ELSEVIER

Journal of Organometallic Chemistry 581 (1999) 51–65

Journal of Organometallic Chemistry

# Functional group compatibilities in boronic ester chemistry

Donald S. Matteson *

*Department of Chemistry, Box 644630, Washington State University, Pullman, WA 99164-4630, USA*

Received 8 July 1998; received in revised form 19 October 1998

**Abstract**

Problems encountered in the chemistry of highly functionalized boronic esters are reviewed. These include β-eliminations of boron and an electronegative group, protodeboronations, and anomalous oxidations. Groups that appear to be particularly compatible with boronic esters or that lead to instability only in certain relationships are also discussed, including azido, alkoxy, cyano and carboxylic ester substituents. 

*Keywords:* Boron; Boronic esters; Functional groups

## 1. Introduction

The utility of boronic ester chemistry in highly stereoselective asymmetric synthesis is well-established, and the author has provided several recent reviews in the past 10 years [1–5]. This review is written for the chemist who has read elsewhere about the great utility of the reaction of asymmetric boronic esters with (dichloromethyl)lithium and would like to plan a synthesis utilizing this chemistry, but who wonders what some of the problems and pitfalls with these unfamiliar boron reagents might be. The strong thermodynamic bias in favor of oxidation of carbon–boron bonds provides the basis for the extreme chemoselectivity that makes boronic ester chemistry useful [1–5], but it also can be a trap that ruins the plans of the unwary chemist.

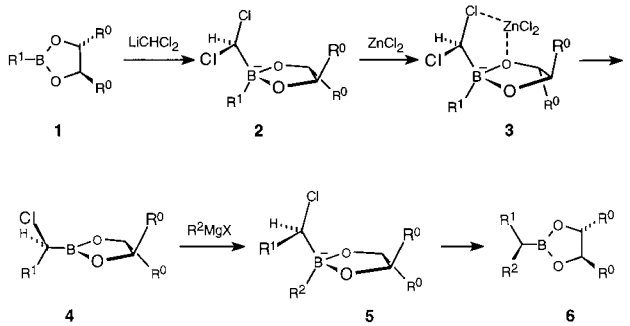
Boronic esters are stable in the presence of a wide variety of functional groups. Reactions intended to affect these functions sometimes involve the boronic ester, not necessarily in intuitively obvious ways. This review collects a wide range of such problems that the author has encountered during 40 years of working in this field. These have often been published in inconspicuous paragraphs in synthetic papers if they have been published at all, and the information is impossible to retrieve in a systematic way.

In other cases, reactions that might be thought hazardous to the carbon–boron bond proceed with no such involvement. This review also points out some of the functional substituents that have proved more compatible with boronic ester chemistry than might have been anticipated.

Before launching into a review of the complications, it seems well to remind readers of the utility of α-halo boronic esters as reagents for asymmetric synthesis. The general sequence illustrated involves reaction of an asymmetric boronic ester (**1**) with (dichloromethyl)-lithium to form a (dichloromethyl)borate complex (**2**), which in the presence of zinc chloride rearranges via a transition state (**3**) [6] that leads to a single α-chloro boronic ester (**4**) in high diastereomeric purity, often $>100{:}1$ dr (diastereomeric ratio) [1–5]. Nucleophilic displacement of the α-chloride is easily accomplished with a wide range of nucleophiles, including RMgX, $RO^-$, $RS^-$, $R_2N^-$ and $N_3^-$, illustrated here with $R^2MgX$. Intermediate borate **5** is analogous to intermediate borate **2**, and the inversion of configuration which has occurred in the conversion of **2** to α-chloro boronic ester **4** places the chlorine of **5** in the favored position for displacement, presumably via a transition state analogous to **3** with magnesium in place of zinc. As a result of this sequential double stereodifferentiation, final boronic ester product **6** has been obtained in 99.9% diastereomeric purity in a set of carefully documented examples [1–5,7].

* Tel.: +1-509-335-1516; fax: +1-509-335-8867..
*E-mail address:* dmatteson@wsu.edu (D.S. Matteson)

0022-328X/99/$ - see front matter 
PII: S0022-328X(99)00064-9



Since the product **6** of the foregoing sequence is a boronic ester analogous to **1** and yields are often very high, this process can be repeated to provide several adjacent chiral centers with extremely high diastereo- and enantioselectivity [1–4]. Alkoxy groups are well tolerated in place of alkyl or aryl group $R^2$, and an azido or silylated amino group is tolerated under some conditions. More reactive substituents such as carboxylic ester or cyano are tolerated at remote positions, though not α to the boronic ester function. It is readily apparent that this chemistry can be used to provide an extremely wide range of possible structures, and must be ranked as among the very broadest in potential scope among the various methods of asymmetric synthesis.

## 2. β-Eliminations

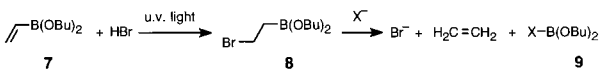
### 2.1. General comments

Thermodynamics tends to favor boron–oxygen bonds over boron–carbon bonds. The exact amount depends on what the carbon becomes bonded to, but it is ca. 40 kcal $mol^{-1}$ if the carbon becomes bonded to oxygen, hydrogen or any other element for which the carbon–element bond is about the same strength as the carbon–boron bond [1]. β-Elimination is an oxidative process in which the boron becomes bonded to oxygen or another electronegative element, carbon loses an electronegative ligand at the β-position, and a carbon–carbon π-bond is formed.

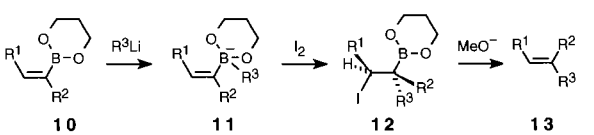
It is not remarkable that β-eliminations of boron and an electronegative atom occur, but boron is unusual for a relatively metallic element in that β-eliminations tend to be very slow. This section emphasizes those structures and situations in which β-eliminations occur. It is important to note that boron becomes tetracoordinate and bonded to an electronegative atom such as oxygen before elimination occurs. Boryl cations, $X_2B^+$, are not intermediates in the reactions to be considered here.

### 2.2. Halides

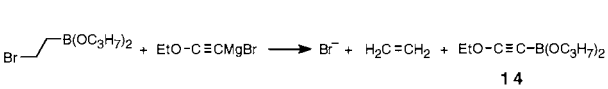
Radical additions to dibutyl vinylboronate provided α-halo boronic esters in 1959 [8], and it was soon shown that nucleophilic displacement of the α-halide is generally facile [9]. This work eventually led to the highly successful applications of α-halo boronic esters in asymmetric synthesis [1–5]. Radical addition of hydrogen bromide to dibutyl vinylboronate (**7**) readily yielded dibutyl (β-bromoethyl)boronate (**8**) [10], and higher homologs were also readily obtained from other α,β-unsaturated boronic esters [11]. However, even a nucleophile $X^-$ as weakly basic as thiocyanate resulted in elimination to ethylene and $XB(OBu)_2$ (**9**), which disproportionated to tributyl borate and, presumably, $BX_3$. Water also caused elimination to occur, and the rate was found to be accelerated by amines [12].



It is readily apparent from the foregoing that β-halo boronic esters cannot be used as intermediates in the kind of asymmetric synthesis outlined for **1**–**6** in Section 1. However, any efficient reaction has its uses. The preferred stereochemistry of the elimination process was shown to be *anti* by the use of a bromination/deboronobromination sequence on *Z* and *E* 2-methyl-2-butenylboronic esters [12]. The stereospecific Zweifel olefin synthesis involves such an elimination [13], illustrated here as the Brown–Bhat modification [14]. *B*-Alkylation of alkenylboronic ester **10** yields intermediate borate **11**, which is converted by iodine to intermediate β-iodo boronic ester **12**, which undergoes stereospecific base-initiated elimination to form **13**. Brown and co-workers have also applied the bromination/deboronobromination of alkenylboronic esters in the stereocontrolled synthesis of *Z* and *E* bromoalkenes [15].

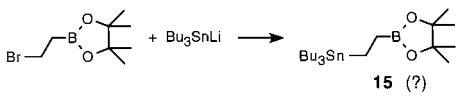


An earlier application of this chemistry involved the use of dipropyl β-bromoethylboronate as a very mild Lewis acid for the transfer of boron to a highly acid sensitive nucleophile, ethoxyacetylide, to prepare dipropyl (ethoxyethynyl)boronate (**14**) [16].



More recently, we have tried to use the (β-bromoethyl)boronic ester function to transfer boron to tributyltin anion without success [17]. NMR evidence

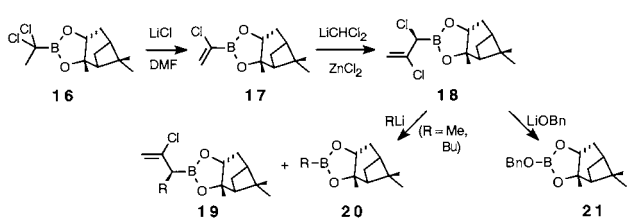
indicated that the substitution product **15** was produced, but the product was not sufficiently characterized for publication. It may be noted that the tributyltin anion functions normally in the displacement of chloride from α-chloro boronic esters [18].




### 2.3. Vinylic chloride

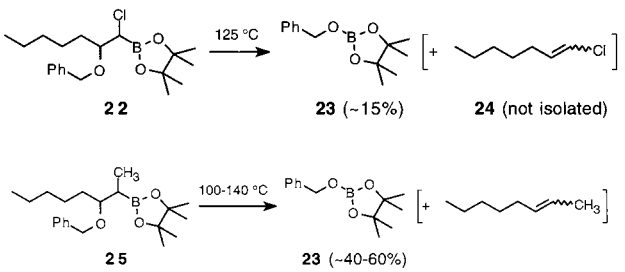
As might be expected, β-elimination of a vinylic chloride from a β-chloroallylic group is not nearly as facile as the halide eliminations discussed above. The unsaturated product from such elimination would be an allene, though this has not been verified. Displacement of an allylic α-chloride by a migrating alkyl group in the presence of a β-chloro substituent has proved feasible under limited conditions.

