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I am submitting herewith a dissertation written by Herbert Charles Hedgecock, Jr. entitled "Synthetic and Mechanistic Aspects of Several Reactions of Organoboranes." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

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SYNTHETIC AND MECHANISTIC ASPECTS OF SEVERAL REACTIONS OF ORGANOBORANES

A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Herbert Charles Hedgecock Jr.

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The author wishes to dedicate this work to his son, Charles Wayne.

ABSTRACT

The properties and reactions of di-3-pinanyl-2-butylborane were the object of an intensive study. The compound was stabilized for an extended period of time such that the chirality was maintained. An unsuccessful attempt was made to induce a redistribution of this compound in order to prepare chiral tri-2-butylborane. Several reactions were performed with di-3-pinanyl-2-butylborane with the intention of preparing a series of chiral compounds and, in the process, elucidating information on the proposed mechanisms of these reactions.

Also, a study was made of the oxidation of organoboranes with trimethylamine N-oxide dihydrate. Variations in solvent, hydroboration technique, oxidation temperature, and amount of oxidant were investigated. A simple, convenient hydroboration-oxidation procedure was developed to convert alkenes into the corresponding anti-Markovnikoff alcohols. Both functionally substituted and simple alkenes were hydroborated and oxidized. A comparison of the efficiency of this procedure to that of the alkaline hydrogen peroxide oxidation procedure was made. The mild conditions of the trimethylamine N-oxide dihydrate oxidation procedure were also demonstrated by oxidizing a solution containing an organoborane along with various functional compounds.

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LIST OF SYMBOLS

BH_3.THF Borane tetrahydrofuran complex

BMS Borane methyl sulfide complex

EE Ethyl ether

glpc Gas-liquid phase chromatography

IAR Intramolecular anionotropic rearrangement

NMR Nuclear magnetic resonance

Ph Phenyl

Pin 3-Pinan-α-yl, or 3-Pinanyl

Pr 1-Propyl

R Alkyl

THF Tetrahydrofuran

CHAPTER I

STATEMENT OF THE PROBLEM

A. Proem

Organoboranes have been developed into one of the most synthetically versatile classes of compounds available to the organic chemist. Numerous techniques are available for their preparation, the most common being the hydroboration reaction. The myriad of organoboranes which can be prepared seems to be limited only by the researcher's imagination. Even more important than their accessibility and structural diversity is the fact that organoboranes are reactive intermediates which may be readily transformed into many different classes of compounds. A comprehensive discussion of the syntheses and reactions of organoboranes is beyond the scope of this work; however, several excellent texts which discuss these as well as other aspects of the chemistry of boron compounds are available.[1-7]

A simple, convenient procedure for the preparation of organoboranes was not available until 1956, at which time the hydroboration reaction was discovered.[8] Since that time the number of syntheses and reactions of organoboranes has increased phenomenally. As a consequence of this rapid growth, the mechanisms of organoborane transformations have often had to take a back seat to the synthetic utility of the reactions. Thus, the object of this dissertation was

to study mechanisms of a variety of organoborane reactions.

B. Di-3-Pinanyl-2-Butylborane

The method of choice for studying the mechanisms was to utilize a chiral organoborane with an enantiomeric substituent. In this way the stereochemistry of the products could be related to that of the organoborane. The compound di-3-pinanyl-2-butylborane, hereafter referred to as $Pin_2B(2\text{-}Bu)$, is just such an organoborane.[9,10]

Several factors made $Pin_2B(2\text{-}Bu)$ a logical choice for studying organoborane reaction mechanisms. First, the compound is easily prepared[9] from α-pinene, a readily available natural product of high optical purity. Second, the stereochemistry and chirality of the organoborane are well defined. Third, extensive literature references can be cited which delineate both the utility and the problems associated with using $Pin_2B(2\text{-}Bu)$. Fourth, the organoborane is relatively stable. Fifth, the anticipated products, formed by transformation of the chiral acyclic 2-butyl group, are enantiomeric compounds with known absolute configurations.

In addition to the advantages, there are a few problems associated with $Pin_2B(2\text{-}Bu)$. First, the organoborane slowly racemizes.[9] Second, several reactions of interest are extremely sluggish or do not occur at all with bulky organoboranes such as $Pin_2B(2\text{-}Bu)$. Third, several of the reactions of interest utilize only one or two of the

alkyl groups on the organoborane. This raises the possibility that the 3-pinanyl groups might react preferentially, with the consequence that none of the desired 2-butyl product would be detected.

Chapter II delineates the attempts to stabilize $Pin_2B(2\text{-}Bu)$ such that racemization of the 2-butyl does not occur. The initial suggestion was that a slow dehydroboration-rehydroboration equilibrium was causing the racemization.[11,12] Two possible answers to the problem were to eliminate either the dehydroboration or the rehydroboration steps. A detailed discussion of each of these possibilities is given.

Chapter II also contains a description of the work directed towards a redistribution of chiral $Pin_2B(2\text{-}Bu)$ in order to synthesize chiral tri-2-butylborane. Such a reaction, if successful, could be anticipated to negate the second and third disadvantages, as previously described, of using $Pin_2B(2\text{-}Bu)$. A redistribution reaction appeared feasible in light of published reports that tri-2-deuterioethylborane could be obtained from di-1-nonyl-2-deuterioethylborane.[13]

The advantages of having chiral tri-2-butylborane to study mechanisms are twofold. First, the compound is much less crowded than $Pin_2B(2\text{-}Bu)$ and, consequently, should react more readily in those reactions which have sterically crowded transition states. Second, the only product

possible from the reaction of tri-2-butylborane would be the 2-butyl derivative, whereas the reaction of $Pin_2B(2\text{-}Bu)$ could lead to products containing either the 3-pinanyl or the 2-butyl groups.

C. Organoborane Mechanisms

Three general types of mechanisms have been proposed for the reactions of organoboranes. They are intramolecular anionotropic rearrangements(hereafter referred to as IAR), free radical reactions, and electrophylic substitutions. The organoborane reactions which were to be studied included hydroxymethylation with carbon monoxide, alkylation of α-halo- and α-diazocarbonyl compounds, amine N-oxide oxidation, and base-induced iodination. All of the above-mentioned reactions, with the possible exception of the last one, were thought to occur via an IAR mechanism. Since retention of configuration is an inherent feature of the IAR mechanism,[14] the stereochemistry of the products from the reaction of $Pin_2B(2\text{-}Bu)$ could be used to add proof to or disprove the proposed mechanism.

In reviewing the literature of the base-induced iodination reaction,[15] the conclusion was reached that nothing was known about its mechanism; none of the organoboranes which had been studied showed any stereochemical evidence to support any mechanism. However, a related reaction, the base-induced bromination of organoboranes, was known to occur with predominant, but not exclusive,

inversion of configuration in the products.[16] Thus, a study of the base-induced iodination seemed appropriate. Chapter III details the mechanistic studies of the reactions mentioned above.

D. Trimethylamine N-Oxide Dihydrate Oxidations

Chapter IV describes the studies with trimethylamine N-oxide dihydrate, a mechanistic study which evolved into a synthetically important reaction. Even though the mechanism of this reaction had been studied before and the results were those expected for an IAR mechanism,[17] the amine N-oxide oxidation still seemed to warrant study because the previous study utilized a benzylic substituted boron compound. A review of the literature showed that reactions involving benzylic-type compounds could, in certain cases, lead to contradictory results.[17,18] It seemed appropriate to study a system which did not involve this benzylic system. Thus, $Pin_2B(2\text{-}Bu)$ appeared to be an excellent choice to study.

There were two additional areas of interest concerning the amine N-oxide oxidations. The oxidations had always been studied using anhydrous trimethylamine N-oxide as an oxidant[17,19-22] and had been performed mainly in hydrocarbon solvents,[17,19,20] which are atypical of those normally used for the preparation of organoboranes.[23] Since the $Pin_2B(2\text{-}Bu)$ reactions were to be carried out in one of the more typical hydroboration solvents, it seemed

appropriate to test the reaction in these solvents.

Furthermore, the reported oxidations had always used anhydrous trimethylamine N-oxide, whose synthesis was, at the least, laborious;[19] on the other hand, trimethylamine N-oxide dihydrate was commercially available. Based on the following facts, the conclusion was made that the hydrated amine N-oxide should work as well as the anhydrous material for oxidizing organoboranes. First, organoboranes are stable in the presence of water.[23] Second, borinic, boronic and boric acid esters readily react with water to produce the corresponding alcohols and boron acids. Third, the products of oxidation of organoboranes with amine N-oxides are borinic, boronic, and boric acid esters.[19] Fourth, the desired product in the mechanistic study was the alcohol. Thus, an extensive study of the reaction conditions of the trimethylamine N-oxide dihydrate oxidation of organoboranes appeared necessary.

The final point of interest was the observation that trimethylamine N-oxide was, in one case,[20] a milder reagent than the normal oxidant, alkaline hydrogen peroxide.[23] Numerous organoboranes can be prepared containing other functionalities,[24] which, if oxidized with alkaline hydrogen peroxide, would possibly be destroyed. Thus, trimethylamine N-oxide dihydrate would appear to be an excellent choice for oxidizing these functional organoboranes. The results of this study are reported in Chapter IV.

CHAPTER II

DI-3-PINANYL-2-BUTYLBORANE

A. General Considerations About Organoboranes

1. Hydroboration Procedures

By far the most important technique for preparing organoboranes has been by hydroboration[1]--the reaction in ethereal solvents of diborane, B_2H_6, or its monomer-solvent complex and a carbon-carbon unsaturated molecule, Equation 1. The reaction of diborane with alkenes in the

$$6\ \text{"Alkene"} + B_2H_6 \longrightarrow 2\ R_3B \qquad (1)$$

gas phase or in non-Lewis base solvents is extremely slow even at elevated tempreatures. However, catalytic amounts of weak Lewis bases such as ethers cause a nearly instantaneous reaction to occur. This suggests that the actual hydroborating agent is the monomeric BH_3 or a BH_3-Lewis base complex rather than diborane itself. Other hydroborating agents are available,[25] but will not be discussed here.

Several methods are available for preparing diborane, the most common being the reactions in ethereal solvents of LiH, NaH, or $NaBH_4$ with BF_3 or BCl_3, Equations 2 and 3.

$$6\ LiH + 2\ BCl_3 \longrightarrow B_2H_6 + 6\ LiCl \qquad (2)$$

$$3\ NaBH_4 + 4\ BF_3 \longrightarrow 2\ B_2H_6 + 3\ NaBF_4 \qquad (3)$$

Diborane is extremely reactive toward oxygen and water or other protic compounds. Consequently, it must be prepared

and used in an inert atmosphere such as nitrogen or argon and stored at low temperatures. Due to its low solubility and reactivity in nonpolar solvents and its high reactivity with protic or easily reduced compounds, diborane is typically prepared and used in ethereal solvents such as ethyl ether, tetrahydrofuran(hereafter referred to as THF), or 2-methoxyethyl ether(hereafter referred to as diglyme).

Hydroborations can be conveniently performed by the in situ generation of diborane in the reaction mixture, by the utilization of a borane-THF solution, or by using the commercially available borane-methyl sulfide complex(hereafter referred to as BMS) to react with an appropriate alkene. Thus, the hydroboration reaction is the simplest, most convenient procedure for the synthesis of organoboranes.

2. Scope and Regioselectivity of Hydroboration

A myriad of cyclic, bicyclic, and acyclic alkyl- and aryl-substituted alkenes have been shown to undergo hydroboration.[1-7] In certain cases additional functionalities, besides the C-C multiple bond, may be present in the molecule without themselves reacting.[24] Since the organoboranes so produced are readily converted into numerous other compounds, the possibility exists for the syntheses of polyfunctional molecules not easily prepared by other methods.

For mono- and most disubstituted alkenes, hydro-

boration readily proceeds to the trialkylborane stage, Equations 4-6. However, tri- and tetrasubstituted alkenes proceed only to the di- and monoalkylboranes, Equations 7 and 8, respectively. Such mono- and dialkylboranes have

$$6\ RCH{=}CH_2 + B_2H_6 \longrightarrow 2\ (RCH_2CH_2)_3B \quad (4)$$

$$6\ R_2C{=}CH_2 + B_2H_6 \longrightarrow 2\ (R_2CHCH_2)_3B \quad (5)$$

$$6\ RCH{=}CHR + B_2H_6 \longrightarrow 2\ (RCH_2CHR)_3B \quad (6)$$

$$4\ R_2C{=}CHR + B_2H_6 \longrightarrow 2\ (R_2CHCHR)_2BH \quad (7)$$

$$2\ R_2C{=}CR_2 + B_2H_6 \longrightarrow 2\ (R_2CHCR_2)BH_2 \quad (8)$$

found wide applicability as highly regioselective hydroborating agents. Except for a few specific cases, they will not be discussed here. Their chemistries have been reviewed elsewhere.[26,27]

For alkenes of the types shown in Equations 4, 5, and 7, hydroboration is highly regioselective, with the B-C bond being formed at the least substituted carbon of the multiple bond.[1-7] 1,2-Disubstituted ethylenes, however, show little preference for site of attack, except where electronic effects play a large roll. The conclusion seems to be that steric effects dominate the regioselectivity of hydroboration, but can be overridden, in part, by either inductive or resonance effects in the alkene.[1,24]

3. Mechanism of Formation

The complexity of the hydroboration reaction has made a detailed description of its mechanism nearly impossible. This is partly due to the fact that three addition

reactions, Equations 9-11, simultaneously occur and cannot be characterized independently, except in special cases.

$$\text{Alkene} + BH_3 \rightleftharpoons RBH_2 \quad (9)$$

$$\text{Alkene} + RBH_2 \rightleftharpoons R_2BH \quad (10)$$

$$\text{Alkene} + R_2BH \rightleftharpoons R_3B \quad (11)$$

Also, five monomer-dimer equilibria, Equations 12-16, and three redistribution equilibria, Equations 17-19, are known.

$$BH_3 + RBH_2 \rightleftharpoons H_2BH_2BHR \quad (12)$$

$$BH_3 + R_2BH \rightleftharpoons H_2BH_2BR_2 \quad (13)$$

$$2\ RBH_2 \rightleftharpoons RHBH_2BHR \quad (14)$$

$$RBH_2 + R_2BH \rightleftharpoons RHBH_2BR_2 \quad (15)$$

$$2\ R_2BH \rightleftharpoons R_2BH_2BR_2 \quad (16)$$

$$BH_3 + R_3B \rightleftharpoons RBH_2 + R_2BH \quad (17)$$

$$2\ RBH_2 \rightleftharpoons R_2BH + BH_3 \quad (18)$$

$$2\ R_2BH \rightleftharpoons R_3B + RBH_2 \quad (19)$$

Several points of interest are known about hydroboration in spite of its complexity, and a discussion of some of these findings is in order.

