Organoboranes. 39. Convenient Procedures for the Preparation of Methylboronic Acid and Trimethylboroxin

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Methylboronic acid and its anhydride, trimethylboroxin, were prepared by three routes. The carbonylation of borane–dimethyl sulfide gives in high yields trimethylboroxin, readily hydrated to methylboronic acid. The reaction of methyllithium with selected trialkoxyboranes and methyl Grignards with 2-methoxy-1,3,2-dioxaborinane yields the corresponding esters, readily hydrolyzed to methylboronic acid in good yields. Methylboronic acid can be dehydrated to trimethylboroxin. Each of these routes was studied in detail to develop efficient, relatively simple routes to both methylboronic acid and trimethylboroxin.

Methylboronic acid, $MeB(OH)_2$, and its anhydride, trimethylboroxin, $(MeBO)_3$, are the simplest of the monoorganylboranes. The preparation of these compounds was first attempted by Khotinsky and Melamed,[1] treating either trimethoxyborane or tributoxyborane with a methyl Grignard. Although this first attempt failed to isolate any desired product, Burg[2] utilized the same reaction under slightly different conditions and successfully isolated small quantities of the methylboronic acid, which was then dehydrated into the corresponding anhydride, trimethylboroxin. This reaction has been used by others to prepare methylboronic acid and other boronic acids.[3,4] Unfortunately, the isolated yields of methylboronic acid are frequently low, less than 33%, caused by a number of factors (vide infra).

Goubeau and Keller have described a high yield route to trimethylboroxin, heating trimethylborane with boric oxide at 300 °C in a sealed bomb[5] (eq 1). However, use of the pyrophoric trimethylborane is not a practical route for the laboratory preparation.

$$Me_3B + B_2O_3 \xrightarrow{300\ °C} (MeBO)_3 \qquad (1)$$

A totally different route was used by Rathke and Brown[6] and others.[7] The carbonylation of borane–tetrahydrofuran complex in the presence of a catalytic amount of a borohydride gave the trimethylboroxin in a yield of 84%.

Boronic acids have found considerable utility as chromatographic reagents for the analysis of bifunctional compounds[8] and for the preparative separation of cis–trans diols.[9] In both cases, the volatility of the cyclic boronate esters influences the ease and speed of the analysis or separation. Were methylboronic acid and trimethylboroxin readily available, it is probable that they would be the reagents of choice for such applications since the low molecular weight of the methylboryl moiety should result in considerably higher volatility of its derivatives. Boronic acids have also been used as protecting agents in the synthesis of carbohydrates[10] and as intermediates to other organoboranes.[11,12]

We have had considerable interest in developing convenient synthetic routes to organoboranes which cannot be realized by direct hydroboration. Thus, methylboronic acid, trimethylboroxin, or their esters may provide easy assess to organoboranes containing methyl groups. In the course of this work, we have developed three convenient routes to trimethylboroxin, methylboronic acid, and their esters.

Results and Discussion

Carbonylation of Borane–Dimethyl Sulfide. The carbonylation of borane–tetrahydrofuran complex to give trimethylboroxin is catalyzed by borohydride.[6] The borane–tetrahydrofuran complex has some limiting characteristics: it is commercially available only as 1 M solutions. These slowly undergo loss of borane due to cleavage of tetrahydrofuran on storage at room temperature. Moreover, this reagent is relatively expensive when compared to other commercially available boranes, such as borane–dimethyl sulfide, BMS. This latter borane complex is available as a neat concentrated liquid, 10 M, stable at room temperature for months. Consequently, it appeared to be the reagent of choice for our studies.

The carbonylation of borane–dimethyl sulfide at atmospheric and higher pressures was studied in detail. There is no significant difference between the reaction of BH_3·THF or BMS and carbon monoxide, other than a somewhat slower rate for the BMS reaction, a rate decrease by a factor of approximately 2. This is presumably due to the slower rate of dissociation of the more stable addition compound into free borane which then reacts with the carbon monoxide. Otherwise, both boranes cleanly react to form trimethylboroxin. The carbonylation reaction is mass transfer limited by the absorption of carbon monoxide into the solvent. Consequently, the observed rate varies with the rate of stirring and can vary significantly from experiment to experiment.

The atmospheric carbonylation reaction must be catalyzed by the addition of a small amount, approximately 1 mol % of a borohydride species. In the absence of any borohydride, only a small amount of carbon monoxide is absorbed, 0.03 equiv, presumably due to the equilibrium formation of a small amount of the carbonyl–borane complex, BH_3·CO. However at higher pressures, ca. 30 atm, in the absence of the catalyst, there occurs a slow absorption of carbon monoxide with formation of trimethylboroxin. It is possible that the higher pressure may shift the equilibrium toward the carbonyl–borane complex,

