_r	$K'=K/K_{a1}$
m-nitrophenylboronic acid	6.96	125	2.1	.17	-.08	7.4×10^2
Phenylboronic Acid	8.7	45	1.7	.98	-.01	4.6×10^1
Boric Acid[20]	9.0	40	1.6	4	.6	6.7
Methylboronic Acid	10.4	50	1.7	16.7	1.2	3.0

Reactions of 4-nitrocatecholate

Boron Acid	pK_a	$k_f, M^{-1}s^{-1}$	log k_f	k_r, s^{-1}	log k_r	$K'=K/K_{a1}$
Phenylboronic Acid	8.7	7.0×10^4	4.8	15	1.2	4.6×10^3
Boric Acid	9.0	5.0×10^4	4.7	68	1.8	7.3×10^2
Methylboronic Acid	10.4	5.0×10^4	4.7	238	2.4	2.1×10^2

less of the nature of $RB(OH)_2$. This is nicely illustrated in Figures IV-1 and IV-2. As the boron acid pK_a changes, there is little variation in the forward rate constant. Because there is no proton transferred and because the rate constants are relatively low, the constancy of these k values is due to an actual dependence upon the ligand, and not to the levelling off effect which produces the constancy in k for the reactions of the fully protonated ligands (see Figures III-3 through III-5). This is consistent with the mechanism involving attack of the protonated ligand oxygen on the boron atom, followed by chelate ring closure via the negative arm of the ligand. Because the rate determining step is one involving ring closure, the forward rate constant is expected to be highly sensitive to ligand specific properties, and relatively insensitive to the pK_a of the boron acid. There is no proton transfer in the rate determining step, and the difference in pK_a of the donor and acceptor which dominated the reactions of the fully protonated ligands with HB is of minimal importance for the reactions of the ligand anions. The reverse rate constants, k_r', on the other hand, increase for a given ligand as the pK_a of the boron acid increases. A similar situation is seen for the reactions of $NiOH^+$ with some internally hydrogen bonded ligands.[6] For these systems, the differences in stability constant are due almost totally to differences in the reverse rate constants. The forward rate constants remain re-

FIGURE IV-1. REACTIONS OF $RB(OH)_2$ WITH THE SALICYLATE ANION

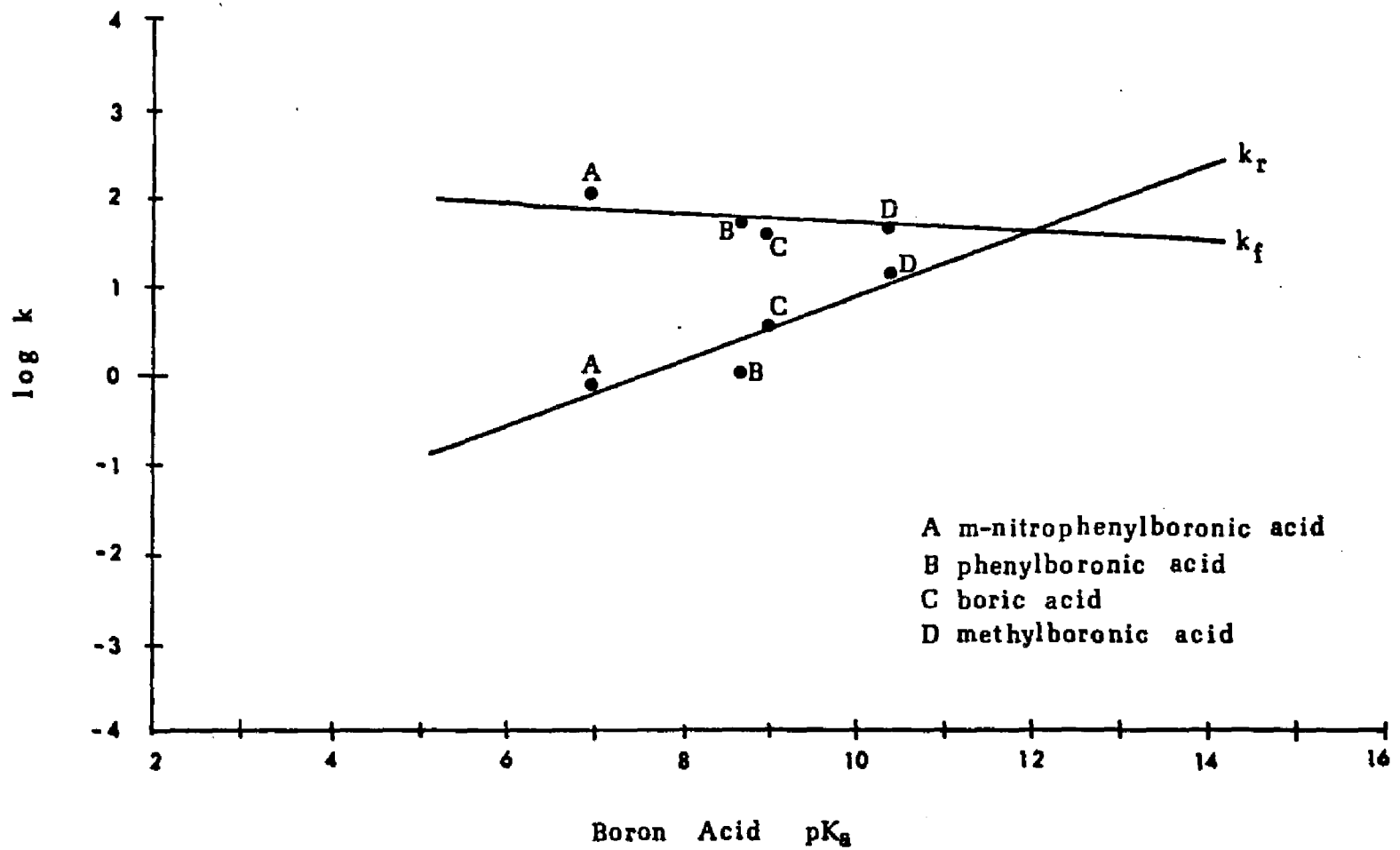
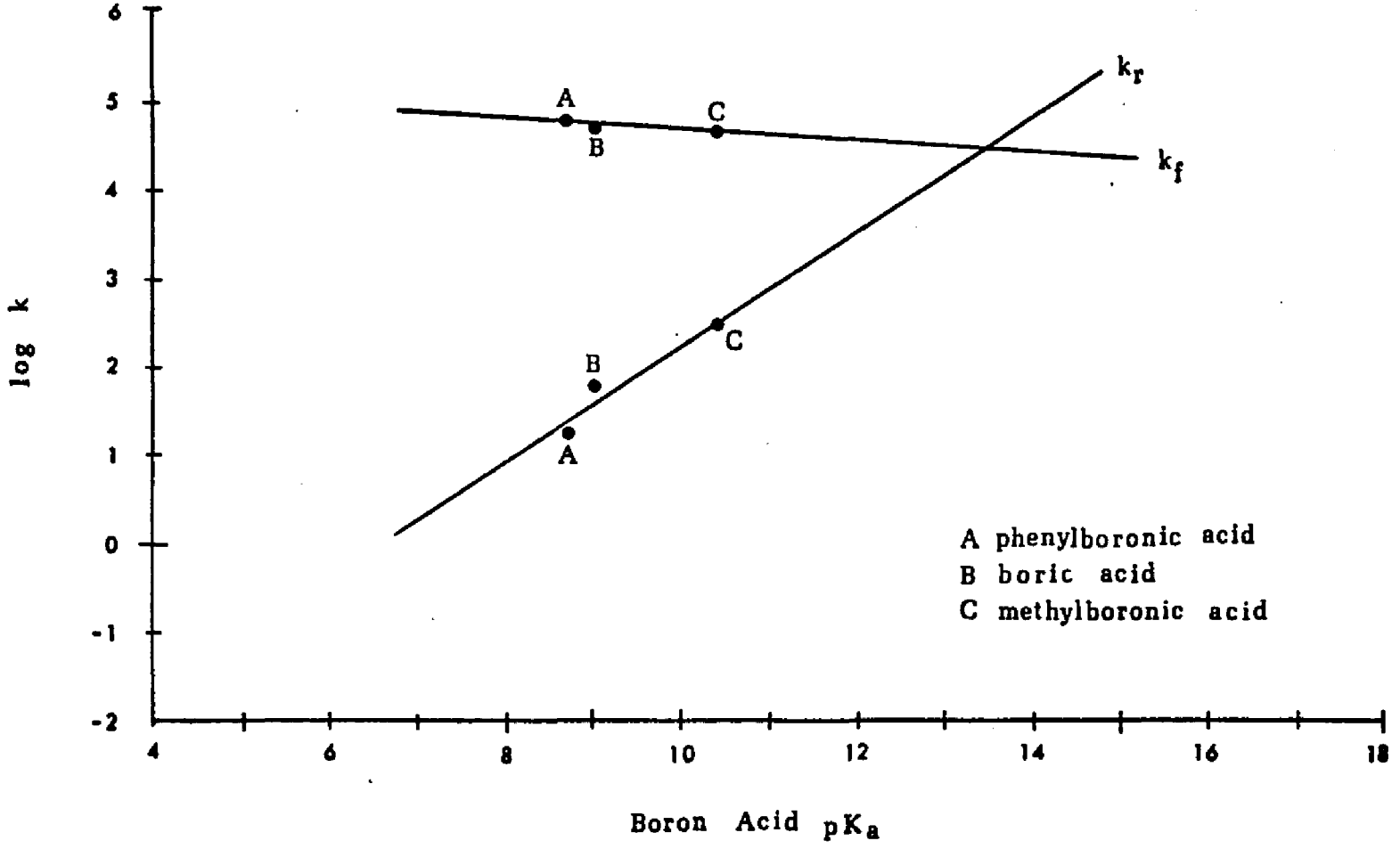


