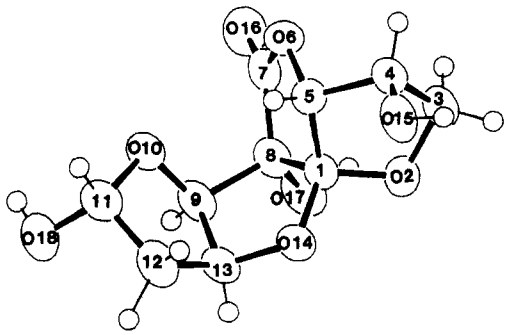

Figure 1. Diagram of **6** as determined by X-ray diffraction. The X-ray numbering scheme is also shown. Atoms in the second molecule in the asymmetric unit were numbered by adding 30 to the number of the equivalent atom shown here.

finement on 422 parameters (coordinates for all atoms, anisotropic thermal parameters for non-hydrogen atoms, and isotropic thermal parameters for the hydrogen atoms) using the 3157 reflections for which $|F_o| > 3\sigma|F_o|$ gave a final R factor of 4.3% (R_w = 6.4%). The absolute configuration of the molecule was determined from the anomalous scattering of the oxygen atoms. The goodness of fit parameter was 2.6, and the final difference map was featureless. All calculations were done using the SHELXTL system of computer programs.[10] Table I (supplementary material) lists the fractional coordinates and equivalent isotropic thermal parameters for the C and O atoms. Hydrogen coordinates and bond lengths and angles for **6** have been deposited with the Crystallographic Data Centre, Cambridge University Chemical Laboratory, Cambridge CB2 1EW, England. Anisotropic thermal parameters and a comparison of observed and calculated structure factors are available from us.

Discussion

The results of the X-ray study on **6** are illustrated in Figure 1, drawn by computer program ORTEP[11] using experimentally determined coordinates. Bond lengths and angles agree well within the two molecules in the asymmetric unit and do not indicate that any unusual characteristics or strains in the molecule caused by ring fusions. All of the five-membered rings have a flattened envelope conformation, and both molecules in the asymmetric unit have the same overall configuration. However, the two molecules do have different out of plane atoms in rings A and B. In molecule **6a**, O-10 and C-8 are the out of plane atoms in rings A and B, respectively, while in molecule **6b**, C-9 is the out of plane atom in both rings. Molecule **6a** is shown in Figure 1. This type of difference is not unusual in five-membered rings and is probably due to differences in the intermolecular environments of the two molecules. The crystal packing is influenced by hydrogen bonding. There are three possible donor hydrogens on each molecule, and they participate in a total of seven hydrogen bonds (see Table 2, supplementary material). In molecule **6a**, O-18 is the donor in a bifurcated hydrogen bond in which O-2 and O-17 of a symmetry related molecule share the role of the acceptor. The only other intermolecular approach less than van der Waals separations is O-46···O-43 at 3.13 Å.

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Registry No. **5b**, 93135-89-8; **6**, 102977-48-0; L-ascorbic acid, 50-81-7; fumaraldehyde, 3675-14-7; succinic anhydride, 108-30-5.

Supplementary Material Available: Tables of X-ray data (coordinates and bonding) for **6** (4 pages). Ordering information is given on any current masthead page.

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Organoboranes. 46. New Procedures for the Homologation of Boronic Esters: A Critical Examination of the Available Procedures To Achieve Convenient Homologation of Boronic Esters

Herbert C. Brown,* Shankar M. Singh,[1a] and Milind V. Rangaishenvi[1b]

Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907

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Two practical and more convenient procedures have been developed to achieve the one-carbon homologation of boronic esters: (1) in situ preparation of $LiCHCl_2$ by treatment of a mixture of methylene chloride and boronic ester with *sec*-butyllithium at −78 °C, followed by in situ reduction of the intermediate with potassium triisopropoxyborohydride, and (2) in situ preparation of (chloromethyl)lithium ($LiCH_2Cl$) by treatment of a mixture of bromochloromethane and boronic ester with *n*-butyllithium at −78 °C. These methods were compared with the previously known procedures: (3) treatment of the boronic ester with preformed $LiCHCl_2$ at −100 °C, followed by the in situ reduction of the intermediate with potassium triisopropoxyborohydride, (4) in situ preparation of $LiCHCl_2$ by treatment of a mixture of methylene chloride and boronic ester with lithium diisopropylamide (LDA) at 0 °C, followed by the reduction of the intermediate with KIPBH, and (5) in situ preparation of $LiCH_2Cl$ by treatment of a mixture of chloroiodomethane and boronic ester with *n*-butyllithium at −78 °C. A critical comparison of these procedures for the homologation of 2-(1-hexyl)- and 2-(3-hexyl)-1,3-dioxaborinane has led to the conclusion that the preferred procedures on the basis of convenience and economy are 2, followed by 4. These two preferred procedures are general, as shown by their applicability to the homologation of 11 different boronic esters.

The homologation of boronic esters[2] is assuming major importance in our efforts to develop a general synthesis of enantiomerically pure compounds via chiral hydroboration[3] (eq 1).

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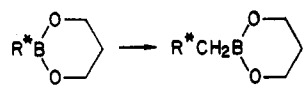


(1)

Two new procedures have been developed and are described here. A critical examination of all of the available procedures[3-5] reveals significant advantages for two procedures. These two methods have been applied to nine representative boronic esters. They are generally applicable and provide simple, convenient, economical procedures to achieve one-carbon homologation in excellent yield.

Background

Since the last decade, many new reactions and reagents have emerged for the conversion of organoboranes into organic molecules of ubiquitous structural features, particularly by C–C bond formation.[4] To achieve this goal, it is desirable not only to find new reactions or reagents but also to define the scope and limitation of their applicability.

Carbanionic reagents bearing a potential leaving group(s) at the α-position homologate the organyl–B linkage. The reaction proceeds through the formation of an ate complex, followed by the 1,2-migration of the organyl group(s) from boron to the carbanionic center by displacement of the leaving group. This offers a convenient, practical way to achieve C–C bond-forming transformations via organoboranes.

Trichloromethyllithium, $LiCCl_3$, is one of such reagents. It is reported to be stable only at low temperature.[5] The marked instability of $LiCCl_3$ led us to explore the possibility of synthesizing the intermediate in situ. Indeed, treatment of chloroform with a suitable base such as $KOCMe_3$ in the presence of trialkylboranes provided a convenient route to trialkylcarbinols[6] (eq 2).

$$R_3B + CHCl_3 + KOCMe_3 \rightarrow \rightarrow R_3COH \qquad (2)$$

The reagents HCF_2Cl and $HCCl_2OMe$ (DCME) also worked. The latter reagent was selected for detailed study. Later the DCME reagent was shown to react also with borinic esters,[7] giving a convenient procedure for the synthesis of ketones (eq 3).

$$R_2BOR' + HCCl_2OMe + LiOCEt_3 \rightarrow \rightarrow R_2C{=}O \qquad (3)$$

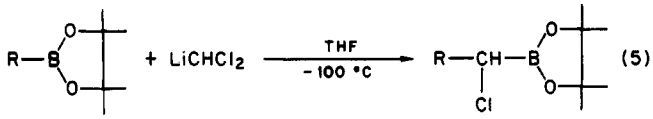
But all attempts to extend the reaction to boronic esters failed.

Another reagent of interest is dichloromethyllithium. It also is reported to be stable only at low temperature.[8] Its reaction with organoboranes was first reported[9] by Kobrich and Merkle in 1967. They established that the reaction of $LiCHCl_2$ with triarylboranes provide a satisfactory route for the preparation of diarylcarbinols (eq 4).

$$Ar_3B + LiCHCl_2 \xrightarrow{-74\ °C} \rightarrow Ar_2CHOH \qquad (4)$$

Later, Rathke et al. demonstrated[10] the utility of $LiCHCl_2$ for preparing diisopropyl (dichloromethyl)boronate, $Cl_2CHB(O\text{-}i\text{-}Pr)_2$, and studied the nucleophilic substitution of this intermediate with organolithium or Grignard reagents.