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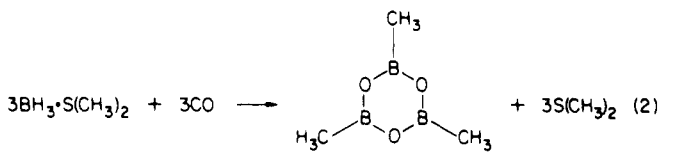
Table I. Methylation of Boron Derivatives with Methylmagnesium Bromide[a]

boron derivative	methylboronic ester, %	dimethylborinic ester, %	Me_3B and $Li(Me_4B)$, %	starting material, %
chlorodimethoxyborane	7	6	12	75
trimethoxyborane	92[b]	2	1	5
triethoxyborane	75	8	[c]	17
triisopropoxyborane	14	43	[c]	43

[a] Estimated accuracy ±5%. [b] Yield can vary from 72% to 92% in individual runs for no apparent reason. [c] No material observed, <1%.

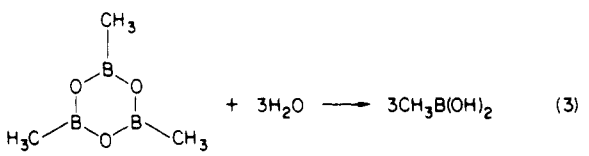
allowing the kinetically slow migration of hydrogen from boron to carbon, forming the boroxin. Unfortunately, considerable byproducts are formed. Therefore, all carbonylation reactions were carried out in the presence of a catalytic amount of lithium borohydride or tetrabutylammonium borohydride, 0.5–2 mol %.

The atmospheric carbonylation of 0.6 mol of borane–dimethyl sulfide in THF (2.5 M) in an adapted automatic hydrogenator[13,14] at room temperature in the presence of 0.5 mol % tetrabutylammonium borohydride proceeds with the smooth uptake of 0.6 mol of carbon monoxide in 12 h. To separate THF (bp 67 °C) from the trimethylboroxin (bp 79–80 °C (751 mmHg)) requires a careful fractional distillation. This yielded 20.3 g of product for a yield of 81% (eq 2).



(2)

Addition of the calculated quantity of water to the THF solution of the boroxin converts it into methylboronic acid,[7] more easily separated from the THF. A yield of 94% of methylboronic acid was realized in this way (eq 3).



(3)

In an attempt to simplify the isolation of trimethylboroxin, more volatile solvents, such as ethyl ether and methylene chloride, were used. In both cases the reactions was considerably slower and gave significant amounts of disproportionation products: trimethylborane, dimethylborane, and polyborate materials (vide infra).[15]

The carbonylation of neat BMS can be carried out at 1 atm but is slow, requiring 50 h for 90% reaction and fails to go to completion, apparently a result of the large excess of free dimethyl sulfide, which competes with the carbon monoxide for the free borane intermediate. However, neat BMS can be carbonylated to trimethylboroxin at 200 psi in 4 h at room temperature. It is essential, however, that the temperature be carefully controlled. The reaction is very sluggish at temperatures less than 15 °C, while at temperatures greater than 30 °C, the reaction can become uncontrollably fast. This results in a loss of 30–40% of the trimethylboroxin transformed into other boron compounds via disproportionation. A solvent greatly adds to the ease of control of the reaction under high-pressure conditions.

Preparation from Methyllithium. A second preparative route to methylboronic acid and its esters is based on methyllithium. A detailed study of the reaction of methyllithium with various trihaloboranes, trialkoxyboranes, and mixed haloalkoxyboranes had been carried out by using conditions similar to those utilized in an early study for the alkylation of *B*-OMe-9-BBN.[16] We discovered that an equivalent of methyllithium reacts rapidly with most of these borane compounds in diethyl ether at −78 °C, forming a mixture of anionic complexes. Protonation of these mixed complexes provided mixtures of methylboron derivatives (eq 4).

$$B(OR)_3 + MeLi \xrightarrow[Et_2O]{-78\ ^\circ C} Li[MeB(OR)_{4-x}] \xrightarrow[HCl]{EE} Me_xB(OR)_{3-x} + ROH + LiCl \quad (4)$$

It was noteworthy that triisopropoxyborane, tri-*sec*-butoxyborane, and triisobutoxyborane gave the monomethylated boronic esters essentially quantitatively.[17] These results can be rationalized in terms of the mechanism. In these cases, the formation of the "ate" complex **1** must proceed essentially irreversibly (eq 5). (In other

$$MeLi + B(O\text{-}i\text{-}Pr)_3 \rightarrow \underset{\mathbf{1}}{Li[MeB(O\text{-}i\text{-}Pr)_3]} \quad (5)$$

cases, such as trimethoxyborane, there must be partial dissociation of the complex into $MeB(OMe)_2 + LiOCH_3$. Reaction with MeLi thus leads to a mixture of compounds $LiMeB(OMe)_3$, $LiMe_2B(OMe)_2$, $LiMe_3B(OMe)$, and $LiMe_4B$.)