FIGURE IV-2. REACTIONS OF $RB(OH)_2$ WITH THE 4-NITROCATECHOLATE ANION



latively uninfluenced by a change in ligand pK_{a1}, while the reverse rate constants decrease as ligand anion basicity increases. This was attributed to the basic nature of $NiOH^+$ which allows for greater ease in breakage of the internal hydrogen bond prior to chelation. Thus, no dependence upon ligand pK_{a1} was observed. There is a very interesting parallel between the reactions of the Ni(II) species with internally hydrogen bonded ligands and the reactions of the trigonal boron acids. The reactions of HB with the fully protonated ligands and the reactions of Ni^{2+} with internally hydrogen bonded ligand anions show a dependence of the forward rate constant upon ligand acidity, and both involve protons which play an important role in the transition state. For the reactions of HB with the ligand anions studied, there is no proton transfer in the transition state, and k_f' is quite sensitive to the nature of the ligand involved. Similarly, the reactions of $NiOH^+$ do not involve a rate determining breakage of the hydrogen bond blocking the reaction site (by virtue of the increased basicity of $NiOH^+$ with respect to Ni^{2+}) and the rates here are also independent of pK_{a1} of the ligand.

The constancy of k_f' for the reactions of a particular ligand anion with different boron acids is due to the fact that ligand dependent properties have been held constant. In both the reactions of boron acids with ligand anions and the reactions of $NiOH^+$ with the internally hydrogen bonded

ligand anions, any differences in the stability constants of the complexes are the result of differences in reverse rate constants for the reactions. Figures IV-1 and IV-2 show the dependence of both the forward and reverse rate constants for the reactions of the different boron acids with the salicylate and 4-nitrocatecholate anions. There is little discrimination among the boron acids for the reactions of a particular ligand anion. The reverse reaction does exhibit a dependence upon boron acid pK_a, and the effect of the electron donating or withdrawing -R group on the bonds which are formed and broken in the transition state may be a factor here.

Summary

The complexation reactions which occur between boron acids and the classes of ligand anion studied are consistent with the mechanism which emphasizes the importance of ligand dependent processes. There is no rate determining proton transfer as in the reactions of H_2L, and the magnitude of the rate constant is determined almost exclusively by the nature of the ligand. The most effective complexation process probably involves attack by the protonated ligand oxygen on the vacant p orbital on boron. The ring is then closed by the anionic oxygen atom, the more basic ligand an-

ions reacting faster. The trend with basicity can be explained on the basis of the ability of the more basic ligand anions to orient solvent molecules around themselves and thereby increase the ease with the hydroxyl group leaves. Minimization of charge repulsion and entropic factors may both be important here. As expected for highly ligand dependent processes, a series of reactions for which the ligand has been held constant shows little variation in forward rate constant with a change in boron acid. Finally, the ligand anion in which the chelation site is blocked by hydrogen bonding, the salicylate anion, has a lowered rate of complexation.

Having discussed separately the reactions of HB with H_2L and the reactions of HB with HL^-, it is interesting now to compare these results. Table IV-6 presents a comparison of rates of reaction for a single boron acid, phenylboronic acid, with a series of ligands, H_2L, and with the corresponding ligand anions, HL^-. The magnitude of k_f (the forward rate constant for the reaction of the fully protonated ligand) decreases as the ligand acidity decreases, while the magnitude of k_f' (the forward rate constant for the reaction of the ligand anion) increases as ligand acidity decreases. These phenomena have been discussed in terms of a transition state which emphasizes proton transfer for the reactions of H_2L and a transition state which emphasizes the ability of the ligand anion to orient solvent molecules

for the reactions of HL^-. In the region where the ligand pK_{a1} is low, k_f is larger than k_f'. This is a combination of two effects: (1) for the more acidic ligands, proton transfer is more facile, and (2) the weakly basic anions of these acidic ligands are poor at orienting the solvent molecules. As the ligand pK_{a1} increases, proton transfer for H_2L becomes less facile, but, at the same time, the conjugate base, HL^-, is increasing in basicity, and becomes more effective in orienting water molecules about the anionic site. Thus, for the ligands with higher values of pK_{a1}, k_f' is larger than k_f.