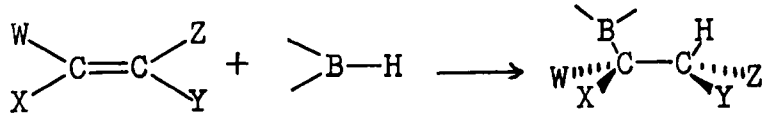
First, the rate of reaction for Equation 9 is second order overall and first order each in BH_3 and alkene.[28] This reaction was studied by hydroborating tetramethylethylene, which reacts with BH_3 to give only the monoalkylborane(which is known to exist as the dimer in solution[29]). Also, kinetic isotope studies were interpreted to indicate that a pre-rate determining π-complex was forming between the p orbital of the BH_3 and the π electrons of the

multiple bond.[28]

For hydroborations of alkenes less hindered than tetramethylethylene, the formation of dialkylboranes is known initially to predominate over the formation of monoalkylboranes.[30,31] However, few attempts have been made to determine what the actual hydroborating species may be for the formation of di- and trialkylboranes. The only exception involves hydroborations using disiamylborane,[32,33] prepared by the reaction of BH_3 with 2-methyl-2-butene. Studies of the reaction of disiamylborane with alkenes have shown that the rate of reaction was second order overall and first order each in the dimer of disiamylborane and alkene. This does not necessarily imply that the dimers of the alkyl- and dialkylboranes are always the hydroborating species. In fact, the above-mentioned data seem to indicate that the monomeric boranes are more reactive than the dimeric species. Otherwise, the above-mentioned reaction would have been first order in the disiamylborane monomer.

4. Stereochemistry of Formation of Organoboranes

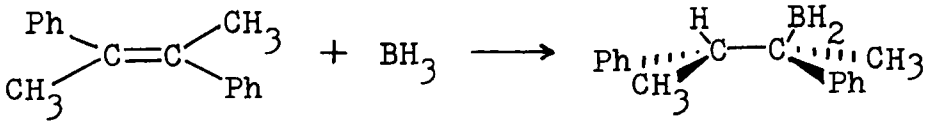
Probably the most important aspect of hydroboration is the stereospecificity of the bond formations in the organoboranes. Although not verified by direct evidence, hydroboration is unanimously believed to be a stereospecific cis addition of the B-H and the C-C multiple bond, Equation 20. The only argument has been as to the exact



(20)

mechanism of this cis addition. The earliest, proposed mechanism involved a four-center transition state.[34] Later mechanisms advanced the idea of a pre-rate determining π-complex between the vacant p orbital of the boron and the π bond of the multiple bond, with a subsequent stereospecific collapse of this complex to give the organoborane.[28,35,36]

There has never been a reported case which has shown unambiguously that hydroboration does, indeed, occur by a stereospecific mechanism. In fact, the mechanism of the hydroboration reaction has nearly always depended on the subsequent alkaline hydrogen peroxide oxidation of the organoborane formed by the hydroboration reaction. Sufficient data exist to state that this oxidation technique occurs by a mechanism whereby the B-C bond becomes an O-C bond with retention of configuration at the carbon attached to boron(see Chapter III for details). Consequently, the structures of numerous organoboranes prepared via hydroboration are known. Equations 21,[18] 22,[37] and 23[38] show the structures of organoboranes which are formed assuming the stereospecificity of hydroboration is as accepted.



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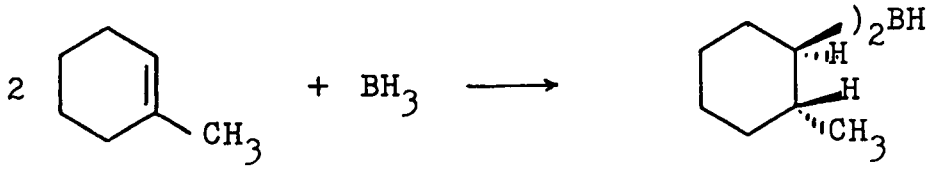

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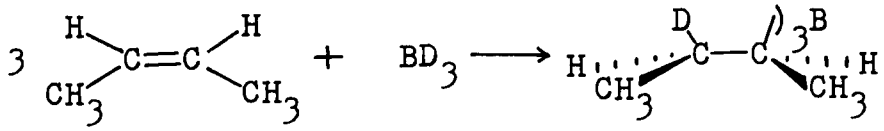

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5. Hydroboration of Functionally Substituted Alkenes

Hydroboration of alkenes containing other functionalities can often be accomplished without affecting the functional groups.[24] This leads to organoboranes containing such substituents. As will be pointed out in Chapter III, organoboranes undergo a myriad of reactions in which they are transformed into other compounds. Thus, the possibility exists for the production of many unique di- or polyfunctional compounds virtually impossible by other techniques.

Functionalities which can be tolerated in the alkene include halides, ethers, thioethers, esters and nitriles, to mention a few. Although such groups as aldehydes, ketones, alcohols, and carboxylic acids do compete with the alkene function for BH_3, their conversion to appropriate acetals, ketals, or esters allows them to be hydroborated without problem. In fact, a less-substituted alkene may even be hydroborated in preference to a more-substituted alkene in the same molecule.

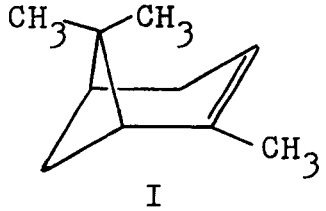
Two problems may arise in the hydroboration of functionally substituted alkenes. First, if the alkene's

functionality is of the vinylic or allylic type, then elimination of this group along with boron may occur. Second, the electronic effects of the functionality may drastically alter the regioselectivity of the hydroboration. For example, the hydroborations of propene and 1-butene both give only 6% of the internal borane, whereas 3-chloropropene and 4-chloro-1-butene give 40 and 18%, respectively, of the internal boranes.[24]

B. Hydroboration Chemistry Involving Chiral α-Pinene

1. Introduction

Probably the most important area of research involving the hydroboration-organoborane field is the hydroboration reactions of chiral α-pinene. (Unless specifically stated, the following discussion will refer to (-)-α-pinene, Structure I. For brevity, the minus sign will be omitted from the name.) The importance of this



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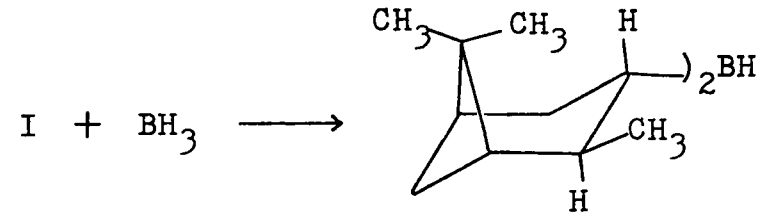
area of research arises from the fact that the products from α-pinene's hydroboration are chiral molecules which can be used for numerous asymmetric syntheses in a variety of systems. Mainly, the α-pinene hydroboration products have been used to induce chirality into a number of

different achiral or racemic alkene systems.[10] Also, these hydroboration products have been used in asymmetric syntheses with allenes,[39-41] carbonyl compounds,[10] imines,[10] nitriles,[42] and polyenes.[43]

2. Reaction Products of α-Pinene and Diborane

α-Pinene is a model compound for demonstrating the concepts of regioselectivity and steric requirements of hydroboration.[44] First, it is a trisubstituted alkene; therefore the B-C bond is formed predominately at the least substituted carbon of the double bond. Second, even with excess α-pinene, only two moles react per mole of BH_3, thus producing the dialkylborane, which then dimerizes.[29,45] Finally, the two faces of the double bond are nonequivalent due to the chirality of the molecule. Thus, the least sterically hindered face--the face on the opposite side of the molecule occupied by the geminal dimethyl group--is preferentially hydroborated. This has been demonstrated in Equation 24.



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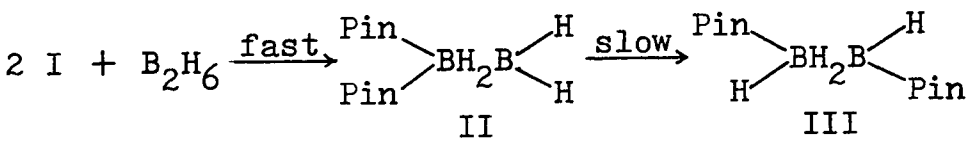
The hydroboration of chiral α-pinene has been studied using two, three, and four equivalents of the alkene per equivalent of diborane.[9,29,39-47] The nature of the resultant products depends on this stoichiometry and, also,

the age of the reaction mixture. Also, a solvent dependence has been noted. Equations 25, 26, and 27 demonstrate what is thought to be the major products of the reaction of diborane with two, three, and four equivalents, respectively, of α-pinene. [The abbreviation "Pin" will be used, hereafter, to indicate the 3-pinanyl moiety. The stereochemistry of this group is shown in Equation 24, (p 15).]



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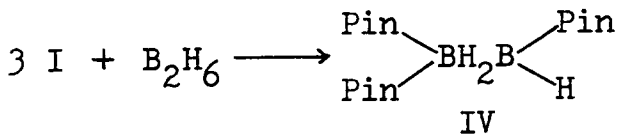

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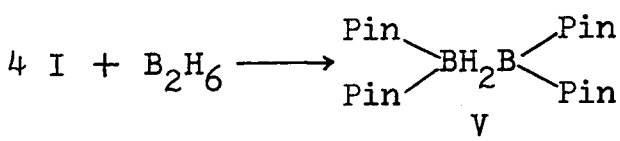

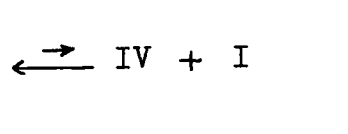

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The most widely studied and used product of α-pinene's hydroboration has been tetra-3-pinanyldiborane, Structure V, hereafter referred to as $Pin_4B_2H_2$. Its structure and chemistry have usually been discussed in terms of the monomer di-3-pinanylborane(also called diisopinocampheylborane), although evidence has shown that it exists as the dimer.[29] Depending on the concentration of excess α-pinene and the concentration of the dimer,[9,29,45] $Pin_4B_2H_2$ is approximately 4%(in diglyme) to 10%(in THF) dissociated into tri-3-pinanyldiborane, Structure IV, hereafter referred

to as $Pin_3B_2H_3$, and α-pinene, Equation 27 (p 16). This is an interesting observation and will be discussed later. $Pin_4B_2H_2$ prepared from (-)-α-pinene has been shown to have a positive absolute rotation, Equation 28; likewise, (+)-α-pinene produces the minus enantiomer, Equation 29.

$$4\ (-)\text{-}\alpha\text{-pinene} + B_2H_6 \longrightarrow (+)\text{-}Pin_4B_2H_2 \qquad (28)$$

$$4\ (+)\text{-}\alpha\text{-pinene} + B_2H_6 \longrightarrow (-)\text{-}Pin_4B_2H_2 \qquad (29)$$

3. Reaction of Chiral $Pin_4B_2H_2$ with Unhindered Alkenes

When (+)-$Pin_4B_2H_2$ is reacted with certain alkenes, unequal amounts of diastereomeric trialkylboranes are produced. When these trialkylboranes are then converted into other compounds (for example, conversion to alcohols using alkaline hydrogen peroxide), an excess of one of the enantiomeric products results. For example, when (+)-$Pin_4B_2H_2$, prepared in diglyme from 93% optically pure α-pinene is reacted with (Z)-2-butene, Equation 30, and the resultant organoborane is oxidized with alkaline hydrogen peroxide, Equation 31, then (S)-(+)-2-butanol which is 87% optically pure is formed.[9] Likewise, (-)-$Pin_4B_2H_2$ produces (R)-(-)-2-butanol of similar optical purity.

$$(+)\text{-}Pin_4B_2H_2 + 2\ \begin{matrix} CH_3 \\ H \end{matrix}\!\!>\!C{=}C<\!\!\begin{matrix} CH_3 \\ H \end{matrix} \longrightarrow 2\ Pin_2B\text{-}\underset{\displaystyle CH_2CH_3}{\overset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}\text{-}CH_3 \qquad (30)$$

VI

$$Pin_2B\text{-}\underset{\displaystyle CH_2CH_3}{\overset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}\text{-}CH_3 + H_2O_2 + NaOH \longrightarrow HO\text{-}\underset{\displaystyle CH_2CH_3}{\overset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}\text{-}CH_3 \qquad (31)$$

If the same set of reactions, Equations 30 and 31 (p 17), are carried out using THF as the solvent rather than diglyme, then 2-butanol of the same configuration is produced, but the optical purity is reduced from 87 to 78%. This decrease in enantiomeric purity is apparently due to the fact that $Pin_4B_2H_2$ is dissociated into $Pin_3B_2H_3$ to a greater extent in THF than in diglyme.

Other unhindered (Z)-alkenes have been hydroborated with chiral $Pin_4B_2H_2$ and a trend has been noted.[9,10] First, each product (normally an alcohol) from the subsequent reaction of the trialkylborane is highly enriched in one enantiomer. Second, the absolute configuration of the enriched enantiomer is related to a specific "fitting" of the alkene when reacting with the chiral $Pin_4B_2H_2$. This has been demonstrated in Equation 32. Thus, for any

$$(+)\text{-}Pin_4B_2H_2 + 2\ \begin{matrix} R & & R \\ & C{=}C & \\ H & & H \end{matrix} \longrightarrow 2\ Pin_2B{-}\overset{\overset{H}{\vdots}}{\underset{\underset{CH_2R}{\vdots}}{C}}{-}R \qquad (32)$$

reaction which stereospecifically converts a B-C bond to a X-C bond, the product of that reaction will be enriched in one of the enantiomers.

