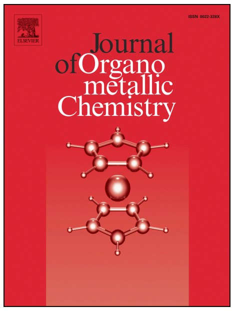


Preparation of alkyltrifluoroborates via Matteson Hydroboration Method

David J. Zillman, Thomas E. Cole

PII: S0022-328X(18)30194-3
DOI: 10.1016/j.jorganchem.2018.03.027
Reference: JOM 20377

To appear in: *Journal of Organometallic Chemistry*

Received Date: 1 January 2018
Revised Date: 15 March 2018
Accepted Date: 16 March 2018

Please cite this article as: D.J. Zillman, T.E. Cole, Preparation of alkyltrifluoroborates via Matteson Hydroboration Method, *Journal of Organometallic Chemistry* (2018), doi: 10.1016/j.jorganchem.2018.03.027.

Preparation of Alkyltrifluoroborates via Matteson Hydroboration Method

David J. Zillman and Thomas E. Cole*

Department of Chemistry & Biochemistry, San Diego State University, San Diego, California 92182-1030
tcole@mail.sdsu.edu

ABSTRACT

An efficient one-pot method for synthesis of simple alkyltrifluoroborate salts has been developed. Alkyldichloroboranes, prepared by the Matteson Hydroboration Method using *in situ* generated $HBCl_2$, were esterified with 2-propanol, treated with aqueous KHF_2 and isolated using standard procedures. The overall isolated yields were generally greater than 90% when fluoridation was conducted under nitrogen. In contrast, reactions using "open air" conditions showed oxidation and gave lower yields of the alkyltrifluoroborate salts.

Keywords:
Matteson Hydroboration Method
Hydroboration
Fluoridation
Potassium Alkyltrifluoroborate salts
Alkylboronic acids

1. Introduction

Boronic compounds are very important intermediates for organic synthesis and medicinal chemistry due to their versatility in synthesizing complex molecules. These reagents have found extensive use in the metal catalyzed carbon-carbon bond forming reactions such as; Suzuki-Miyaura [1] and Liebersking-Srogl [2] coupling reactions, conjugate additions [3] and carbon-heteroatom Chan-Lam couplings [4]. The boronic derivatives can also be used as building blocks to form new types of boronic compounds using homologation [5] and transformation of pendent functional groups [6].

A number of routes have been developed to prepare alkylboronic compounds using the hydroboration reaction. Catecholborane is slow to hydroborate most alkenes, therefore, require longer reaction times and elevated temperatures [7]. The related pinacolborane is even less reactive, requiring a catalyst to achieve good yields [8]. Catecholborane can also be catalyzed, however, the metal catalyst may adversely affect regioselectivity [9]. Complexed dihaloboranes have frequently been used to prepare the alkylboronic derivatives. Unfortunately, the dichloroborane reagents form a mixture of organoborane products, especially with less reactive alkenes [10]. In contrast, dibromoborane cleanly forms the corresponding alkyldibromoboranes, but requires 5-20 mol% boron tribromide to catalyze the hydroboration reaction. Matteson developed a simple and efficient route to alkyldihaloboranes using boron trihalides and trialkylsilanes, circumventing the limitations of preformed dihaloboranes [11,12]. In addition, the Matteson Hydroboration Method using ligand free $HBCl_2$ is faster, cheaper and less expensive than other hydroboration reactions. While we had good success in using this method to prepare alkyldichloroboranes for the conversion to the corresponding alkyldimethylboranes [13], attempts to convert the alkyldichloroboranes into the boronic acids or esters gave low yields and purity. It is believed that the trialkylhalosilane side-products interfere with the boronic acid isolation [14,15,16]. Matteson's solution for the removal of sterically bulky diol ligands from boronic esters using potassium bifluoride suggested this as a solution to the separation of the boronic and silane materials [17]. The separation of the potassium alkyltrifluoroborate salt from the silane and other organic products are expected be straight forward and high yielding. In addition, organotrifluoroborate salts have a number of desirable properties; they are stable to air and moisture allowing long term storage. The preparation of organyltrifluoroborates and their application to organic synthesis have been reviewed [18,19]. In contrast to the boronic acids, they have known compositions and are readily purified. The tetracoordinate bonding gives extraordinary stability, protecting the boron. Yet, these organotrifluoroborates can also be readily converted into the corresponding boronic acids and esters [20,21,22,23]. Literature shows a rather significant variation in the isolated yields in the conversion of the boronic acids or esters to the corresponding alkyltrifluoroborates, generally between 70-90% yields. We wished to develop an effective route using the non-coordinated $HBCl_2$ to form the corresponding potassium alkyltrifluoroborate salts with overall greater than 90% isolated yields.

