SYNTHESIS OF α-HALOORGANOBORON COMPOUNDS

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ABSTRACT

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By

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Since α-haloorganoboron compounds are useful in organic synthesis and mechanistic studies, convenient methods to prepare these compounds are desirable. It is found that reactions between phenyl(trichloromethyl)mercury and boron trihalides do not produce the expected α-haloorganoboron compounds. Similar reactions of sodium trichloroacetate with boron trihalides are also unsuccessful. However, the reaction of trimethyl borate with dichloromethyllithium gives a salt with the structure $Cl_2HCB(OCH_3)_3\overset{\oplus}{Li}$. Hydrolysis of the salt affords the dichloromethaneboronic acid, $Cl_2HCB(OH)_2$, in very good yields, 90-95%. Subsequently, the acid derivative of diethanolamine, $Cl_2HCB(OCH_2CH_2)_2NH$, is made very readily in 70-75% yield. In addition, di-n-propyl dichloromethaneboronate, $Cl_2HCB(OCH_2CH_2CH_3)_2$, is obtained in 50-60% yield.

SYNTHESIS OF α-HALOORGANOBORON COMPOUNDS

By

Esther Yu-hsuan Chao

A THESIS

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To

My Parents

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INTRODUCTION

The reactivity of α-halogens to nucleophilic displacement is known to be greatly enhanced by a neighboring boron atom. α-Haloorganoboron compounds, especially the boronic esters which are relatively quite stable, are therefore potentially useful for synthetic applications and mechanistic studies. Consequently, it was decided to develop methods for the convenient preparation of α-haloorganoboron compounds. The reactions of α-haloorganometallic compounds with boron halides or borate esters were chosen for study.

This thesis reports the results of this study.

LITERATURE REVIEW

Recently, the ability of the neighboring boron atom to increase the reactivity of α-halogen as a leaving group in nucleophilic displacements has been studied in synthetic and mechanistic aspects. Work has been done mostly by D.S. Matteson on the formation of halogen-carbon-boron bonds during the last ten years.

In 1960, D. S. Matteson obtained the first α-halogen aliphatic boron compound by radical-catalyzed addition of polyhalomethane to α,β-unsaturated boronic esters.[1] For example,

$$CH_2{=}CHB(OBu)_2 + Cl_3CBr \xrightarrow[\text{initiator}]{\text{radical}} Cl_3CCH_2CHBrB(OBu)_2$$

b.p. 95-96°/0.08 mm

94%

The intermediate radical of the reaction is resonance-stabilized. The canonical structures are expressed as:

$$Cl_3CCH_2\dot{C}H\text{-}B(OBu)_2 \longleftrightarrow Cl_3CCH_2\overset{\oplus}{C}H\text{-}\dot{\underset{\ominus}{B}}(OBu)_2$$

If the α-halo boronic ester is contacted with base, hydrolysis of both the ester and α-halo group occurs, but with cold water only the corresponding boronic acid is obtained. The acid polymerizes with evolution of hydrogen halide either on storage or on heating.[1]

In 1961, Zeldin and Girardot described the synthesis of chloromethyldimethylborane (I) by direct chlorination of trimethylborane at -95^0[2]. They found this derivative (I) to be reasonably stable at 0^0.

$$(CH_3)_3B + Cl_2 \xrightarrow{-95^0} \underset{\text{(I)}}{H_2CClB(CH_3)_2} \quad \text{(vapor tension 36.5 mm at } 0^0\text{)}$$

34%

The ionic addition of hydrogen bromide or iodide to α,β-unsaturated boron compounds was carried out by D. S. Matteson and his coworker in 1963 when the first simple α-haloorganoboron compounds became available.[3]

$$CH_3CH{=}\underset{CH_3}{C}B(OBu)_2 + HBr\,(liquid) \xrightarrow[2\ hrs]{-75^0} CH_3CH_2\underset{Br}{\overset{CH_3}{C}}B(OBu)_2$$

(II)

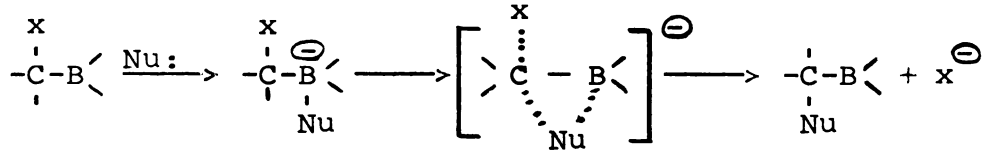
The dibutyl 2-bromobutane-2-boronate (II) (boiling point $64\text{-}65^0/0.1$ mm) was obtained in 61% yield. The addition of hydrogen halide across the double bond is directed by the electron-donating inductive effect of the boryl group which stabilizes form (A) over form (B).[3]

$$CH_3CH_2\overset{\oplus}{\underset{CH_3}{C}}B(OBu)_2 \qquad CH_3\overset{\oplus}{C}HCHB(OBu)_2$$

(A) (B)

The displacement reaction of α-halo boron compounds with sodium iodide in acetone was studied by D. S. Matteson in 1966.[4] Comparison with literature values for simple

alkyl halide gives the following relative rate constants: isopropyl bromide 1.0; ethyl bromide, 40; dibutyl 2-bromopropane-2-boronate, 1600; allyl bromide, 4000; dibutyl 1-bromoethaneboronate, 6000.[4] It was concluded that the neighboring boron atom participates in and greatly accelerates nucleophilic displacement of the α-halide ion.[5] Attack of the nucleophile was assumed to occur initially on the boron atom, followed by migration of the nucleophile to the α-carbon atom with expulsion of the α-halide ion. The following mechanism is representative:[6]



The preparation of halomethaneboron compounds has proved difficult. A very small yield of chloromethaneboronic ester was made by chlorination of methaneboronic acid derivative with t-butyl hypochlorite.[7] Irradiation of t-butyl hypochlorite and di-t-butyl methaneboronate at 0^0 did produce some chloromethylboron compound. The product which was isolated was obtained in only 9% yield as the di-n-butyl ester (III).[8]

$$CH_3B(Ot\text{-}Bu)_2 + t\text{-}BuOCl \longrightarrow ClCH_2B(Ot\text{-}Bu)_2 + CH_3BOC(CH_3)_2CH_2Cl$$

$$+ \text{other products} \xrightarrow{n\text{-}BuOH} ClCH_2B(On\text{-}Bu)_2$$

(III)

The problem is that chlorination of the B-methyl group is

barely favored energetically over attack on C-methyl groups, which outnumber the former nine to one.[8]

However, by starting from boron tribromide and iodomethylmercuric iodide, useful quantities of dibutyl iodomethaneboronate (IV) were obtained.[9]

$$ICH_2HgI + BBr_3 \xrightarrow[\text{temperature}]{\text{room}} ICH_2BBr_2 \xrightarrow{BuOH+NaI} \underset{\text{(IV)}}{ICH_2B(OBu)_2}$$

b.p. $60^0/0.1$ mm
35-40%

Ethyleneboronic ester (V) at first was found to be inert to liquid hydrogen bromide at -70^0.[3] By refluxing with hydrogen iodide, the corresponding α-iodo compound (VI) is obtained as the predominant product as follows:[4]

$$\underset{\text{(V)}}{CH_2{=}CHB(OBu)_2} + HI \xrightarrow{\text{reflux}} \underset{\text{I}}{\underset{\text{(VI)}}{CH_3CHB(OBu)_2}} + ICH_2CH_2B(OBu)_2$$