Table IV-7 shows the reactions of salicylic acid and of the salicylate anion with the four different boron acids. For this ligand, all k_f values are larger in magnitude than the corresponding k_f' values. This may be a combination of the low pK_{a1} of the ligand which favors k_f over k_f' (proton transfer is fairly easy, while the ability of the ligand anion to orient water is not great) and also of the lowering of the forward rate constant of the salicylate anion as a result of the hydrogen bonding.

Table IV-6. Reactions of H_2L and HL^- with $\phi B(OH)_2$

Ligand	pK_{a1}	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	$k_f, M^{-1}s^{-1}$	k_r, s^{-1}	K
Oxalic Acid[2]	1.04	$2x10^3$	$6.2x10^2$	$3.3x10^2$	10	3.2
Malonic Acid[6]	2.59	350	$1.3x10^4$	$1.5x10^2$	15	$2.6x10^{-2}$
Salicylic Acid	2.83	225	$3.3x10^3$	45	1	$6.8x10^{-2}$
Mandelic Acid	3.22	175	$4.7x10^4$	$1.3x10^3$	52	$1.5x10^{-2}$
Lactic Acid[3]	3.70	140	$3.8x10^4$	$1.5x10^3$	83	$3.7x10^{-3}$
4-nitrocatechol	6.69	650	$6.8x10^5$	$7.0x10^4$	15	$9.5x10^{-4}$

Table IV-7. Reactions of $RB(OH)_2$ with Salicylic Acid and with Salicylate

Boron Acid	pK_a	$k_f, M^{-1}s^{-1}$	$k_r, M^{-1}s^{-1}$	$k_f, M^{-1}s^{-1}$	k_r, s^{-1}	K
m-nitrophenylboronic Acid	6.96	650	590	125	.17	1.1
Phenylboronic Acid	8.7	225	3.3×10^3	45	1	6.8×10^{-2}
Boric Acid[20]	9.0	135	4.5×10^3	40	4	3×10^{-2}
Methylboronic Acid	10.4	55	1.2×10^4	50	16.6	4.5×10^{-3}

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CHAPTER FIVE

Reactions of the Tetrahedral Borate Anion

The last two terms of the expression for the relaxation time as derived from the general reaction scheme for substituted boron acids with bidentate ligands (see Chapter Two) represent contributions from the reactions of the tetrahedral borate anion, B^-, with the fully protonated protonated ligand, H_2L, and with the ligand anion, HL^-. For phenylboronic acid (pK_a = 8.7[1]), boric acid (pK_a = 9.0[2]), and methylboronic acid (pK_a = 10.4) these terms did not contribute significantly to the relaxation times measured, since studies were carried out at pHs of six and below. At these pHs, the amount of tetrahedral borate anion present is too small to allow determination of specific rate constants for $RB(OH)_3^-$ reactions with H_2L and with HL^-. In the case of m-nitrophenylboronic acid which has a pK_a of 6.96, however, it was possible to obtain values for the tetrahedral complexation rate constants with two ligands, mandelic acid and salicylic acid. For mandelic acid, studies could be carried out at pHs as high as six, and in this manner, values of k_f'' (characteristic of the B^-/H_2L reactions) and also of k_f''' (characteristic of the B^-/HL^- reactions) were calculated. The relaxation times for the m-nitro-

phenylboronic acid/salicylic acid system were too long to be measured at pH~6, and so, data were collected for pHs only as high as four. Consequently, it was not possible to obtain a precise value of the rate constant for the reaction of B^- with the salicylate anion, but an upper limit could be set. It was possible, though, to obtain a good value of k_f'' for the complexation reaction of the tetrahedral anion with the fully protonated ligand, H_2L. The results of these studies are presented in Table V-1.

The tetrahedral anion of this substituted boron acid appears to react with the ligand and with the ligand anion with reasonably high rates. In addition, Table V-2 indicates that the tetrahedral reactions seem to have larger rate constants than do the analogous reactions of the trigonal form of the boron acid.

While it is not possible to definitively discuss the reactions of the tetrahedral borate anion on the basis of only two points, it is interesting to note some similarities between these results and the results of work done on oxyanion complexation reactions, and to speculate on factors which influence the more general class of reaction which is highly ligand dependent. In contrast to di- and tri-valent metal ion chemistry where much work has been done in elucidation of complexation mechanisms,[3,4] metal oxyanion reactions have not been as thoroughly studied, even though they, in many cases, are the predominant species at high pHs, and

Table V-1. Reactions of $RB(OH)_3^-$ with H_2L and HL^-

Ligand	pK_{a1}	k_f'', $M^{-1}s^{-1}$	k_r'', s^{-1}	k_f''', $M^{-1}s^{-1}$	k_r''', $M^{-1}s^{-1}$
Salicylic Acid	2.83	$1x10^6$	0.1	$<1x10^4$	$<1.5x10^8$
Mandelic Acid	3.22	$2.4x10^7$	14	$1.5x10^4$	$5.2x10^8$

Table V-2. Rate Constants for Reactions of HB and B^- with H_2L and HL^-

Ligand	pK_{a1}	k_f, $M^{-1}s^{-1}$	k_f', $M^{-1}s^{-1}$	k_f'', $M^{-1}s^{-1}$	k_f''', $M^{-1}s^{-1}$
Salicylic Acid	2.83	650	125	$1x10^6$	$<1x10^4$
Mandelic Acid	3.22	$2.5x10^3$	$1.5x10^4$	$2.4x10^7$	$1.5x10^4$

even though many are of biological importance.[5] Experimentally, the investigation of metal oxyanions is difficult for two reasons: one, they tend to polymerize, and two, there is some uncertainty as to the structures in solution of the protonated forms of these oxyanions. Recent studies of the molybdate and tungstate complexation reactions with catechol and catechol derivatives have been carried out by Gilbert and Kustin.[6] These ions exist in an unprotonated form, XO_4^{2-}, which is tetrahedral, and in a protonated form, HXO_4^-, which is most likely octahedral;[7] the complexes are thought to be octahedral.[8] Thus, complexation reactions of the unprotonated, tetrahedral oxyanions are addition reactions while the reactions of the protonated HXO_4^- species are substitution or condensation reactions. These reactions are analogous respectively to the reactions of trigonal boron acids, which occur with expansion of coordination number, and to the reactions of tetrahedral borate anions, which are condensation reactions. In the case of molybdate and tungstate, the authors found a general tendency for the protonated oxyanion to react faster than the unprotonated oxyanion (i.e. the substitution reaction has a larger rate constant than does the analogous addition reaction). This same trend is observed in the reactions of trigonal and tetrahedral boron acids, as seen in Table V-2. For the oxyanion complexation reactions, the unprotonated XO_4^{2-} ion reacted faster with the least basic forms of the ligands

studied, while the rate constants of the reactions of the protonated HXO_4^- increased as ligand basicity increased. This order of relative rate constants as a function of ligand pK_{a1} is also observed for the two ligands studied. The substitution reactions for the more basic ligand, mandelic acid, occur with greater rate constants.