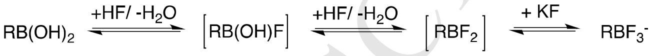
2. Results and Discussion

Our initial investigation was focused on the fluoridation step, since ligand free $HBCl_2$ gave excellent selectivity, generally > 98% formation of the alkyldichloroborane. The major variations are attributed to inefficient conversion of the boronic acids or esters to the trifluoroborate salt; or cleavage of the alkyl group during treatment with KHF_2. Preformed alkylboronic acid was used in preliminary reactions to avoid potential interference of the silane products formed in the Matteson Hydroboration Method. The *n*-decyl group was chosen because of the lower volatility and aqueous solubility of the boronic acid and possible cleavage products, which would allow for a more accurate determination of the mass balance. The boronic acid was prepared by hydroboration of 1-decene with dibromoborane dimethyl sulfide with 5 mol% tribromoborane, then hydrolyzed to give the *n*-decylboronic acid [24]. Fluoridation reaction conditions were based on the methods reported by Vedejs [25] and Genêt [26]. Decylboronic acid was first dissolved in methanol then a concentrated aqueous solution of the KHF_2 was then added to the open flask, resulting in an immediate formation of a thick slurry. The reaction was stirred for 15-30 min and the volatiles, were removed *in vacuo* until the solid appeared dry. The solid material was dissolved in hot acetone, inorganic salts were removed by filtration, acetone was removed *in vacuo* and the solid was then triturated with ether to afford ca. 76% yield of the potassium decyltrifluoroborate. The ^{11}B NMR spectrum in acetone-d_6, showed a single species at 5.1 ppm, corresponding to the expected potassium alkyltrifluoroborate salt. The proton, carbon and fluorine NMR spectra were also in agreement with literature values [27]. The ether trituration liquid was evaporated to dryness yielding a colorless oil. The ^{11}B NMR spectra showed a very weak signal at 32 ppm, indicating the boron acid was a minor constituent of the oil. However, the amount of this material appeared to account for the majority of the missing mass balance. This oil was analyzed by capillary gas chromatography. A single major peak corresponding to the retention time of a C_{13} compound was seen, but no decene or decane was detected. Proton NMR spectrum showed a downfield triplet at 3.62 ppm, consistent with a primary alcohol. The ^{13}C NMR spectrum showed 10 unique resonances with the furthest downfield signal at 63.12 ppm. These spectral values were in agreement with literature values for 1-decanol [28]. These results indicated oxidation of the alkylboronic acid, forming the corresponding 1-decanol.

In an effort to determine at which point oxidation occurred, we prepared and isolated a sample of 1-decylboronic acid by the sodium bicarbonate hydrolysis of potassium *n*-decyltrifluoroborate under an inert atmosphere. The ^{11}B NMR spectrum showed single specie at 30.8 ppm with no detectable materials in the region of the boric acids between 17-20 ppm. The remainder of this boronic acid was dissolved in a methanol/water mixture (90/10) and stirred in air for 24 h at room temperature. The ^{11}B NMR spectrum showed a trace amount, ~ 0.1%, of boric acid material indicating very little oxidation even over an extended period of time. This result is consistent with the air-stability of boronic acids in the presence of water.

While alkylboronic acids are generally considered to be stable toward oxidation, we have noted occasional air-sensitivity that is largely dependent on the isolation technique and subsequent handling of the solid material [29]. Alkylboronic acids isolated from solvent containing water using modestly reduced pressures at lower temperatures over minimal time, showed no indication of oxidation after exposure to air as seen in ^{11}B NMR spectra by the absence of boric acid at ca. 18 ppm. This is consistent with the general agreement that hydrated boronic acids are stable in air. However, exposure of solid boronic acids to reduced pressure for extended periods of time, or higher temperatures or prolonged sweeping of flasks with dry nitrogen, leads to a change in appearance from a dull translucent white to a bright opaque white solid. To illustrate this effect, an ether extract containing decylboronic acid was pumped down, ca. 5mmHg, using evaporative cooling, < 0 °C, until the ether was just removed and a dull translucent white solid remained. This sample was exposed to air for 7 min, then under nitrogen, dissolved in methanol/water (6:1). The boron NMR spectrum showed in addition to the expected boronic acid at 30.8 ppm, ~ 3% of boric acid at 18.2 ppm. Repeating the isolation of the decylboronic acid under essentially identical conditions, but allowing the ether to be removed over a longer period of time while the sample warmed to room temperature, gave a change in color from dull white to opaque bright white. Exposure to air for 7 min, followed by transfer to a nitrogen atmosphere and dissolving in methanol/water mixture gave an increased amount of boric acid to approximately 7%. As a consequence, all boronic acids used in this study were isolated under conditions that showed reduced sensitivity to oxidation.

Next, we wanted to study the effects of air on the reaction of KHF_2 with decylboronic acid. The decylboronic acid was dissolved in methanol under a nitrogen atmosphere. This solution was then exposed to air for 5-7 minutes before a concentrated aqueous solution of KHF_2 (2.2 eq) was added and the mixture stirred for approximately 15 minutes. The volatiles were removed under reduced pressure to give a dry solid, then under an inert atmosphere and the entire sample was dissolved in a 3:1 mixture of acetone/D_2O. The ^{11}B NMR spectrum showed three species. The largest corresponded to the expected alkyltrifluoroborate with an area of 74.2%. This amount is in agreement with the earlier isolated yield. There was a relative small amount of unreacted boronic acid, 7.3%. In addition, there was an upfield quartet at -0.22 ppm that corresponds to the potassium tetrafluoroborate with 18.5% area. The presence of this signal indicated oxidation of the boronic acid forming boric acid, which is converted to the tetrafluoroborate. Since no boric acid was present in the initial decylboronic acid, oxidation had to occurred during fluoridation since very little oxidation of decylboronic was found in methanol solution alone. While boronic acids are relative air-stable and organotrifluoroborates are inert to oxygen, the intermediates formed in this reaction are air-sensitive. Alkydifluoroboranes, RBF_2, are known to be air-sensitive [30,31], while alkylhydroxyfluoroboronic acids, RB(OH)F, are also expected to be reactive to oxygen, (Scheme 1). This indicates oxidation of the intermediates can represent a significant loss of



Scheme 1. Intermediates formed in the fluoridation of boronic acids to give trifluoroborates. (remove –graphics ChemDraw Helvetica ~ 7 pt, template ACS document 1996, scaled 60%. Planned width 90 mm, single column. - remove)

boron materials. The amount of oxidation is likely to be dependent on transfer of oxygen into the reaction solution.