Treatment of the "ate" complex **1** with an equivalent of hydrogen chloride[18] (eq 6) liberates the diisopropyl ester of methylborinic acid **2**. The ester can be recovered by distillation in a yield of 71%.

$$Li[MeB(O\text{-}i\text{-}Pr)_3] + HCl \rightarrow \underset{\mathbf{2}}{MeB(O\text{-}i\text{-}Pr)_2} + i\text{-}PrOH + LiCl \quad (6)$$

Hydrolysis of the ester with water proceeds readily (eq 7). The isopropyl alcohol (bp 82 °C) can readily be sep-

$$MeB(O\text{-}i\text{-}Pr)_2 + 2H_2O \rightarrow MeB(OH)_2 + i\text{-}PrOH \quad (7)$$

arated from the water solution of the methylboronic acid by distillation. However, separation of the water from the $MeB(OH)_2$ is difficult. The methylboronic acid is not readily extracted from the water by ethyl ether or any immiscible solvent tried. Fortunately, acetone forms a favorable azeotrope with water (bp 56 °C)[19] and azeotropic distillation of water with acetone provides the pure methylboronic acid in a yield of 79%.

Preparation from Methyl Grignard. Boronic acids and esters have previously been prepared from the reaction of a Grignard reagent with a trialkoxyborane.[1-4] Unfortunately, most of the simpler alkylboronic acids and esters give low isolated yields of the desired derivatives. The reaction of methyl Grignard itself with trimethoxyborane

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Table II. Methylation of Cyclic Boron Derivatives with Methylmagnesium Bromide[a]

cyclic boron derivative	methylboronic ester, %	dimethylborinic ester, %	Me_3B and $Li(Me_4B)$, %	starting material, %
2-chloro-1,3,2-dioxaborolane	17	6	17	60
2-chloro-1,3,2-benzodioxaborole	27	*b*	39	34
2-chloro-1,3,2-dioxaborinane	31	7	24	38
2-chloro-1,3,2-tetramethyldioxaborolane	8	14	1	76
trimethylene borate	73	10	*b*	17
2-methoxy-1,3,2-dioxaborolane	46	*b*	2	52
2-methoxy-1,3,2-dioxaborinane	98	1	*b*	1

[a] Estimated accuracy ±5%. [b] No material observed, <1%.

results in the formation of a variety of methylated boranes, including the pyrophoric trimethylborane, and gives low isolated yields of methylboronic acid, due both to the nonselective methylation and the difficulties involved in isolating this highly water-soluble volatile compound. In the hope of improving the selectivity and ease of isolation, we systematically explored the reaction of methyl Grignard with various boron compounds. These results are summarized in Table I. It was surprising that, unlike the reaction of methyllithium with similar compounds, methyl Grignard exhibits only minor variations in the selectivity.[20] Thus, other factors must be controlling this reaction. The reaction of phenylmagnesium bromide with trimethoxyborane to give phenylboronic acid has been studied in detail by Washburn and co-workers.[21] It was proposed that there is a rapid redistribution of methoxy groups between the various boron species (eq 8–10). The boronic

$$PhMgBr + B(OMe)_3 \rightleftharpoons MgBr[PhB(OMe)_3] \quad (8)$$

$$MgBr[PhB(OMe)_3] \rightleftharpoons PhB(OMe)_2 + MgBr(OMe) \quad (9)$$

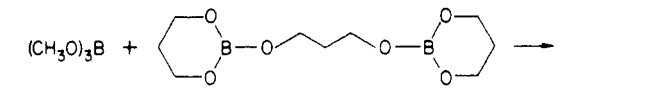
$$MgBr[PhB(OMe)_3] + B(OMe)_3 \rightleftharpoons PhB(OMe)_2 + MgBrB(OMe)_4 \quad (10)$$

ester formed in eq 9 and 10 may react further with additional Grignard reagent to form the borinic ester (eq 11) and, in a similar fashion, the higher arylated products.

$$PhB(OMe)_2 + PhMgBr \rightleftharpoons MgBr[Ph_2B(OMe)_2] \quad (11)$$

The selective monomethylation of an alkoxyborane would seem possible if the redistribution of the alkoxy groups could be suppressed, for example, by using a cyclic or bicyclic alkoxyborane. A series of cyclic monochlorodialkoxyboranes were prepared[22-24] and reacted with methylmagnesium bromide in ether at −78 °C. Analysis by ^{11}B NMR of the protonated reaction established that a mixture of methylated boranes were formed.