60% 40%

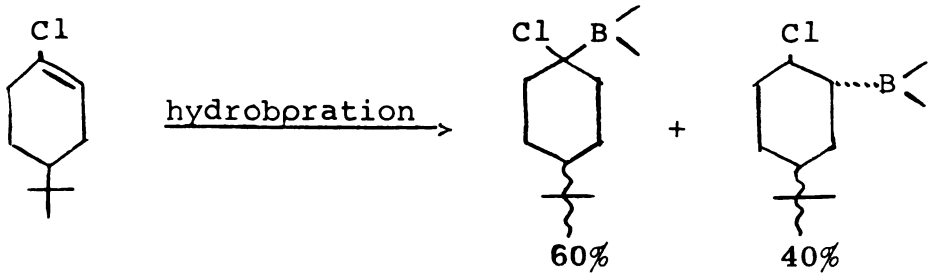
The pure α-iodoethaneboronic ester (VI) is light sensitive and unstable on storage. Decomposition products include iodine and butyl borate.[4]

D. Seyferth and B. Prokai, in 1966, proposed that α-haloalkaneboron compounds (VII) are formed as intermediates in the reaction of trialkylboranes with bromodichloromethyl phenyl mercury.[10]

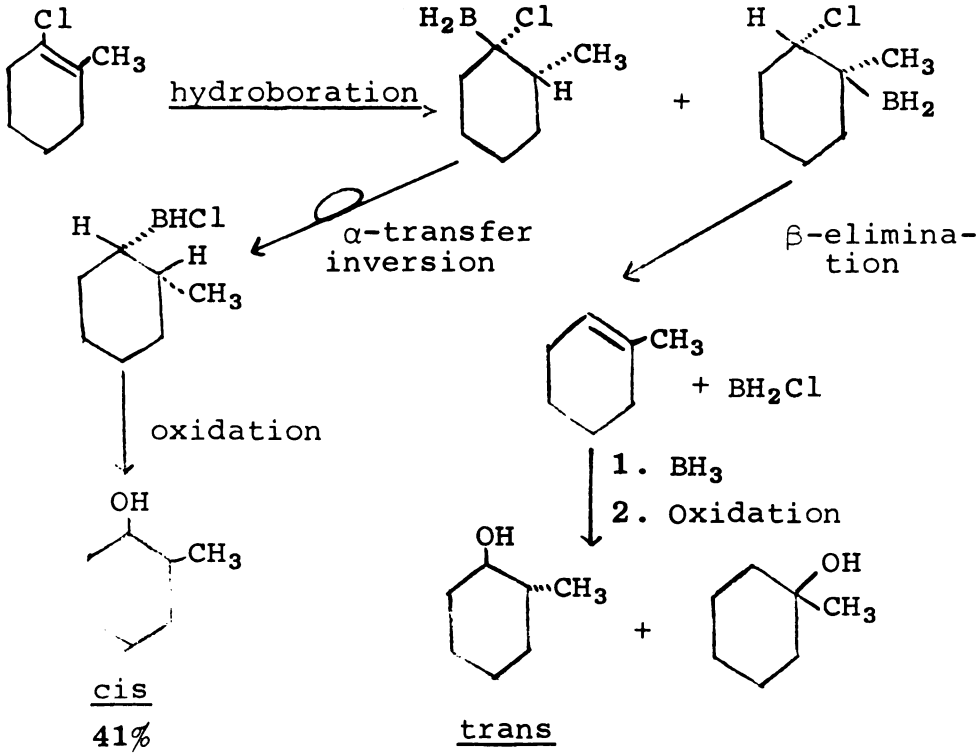
$$3RCH{=}CH_2 \xrightarrow{\text{hydroboration}} (RCH_2CH_2)_3B \xrightarrow{C_6H_5HgCCl_2Br}$$

$$\underset{\text{(VII)}}{(RCH_2CH_2)_2BCCl_2CH_2CH_2R} \longrightarrow RCH_2CH_2BCl_2 + RCH_2CH_2CH{=}CHCH_2R$$

Attempts to isolate the intermediate (VII) were not successful. In the meantime, D. J. Pasto and his coworker found that hydroboration of vinyl halides leads to the formation of highly reactive intermediate adducts which undergo further reactions.[11] The addition of the boron occurs predominantly to the carbon bearing the halogen.[12]



Furthermore, the stereochemistry of the rearrangement of α-haloorganoboranes was shown to be as follows:[13]



In 1968, D. J. Pasto prepared 1-chloro-2-methylpropylboronic acid (VIII) by hydrolysis of the corresponding borane in excellent yields, ≥ 84%.[14] The reaction is shown as:

$$(CH_3)_2C{=}CHCl \xrightarrow[\text{tetrahydrofuran}]{BH_3} (CH_3)_2CHCHClBH_2 \xrightarrow{H_2O} (CH_3)_2CHCHClB(OH)_2$$

(VIII)
m.p. 63-64°

At present, efforts are still being made to find convenient synthetic methods for preparing α-haloorganoboron compounds. This thesis describes the successful synthesis of dichloromethaneboronic acid and its esters.

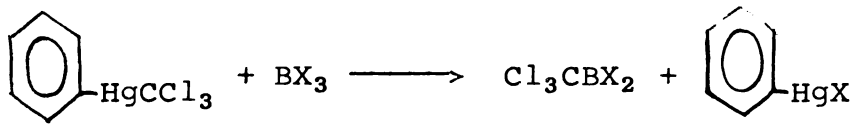
RESULTS

The reaction between α-haloalkylmetallic derivatives and boron compounds is a reasonable synthetic approach to α-haloorganoboron compounds. The reaction could be generalized as:

$$RCHM + BX'_3 \longrightarrow RCHBX'_2 + MX'$$

X = halogen, X' = halogen, methoxide, etc.

Phenyl(trichloromethyl)mercury is a stable compound. Therefore it was, initially, used as the α-haloalkylmetallic intermediate in this synthetic work. The reaction between phenyl(trichloromethyl)mercury and boron trihalide would be expected to produce compounds of the type Cl_3CBX_2 as follows:



A mixture of phenyl(trichloromethyl)mercury and excess boron trichloride was refluxed under a dry-ice condenser overnight at 0^0 under nitrogen. Simple distillation of the reaction mixture led to decomposition. A dark solution was obtained from which no definite products could be isolated.

Since it is known that the B-O bond is stronger than the B-X bond, the ethylene glycol ester of the boron compound might be expected to be more stable than organoboron dihalide. The ethylene glycol ester of the Cl_3CBX_2 might be prepared as follows:

$$Cl_3CBX_2 + (CH_2OH)_2 \longrightarrow Cl_3CB(OCH_2)_2 + 2HX$$

Reaction of stoichiometric quantities of phenyl(trichloromethyl)mercury and boron trichloride was performed in chlorobenzene solution. The reaction mixture was stirred for one hour at 0^0 under nitrogen, followed by esterification with ethylene glycol. Attempts to distill the corresponding ethylene glycol ester under reduced pressure afforded only boric acid which melted at 180^0 with decomposition. Similar attempts to react phenyl(trichloromethyl)mercury with boron trifluoride etherate were also unsuccessful.

The thermal decomposition of sodium trichloroacetate produces $NaCCl_3$. The trichloromethyl anion is unstable in the reaction media and decomposes to give dichlorocarbene by prolonged reaction time.[15]

An attempt was made to intercept the trichloromethyl anion with boron trihalide to obtain α-haloorganoboron compounds of the type Cl_3CBX_2. The ethylene glycol ester of Cl_3CBX_2, which might be relatively stable, was desired. The overall reaction could be shown as follows:

$$NaO\overset{O}{\overset{\|}{C}}CCl_3 \xrightarrow{\Delta} CO_2\uparrow + NaCCl_3 \xrightarrow{BX_3} Cl_3CBX_2 + NaX$$

$$\downarrow (CH_2OH)_2$$

$$Cl_3CB(OCH_2)_2 + 2HX$$

A solution of stoichiometric amounts of sodium trichloroacetate and boron trichloride was refluxed under a dry-ice condenser for one hour at 0^0 under nitrogen. The evolution of carbon dioxide gas was observed. Esterification with ethylene glycol and distillation of the reaction mixture under reduced pressure afforded only boric acid. Similar reactions between sodium trichloroacetate and boron trifluoride etherate gave identical results.