It remained to be seen whether the presence of the silane products from the Matteson Hydroboration Method has an adverse effect on the fluoridation. Decyldichloroborane was prepared using $HBCl_2$ as described in the experimental. The alkyldichloroborane was hydrolyzed under nitrogen, using an ether/water mixture, washed with brine and the ether removed under vacuum to give the crude boronic acid/silane mixture. This material was dissolved in methanol in air and a concentrated KHF_2 aqueous solution, 2.2 eq, was added and stirred 15 min. Removal of volatiles was complicated with persistent foaming, resulting in a minor loss of material, eventually forming a dry solid. The crude alkyltrifluoroborate mixture was dissolved in hot acetone, filtered to remove the insoluble materials. Acetone was then removed under reduced pressure, to give solid material. This white solid was triturated with ether, filtered in air, washed with additional ether and then dried as described in the experimental procedure. The yield of potassium *n*-decyltrifluoroborate was 78.9%. While there was some loss of product due to foaming, the isolated yield of the alkyltrifluoroborate salt was in agreement with the earlier preparations and the general average yields reported in literature. This clearly indicates the presence of silane materials does not negatively affect the yields. Taking all of these results together; the lower yields, formation of significant amounts of tetrafluoroborate and presence of the corresponding alcohol from the alkyl group all indicate oxidation of the boronic derivative likely occurs during fluoridation in the presence of air. This indicates the necessity of converting boronic acids to the trifluoroborate under an inert atmosphere. Unfortunately, many of the literature preparations use “open flask” reaction conditions with plastic ware to avoid etching of glassware with hydrofluoric acid.

Table 1
Effects of inert reaction conditions on fluoridation reactions.

$$\text{DecylB(OH)}_2 \xrightarrow[\text{Conditions}]{\text{Reaction}} + \ \text{KHF}_2 \longrightarrow \text{DecylBF}_3^- \text{K}^+$$

Entry	Source $DecylB(OH)_2$	Reaction Conditions	KHF_2 eq	% Isolated $DecylBF_3^-$	^{11}B NMR Analysis				Comments
					% $DecylBF_3^-$	% KBF_4^-	% $DecylB(OH)_2$	% $B(OH)_3$	
1	a	Air, $MeOH/H_2O$, 0.25 h, RT	2.2	76					1-decanol
2	b	Air, $MeOH /H_2O$ (9:1) 24h, RT	0				99.9	0.1	
3	b	Air, $MeOH/H_2O$, (9:1), 0.25h, RT	2.2		74.2	18.5	7.3		
4	c	Air, $MeOH/H_2O$ (9:1), 0.5h, RT	2.2	78.9					
5	d	N_2, $MeOH/H_2O$, (9:1). 0.5 h, RT	3.3	92.9					

[a] Prepared from 1-decene and $HBBr_2{\cdot}SMe_2$ + 10 mol% BBr_3 and isolated as boronic acid.
[b] Prepared by $NaHCO_3$ hydrolysis of K $DecylBF_3$.
[c] Prepared by Matteson Hydroboration Method and hydrolysis of the alkyldichloroborane using ether/water.
[d] Prepared by Matteson Hydroboration Method followed by THF/*i*-PrOH.

(remove – Table created in Word, cambria 7 pt. Should be scaled to 190 mm width - remove)

To verify the importance of an inert atmosphere, the entire synthetic sequence was repeated under N_2 up to the isolation of the product. Decyldichloroborane was directly converted into the corresponding boronic ester using a mixture of oxygen free THF and isopropanol. The bulk of the solvents were removed under reduced pressure and the flask refilled with N_2. The crude boronic ester was dissolved in additional *i*-PrOH, cooled to 0 °C and a concentrated deoxygenated aqueous solution of KHF_2 (3.3 eq) was added dropwise and stirred for 30 min. Volatiles were then removed under reduced pressure. A larger than normal round-bottomed flask was used to reduce loss of material due to viscous foaming. The product was isolated in the usual manner giving a 92.9% yield of potassium decyltrifluoroborate (**2b**). This reaction demonstrated the importance of carrying out the fluoridation under inert conditions, resulting in significant increased yields. The NMR analysis showed a pure product, identical to the potassium *n*-decyltrifluoroborate salts isolated earlier. Since our initial goal of an isolated yield greater than 90% were met, this reaction was not further optimized.

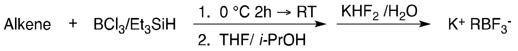
Using the general synthetic procedure, 1-hexyldichloroborane was prepared and converted into the corresponding isopropyl ester. The crude ester was treated with KHF_2 (3.0 eq) to give the crude alkyltrifluoride salt. The potassium 1-hexyltrifluoroborate salt (**3**) was isolated in the usual manner in a 93.4% yield. The spectral data were in agreement with literature values [17].

Cyclohexene is rapidly hydroborated by $HBCl_2$, selectively forming the cyclohexyldichloroborane. The ^{11}B NMR spectra showed the cyclohexldichloroborane as the only hydroboration product. This is in contrast to dibromoborane dimethylsulfide, which is slow to react and must be catalyzed with BBr_3 [32]. Hydroborations with coordinated dichloroboranes, undergo extensive disproportionation with these sterically large alkenes, even when catalyzed with boron trichloride [33]. The Matteson Method is the superior method for these sterically demanding alkenes. The product was prepared using the general synthetic procedure. After the reaction with KHF_2, removal of solvents was best accomplished using a larger than normal reaction flask due to the persistent foaming. Also, cyclohexyltrifluoroborate salt was considerably more soluble in hot acetone than **2b** and **3**. As a consequence, all of the acetone must be removed before trituration with ether, otherwise significant loss of product occurs during this step. The isolated yield for potassium cyclohexyltrifluoroborate (**4**) was 89.3%. We did not further optimize this reaction since the yield essentially met our targeted yield. The full spectral analysis was in agreement with literature or expected values [17,34].

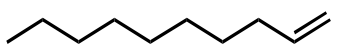
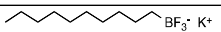
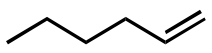
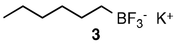
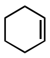
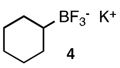
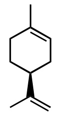
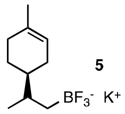
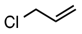
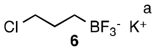
Previously, we have used ligand free $HBCl_2$ to selectively prepare 2-ethylcyclohex-3-enyldichloroborane from vinylcyclohexene [13]. We selected (S)-(–)-limonene as an example to demonstrate the selective hydroboration of non-conjugated dienes. The alkyltrifluoroborate was prepared according to the general synthetic procedure. The ^{11}B NMR after conversion to the boronic ester showed no detectable presence of borinic product, indicating clean formation of the alkyldichloroborane. Unlike the previous reactions, the filtered acetone solution was turbid. After isolation of the product, the fluorine and boron NMR spectra showed a broad signal without coupling, indicating fluoride exchange. Repeated purification with hot acetone and trituration with ether did not give a coupled fluorine or boron NMR spectra, only further loss of product. This problem was solved in the repeated reaction. The crude product was dissolved in methanol, an additional 5-10 mol% KHF_2 was added and isolation of the product gave a clear acetone filtrate. The potassium trifluoro((R and S)-2-((S)-4methylcyclohex-3-enyl)propyl)borate (**5**) was isolated in 93.1% yield. The proton and carbon NMR spectra showed an equal molar diasteromeric mixture as expected, however, the fluorine and boron spectra did not resolve into the expected quartets, but remained a broad singlet, albeit better defined than the initially isolated product.