The in situ generation of (1,1-dichloroethyl)lithium in the presence of trimethyl borate [19] followed by *trans*-esterification yielded (*S*)-pinanediol (1,1-dichloroethyl)-boronate (**16**), which was dehydrochlorinated to the (1-chlorovinyl)boronate (**17**) [20]. The reaction with (dichloromethyl)lithium and zinc chloride proceeded normally to produce pinanediol (1,2-dichloroallyl)boronate (**18**). With methylmagnesium bromide or butylmagnesium chloride, **18** was converted to a mixture of the (1-alkyl-2-chloroallyl)boronic ester **19** (the halide displacement product) and the alkylboronic ester **20** (replacement of the entire dichloroallyl group) in ~3:1 ratio. The α-bromo analog of **18** was also prepared but epimerized to a considerable extent and yielded mainly **20** with butylmagnesium chloride. Lithium benzyl oxide converted **18** to pinanediol benzyl borate (**21**).

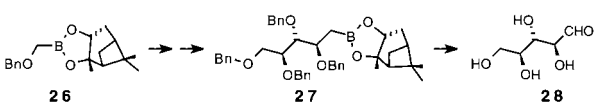



### 2.4. Alkoxides

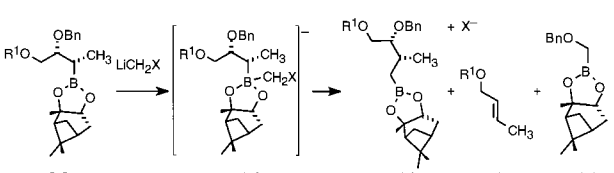
In contrast to halides, the alkoxy functionality is remarkably stable in the β-relationship to boron. This was tested soon after the chain extension process via (dichloromethyl)lithium was discovered, and it was found that a β-benzyloxy boronic ester (**22**) (a mixture of diastereomers) underwent ~15% decomposition to pinacol benzyloxyboronate (**23**) during vacuum distillation at 125°C, though it survived several hours at 50–65°C while the contaminant **23** was removed by molecular distillation, yielding an analytical sample of **22** that showed correct values for C, H and B, and was 0.8% low in Cl [21]. The other product was presumed to be the chloroalkene **24**, but this was not isolated. The β-benzyloxy boronic ester **25**, derived from **22** by methylation with the Grignard reagent, proved somewhat more labile, only ~40% surviving distillation at 100–140°C.




There being no need to heat β-alkoxy boronic esters for most synthetic purposes, we have avoided the foregoing decomposition by working at rt. Successive installation of benzyloxymethylene groups, starting from pinanediol [(benzyloxy)methyl]boronate (**26**) has been used in a synthesis of L-ribose (**28**) [22]. It may be noted that key intermediate **27** has a plain methylene group next to boron, because the usual insertion of $LiCHCl_2$ gave poor results and the insertion of $LiCH_2Cl$ proved somewhat better.



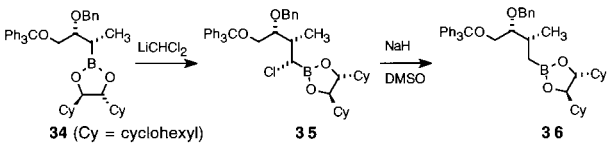

In view of the data obtained during the preparation of **28**, it came as a surprise that β-benzyloxy boronic ester **29** ($R^1$ = *p*-methoxybenzyl) reacted with (bromomethyl)lithium [23] to produce ~30–40% elimination products (**32** + **33**) instead of the homologation product (**31**). With (chloromethyl)lithium [24] the proportion of (**32** + **33**) rose to ~57%.




Although the stereochemistry of **32** was not rigorously proved, it appeared from the $^1H$–$^1H$ coupling constant (15.6 Hz) that the alkene is probably *trans*. This requires that the elimination follow a *syn* pathway. Perhaps the displacement of the halide by the benzyloxy group is concerted with the elimination, in accord with the *syn* stereochemistry, though $X^-$ and **33** are the

expected products even if the initial elimination produces benzyloxide and (halomethyl)boronic ester.

Concerted benzyloxide displacement and elimination is also consistent with the much better result obtained with (dichloromethyl)lithium in a similar process. Direct conversion of **34** to **36** with (chloromethyl)lithium resulted in the same sort of elimination as observed with **29**, but (dichloromethyl)lithium reacted cleanly to provide **35**. Reduction of the α-chloro boronic ester **35** to **36** was easily accomplished by treatment with sodium hydride in DMSO [22].

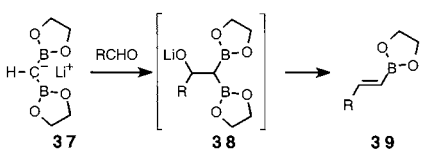



**34** (Cy = cyclohexyl) **35** **36**

Similar reductions have been carried out with K(*i*-PrO)$_3$BH [25], LiEt$_3$BD [26], or K(*i*-PrO)$_3$BD [27]. Normally the direct reaction of boronic esters with LiCH$_2$Cl [24] or LiCH$_2$Br [23] is at least as efficient as any two-step process with LiCHCl$_2$ followed by reduction.

## 2.5. Oxide anions

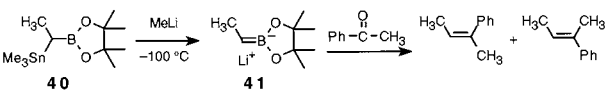
Anionic oxide β to boron arises in a totally different context, the reaction of a lithiated methanediboronic ester such as **37** with an aldehyde or ketone [28,29]. One of the two boronic ester functions and the oxide undergo β-elimination to yield the alkenylboronic ester. The products derived from aldehydes (**39**) are usually ~90% *trans*. It is not known whether the presumed lithiated intermediate **38** undergoes elimination directly or whether the elimination is delayed until work up with aqueous acid.




**37** **38** **39**

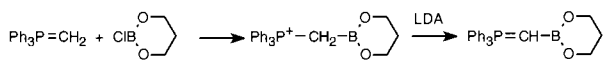
Although the labor of preparing **37** is a deterrent to casual use, this route to **39** provides an alternative to alkyne hydroboration. In Kishi's famous synthesis of palytoxin, alkyne hydroboration failed because of a functional group conflict, and the route via **37**–**39** provided a key intermediate [30].

A stannylboronic ester **40** has been converted to a simple (α-lithioethyl)boronic ester **41**, which with acetophenone yielded a mixture of *Z*- and *E*-2-phenyl-2-butene [31]. In the light of all of the β-alkoxy boronic ester chemistry discovered since that reaction was run, it seems unlikely that elimination occurred before acidic aqueous work-up.

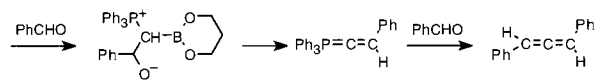



**40** **41**

Another β-oxide elimination has apparently occurred in the reaction of a boron substituted Wittig reagent **42** with benzaldehyde to form 1,3-diphenylallene (48% isolated) [32]. It was postulated that intermediate **43** underwent boron oxide β-elimination and proton loss to form Wittig reagent **44**, which reacted with a second mole of aldehyde to form the allene. (Phosphorus elimination would have led to an alkenylboronic ester, which would not react further with the aldehyde.) Benzophenone under similar conditions yielded tetraphenylallene (47%), but heptanal did not yield any allenic product, as if the saturated analog of **43** did not eliminate boron, though the actual products were not identified.



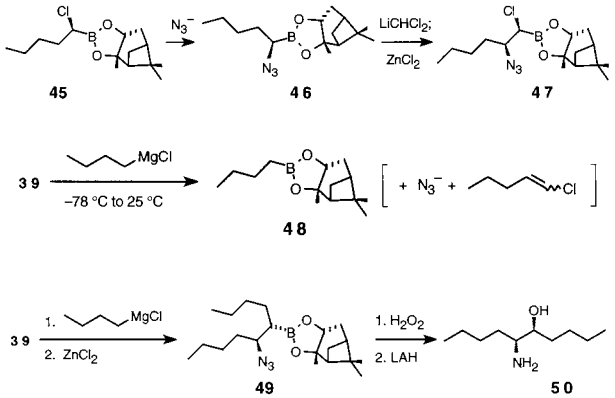

**42**



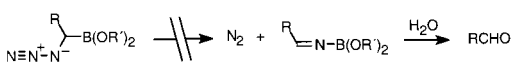

**43** **44**

## 2.6. Azides

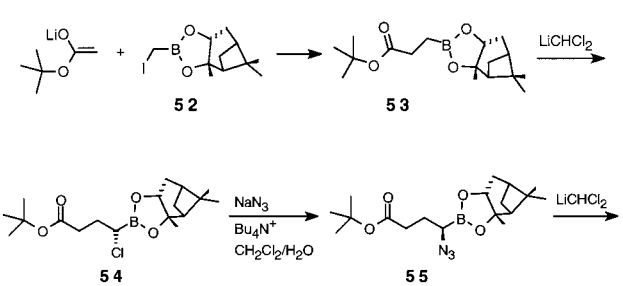
It is remarkable that azide can be used as a functional substituent with boronic esters, but it has proved to be a fairly stable and inert substituent [33,34]. However, it is a bit more labile than alkoxy groups toward β-elimination. The conditions for converting chloro boronic ester **45** to azide **46** involved excess sodium azide, a phase transfer catalyst, and dichloromethane/water. [Caution: diazidomethane is a possible explosive by-product if this reaction is prolonged. Development of safer solvents for this reaction is in progress [35].] Conversion to **47** followed the usual procedure, reaction with LiCHCl$_2$ followed by addition of zinc chloride and warming to rt. Treatment of α-chloro-β-azido boronic ester **47** with butylmagnesium chloride resulted in formation of pinanediol butylboronate (**48**), presumably accompanied by azide ion and 1-chloropentene. This elimination was avoided and the substitution product **49** was formed in high yield when zinc chloride (four equivalents) was added to the mixture after the initial reaction with the Grignard reagent. Oxidation of **49** to **50** under basic conditions resulted in the formation of 5-decene as a major by-product, but proved efficient when buffered at pH 7.6.