In 1964, Köbrich and Flory described the preparation of trichloromethyllithium solutions[16,17] by slow addition of an equivalent amount of n-butyllithium to a tetrahydrofuran|ether|pentane (4:1:1) solution of chloroform at -108^0 under nitrogen, as shown by the following equation:

$$HCCl_3 + CH_3CH_2CH_2CH_2Li \xrightarrow[-108^0]{\text{tetrahydrofuran}|\text{ether}|\text{pentane}} LiCCl_3 + CH_3CH_2CH_2CH_3$$

It was thought that trichloromethyllithium might react with the boron compound to give a product of the structure Cl_3CBX_2 as shown in the following equation.

$$LiCCl_3 + BX_3 \xrightarrow[-108^0]{\text{tetrahydrofuran}|\text{ether}|\text{pentane}} Cl_3CBX_2 + LiX$$

In order to verify the formation of trichloromethyllithium, the reaction between trichloromethyllithium solution and

benzophenone was performed as follows:

$$LiCCl_3 + \Phi CO\Phi \xrightarrow[-108^0]{\text{tetrahydrofuran} \mid \text{ether} \mid \text{pentane}} \Phi\overset{\Phi}{\underset{}{C}}(\bar{O}Li^+)-CCl_3 \xrightarrow[-108^0]{H_3O^+ + \text{methanol}}$$

$$\Phi_2C(OH)CCl_3$$

It was found that hydrolysis of the lithium salt with concentrated sulfuric acid and methanol at -108^0 instead of at room temperature afforded $\Phi_2C(OH)CCl_3$ in a higher yield (30%) than reported by Köbrich (20%).[17]

The reaction between trichloromethyllithium and boron trihalide was performed. An equivalent amount of $BF_3 \cdot O(CH_2CH_3)_2$ was added to a trichloromethyllithium solution at -108^0 under nitrogen to produce a clear solution. The reaction mixture turned a black color as the temperature was raised to room temperature, indicating decomposition. No definite product could be isolated. Use of trimethyl borate in place of boron trifluoride etherate gave similar results. Attempts to isolate any trihalomethylboron product were unsuccessful.

Dichloromethyllithium was first prepared by Köbrich and Flory in 1964.[18] Dichloromethyllithium, which is more stable than trichloromethyllithium, was prepared by slow addition of an equivalent amount of n-butyllithium to methylene chloride in tetrahydrofuran solution at -100^0 under nitrogen. The reaction is shown as:

$$CH_2Cl_2 + CH_3CH_2CH_2CH_2Li \xrightarrow[-100^0]{\text{tetrahydrofuran}} LiCHCl_2 + CH_3CH_2CH_2CH_3$$

It was proposed that dichloromethyllithium would react with trimethyl borate to produce a compound like $Cl_2HCB(OCH_3)_2$ as follows:

$$LiCHCl_2 + B(OCH_3)_3 \xrightarrow[-100^0]{\text{tetrahydro-furan}} Cl_2HCB(OCH_3)_2 + LiOCH_3$$

Addition of trimethyl borate to a dichloromethyllithium solution at -100^0, followed by removal of solvent afforded an oil-like material with a positive flame test for boron. The nmr spectrum showed a singlet at δ 5.3 (1H) and a singlet at δ 3.3 (9-10H). The results suggest the structure of the product as $Cl_2HC\overset{\ominus}{B}(OCH_3)_3Li^{\oplus}$ (IX) which is formed according to the following equation:

$$LiCHCl_2 + B(OCH_3)_3 \xrightarrow[-100^0]{\text{tetrahydrofuran}} \underset{\text{(IX)}}{Cl_2HC\overset{\ominus}{B}(OCH_3)_3Li^{\oplus}}$$

The compound (IX) is soluble in ethyl ether and chloroform. However, attempts to crystallize it from these solvents failed.

Hydrolysis of the lithium salt (IX) should give the corresponding boronic acid (X) as follows:

$$\underset{\text{(IX)}}{Cl_2HC\overset{\ominus}{B}(OCH_3)_3Li^{\oplus}} \xrightarrow[\text{tetrahydrofuran}\ -100^0]{\text{dilute HCl}} Cl_2HCB(OCH_3)_2 + CH_3OH + LiCl$$

$$\downarrow H_2O,\ \text{room temperature}$$

$$\underset{\text{(X)}}{Cl_2HCB(OH)_2}$$

It was found that hydrolysis of the lithium salt (IX) with dilute hydrochloric acid at -100^0, followed by extraction

with ethyl ether, and concentration of the organic phase afforded a white solid with a positive flame test for boron. After recrystallization from ethyl ether, the material melted at 97-98°. The nmr spectrum showed a singlet at δ 5.25 (1H) and a singlet at δ 4.88 (2-3H) in $(CD_3)_2SO$. The nmr spectrum indicated the presence of boric acid, $B(OH)_3$, together with the product (X). The overall yield of (X) was 90-95%. The material is soluble in alcohols and tetrahydrofuran, but insoluble in diethyl ether, chloroform, carbon tetrachloride, and benzene. Although it is quite stable in air, the α-halo boronic acid (X) might lose water readily and reversibly to form the corresponding boroxine (XI):[19,20]

$$3Cl_2HCB(OH)_2 \underset{3H_2O}{\overset{-3H_2O}{\rightleftharpoons}} \underset{(XI)}{\text{boroxine}}$$

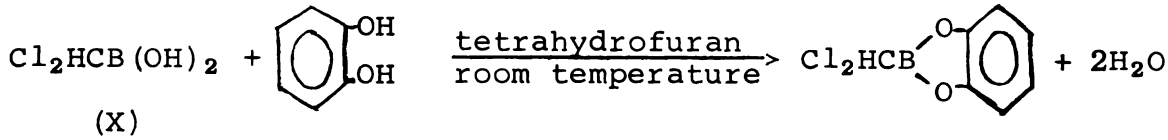
(X)

The presence of boric acid and boroxine (XI) could explain the variable ratios of protons in the nmr spectra.

Since the α-halo boronic acid was not fully characterized, derivatives of the acid were desired. An attempt was made to synthesize the corresponding boroxine (XI) by dissolving the acid in benzene and distilling the benzene-water azeotrope at 70°. However, the reaction mixture turned brown and then gave a black residue of carbon under the reaction conditions.

It is known that the boronic acid derivatives of catechol and diethanolamine are solids in many cases, which makes them useful derivatives for the characterization of boronic acids. The preparation of dichloromethaneboronic acid (X) derivatives of catechol and diethanolamine was therefore attempted.

The reaction of the acid and catechol can be shown as:



(X) (XII)

A mixture of stoichiometric amounts of the acid and catechol in tetrahydrofuran was stirred for one hour at room temperature under nitrogen. A white solid with a positive flame test for boron was obtained, but it turned to a deep purple color soon after it was isolated.

The reaction of the acid and diethanolamine is shown as:

$$\underset{(X)}{Cl_2HCB(OH)_2} + NH(CH_2CH_2OH)_2 \xrightarrow[\text{room temperature}]{\text{tetrahydrofuran}} Cl_2HCB(OCH_2CH_2)_2NH + 2H_2O$$

(XIII)

An equivalent amount of diethanolamine was added dropwise to the tetrahydrofuran solution of dichloromethaneboronic acid (X) at room temperature under nitrogen. A white solid formed immediately. Filtration of the reaction mixture under nitrogen afforded a solid with a positive flame test

for boron. Recrystallization from acetonitrile gave white needles which melted at 134° with decomposition. The derivative (XIII) is hydroscopic, but quite stable in air since its melting point stays constant over a period of one week when exposed to air. It was found that compound (XIII) is insoluble in many common organic solvents such as ether, chloroform, carbon tetrachloride and benzene, but soluble in alcohols, pyridine and hot acetonitrile. The nmr spectrum showed an H-C-B and H-N-C singlet at δ 5.25 (1H), an O-CH_2-C triplet at δ 4.35 (2H), and a C-CH_2-N triplet at δ 3.9 (2H) in D_2O. The results are consistent with the structure of the dichloromethaneboronic acid derivative of diethaneolamine (XIII). The yield of the pure compound was 70-75%.