The hydroboration of allyl chloride was different from the other alkenes studied. Matteson reported that triethylsilane formed small amounts of the R_2BCl product, even when carried out at -78 °C [12]. In contrast, trimethylsilane exclusively formed the desired alkyldichloroborane. However, use of this more volatile silane, BP 6.7 °C, is inconvenient and is more difficult to handle in laboratory preparations. In an effort to minimize the amount of the dialkylchloroborane, a larger excess of BCl_3, 10 mol% versus the usual 5 mol% and a lower reaction temperature of -78 °C was used following the general synthetic procedure. After the reaction mixture was esterified, the boron NMR spectrum showed 7.8% borinic ester. The solvents were removed under reduced pressure at 0 °C instead of 30-40 °C to reduce the loss of this more volatile ester. The potassium 1-chloropropyl-3-trifluoroborate (**6**) was isolated in a 76.5% yield. The spectroscopic data is in excellent agreement with literature values [35]. This yield was considerably lower than previous reactions. Repeated attempts to increase the yield gave essentially the same result. An interesting relationship is found, the ratio of isolated alkyltrifluoroborate to boronic ester in all of the previous reactions indicated a ~ 90% conversion. The hydroboration of allyl chloride give about 84% conversion to the corresponding boronic ester. The isolated 76.5% yield is consistent with these fluorination reactions. This suggested that the borinic esters are not converted to form the alkyltrifluoroborate product.

Table 2.
Yields of the alkyltrifluoroborates via Matteson Hydroboration Method and fluorination.



$$\text{Alkene} + BCl_3/Et_3SiH \xrightarrow[\text{2. THF/ }i\text{-PrOH}]{\text{1. 0 °C 2h} \rightarrow \text{RT}} \xrightarrow{KHF_2/H_2O} K^+\ RBF_3^-$$

Entry	Alkene	Product	Isolated Yield(%)
1		 **2b**	92.9
2		 **3**	93.4
3		 **4**	89.1
4		 **5**	93.1
5	 [a]	 **6** [a]	76.5

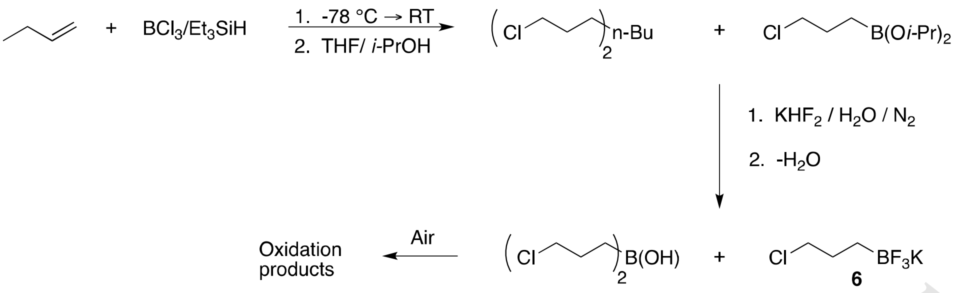
[a] Hydroboration done at -78 °C 2 h then warmed to room temperature 2h.

(remove – Table drawn in Word, text Cambria 7 pts, graphics ChemDraw Helvetica ~ 7 pt, template ACS document 1996, scaled 60%. Proposed width 90 mm - remove)

While diaryldifluoroborate salts have been known for some time [36] a detailed literature search revealed no examples of dialkyldifluoroborate salts other than the bis(trifluoromethyl)difluoroborate salt $K[(CF_3)_2BF_2]$. [37]. This suggests that diorganodifluoroborates may be thermodynamically unstable in the absence of strongly electron withdrawing groups. In an effort to better understand whether borinic derivatives undergo fluoridation, we investigated this class of boron compounds. We chose dicyclohexylborinic ester as our model system as it is readily prepared by hydroboration of cyclohexene with BMS followed by esterification with an alcohol. A THF solution of dicyclohexylisopropylborinic ester was prepared and analyzed by ^{11}B NMR. Analysis of the reaction solution showed 2.2% Cy_3B, 97.1% $Cy_2B(O\textit{i}Pr)$ and 0.7% $CyB(O\textit{i}Pr)_2$. When the remainder of the THF solution was treated with concentrated KHF_2, only a small amount of precipitate formed and the reaction solution separated into two layers. The solvents were removed under vacuum and the residue was dissolved in Et_2O. Analysis of this solution showed 1.9% Cy_3B and 98.1% Cy_2BOH; the ratios of Cy_3B to the borinic species in the two experiments were essentially the same. After removal of the Et_2O, the remaining solids were exposed to air, resulting in an exothermic reaction with almost complete conversion of the Cy_3B and the borinic species to boric acid products.

Thus, these finding suggest that the borinic products formed in the hydroboration of allyl chloride do not react with the KHF_2 and remain as the borinic material (Scheme 2). Removal of the solvent after fluoridation and exposure to air during the hot acetone extraction leads to the complete oxidation of the borinic materials to form the boric compounds. These materials are not trapped with excess bifluoride, since water is not present at this point. Oxidation products are removed during product isolation. Thus, one either accepts a lower yield when working with reactive alkenes such as allyl chloride and triethylsilane or one uses the somewhat more experimentally demanding liquefied trimethylsilane, (BP

7.6 °C) and neat boron trichloride (BP 12.6 °C) which has been demonstrated to give clean product formation [12]. However, for the majority of alkenes, there is no significant difference between triethylsilane and trimethylsilane.