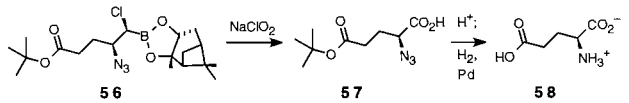


The foregoing results were unanticipated. Trialkylboranes and alkyldichloroboranes react with alkyl azides to eliminate nitrogen and form secondary amines [36]. The analogous reaction of boronic esters has not been observed, but in view of the instability of α-amino boronic esters and the strongly favorable thermodynamics, rearrangement of the α-azido boronic ester to an imine (**51**), which would hydrolyze to an aldehyde, seemed a likely possibility. This reaction has not been observed.



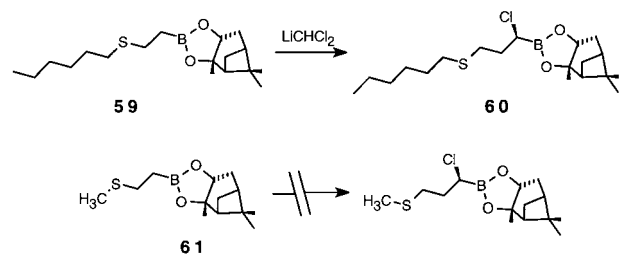
The stability of α-azido boronic esters has been utilized in a straightforward asymmetric synthesis of amino acids, e.g. glutamic acid (**58**) [34]. *tert*-Butyl lithioacetate reacted with pinanediol iodomethylboronate (**52**) to produce the *tert*-butyl 3-borylpropionate **53**, which underwent chain extension with (dichloromethyl)lithium to **54** and azide substitution to **55**. A second chain extension to **56** followed by oxidation with buffered sodium chlorite (in the presence of 2-methyl-2-butene to suppress radical side reactions) yielded crude azido acid **57**. The *tert*-butyl ester was cleaved with trifluoroacetic acid and the azido group reduced catalytically to provide glutamic acid (**58**). Three other amino acids were prepared in an analogous manner to the conversion of **53** to **58** [34], and asymmetrically deuterated pinanediol benzylboronate was also converted to asymmetrically deuterated phenylalanine [26].





## 2.7. Thioethers

Pinanediol [(2-hexylthio)ethyl]boronate (**59**) with (dichloromethyl)lithium underwent normal chain extension to form **60** [33]. Unexpectedly, pinanediol [(2-methylthio)ethyl]boronate (**61**) failed to undergo chain extension [37]. It was suspected that the problem might be β-elimination of boron and sulfur, but this was not proved. A low yield of chain extension product was obtained when the 2,3-butanediol ester was used in place of **61**.



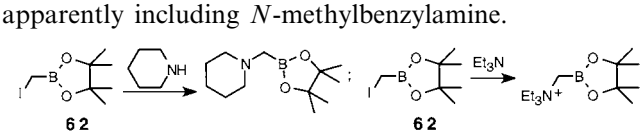
# 3. Protodeboronations

## 3.1. General remarks

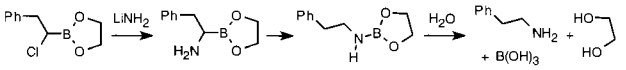
Hydrolysis of boronic acids to boric acid and a hydrocarbon is highly exothermic [1]. However, hydrolysis is normally a very slow process, and most boronic acids are stable to water, acids and bases. Boronic esters are similarly stable, though oxygen ligand exchange may occur. Exceptions are generally those compounds that can form some kind of stabilized carbanion if a base is added to form a tetracoordinate boron.

## 3.2. α-Amino boronic esters

Secondary amines react readily with iodomethylboronic esters to produce stable (dialkylamino)methylboronic esters, and tertiary amines produce the quaternary ammonium salts [38,39]. These reactions are illustrated by the conversion of pinacol iodomethylboronate (**62**) to piperidine and triethylamine derivatives [39]. Attempts to achieve similar reactions with benzylamine resulted only in decomposition products, apparently including *N*-methylbenzylamine.

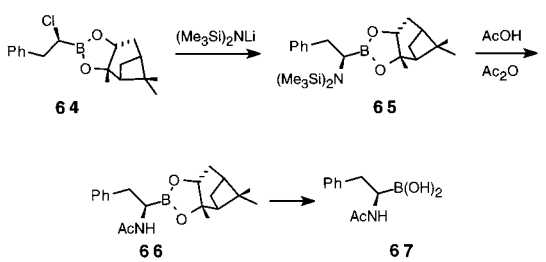


It was subsequently found that α-amino boronic esters or acids which contain an NH group deboronate spontaneously over a period of a few hours, as illustrated by ethylene glycol 1-amino-2-phenylethylboronate (**63**) [40,41].



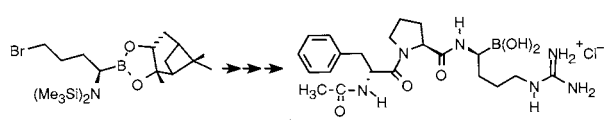
**63**

This instability is associated with the basicity of the amine. Salts and acyl derivatives of amino boronic acids are stable indefinitely [40–42]. The first α-amido boronic acid, the boronic acid analog of *N*-acetylphenylalanine (**67**), proved to be a good inhibitor of chymotrypsin [40]. The key to making this compound was the reaction of pinanediol (1-chloro-2-phenylethyl)boronate (**64**) with lithiohexamethyldisilazane, which provides the *N*-protected intermediate **65**. Acid cleavage of **65** in the presence of acetic anhydride yielded the amido boronic ester **66**. The harsh conditions used to cleave the pinanediol to make the boronic acid **68** are obsolete, as water soluble pinanediol boronic esters are easily equilibrated with water insoluble phenylboronic acid [42].



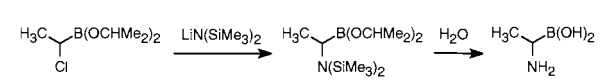
**64** **65** **66** **67**

A number of peptidyl boronic acids have been developed subsequently as enzyme inhibitors. One of the most notable is the thrombin inhibitor DuP 714 (**69**) [42]. The boraarginine component is derived from a (3-bromopropyl)boronic ester, which reacts with $LiCHCl_2$ followed by substitution with $LiN(SiMe_3)_2$ in the normal way to produce precursor **68** [43].



**68** **69**

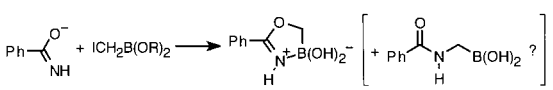
Free amino boronic acids have a sufficient lifetime to show enzyme inhibition. An example is (1-aminoethyl)boronic acid (**71**), which was generated in situ from a stable silylated precursor (**70**) [44].



**70** **71**

Lithiohexamethyldisilazane is well known as a sterically hindered base that normally abstracts protons rather than adding to Lewis acid sites, and the substitution of α-chloro boronic esters by this reagent illustrates how remarkably the boronic ester group facilitates displacement over other reaction pathways, no doubt as a result of the formation of a borate complex with the base and subsequent rearrangement. The initial use of this base was prompted by Majumdar's report (unpublished) that he had tried to deprotonate an α-chloro boronic ester with lithio-2,2,6,6-tetramethylpiperidide, but all that appeared to have happened was partial displacement of the chloride by the piperidide, and he did not investigate further.

It was originally thought that α-amido boronic esters could be made directly via the reaction of a metallated amide with an α-halo boronic ester [45], but it was subsequently found that the major isolated products from such reactions were carbon–oxygen linked, as in **72** [46]. These imino esters tend to have low solubility in water or ether, are undoubtedly chelated, and appear to be highly hydrated. In view of the fact that the imido ester **72** bound slightly more strongly to chymotrypsin than did its isomer **73** [46] it would seem worthwhile to examine further examples for their possible activity, but it appears that this has not been done.

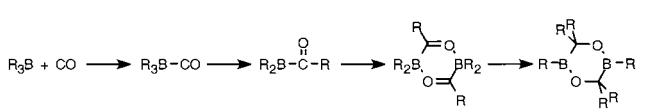


**72** **73** (not isolated)

It is also possible that α-amido boronic esters are formed in major amounts in these reactions, and were overlooked in earlier work merely because of their relatively high water solubility. A change in the metal cationic counterion might increase or decrease the relative proportions of **72** and **73**.

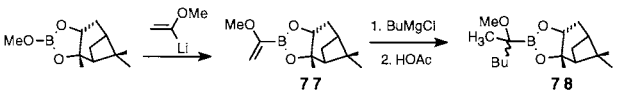
### 3.3. α-Keto boranes

To the reviewer's knowledge, no α-keto boronic ester has ever been reported, but carbon monoxide insertion into trialkylboranes is well established [47,48], and is useful for introducing labeled carbon atoms [49]. All evidence indicates that the initially formed α-keto borane **74** dimerizes rapidly to **75** and rearranges further to 1,4-dioxa-2,5-diborin **76**. The analogous isonitrile insertion into trialkylboranes involves similar but slower rearrangements, and the α-imino borane intermediates are similarly not isolable [50].