A possible explanation for the increased reactivity of the species undergoing the substitution reaction (B^- or HXO_4^-) with respect to the species which undergoes the addition reaction (HB or XO_4^{2-}) may lie in the relative bond lengths of the B-O or X-O bonds. In the borate anion[9] and in the octahedral[6] oxyanion as well, this bond is lengthened in comparison to the corresponding bond in the form which displays a lower coordination number. This lengthening of the bond may decrease the activation energy necessary to enter the transition state. In the case of complex formation between the tetrahedral borate anion and the ligand anion, this favorable increase in bond distance may be offset partially by the charge repulsion between B^- and HL^-. Hence, the rates of complexation of the ligand anion with B^- are expected to be lowered with respect to those for the analogous reactions of the fully protonated forms of the ligands. This is the trend which is indeed observed in both of the cases examined.

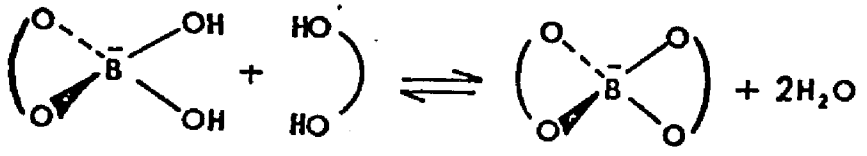
Finally, Gilbert and Kustin[6] report that the octahedral, protonated oxyanions do not complex with the fully

protonated form of catechol and the catechol derivatives. The results of the work on the reactions of the tetrahedral borate anions indicate that, in these cases, a substitution reaction with the fully protonated form of the ligand will take place. However, the ligands used in the boron acid work have pK_{a1} values which are considerably lower than those of catechol and its derivatives. It may be that the ligands employed in the oxyanion studies are sufficiently less acidic such that the reaction between HXO_4^- and H_2L either does not proceed or has associated with it a very small rate constant.

In view of the striking similarities between boron acid reactions and metal oxyanions, the results of boron acid studies may be characteristic of a more general class of ligand dependent substitution reactions. By an investigation of boron acid complexation reactions, one may obtain a more definitive picture of the mechanism involved. A strong mechanistic resemblance exists between reactions of trigonal $RB(OH)_2$ and metal oxyanion additions; there are many similarities between the reactions of the tetrahedral borate anion and the octahedral substitution reactions of metal oxyanions. In addition, boron acid studies may be more informative since the structures of the $RB(OH)_3^-$ species in solution have been well characterized, and since the substituted boron acids do not undergo complicating polymerization reactions, even at high pHs.

Relation to 1:2 Complexes of Boric Acid

The mechanistic question of the dynamics of reaction of the tetrahedral form of the boron acids bears on the possibility of formation of 1:2 complexes which is present in the case of boric acid. Addition of a second ligand molecule to form the 1:2 boric acid:ligand complex must have different geometric constraints and requirements from those characteristic of 1:1 complex formation. Elucidation of the mechanism of and factors influencing the reactions of tetrahedral borate should shed some light on the condensation reaction shown below:



The subsequent section deals with the dynamics of 1:2 complex formation and the influence of a first-bound ligand upon addition of a second chelating ligand.

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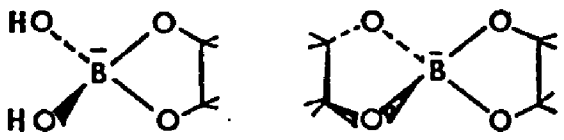
CHAPTER SIX

1:2 Complexes of Boric Acid. Reactions Which Emphasize the Importance of an Already Bound Ligand

Boric acid, $B(OH)_3$, affords a complexation possibility which is not available to the substituted boron acids, $RB(OH)_2$. It can form not only the 1:1 boric acid/ligand complex, but also the 1:2 species pictured below.



1:1 1:2

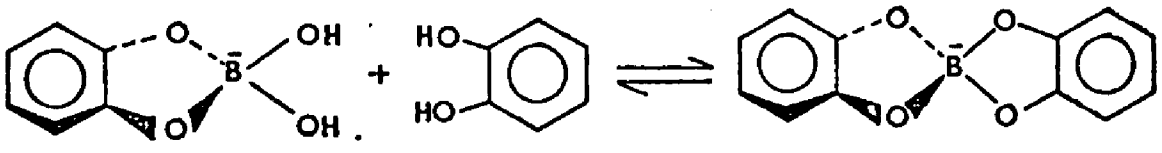
The 1:2 complex can be thought of as being formed via a condensation reaction in which a second ligand molecule displaces two of the hydroxyl groups on boron. Unlike the formation of the 1:1 complex which involves both an addition and a substitution, the addition of the second ligand is only a substitution reaction, the coordination number of the boron atom remaining the same. Therefore, one would expect the stereochemical requirements for the formation of the two complexes, 1:1 and 1:2, to differ from each other.

There have been many reports in the literature which indicate the presence of both 1:1 and 1:2 complexes for

several boric acid/ligand systems.[1,2,3] Infrared and Raman studies have established the existence of both one and two chelate rings for complexes of boric acid and salicylic acid,[4] lactic acid,[5] and some 1,2- and 1,3-alkyldiols.[6]

Solution Studies of Boric Acid Complexation with Catechols

In the studies of boric acid reactions with catechol and two catechol derivatives (4-nitrocatechol and 4-methylcatechol) which were carried out, there was no evidence, either thermodynamic or kinetic, which indicated the presence of a 1:2 complex in solution. This is somewhat surprising, since it is easy to visualize, thermodynamically, the formation of the 1:2 species via a condensation reaction between the 1:1 complex and a second ligand:



Stability constant calculations performed using equations derived for the 1:1 complexes of boron acids (see sections II.B and II.C) gave good, constant values for K_{stab} up to pHs of about seven for the boric acid/4-nitrocatechol, boric acid/catechol, and boric acid/4-methylcatechol systems. In cases where 1:2 complexes as well as 1:1 complexes are

formed, both species must be taken into account to obtain good values of the thermodynamic formation constants.[7] Kinetic results also support the thermodynamic conclusion that there is no detectable 1:2 species in solutions of catechol and the substituted catechols. Only a single relaxation time for each of these systems is observed, and it can be fit very well to the expression obtained in section II.A which assumes 1:1 complex formation only. That two relaxation times are present for some boric acid systems has been determined in studies of boric acid with lactic acid[8] and of boric acid with mandelic acid.[9] In both cases, these two relaxation times are quite separable, the second one appearing at rather long times. This lack of evidence for the formation of 1:2 complexes of boric acid with catechol and sustituted catechols is consistent with the thermodynamic results of other studies. Conner and Bulgrin[10] report the absence of a 1:2 boric acid/catechol complex. Bartusek[2,11,12] and coworkers have made an extensive investigation of the stability constants of complexes of boric acid. They report only 1:1 complex formation in the cases of the following ligands: tiron, catechol, 4-nitrocatechol, Alizarin Yellow S, and pyrocatecuic acid, the conclusion being that boric acid does not form 1:2 complexes with o-diphenols. In addition, Bartusek and Martell[13] studied the formation constants of some amide derivatives of salicylic acid with boric acid, and found that, although salicylic

acid itself will complex in both a 1:1 and a 2:1 ratio with boric acid, the amides form only 1:1 species. The formation constants of the boric acid/amide systems were also found to be lowered, indicating a decreased tendency toward complexation when one of the ligand hydroxyl groups is replaced by an amide.