Scheme 2. Hydroboration of allyl chloride and product formation.
(remove – Table drawn in Word Cambria 7 pts, graphics ChemDraw Helvetica ~ 7 pt, template ACS document 1996, scaled 60%. Proposed width 140 mm - remove)

3. Conclusions

The Matteson Hydroboration Method, using triethylsilane and solutions of 1 M boron trihalides, is a superior route to the formation of the alkyldihaloboranes for most alkenes. The triethylsilane side products are effectively removed on conversion to the alkyltrifluoroborate salt, generally giving overall isolated yields of greater than 90%. The alkyltrifluoroborate salts can be handled and stored for extended periods of time. They can readily be converted to other boronic derivatives. Importantly, we have demonstrated the importance of carrying out the fluoridation reactions under an inert atmosphere, avoiding oxidation seen in "open air" reactions.

4. Experimental

4.1. Instrumentation

^{1}H and ^{13}C NMR spectra were recorded on a Varian VNMR 600 at 599 and 150 MHz respectively using DMSO-d_6 as the solvent and were referenced to the residual proton or carbon signals of DMSO-d_6 (^{1}H = 2.50 ppm) and (^{13}C = 39.52 ppm). ^{13}B and ^{19}F NMR spectra were recorded on a Varian VNMR 400 at 128 and 376 MHz respectively and were referenced to an external reference capillary. The external reference contained 0.56 M $BF_3 \cdot OEt_2$ dissolved in C_6D_6; using neat $BF_3 \cdot OEt_2$ (^{11}B = 0.00 ppm) and α,α,α trifluorotoluene in $CDCl_3$ (^{19}F = -63.72 ppm) as references for the capillary (^{11}B = -0.45 ppm) and (^{19}F = -

152.80 ppm) respectively. ^{11}B NMR spectra were recorded using, singly or in mixture, MeOH, *i*-PrOH, THF, Et_2O, D_2O or acetone-d_6 as the solvent. ^{19}F NMR spectra were recorded using acetone-d_6 as the solvent. Chemical shift and coupling constant data are apparent and reported in units of δ (ppm) and *J* (Hz). Infrared spectra were recorded on a Perkin Elmer ATR Spectrum RX-1 FTIR spectrophotometer and reported in units of cm^{-1}.

4.2 Equipment and reagents

All glassware was dried at 150 °C for at least of 4 hours; the typical reaction apparatus was assembled hot and cooled by an internal stream of N_2. Alkenes were distilled from $LiAlH_4$, allyl chloride from CaH_2, under N_2 atmosphere. THF was distilled from sodium benzophenone ketal, MeOH and *i*-PrOH from magnesium and CH_2Cl_2 from CaH_2; all under N_2. Anhydrous Et_2O and acetone were used as received. Dibromoborane dimethylsulfide was dissolved in CH_2Cl_2 under N_2, forming a solution ca. 2.1 M in $HBBr_2•SMe_2$. Triethylsilane, 1M BBr_3 in CH_2Cl_2 and 1M BCl_3 in hexanes were used as received. De-ionized H_2O was boiled and sparged under N_2. All alkenes, solvents and liquid reagents were stored under N_2 in storage bottles fitted with Teflon stopcocks.

4.3 General conditions

Hydroboration of alkenes using $HBBr_2•SMe_2$ or $HBCl_2$, hydrolysis to the alkylboronic acid, alcoholysis to the alkylboronic ester and conversion to the potassium alkyltrifluoroborate salts were conducted based on procedures described in the literature [24,38]. Potassium decyltrifluoroborate was hydrolyzed to decylboronic acid using aqueous $NaHCO_3$ under N_2. Unless otherwise noted, all synthetic reactions and manipulations were conducted under N_2 using standard air-sensitive techniques. Yields of potassium alkyltrifluoroborate salts derived from alkyldichloroboranes were calculated according to the limiting reagent of the hydroboration with $HBCl_2$.

4.4 Optimization

*4.4.1 (decylboronic acid) (**1**)*

A 100 mL flask was charged with 2.1M $HBBr_2•Me_2S$ in CH_2Cl_2 (26.2 mL, ca. 55.0 mmol) and 1-decene (9.5 mL, 50.0 mmol) was added dropwise to the stirred solution at 20 °C. One molar BBr_3 in CH_2Cl_2 (2.5 mL, 2.5 mmol) was added dropwise while the reaction mixture was cooled to 0 °C; the reaction was stirred for 15 min; then warmed spontaneously to 20 °C; and stirred for 30 min. The solution of boranes was hydrolyzed by dropwise transfer to another flask containing a stirred mixture of Et_2O (100 mL) and H_2O (20 mL) at 0 °C then stirred for 20 min. The solution was transferred to a separatory funnel with minimal exposure to air; the aqueous layer was separated and discarded; the organic phase was washed with H_2O (2 × 30 mL) and brine (2 × 30 mL); dried over $MgSO_4$ and filtered; then concentrated on a rotary evaporator. The yield of free-flowing white powder was 8.71g, 93%. ^1H NMR δ 6.50 (s, 2H), 1.41 (p, *J* = 7.8, 7.2 Hz, 2H), 1.28 (s, 14H), 0.92 – 0.84 (m, 3H), 0.71 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 32.55, 32.07, 29.79, 29.73, 29.62, 29.50, 24.53, 23.50, 22.85, 14.28. ^{11}B NMR δ 32.32.