**74** **75** **76**

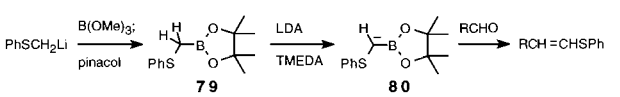
Boronic esters are unreactive toward carbon monoxide. An enol ether of an acetylboronic ester (**77**) has been prepared [20], but attempted hydrolysis to the acetylboronic ester failed to yield any product that could be identified. Treatment of the enol ether with butylmagnesium chloride followed by acetic acid resulted in migration of the butyl group from the boron to the masked carbonyl carbon to form **78** as a mixture of diastereomers [20]. This transformation is analogous to what might be expected of an α-keto boronic ester with a Grignard reagent. Inasmuch as the Grignard reagent presumably attacks the less hindered face of the boron atom, which is known from previous work to yield gross mixtures of isomers from pinanediol esters [51], there remains an unexplored possibility that a chiral director of $C_2$ symmetry might provide useful stereocontrol.



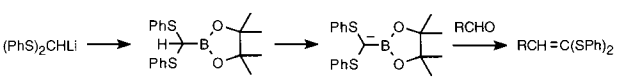

77 78

### 3.4. α-Sulfur substituents

Pinacol (phenylthiomethyl)boronate (**79**) is a well established and useful synthetic intermediate via deprotonation to anion **80** [52]. The bis(phenylthiomethyl)boronate **81** has been prepared and deprotonated to **82** in an analogous manner[53]. These anions can be alkylated, or they react with aldehydes or ketones in the same manner as the diborylmethide anion **37** (Section 2.5), with boron–oxygen elimination as the final step. Obviously, protodeboronation or sulfur stabilized anion formation is not a rapid reaction during the ordinary handling of these compounds.

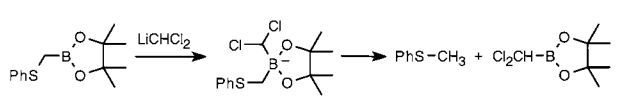



79 80



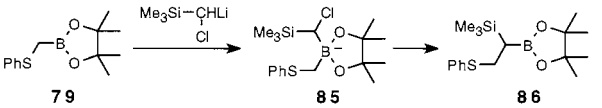

81 82

Although sulfur substituted compounds such as **79** and **81** are stable to a variety of conditions, attempted chain extension of **79** with (dichloromethyl)lithium failed. Dissociation of the (phenylthio)methyl anion from intermediate (dichloromethyl)borate ion **83** is the apparent route to phenyl methyl sulfide and the (dichloromethyl)boronic ester **84**.



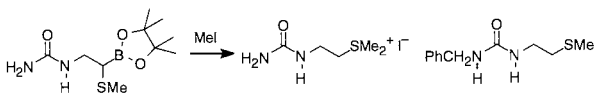

79 83 84

The phenylthiomethide anion did migrate efficiently from boron to carbon in the reaction of **79** with [(chloromethyl)(trimethylsilyl)methyl]lithium to form the [α-silyl-β-(phenylthio)ethyl]boronic ester **86**. The chlorine in borate intermediate **85** is expected to be much more reactive toward nucleophilic displacement than that in **83** [32].




79 85 86

In recent work, an attempt was made to methylate the α-(methylthio) boronic ester **87** in the hope of obtaining the corresponding dimethylsulfonium substituted boronic ester, but only deboronated product, presumably **88**, was obtained. Subjecting an *N*-benzyl analog of **87** to basic conditions led to *N*-benzyl-*N*′-[(methylthio)ethyl]urea (**89**). These facile deboronations are in accord with the carbanion stabilizing properties of the sulfur substituents [54].



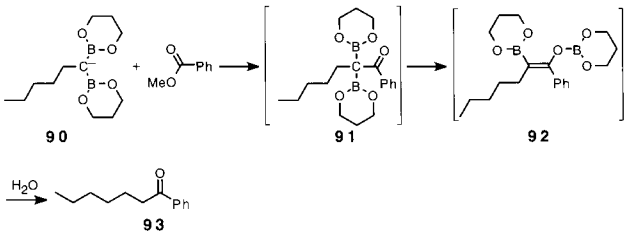

87 88 89

No examples of α-sulfoxide or α-sulfone substituted boronic esters have come to the author's attention. Such compounds would be expected to be highly labile toward deboronation. More remote sulfoxide or sulfone groups are stable, and alkenylboronic esters bearing such substituents b to boron have been prepared and used as dienophiles [55].

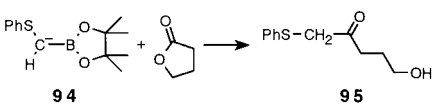
### 3.5. α-Carbonyl substituents

Rearrangement of α-boryl carbonyl groups (B–C–C=O) to the boron enolate (C=C–O–B) is highly exothermic [1] and can be postponed long enough to observe the α-boryl carbonyl compound only in certain special cases. Boranes α to a carboxylic ester group have been produced via hydroboration of α,β-acetylenic esters [56]. (Esters of propargylic acid itself yield β-boryl derivatives [57], and a pinylborane of this class has been converted to a boronic ester [58], but there is no instability once the carbonyl group is this remote from the boron.)

Examples of such deboronations have been encountered in the reactions of diborylmethide or triborylmethide ions with carboxylic esters [29]. For example, the reaction of the hexane-1,1-diboronic ester anion **90** with methyl benzoate presumably produces the keto diboronic ester **91** as an intermediate, but this may rearrange to the boron enolate **92**, and on aqueous work up the only product isolated was hexyl phenyl ketone (**93**).

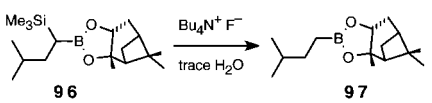


Similar deboronation occurs when a phenylthiomethylboronic ester anion reacts with a carboxylic ester, which results in a useful synthesis of (phenylthio)methyl ketones. An example is the reaction of **94** with butyrolactone to produce the (phenylthio)methyl ketone **95** [52].



### 3.6. α-Silyl substituent—desilylation

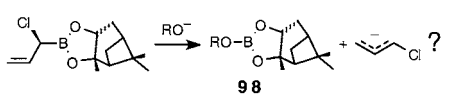
With fluoride as the base, protodesilylation of the trimethylsilyl group rather than protodeboronation occurs, as in the desilylation of **96** to **97** [59].



Evidence that chloride in the $Me_3SiCHCl$ group is activated toward displacement has been provided by the homologation of the (phenylthio)methyl boronic ester **79** to the α-silyl β-phenylthio boronic ester **86** noted above [32]. In cases where homologation of boronic esters with (dichloromethyl)lithium or (chloromethyl)lithium fails, it might be possible to insert a methylene group in the C–B bond via the more facile reaction with $Me_3SiCHClLi$ followed by protodesilylation, but this has not been tested.

### 3.7. α-Chloroallyl anomaly

Although (α-chloroallyl)boronic esters undergo normal substitution with some nucleophiles, for example, $LiN(SiMe_3)_2$ [37], repeated attempts to carry out substitution by alkoxide have failed[60,61]. Perhaps the problem is cleavage to a stable trialkoxyborane such as **98** and chloroallyl anion, but no clear evidence was ever obtained.



An α-bromoallyl boronic ester underwent normal substitution with lithium methoxide [60], and α-chlorocrotyl boronic esters substituted normally, though they were not accessible in satisfactory purity via the usual homologation process and had to be made via a roundabout route [62].

## 4. Oxidations

### 4.1. General remarks

Deboronation with alkaline hydrogen peroxide is normally quantitative, and stereospecifically yields the alcohol with retention of the configuration of the boronic ester [1]. The mechanism of typical peroxidic deboronations was investigated in considerable detail by Kuivila in the 1950s [63]. However, anomalous reactions with hydrogen peroxide have been observed in a number of instances where there are nearby functional substituents, and these will be discussed in this section.

Typically, oxidation of the carbon–boron bond is initiated by nucleophilic attack at boron, and weakly nucleophilic oxidizing agents may attack other substituents faster. Thus, there are a number of examples of oxidation of other functionality without disturbing the boronic ester group, or of oxidations that do result in deboronation but are initiated at a neighboring function. These useful oxidations will also be discussed in this section.

### 4.2. Air oxidation: caution

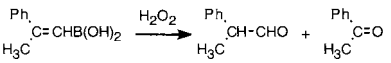
Cyclic boronic esters generally appear to be stable in air, and storage for a number of days or weeks without protection from atmospheric oxygen usually results in no measurable change. This can be deceptive! Air oxidation of the carbon–boron bond is highly exothermic even though it is normally slow [1]. For the reaction $1/2O_2 + H_2O + CH_3B(OH)_2 \rightarrow CH_3OH + B(OH)_3$, $\Delta H^\circ = -239.1$ kJ mol$^{-1}$ ($-57.1$ kcal mol$^{-1}$).

Autoxidations are generally radical initiated reactions. After long exposure to air, peroxidic impurities tend to build up, and once autoxidation gets started, the entire sample can be consumed in a relatively short time. We have had experience with compounds that were stable for a number of weeks, but after a few months had entirely decomposed. A rubber septum cap is not an adequate oxygen barrier for long term storage. Analytical samples of boronic esters stored in screwcap vials are usually obviously decomposed after a few years. It is difficult to document such decompositions, and it is reasonable to suspect that they are more common than has been recognized or reported.

### 4.3. Anomalous reactions with hydrogen peroxide

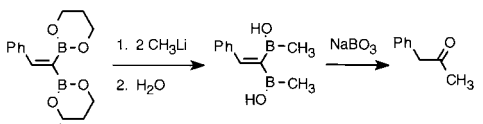
Although the usual ionic internal migration mechanism for peroxidic oxidation of boronic esters requires retention of configuration of the migrating carbon [63], and this is the only measurable pathway in standard cases [7,64], non-specific radical reactions become the major pathways when trialkylboranes are treated with hydrogen peroxide in the absence of base [65]. For the oxidation of α-chloro boronic esters to aldehydes, inclusion of a buffer such as bicarbonate or phosphate provides sufficient base to prevent side reactions [66].