It is interesting to speculate on the reasons for the absence of a 1:2 species in solution when the ligand is an o-diphenol. Boric acid is known to form 1:1 and 1:2 complexes with ligands which are more acidic than the catechols (lactic acid,[5] tartaric acid,[14] and salicylic acid[4]) and also with ligands which are less acidic than the catechols (mannitol[15] and other polyhydroxy compounds). Bartusek[2] postulated that perhaps chelate ring size was the factor controlling the presence or absence of the 1:2 species. His studies demonstrated that chromotropic acid and its 2-bromo- and 2,7-dibromo- derivatives as well as salicylic acid, all of which form six membered rings, are capable of complexing in 1:1 and 2:1 ratios with boric acid, while the o-diphenols which form five membered rings form only 1:1 complexes in solution. This argument, however, conflicts with the IR evidence and kinetic evidence that lactic acid/boric acid 2:1 complexes exist in aqueous solutions[8] and also the indication that mandelic acid[9] and some 1,2-alkyldiols[6] yield 2:1 complexes with solutions of boric acid. While ring size may not be the major factor in determining whether or not

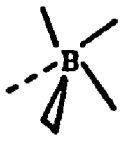
boric acid will combine in a 1:2 ratio with the ligand, the flexibility and geometry of the ligand may be important. It is known that ligand geometry exerts an influence on complexation reactions of boron acids. For example, no complex is formed between boric acid and trans 1,2-cyclohexanediol, and there is evidence of only minimal complex formation of the cis form of the ligand.[10] Presumably, this is due to the inability of the trans form to assume the geometry necessary for complexation, and the fact that only the boat form of the cis isomer (which is present in very small amounts) has the proper geometry. In addition, it is seen that the catechols show rates for formation of the 1:1 complex which are higher than the values predicted by pK_{a1} of the ligand.[3] In this case, ligand geometry results in an increased rate of complexation since the rigidity of the ligand must hold it in a geometry which is favorable to reaction. The conclusion is, then, that ligand geometry and flexibility can either increase or decrease the observed rate of reaction depending upon whether the lack of flexibility constrains the ligand to a favorable or to an unfavorable conformation with regard to the transition state.

It is reasonable to assume that the reaction in which addition of a second ligand occurs is also sensitive to ligand flexibility and stereochemistry. Surely the geometric requirements for the formation of the 1:1 complex from boron acid and ligand are different from those of the

condensation reaction of the 1:1 complex with a second ligand molecule. Thus, while the rigidity of catechol and the substituted catechols may enhance the formation of the 1:1 species, this same factor may hinder the formation of the 1:2 species. Preliminary studies on boric acid/lactic acid[8] and boric acid/mandelic acid[9] systems indicate the presence of a long relaxation time in addition to a shorter one, pointing to the fact that the second chelation may be slow. Recall that in the preceeding chapter, the rates of complexation of the tetrahedral borate anions appear to be rather high. The fact that the tetrahedral borate reactions proceed with relatively large rate constants while the 1:2 complexation reactions mentioned seem to have characteristically long relaxation times could be indicative of the fact that the already coordinated ligand may make it difficult for the 1:1 complex to assume the required transition state geometry.

The effect of an already bound ligand on subsequent chelation steps is seen in the reactions of some metal ions. A study by Margerum[16] has determined the rate constants for the formation of bis complexes of aromatic heterocyclic ligands with a complex in which the Ni^{2+} cation is already bonded to an aromatic ligand. The effect of the first bound ligand in this case is an enhancement of the rate of the second chelation over that observed for aquo Ni^{2+}. Kinetically, the substitution reactions of square planar metal

complexes exhibit a dependence upon already bound ligands. The well known trans effect is a kinetic effect which results in the labilization of certain bonds upon chelation with a first ligand.[17] In the case of boric acid with o-diphenols, the complexation of the first ligand may impose conformational restraints upon the complex, and the geometry required for the second step to occur may be difficult for the 1:1 species to assume. The second chelation must proceed either via a dissociative mechanism (a three coordinate boron in the transition state) or via an associative mechanism (a five coordinate boron in the transition state). The dissociative mechanism would require the four coordinate complex to approach a trigonal structure, and the rigidity of the chelate rings formed by the o-diphenols may hinder this. For an associative mechanism to be in operation, the boron would have to approach a five coordinate structure. Recently, calculations have been done[18] on possible geometries of five coordinate boron, since it has been proposed that the hydrolysis of BH_4^- proceeds through a metastable five coordinate intermediate.[19] The most favorable structure for this metastable intermediate was found to be the one of C_s symmetry shown below:

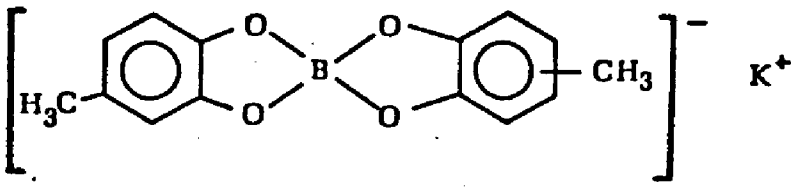


Because the five coordinate intermediate shown here has five identical ligands, the total symmetry is C_s. For the complexes of boric acid, although all coordinating species are not identical, the local symmetry is C_s, involving a boron atom and five ligand oxygen atoms. Again, the constraints imposed by the first bound ligand may make entrance into the transition state difficult. Complexes of ligands which are more flexible than the o-diphenols would be expected to assume the transition state geometry more easily, hence the presence of 1:2 complexes in these cases.