*4.4.2 (potassium decyltrifluoroborate) (**2**)*

A 50 mL round bottom flask equipped with a magnetic stir bar was charged with 1-decylboronic acid (1.489g, 8.00 mmol) and MeOH (4.0, 5.0, 6.0 or 7.0 mL) under air. A concentrated aqueous solution of KHF_2 (1.375 g, 17.6 mmol) was added dropwise and the contents stirred for 15 min. Methanol and H_2O were removed *in vacuo* for 4 h. The solids were extracted with hot acetone (400 mL) and the solution was filtered through a Büchner funnel; the solids were washed with acetone the combined organics were concentrated on a rotary evaporator, leaving a white solid. The solid was triturated with Et_2O (20 mL); filtered onto a tared Büchner funnel and washed with Et_2O (2 × 10mL); then dried at 40 °C for 4 h. Methanol (4.0 mL); isolated yield 1.29 g, 65%. Methanol (5.0 mL); isolated yield 1.36 g, 69%. Methanol (6.0 mL); isolated yield 1.48 g, 75%. Methanol (7.0 mL); isolated yield 1.51 g, 76%.

*4.4.3 (decylboronic acid) (**1a**)*

A 50 mL flask was charged with (**2**) (0.248 g, 1.00 mmol) and ~ 2 mL of Et_2O. The flask was fitted with a gas inlet valve and most of the Et_2O was removed with the aid of reduced pressure; the flask was refilled with N_2. Additional Et_2O (4 mL) and 2 mL of 1.1M $NaHCO_3$ were added to the flask; the contents were vigorously stirred until no solids remained; usually 3.5-4 h. Additional Et_2O (4 mL) and H_2O (2 mL) were added to the flask and the contents gently stirred for 10 min; the aqueous layer was carefully removed; the organic phase was washed with H_2O (2 × 4 mL), brine (2 × 4 mL) and H_2O (2 × 4 mL).

*4.4.4 (potassium decyltrifluoroborate) (**2a**)*

A 50 mL flask was charged with 1M BCl_3 (10.0 mL, 10.0 mmol) in hexane and cooled to 0 °C. A 10 mL vial was charged with 1-decene (1.403 g, 10.0 mmol) and triethylsilane (1.163 g, 10 mmol); the mixture was added dropwise to the vigorously stirred BCl_3 over 10 min; with continued stirring at 0 °C for 4 h. A 100 mL flask was charged with Et_2O (20 mL) and H_2O (10 mL) and cooled to 0 °C. The contents in the 50 mL flask were transferred to the 100 mL flask and stirred for 30 min. With minimal exposure to air, the contents of the 100 mL flask were transferred to a separatory funnel; the aqueous phase was discarded and the organic phase was washed with H_2O (2 × 15 mL), brine (2 × 20 mL) and partially concentrated with the aid of reduced pressure; then transferred to a 50 mL round-bottom flask and the rest of the solvents removed with the aid of reduced pressure. In the presence of air, the contents of the flask were dissolved with MeOH (8.0 mL) and a concentrated aqueous solution of KHF_2 (1.72 g, 22 mmol) was added dropwise and stirred for 15 min. Methanol and H_2O were removed *in vacuo* for 4 h at 40 ˚C. The solids were extracted with hot acetone (400 mL), the solution was filtered and the solids were washed with acetone (20 mL); the combined organics were concentrated on a rotary evaporator, leaving an oily white solid. The solid was triturated with Et_2O (20 mL), filtered onto a tared Büchner funnel and washed with Et_2O (2 × 10mL); then dried at 40 ˚C for 4 h. The yield was 1.90 g, 78.9%.

4.5 General synthetic procedure

A 100 mL flask was charged with 1M BCl_3 (21.0 mL, ~21 mmol) in hexane (BCl_3) and cooled to 0 ˚C in an ice/H_2O bath. A 10 mL serum vial was charged with an alkene (20 mmol) and triethylsilane (2.33 g, 20 mmol). The alkene-Et_3SiH mixture was added dropwise with stirring over a period of 8-10 min and stirred at 0 ˚C for 2 h then spontaneously warmed to 25 ˚C; total time of reaction was 4 h. A 20 mL vial was charged with oxygen free THF (~11 mL) and *i*-PrOH (4 mL, ~54 mmol); the mixture was transferred to the stirred contents of the reaction flask and stirred for 30 min. The hexane-THF solution of esters was transferred to a N_2 flushed graduated cylinder and the volume was recorded; an aliquot was withdrawn for analysis by ^{11}B NMR. The solution in the cylinder was transferred to a 250 mL flask and the bulk of the hexane, THF and *i*-PrOH were removed with the aid of reduced pressure; the flask was refilled with N_2 and isopropanol (20 mL) was added to the flask. A solution of KHF_2 (4.68 g, 60 mmol) prepared in oxygen free H_2O (11.8 mL) was added dropwise to the vigorously stirred contents of the 250 mL flask and stirred for an additional 15 min. The solvents were removed with the aid of reduced pressure for 12 h. The flask was connected to vacuum line and volatiles further removed *in vacuo* at 40 ˚C for 4 h. The crude product was quantitatively transferred to an Erlenmeyer flask and dissolved in sufficient boiling acetone to dissolve the alkyltrifluoroborate salt. The hot acetone solution was filtered through a Büchner funnel and the salts were washed with hot acetone (2 × 10 mL); the combined organics were concentrated on a rotary evaporator. The remaining solids were triturated with Et_2O (100 mL) and filtered onto a tared Büchner funnel then washed with Et_2O (4 × 15 mL) and dried at 40 ˚C for 4 h. To calculate the yield: the cooled Büchner funnel was weighed, the tare weight was subtracted and the difference multiplied by the quotient of the initial and final volume of the graduated cylinder.

*4.5.1 (potassium decyltrifluoroborate) (**2b**)*

BCl$_3$ (19.7 mL, 19.7 mmol), 1-decene (2.588 g, 18.45 mmol) and Et$_3$SiH (2.152 g, 18.51 mmol); yield 4.254 g, 92.9%. ^{1}H NMR δ 1.34 – 1.03 (m, 16H), 0.85 (t, J = 6.9 Hz, 3H), -0.05 (dt, J = 9.1, 6.3 Hz, 2H). ^{13}C NMR δ 33.16, 31.31, 29.47, 29.27, 29.16, 28.76, 25.54, 22.08, 20.00, 13.87. ^{11}B NMR (Acetone-d_6) δ 5.79 (q, J = 64 Hz). ^{19}F NMR δ -141.00 (m). IR 2954, 2915, 2849, 1232, 1094, 1020, 917, 722 cm^{-1}.