Certain alkenylboron compounds appear particularly prone to oxidize via pathways other than the usual one. The anomalous reaction of purified 2-phenylpropeneboronic acid (**99**) with basic hydrogen peroxide came as a considerable surprise [67]. Not only the expected α-methyl phenylacetaldehyde but also acetophenone were obtained as products. If only bicarbonate buffer was used, the proportion of acetophenone rose to ~40%, but even in strongly basic solution several percent of the anomalous cleavage occurred. Sodium perborate proved more selective, and in strongly basic solution reduced the amount of anomalous cleavage to 1–2% [67].



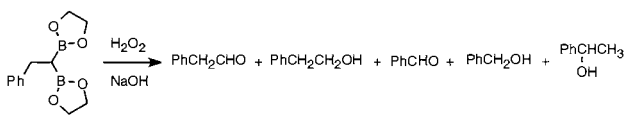

**99**

A stranger cleavage was observed when the phenylethenediboronic ester **100** was methylated with methyllithium and then treated with alkaline sodium perborate [68]. Methyl migration from boron to carbon occurred, and phenylacetone was isolated in yields up to 75%.



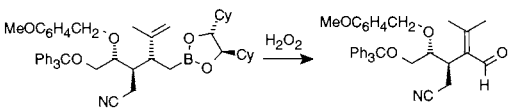

**100** **101**

Anomalous oxidation/fragmentation of a diboronic ester was reported previously by Pasto et al. [69]. The phenylethanediboronic ester **102** yielded a variety of fragmentation products. However, some caution is needed in the interpretation of older results such as these, inasmuch as NMR instruments in that era were inadequate to prove the purity of **102**.




**102**

Homoallylic boronic esters may also yield anomalous results. An example is the oxidation of the homoallylic boronic ester **103** to the α,β-unsaturated aldehyde **104** as the only isolable product [70]. The amount of sodium hydroxide used in this oxidation was a little more than one equivalent relative to the boronic ester and a little less than the stated amount of hydrogen peroxide used. These conditions were basic enough that ordinarily only direct replacement of the boronic ester group by hydroxide ion would be observed, and the fact that none of the normal reaction product was observed is significant.

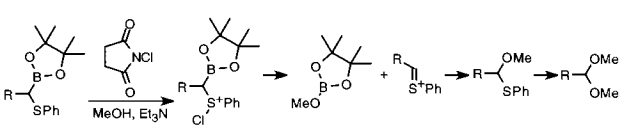



**103** **104**

The foregoing anomalies cast doubt on any unusual results interpreted solely on the basis of hydroboration/oxidation data, without direct characterization of the borane intermediates.

In contrast to the results obtained with boronic ester **103**, earlier oxidations of homoallylic boranes or borinic esters yielded the expected homoallylic alcohols [71,72]. Perhaps the greater acidity of these boranes encourages ionic reactions.

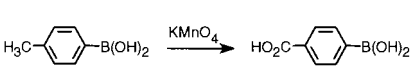
Products **105** from the alkylation of pinacol (phenylthiomethyl)boronate (**79**) react with *N*-chlorosuccinimide or similar reagents under basic conditions to produce monothioacetals (**108**), which are converted to acetals (**109**) if a second mole of *N*-chlorosuccinimide is included [73]. In this case the oxidative deboronation may involve β-elimination of chloride and borate ester from **106** to form the thiol cation **107**. Protodeboronation is not encountered under these conditions.




**105** **106** **107** **108** **109**

### 4.4. Oxidation of other functions in the presence of boronic esters

The carbon–boron bond is relatively inert to oxidizing agents that do not coordinate with boron. The oldest example is the rather surprising oxidation of the methyl group of tolylboronic acid (**110**) with potassium permanganate [74].

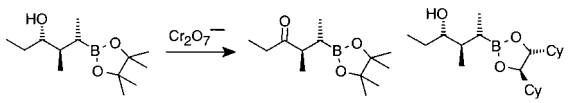



**110**

Chromate ion at pH 3–7 oxidizes boronic acids to the corresponding alcohols, which are stable under these conditions [75]. *tert*-Butylboronic acid reacts four

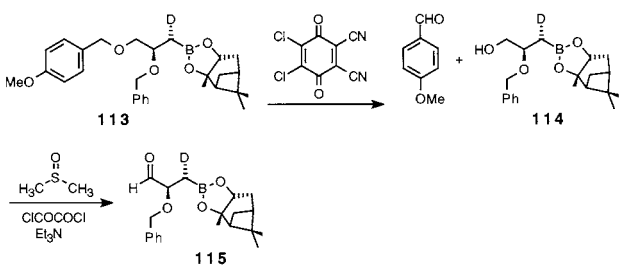
orders of magnitude faster than ethylboronic acid. In strong acid, *sec*-alkylboranes are oxidized directly to ketones [76]. Pyridinium chlorochromate oxidizes primary trialkylboranes to aldehydes [77].

In spite of this susceptibility of carbon–boron bonds to attack by chromium(VI), oxidation of a secondary alcohol to a ketone by pyridinium dichromate in the presence of the pinacol boronic ester function of **111** has proved efficient [66]. Although the dicyclohexylethanediol ester **112** could also be oxidized to the ketone, some loss occurred because of cleavage and oxidation of the diol. Oxidation of **112** by tetrapropylammonium perruthenate/*N*-methylmorpholine *N* oxide or Swern's method also yielded the ketone together with some cleavage and oxidation of the diol.



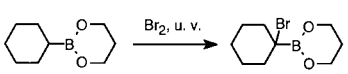

111 112

DDQ oxidation converted the *p*-methoxybenzyl ether of **113** to alcohol **114**, and Swern oxidation converted the primary alcohol function of **114** to the aldehyde of **115**.




113 114 115

Free radical bromination of *sec*-alkylboronic esters such as **116** replaces the hydrogen α to boron without affecting the carbon–boron bond [78].




116

The carbon–boron bond tends to be fairly insensitive to radical attack in general, a fact that was taken advantage of in the author's earliest work [79]. *tert*-Butyl hypochlorite with an equimolar amount of di-*tert*-butyl methylboronate, $CH_3B[OC(CH_3)_3]_2$, yielded 9–10% chloroboronic ester, $ClCH_2B(OR)_2$, and 10–15% trialkylborate, $B(OR)_3$, with the major reaction being chlorination of the abundant *tert*-butyl methyl groups [80]. Thus, the statistically corrected C–B bond cleavage in this instance was ~5 times faster than the methyl C–H bond, though when methylboronic anhydride (trimethylboroxine) was similarly chlorinated, the only observed reaction was C–B cleavage.

## 5. Problems involving the homologation/displacement process

### 5.1. Introductory comments

The reaction of boronic esters of chiral diols with (dihalomethyl)lithium is a complex process which involves several important considerations. These include (1) choice of chiral diol; (2) protection of the α-halo boronic ester from epimerization during its formation or subsequent work up; (3) catalysis of the reaction; (4) low temperature required for the reaction; (5) displacement of the halide by a nucleophile; (6) involvement of neighboring functional groups.

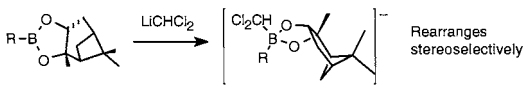
### 5.2. Chiral diols

The author is often asked about alternative diols as chiral directors. Given that both pure enantiomers of chiral 1,2-dicyclohexyl-1,2-ethanediol are easy to make in substantial quantities [81], and that the diastereoselection attainable with diols of this type is normally very high, up to 99.9% [7], it is hard to see how the results could be improved. Pinanediol is made even more easily [82], and can be used if greater stability of the boronic ester toward hydrolysis is needed, or if lower cost takes precedence and stereoselectivity in the 98–99% range (from purified pinene/pinanediol) or ~90% ee (from inexpensive pinene) will do. Diisopropylethanediol works as well as dicyclohexylethanediol [7], but it is harder to make.

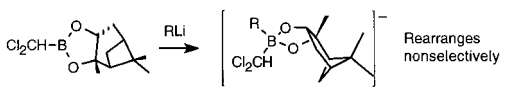
(*R*,*R*)-2,3-Butanediol yields about 20:1 diastereomeric ratios, sufficient to be useful if this natural fermentation product were cheaper [83]. 2,4,5,6-Di-*o*-cyclohexylidenemannitol with normal amounts of zinc chloride has led to secondary alcohols in 90–99% ee's, though only 41–77% yields [84]. However, diacetonemannitol yields very low diastereoselection unless about four equivalents of zinc chloride are added, which brings it into the 90–95% range [85].

Diols that do not work include the following. Boronic esters of dialkyl tartrates fail to undergo the CHCl insertion reaction [33]. A boronic ester of an enantiomerically pure 1,3-diol, 2,4-pentanediol, yielded a negligible diastereomeric excess [86]. The six-membered dioxaborin ring will have one methyl substituent axial and the other equatorial, and cannot provide the significant $C_2$-symmetry of the dioxaborolanes derived from 1,2-diols. 2,5-Dimethoxy-2,5-dimethyl-3,4-hexanediol, which is easier to make than diisopropylethanediol, required two equivalents of zinc chloride, and the ester of butylboronic acid gave only 12:1 diastereoselection [87]. Binaphthol is a popular chiral diol, but it is expensive and not likely to form very stable boronic esters, and there has not been any good theoretical or practical reason to test it.

There is one cautionary note about the choice of chiral diols. With boronic esters of $C_2$-symmetry, it makes no difference whether one starts with $Cl_2CHB(OR)_2$ and RLi or $RB(OR)_2$ and $LiCHCl_2$, as both produce identical intermediate borate complexes. However, the asymmetry of pinanediol generates two non-equivalent faces on the boron atom, consequently two different borate complexes and two different stereochemical outcomes [51]. Thus, borate complex **118** derived from pinanediol alkylboronate **117** rearranges stereoselectively, but borate complex **120** from pinanediol (dichloromethyl)borate **119** yields a gross mixture of diastereomeric α-chloro boronic esters.