The (methylchloro)dialkoxyborate formed is expected to undergo a facile elimination and precipitation of the magnesium halide, forming the cyclic methyldialkoxyborane. This compound would be susceptible to additional attack by another equivalent of Grignard, giving rise to higher methylated boranes. The bicyclic trialkoxyboranes that were attempted, triethanolamine borate and tris(hydroxymethyl)ethane borate, were insoluble in the aprotic solvents at reaction conditions and gave a mixture of products. However, trimethylene borate gave good selectivity with methylmagnesium bromide and 2-methoxy-1,3,2-dioxaborinane,[25] readily prepared merely by mixing trimethylborate with trimethylene borate, gave one product in better yield than either trimethylene borate or trimethoxyborane (eq 12 and 13). Trimethoxyborane in



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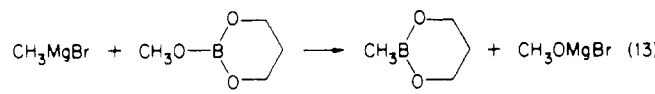

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our hands sometimes gave variable results, apparently dependent on other factors. The 2-methoxy-1,3,2-dioxaborinane consistently gave excellent selectivity with methylmagnesium chloride, bromide, or iodide. On the other hand, 2-methoxy-1,3,2-dioxaborolane gave much poorer results (Table II).

The reaction of 0.05 mol of 2-methoxy-1,3,2-dioxaborinane with an equivalent of methylmagnesium bromide in ether, 0.5 M, at −78 °C, followed by protonation with anhydrous hydrogen chloride, was extracted with pentane and isolated as the sodium hydroxide complex. This complex was hydrolyzed and transesterified to the methyldimethoxyborane to remove the 1,3-propanediol and isolated as the sodium hydroxide complex. The protonation with hydrogen chloride in ether afforded 2.2 g of methylboronic acid, a yield of 73%.

The hydrolysis of the esters to methylboronic acid could be achieved by treatment with sodium hydroxide and evaporation of the water away from the sodium salt $CH_3B(OH)_3Na$ followed by suspending the salt in ether and treating it with the calculated quantity of hydrogen chloride in ether (eq 14 and 15).

$$CH_3B[OCH(CH_3)_2]_2 + NaOH \rightarrow CH_3B(OH)_3Na + 2(CH_3)_2CHOH \quad (14)$$

$$CH_3B(OH)_3Na + HCl \xrightarrow{\text{ethyl ether}} CH_3B(OH)_2 + NaCl \quad (15)$$

Hydration–Dehydration. Methylboronic acid and its anhydride, trimethylboroxine, can be interconverted. The addition of 3 equiv of water to neat trimethylboroxin results in the rapid exothermic quantitative precipitation of methylboronic acid. The reverse reaction is somewhat more difficult to achieve in high yield. Suitable dehydrating agents for this reaction are not immediately obvious. Basic dehydrating agents form addition complexes with the boronic acid and therefore are unsuitable.[2] Acidic agents, such as phosphorus pentoxide and 85% phosphoric

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acid, have failed to produce any product, while concentrated sulfuric acid has given only moderate yields of trimethylboroxin, 36%.[4] Azeotropic removal of water could not easily be carried out due to the high relative volatility of methylboronic acid and the small differences in boiling points of the azeotropes. Matteson[26] was able to circumvent some of these problems by preparing the pyridine complex trimethylboroxin (bp 139–143 °C (700 mm Hg)) by using a benzene–pyridine azeotrope and an efficient distillation column. This gave an isolated yield of 82% for this complex. Others have reported that the gas-phase dehydration of methylboronic acid over anhydrous calcium sulfate, 0.25 equiv, gave unspecific yields of trimethylboroxin.[2,7] We have monitored the disappearance of the hydroxyl absorption band at 3400 cm^{-1} by infrared spectrometry in the dehydration of methylboronic acid in ether. Magnesium sulfate did not result in the formation of trimethylboroxin, while 4 Å molecular sieves and calcium sulfate rapidly removed water of dehydration, but also absorbed significant quantities of boron material. We have also found that either calcium hydride in refluxing ether or thionyl chloride[3] at room temperature gives relative good yields of isolated trimethylboroxin, 58% and 63%, respectively.

Physical Properties. Trimethylboroxin, $(MeBO)_3$, the cyclic trimeric anhydride of methylboronic acid, is a relatively volatile compound, bp 79–80 °C. It is mildly air-sensitive and can be stored under an inert gas for extended periods of time; however, it readily reacts with water to form the solid methylboronic acid. The melting point of this compound is variable, dependent not only on the purity but also on the degree of hydration. The melting point has been reported between 73 to 100 °C.[4] The methylboronic acid can be purified by recrystallization from benzene–petroleum ether or by sublimation (0.05 mm of Hg at 100 °C). On stainding at room temperature and atmospheric pressure, this compound slowly sublimes. Storage in air for 47 days resulted in the oxidation of only 2–3% of the material, suggesting only mild air sensitivity.

Trimethylboroxin is infinitely soluble in all nonprotic solvents tested. However, methylboronic acid is soluble in only relatively polar solvents at room temperature: acetone, 5.8 M; water, 5.5 M; tetrahydrofuran, 5.4 M; ethyl ether, 2.0 M; ethyl acetate, 1.9 M; methylene chloride, 1.0 M; chloroform, 1.0 M; benzene, trace amount hexane, trace amounts.