*4.5.2 (potassium hexyltrifluoroborate) (**3**)*

BCl$_3$ (21 mL, ~21 mmol), 1-hexene (1.716 g, 20.39 mmol) and Et$_3$SiH (2.405 g, 20.68 mmol); yield 3.658 g, 93.4%. ^{1}H NMR δ 1.37 – 1.01 (m, 8H), 0.84 (t, J = 7.0 Hz, 3H), -0.05 (h, J = 6.5 Hz, 2H). ^{13}C NMR δ 32.8, 31.7, 25.5 (q, J = 2.3 Hz), 22.2, 20.09 (bs), 14.1. ^{13}B NMR (Acetone-d_6) δ 4.36 (q, J = 63.5 Hz). ^{19}F NMR δ -140.04 (m). IR 2953, 2914, 2847, 1221, 1091, 1068, 908, 724 cm^{-1}.

*4.5.3 (potassium cyclohexyltrifluoroborate) (**4**)*

BCl$_3$ (19.5 mL, ~19.5 mmol), cyclohexene (1.583 g, 19.27 mmol) and Et$_3$SiH (2.244 g, 19.30 mmol); yield 3.269 g, 89.3%. ^{1}H NMR δ 1.65 – 1.54 (m, 3H), 1.53 – 1.43 (m, 2H), 1.20 – 0.98 (m, 3H), 0.90 (qd, J = 12.3, 2.7 Hz, 2H), -0.01 (dtq, J = 11.8, 7.7, 3.8 Hz, 1H). ^{13}C NMR δ 29.58 (br), 28.78 (q, J = 1.4 Hz), 28.17, 27.44. ^{11}B NMR (Acetone-d_6) δ 4.84 (q, J = 61.6). ^{19}F NMR δ -147.99 (m). IR 2929, 2849, 1221, 1089, 911, 879, 725 cm^{-1}.

*4.5.4 (potassium trifluoro((R and S)-2-((S)-4-methylcyclohex-3-enyl)propyl)borate (**5**)*

BCl$_3$ (19.5 mL, ~19.5 mmol), (S)(-) limonene (2.60 g, 19.11 mmol) and Et$_3$SiH (2.21 g, 18.98 mmol); yield 4.314 g, 93.1%. ^{1}H NMR δ 5.34 (ddt, J = 4.0, 2.5, 1.3 Hz, 1H), 2.01 – 1.80 (m, 3H), 1.79 – 1.62 (m, 1H), 1.62 – 1.56 (m, 3H), 1.50 (ddp, J = 13.9, 6.3, 3.5 Hz, 1H), 1.30 (dddd, J = 16.8, 8.4, 7.0, 4.1 Hz, 1H), 1.24 – 1.10 (m, 1H), 0.84 (dd, J = 6.8, 2.2 Hz, 3H), 0.31 (h, J = 6.2 Hz, 1H), 0.07 – -0.11 (m, 1H). ^{13}C NMR δ 132.78, 132.77, 121.73, 121.71, 40.56, 40.41, 33.96 (q, J = 2.0 Hz), 33.80 (q, J = 1.97 Hz), 30.83, 30.73, 28.90, 27.35, 26.79, 25.20, 24.31, 23.29, 18.78, 18.40. ^{11}B NMR (Acetone-d_6) δ 5.66. ^{19}F NMR δ -137.89. IR 2963, 2915, 2881, 2852, 1262, 1075, 931, 903, 716 cm^{-1}.

*4.5.5 (potassium 1-chloropropyl-3-trifluoroborate) (**6**)*

BCl$_3$ (21.0 mL, ~21.0 mmol), Et$_3$SiH (2.377 g, 20.44 mmol) and 3-chloropropene (1.527 g, 19.95 mmol); yield 2.815 g, 76.5%. ^{1}H NMR δ 3.49 (t, J = 7.5 Hz, 2H), 1.60 (p, J = 7.7 Hz, 2H), 0.04 (h, J = 6.5 Hz, 2H). ^{13}C NMR δ 48.95, 29.90 (q, J = 2.4 Hz), 17.36. ^{11}B NMR δ 4.90 (q, J = 61.1 Hz). ^{19}F NMR δ -141.41 (m). IR 2963, 2939, 2914, 2851, 1271, 1080, 920, 718 cm^{-1}.

*4.5.6 (potassium dicyclohexyldifluoroborate) (**7**)*

The 50 mL flask was charged with BMS (0.7597 g, 10 mmol) and THF (10 mL) then cooled to 0 ˚C. Cyclohexene (2.0 mL, *ca.* 20 mmol) was added dropwise over 7 min and stirred for 2 h at 0 ˚C. Isopropanol (1.3 mL, *ca.* 15.4 mmol) was added (*very carefully-*H_2 *gas evolution*) and stirred for 15 min; the flask warmed to room temperature and stirred for 1 h. An aliquot of the esters was withdrawn for NMR analysis. ^{11}B NMR (THF- *i*-PrOH) δ 80.25 (bs, 2.21%), 49.68 (s, 97.06%) 31.76 (s, 0.73%). A concentrated solution of KHF_2 (1.72 g, 22 mmol) was added dropwise to the vigorously stirred solution of esters and stirred for an additional 10 min; and the solvents were removed *in vacuo* 12 h. The dried reaction products were dissolved in THF (10 mL) and an aliquot withdrawn for NMR analysis. ^{11}B NMR (Et_2O-MeOH, 6:1 v:v) δ 80.30 (bs, 1.88%), 51.71 (s, 98.12%).

Acknowledgements

We thank the San Diego Foundation, Blasker Foundation and San Diego State University for Financial support of this project. We also thank Dr. LeRoy Lafferty for his valuable assistance in the NMR characterizations.