117 118

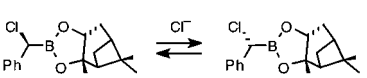



119 120

Another aspect to this asymmetry is that pinanediol esters can be used in some sequences, for example, double inversion [88], that will probably fail with esters of $C_2$-symmetry because the diastereoselection in the second step will oppose the second inversion.

### 5.3. Epimerization

α-Halo boronic esters are reactive in $S_N2$ reactions and consequently epimerize readily in the presence of halide ion. The kinetics of epimerization of pinanediol (α-chlorobenzyl)boronate (**121**) have been studied in considerable detail [89]. It was found that free chloride ion and **121** react in a typical second-order process. The reaction in THF was greatly accelerated by a small amount of water or dimethyl sulfoxide, and was suppressed by reagents such as zinc chloride or mercuric chloride that complex with chloride ion.



121

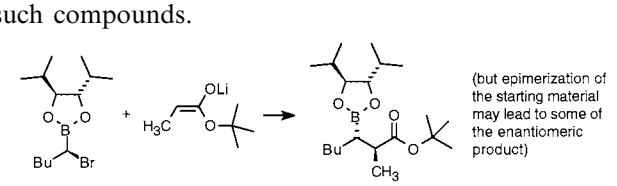
The half-life for epimerization of **121** at rt under the usual conditions used to make the compound in the absence of zinc chloride is on the order of 3–4 h ($k = 5.7 \times 10^{-5}$ $s^{-1}$ for 0.45 M LiCl at 25°C). Compounds having an alkyl group in place of phenyl epimerize much more slowly, ca. 10–20% in a day. The minimum rate of epimerization, about two orders of magnitude slower, occurs when there is just enough $ZnCl_2$ to convert all of the $Cl^-$ ion to $ZnCl_3^-$. A small amount of $ZnCl_4^{2-}$ does no harm, though larger amounts evidently dissociate to some extent and are less effective at suppressing epimerization.

It is important that zinc chloride not be used in excess of the necessary amount for synthetic purposes. Under the relatively dilute conditions used for allowing the (dichloromethyl)borate ester to rearrange to **121**, a small amount of free $ZnCl_2$ does no harm, but at higher concentrations there is a third-order term in **121**, $ZnCl_2$, and $ZnCl_3^-$. This term in the rate law becomes very large when all of the reactants are concentrated to above 1 M, and could result in substantial epimerization of a product during work up.

For boronic esters that lack any functionality except perhaps unsaturation or halogen, the theoretically correct amount of zinc chloride is one equivalent. Free zinc chloride is required in order to catalyze the reaction, and will do no harm until the solution is concentrated. Polar substituents add another complication. Alkoxy substituted boronic esters react sluggishly, as if they tie up additional zinc chloride by complexation. The rule of thumb developed during the synthesis of L-ribose was that an additional mole of zinc chloride should be added for each benzyloxy group (or other functional substituent) present in the boronic ester [90]. This practice has been followed in subsequent syntheses, and in the few cases where the amount of zinc chloride has been varied to optimize conditions, it appears to be a good first approximation. If epimerization during work up resulting from catalysis by excess zinc chloride has occurred, it has never been sufficient to attract our attention.

The accelerating effect of water on the epimerization rate can cause problems. The zinc chloride has to be strictly anhydrous. Drying at 100°C under vacuum while stirring has been successful with small batches [33], but fusion has been preferred for larger amounts. Commercial solutions of zinc chloride in ether or THF appear to work well and are the most convenient. When work up is begun, it can be important to (a) distill the THF under vacuum first and (b) add ether or pentane to the mixture followed by saturated ammonium chloride, not plain water, in order to avoid having the α-chloro boronic ester in the same solution that contains water and chloride.

For some purposes, α-bromo boronic esters are preferred, as in the homologation of boronic esters containing several alkoxy groups [90] or the reaction of α-halo boronic esters such as **122** with ester enolates, which attack α-chloro boronic esters sluggishly [87]. Because **123** was formed in a good diastereomeric ratio ($\sim$ 50:1), this reaction was suggested as a good route to such compounds.




122 123

However, later observations cast doubt on the enantioselectivity of the foregoing route [91]. A dicyclohexylethanediol (bromoalkyl)boronate similar to **122** was found to epimerize unexpectedly rapidly (one sample ~10% after a day of storage), and both epimers were found to react readily with the ester enolate to produce the same diastereomeric relationship between the carbons connected. This was unexpected in view of the double diastereoselection observed when the nucleophile was an alkyl anion from a Grignard reagent [7], and the 200 MHz NMR spectra available in the earlier work [87] would not necessarily have revealed the epimer even in fairly substantial amounts. Thus, some rechecking and possibly new experimental details are needed if this ester enolate reaction is to be used for synthetic purposes. Epimerization was never observed in the earlier work with the benzyloxy substituted boronic esters [90], which undergo bromide displacement much more slowly.

### 5.4. Catalysis

Zinc chloride obviously serves a double function of catalysis and sequestration of chloride ion. As pointed out in Section 1, a satisfying interpretation of the mechanism has been proposed [6], in which a Lewis acid forms a cage structure and assists departure of chloride ion. Much of the practical problem with respect to catalysis involves use of the correct amount of catalyst, which is discussed in the preceding section.

Catalysis of the reaction of an achiral boronic ester with a chiral ytterbium complex has been reported recently [92]. A good ee in the product was obtained only when the catalyst was present in excess of the reactants. This may merely reflect the lack of separation of the chloride sequestering effect from the catalytic effect. In order to achieve an effective chiral catalytic route for this reaction, it will be necessary to find a Lewis acid that binds chloride ion well enough to assist the reaction, but not as strongly as a second reagent that sequesters chloride ion without catalyzing the reaction significantly.

### 5.5. Temperature problem

The need for low temperatures is the costliest aspect of the reaction of (dichloromethyl)lithium with boronic esters. The classical method of generating (dichloromethyl)lithium is the addition of butyllithium to dichloromethane in THF at −100°C [93]. Although (dichloromethyl)lithium was reported to have a lifetime of hours at temperatures as high as −65°C [93], we were initially baffled that it could not be generated with dry ice cooling [21]. The highly exothermic nature of the reaction may be the cause, as a drop of butyllithium solution falling into dichloromethane/THF even at −100°C makes an audible noise, as if the solvent boils. Better results are usually obtained if the butyllithium runs down the cold wall of the reaction vessel before contacting the dichloromethane [33].

Addition of LDA to dichloromethane generates (dichloromethyl)lithium in the presence of the boronic ester at temperatures up to −20°C [33]. This in situ method generates diisopropylamine as a by-product, and requires approximately an additional mole of zinc chloride to compensate for amine–zinc complexation, but is more practical for large scale preparations. Using the in situ method, this process has been scaled up to ~50 kg of boronic ester at Boulder Scientific Company [94].

### 5.6. Displacements on α-halo boronic esters

Most of the likely problems involving displacements of halide from α-chloro boronic esters have been discussed in Sections 5.2 and 5.3. Ordinarily, α-halo boronic esters are considerably more reactive than ordinary alkyl halides, and competing elimination reactions are rare.

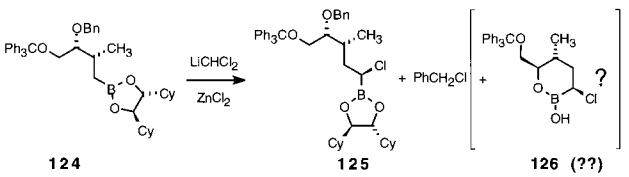
It is normally much easier to displace chloride from (α-chloroalkyl)boronic esters than from (dichloromethyl)boronic esters. Although alkoxides displace chloride ion from every α-chloro boronic ester tested except for (otherwise unsubstituted) α-chloroallylboronic esters, it has not been found possible to substitute (dichloromethyl)boronic esters by alkoxides. Migrating carbon atoms appear to be the only nucleophiles capable of displacing the first of two halides, and these cannot be in structures that would be stable carbanions if dissociated, such as enolates.

Displacement of bromide from (bromomethyl)boronic esters by trityloxide anion, an extremely hindered nucleophile, requires dimethyl sulfoxide as solvent [95]. On the other hand, dimethyl sulfoxide did not appear to help the reaction of azide ion with a sluggish α-chloro boronic ester [96], and the use of a two-phase system for such displacements has been described in Section 2.6.

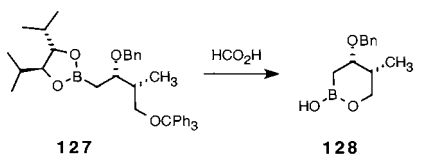
### 5.7. Functional group reactions

The synthesis of L-ribose ran into difficulties during installation of the fifth carbon, and further extension was not possible, in spite of the fact that the benzyloxy groups had not appeared to cause any problem during installation of the first four carbons [90]. More recent work suggests that a possible source of the problem might be some kind of direct interaction

with a benzyloxy function, as was found in the reaction of boronic ester **124** with (dichloromethyl)lithium [22]. The yield of the homologation product **125** was ~60%, and benzyl chloride was identified as a byproduct by mass spctroscopic analysis. Perhaps the oxygen of the benzyloxy group formed a six-membered ring borate with the boron atom of **125**, which might lose dicyclohexylethanediol to form **126** or other derivative that failed to elute and was not identified.