In general, boronic esters of the type $RB(OR')_2$ can be made by removal of water formed in the reaction of the boronic acid with an alcohol. The reaction of dichloromethaneboronic acid (X) with various alcohols can be generalized as:

$$\underset{(X)}{Cl_2HCB(OH)_2} + 2ROH \xrightarrow{\text{distillation}} Cl_2HCB(OR)_2 + 2H_2O$$

Usually, a solution of α-halo boronic acid containing excess alcohol and benzene was distilled under nitrogen at atmospheric pressure to remove the water-alcohol-benzene azeotrope. The product was collected by distillation under reduced pressure. The results of esterifications of the acid (X) with ethylene glycol, ethanol, n-butanol, and n-propanol are summarized as follows:

The reaction between α-halo boronic acid (X) and ethylene glycol can be shown as:

$$\underset{(X)}{Cl_2HCB(OH)_2} + (CH_2OH)_2 \xrightarrow{-2H_2O} \underset{(XIV)}{Cl_2HCB(OCH_2)_2}$$

The ethylene glycol ester obtained after removal of solvent, was recrystallized from ethyl ether to give a white solid, mp **97-99°**, which gave a positive flame test for boron. The nmr spectrum showed an H-C-B singlet at δ 5.3 (1H), an O-H singlet at δ **4.8** (3-5H), and an $O-CH_2-C$ singlet at δ **3.8** (4-7H) in $(CH_3)_2SO$ with variable ratios of the respective protons. The mass spectrum proved the formation of the ethylene glycol ester (XIV) by the parent peak at m/e **154** and an isotope peak at m/e **156** in the ratio of intensity **1.7:1** identical to the theoretical value. Further attempts at purification failed. It is possible that monomer, dimer and polymer by-products are formed as follows:

$$\underset{(X)}{Cl_2HCB(OH)_2} + (CH_2OH)_2 \xrightarrow[-H_2O]{\text{distillation}} Cl_2HCB(OCH_2)_2 + \underset{(XIV)}{}$$

$$\underset{\text{monomer}}{HOCH_2CH_2O\overset{CHCl_2}{\overset{|}{B}}OCH_2CH_2OH} + \underset{\text{dimer}}{H(OCH_2CH_2O\overset{CHCl_2}{\overset{|}{B}}OCH_2CH_2O)_2H}$$

$$+ \underset{\text{polymer}}{H(OCH_2CH_2O\overset{CHCl_2}{\overset{|}{B}}OCH_2CH_2O)_nH}$$

Esterification of the α-halo boronic acid with ethanol was attempted as follows:

$$\underset{(X)}{Cl_2HCB(OH)_2} + 2CH_3CH_2OH \xrightarrow[-2H_2O]{\text{distillation}} \underset{(XV)}{Cl_2HCB(OCH_2CH_3)_2}$$

The product was collected at 26-32°/0.5-0.6 mm and showed a positive flame test for boron. The nmr spectrum showed a singlet at δ 5.25 (1H), a quartet at δ 3.5 (2-5H), a triplet at δ 1.0 (3-7H) (neat). It was concluded that the unreacted ethanol distilled together with the expected ethanol ester, $Cl_2HCB(OCH_2CH_3)_2$, under reduced pressure. Attempts to isolate the ester product in good yields were unsuccessful. However, 10-15% yield of the pure ethanol ester which gave an nmr spectrum with correct proton ratio (1:4:6) was obtained.

The n-butanol ester of the α-halo boronic acid (X) was prepared by the following equation:

$$\underset{(X)}{Cl_2HCB(OH)_2} + 2CH_3CH_2CH_2CH_2OH \xrightarrow[-2H_2O]{\text{distillation}} \underset{(XVI)}{Cl_2HCB(OCH_2CH_2CH_2CH_3)_2}$$

The ester (XVI) was obtained at 103-104°/5-6 mm and showed a positive flame test for boron. The nmr spectrum showed an H-C-B singlet at δ 5.3, an $O-CH_2-C$ (of boronate (XVI)) triplet at δ 4.1, an $O-CH_2-C$ (of tri-n-butyl borate) triplet at δ 3.8, a $C-CH_2-C$ multiplet at δ 1.9 and a $C-CH_3$ triplet at δ 1.0 with variable proton ratios. The boiling point of tri-n-butyl borate, $B(OCH_2CH_2CH_2CH_3)_3$, is found to be 103-105°/8 mm or 114-115°/15 mm. Evidently,

tri-n-butyl borate was present together with the expected product (XVI). Further attempts to isolate the desired ester (XVI) failed.

An ester of the boronic acid (X) with a sufficient boiling point difference under reduced pressure from the corresponding borate ester or the alcohol was desired. The n-propanol ester of the boronic acid (X) was prepared as follows:

$$\underset{(X)}{Cl_2HCB(OH)_2} + 2CH_3CH_2CH_2OH \xrightarrow[-2H_2O]{\text{distillation}} \underset{(XVII)}{Cl_2HCB(OCH_2CH_2CH_3)_2}$$

Esterification of the boronic acid with n-propanol gave the n-propanol ester (XVII) in 40% yield. The n-propanol ester (XVII), collected at $103^0/15$ mm, showed $N^{23}D$ 1.4230 and a positive flame test for boron. The nmr spectrum showed an H-C-B singlet at δ 5.32 (1H), an $O-CH_2-C$ triplet at δ 4.0 (4H), a $C-CH_2-C$ sextet at δ 1.56 (4H) and a $C-CH_3$ triplet at δ 0.95 (6H) (neat). These results are consistent with the structure of di-n-propyl dichloromethaneboronate (XVII) which is soluble in almost all organic solvents including alcohols, ethers, chloroform and benzene. It was found that moisture in the air could slowly hydrolyze the n-propanol ester (XVII) to the corresponding boronic acid (X) as follows:

$$\underset{(XVII)}{Cl_2HCB(OCH_2CH_2CH_3)_2} \xrightarrow[\text{temperature}]{\text{moisture room}} \underset{(X)}{Cl_2HCB(OH)_2} + 2CH_3CH_2CH_2OH$$

Therefore, the n-propanol ester (XVII) should be stored

under a nitrogen atmosphere. Finally, preparation of dichloromethaneboronic acid (X), directly followed by esterification with n-propanol afforded the ester (XVII) in an overall yield of 55-60%.

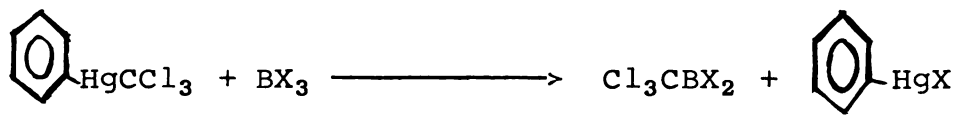
The results of elemental analyses of boronic acid (X), and boronate (XIII), (XVII) are not acceptable. The reasons are probably due to: first, the formation of an inert boron carbide under analytic operation conditions; second, the highly hydroscopic quality of boronate (XIII) and moisture-sensitivity of boronate (XVII). These make the operation of elemental analyses determination difficult. The analytic data obtained is listed in Table (A).