4. Reaction of $Pin_3B_2H_3$ and $Pin_4B_2H_2$ with Hindered Alkenes

The reaction of moderately to highly hindered alkenes with $Pin_3B_2H_3$ and $Pin_4B_2H_2$ is known to be mechanistically different from the reaction of unhindered alkenes with $Pin_4B_2H_2$.[10,46] (The terms unhindered, moderately and

highly hindered alkenes refer, here, only to the steric interactions which result when $Pin_4B_2H_2$ reacts with such alkenes. The terms do not imply steric interactions within the alkene structure itself.) The following observations suggest this is true:

1. Hydroborations are much slower than for unhindered alkenes.
2. Enantiomeric purities of the resultant products are much lower.
3. α-Pinene is displaced from the hydroborating agent.
4. Hydroborations using $Pin_3B_2H_3$ give nearly the same enantiomeric mixtures as those obtained by using $Pin_4B_2H_2$.
5. Absolute configurations of the products are opposite to those formed from unhindered alkenes.

Rather than trying to give a comprehensive discussion of this area, two representative examples--(E)-2-butene and 2-methyl-2-butene--will be discussed in detail. Further examples can be found elsewhere.[10,46]

The reaction of (Z)-2-butene with (+)-$Pin_4B_2H_2$ was essentially complete within two hours at 0°, Equation 30 (p 17). Oxidation of the resulting organoborane gave 87% optically pure (S)-(+)-2-butanol, Equation 31 (p 17). However, the reaction of (E)-2-butene was complete only after 24 hours at 0°, and the resultant organoborane, when oxidized, gave 13% optically pure (R)-(-)-2-butanol.

Hydrolysis of the reaction mixture between (E)-2-butene and (+)-$Pin_4B_2H_2$ resulted in the liberation of one mole of hydrogen for each two moles of the reacted alkene. Finally, gas chromatographic analysis of the reaction mixture showed the presence of one mole of α-pinene for each two moles of reacted alkene. These observations suggest that (E)-2-butene is reacting by the sequence shown in Equations 33-36.

$$\underset{\text{V}}{Pin_4B_2H_2} \longrightarrow \underset{\text{IV}}{Pin_3B_2H_3} + \alpha\text{-pinene} \qquad (33)$$

$$\text{IV} + \begin{matrix} CH_3 \\ H \end{matrix}\!\!>\!C{=}C<\!\!\begin{matrix} H \\ CH_3 \end{matrix} \longrightarrow \underset{\text{VII}}{PinB(2\text{-Butyl})} + Pin_2BH \qquad (34)$$

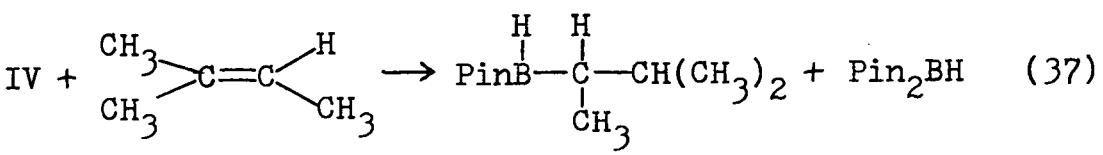
$$\text{VII} + \begin{matrix} CH_3 \\ H \end{matrix}\!\!>\!C{=}C<\!\!\begin{matrix} H \\ CH_3 \end{matrix} \longrightarrow \underset{\text{VIII}}{PinB(2\text{-Butyl})_2} \qquad (35)$$

$$2\ Pin_2BH \longrightarrow \text{V} \qquad (36)$$

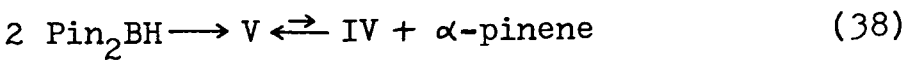
No attempt has been made here to show the absolute configurations of the 2-butyl groups in Structures VII and VIII. Presently, the only detail which is known is that a small excess (13%) of the (S)-enantiomeric 2-butyl group is formed in these structures when (E)-2-butene is reacted with (+)-$Pin_4B_2H_2$.

The reaction of the more hindered alkene 2-methyl-2-butene with (+)-$Pin_4B_2H_2$ was shown to be even slower than that for (E)-2-butene; the reaction was only 72% complete after 60 hours at 0°. After oxidation of the resultant

organoborane with alkaline hydrogen peroxide, the product (R)-(-)-3-methyl-2-butanol was found to be 14% optically active. Again, α-pinene was observed in the reaction mixture. However, this time approximately one mole was displaced for each mole of alkene which reacted. This would again suggest that the actual hydroborating species is not $Pin_4B_2H_2$; rather it is $Pin_3B_2H_3$. This hypothesis has been tested, with the results indicating that this is the case. $Pin_3B_2H_3$ was prepared, Equation 26 (p 16), and reacted with 2-methyl-2-butene. The reaction was essentially complete after three hours. After oxidation, the product 3-methyl-2-butanol was found to be 17% enriched in the (R)-enantiomer. Thus, the reactions of $Pin_4B_2H_2$ and $Pin_3B_2H_3$ with 2-methyl-2-butene both produce nearly the same enantiomeric excess (14 and 17%, respectively) of the same enantiomer. The reaction for $Pin_3B_2H_3$ is probably proceeding as described in Equations 37 and 38.



(37)



(38)

then (37), (38), etc.

The reaction of other hindered alkenes with $Pin_4B_2H_2$ or $Pin_3B_2H_3$ produces diastereomeric organoboranes with one diastereomer predominating.[10,46] Even though the diastereomeric excess is not as pronounced as was the case with

unhindered alkenes, the absolute configuration of the enriched enantiomeric product from reaction of the organoborane can again be accurately predicted.[10] Thus, the reaction of $Pin_4B_2H_2$ or $Pin_3B_2H_3$ can be a valuable tool for both preparation of chiral molecules and prediction of their absolute configurations.

5. Other Reactions of $Pin_4B_2H_2$ and $Pin_3B_2H_3$

As previously mentioned, an exhaustive review of this area of research is far beyond the scope of this text. In addition, the reported studies have been carried out by several research groups, making a standardization of the results extremely difficult, if not impossible. Furthermore, there are instances where results from one research group contradict those of another's.[10] However, a brief mention of some of the other uses of $Pin_4B_2H_2$ and $Pin_3B_2H_3$ are in order.[10]

Optical activity has been induced into a number of other alkene systems by their reactions with $Pin_4B_2H_2$ or $Pin_3B_2H_3$. A few such systems include 2-substituted-1-alkenes, 1- and 2-deuterioalkenes, and 1-alkenes(using $Pin_4B_2D_2$). Other uses include the partial kinetic resolution of racemic mixtures of alkenes and allenes, the reduction of aldehydes and ketones to give chiral alcohols, and the reaction with imines and nitriles to prepare chiral products.[10] Chirality has also been induced in polymers.[43]

6. Proposed Models for $Pin_4B_2H_2$ and $Pin_3B_2H_3$

Numerous models have been advanced to predict which diastereomeric organoborane will predominate when $Pin_4B_2H_2$ is reacted with an appropriate alkene.[9,34,41,48,49] All of these models, except one,[48] are based on the monomeric di-3-pinanylborane. The major differences in the models are based mainly on different rotational conformations of the 3-pinanyl groups relative to each other, mechanism of the hydroboration step, or simplicity of presenting the models. An exhaustive review of the intricacies of each model is not warranted here; besides, for the reaction with unhindered alkenes, all of the models make the same prediction.

Despite their success with unhindered alkenes, none of these models correctly predicts the configuration of the products in the reaction of hindered alkenes. The reason for this is that all of the models make use of the chiral di-3-pinanylborane; whereas the actual hydroborating species is, in fact, the mono-3-pinanylborane, or more correctly, a dimeric borane which contains this species, Structure III or IV (p 16). A review of the literature shows only one reference to such a proposed model;[6] however, sufficient evidence can be cited to give credence to the proposal.

For example, the reaction of (Z)-3-hexene with (+)-$Pin_4B_2H_4$ in diglyme, followed by oxidation, produces

(S)-(+)-3-hexanol which is approximately 91% optically pure.[9] Second, when the product of two moles of (-)-α-pinene and one mole of diborane is formed and reacted immediately with (Z)-3-hexene, then 21% optically pure (S)-(+)-3-hexanol is formed after oxidation.[47] However, if this same hydroboration mixture is allowed to stand for 21 hours before reacting it with the (Z)-3-hexene, then the 3-hexanol produced after oxidation has the (R)-configuration and is 11% optically pure. Based on the above information and Equations 25 and 27 (p 16), it would be logical to conclude that hydroborations of appropriate alkenes with di-3-pinanylborane produce only one enantiomeric alkyl group from that alkene; whereas reactions involving mono-3-pinanylborane yield unequal amounts of both enantiomeric alkyl groups, with the excess enantiomer having the opposite configuration to that produced by di-3-pinanylborane.

C. Restatement Of The Problem

As was stated in Chapter I, the mechanisms of several reactions of organoboranes seemed appropriate to study, and the method of choice was to employ chiral di-3-pinanyl-2-butylborane. In order to study the mechanisms, the reagent needed to be pure and stable. However, di-3-pinanyl-2-butylborane was reported to lose optical purity upon standing.[9] Thus, it seemed appropriate to attempt to

stabilize the compound. The initial suggestion was that a dehydroboration-rehydroboration process was causing the instability of the reagent. Since the dehydroboration reaction occurs faster at higher temperatures, then the first plan of attack was simply to cool the reagent. Also, since the rehydroboration step apparently causes the actual loss in optical activity, an effort to stop this reaction was suggested. The method for accomplishing this was to add an active proton source which would react with any B-H bonds which might form.

The second problem was to attempt a redistribution reaction of the chiral di-3-pinanyl-2-butylborane to give chiral tri-2-butylborane. Since several of the reactions of interest utilized only one alkyl group of the organoborane and since these same reactions were extremely sluggish with sterically hindered organoboranes, it was anticipated that these reactions might prove impossible to study. Chiral tri-2-butylborane should alleviate such problems. That the redistribution might occur was based on the observation that di-1-nonyl-2-deuterioethylborane was successfully converted into tri-2-deuterioethylborane.[13] For such a process to occur, then the 2-deuterioethyl group must be transferred from one boron to another via an alkyl bridge species.[6] It was anticipated that such an alkyl migration would occur with the alkyl substituent retaining its stereochemistry.

The anticipated products from this redistribution reaction of di-3-pinanyl-2-butylborane were expected to be chiral tri-2-butylborane, α-pinene, and $Pin_4B_2H_2$. Noting that the boiling points of α-pinene and tri-2-butylborane were nearly the same, it was anticipated that the reaction could possibly be driven to completion by distilling off these two products as they formed, thus leaving $Pin_4B_2H_2$ in the reaction flask to be, subsequently, reused.

If this reaction were successful, then separation of the tri-2-butylborane from the α-pinene appeared to present a new problem. Therefore, research was necessitated to overcome this. One answer seemed to be the possibility of forming a solid organoborane derivative. The suggestion was made to form an amine-borane complex which could then be purified. The experimental results of these studies are described in the following sections.

D. Experimental

1. General Techniques

NMR spectra were recorded using either a Varian A-60 or T-60 spectrometer. Samples were run either as pure liquids or as solutions in an appropriate solvent, using tetramethylsilane (TMS) as the internal standard. The chemical shifts were recorded in δ units relative to the TMS signal. Spectra of those compounds which were isolated

from reaction mixtures were compared to the spectra of authentic samples, when available.

Analytical glpc was performed on either a Varian Aerograph 90-P or an Aerograph Autoprep Model A-700. Both instruments were equipped with thermal conductivity detectors, used helium as the carrier gas, and had interchangeable, stainless steel columns. The specific columns used were:

A. 6 ft x 1/4 in, 5% SE-30 on 60/80 Chromosorb W.

B. 10 ft x 1/4 in, 10% SE-30 on 60/80 Chromosorb W.

C. 10 ft x 1/4 in, 15% SE-30 on 60/80 Chromosorb W.

D. 6 ft x 1/4 in, 5% Carbowax 20-M on 60/80 Chromosorb W.

E. 10 ft x 1/4 in, 9.1% Carbowax 20-M on 60/80 Chromosorb W.

All columns were hand packed and pre-conditioned using standard techniques.[50]

Preparative glpc was performed using a Varian Autoprep Model 711, equipped with a flame ionization detector and nitrogen carrier gas. The column was a 20 ft x 3/8 in, 30% DEGS on 45/60 Chromosorb W.

The optical rotation of α-pinene was measured with a Josef and Jan Fric Polarimeter(E. H. Sargent and Co.), using a sodium-D-lamp and a 0.100 dm cell. Rotations were made by making ten consecutive readings on alternating sides of balance and averaging the results. Measurements

were made on pure liquids using distilled water for optical zero. Specific rotations were calculated with the standard formula:

$$[\alpha]_D^{^oC} = \frac{\text{Observed Rotation}}{\text{Length Of Tube(dm) x Density(g/ml)}}$$

Optical rotations of the 2-butanol were made using a Bendix-Ericsson ETL-NPL Automatic Polarimeter-143A, using a 0.0668 dm cell. The polarimeter was equipped with a sodium-D filter. Duplicate readings were obtained for each sample over a 1 min time span. Optical zero was measured with distilled water.

All commercial chemicals used in this research have been noted, when appropriate, along with their suppliers (listed in parentheses after their names). Purity was determined by NMR and glpc. Anhydrous, oxygen-free THF(Aldrich) and diglyme(Ansul Co.) were prepared by the method of Brown.[51] Microanalyses of new compounds were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

In the experiments involving air-sensitive compounds, the glassware was assembled and equipped with a rubber septum inlet and a mercury bubbler outlet. The equipment was then flame-dried and allowed to cool while passing a slow stream of nitrogen through the system. The nitrogen atmosphere was maintained throughout such experiments. Standard laboratory thermometers were used without

correction. All syringes were dried in an oven and pre-assembled while hot. Syringe needles were stainless steel, and were, likewise, dried in an oven. The syringes, equipped with needles, were flushed with nitrogen before use.

2. Stability Study of Di-3-Pinanyl-2-Butylborane

(-)-α-Pinene was prepared from (-)-β-pinene (Crosby Chemical Co.) by the method of Settine.[52] The α-pinene had a specific rotation of -47.4°, which corresponds to a 92% optical purity.[9,52] The product was at least 99% pure by glpc, using Columns D and E (p 27). The major impurity was β-pinene. The following data were used to calculate the specific rotation:

Optical zero: (+) 0.11, 0.11, 0.11, 0.12, 0.11, 0.12, 0.11, 0.10, 0.11, 0.11; Avg. +0.11°.