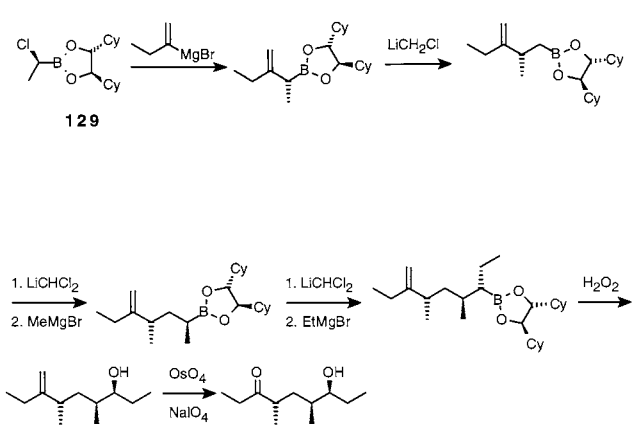



In a better documented example of neighboring group interaction, **127** was detritylated with formic acid and closed to what appeared to be **128** on the basis of NMR evidence [22].

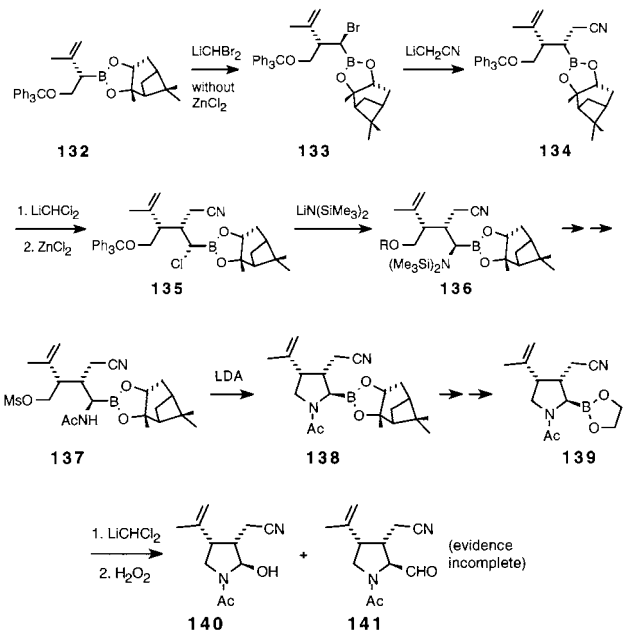



### 5.8. Functional group polarity effects

The boronic ester homologation process is most efficient in the absence of neighboring functionality or polar substituents. A recent example, the synthesis of the insect pheromone serricornin (**131**), illustrates how efficient this process can be [97]. The conversion of **129** through the entire sequence does not require chromatography until deboronated intermediate **130** is reached. After chromatography and distillation, **130** is readily oxidized to serricornin (**131**). The yield of **131** based on **129** was 59%.

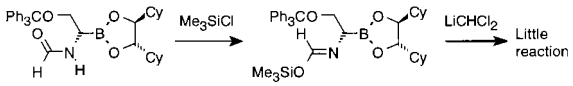



Another recent example, a failed synthesis of the neurotoxin kainic acid, illustrates the kind of problems polar functional groups can cause [98]. The allylic functionality in intermediate **132** underwent some kind of decomposition or rearrangement if the reaction with (dibromomethyl)lithium was carried out in the presence of zinc chloride, and yielded a 9:1 mixture of **133** and its epimer without zinc chloride. Fortunately, **133** crystallized and could thus be purified easily. The next step, reaction with lithioacetonitrile, was fairly efficient with bromo compound **133** but not with its chloro analog. Conversion of **134** to **135** was straightforward.




Reaction of **135** with azide ion was so slow as to create a hazard of diazidomethane formation in the dichloromethane/water phase transfer system, and the reaction with lithiohexamethyldisilazane to form **136** was used instead. Conversion to the amido boronic ester with a methanesulfonyl substituent (**137**) in several steps was then straightforward, and base initiated ring closure to the pyrrolidineboronic ester **138** was facile. However, attempts to carry out the homologation of **138** with (dichloromethyl)lithium resulted in low yields, and the pinanediol ester was therefore cleaved and converted to the ethylene glycol ester **139**. Attempted homologation of **139** followed by peroxidic oxidation yielded mainly the simple deboronation product **140** derived from unchanged **139**, but a small yield of what appeared to be the desired aldehyde **141** on the basis of mass spectral and NMR evidence was also obtained. Further work with the few milligrams of **141** was considered impractical, though all that remained to be done to reach kainic acid was oxidation of the aldehyde and hydrolysis of the acetyl and nitrile functions [98].

Similar resistance to homologation by compounds having polar nitrogen functionality was encountered in another study [54]. It was unclear whether any homologation of silylated amido boronic ester **142** or similar compounds took place.




**142**

## Acknowledgements

This work has been supported by the National Science Foundation, most recent grants numbered CHE8922672, CHE9303074 and CHE9613857, and the National Institutes of Health, grants GM39063, GM44995 and GM50298.

## References

[1] D.S. Matteson, Stereodirected Synthesis with Organoboranes, Springer, Berlin, 1995.
[2] D.S. Matteson, in: G. Helmchen, R.W. Hoffmann, J. Mulzer, E. Schaumann (Eds.), Houben-Weyl, Methods of Organic Chemistry, Georg Thieme, Stuttgart, 1995. Stereoselect. Synth. E21a, 1077–1100.
[3] D.S. Matteson, Tetrahedron 54 (1998) 10555–10607.
[4] D.S. Matteson, in: W. Siebert (Ed.), Advances in Boron Chemistry, The Royal Society of Chemistry, Cambridge, UK, 1997, p. 185.
[5] Older reviews: (a) D.S. Matteson, Acc. Chem. Res. 21 (1988) 294–300. (b) D.S. Matteson, Chem. Rev. 89 (1989) 1535–1551. (c) D.S. Matteson, Tetrahedron 45 (1989) 1859–1885. (d) D.S. Matteson, Pure Appl. Chem. 63 (1991) 339–344. (e) D.S. Matteson, in: Atta-ur-Rahman (Ed.), Studies in Natural Products Chemistry, Vol. 11, Elsevier, Amsterdam, 1992, p. 409–427. (f) D.S. Matteson, in: G.W. Kabalka (Ed.), Current Topics in the Chemistry of Boron, The Royal Society of Chemistry, Cambridge, UK, 1994, p. 119–124.
[6] (a) M.M. Midland, J. Org. Chem. 63 (1998) 914–915. (b) E.J. Corey, D. Barnes-Seeman, T.W. Lee, Tetrahedron: Asymmetry 8 (1997) 3711–3713.
[7] P.B. Tripathy, D.S. Matteson, Synthesis (1990) 200–206.
[8] (a) D.S. Matteson, J. Am. Chem. Soc. 81 (1959) 5004. (b) D.S. Matteson, J. Am. Chem. Soc. 82 (1960) 4228–4233.
[9] D.S. Matteson, R.W.H. Mah, J. Am. Chem. Soc. 85 (1963) 2599–2603.
[10] D.S. Matteson, J.D. Liedtke, J. Org. Chem. 28 (1963) 1924.
[11] D.S. Matteson, J.D. Liedtke, Chem. Ind. (London) (1963) 1241.
[12] D.S. Matteson, J.D. Liedtke, J. Am. Chem. Soc. 87 (1965) 1526.
[13] G. Zweifel, H. Arzoumanian, C.C. Whitney, J. Am. Chem. Soc. 89 (1967) 3652–3653.
[14] H.C. Brown, N.G. Bhat, J. Org. Chem. 53 (1988) 6009–6013.
[15] (a) H.C. Brown, V. Somayaji, Synthesis (1984) 919–920. (b) H.C. Brown, T. Imai, N.G. Bhat, J. Org. Chem. 51 (1986) 5277–5282. (c) H.C. Brown, N.G. Bhat, Tetrahedron Lett. 29 (1988) 21–24.
[16] D.S. Matteson, K. Peacock, J. Organomet. Chem. 2 (1964) 190–192.
[17] D.S. Matteson, P.B. Tripathy, Unpublished.
[18] D.S. Matteson, P.B. Tripathy, A. Sarkar, K.M. Sadhu, J. Am. Chem. Soc. 111 (1989) 4399–4402.
[19] D.S. Matteson, G.D. Hurst, Organometallics 5 (1986) 1465–1467.
[20] D.S. Matteson, E.C. Beedle, Heteroatom Chemistry 1 (1990) 135–140.
[21] D.S. Matteson, D. Majumdar, Organometallics 2 (1983) 1529–1535.
[22] D.S. Matteson, R. Soundararajan, O.C. Ho, W. Gatzweiler, Organometallics 15 (1996) 152–163.
[23] K.M. Sadhu, D.S. Matteson, Organometallics 4 (1985) 1687–1689.
[24] T.J. Michnick, D.S. Matteson, Synlett. (1991) 631–632.
[25] (a) H.C. Brown, T. Imai, P.T. Perumal, B. Singaram, J. Org. Chem. 50 (1985) 4032. (b) H.C. Brown, R.G. Naik, R.K. Bakshi, C. Pyun, B. Singaram, J. Org. Chem. 50 (1985) 5586. (c) H.C. Brown, R.G. Naik, B. Singaram, C. Pyun, Organometallics 4 (1985) 1925.
[26] D.S. Matteson, E.C. Beedle, E. Christenson, M.A. Dewey, M.L. Peterson, J. Label. Compd. Radiopharm. 25 (1988) 675–683.
[27] D.S. Matteson, A.A. Kandil, R. Soundararajan, J. Am. Chem. Soc. 112 (1990) 3964–3969.
[28] (a) D.S. Matteson, R.J. Moody, P.K. Jesthi, J. Am. Chem. Soc. 97 (1975) 5608. (b) D.S. Matteson, P.K. Jesthi, J. Organomet. Chem. 110 (1976) 25–37.
[29] D.S. Matteson, R.J. Moody, Organometallics 1 (1982) 20–28.
[30] J. Uenishi, J.M. Beau, R.W. Armstrong, Y. Kishi, J. Am. Chem. Soc. 109 (1987) 4756.
[31] D.S. Matteson, J.W. Wilson, Organometallics 4 (1985) 1690–1692.
[32] D.S. Matteson, D. Majumdar, Organometallics 2 (1983) 230–236.
[33] D.S. Matteson, K.M. Sadhu, M.L. Peterson, J. Am. Chem. Soc. 108 (1986) 812–819.
[34] D.S. Matteson, E.C. Beedle, Tetrahedron Lett. 28 (1987) 4499–4502.
[35] D.S. Matteson, R.P. Singh, Unpublished results.
[36] (a) A. Suzuki, S. Sono, M. Itoh, H.C. Brown, M.M. Midland, J. Am. Chem. Soc. 93 (1971) 4329. (b) H.C. Brown, M.M. Midland, A.B. Levy, J. Am. Chem. Soc. 95 (1973) 2394. (c) H.C. Brown, M.M. Midland, A.B. Levy, A. Suzuki, S. Sono, M. Itoh, Tetrahedron 43 (1987) 4079.
[37] D.S. Matteson, T.J. Michnick, R.D. Willett, C.D. Patterson, Organometallics 8 (1989) 726–729.
[38] D.S. Matteson, T.C. Cheng, J. Org. Chem. 33 (1968) 3055.
[39] D.S. Matteson, D. Majumdar, J. Organomet. Chem. 170 (1979) 259–264.
[40] D.S. Matteson, K.M. Sadhu, G.E. Lienhard, J. Am. Chem. Soc. 103 (1981) 5241–5242.
[41] D.S. Matteson, K.M. Sadhu, Organometallics 3 (1984) 614–618.
[42] J. Wityak, R.A. Earl, M.M. Abelman, Y.B. Bethel, B.N. Fisher, G.S. Kauffman, C.A. Kettner, P. Ma, J.L. McMillan, L.J. Mersinger, J. Pesti, M.E. Pierce, F.W. Rankin, R.J. Chorvat, P.N. Confalone, J. Org. Chem. 60 (1995) 3717–3722.
[43] D.S. Matteson, P.K. Jesthi, K.M. Sadhu, Organometallics 3 (1984) 1284–1288.
[44] K. Duncan, S.W. Faraci, D.S. Matteson, C.T. Walsh, Biochemistry 28 (1989) 3541–3549.
[45] R.N. Lindquist, A.C. Nguyen, J. Am. Chem. Soc. 99 (1977) 6435–6437.
[46] P. Amiri, R.N. Lindquist, D.S. Matteson, K.M. Sadhu, Arch. Biochem. Biophys. 234 (1984) 531–536.
[47] (a) M.E.D. Hillman, J. Am. Chem. Soc. 84 (1962) 4715. (b) M.E.D. Hillman, J. Am. Chem. Soc. 85 (1963) 982. (c) M.E.D. Hillman, J. Am. Chem. Soc. 85 (1963) 1626.