Table (A). Results of Elemental Analyses

Formula		C%	H%	Cl%	N%
$Cl_2HCB(OH)_2$	Calcd	9.32	2.33	55.12	--
(X)	Found	5.52	2.84	32.21	--
$Cl_2HCB(OCH_2CH_2)_2NH$	Calcd	30.40	5.05	35.89	7.08
(XIII)	Found	29.86	6.69	28.51	11.21
		30.94	5.06	34.28	7.93
		28.83	4.84	--	6.11
$Cl_2HCB(OCH_2CH_2CH_3)_2$	Calcd	39.46	7.05	33.35	--
(XVII)	Found	38.80	6.89	34.19	--
		24.28	4.08	--	--

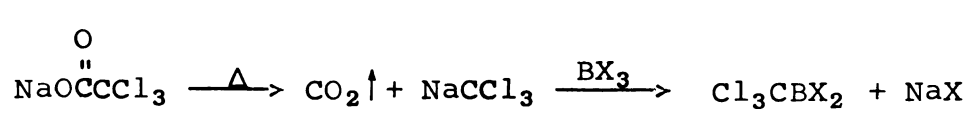
DISCUSSION

The reactions between phenyl(trichloromethyl)mercury and boron trihalide are unsuccessful for preparing boron compounds of the type Cl_3CBX_2, according to the proposed scheme:



The difficulties of synthesizing Cl_3CBX_2 by this method may be due to the low reactivity of the organomercury compound or the instability of the product Cl_3CBX_2. Furthermore, the side-product, phenylmercuric halide is partially soluble under the reaction conditions, thereby making work-up difficult.

Consequently, the relatively more reactive $NaCCl_3$ species, which can be generated by thermal decomposition of sodium trichloroacetate was attempted. The reaction between $NaCCl_3$ and the boron trihalide possibly produces trichloromethylboron dihalide, Cl_3CBX_2, as follows:



The evolution of carbon dioxide gas is observed from the reaction, but the desired product is not obtained. It is

assumed that carbon dioxide might react with $\overset{\ominus}{C}Cl_3$ or $:CCl_2$ to produce other compounds under the reaction conditions.

Thus, milder reaction conditions to generate the trihalomethyl anion are desirable. Köbrich and Flory describe the preparation of chloromethyllithium solution as follows:[16,17]

$$HC\text{-}XCl_2 \xrightarrow[-100^0,\text{ether}]{CH_3CH_2CH_2CH_2Li} LiC\text{-}XCl_2 + CH_3CH_2CH_2CH_3$$

$X = Cl, H.$

The reaction between trichloromethyllithium, $LiCCl_3$, and boron trihalide leads to decomposition products presumably due to the instabilities of both the Cl_3CBX_2 product and $LiCCl_3$. In fact, it is known that $LiCCl_3$ is stable at -115^0 but decomposes exothermally at -80^0 to form a mixture of tetrahaloethylene.[21]

Dichloromethyllithium is relatively more stable than trichloromethyllithium.[16,18] Therefore, dichloromethyllithium can be handled easily in preparation of α-haloorganoboron compounds. An oil-like product (IX) is obtained from the reaction of dichloromethyllithium and trimethyl borate at -100^0 under a nitrogen atmosphere.

$$LiCHCl_2 + B(OCH_3)_3 \xrightarrow[-100^0]{\text{tetrahydrofuran}} Cl_2HC\overset{\ominus}{B}(OCH_3)_3\overset{\oplus}{Li}$$

(IX)

The nmr spectrum probably suggests the reasonable structure

of (IX). Crystallization of the lithium salt (IX) fails possibly because the material is highly air-sensitive or the material may actually be an oil.

Usually, the reaction between organolithium compounds and boron derivatives gives a mixture of products[22] as follows:

$$RLi + BX_3 \longrightarrow RBX_2 + R_2BX + R_3B + R_4\overset{\ominus}{B}\overset{\oplus}{Li}$$

However, the reaction between dichloromethyllithium and trimethyl borate produces mainly monoalkylation of the boronic ester. The electron withdrawing effects of the chlorine atoms attached to the α-carbon make the boron atom highly electron-deficient; thus the product is isolated as a salt with the structure $Cl_2HC\overset{\ominus}{B}(OCH_3)_3\overset{\oplus}{Li}$ (IX). This salt is presumably resistant to further alkylation by the organolithium reagent.

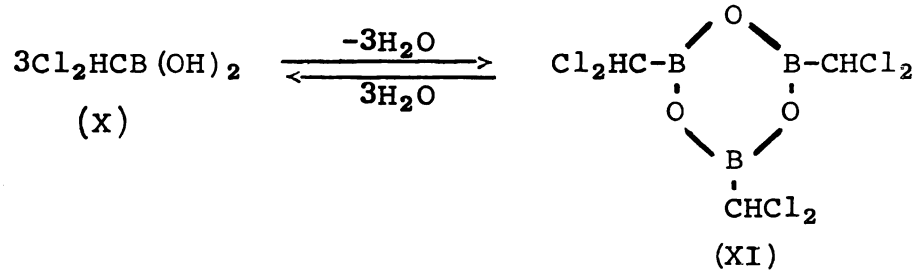
It is known that the boron-carbon bond is very strong and is not easily broken by strong acids such as hydrochloric acid and sulfuric acid, or by sodium hydroxide at room temperature. Therefore, hydrolysis of $Cl_2HC\overset{\ominus}{B}(OCH_3)_3\overset{\oplus}{Li}$ (IX) with dilute hydrochloric acid at -100^0 under nitrogen produces the desired compound, dichloromethaneboronic acid (X), in very good yields (90-95%).

$$\underset{\text{(IX)}}{Cl_2HC\overset{\ominus}{B}(OCH_3)_3\overset{\oplus}{Li}} \xrightarrow[-100^0]{\text{dil HCl}} Cl_2HCB(OCH_3)_2 \xrightarrow[\text{room temperature}]{H_2O} Cl_2HCB(OH)_2$$

(X)

mp 97-98°

The acid (X) is found to be soluble in alcohols and tetrahydrofuran, but insoluble in diethyl ether, chloroform, carbon tetrachloride and benzene. The nmr spectrum of the acid (X) shows an H-C-B singlet at δ 5.25 (1H) and B-O-H singlet at δ 4.88 (2-3H) in $(CD_3)_2SO$. It indicates the presence of boric acid, $B(OH)_3$, together with the boronic acid (X). In addition, the α-halo boronic acid (X) might lose water to form the corresponding boroxine (XI) readily and reversibly[19,20] as follows:



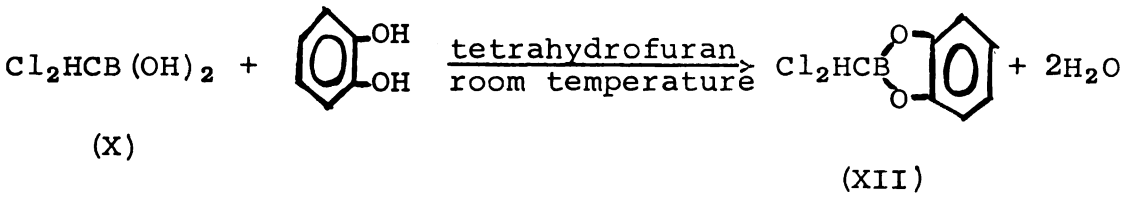
(XI)

The boronic acid (X) in the presence of boric acid and boroxine (XI) could explain the variable proton ratios of the nmr spectra.

Attempts to prepare the pure boroxine (XI) by dehydration of (X) in refluxing benzene are unsuccessful, possibly because of the heat-sensitivity of the α-haloorganoboron compound under the reaction conditions at 70-110°.