α-Pinene: (-) 3.96, 3.95, 3.94, 3.97, 3.97, 3.96, 3.98, 3.96, 3.96, 3.96; Avg. -3.96°.

Length of tube: 0.100 dm; Density: 0.859 g/ml; $[\alpha]_D$ max: -51.5°, Temperature: 23°.

Di-3-pinanyl-2-butylborane was prepared by the method of Brown[9] with slight modifications. A 1-l, three-necked flask, calibrated in 50-ml increments, was equipped with a stirring bar, a 250-ml, pressure-equalizing funnel, a rubber septum, and a mercury bubbler. After flame drying and flushing the apparatus with nitrogen, 350 ml of diglyme, 180 ml (1.13 mol) of (-)-α-pinene, and 15.39 g

(0.41 mol) of sodium borohydride (Alfa Products) were added to the flask. The flask was immersed in an ice bath, and the contents were stirred. Boron trifluoride diglymate, prepared from 72.5 ml (0.54 mol) of boron trifluoride etherate (Aldrich) and 150 ml of diglyme, was introduced into the separatory funnel and added to the contents of the flask over a period of 80 min. The $Pin_4B_2H_2$, thus produced, was allowed to stir for 4 hr.

During this 4-hr reaction period, 50.5 ml (0.57 mol) of (Z)-2-butene (Matheson) was condensed into a Dry Ice-acetone gas trap. The outlet of the gas trap was equipped with a piece of Tygon tubing, fitted with a 12 in syringe needle. Approximately 5 cm of the Tygon tubing was filled with Ascarite (Arthur H. Thomas Co.), held in place with plugs of glass wool.

Following the 4-hr reaction period, the (Z)-2-butene was transferred to the reaction flask by positioning the syringe needle directly above the surface of the well-stirred mixture and warming the (Z)-2-butene (bp 3.7°) with a lukewarm water bath; the addition required 65 min. After allowing the reaction mixture to stir for an additional 20 min, the stirring was stopped, and the volume in the flask was estimated to be 720 ml. Three-tenths (i.e., 216 ml) of this mixture was transferred via syringe to an appropriate flask, equipped with a stirring bar, septum inlet, and mercury bubbler. The larger flask (i.e., the one con-

taining 504 ml of solution) was charged with 2.2 ml of ethylene glycol (Fisher), and the contents were stirred for 10 min, during which time the funnel was replaced by a glass stopper. The two flasks were stored in the cold room (0-3°). From the theoretical yield of di-3-pinanyl-2-butylborane (0.54 mol) and the total volume of the solution (720 ml), the concentration of the organoborane was calculated to be 0.75 M.

The two flasks of di-3-pinanyl-2-butylborane were studied over a 306-hr period by oxidizing 70-ml aliquots (53 mmol) of the organoborane, using the standard alkaline hydrogen peroxide oxidation technique,[23] and subsequently isolating and analyzing the chiral 2-butanol. A total of nine oxidations, each using 18 ml of 3 N sodium hydroxide and 18 ml of 30% hydrogen peroxide, were performed--six on the large flask and three on the small one.

The chiral 2-butanol from each oxidation reaction was isolated and purified according to the procedure that follows. After pouring the oxidation mixture into a separatory funnel, the oxidation flask was twice rinsed with 100 ml of ethyl ether, which was added to the funnel. This mixture was then extracted with 3 x 100 ml of saturated, aqueous sodium chloride and dried over magnesium sulfate for one day. After decanting the solution from the magnesium sulfate into a 500-ml flask, most of the ether was removed using a rotary evaporator until approximately

100 ml of solution remained. The 2-butanol was concentrated using a Nester-Faust spinning band distillation column. High purity (99+%) 2-butanol was then obtained by preparative glpc (p 27). The purity of each sample of 2-butanol was confirmed by NMR (p 26) and analytical glpc (p 27), using Columns A and D. Optical rotations were measured as described (p 28).

The results of the nine experiments have been summarized in Table I (p 33).

3. Attempted Redistribution of Di-3-Pinanyl-2-Butylborane

A flask similar to that described in the previous experiment was readied. Next, 500 ml of hexane (Eastman), distilled from calcium hydride (Alfa Products), and 143 g (1.05 mol) of α-pinene were added to the flask. The flask was placed in an ice bath and stirring was initiated. The dropping funnel was charged with 48 ml (0.50 mol) of borane methyl sulfide complex (Aldrich Boranes), which was then added to the reaction mixture over a 45-min period. After the addition was complete, the flask was removed from the ice bath and allowed to stir for 24 hr. After this time, 46 ml (0.5 mol) of (Z)-2-butene was introduced, as described in the previous experiment, over a 1-hr period. The contents of the flask were stirred for an additional hour.

While maintaining a nitrogen flow into the flask, the mercury bubbler was replaced with a glass stopper, and the

TABLE I

ATTEMPTED STABILIZATION OF DI-3-PINANYL-2-BUTYLBORANE

Aliquot No.[a,b]	Time[c] (hr)	Temp.[d] (°)	$[\alpha]_D$[e]	Optical Purity(%)[f]
1	0	22	+12.1°	87
2	48	22	12.1°	87
3	48	22	11.7°	84
4	96	22	12.1°	87
5	114	23	12.1°	87
6	150	23	11.9°	86
7	216	23	12.1°	87
8	246	23	12.1°	87
9	306	23	12.1°	87

a. The synthesis and oxidation of the organoborane and the isolation and purification of the 2-butanol from each aliquot were carried out as described in Section D-2 (p29).

b. Aliquots 1,2,4,6,7, and 9 were taken from the large flask of organoborane described in Section D-2 (p 29). Aliquots 3,5, and 8 were taken from the small flask of organoborane.

c. The time of oxidation of each aliquot relative to the time of synthesis of the organoborane.

d. Optical rotation temperature.

e. Measured as described in Section D-1 (p 28).

f. Based on a maximum specific rotation of +13.87° for 2-butanol.[53]

dropping funnel was replaced with a distilling head and condenser, connected to a 1-l, receiving flask. After placing the receiving flask into a Dry Ice-acetone bath and the reaction flask into a lukewarm water bath, the hexane, methyl sulfide, and residual butene were removed from the reaction mixture using a vacuum pump until nothing was being collected at 20 mmHg. At this point, nitrogen was introduced and the system was allowed to return to atmospheric pressure. While maintaining a nitrogen atmosphere, the distillation equipment was removed and replaced with a mercury bubbler. The viscous clear liquid which remained in the flask was allowed to stir at room temperature for 20 days.

During the 20-day redistribution period, racemic tri-2-butylborane was prepared by the method of Brown.[54] To test the air sensitivity of this compound, approximately 5 ml of the liquid was placed in a small beaker in a hood. Contrary to earlier reports,[54] the borane did burn in air after being exposed for approximately 1 min. An NMR spectrum of the organoborane was recorded in carbon tetrachloride. The spectrum consisted of a set of broad overlapping peaks from 0.6 to 1.7 δ, with the most prevalent band--probably due to the two signals from the two methyl groups--centered at 0.9 δ. Approximately 0.9g (5 mmol) of this compound was mixed with 0.45 g (5.3 mmol) of piperidine (Fisher) in 5 ml of ethyl ether. A white solid

precipitated from solution. The ethyl ether was removed with a water aspirator and the solid was exposed to the air. The compound immediately began to smoke. An NMR spectrum in D_2O (Bio-Rad Laboratories) showed the presence of the 2-butoxy group (similar to that of 2-butanol). This research was stopped in order to return to the redistribution problem.

After the 20-day redistribution period, the mercury bubbler was removed from the flask containing the hydroboration mixture and, again, replaced with the distillation equipment. Vacuum distillation at 0.1 mmHg and 25-35° was carried out for 4 days, 8 hr per day. Each day's distillate was checked by NMR and by burning a small amount. No boron compounds were evident by either test. The distillate (approximately 20 ml total) was composed almost completely of α-pinene. Distillation was stopped after the fourth day, at which time the pot residue partially solidified (white). An NMR spectrum in deuteriochloloform (Mallinckrodt) showed a complex set of overlapping multiplets from 0.6 to 2.6 δ. No attempt was made to characterize the spectrum. A small amount of the crystals were oxidized with alkaline hydrogen peroxide. Glpc analysis indicated the presence of 2-butanol. After two weeks at room temperature, the semi-solid crystals had liquified. This area of research was subsequently abandoned.

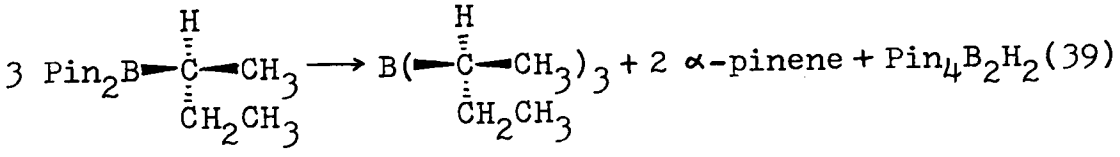
E. Discussion Of Results And Conclusions

1. Stability of Di-3-Pinanyl-2-Butylborane

The optical integrity of the 2-butyl group in di-3-pinanyl-2-butylborane can be maintained for an extended period of time simply by storing the reagent at 0°. The results, summarized in Table I (p 33), **indicate that di-3-pinanyl-2-butylborane has not racemized after 306 hours, as shown by the alkaline hydrogen peroxide oxidation of this organoborane.** This can be contrasted to a reported 16% decrease when the reagent is stored at room temperature.[9] Thus, the conclusion can be made that di-3-pinanyl-2-butylborane can be prepared and stored at 0° for several weeks without significantly effecting its chirality.

2. Attempted Redistribution of Di-3-Pinanyl-2-Butylborane

Based on Köster's reported redistribution reaction,[13] an attempt was made to prepare chiral tri-2-butylborane from chiral di-3-pinanyl-2-butylborane, Equation 39.



$$3\ Pin_2B{-}\overset{H}{\overset{|}{C}}{-}CH_3 \longrightarrow B\left({-}\overset{H}{\overset{|}{C}}{-}CH_3\right)_3 + 2\ \alpha\text{-pinene} + Pin_4B_2H_2 \quad (39)$$

$$\qquad\qquad\quad CH_2CH_3 \qquad\qquad\qquad\qquad\quad CH_2CH_3$$

The procedure involved an attempt to shift the equilibrium towards the product by distilling away the tri-2-butylborane (bp 63-64° at 3 mmHg) and α-pinene (bp 37.3° at 10 mmHg) as they formed.

As was described in Section D-3 (p 32), the reaction

failed. The conclusion would appear to be that this procedure, as described, cannot be used to prepare chiral tri-2-butylborane.

The one point of interest which came out of this research was the attempt to form a stable amine-organoborane complex. Although this reaction also failed, *per se*, the formation of a solid complex was realized. However, the solid was not stable in air. The conclusion would seem to be that solid complexes can, indeed, be formed and possibly even used for the purification of organoboranes. A procedure using an inert atmosphere (i.e., a glove box or some other suitable equipment) would simply have to be adapted for handling the compounds. Further research into this area might be of interest.

CHAPTER III

ORGANOBORANES: REACTIONS AND MECHANISMS

A. Introduction

Since the discovery of the hydroboration reaction,[8] organoboranes have been developed into one of the most versatile groups of compounds available to the organic chemist.[1-7] The hydroboration reaction introduced a simple, convenient procedure which permitted the regioselective and stereospecific conversion of carbon-carbon unsaturated molecules into the corresponding organoboranes. The significance of this straightforward preparative technique was accentuated by the fact that the organoboranes could be transformed into a variety of useful products (e.g.: alcohols, aldehydes, alkanes, alkenes, alkynes, alkyl halides, amines, dienes, diynes, esters, ketones, nitriles, peroxides, and thioethers). Besides this variety in classes of compounds which are available, there are numerous structural features which can also be incorporated into these products (e.g.: stereospecific bond formations, chirality, and polyfunctionality, to mention a few). Thus, with such a broad basis for their synthesis and utilization, organoboranes have vast potentials which can be, and have been, utilized in the realm of synthetic organic chemistry.

B. Organoborane Transformations

As described in Chapter II, organoboranes are readily formed by the regioselective and stereospecific hydroboration reaction. Numerous structural variations are also possible in the alkenes which are used for preparing these compounds. Thus, an extremely large number of organoboranes are available. These compounds have found wide-spread utility as reaction intermediates in organic syntheses. A description of all organoborane transformations is far beyond the scope of this text. However, several reactions are summarized in Table II (p 40) which demonstrate the flexibility of these compounds. For details of these and other reactions of organoboranes (especially those involving vinylboranes) several texts may be consulted.[1-7] The discussion, herein, will focus on the mechanistic aspects of the reactions of organoboranes.

C. Organoborane Reaction Mechanisms

1. Intramolecular Anionotropic Rearrangements

a. General considerations. The most common mechanism by which organoboranes react is that of the intramolecular anionotropic rearrangement,[14] hereafter referred to as IAR. The IAR mechanism is also called the ate-complex mechanism, being derived from the nomenclature of four-coordinate boron compounds.