[48] (a) H.C. Brown, M.W. Rathke, J. Am. Chem. Soc. 89 (1967) 2737. (b) H.C. Brown, Science 210 (1980) 485.
[49] G. Kabalka, R.S. Varma, Tetrahedron 45 (1989) 6601.
[50] (a) J. Casanova Jr., R.E. Schuster, Tetrahedron Lett. (1964) 405. (b) G. Hesse, H. Witte, G. Bittner, Justus Liebigs Ann. Chem. (1965) 687. (c) J. Casanova Jr., H. Kiefer, J. Org. Chem. 34 (1969) 2579.
[51] D.J.S. Tsai, P.K. Jesthi, D.S. Matteson, Organometallics 2 (1983) 1543–1545.
[52] (a) D.S. Matteson, K. Arne, J. Am. Chem. Soc. 100 (1978) 1325. (b) D.S. Matteson, K.H. Arne, Organometallics 1 (1982) 280–288.
[53] A. Mendoza, D.S. Matteson, J. Org. Chem. 44 (1979) 1352–1354.
[54] D.S. Matteson, R.P. Singh, C.H. Sutton, J.D. Verheyden, J. Lu, Heteroatom Chem. 8 (1997) 487–494.
[55] C. Rasset-Deloge, P. Martinez-Fresneda, M. Vaultier, Bull. Soc. Chim. Fr. 129 (1992) 285.
[56] J. Plamondon, J.T. Snow, G. Zweifel, Organomet. Chem. Syn. 1 (1971) 249.
[57] E. Negishi, T. Yoshida, J. Am. Chem. Soc. 95 (1973) 6837.
[58] P. Martinez-Fresneda, M. Vaultier, Tetrahedron Lett. 30 (1989) 2929.
[59] D.J.S. Tsai, D.S. Matteson, Organometallics 2 (1983) 236–241.
[60] R.W. Hoffmann, B. Landmann, Chem. Ber. 119 (1986) 1039.
[61] D.S. Matteson, T.J. Michnick, Unpublished.
[62] R.W. Hoffmann, S. Dresely, Synthesis (1988) 103.
[63] (a) H.G. Kuivila, J. Am. Chem. Soc. 76 (1954) 870. (b) H.G. Kuivila, J. Am. Chem. Soc. 77 (1955) 4014. (c) H.G. Kuivila, A.G. Armour, J. Am. Chem. Soc. 79 (1957) 5659.
[64] H.C. Brown, G. Zweifel, J. Am. Chem. Soc. 83 (1961) 2544.
[65] D.B. Bigley, D.W. Payling, J. Chem. Soc. B (1970) 1811.
[66] (a) D.S. Matteson, H.-W. Man, J. Org. Chem. 58 (1993) 6545–6547. (b) D.S. Matteson, H.-W. Man, O.C. Ho, J. Am. Chem. Soc. 118 (1996) 45604566.
[67] D.S. Matteson, R.J. Moody, J. Org. Chem. 45 (1980) 1091.
[68] D.S. Matteson, R.J. Moody, J. Organomet. Chem. 152 (1978) 265.
[69] D.S. Matteson, J.-J. Yang, Tetrahedron: Asymm. 8 (1997) 3855–3861.
[70] (a) D.J. Pasto, J. Chow, S.K. Arora, Tetrahedron Lett. (1967) 723. (b) D.J. Pasto, S.K. Arora, J. Chow, Tetrahedron 25 (1969) 1571.
[71] H.C. Brown, R. Liotta, G.W. Kramer, J. Org. Chem. 43 (1978) 1058.
[72] G. Zweifel, S.J Backlund, T. Leung, J. Am. Chem. Soc. 99 (1977) 5192.
[73] A. Mendoza, D.S. Matteson, J. Organomet. Chem. 156 (1978) 149.
[74] (a) A. Michaelis, Justus Liebigs Ann. Chem. 315 (1901) 19. (b) W. König, W. Scharrnbeck, J. Prakt. Chem. 128 (1930) 153. (c) B. Bettman, G.E.K. Branch, D.L. Yabroff, J. Am. Chem. Soc. 56 (1934) 1865.
[75] J.C. Ware, T.G. Traylor, J. Am. Chem. Soc. 85 (1963) 3026.
[76] H.C. Brown, C.P. Garg, J. Am. Chem. Soc. 83 (1961) 2951, 2952.
[77] (a) C.G. Rao, S.U. Kulkarni, H.C. Brown, J. Organomet. Chem. 172 (1979) C20. (b) H.C. Brown, S.U. Kulkarni, C.G. Rao, Synthesis (1980) 151.
[78] H.C. Brown, N.R. De Lue, Y. Yamamoto, K. Maruyama, J. Org. Chem. 42 (1977) 3252.
[79] D.S. Matteson, J. Am. Chem. Soc. 82 (1960) 4228.
[80] D.S. Matteson, J. Org. Chem. 29 (1964) 3399.
[81] W.C. Hiscox, D.S. Matteson, J. Org. Chem. 61 (1996) 8315–8316.
[82] (a) R. Ray, D.S. Matteson, Tetrahedron Lett. 21 (1980), 449–450. (b) R. Ray, D.S. Matteson, J. Indian Chem. Soc. 59 (1982) 119–123.
[83] K.M. Sadhu, D.S. Matteson, G.D. Hurst, J.M. Kurosky, Organometallics 3 (1984) 804–806.
[84] G.W. Kabalka, G. Li, J. Organomet. Chem. 581 (1999) 67–70.
[85] J.D. Patterson, D.S. Matteson, Unpublished observation.
[86] K.M. Sadhu, D.S. Matteson, Unpublished observation.
[87] D.S. Matteson, T.J. Michnick, Organometallics 9 (1990) 3171–3177.
[88] D.S. Matteson, A.A. Kandil, J. Org. Chem. 52 (1987) 5121–5124.
[89] D.S. Matteson, E. Erdik, Organometallics 2 (1983) 1083–1088.
[90] D.S. Matteson, M.L. Peterson, J. Org. Chem. 52 (1987) 5116–5121.
[91] D.S. Matteson, H.-W. Man, J. Org. Chem. 59 (1994) 5734–5741.
[92] P.K. Jadhav, H.-W. Man, J. Am. Chem. Soc. 119 (1997) 846–847.
[93] (a) G. Köbrich, K. Flory, W. Drischel, Angew. Chem. Int. Ed. Engl. 3 (1964) 513. (b) G. Köbrich, H.R. Merkle, H. Trapp, Tetrahedron Lett. (1965) 969–972.
[94] C. Blankenship, Personal communication, 1996.
[95] O.C. Ho, R. Soundararajan, J. Lu, D.S. Matteson, Z. Wang, X. Chen, M. Wei, R.D. Willett, Organometallics 14 (1995) 2855–2860.
[96] J. Lu, D.S. Matteson, Unpublished.
[97] D.S. Matteson, R.P. Singh, B. Schafman, J. Yang, J. Org. Chem 63 (1998) 4466–4469.
[98] D.S. Matteson, J. Lu, Tetrahedron: Asymm. 9 (1998) 2423–2436.