References

---

[1] A. Suzuki, Angew. Chem. Int. Ed. 50 (2011) 6723-6733.
[2] H. Prokopcová, C.O. Kappe, Angew. Chem. Int. Ed. 48 (2008) 2276-2286.
[3] G. Berthon-Gelloz, T. Hayashi, Rhodium- and palladium-catalyzed asymmetric conjugate additions of organoboronic acids, Chapter 5 in: D.G. Hall (Ed.), Boronic Acids, 2nd ed., Wiley-VCH Verlag Gmbh & Co. KGaA, Weinheim, Germany, 2011, pp 263-314.
[4] J.X. Qiao, P.Y.S. Lam, Synthesis 6 (2011) 829-856.
[5] D.S. Matteson, (α-Haloalkyl)boronic esters in asymmetric synthesis, Chapter 8 in: D.G. Hall (Ed.), Boronic Acids, Wiley-VCH Verlag Gmbh & Co. KGaA, Weinheim, Germany, 2005, pp 305-342.
[6] G.A. Molander, L. Jean-Gérard, Organotrifluoroborates: Organoboron reagents for the twenty-first century, Chapter 11, Vol 2 in: D.G. Hall (Ed.), Boronic Acids, 2nd ed., Wiley-VCH Verlag Gmbh & Co. KGaA, Weinheim, Germany, 2011, pp 507-550.
[7] H.C. Brown, J. Chandrasekharan, J. Org. Chem. 48 (1983) 5080-5082.
[8] Y. Yamamoto, R. Fujikawa, T. Umemoto, N. Miyaura, Tetrahedron 60 (2004) 10695-10700.
[9] K. Burgess, W.A. van der Donk, S.A. Westcott, T.B. Marder, R.T. Baker, J.C. Calabrese, J. Am. Chem. Soc. 114 (1992) 9350-9349.
[10] M. Zaidlewicz, J.V.B. Kanth, H.C. Brown, J. Org. Chem. 65 (2000) 6697-6702.
[11] R. Soundararajan, D.S. Matteson, J. Org. Chem. 55 (1990) 2274-2275.
[12] R. Soundararajan, D.S. Matteson, Organomet. 14 (1995) 4157-4166.
[13] D.J. Zillman, G.C. Hincapié, M.R. Savari, F.G. Mizori, T.E. Cole, Tetrahedron Lett. 51 (2010) 3033-3036.
[14] E.W. Abel, A. Singh, J. Chem. Soc. 1959, 690-693.

[15] S.K. Mehrotra, G. Srivastava, R.C. Mehrotra, J. Organomet. Chem. 73 (1974), 277-296.

[16] M. Beckett, P. Owen, K.S. Varma, J. Organomet. Chem. 588 (1999) 107-112.

[17] D. S. Matteson, G.Y. Kim, Org. Lett. 4 (2002) 2153-2155.

[18] H.A. Stefani, R. Cella, A.S. Vieira, Tetrahedron 63 (2007) 3623-3658.

[19] S. Darses, J.-P. Genêt, Chem. Rev. 108 (2008) 288-325.

[20] B.J. Kim, D.S. Matteson, Angew. Chem. Int. Ed. 43 (2004) 3056-3056.

[21] G.A. Molander, L.N. Cavalcanti, B. Canturk, P.-S. Pan, L.E. Kennedy, J. Org. Chem. 74 (2009) 7364-7369.

[22] G.W. Kabalka, V. Coltuclu, Tetahedron Letters 50 (2009) 6271-6272.

[23] Q.I. Churches, J.F. Hopper, C.A. Hutton, J. Org. Chem. 80 (2015) 5428-5435.

[24] H.C. Brown, J. Chandrasekharan,. Organometallics 2 (1983) 1261-1263.

[25] E. Vedejs, R.W. Chapman, S.C. Fields, S. Lin, M.R. Schrimpf, J. Org. Chem 60 (1995) 3020-3037.

[26] S. Darses, J.-P. Genêt, J.-L. Brayer, J.-P. Demoute, Tetrahedron Lett. 38 (1998) 4393-4396.

[27] J.-J. Dai, W.-M. Zhang, Y.-J. Shu, Y.-Y. Sun, J. Xu, Y.-S. Feng, H.-J. Xu, Chem. Comm. 52 (2016) 6793-6796.

[28] J.D. Roberts, F.J. Weigert, J.I. Kroschwitz, H.J. Reich, J. Am. Chem. Soc. 92 (1970) *92*, 1338-1347.

[29] D.G. Hall, Structure, properties, and preparation of boronic acids, Chapter 1, Vol 1 in: D.G. Hall (Ed.), Boronic Acids, 2nd ed., Wiley-VCH Verlag Gmbh & Co. KGaA, Weinheim, Germany, 2011, pp 1-133.

[30] P.A. McCusker, L.J. Glunz, J. Am. Chem. Soc. 77 (1955) 4253-4255.

[31] P.A. McCusker, H.S. Makowski, J. Am. Chem. Soc. 79 (1957) 5185-5188.

[32] H.C. Brown, J. Chandrasekharan, J. Org. Chem. 53 (1988) 4811-4814.

[33] J.V. Kanth, H.C. Brown, J. Org. Chem. 66 (2001) 5359-5365.

[34] C. Cazorla, E. Métay, M. Lemaire, Tetrahedron 67 (2011) 8615-8621.

[35] G.A. Molander, C.-S. Yun, M. Ribagorda, B. Biolatto, J. Org. Chem. 68 (2003) 5534-5539.

[36] D. Thierig, F. Umland, Naturwissenschaften 54 (1967), 563.

[37] G. Pawelke, F. Heyder, H. Bürger, J. Organomet. Chem. 178 (1979) 1-4.

[38] H.C. Brown, N.G. Bhat, V. Somayaji, Organometallics 2 (1983) 1311-1316.

Highlights:

- Matteson Hydroboration Method using ligand free $HBCl_2$ is fast and highly selective
- Fluoridation of boronic compounds require oxygen-free conditions to prevent loss
- Isolated yields of alkyltrifluoroborates generally greater than 90%
- Alkene to alkyltrifluoroborate conversion without isolation of intermediates
- Dialkylborinic derivatives do not form fluoroborate salts