The nuclear magnetic resonance spectra of both the acid and boroxine are summarized in Table III. The infrared spectrum of these two compounds are virtually identical except for the very strong hydroxyl absorption band at 3400 cm^{-1}. The mass spectrum of the boroxin gives a molecular ion at m/z 126 and very strong loss of a methyl group at m/z 111. The mass spectrum of methylboronic acid does not show a molecular ion and undergoes a strong loss of the methyl group, forming an ion at m/z 45.

Conclusion

The reaction of carbon monoxide with borane–dimethyl sulfide in the presence of borohydride catalyst provides an excellent synthetic route of trimethylboroxin in yields of 81–84%. Hydration of the boroxin with water priovides methylboronic acid in a yield of 94%. The reaction of methyllithium with triisopropylborate gives a complex, readily converted by hydrogen chloride in diisopropyl methylboronate. Similarly, treatment of 2-methoxy-1,3,2-dioxaborinane with methylmagnesium bromide gives the corresponding ester of methylboronic acid in 98% yield. These esters are readily converted to the methylboronic acid. Finally, dehydration of methylboronic acid, either with calcium hydride or thionyl chloride, forms trimethylboroxin. Consequently, these developments provide three reliable methods for the preparation of either trimethylboroxin or methylboronic acid.

Experimental Section

General Comments. All glassware was dried at 140 °C for at least 3 h, assembled hot and cooled under a stream of dry nitrogen. All reactions were carried out under a static pressure of nitrogen.[27] Anhydrous ethyl ether (Mallinckrodt) was stored over 4-Å molecular sieves and used without further purification. Tetrahydrofuran was distilled from sodium benzophenone ketal and stored under a nitrogen atmosphere.

The borane–dimethyl sulfide, borane–tetrahydrofuran, and lithium, or tetrabutylammonium borohydrides are commercial materials (Aldrich). The concentrations of these materials were estimated by hydrolysis.[27] The trialkoxyboranes are available from commercial sources (Aldrich or Callery) or are prepared by using the method of Brown and Krishnamurthy.[28] The haloalkoxyboranes were prepared by redistribution of the trialkoxyborane and boron trichloride or the addition of an alcohol or diol to boron trichloride.[22-24] The anhydrous hydrogen chloride in ether was prepared from hydrochloric acid and sulfuric acid with the automatic hydrogenator. The ether solution was standardized by titrating a hydrolyzed aliquot with sodium hydroxide.

The atmospheric carbonylation of boranes was carried out in a modified automatic hydrogenator, Brown[13] apparatus, generating carbon monoxide from formic acid and sulfuric acid.[13] The carbonylations at higher pressures were carried out by using a Parr Instruments 0.31 L "mini" pressure reactor, Model 4561.

The ^{11}B and ^{13}C NMR spectra were recorded on a Varian FT-80A spectrometer, 25.517 and 20.000 MHz, relative to boron trifluoride etherate and tetramethylsilane, respectively. Proton spectra were obtained on a Varian T-60 relative to tetramethylsilane. The infrared spectra were recorded by using a Perkin-Elmer 1420 ratio recording spectrometer. The mass spectra data were obtained from a Finnigan, Model 4000, gas chromatographic mass spectrometer.

General Procedure for the Atmospheric Carbonylation of Borane. The experimental detail for the atmospheric carbonylation of trialkylboranes has been previously described[14] and was essentially the same as used here. The apparatus was oven-dried, assembled hot, and cooled under a flow of nitrogen. The carbon monoxide was generated from the slow addition of formic acid to concentrated sulfuric acid at 90 °C. A drying tube filled with a mixture of Drierite and Ascarite was placed between the generation and reaction flask for the removal of water and carbon dioxide. Borane–dimethyl sulfide (600 mmol, 60 mL of 10 M, neat material) in 250 mL of tetrahydrofuran solution was placed in the 500-mL reaction flask containing a magnetic stirring bar. The apparatus was checked for leaks and then flushed with carbon monoxide generated from 2 mL of formic acid. The catalyst, tetrabutylammonium borohydride (0.7 g, 2.85 mmol), was dissolved in 3 mL of THF and the solution added via syringe to the borane solutions. Absorption of carbon monoxide began shortly after the reaction solution was rapidly stirred. The extent of the reaction was followed by measuring the amount of formic acid added to the sulfuric acid, 1 mL of formic acid generated 26.6 mmol of carbon monoxide. The borane solution was maintained at approximately 25 °C by using a water bath. The reaction was approximately 90% complete after 6–8 h at which time the absorption of carbon monoxide had slowed considerably. The reaction was allowed to proceed for a total of 12–16 h. At this point, 0.65 mol of water (11.7 g) was carefully added to the solution, and a small amount of gas was evolved. This solution was transferred to another round-bottom flask, and the dimethyl sulfide and tetrahydrofuran were removed at 14 mm of Hg

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Table III. Nuclear Magnetic Resonance Data (δ) of Methylboronic Acid and Methylboroxine

	^{11}B	^{1}H	^{13}C
methylboronic acid	+31.9 (D_2O)	+0.26 (br) ($CDCl_3$)	−3 (br s) (D_2O)
trimethylboroxin	+32.5 ($CDCl_3$)	+0.25 (br s) ($CDCl_3$)	−3 (br s) ($CDCl_3$)

pressure at 0 °C. The resultant white solid, methylboronic acid, was isolated in 94% yield (33.75 g).