Most known α-halo boronic acid derivatives of catechol and diethanolamine are solids. In order to characterize the dichloromethaneboronic acid (X), the catechol and diethanolamine derivatives were made.

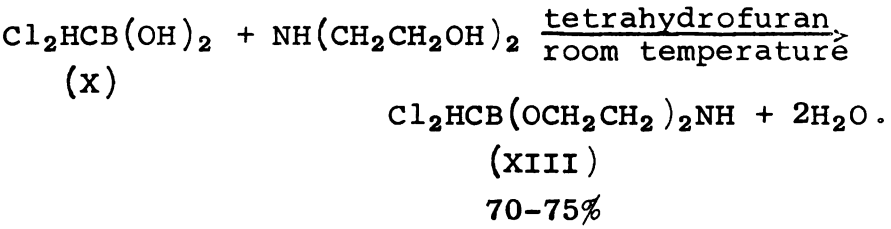
A sample of the catechol ester (XII) was prepared according to the following equation:



(X) (XII)

It is known that compounds such as catechyl 2-bromopropane-2-boronate and catechyl 1-bromoethaneboronate are unstable on storage, turning to a black liquid.[4] Likewise, a pure sample of the type (XII) could not be obtained.

However, the boronic acid derivative of diethanolamine (XIII) is obtained very readily. The reaction is shown as:

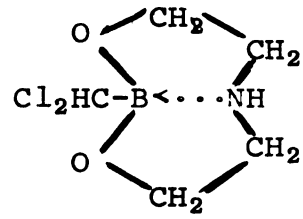


(X) (XIII)

70-75%

The product (XIII) melts at 134° with decomposition. It is hydroscopic but otherwise stable in air as indicated by its constant melting point when exposed to air. The boronic acid derivative of diethanolamine (XIII) is insoluble in many common organic solvents such as ethers, chloroform, carbon tetrachloride and benzene, but soluble in alcohols, pyridine and hot acetonitrile. The easy synthesis and high stability of the acid derivative of diethanolamine (XIII) is probably due to the presence of the coordinatively

saturated boron atom as shown below:[23,24]



(XIII)

The nmr spectrum of the acid derivative (XIII) shows an H-C-B and N-H singlet at δ 5.25 (1H), an O-CH_2-C triplet at δ 4.35 (2H), and a C-CH_2-N triplet at δ 3.9 (2H) in D_2O. These results are consistent with the structure of the compound (XIII).

Efforts have been made to convert the α-halo boronic acid (X) to the corresponding esters.

$$\underset{(X)}{Cl_2HCB(OH)_2} + 2ROH \xrightarrow[-2H_2O]{\text{distillation}} Cl_2HCB(OR)_2$$

This reaction is reversible and water is usually removed as the benzene azeotrope.

A solid product is obtained from the esterification of the α-halo boronic acid (X) with ethylene glycol.

$$\underset{(X)}{Cl_2HCB(OH)_2} + (CH_2OH)_2 \xrightarrow{-2H_2O} \underset{(XIV)}{Cl_2HCB(OCH_2)_2}$$

Both mass and nmr spectra show that materials other than the desired ethylene glycol ester (XIV) are present. Attempts to purify the ester (XIV) failed. The impurities could be the unreacted α-halo boronic acid (X) which is

hard to remove from the ethylene glycol ester (XIV) presumably because of similar solubility. It is also likely that monomer, dimer and polymers of the ethylene glycol ester form under the reaction conditions.

$$\underset{\text{(X)}}{Cl_2HCB(OH)_2} + (CH_2OH)_2 \xrightarrow[-\,H_2O]{\text{distillation}} \underset{\text{(XIV)}}{Cl_2HCB(OCH_2)_2} +$$

$$HOCH_2CH_2O\overset{\overset{CHCl_2}{|}}{B}OCH_2CH_2OH + H(OCH_2CH_2O\overset{\overset{CHCl_2}{|}}{B}OCH_2CH_2O)_2H +$$

monomer dimer

$$H(OCH_2CH_2O\overset{\overset{CHCl_2}{|}}{B}OCH_2CH_2O)_nH$$

polymer

Esterification of the acid with ethanol according to the following equation

$$\underset{\text{(X)}}{Cl_2HCB(OH)_2} + 2CH_3CH_2OH \xrightarrow[-2H_2O]{\text{distillation}} \underset{\text{(XV)}}{Cl_2HCB(OCH_2CH_3)_2}$$

was attempted. Quantitative yield of the product was not obtained. It is assumed that unreacted ethanol distilled together with the ethanol ester, $Cl_2HCB(OCH_2CH_3)_2$ (XV), at 26-32°/0.5-0.6 mm. Further isolation gave only 10-15% yield of pure diethyl dichloromethaneboronate which showed the correct nmr spectrum.

The n-butanol ester of the acid was prepared as follows:

$$\underset{\text{(X)}}{Cl_2HCB(OH)_2} + 2CH_3CH_2CH_2CH_2OH \xrightarrow[-2H_2O]{\text{distillation}}$$

$$\underset{\text{(XVI)}}{Cl_2HCB(OCH_2CH_2CH_2CH_3)_2}$$

A product was collected at 103-104°/5-6 mm. The nmr spectrum indicated the presence of a mixture of di-n-butyl dichloromethaneboronate (XVI) and tri-n-butyl borate in variable proportions. The boiling point of tri-n-butyl borate is 114-115°/15 mm, which is so close to that of the n-butanol ester (XVI) under reduced pressure that it is impossible to separate the mixture by simple distillation.

However, useful quantities of pure di-n-propyl dichloromethaneboronate (XVII) were collected at 103°/15 mm according to the following equation:

$$\underset{(X)}{Cl_2HCB(OH)_2} + 2CH_3CH_2CH_2OH \xrightarrow[-2H_2O]{\text{distillation}} \underset{\substack{(XVII)\\ 40\%}}{Cl_2HCB(OCH_2CH_2CH_3)_2}$$

Since tri-n-propyl borate boils at 90°/15 mm, separation by distillation is more facile in this case than for the butyl esters. The nmr spectrum of the ester (XVII) shows an H-C-B singlet at δ 5.32 (1H), an O-CH_2-C triplet at δ 4.0 (4H), a C-CH_2-C sextet at δ 1.56 (4H), and a C-CH_3 triplet at δ 0.95 (6H) (neat). These results are consistent with the structure of the ester (XVII). The ester (XVII), $N^{23}D$ 1.4230, is soluble in many common organic solvents such as ethers, alcohols, chloroform, and benzene. Exposure of the ester (XVII) to air does not result in oxidation but rather in the formation of the boronic acid (X).

$$\underset{(XVII)}{Cl_2HCB(OCH_2CH_2CH_3)_2} \xrightarrow[\text{room temperature}]{\text{moisture}} \underset{(X)}{Cl_2HCB(OH)_2} + 2CH_3CH_2CH_2OH$$

It is observed that α-haloorganoboronic acid (X) gives black residue of carbon as the reaction temperature exceeds 110^0. Possibly the solid α-haloorganoboron compounds are sensitive to heat, therefore the mildest reaction condition would be optimum for the synthesis of the α-haloorganoboron compounds. Starting from methylene chloride and n-butyllithium reaction, directly followed by hydrolysis and esterification with n-propanol, the stable di-n-propyl dichloromethane boronate (XVII) is obtained in 55-60% yield. This ester may be useful for further studies. Subsequent nucleophilic substitution reactions of ester (XVII) could be proposed as follows:

1. Reaction with Grignard reagents,

$$\underset{\text{(XVII)}}{Cl_2HCB(OCH_2CH_2CH_3)_2} + RMgX \longrightarrow ClHCB(OCH_2CH_2CH_3)_2 + MgXCl$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad R$$

2. Reaction with NaH,

$$\underset{\text{(XVII)}}{Cl_2HCB(OCH_2CH_2CH_3)_2} + NaH \longrightarrow ClH_2CB(OCH_2CH_2CH_3)_2 + NaCl$$

3. Formation of chlorocarbene,

$$\underset{\text{(XVII)}}{Cl_2HCB(OCH_2CH_2CH_3)_2} \xrightarrow{\Delta} Cl\ddot{C}H + ClB(OCH_2CH_2CH_3)_2 \ .$$

EXPERIMENTAL

Melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (nmr) spectra were obtained using a Varian A-60 spectrometer. All spectra are recorded in δ units relative to tetramethylsilane (TMS).