Isolation and Characterization of a Solid 1:2 Complex

During the course of determining the stability constant for the boric acid/4-methylcatechol system by titration with standard sodium hydroxide, it was noticed that small amounts of a solid white precipitate formed as the solution became more basic. The quantity of precipitate formed was quite small, and only appeared at pHs above seven, so it did not interfere with the collection or evaluation of either thermodynamic or kinetic data for the system. In a separate experiment, this solid was collected by filtration from a basified aqueous solution of boric acid and 4-methylcatechol, where μ=0.1 by addition of potassium nitrate. Characterization of this substance was performed us-

ing the solubility, melting point, conductance, NMR, IR, mass spectral, and elemental analysis data presented below. These data indicate that the solid is the potassium salt of the 1:2 complex of boric acid and 4-methylcatechol:



The solid does not exhibit a sharp melting point up to temperatures of 355°C, but becomes slightly discolored at these high temperatures. High melting points are generally characteristic of salts, and it has been reported that tetraalkylboronate salts are amorphous or crystalline, and decompose upon heating.[20] There was no appreciable solubility of the solid in the following solvents: water, cyclohexane, benzene, o-dichlorobenzene, nitrobenzene, toluene, methylethyl ketone, and acetyl chloride. Ethanol, methanol, ethylene glycol, and an ethanol- water mixture will dissolve the precipitate when hot, but the solutions quickly become discolored-most likely due to the decomposition of the complex followed by oxidation of the 4-methylcatechol. The solid does dissolve in tetrahydrofuran (THF) and in dimethylsulfoxide (DMSO), both polar, aprotic solvents. These solubility results are consistent with the observation that most tetraalkylboronate compounds are only sparingly

soluble in all solvents except alcohols and THF.[20] A second important result of the solubility studies has to do with the concept of proton transfer. The fact that the solid dissolves in DMSO and the solution does not become discolored indicates that the complex is not dissociated in this solvent. In the polar, protic solvents such as ethanol, complex dissociation occurs as evidenced by rapid discoloration of the solution. This discoloration is characteristic of the oxidation of 4-methylcatechol to the quinone. This supports the idea that proton transfer is vital to the reactions of boron acids with these ligands, the complex being unable to undergo the dissociative reaction in a polar but aprotic solvent.

The solid was sent out for elemental analysis for hydrogen, carbon, boron, oxygen, and sodium. The percentage of sodium present in the sample was so low as to indicate that it is not the sodium salt which is formed, but most likely the potassium salt. Table VI-1 compares the experimentally obtained percentages of boron, carbon, hydrogen, and oxygen with those expected for the 1:2 potassium salt of boric acid and 4-methylcatechol shown previously. It is seen that the experimentally obtained amounts of boron, carbon, hydrogen, and oxygen are in good agreement with those expected for the potassium salt of the 1:2 boric acid/4-methylcatechol complex.

Infrared spectra[21] of the solid in KBr pellets and in a

Table VI-1. Comparison of Experimental and Predicted Elemental Analyses

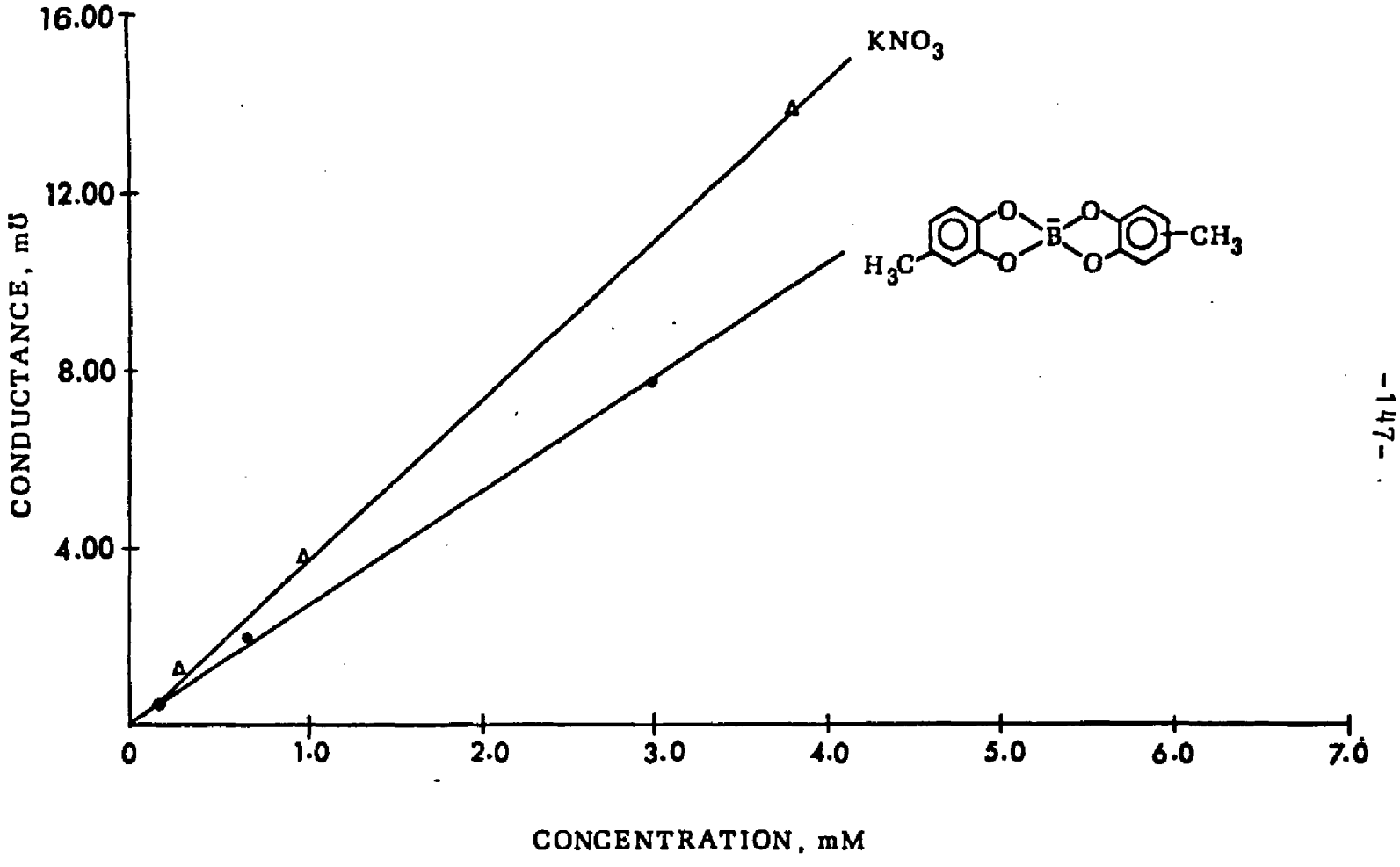
Element	%, Experimental	%, Calculated
Boron	3.33	3.74
Carbon	56.29	57.14
Hydrogen	3.97	4.08
Oxygen	16.67[a]	21.77

[a] a lower limit

nujol mull were taken, and also indicate the complex presented earlier. Comparison of spectra of solid $B(OH)_3$ and of the sample show a disappearance of the characteristic $B(OH)_3$ band at 3400 cm^{-1}. In addition, the precipitate showed major bands at 1490, 1450, 1270, 1100, 950, and 900 cm^{-1}. In studies of boric acid with salicylic acid[4] and with lactic acid,[5] Larsson and Nunziata have made the following assignments: (1) upon complexation, one or two new bands appear at 1470 cm^{-1}, (2) a new band at 1269 cm^{-1} appears and is characteristic of the C-O bond in the complex, (3) the tetrahedral stretch due to the tetrahedral BO_4^- moiety is a triply degenerate vibration which is split, and has bands appearing at 1080 and 965 cm^{-1}. For the less symmetric 1:2 complex (as opposed to the 1:1 complex), the band at 965 may be even further split. Finally, the authors note that complexation should result in the loss of the vibrational band at 1340 cm^{-1} which is characteristic of the ligand C-O-H bond ; this is absent in the spectra of the solid sample. The spectra of the complex isolated from the solution of boric acid and 4-methylcatechol contain bands which are in close agreement with those predicted above, and lend support to the proposed 1:2 structure. The lack of an O-H stretching band also supports this conclusion.