Alternatively, 0.79 g (14 mmol) of acetone was added to the reaction mixture in place of water, destroying the residual borane. This reaction mixture was distilled through an efficient 90-cm distillation column separating the dimethyl sulfide and tetrahydrofuran from trimethylboroxin (bp 79–80 °C 748 mmHg)), isolating 20.4 g: 81% yield; n^{20}_D 1.3638; proton NMR (neat) δ 0.15–0.35 (br, 9 H); boron NMR (neat) +32.5 ppm (s).

General Procedure for the Carbonylation of Borane at Pressures Greater Than 1 Atm. The base of a Parr "mini" reactor was oven-dried and cooled under a stream of nitrogen and assembled. The neat borane–dimethyl sulfide (500 mmol, 50 mL) was added along with 2 mmol of lithium borohydride in 1 mL of ether. The reactor was assembled and pressurized to 200 psi with carbon monoxide (Matheson). Careful maintanence of the internal temperature to less than 25 °C by using an external water bath was essential to minimize disproportionation, repressurizing the reactor to 200 psi three times and adding 0.5 mol of carbon moxide in 6 h time, at which point the absorption of carbon monoxide had ceased and the excess was vented. The reaction was transferred to the distillation apparatus. Remaining in the reactor was 4.1 g of polyborate material. Distillation of the clear solution gave 10.66 g (85 mmol) of trimethylboroxin: bp 79–80 °C (748 mm Hg); 51% yield.

Preparation of Methylboronic Acid from Methyllithium. To a 500-mL round-bottom flask with a magnetic stirring bar, side-arm, and gas inlet adaptor was added 330 mL of anhydrous ethyl ether and 100 mmol (19.0 g, 22.95 mL) of triisopropoxyborane. The solution was cooled with a dry ice–acetone bath. A 100-mmol (68-mL) sample of methyllithium was added slowly via double-ended needle in 1 h. The reaction mixture was stirred an additional hour and allowed to warm to room temperature with stirring, (3 h). The mixture was then cooled to 0 °C, 107 mmol of anhydrous hydrogen chloride in ether was added by syringe, and the solution stirred for 0.5 h. The ether solution was decanted by double-ended needle from the lithium chloride precipitate and combined with the ether washings of the solid. The boronic ester was hydrolyzed with 20 mL of water and the ether removed by atmospheric distillation. The water was removed by azeotropic distillation with 600 mL of acetone, and the residue was dried under a stream of nitrogen, yielding 4.7 g, (79 mmol): 79% yield; mp 88–90 °C; proton NMR (D_2O) δ 0.13 (br, s, 3 H), 4.5 (br, s, 2 H); boron NMR (D_2O) +32.6 ppm (s).

General Procedure Determining the Selectivities of Methyl Grignard with Various Boron Compounds. To a 50-mL flask with a side-arm fitted with a magnetic stirring bar and gas inlet adaptor was added 10 mL of ether and 5 mmol of the boron compound. The solution was cooled with a dry ice–acetone bath, and 5 mmol of methylmagnesium bromide or methylmagnesium iodide in ether was added dropwise via syringe. The resultant mixture was stirred for a 0.5 h and then allowed to warm to room temperature with stirring for an additional 0.5 h. The reaction mixture was cooled to 0 °C, and 5 mmol of anhydrous hydrogen chloride in ether was added. After the mixture was warmed to room temperature, a sample was analyzed by ^{11}B NMR for the various methylated boranes. The percentages of trimethylborane, starting material, and borinic and boronic esters were estimated by using peak heights for these species. This procedure appears to give good mass balance, ±5% for compounds having similar peak width. These results are summarized in Tables I and II.

Preparation of Methylboronic Acid from Methyl Grignard. 2-Methoxy-1,3,2-dioxaborinane was prepared by the redistribution of 16.67 mmol of each: trimethylene borate (4.065 g, 3.52 mL) and trimethoxyborane (1.732 g, 1.89 mL) in a 250-mL side-armed flask with a magnetic stirring bar and gas inlet adaptor. After the solution was stirred for 15 min, 100 mL of anhydrous ether was added, the 2-methoxy-1,3,2-dioxaborinane solution was cooled in a dry ice–acetone bath, and 50 mmol (20.0 mL) of methylmagnesium chloride was added dropwise via syringe in 0.5 h. The reaction was stirred for 3–4 h before it was allowed to warm to room temperature. A 100-mL solution of pentane was added and stirred an additional hour. The reaction mixture was protonated with 53 mmol of anhdrous hydrogen chloride in ether (17.7 mL) at 0 °C and stirred for 0.5 h. The clear supernatant was transferred from the solid magnesium salt and combined with the three 50-mL pentane washings of the solid. The pentane solution was extracted with 60 mmol of sodium hydroxide in 10 mL of water, and the pentane layer was discarded. The water was removed under a reduced pressure (14 mm of Hg) at 60 °C until a white solid was obtained. This complex was destroyed by the addition of 6 mL of concentrated hydrochloric acid and 30 mL of methanol. The methyl ester of the boronic acid was distilled from the solution into 55 mmol of sodium hydroxide in 9.2 mL of water. The sodium salt of methylboronic acid was isolated by removing the volatiles under reduced pressure. To this solid was added 55 mmol of anhydrous hydrogen chloride in ether, and the solution was stirred overnight. The solution of methylboronic acid was transferred to a tared vial and the ether removed under a reduced pressure, obtaining 2.2 g (36 mmol) of methylboronic acid (73% yield).