TABLE II

SELECTED REACTIONS OF TRIETHYLBORANE

No.	Reagent[a]	Product[b]
1	H_2O_2 + aq NaOH	3 CH_3CH_2OH (34,55,56)
2	$(CH_3)_3NO$	$(CH_3CH_2O)_3B$ (17,19)
3	C_5H_5NO	$CH_3CH_2OB(CH_2CH_3)_2$ (19)
4	H_2NOSO_3H	2 $CH_3CH_2NH_2$ (57,58)
5	$CH_3CH_2CO_2H$	3 CH_3CH_3 (59,60)
6	$CH_3CH_2CO_2D$	3 CH_3CH_2D (59,60)
7	$CO + (CH_2OH)_2$ (H_2O_2 + NaOH)	$(CH_3CH_2)_3COH$ (61)
8	$CO + H_2O$ (H_2O_2 + NaOH)	$(CH_3CH_2)_2CO$ (61)
9	$CO + NaBH_4$ (aq KOH)	$CH_3CH_2CH_2OH$ (61)
10	$BrCH_2X$ + base (X=-COR,-CO_2R,-CHO)	$CH_3CH_2CH_2X$ (62-64)
11	N_2CHX (H_2O) (X=-COR,-CO_2R,-CN,-CHO)	$CH_3CH_2CH_2X$ (65-67)
12	$(CH_3)_3SI$ + base (H_2O_2 + NaOH)	$CH_3CH_2CH_2OH$ (68)
13	$(CH_3)_2SCHCO_2R$ + base (H_2O_2 + NaOH)	$CH_3CH_2CH_2CO_2R$ (69)
14	O_2 (H_2O)	3 CH_3CH_2OH (70,71)
15	O_2 (H_2O_2)	2 $CH_3CH_2O_2H$ (71,72)
16	Br_2	CH_3CH_2Br (73,74)
17	R_2NCl	CH_3CH_2Cl (75)

TABLE II (continued)

No.	Reagent[a]	Product[b]
18	$AgNO_3$ + aq NaOH	$CH_3CH_2CH_2CH_3$ (76)
19	CH_3SSCH_3 + light	$CH_3CH_2SCH_3$ (77)
20	$CH_2{=}{=}CHX$ + radical initiator (H_2O) (X=—COR,—CHO)	$CH_3CH_2CH_2CH_2X$ (78-80)
21	Br_2 + H_2O (H_2O_2 + NaOH)	$CH_3CH_2CH(OH)CH_3$ (81)
22	Br_2 + $NaOCH_3$	3 CH_3CH_2Br (16,82)
23	I_2 + NaOH	2 CH_3CH_2I (15)

a. Reagents in parentheses are used in subsequent steps.

b. Numbers in parentheses are references to these reactions.

The most important aspect of IAR mechanisms is that the products are formed stereospecifically[14] with retention of configuration in the alkyl group, or groups, of the organoborane.[1-7] Several reactions--not involving organoboranes--which are also thought to proceed by similar mechanisms are known to occur with retention of configura- in the products. Examples of these reactions include the Hofmann,[83] Curtius,[84] Beckmann,[85] Lossen,[85] Schmidt,[85] Stevens,[86] and Baeyer-Villiger[87] rearrangements. In fact, the mechanism of the Baeyer-Villiger reaction is very closely related to the proposed mechanisms of a number of organoborane reactions.

The proof that hydroboration occurs by a stereospecific cis addition relies entirely on the stereochemical pathway of product formation of organoborane reactions which are believed to occur by IAR mechanisms. Therefore, a description of the most widely studied of these reactions, the alkaline hydrogen peroxide oxidation, is in order.

b. Alkaline hydrogen peroxide oxidations. Organoboranes have been shown to readily react with alkaline hydrogen peroxide,[23,88,89] converting all of the alkyl groups to the corresponding alcohols, Equation 40. The

$$R_3B + 3\ H_2O_2 + NaOH \longrightarrow 3\ ROH + NaB(OH)_4 \qquad (40)$$

groups attached to boron can also be aromatic or vinyl derivatives; however the products from oxidation in these cases would be phenols, aldehydes, or ketones. The

mechanism has been studied in detail, and the following facts are known:

1. Oxidation of boronic acids, $RB(OH)_2$, is second order overall and first order each in boronic acid and hydrogen peroxide.[55,56,90]
2. Oxidation of benzene-[^{18}O]-boronic acid with isotopically normal hydrogen peroxide in [^{18}O] water produces isotopically normal phenol.[91]
3. Oxidation of benzeneboronic acid with chiral 1-phenylethylhydroperoxide produces, besides the phenol, chiral 1-phenylethanol with complete retention of stereochemistry.[91]
4. <u>exo</u>- and <u>endo</u>-5-norbornene-2-boronic acids are oxidized to give the <u>exo</u>- and <u>endo</u>-alcohols, respectively.[92]
5. Oxidation of chiral 1-phenylethylboronic acid produces chiral 1-phenylethanol.[93]

From these facts the following mechanism has been proposed, Equations 41-44:

$$H_2O_2 + {}^{-}OH \rightleftarrows HOO^{-} + H_2O \qquad (41)$$

$$R_3B + HOO^{-} \longrightarrow [R_3BOOH]^{-} \qquad (42)$$

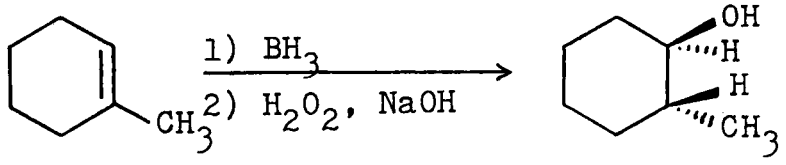
$$\left[R_2\overset{\overset{R}{|}}{B}-O-OH\right]^{-} \longrightarrow R_2BOR + {}^{-}OH \qquad (43)$$

$$R_2BOR + H_2O \longrightarrow R_2BOH + ROH \qquad (44)$$

The second and third alkyl groups are oxidized in a similar manner, thus converting all of the alkyl groups

into alcohols, Equation 40 (p 42).

Since the alkaline hydrogen peroxide oxidation of organoboranes apparently occurs with retention of configuration, and the hydroboration-oxidation sequence is known to proceed by an overall cis hydration of alkenes,[39] then it follows that the hydroboration reaction must also be a stereospecific process. Thus, the hydroboration-oxidation reaction sequence constitutes a simple, convenient procedure for the conversion of alkenes into the corresponding anti-Markovnikoff alcohols. This is illustrated in Equations 45 and 46.



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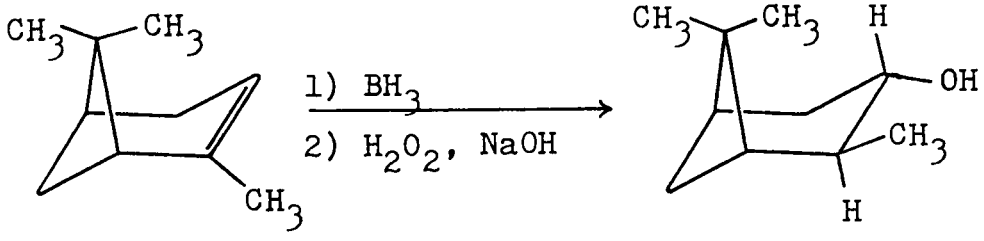


(46)

c. Other intramolecular anionotropic rearrangements. Numerous transformations of organoboranes are known in which the products are formed with retention of configuration. Reactions 1-13 in Table II (p 40) are a partial list of these reactions. With the exceptions of Reactions 5 and 6, these transformations are believed to occur by a 1,2-alkyl migration similar to that proposed for the

alkaline hydrogen peroxide oxidation. The two exceptions are believed to occur by a 1,6-alkyl rearrangement,[60] which also proceeds with retention of configuration in the products.

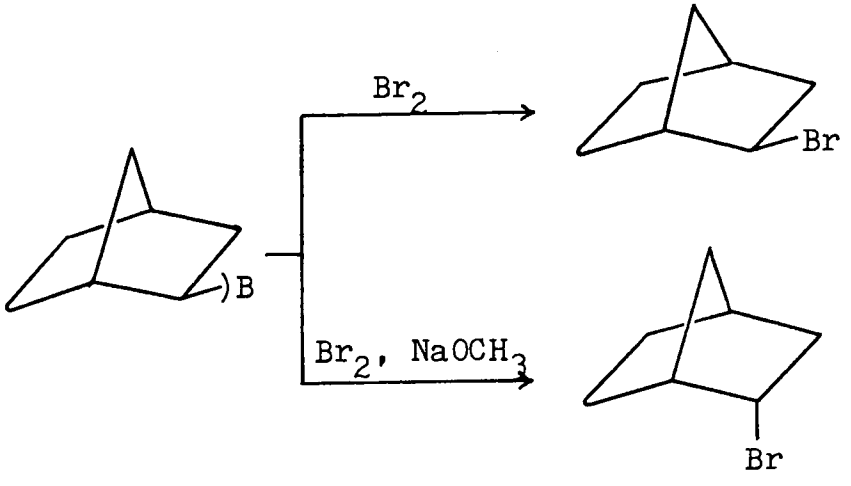
2. Free Radical Chain Reactions

Several organoborane reactions are believed to occur by free radical mechanisms. Reactions 14-21 in Table II (p 40) are a partial list. Two mechanistic variations have been forwarded for these reactions. The first involves alkyl radical formation; whereas the second involves the abstraction of a hydrogen atom on a carbon attached α to the boron. Even though the free radical reactions are both synthetically and mechanistically important, a comprehensive discussion of their chemistries is not appropriate here. Suffice it to say that stereochemistry of product formation, rate studies, and effects of free radical initiators and scavengers have been used to deduce the mechanisms of these reactions.[71,73-75,78-80]

3. Electrophylic Substitutions

Sufficient evidence exists to say that the reaction of bromine with organoboranes occurs by a free radical mechanism.[73,74] However, the base-induced bromination, Reaction 22 in Table II (p 40), is thought to occur by a different mechanism -- electrophylic substitution--because predominant inversion of configuration is observed in the product of this reaction.[16] For example, the reaction of

tri-exo-norbornylborane with bromine produces norbornyl bromide which is at least 99% exo,[74] Equation 47; however, the reaction with bromine and sodium methoxide produces the endo isomer predominately,[16] Equation 48.

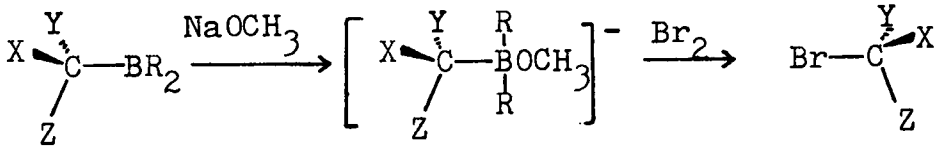


(47)

(48)

Typically, electrophylic substitution reactions occur either with retention or racemization of the products;[94-96] few have been reported which occur via inversion.[97,98] Thus, the base-induced bromination is somewhat of a novelty.

The mechanism of the base-induced bromination has been described as formation of an ate complex between the organoborane and methoxide, followed by the electrophylic substitution (with inversion) by bromine,[16] Equation 49.



(49)

The base-induced iodination of organoboranes, Reaction 23 in Table II (p 40), would appear to be similar mechanistically to the base-induced bromination.[15]

However, all of the alkyl iodides which have been prepared are void of any stereochemical information to justify a mechanism.

D. Restatement Of The Problem

Several of the mechanisms of organoborane reactions have relied almost exclusively of the stereochemistry of product formation involving cyclic or bicyclic systems. Normally the products have been the thermodynamically, most-stable diastereomers. A more rigorous proof for a mechanism is a study involving enantiomeric substrates. Since the reagent di-3-pinanyl-2-butylborane, Structure VI (p 17), has the enantiomeric 2-butyl moiety, then this reagent would appear to be an appropriate substrate to use in the investigation of organoborane mechanisms. The fact that this reagent was successfully used to study the amination reaction,[58] Reaction 4 in Table II (p 40), is a precedent which shows that this reagent can, indeed, be used to study organoborane reaction mechanisms.

The reactions whose mechanisms were of interest included hydroxymethylation with carbon monoxide and sodium borohydride,[61] Reaction 9 in Table II (p 40), alkylation of α-bromo-[62] and α-diazoesters,[66] Reactions 10 and 11, respectively, in Table II (p 40), trimethylamine N-oxide oxidation,[19] Reaction 2 in Table II (p 40), and base-induced iodination,[15] Reaction 23 in Table II (p 40).

No mechanism had been proposed for the base-induced iodination. However, the other reactions were believed to occur by IAR mechanisms.

It was anticipated that the hydroxymethylation reaction and the alkylation of the α-substituted esters might not occur with di-3-pinanyl-2-butylborane. The basis for this conclusion was the fact that these reactions were reported to not occur with sterically hindered organoboranes, e.g., tris(trans-2-methylcyclopentyl-)borane.[100,101] The decision was made to at least attempt the reactions.

The mechanism of the amine N-oxide oxidation had been previously studied.[17] However, the system which was studied was suspect because of contradictory results reported for this and a similar system in a different organoborane reaction (the alkaline protonolysis of benzylic-type organoboranes). Whereas the reaction of aqueous hydroxide with the hydroboration products of the isomeric 2,3-diphenyl-2-butenes gave retention of configuration in the respective alkane products,[18] the D_2O/OD^- reaction of chiral 1-phenylethylboronic acid gave predominant inversion.[17] Because of this anomaly in the alkaline protonolysis of these two similar systems, a study of the amine N-oxide oxidation reaction using di-3-pinanyl-2-butylborane was proposed to retest the previous study.[17]

As noted earlier, there had been no effort to study the mechanism of the base-induced iodination reaction.

Because of the reported results with the apparently-similar, base-induced bromination reaction,[16] a study seemed appropriate.

E. Experimental And Results

1. General Techniques

The general techniques were previously described in Chapter II in Section D-1 (p 26), with two exceptions. All measurements of optical activity were made with the Josef and Jan Fric polarimeter, using the sodium-D-lamp and the 0.0668 dm cell. Also, the preparative glpc was carried out using the Autoprep Model A-700. The column was a 20 ft x 3/8 in, 20% DOW-11 on 45/60 Chromosorb P.

2. Hydroxymethylation Reaction

Tetra-3-pinanyldiborane and di-3-pinanyl-2-butylborane were prepared by the procedures of Brown and co-workers,[9] using three times the original quantities (i.e., 0.3 mol of the organoborane). Once the di-3-pinanyl-2-butylborane was formed, the reaction mixture was subjected to the carbonylation reaction described by Rathke and Brown.[99] As determined by carbon monoxide uptake--almost no uptake--very little reaction occurred. After work-up of this reaction mixture as described,[99] analytical glpc (Columns B and D, p 27) indicated the absence of the expected 2-methyl-1-butanol. The study of this reaction was terminated.

3. Alkylation Reactions

a. Ethyl α-bromoacetate. Tetra-3-pinanyldiborane and di-3-pinanyl-2-butylborane were prepared by the procedure described in the previous experiment. The trialkylborane was subjected to the α-bromoester alkylation reaction described by Brown and co-workers.[62] Analytical glpc (Columns B and D, p 27) indicated the absence of the expected product, ethyl 3-methylpentanoate.

The reaction mixture was poured into approximately 1000 g of ice and extracted with 5 x 100 ml of pentane. The pentane layer was washed with 4 x 100 ml of ice water. The pentane layer was dried with magnesium sulfate, separated, and the pentane was removed using a rotary evaporator. A thick yellow liquid remained. Glpc analyses (Columns B and D, p 27) of this extract again showed the presence of none of the anticipated product.