Conductance studies of the solid dissolved in DMSO were carried out along with parallel measurements of DMSO solutions of potassium nitrate. Figure VI-1 shows the results of

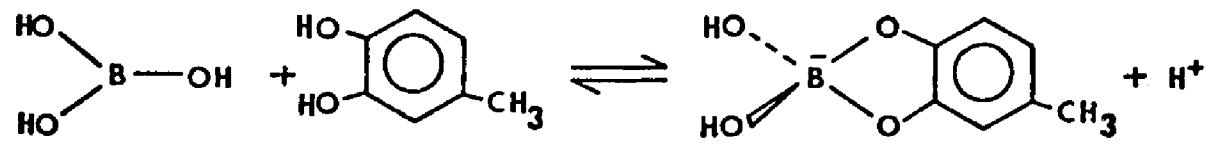
FIGURE VI-1. CONDUCTANCE OF K^+ SALT OF 1:2 COMPLEX ANION IN DMSO

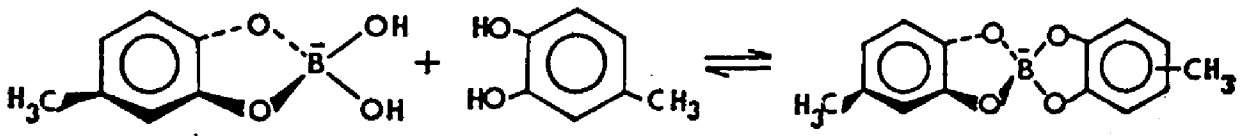


these measurements which indicate that the sample is a 1:1 electrolyte. They also are consistent with the idea that the complex does not dissociate in aprotic solvents.

Finally, NMR spectra of boric acid, 4-methylcatechol, and the solid precipitate dissolved in deuterated DMSO were taken. These support the conclusion that the complex formed is indeed the 1:2 species. There is no evidence of an O-H proton which would be present if the substance isolated were the 1:1 complex. The peak heights were integrated, and the values are consistent with the 1:2 potassium salt shown previously.

The reason behind precipitation from solution of a species which is both thermodynamically and kinetically undetectable in solution could possibly be a combination of the dynamics of formation and of the solubility and equilibria of the product. For the reasons discussed previously, the first bound ligand may make the formation of a 1:2 complex kinetically unfavorable. The low forward rate constant would then result in undetectably small amounts of the second complex in solution. However, thermodynamically, the reaction scheme can be represented as follows:

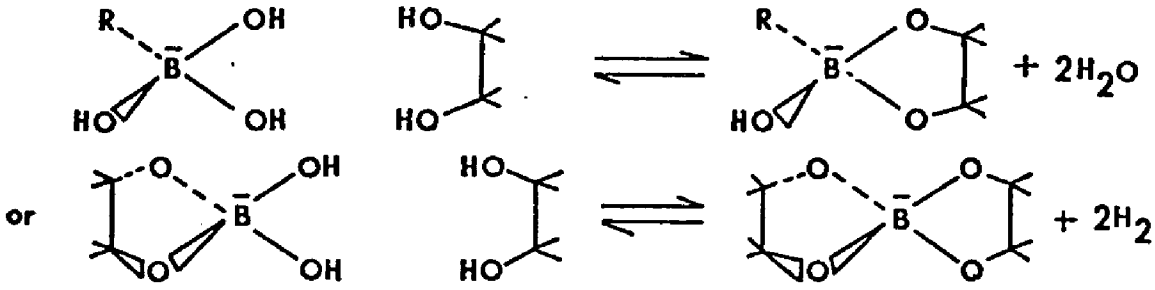




It is clear that at higher pH values, LeChatalier's principle predicts an increase in the concentration of the 1:1 species, and hence an increase in the 1:2 species also. As the pH of the solution is increased (as in a titration with sodium hydroxide), the concentration of 1:2 complex also increases, and, if the solubility of the complex in aqueous solution is not great, it will begin to precipitate out of solution. From the solubility studies of the solid, it was seen that the product is quite insoluble in water, so it is not surprising that small amounts begin to come out of solution. Once precipitation of the 1:2 complex has begun, the equilibria will continue to shift to produce more of the complex. The species is not detectable kinetically or thermodynamically because the pH must be above seven for precipitation to occur, since the concentration of complex in acidic solution is very low. No solid was obtained upon basification of solutions of boric acid and 4-nitrocatechol and of boric acid and catechol (μ = 0.1M in KNO_3 in all cases). If the above interpretation is correct, then this difference presumably lies in the differences in solubility of the various complexes. For catechol and 4-nitrocatechol, if the 1:2 complex is soluble in the small amounts formed, then no precipitation will occur.

The study of the dynamics of the formation of 1:2 complexes of boric acid with the catechols emphasizes the importance of a first bound ligand upon subsequent chelation

processes. The stringent geometric requirements imposed on the 1:1 complexes upon chelation with a single molecule of o-diphenol may make entrance into the transition state preceeding 1:2 complex formation kinetically unfavorable. Evidence of 1:2 complexation in the case of more basic and of less basic ligands points out that the more flexible ligands, regardless of pK_{a1}, will undergo the second chelation step. Preliminary data for the boric acid/lactic acid[8] and for the boric acid/mandelic acid[9] systems show a long relaxation time, perhaps indicating that, even for these more flexible ligands, the second complexation step may be difficult. Again, the greater flexibility of the tetrahedral borate anion may be a factor responsible for the relatively high rates with which these react to form the 1:1 complex, as opposed to the lower rates observed for the 1:2 formation:



The isolation of the 1:2 potassium salt of boric acid and 4-methylcatechol may be the result of thermodynamic as well as kinetic factors. This species precipitates from an aqueous solution at higher pHs, while remaining both thermodynamically and kinetically undetectable when in solution.

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21. We gratefully acknowledge the help of Russell Selzer who took all of the infrared spectra of the solid.

CHAPTER SEVEN

Concluding Remarks

Through the study of the complexation reactions of boron acids, the effects and dynamics of ligand dependent processes have been well demonstrated. The influence of ligand donor atom protonation, ligand geometry and orientation, and chelate ring size are seen in the reactions of trigonal boron acids with fully protonated ligands, and the reactions of the ligand anions have emphasized the importance of such additional ligand specific effects as intramolecular hydrogen bonding and ligand basicity. These results bear not only upon the complexation reactions of boron acids, but also upon the more general class of reaction which is dependent upon the properties of the ligand involved. Because of the many similarities between the boron acid reactions and the reactions of oxyanions, the ideas concerning complexation dynamics which have been developed here also find application in the oxyanion work. Oxyanions exist both in a form of low coordination number (tetrahedral), and also in a form of higher coordination number (octahedral).[1] Thus, they undergo reactions which can be either addition reactions or substitution reactions; trigonal boron acids undergo reactions which are both addi-

tion and substitution, while the tetrahedral anions undergo substitution reactions. The complexation of both boron acids and oxyanions with ligand anions depends heavily upon the ligand basicity, the ability of the ligand to orient water perhaps playing a major role here. In addition, the failure of the fully protonated form of catechol to react with the octahedral molybdate in a substitution process[2] is reminiscent of the lack of formation of the 1:2 complexes in the case of the reactions of boric acid with catechol and the substituted catechols.