Elemental analyses were carried out by Crobaugh Laboratories, Cleveland, Ohio.

A. Phenyl(trichloromethyl)mercury. Method of Schweizer and O'Neill.[25]

In a 1-l three-necked, round bottomed flask equipped with a reflux condenser and an efficient mechanical stirrer were placed 400 ml of dry benzene, 48 g (0.36 mole) of ethyl trichloroacetate and 26.4 g (0.074 mole) of phenylmercuric bromide. The mixture was stirred and cooled in an ice-water bath for 15 min. Sodium methoxide (16.8 g, 0.308 mole) was added all at once. The mixture was stirred for 1.5 hr with cooling, then quenched with an equal volume of water. After thorough mixing, the benzene layer was decanted and filtered. The aqueous mixture was extracted with three 100-ml portions of benzene after which the organic layers were combined and evaporated to dryness under

a stream of air. Phenyl(trichloromethyl)mercury (7.3 g, 50% yield), a white solid, mp 102-107°, was obtained. After one washing with 20 ml of cold ethanol, 4.8 g (40%) of the desired product was obtained, mp 107-108° (lit. mp 114-115°).[25]

B. Attempted Reaction of Phenyl(trichloromethyl)mercury and Boron Trichloride

In a 100-ml three-necked, round bottomed flask equipped with a dry-ice condenser was placed 7.3 g (18 mmole) of phenyl(trichloromethyl)mercury. Around 20 ml (25 mmole) of boron trichloride was allowed to evaporate into the flask at 0° under nitrogen. The reaction mixture was stirred overnight at 0° and then warmed gradually to room temperature. At this time, evolution of boron trichloride gas was observed. A white solid precipitated. After addition of 10 ml of ethylene glycol, the esterified mixture was stirred for 1 hr at room temperature and then distilled under reduced pressure. The distillate collected showed the negative flame test for boron. The white solid left in the flask melted >250°.

A similar experiment using stoichiometric amounts of both reagents in chlorobenzene solution was also unsuccessful.

C. Attempted Reaction of Phenyl(trichloromethyl)mercury and Boron Trifluoride Etherate

To a solution of 0.8 g (2 mmole) of phenyl(trichloromethyl)merucry in 10 ml of anhydrous ethyl ether at room temperature was added, under nitrogen, 0.25 ml (2 mmole) of boron trifluoride etherate. The reaction mixture was stirred for one hour at room temperature, hydrolyzed with 5 ml of water and concentrated. Only phenylmercuric fluoride with a melting point >250^0 was obtained.

A similar experiment in the presence of sodium iodide as catalyst was also unsuccessful.

D. Sodium Trichloroacetate.[26]

Trichloroacetic acid (163.4 g, 1 mole) was put in a 2-l Erlenmeyer flask with a side arm and cooled in an ice-bath. After the addition of 9/10 of 150 ml of 0.15 N, ice-cold sodium hydroxide solution, the mixture was titrated with the remaining solution to a methyl orange end-point. The flask was then covered with a rubber stopper, connected to an aspirator and mounted on a steam bath in order to remove water. Finally, quantitative amount of white solids was collected and dried in a dessicator under vacuum overnight.

E. Attempted Reaction of Sodium Trichloroacetate and Boron Trichloride

In a 100-ml three-necked, round bottomed flask equipped with a dry-ice condenser was placed 4.63 g (25 mmole) of sodium trichloroacetate under nitrogen. Boron trichloride initially was collected in a trap which was immersed in a dry-ice and acetone bath to prevent the compound from evaporating. Around 15-20 ml (25 mmole) of boron trichloride was evaporated into the round bottomed flask at 0^0. The reaction mixture was stirred for one-half hour at 0^0 and then warmed to room temperature gradually. A gas was evolved and identified as CO_2 by a positive $Ba(OH)_2$ test. However, the unreacted boron trichloride evolved from the reaction mixture spontaneously at a temperature higher than 12^0. Esterification of the resulting solution with 5 ml of ethylene glycol and distillation under reduced pressure gave a distillate with a negative flame test for boron. The solid left in the flask was shown to be boric acid which melts at 180^0 with decomposition, in 80% yield.

F. Attempted Reaction of Sodium Trichloroacetate and Boron Trifluoride Etherate

In a 50-ml round bottomed flask was placed 9.27 g (50 mmole) of sodium trichloroacetate under nitrogen. Soon after injection of 6.3 ml (50 mmole) of boron trifluoride etherate, the evolution of gas which is identified as

carbon dioxide by a positive $Ba(OH)_2$ test, was observed. When the evolution of CO_2 gas stopped, 20 ml of ethylene glycol was added, then the mixture was stirred overnight at 25°. Distillation under reduced pressure gave only boric acid which melts at 180° with decomposition, in 80% yield.

G. Trichloromethyllithium Solution. Method of Köbrich and Flory[16,17]

In a 100-ml three-necked, round bottomed flask equipped with a mechanical stirrer were placed 1.60 ml (20 mmole) of chloroform and 48 ml of the combined solvents tetrahydrofuran/ethyl ether/pentane in 4:1:1 ratio at -108° by immersing the flask in an absolute alcohol-liquid nitrogen mixture in a dewar flask under nitrogen. To the solution was added dropwise with stirring at -108°, 12.6 ml (20 mmole) of n-butyllithium over a 15-minute period. Stirring at this temperature for an additional 20 minutes resulted in a colorless suspension of trichloromethyllithium.

H. Reaction of Trichloromethyllithium and Benzophenone[17]

The trichloromethyllithium solution (20 mmole) obtained from the previous procedure, was treated with 3.5 g (< 20 mmole) of benzophenone in 20 ml of ethyl ether. The reaction mixture was stirred for 20 min, then hydrolyzed with concentrated sulfuric acid and methanol at -108°. Evaporation of solvents and crystallization from ice-cold

pentane afforded 1.65 g (30%), (lit 1.33 g, 20%), of $\Phi_2C(OH)CCl_3$, mp 64-65° (lit 64.5-65.5°).

I. Attempted Reaction of Trichloromethyllithium and Boron Trifluoride Etherate

Trichloromethyllithium solution (50 mmole) obtained from the method of Köbrich and Flory, was treated dropwise during 15 min with stirring with 6.3 ml (50 mmole) of boron trifluoride etherate. The colorless reaction mixture was stirred for 30 min at -108°, then warmed gradually to room temperature. However, a dark colored solution resulted. It possibly indicates the decomposition of trichloromethyllithium reagent or the expected product, Cl_3CBF_2.

A similar reaction was performed using trimethyl borate instead of boron trifluoride etherate. It also resulted in the formation of a dark colored solution.

J. Dichloromethyllithium Solution. Method of Köbrich and Flory[18]

The dichloromethyllithium solution was prepared by adding 15.75 ml (25 mmole) of n-butyllithium dropwise over a period of 30 min, under nitrogen, to a vigorously stirred solution of methylene chloride (1.59 ml, 25 mmole) in 50 ml of tetrahydrofuran at -100° obtained by immersing the container in a dewar flask containing a mixture of absolute alcohol-liquid nitrogen. The reaction mixture was stirred for one-half hour at this temperature. A colorless solution of dichloromethyllithium resulted which was stable even at -74°.