After standing for one day, the pentane extract formed clear crystals. These crystals were filtered under nitrogen and stored in a nitrogen-flushed flask. An NMR spectrum of these crystals in carbon tetrachloride was identical to the spectrum recorded in the redistribution reaction (p 35). After oxidizing a small portion of these crystals with alkaline hydrogen peroxide, glpc analysis indicated the presence of 2-butanol. It was concluded that di-3-pinanyl-2-butylborane had been isolated. The study of this reaction was terminated.

b. Ethyl α-diazoacetate. Approximately 0.2 g (0.6 mmol) of the crystals from the previous experiment were placed in a nitrogen-flushed, septum-capped Erlenmeyer flask, equipped with a stirring bar. Diglyme (2 ml) was added to dissolve the crystals. Then 1.0 ml (10 mmol) of ethyl diazoacetate (Fisher) was added to the flask. The contents of the flask were allowed to stir at room temperature for 1 day. After adding 0.2 ml (11 mmol) of water, the reaction mixture was allowed to stir for an additional day. Analytical glpc indicated the absence of the expected product, ethyl 3-methylpentanoate. The study of this reaction was terminated.

4. Trimethylamine N-Oxide Dihydrate Oxidation

A 250-ml, side-armed flask, equipped with a septum, stirring bar, and condenser leading to a mercury bubbler (in a hood), was flame dried and flushed with nitrogen. The flask was charged with 28.6 g (0.21 mol) of α-pinene (p 29) and 70 ml of diglyme. The flask was placed in an ice bath and stirring was initiated. Preparation of tetra-3-pinanyldiborane was carried out using a modification of the Zweifel and Brown technique for the external generation of diborane.[23,102] The modification involved directing the diborane into the reaction flask by means of a syringe needle positioned slightly above the well-stirred solution rather than using a gas dispersion tube placed in the solution. Di-3-pinanyl-2-butylborane was prepared from

this reaction mixture by the procedure of Brown and co-workers.[9]

While maintaining a nitrogen atmosphere in the flask, the condenser was removed; 34 g (0.3 mol) of trimethylamine N-oxide dihydrate (Eastman) was quickly added; and the condenser was replaced. With stirring initiated, the flask was slowly placed into an oil bath which had been pre-heated to 140°. The contents of the flask were allowed to stir for 2 hr.

Following the 2-hr oxidation period, the reaction mixture was removed from the oil bath, allowed to cool, and transferred to a separatory funnel. The reaction flask was rinsed with 100 ml of saturated aqueous sodium chloride and 200 ml of methylene chloride (Fisher), both of which were added to the separatory funnel. The layers were mixed and separated. The methylene chloride layer was extracted with 4 x 100 ml of saturated aqueous sodium chloride and dried with magnesium sulfate. The 2-butanol was concentrated by fractional distillation and purified by preparative glpc (p 49) to 99+% purity as indicated by analytical glpc and NMR analyses (p 32). The optical rotation (p 49) was determined to be +11.87°, indicating an 86% optical purity.[53] The following measurements were recorded for the optical rotation of the 2-butanol:

Optical zero: (+) 0.10, 0.12, 0.12, 0.10, 0.10, 0.10, 0.10, 0.10, 0.10, 0.10; Avg. +0.10°

2-Butanol: (+) 0.75, 0.73, 0.73, 0.73, 0.73, 0.75, 0.75, 0.73, 0.74, 0.75; Avg. +0.74°.

Length of tube: 0.0668 dm; Density: 0.807 g/ml; $[\alpha]_D$ max: 13.87°; Temperature: 23°.

5. Base-Induced Iodination

Di-3-pinanyl-2-butylborane was prepared using twice the quantities described in the procedure by Brown and coworkers[9] (i.e., 0.2 mol of organoborane). This solution was divided into two equal portions and placed into separate, three-necked flasks. All manipulations were carried out under an atmosphere of nitrogen.

The first flask was equipped with two pressure equalizing funnels, a thermometer, and a stirring bar. A solution of 50.8 g (0.2 mol) of iodine (Allied Chemical and Dye Co.) in 100 ml of diglyme was placed into one of the dropping funnels. A solution of sodium methoxide (0.2 mol) in methanol[103]--prepared by reacting 4.6 g (0.2 mol) of sodium (J. T. Baker) with 100 ml of methanol (Fisher) distilled from magnesium[104] (Mallinckrodt)--was placed into the second dropping funnel. The flask was covered with aluminum foil and immersed in an ice bath. The two solutions were simultaneously added to the reaction flask over a 1-hr period. This mixture was allowed to stir for an additional hour.

The contents of the reaction flask were poured into a separatory funnel containing approximately 300 ml of ice

water and 50 ml of pentane. A small portion (0.1-0.3 g) of sodium thiosulfate (Matheson) was added to the separatory funnel and the contents were agitated. This process was repeated several times until the brown color of the iodine was dissipated. A slight yellow color remained in the pentane layer. The aqueous layer was then extracted with a total of 5 x 50 ml of pentane. The combined pentane layers were extracted with 50 ml of 2% aqueous sodium thiosulfate, 5 x 50 ml of ice water, and 50 ml of saturated aqueous sodium chloride. The pentane layer was dried with magnesium sulfate in an aluminum foil-covered flask. After separating the pentane layer from the magnesium sulfate, fractional distillation yielded approximately 10 ml of a mixture which was shown by analytical glpc--Column B (p 27)--to consist of 2-iodobutane (major), ∝-pinene (minor), and pentane (minor).

This mixture was cooled in ice, poured into a separatory funnel along with 7 ml of chilled sulfuric acid, mixed and separated. The product was then washed with 5 x 10 ml of cold water, 10 ml of cold 5% sodium bicarbonate, and 10 ml of cold water. After drying over magnesium sulfate, the product was then placed into a 10-ml flask along with 2 ml of tetradecane (Aldrich) and distilled at reduced pressure (47-49° at 60 mmHg). Purity (at least 99%) was determined by analytical glpc--Column B (p 27)--and NMR. The specific rotation of the 2-iodobutane was found to be

-26.9°, which corresponds to an 84% optical purity.[53] The following data were used for this determination:

Optical zero: (+) 0.06, 0.03, 0.04, 0.04, 0.05, 0.06, 0.04, 0.05, 0.05, 0,05; Avg. $+0.05^{\circ}$

2-Iodobutane: (-) 2.80, 2.81, 2.80, 2.81, 2.81, 2.81, 2.81, 2.80, 2.81, 2.80; Avg. -2.81°

Length of tube: 0.0668 dm; Density: 1.59 g/ml; $[\alpha]_D$ max: -31.98°; Temperature: 25°.

The second portion of di-3-pinanyl-2-butylborane(p53) was oxidized using the procedure of Brown and co-workers.[9] The reaction mixture was transferred to a separatory funnel along with 200 ml of ether, extracted with 3 x 200 ml of saturated aqueous sodium chloride, and dried over magnesium sulfate. The 2-butanol was concentrated by fractional distillation and purified by preparative glpc (p 52). Analytical glpc and NMR analyses (p 52) indicated that the product was at least 99% pure. The specific rotation was calculated to be $+11.9^{\circ}$, which corresponds to an 86% optical purity. The following data were used to calculate the specific rotation:

Optical zero: (+) 0.06, 0.03, 0.04, 0.04, 0.05, 0.06, 0.04, 0.05, 0.05, 0.05; Avg. $+0.05^{\circ}$

2-Butanol: (+) 0.69, 0.68, 0.68, 0.68, 0.67, 0.70, 0.70, 0.69, 0.70, 0.69; Avg. $+0.69^{\circ}$

Length of tube: 0.0668 dm; Density: 0.807 g/ml; $[\alpha]_D$ max: 13.87°; Temperature: 25°.

F. Discussion Of Results And Conclusions

Studies of the mechanisms of the hydroxymethylation reaction,[61] Equation 50, and the alkylation of α-substituted esters,[62,66] Equations 51 and 52, were attempted and failed. The conclusion would appear to be that the

$$R_3B \xrightarrow[2)\ aq\ NaOH]{1)\ CO + NaBH_4} RCH_2OH \qquad (50)$$

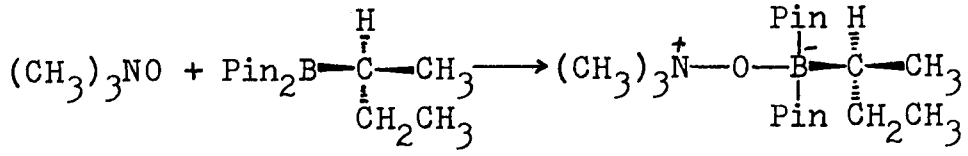
$$R_3B \xrightarrow[K^+\bar{O}C(CH_3)_3]{BrCH_2CO_2CH_2CH_3} RCH_2CO_2CH_2CH_3 \qquad (51)$$

$$R_3B \xrightarrow[2)\ H_2O]{1)\ N_2CHCO_2CH_2CH_3} RCH_2CO_2CH_2CH_3 \qquad (52)$$

transition states of these reactions are too sterically crowded in the case of di-3-pinanyl-2-butylborane. A similar problem had been reported with these same reactions in attempting to use tris(trans-2-methylcyclopentyl-)borane.[100,101] Consequently, the failure of these reactions was not altogether unexpected.

The oxidation of di-3-pinanyl-2-butylborane with trimethylamine N-oxide dihydrate was attempted and was quite successful. (S)-(+)-2-Butanol was isolated and shown to have a specific rotation of +11.9°, corresponding to an optical purity of 86%. This can be compared to optical purities of 86 and 87% which were obtained using the alkaline hydrogen peroxide oxidation procedure (cf., p 33 and 55). Thus, the conclusion can be made that the amine N-oxide oxidation of organoboranes does, indeed,

occur by an intramolecular anionotropic rearrangement mechanism as previously suggested.[17] The mechanism is demonstrated in Equations 53 and 54.



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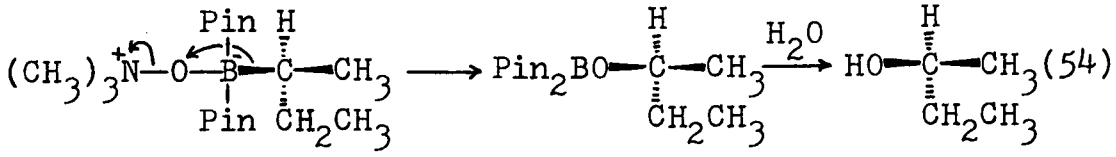
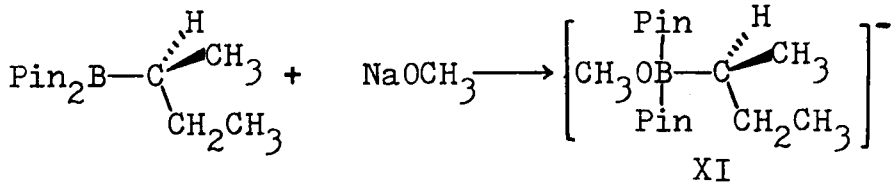


(54)

The base-induced iodination of di-3-pinanyl-2-butylborane produces optically active 2-iodobutane of high chirality with a configuration opposite to that of the 2-butanol produced in the oxidation of the borane by alkaline hydrogen peroxide. A solution of di-3-pinanyl-2-butylborane in diglyme was prepared and divided into two equal portions. One portion was reacted with iodine and sodium methoxide to give 2-iodobutane. The second portion was converted to 2-butanol using the standard alkaline hydrogen peroxide procedure. The 2-butanol had the S-configuration with a specific rotation of $+11.9^{\circ}$, which corresponds to an 86% optical purity. The 2-iodobutane, however, had the R-configuration with a specific rotation of -26.9°, which corresponds to an 84% optical purity.[105]

These exciting results indicate that the base-induced iodination reaction, in contrast to the majority of reactions of organoboranes, involves substitution of the

boron-carbon bond with clean inversion. The mechanism is proposed to be coordination of the base with the organoborane, followed by electrophylic substitution, with inversion, of iodine with the four-coordinate boron species. This has been demonstrated in Equations 55 and 56.



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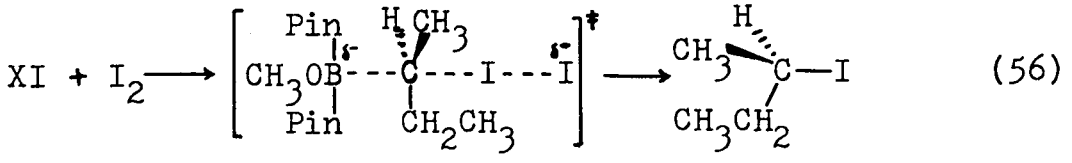


(56)

In conclusion, di-3-pinanyl-2-butylborane appears to be a good choice for studying the mechanisms of organoborane reactions. The major drawback is that this organoborane will not undergo those reactions involving sterically-demanding transition states. Besides being a good choice for mechanistic studies, di-3-pinanyl-2-butylborane is also an excellent choice for the preparation of optically active compounds.

CHAPTER IV

AMINE N-OXIDE OXIDATIONS OF ORGANOBORANES

A. Background

A variety of alkyl- and arylboranes have been shown to be efficiently oxidized by amine N-oxides; however, vinyl and acetylenic boranes do not react.[19-22] Three compounds have been used as oxidants: trimethylamine N-oxide, pyridine N-oxide, and 4-methylpyridine N-oxide. The first, trimethylamine N-oxide, is of the most importance and will be discussed in detail. The latter two are of lesser importance and will be alluded to when necessary.

Trimethylamine N-oxide oxidizes organoboranes to the corresponding borate esters,[19] Equation 57. The reaction

$$R_3B + 3\ (CH_3)_3NO \longrightarrow (RO)_3B + 3\ (CH_3)_3N \qquad (57)$$

was initially developed into an analytical procedure for the quantitative determination of boron-carbon bonds in organoboranes.[19] Besides being used as an analytical tool, this reaction exhibited features which made it equal or superior to other organoborane oxidation techniques.

First, organoboranes are oxidized stereospecifically by trimethylamine N-oxide to give products with the same configurations as those obtained by alkaline hydrogen peroxide oxidations. For example, oxidation of chiral 1-phenylethylboronic acid was shown to proceed with nearly complete retention of configuration in the product

1-phenylethanol.[17] An IAR mechanism similar to that proposed for the alkaline hydrogen peroxide oxidation has been suggested. The proof of this mechanism was discussed in Chapter III. [Equations 53 and 54 (p 57) describe the stereochemistry of the oxidation technique.]