Dehydration of Methylboronic Acid to Trimethylboroxin Using Calcium Hydride. Methylboronic acid (5.98 g, 100 mmol) was placed in a 100-mL round-bottom flask containing 100 mmol (4.21 g) calcium hydride and a magnetic stirring bar and fitted with a reflux condenser. The boronic acid was dissolved in 50 mL of ether and refluxed for 3 h. During this time the hydrogen gas was vented. The reaction mixture was cooled, and the clear supernatant was transferred via double-ended needle to a distillation flask and combined with the ether washings (2 × 20 mL) of the solid. The careful atmospheric pressure distillation gave 2.42 g (19.3 mmol, 58% yield) of trimethylboroxin.

Dehydration of Methylboronic Acid to Trimethylboroxin Using Thionyl Chloride. In a 35-mL side-armed flask fitted with a magnetic stirring bar and gas inlet adaptor was placed 100 mmol of methylboronic acid (5.98 g). The thionyl chloride (100 mmol, 7.4 mL) was added via syringe. The reaction was exothermic with a slow evolution of sulfur dioxide and hydrogen chloride. The careful distillation gave 2.63 g (21.0 mmol, 63% yield) and 0.7 g (11.7 mmol) of solid methylboronic acid as distillation residue.

General Procedure Determining the Solubility of Methylboronic Acid in Various Solvents. The solubility of methylboronic acid was estimated by using two procedures. The first procedure, 3 mL of the solvent was added to an ampule containing 1.5 g of methylboronic acid. The mixture was stirred for at least 15 min at room temperature to ensure that the solution was saturated. Exactly 1.00 mL of this clear solution was transferred to a tared ampule, and the solvent was removed under a stream of nitrogen. This gave an estimated accuracy of ±10%. The solubilities of methylboronic acid: in acetone, 5.8 M; in tetrahydrofuran, 5.4 M; in ethyl ether, 2.0 M; in ethyl acetate, 1.9 M; in benzene, trace amount; in hexane, trace amount.

The second procedure was used to only estimate the solubility. A known amount of methylboronic acid was placed in an ampule, and the solvent was slowly added via calibrated syringe with stirring until all solid dissolved: water, 5.4 M; methylene chloride, 1.0 M; chloroform, 1.0 M.

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Registry No. $BH_3S(CH_3)_2$, 13292-87-0; $MeB(OH)_2$, 13061-96-6; $(MeBO)_3$, 823-96-1; $[OCH(CH_3)_2]_3B$, 5419-55-6; $(CH_3O)_3B$, 121-43-7; $(CH_3CH_2O)_3B$, 150-46-9; Me_3B, 593-90-8; $Li(Me_4B)$, 2169-38-2; MeMgBr, 74-83-9; MeLi, 917-54-4; CO, 630-08-0; tetrabutylammonium borohydride, 33725-74-5; lithium borohydride, 16949-15-8; methylmagnesium iodide, 74-88-4; chlorodimethoxyborane, 868-81-5; dimethyl methylboronate, 7318-81-2; methyl dimethylborinate, 4443-43-0; diethyl methylboronate, 86595-26-8; ethyl dimethylborinate, 86610-16-4; diisopropyl methylboronate, 86595-27-9; isopropyl dimethylborinate, 95407-90-2; 2-methoxy-1,3,2-dioxaborinane, 1121-48-8; 2-chloro-1,3,2-dioxaborolane,

1192-03-6; 2-chloro-1,3,2-benzodioxaborole, 55718-76-8; 2-chloro-1,3,2-dioxaborinane, 1003-43-6; 2-chloro-1,3,2-tetramethyldioxaborolane, 67975-91-1; trimethylene borate, 52876-41-2; 2-methoxy-1,3,2-dioxaborolane, 1003-24-3; 2-methyl-1,3,2-dioxaborolane, 37003-57-9; 2-methyl-1,3,2-benzodioxaborole, 78336-63-7; 2-methyl-1,3,2-dioxaborinane, 51901-48-5; 2-methyl-1,3,2-tetramethyldioxaborolane, 94242-85-0; calcium hydride, 7789-78-8; thionyl chloride, 7719-09-7; methyl chloride, 74-87-3.