K. Reaction of Dichloromethyllithium and Trimethyl Borate

An equivalent amount of trimethyl borate (5.7 ml, 50 mmole) was added to the colorless solution of dichloromethyllithium (50 mmole) obtained from the previous preparation, at -100° under nitrogen. The reaction mixture was stirred for one-half hour at -100°, then warmed gradually to room temperature. Removal of the solvents afforded an oil-like material. The nmr spectrum showed singlets at δ 5.25 (1H), and δ 3.3 (9-10H) which suggested the formation of a compound having a reasonable structure as $Cl_2HC\overset{\ominus}{B}(OCH_3)_3\overset{\oplus}{Li}$ (IX). However, crystallization of the oil-like material from ethyl ether or chloroform failed.

L. Preparation of Dichloromethaneboronic Acid (X)

The $Cl_2HC\overset{\ominus}{B}(OCH_3)_3\overset{\oplus}{Li}$ (IX) solution obtained from the previous reaction, was hydrolyzed with dilute hydrochloric acid at -100° under nitrogen. The reaction mixture was stirred vigorously for 30 min at -100°, then warmed to room temperature gradually. After extraction with ethyl ether and removal of solvents, a white solid, mp 92-95°, which gave a positive flame test for boron was collected from ice-cold pentane. It melted at 97-98° after recrystallization from anhydrous ethyl ether. The acid (X) is soluble in alcohols and tetrahydrofuran but insoluble in diethyl ether, chloroform and benzene. The nmr spectrum showed a singlet at δ 5.25 (1H) and a singlet at δ 4.88 (2-3H) in $(CD_3)_2SO$.

The crude product, dichloromethaneboronic acid (X), was obtained in 90-95% yield. The results of elemental analysis are not acceptable possibly due to the presence of the corresponding boroxine (XI) and boric acid.

M. Derivatives of Dichloromethaneboronic Acid (X)

a. Attempted Preparation of Boroxine (XI). A mixture of 1.29 g (10 mmole) of dichloromethaneboronic acid (X) and a5 ml of dry benzene was distilled at atmospheric pressure under nitrogen. The benzene-water azeotrope was collected at 70°. The reaction mixture turned brown and then gave a black residue of carbon as the temperature exceeded 110°. No boroxine (XI) was obtained.

b. Acid Derivative of Catechol (XII). A solution of 0.79 g (5 mmole) of dichloromethaneboronic acid and 0.55 g (5 mmole) of catechol in 10 ml of tetrahydrofuran was stirred at room temperature for two hours under nitrogen. The reaction mixture, after drying ($MgSO_4$) and removal of the solvents gave a white solid which turned to a deep purple color immediately after it was isolated. Attempts to obtain the pure sample were unsuccessful.

c. Acid Derivative of Diethanolamine (XIII). Diethanolamine (0.96 ml, 10 mmole) was added dropwise to a clear solution of dichloromethaneboronic acid (1.29 g, 10 mmole) in 10 ml of tetrahydrofuran at room temperature under nitrogen. A white solid formed immediately. The reaction mixture was stirred gently for 10 min. Filtration under nitrogen afforded 1.48 g of $Cl_2HCB(OCH_2CH_2)_2NH$ (XIII) in 70-75% yield. Recrystallization from acetonitrile gave white needles which melted at 134° with decomposition. The

derivative (XIII) is insoluble in many common organic solvents such as ethers, chloroform and benzene but soluble in alcohols, pyridine and hot acetonitrile. It is hydroscopic but rather stable in air by its constant melting point over a period when exposed to air. The nmr spectrum showed an H-C-B and H-N-C singlet at δ 5.25 (1H), an O-CH_2-C triplet at δ 4.35 (2H), and a C-CH_2-N triplet at δ 3.9 (2H) in D_2O.

N. Esters of Dichloromethaneboronic Acid (X)

a. Ethylene Glycol Ester (XIV). A solution of 1.29 g (10 mmole) of dichloromethaneboronic acid and 0.73 ml (11 mmole) of ethylene glycol in 10 ml of tetrahydrofuran containing anhydrous $MgSO_4$ (1 teaspoon) as dehydrating agent was refluxed for two hours under nitrogen. Removal of the $MgSO_4$ by filtration and evaporation of the solvent yielded an off-white compound which melted at 90-99°. Recrystallization from anhydrous ethyl ether gave a white solid, mp 97-99°.

The mass spectrum proved the formation of ethylene glycol ester (XV) by the parent peak at m/e 154 and an isotope peak at m/e 156 with a ratio of intensity 1.7:1, identical to the theoretical value. The nmr spectrum showed singlets at δ 5.3 (1H), δ 4.8 (3-5H), δ 3.8 (4-7H) in variable proton ratios. Both spectra indicated the unexpected compounds present in the product. Further purification was unsuccessful.

b. Ethanol Ester (XV). A solution of 3.87 g (30 mmole) of dichloromethaneboronic acid in 20 ml of ethanol and 15 ml of benzene was distilled at atmospheric pressure under nitrogen. The water-ethanol-benzene azeotrope distilled at 70°. The solvents were removed by distillation under reduced pressure and the main product, which gave a positive flame test for boron, was collected at 26-32°/ 0.5-0.6 mm. The nmr spectrum showed a singlet at δ 5.25 (1H), a quartet at δ 3.5 (2-5H), and a triplet at δ 1.0 (3-7H). Further isolation only gave 10-15% of the pure diethyl dichloromethaneboronate which showed an nmr spectrum with correct proton ratios, (1:4:6).

c. n-Butanol Ester (XVI). In a 100-ml round bottomed flask equipped with a fractionating column were placed 3.87 g (30 mmole) of dichloromethaneboronic acid and 30 ml of n-butanol. The reaction mixture was distilled at atmospheric pressure under a nitrogen atmosphere to give the water-n-butanol azeotrope at 90-91°. The unreacted n-butanol was removed by distillation under reduced pressure until the thermometer registered a sudden rise in temperature. The product distilled almost entirely at 103-104/5-6 mm. However, the product, di-n-butyl dichloromethaneboronate (XVI) (H-C-B peak in the nmr at δ 5.3) constituted a variable proportion of the by-product. tri-n-butyl borate, which boiled too close to that of di-n-butyl dichloromethaneboronate (XVI) to be removed easily by simple distillation.

d. n-Propanol Ester (XVII). A solution of 3.23 g (25 mmole) of dichloromethaneboronic acid in 25 ml of n-propanol was heated to gentle boiling and the water-n-propanol azeotrope was distilled at 70^0 at atmospheric pressure under nitrogen. The unreacted n-propanol was removed by distillation under reduced pressure until the thermometer registered a sudden rise in temperature. Initially, small quantities of the distillate were collected at $85\text{-}97^0/15\text{-}16$ mm, which was proved to be a mixture of tri-n-propyl borate and di-n-propyl dichloromethaneboronate (XVII) by its nmr spectrum. The pure di-n-propyl dichloromethaneboronate (XVII) was obtained at $103^0/15$ mm, $N^{23}D$ 1.4230, in 40% yields. However, the overall preparation of the ester (XVII), starting from the reaction of dichloromethyllithium and trimethyl borate, followed by hydrolysis and esterification, gave a yield of 55-60% based on trimethylborate. The ester (XVII) is soluble in many common organic solvents such as alcohols, ethers, chloroform and benzene. It also found that ester (XVII) is slowly hydrolyzed by the moisture in air to the corresponding boronic acid (X). The nmr spectrum showed an H-C-B singlet at δ 5.32 (1H), an $O\text{-}CH_2\text{-}C$ triplet at δ 4.0 (4H), a $C\text{-}CH_2\text{-}C$ sextet at δ 1.56 (4H) and $C\text{-}CH_3$ triplet at δ 0.95 (6H).

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