Second, oxidations using amine N-oxides can be controlled by reaction temperature, by stoichiometry of the oxidant, and by the nature of the amine N-oxide, itself, such that the extent of oxidation can be controlled.[19] For example, the oxidation of tri-1-propylborane with one, two, and three equivalents of trimethylamine N-oxide produces the mono-, di-, and tripropoxyboranes, Equations 58, 59, and 60, respectively.

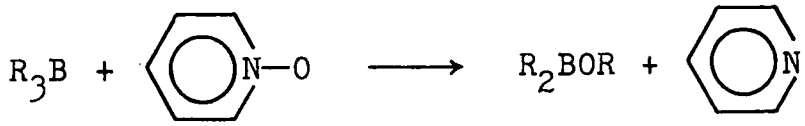
$$Pr_3B + (CH_3)_3NO \longrightarrow Pr_2BOPr \quad (58)$$

$$Pr_2BOPr + (CH_3)_3NO \longrightarrow PrB(OPr)_2 \quad (59)$$

$$PrB(OPr)_2 + (CH_3)_3NO \longrightarrow B(OPr)_3 \quad (60)$$

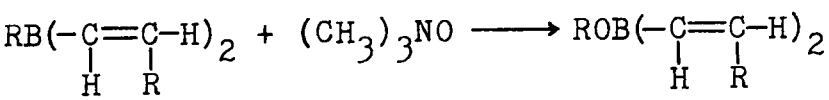
Although no related comparative studies have been attempted with less than the stoichiometric quantity of hydrogen peroxide, evidence suggests that the alkaline hydrogen peroxide oxidation occurs too rapidly to be used for the partial oxidation of organoboranes.[23,88,89,106] By using the more stable aromatic amine N-oxides, such as pyridine N-oxide or 4-methylpyridine N-oxide, one group on the organoborane can be cleanly oxidized to give the corresponding borinate ester, even in the presence of excess

oxidant,[19] Equation 61.



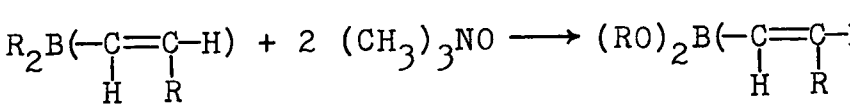
$$R_3B + \text{(pyridine N-oxide)} \longrightarrow R_2BOR + \text{(pyridine)} \qquad (61)$$

The partial oxidation of organoboranes has been put to effective use in the selective oxidation of the alkyl groups in mixed alkylvinylboranes. For example, if thexyldivinylboranes are oxidized with one equivalent of trimethylamine N-oxide, only the thexyl group is oxidized,[21] Equation 62. The resultant divinylborinate esters are



$$RB(-\underset{H}{\overset{|}{C}}=\underset{R}{\overset{|}{C}}-H)_2 + (CH_3)_3NO \longrightarrow ROB(-\underset{H}{\overset{|}{C}}=\underset{R}{\overset{|}{C}}-H)_2 \qquad (62)$$

useful intermediates for the synthesis of conjugated cis,trans-dienes.[21] A second example is the oxidation of dialkylvinylboranes with two equivalents of trimethylamine N-oxide, giving as products the vinylboronate esters,[22] Equation 63.

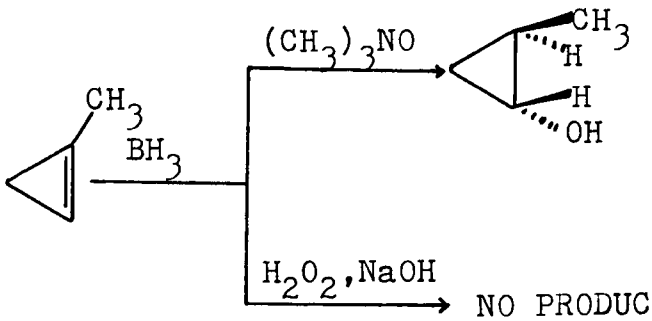


$$R_2B(-\underset{H}{\overset{|}{C}}=\underset{R}{\overset{|}{C}}-H) + 2\ (CH_3)_3NO \longrightarrow (RO)_2B(-\underset{H}{\overset{|}{C}}=\underset{R}{\overset{|}{C}}-H) \qquad (63)$$

The examples given in Equations 62 and 63 would suggest that the possibility exists for preferentially oxidizing a particular group (or groups) in mixed trialkylboranes, $R^1R^2R^3B$. However, research in this area has led to only limited success.[107] Typically, one of the alkyl groups in mixed trialkylboranes preferentially reacts, but all groups are oxidized to some extent. However, a relative rate of oxidation for several types of

alkyl substituents has been ascertained. The relative rate of oxidation, in decreasing order of reactivity, for the alkyl groups is as follows: tertiary > cyclohexyl > secondary > normal primary > 2-substituted primary >> vinyl. (This order of oxidation is the exact opposite, with the exception of the 2-substituted primary case, to the relative rates of hydroboration of the appropriate alkene as described in experiments by Köster and co-workers;[13] i.e., the faster an alkene hydroborates, the slower it oxidizes.) The oxidations in this study were limited in scope. Also, no attempt was made to maximize the efficiency of the oxidations. Consequently, the question of whether this technique can be used for mixed trialkylboranes remains unresolved.

Trimethylamine N-oxide is apparently a milder oxidant than alkaline hydrogen peroxide. For example,[20] the hydroboration-oxidation of 1-methylcyclopropene readily occurs using trimethylamine N-oxide as the oxidant, but fails using alkaline hydrogen peroxide, Equations 64 and 65.



(64)

(65)

This is apparently due to the fact that cyclopropanols are unstable in both base[108] and peroxides.[109]

Numerous functionalities--for example, halides, enol ethers, esters, sulfides and nitriles--which can be incorporated into organoboranes[24] are susceptible to reaction with either sodium hydroxide or hydrogen peroxide. Oxidations have been achieved with some of these functionally substituted organoboranes, but special techniques and reagents had to be employed.[110-113] Trimethylamine N-oxide would appear to be a much milder oxidant and, as such, should be especially valuable for the oxidation of functionally substituted organoboranes.

B. Restatement Of The Problem

Anhydrous trimethylamine N-oxide was known to oxidize most organoboranes to the corresponding boric acid esters. Based on the fact that such esters are readily hydrolyzed by water to give the corresponding alcohols, the commercially-available trimethylamine N-oxide dihydrate would seem to be an excellent choice for oxidizing organoboranes to the corresponding alcohols.

First, the hydrated amine N-oxide could be used as is without the necessity of subliming the material in order to obtain the anhydrous amine N-oxide. Second, trimethylamine N-oxide dihydrate is more convenient and far safer to handle than the 3N sodium hydroxide and 30% hydrogen peroxide which are typically used to oxidize organoboranes.[23]

The amine N-oxide could also be a superior oxidant of organoboranes which are susceptible to the standard oxidation conditions.

Since all amine N-oxide oxidations reported the use of the anhydrous oxidant and since nearly all oxidations were performed in atypical hydroboration solvents, then it seemed appropriate to carry out an extensive study of the reaction conditions and develop a simple procedure (or procedures) for organoborane oxidations using trimethylamine N-oxide dihydrate.

C. Experimental

1. General Techniques

The general techniques were described in Chapter II (p 26). All hydroborations and oxidations were carried out in flame-dried, nitrogen-flushed flasks which were equipped with a stirring bar, a septum inlet, and a condenser. The condenser was attached to a mercury bubbler which was vented into an aqueous solution of hydrochloric acid (in a hood). The alkenes which were hydroborated and the internal standards for glpc analyses were weighed and transferred with dry, nitrogen-flushed syringes.

The alcohols produced by the oxidation reactions were analyzed by one of two methods. The first was the direct analysis of the reaction mixture by injecting 1-10 μl aliquots onto an appropriate glpc column. The second

involved the silation of the product alcohols prior to their analyses.[114,115] This was carried out by placing 0.10-0.15 ml of the reaction mixture into a nitrogen-flushed vial, equipped with a septum cap. Next, 0.4 ml of the reaction solvent was added, followed by 0.3 ml of hexamethyldisilizane, $[(CH_3)_3Si]_2NH$, and 0.15 ml of trimethylchlorosilane, $(CH_3)_3SiCl$, (Pierce Chemical Co.). The mixture was heated on a steam bath for 5-10 min. Yield calculations were made using the internal standard method described by Brown.[116]

2. Hydroborations

a. Method A. A flask was charged with 15 ml of tetrahydrofuran (THF), 30 mmol of alkene, and a weighed quantity of internal standard. The flask was cooled in an ice bath, and the mixture was stirred. Then 10 mmol of standardized 2 M BH_3.THF, prepared by the method of Brown,[102] was added via syringe over a period of 10 min. When the addition was complete the ice bath was removed and the reaction was allowed to stir for 1 hr. When the alkene was cyclohexene, the reaction was either stirred overnight or heated for 4 hr at 60-70° to insure complete hydroboration.

b. Method B. The procedure described above was used with three exceptions. First, the solvent was not necessarily THF. Experiments employed a total of 20 ml of the following solvents: diglyme, THF, ethyl ether, or mixed

xylenes. Also, the BH_3.THF was replaced by an equivalent quantity (0.95 ml) of borane methyl sulfide, $BH_3.S(CH_3)_2$.[117]

3. Oxidations

a. Alkaline hydrogen peroxide. Oxidations were carried out using the standard technique of Brown and co-workers.[23] The organoborane (10 mmol) was oxidized using 3.4 ml of 3 N aqueous sodium hydroxide and 3.4 ml of 30% hydrogen peroxide. Products were isolated using standard techniques.[23] Purity of the products was determined by glpc and NMR analyses (pp 26,27).

b. Trimethylamine N-oxide dihydrate. The organoborane (10 mmol) was treated with 0.18 ml (10 mmol) of water to destroy residual hydride. As nitrogen was passed into the flask, the condenser was removed and a weighed quantity of trimethylamine N-oxide dihydrate was added. After replacing the condenser, the flask was immersed into a pre-heated oil bath, and the contents were stirred. After 2-5 min the nitrogen flow was stopped. Progress of the oxidation was monitored by glpc (p 64).

Products were isolated by extraction and distillation. After cooling the reaction mixture, the contents of the flask were transferred to a separatory funnel. The flask was rinsed with 50 ml of ethyl ether, which was added to the separatory funnel. The ether layer was then extracted with 5 x 50 ml of saturated aqueous sodium chloride, dried over magnesium sulfate, and distilled. Product purity was

determined by glpc and NMR analyses (pp 26,27).

4. Trimethylamine N-Oxide Dihydrate Oxidations with Added Substrates

Cyclohexene (Eastman) was hydroborated in diglyme [Section C-2-b (p 65)] on a ten-fold scale. Ten ml of dodecane (Aldrich) was added as an internal standard. By filling an identical flask to the same level with water and measuring the volume, the quantity of organoborane solution was found to be 250 ml.

Twenty-five ml aliquots (10 mmol of organoborane) were transferred via syringe to a reaction flask (p 64). After adding 10 mmol of water, 10 mmol of the test substrate was introduced. Glpc analysis [Columns C and E (p 27)] was carried out in order to standardize test substrate to internal standard. The oxidation was then carried out by adding 3.33 g (30 mmol) of trimethylamine N-oxide dihydrate to the reaction and heating the mixture to 140° for 2 hr (p 66). The mixture was again subjected to glpc analysis to determine the yields of cyclohexanol and test substrate. (The results of these experiments will be described later.)

5. Hydroboration-Oxidation of Functionally Substituted Alkenes

a. Method A. The alkenes were hydroborated [Section C-2-b (p 65)] in diglyme. Oxidations of the resultant organoboranes [Section C-3-b (p 66)] were carried out at

140° using 3.33 g (30 mmol) of trimethylamine N-oxide dihydrate. (The results of these experiments will be described later.)

b. Method B. The alkenes were hydroborated [Section C-2-a (p65)], and the resultant organoboranes were oxidized [Section C-3-a (p 66)] as described. (The results of these experiments will be described later.)

c. Method C. The alkenes were hydroborated [Section C-2-a (p 65)] in THF. Oxidations of the resultant organoboranes [Section C-3-b (p 66)] were carried out at 70° using 4.00 g (36 mmol) of trimethylamine N-oxide dihydrate. (The results of these experiments will be described later.)

6. Preparation and Identification of New Compounds

a. 5-Benzoxy-1-hexene. Thirty g (0.3 mol) of 5-hexene-2-one (Aldrich) was slowly added to aqueous sodium borohydride (0.1 mol, 1 M). The mixture was stirred for 1.5 hr and the product, 1-hexen-5-ol, was isolated by extraction. The mixture was poured into a separatory funnel. The reaction flask was rinsed with 100 ml of ether, which was added to the separatory funnel. The layers were mixed and separated. The ether layer was extracted with 50 ml of saturated aqueous sodium chloride, dried over magnesium sulfate, and distilled: bp 135° (740 mmHg) [lit. bp 138-139° (752 mmHg)][118]; yield of alcohol 90% (27 g); NMR ($CDCl_3$) δ 1.2 (d, 3, $-CH_3$), 1.5

(m, 2, $-CH_2-$), 2.1 (m, 2, $-CH_2C=C$), 3.0 (s, 1, OH), 3.8 (sextet, 1, methine), 5.1 (m, 2, $H_2C=C$), 5.8 (m, 1, $-CH=C$).

The benzoate ester was prepared by adding benzoyl chloride (Eastman) (42 g, 0.3 mol) to 1-hexen-5-ol dissolved in 50 ml of pyridine (Fisher). This mixture was stirred for 0.5 hr. The product was isolated by pouring the reaction mixture into 100 g of ice and 100 ml of ether in a separatory funnel, separating the two layers, and extracting the product with 3 x 50 ml of water. The product was dried over magnesium sulfate and potassium carbonate and distilled: bp 95° (0.5 mmHg); NMR ($CDCl_3$) δ 1.4 (d, 3, $-CH_3$), 2.0 (m, 4, $-CH_2CH_2-$), 4.9-6.3 (m, 4, methine, $H_2C=C$, and $-CH=C$), 7.6 (m, 3, ArH), 8.3 (m,2,ArH).

b. 5-Benzoxy-1-hexanol. 5-Benzoxy-1-hexene was hydroborated and oxidized as described in Section C-5-a (p 67). The product, 5-benzoxy-1-hexanol, was isolated by distillation: bp 121-125° (0.05-0.1 mmHg); NMR ($CDCl_3$) δ 1.3 (d, 3,$-CH_3$), 1.5 [broad envelope, 6, $-(CH_2)_3-$], 3.3 (s, 1, -OH), 3.7 (t, 2, OCH_2-), 5.2 (m, 1, OCH—), 7.6 (m, 3, ArH), 8.2 (m, 2, ArH).