Electrophilic Cleavages in $(CH_3)_3SnCH_2M(CH_3)_3$ (M = Sn, Ge, Si, C). 1. Product Distribution

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The extent to which Sn–CH_2 and/or Sn–CH_3 cleavage occurs in $(CH_3)_3SnCH_2M(CH_3)_3$ (M = Sn, Ge, Si) in reactions with several electrophiles has been determined. With iodine and with bromine in various solvents both sites are attacked with Sn–CH_2 cleavage favored for nonpolar solvents and for M = Sn. Protolysis leads to Sn–CH_2 cleavage only, and this site appears to be activated by the $(CH_3)_3M$ groups. On the other hand organometallic electrophiles exclusively attack the Sn–CH_3 groups and the $(CH_3)_3MCH_2$ groups are deactivating. With all reagents only the Sn–CH_3 groups are reactive in $(CH_3)_3SnCH_2C(CH_3)_3$. The complex mechanistic situation for halogenolysis can lead to variations in the relative reactivities of various sites during reaction and introduce serious errors into internal selectivity measurements.

Introduction

Substrates of the type $(CH_3)_3SnCH_2M(CH_3)_3$, where M = Sn, Ge, Si, and C, may undergo reactions with electrophiles to cleave the Sn–CH_3 and/or the Sn–CH_2 bonds. Comparison of the individual rates of these processes with one another and with the reference substrate $(CH_3)_4Sn$ provides information on the substituent effects of the $(CH_3)_3M$ and $(CH_3)_3MCH_2$ groups. In this paper we concentrate attention on the extent of reaction at these two sites and will deal with the rates of the processes, particularly halogenolysis for which there are a number of complications, subsequently.

A number of reactions of these related substrates have been described previously. The most reactive member of this set, M = Sn, when first prepared was reported[1] to be inert toward bromine at ambient temperatures, although reaction took place slowly in refluxing CCl_4 to yield $(CH_3)_2SnBr_2$ and other volatile products. Both Sn–CH_3 and Sn–CH_2 cleavage has clearly occurred but there is no indication of the preferred path. However, a recent report[2] notes that with bromine in a methanol/carbon tetrachloride mixture at −60 °C the major products are $(CH_3)_3SnBr$ and $(CH_3)_2SnBr_2$ implying predominant Sn–CH_2 cleavage. On the other hand, the reaction of $[(CH_3)_3SiCH_2]_2Sn(CH_3)_2$ with Br_2/CCl_4 gives a 65% yield of Sn–CH_3 cleavage product with a 31% yield of $(CH_3)_3SiCH_2Sn(CH_3)_2Br$, the result of Sn–$CH_2$ cleavage.[3] Furthermore, it is well-known that the solvent plays an important role in the differential reactivity of the alkyl groups in tetraalkylstannanes[4] (see below), and in a case related to the present studies, it is reported[5] that Br_2/CCl_4 opens the ring of 1,1,3,3-tetramethyl-2,2,4,4-tetrakis(trimethylsilyl)-1,3-distannacyclobutane whereas Br_2/CH_3OH can be employed to cleave one Sn–CH_3 bond.

Table I. Halogenolysis of $(CH_3)_3SnCH_2M(CH_3)_3$—Product Composition

reagent/solv	% reaction at CH_2[a]			
	M = C	Si	Ge	Sn
Br_2/DMF[b]	<<1	5	6	16
Br_2/CH_3OH	<<1	10	<<1	31
Br_2/CH_2Cl_2	<<1	10	7	10
$Br_2/CHCl_3$	<<1	13	6	13
Br_2/CCl_4	<<1	24	31	75
I_2/C_6H_5Cl	<<1	4	9	12.5
I_2/CH_3OH	<<1	8	10	24
I_2/CCl_4	<<1	10	12	54

[a] Mean of several reactions with ca. 0.1 M reactants analyzed by ^1H NMR. [b] Dimethylformamide.

Iodinolysis of $(CH_3)_3SnCH_2Si(CH_3)_3$ without solvent resulted[3] in a 79% yield of $(CH_3)_3SiCH_2I$. Presumably this was accompanied by $(CH_3)_3SnI$ although not mentioned. Reaction with $I_2/CHCl_3$ was used to convert $(CH_3)_3SnCH_2Sn(CH_3)_3$ to 2 equiv of $(CH_3)_3SnI$ and impure CH_2I_2 thus providing its structure proof.[6] These two results imply almost exclusive Sn–CH_2 cleavage.

Reaction of $(CH_3)_3SnCH_2Sn(CH_3)_3$ with 1 equiv of dry HCl has been reported[7] to yield chlorotrimethylstannane and tetramethylstannane in equal proportions, while excess acid reacts with the latter to form methane. Clearly the Sn–CH_2 site is once again preferentially attacked.

We have found[8] that substrates of the type $(CH_3)_3SnM(CH_3)_3$ may react at different sites with acids and with

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