The investigations carried out thus far have begun to yield an understanding of the dynamics of formation of the 1:2 complexes of boric acid and of the reactions of the tetrahedral borate anions. Much work remains to be done in this area before a complete picture of the reaction mechanism is obtained. First, studies of boron acids with a series of ligands must be carried out at high pHs. In this manner, more will be learned about factors which influence the rates of reaction of the tetrahedral borate anions. Preliminary results indicate that these complexation reactions proceed fairly rapidly (at least with the more acidic ligands mandelic acid and lactic acid), but effects such as ligand acidity, ligand donor atom protonation, ligand flexibility, and other ligand specific properties still remain to be evaluated. While one would expect some similarity between the reactions of tetrahedral borate anions to form

the 1:1 complexes and the reactions of the tetrahedral 1:1 species to form the 1:2 complex, the two will surely not have precisely the same ligand requirements and dependencies. Therefore, the second facet of boron acid chemistry to be investigated is the formation of the 1:2 complex via a condensation reaction between the 1:1 species and a second ligand molecule. In contrast to the results of the reactions of the tetrahedral borate anions, preliminary data for the formation of the 1:2 species indicate that it is difficult for the 1:1 complex to undergo the second chelation. Studies of the dynamics of this process will elucidate the effect of an already bound ligand upon any further chelation steps which occur. The boron acid systems lend themselves nicely to a study of this type. Because the boron acids undergo geometric changes upon complexation, the reactions are quite sensitive to the nature and flexibility of the coordinated ligand. This is not true in the case of normal aquo metal ion chemistry, where the geometry about the cation remains fixed. A comparison of the reactions of tetrahedral borate anions with the reactions of the 1:1 borate species will allow assessment of the influence of an already bound ligand and the factors which are important in subsequent chelation steps. The results of studies of the reactions of the tetrahedral boron compounds will shed light on the more general class of substitution reaction which is ligand dependent, and, in this respect, will find widespread appli-

cation.

For all of the boron acids studied thus far, the rate determining step involved chelate ring closure; the attack by the ligand upon the empty boron p_z orbital occurs rapidly and the trigonal - tetrahedral interconversion is a facile process ($k_f = 10^{10}$ $M^{-1}s^{-1}$ and $k_r = 10^5$ s^{-1} for boric acid).[3] In the case of a sufficiently less acidic boron acid, the attack by the ligand uopn the empty orbital and the trigonal - tetrahedral interconversion may become competitive with ring closure. Mesityleneboronic acid has a pKa of 11.5,[4] one pK unit higher than the least acidic boron acid which has been examined (methylboronic acid with a pK of 10.4). By studying the complexation kinetics of this boron acid, it may be possible to gain some insight into the nature of the trigonal - tetrahedral interconversion process.

It would be interesting as well as informative to look at the reactions of boron acids with ligands which contain donor atoms other than oxygen. Sulfur analogs of some of the oxygen containing ligands (for example, benzene dithiol) present opportunities for future work. Pearson's hard soft acid base theory[5] predicts that the stability constants for boron acid - thiol complexes should be lower than those of the corresponding diol. This offers the possibility that the rate of ligand attack on the boron acid will be competitive with ring closure, and here (as in the case of boron acids of high pK_a values) there may be a shift in the rate

determining step in the complexation process. Whether or not this is the case, the sulfur ligands have different properties with respect to such things as hydrogen bonding and ability to orient solvent molecules. From this point of view, the sulfur analogs will permit further investigation of the dynamics of ligand dependent mechanisms and the factors which influence the rates of reactions of this type. For this same reason, work with nitrogen donor atoms would also be an interesting avenue for future research in boron acid complexation reactions.

Although the present work concerns only the reactions of boron acids, the kind of ligand dependence observed here is surely not confined to boron chemistry alone. Similarities to metal oxyanion reactions have already been discussed. The mechanistic considerations which have been shown to be important in these reactions may prove to be of considerable generality.

Perhaps the most universally applicable use of boric acid appears in a book by R. Yee.[6] The recipe for Chinese tamales calls for one teaspoon of boric acid (poun sa).

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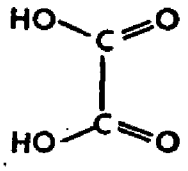
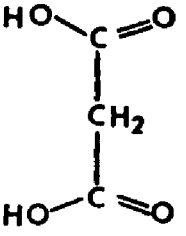
APPENDIX A

Ligands:

DICARBOXYLIC ACIDS

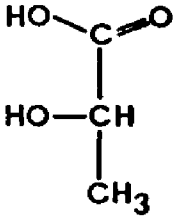


oxalic acid

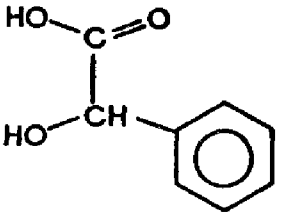


malonic acid

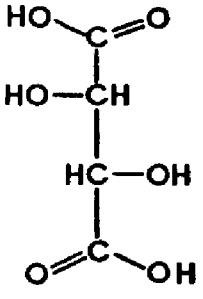
α-HYDROXYCARBOXYLIC ACIDS



lactic acid

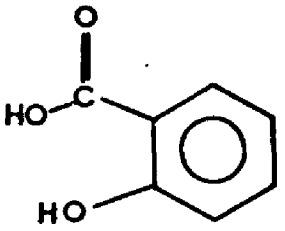


mandelic acid



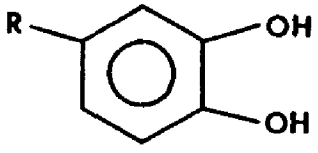
tartaric acid

o-HYDROXYCARBOXYLIC ACIDS



salicylic acid

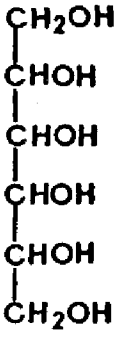
DIOLS AND POLYOLS



catechol: R=H

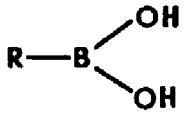
4-nitrocatechol: R=NO_2

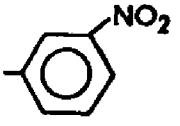
4-methylcatechol: R=CH_3

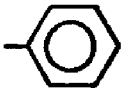


mannitol

Boron Acids:



m-nitrophenylboronic acid: R= 

phenylboronic acid: R= 

boric acid: R= −OH

methylboronic acid: R= $-CH_3$