Elemental analysis calculated for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.05; H, 8.06.

c. 3-p-Tolylthio-2-methylpropene. p-Tolylthiol (Aldrich) (37.2 g, 0.3 mol) was added to a flask containing aqueous sodium hydroxide (12 g, 0.3 mol, in 50 ml of water) and stirred at room temperature for 4 hr. The water was

removed at room temperature under reduced pressure. After mixing the residual salt with 50 ml of methanol, 3-chloro-2-methylpropene (Aldrich) (27.5 g, 0.33 mol) was added, and this mixture was stirred overnight.

The solution was added to 100 ml of water in a separatory funnel, and the product was extracted with 3 x 50 ml of ether. The ether layer was dried over magnesium sulfate and the product was distilled: bp 67° (0.3 mmHg) and 88-90° (1.4 mmHg); yield 43 g (80%); NMR (neat) δ 1.8 (s, 3, $CH_3C=$), 2.2 (s, 3, CH_3Ar), 3.4 (s, 2, $-CH_2S$), 4.8 (broad s, 2, $H_2C=$), 7.2 ($A_2'X_2'$, 4, ArH).

Elemental analysis calculated for $C_{11}H_{14}S$: C, 74.09; H, 7.92; S, 17.99. Found: C, 74.20; H, 8.06; S, 18.40.

d. 3-p-Tolylthio-2-methylpropanol. 3-p-Tolylthio-2-methylpropene (6.12 g, 0.03 mol) was hydroborated and oxidized as described in Section C-5-a (p 67). The product, 3-p-tolylthio-2-methylpropanol, was isolated by distillation: bp 112-113° (0.15 mmHg); NMR ($CDCl_3$) δ 1.0 (d, 3, $-CH_3$), 1.9 (broad m, 1, CH), 2.3 (s, 3, CH_3Ar), 2.9 [m(AB), 2, CH_2S], 3.0 (s, 1, -OH), 3.6 (d, 2, $-CH_2O$), 7.3 ($A_2'X_2'$, 4, ArH).

Elemental analysis calculated for $C_{11}H_{16}OS$: C, 67.28; H, 8.22; S, 16.34. Found: C, 67.20; H, 8.16; S, 16.53.

D. Results

1. Oxidation of Tri-1-Hexylborane with Trimethylamine N-Oxide Dihydrate

1-Hexene (Aldrich) was hydroborated and oxidized with trimethylamine N-oxide dihydrate in various solvents and at a variety of temperatures in order to establish a suitable set of reaction conditions which could be used in later studies. Five experiments using the procedures described in Sections C-2-a (p 65), C-2-b (p 65), and C-3-b (p 66) were carried out; **the results have been summarized in Table III (p 72). All oxidations used** 3.33 g (30 mmol) of trimethylamine N-oxide dihydrate. The yields of 1- and 2-hexanol were determined by glpc analysis (p 64).

2. Trimethylamine N-Oxide Dihydrate Concentration Effects

Three separate oxidations of tri-1-hexylborane [Section C-2-a (p 65)] were carried out in THF at 70° with varying quantities of trimethylamine N-oxide dihydrate. Oxidations [Section C-3-b (p 66)] of 10 mmol of the organoborane were carried out using 30, 36, and 45 mmol of trimethylamine N-oxide dihydrate. The yields of 1- and 2-hexanol were determined by glpc analysis (p 64). The results have been summarized in Table IV (p 73).

3. Comparison of Oxidation Techniques for Simple Organoboranes

Five simple alkenes were hydroborated and oxidized using both the trimethylamine N-oxide dihydrate and the

TABLE III

OXIDATION OF TRI-1-HEXYLBORANE WITH TRIMETHYLAMINE N-OXIDE DIHYDRATE

Expt No.	Solvent[c]	Oxidn Temp(°)[d]	Yield of hexanols[e] (%)[f]								
			0.5hr	1.0hr	1.5hr	2.0hr	2.5hr	4.0hr	6.0hr	24hr	48hr
1[a]	EE	36	-	28	-	30	-	33	36	50	-
2[b]	THF	70	61	63	67	70	71	73	76	81	84
3[a]	Diglyme	70	-	-	62	65	-	67	69	76	80
4[a]	Diglyme	140	83	86	-	90	92	-	95	-	-
5[a]	Xylenes	140	76	-	92	-	-	94	95	-	-

a. The organoborane was prepared as described in Section C-2-b (p 65).

b. The organoborane was prepared as described in Section C-2-a (p 65).

c. EE: ethyl ether; THF: tetrahydrofuran

d. Oxidations [Section C-3-b (p 66)] utilized 3.33 g (30 mmol) of trimethylamine N-oxide dihydrate.

e. Yields consist of a 94:6 ratio of 1- and 2-hexanols, respectively.

f. Yields were determined by glpc analysis (p 64).

TABLE IV

EFFECT OF TRIMETHYLAMINE N-OXIDE DIHYDRATE CONCENTRATION ON THE OXIDATION OF TRI-1-HEXYLBORANE

Expt[a] No.	Oxidant[b] (mmol)	Yield (%)[c,d] 24hr	Yield (%)[c,d] 48hr
1	30	81	84
2	36	88	93
3	45	93	95

a. The organoborane was prepared as described in Section C-2-a (p 65).

b. The oxidation was carried out as described in Section C-3-b (p 66) at 70°.

c. Yields consist of a 94:6 ratio of 1- and 2-hexanols, respectively.

d. Yields were determined by glpc analysis (p 64).

alkaline hydrogen peroxide procedures. For the amine N-oxide reactions, preparations of the organoboranes were described in Section C-2-b (p 65), and oxidations were described in Section C-3-b (p 66). For the alkaline hydrogen peroxide reactions, preparations of the organoboranes were described in Section C-2-a (p 65), and oxidations were described in Section C-3-a (p 66). The yields of alcohols were determined by glpc analysis (p 64). The results have been summarized in Table V (p 75).

4. Selective Oxidations with Added Substrates

Using the experimental procedure outlined in Section C-4 (p 67), tricyclohexylborane (10 mmol) in diglyme was oxidized with trimethylamine N-oxide dihydrate (30 mmol) in the presence of several functionally substituted reagents. Yields of cyclohexanol and recovered reagents were made by glpc analysis (p 67). The results have been summarized in Table VI (p 76).

5. Hydroboration-Oxidation of Functionally Substituted Alkenes

A study was made of the efficiencies of the trimethylamine N-oxide dihydrate oxidations in diglyme and THF and the alkaline hydrogen peroxide oxidations in THF for six functionally substituted organoboranes. The experimental procedures were described in Section C-5 (pp 67,68). Yields were determined by glpc analysis (p 64). The results have been summarized in Table VII (p 77).

TABLE V

COMPARISON OF OXIDATION TECHNIQUES

FOR SIMPLE ORGANOBORANES

Alkene[a]	Oxidn Time(hr)	Product	Yield (%)[e] $(CH_3)_3NO \cdot 2H_2O$[f]	Yield (%)[e] $H_2O_2/NaOH$[g]
1-hexene	3	1-hexanol[b]	95	95
1-octene	2	1-octanol[b]	95	95
(E)-2-butene	1	2-butanol[c]	94	94
cyclohexene	2	cyclohexanol	94	92
norbornene	1	norbornanol[d]	100	100

a. The organoboranes were formed via the hydroborations of the alkenes listed in the table.

b. The product contained 6% of the secondary isomer.

c. The product contained no 1-butanol.

d. The product was the <u>exo</u> isomer.

e. Yields were determined by glpc analysis (p 64).

f. The oxidations were carried out in diglyme at 140° using 3.33 g (30 mmol) of trimethylamine N-oxide dihydrate as described in Section C-3-b (p 66).

g. The oxidations were carried out as described in Section C-3-a (p 66).

TABLE VI

OXIDATION OF TRICYCLOHEXYLBORANE IN THE PRESENCE OF ADDED REAGENTS

Reagent[a]	Cyclohexanol Yield (%)[b,c]	Recovered Reagent (%)[c]
Benzaldehyde	94	100
Butyrophenone	94	100
Ethyl valerate	94	100
Ethyl cinnamate	94	100
Phenylethylene oxide	94	100
Benzonitrile	94	100
Thiophene	94	100
1-Bromohexane	94	100
3-Penten-2-one	94	95

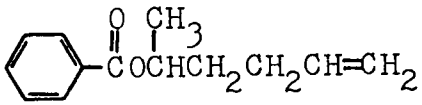
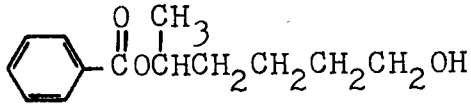
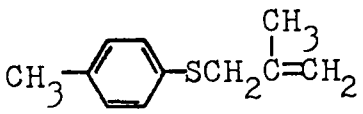
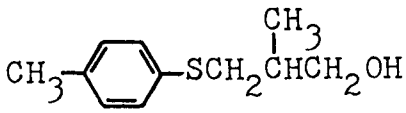
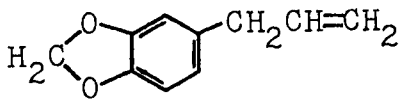
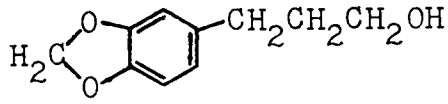
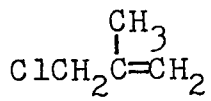
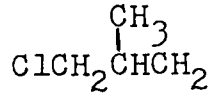
a. Ten mmol of the reagent was added to the oxidation flask prior to the oxidation.

b. The oxidations were carried out by adding 3 equiv of trimethylamine N-oxide dihydrate to 10 mmol of tricyclohexylborane in diglyme and heating the mixture to 140° for two hours (p 67).

c. Yields were determined by glpc analysis (p 67).

TABLE VII

COMPARISON OF OXIDATION TECHNIQUES FOR FUNCTIONALLY SUBSTITUTED ORGANOBORANES

Alkene[a]	Product[b]	Yield (%)[c]		
		Method A[d]	Method B[e]	Method C[f]
		95	91	94
$ClCH_2CH_2CH_2CH{=}CH_2$	$ClCH_2CH_2CH_2CH_2CH_2OH$	95	89	89
		92	83	81
		75	75	73
		67	61	61
$(CH_3)_2CHCH_2OCH{=}CH_2$	$(CH_3)_2CHCH_2OCH_2CH_2OH$	62	61	59

a. The organoborane was formed via hydroboration of the alkene.

TABLE VII (CONTINUED)

b. Only the major product is shown.

c. Yields were determined by glpc analysis (p 64) of the reaction mixtures.

d. The organoborane in diglyme was oxidized with 3.33 g of trimethylamine N-oxide dihydrate. The oxidation was carried out at 140° for 2 hr.

e. The organoborane was oxidized as described in Section C-3-a.

f. The organoborane in THF was oxidized with 4.00 g of trimethylamine N-oxide dihydrate. The oxidation was carried out at 70° for 48 hr.

E. Discussion Of Results And Conclusions

Organoboranes can be efficiently oxidized with trimethylamine N-oxide dihydrate in either hydrocarbon or ethereal solvents. The rate of the oxidation appears to be insensitive to the solvent used. This is apparently a consequence of the low solubility of the amine N-oxide in all of the solvents used in this study.[119,120]

A comparison of Experiments 2 and 3 in Table III (p 72) shows only a slight difference in the rates of formation of 1-hexanol for oxidations carried out at 70° in THF and diglyme. Similarly, oxidations at 140° in diglyme and mixed xylenes, Table III (p 72), show nearly the same rates of formation of 1-hexanol.

The data also indicate that the oxidation is temperature dependent. For example, after two hours one alkyl group (30%) is oxidized at 36°, two groups (65-70%) at 70°, and three groups (90%) at 140°. This would suggest that trimethylamine N-oxide dihydrate oxidations should be a convenient procedure for preparing borinic and boronic acids by the sequential oxidation of the alkyl groups of the organoborane.

The rate of the oxidation reaction can be increased by increasing the concentration of trimethylamine N-oxide dihydrate. This has been demonstrated in Table IV (p 73). Thus, for organoboranes which are thermally unstable, a convenient oxidation rate can be obtained simply by

increasing the amount of the oxidant.

Several representative, simple alkenes were hydroborated and oxidized using both the amine N-oxide and the alkaline hydrogen peroxide procedures. The results, described in Table V (p 75), indicate that oxidation with trimethylamine N-oxide dihydrate produces nearly quantitative yields of alcohols from the corresponding organoboranes. In all cases the yields of alcohols were as good as or better than the yields in the alkaline hydrogen peroxide procedure.

The fact that trimethylamine N-oxide dihydrate is an exceptionally mild oxidant is demonstrated in Tables VI (p 76) and VII (p 77). Oxidation of tricyclohexylborane in the presence of a variety of added functional compounds, Table VI (p 76), shows that this oxidation technique has little or no effect on the added substrates. Furthermore, oxidation of functionally substituted organoboranes, Table VII (p 77), using the amine N-oxide procedure was shown to be as good as or better than oxidation by the standard oxidation technique.[23] Also, the yields of alcohols using the amine N-oxide procedure in THF were comparable to those using the standard oxidation procedure.

The conclusion would seem to be that the trimethylamine N-oxide dihydrate oxidation of organoboranes constitutes a viable alternative to the standard alkaline hydrogen peroxide oxidation. The amine N-oxide procedure

is simple, convenient, and versatile. Trimethylamine N-oxide dihydrate is easier to handle and, by far, safer to use than sodium hydroxide and hydrogen peroxide. Finally, trimethylamine N-oxide dihydrate is an exceedingly mild oxidant. Consequently, this reagent should be of great value for the syntheses of polyfunctional molecules not easily obtainable by other methods.

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