In 1980 Matteson and Majumdar established[11] that $LiCHCl_2$ successfully homologates boronic esters to α-chloroalkyl derivatives (eq 5). Matteson also developed



(5)

a most elegant asymmetric synthesis based on this method.[12] He did show that LDA would induce a reaction between methylene chloride and boronic ester at −78 °C but did not pursue this approach. In our laboratory a method for the in situ reduction of the α-haloboronic ester using KIPBH has been developed.[13] This procedure of preparing α-haloboronic ester, followed by in situ reduction with KIPBH, appeared to offer major advantages to achieve the simple homologation of boronic esters. Consequently, we applied it to representative boronic esters.[3]

More recently, Matteson has reported the in situ generation of (chloromethyl)lithium ($LiCH_2Cl$) by reacting chloroiodomethane with n-BuLi at −78 °C to achieve homologation.[2] He has also shown that the LDA-induced reaction with CH_2Cl_2 in the presence of $B(O\text{-}i\text{-}Pr)_3$ occurs at 0 °C.[14] Consequently, we appear to have returned essentially to the conditions of our original study with methylene chloride in place of chloroform.

The homologation reaction is highly important to our program of asymmetric synthesis.[3] We decided to forego all preconceived ideas and to examine possible procedures for achieving homologation and then to select the most favorable procedure or procedures. After considerable experimentation, we examined the following nine procedures: (a) preformed $LiCHCl_2$ at −100 °C; (b) $LiCHCl_2$ prepared in situ from CH_2Cl_2 and LDA at 0 °C; (d) $LiCHCl_2$ prepared in situ from CH_2Cl_2 and *sec*-BuLi at −78 °C; (e) $LiCHCl_2$ prepared in situ from CH_2Cl_2 and *sec*-BuLi at 0 °C; (f) $LiCH_2Cl$ prepared in situ from ICH_2Cl and n-BuLi at −78 °C; (g) $LiCH_2Cl$ prepared in situ from ICH_2Cl and n-BuLi at 0 °C; (h) $LiCH_2Cl$ prepared in situ from $BrCH_2Cl$ and n-BuLi at −78 °C; (i) $LiCH_2Cl$ prepared in situ from $BrCH_2Cl$ and n-BuLi at 0 °C.

Results and Discussion

Each of the nine procedures was run with 2-(1-hexyl)-1,3-dioxaborinane. If the results were promising, the procedure was repeated with 2-(3-hexyl)-1,3-dioxaborinane. We then selected the two most promising procedures, d and h above, and applied them to 11 representative boronic esters.

We also undertook to improve the preparative procedure. Previously we had followed Matteson's procedure and had utilized reaction periods of 12 h to achieve complete transfer of the organic group from the boron atom in the ate complex to the carbenoid center with the displacement of the leaving group. The long reaction time

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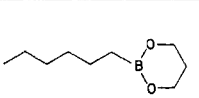
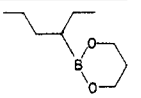
Table I. One-Carbon Homologation of Boronic Esters

no.	procedure	temp, °C	% yield[a] of the homologated product 	
1	performed $LiCHCl_2$	−100	93	92
2	in situ $LiCHCl_2$ from CH_2Cl_2 + LDA	−78	91	90
3	in situ $LiCHCl_2$ from CH_2Cl_2 + LDA	0	93	90
4	in situ $LiCHCl_2$ from CH_2Cl_2 + *sec*-BuLi	−78	86	87
5	in situ $LiCHCl_2$ from CH_2Cl_2 + *sec*-BuLi	0	6	10
6	in situ $LiCH_2Cl$ from ICH_2Cl + *n*-BuLi	−78	97	96
7	in situ $LiCH_2Cl$ from ICH_2Cl + *n*-BuLi	0	*b*	
8	in situ $LiCH_2Cl$ from $BrCH_2Cl$ + *n*-BuLi	−78	91	89
9	in situ $LiCH_2Cl$ from $BrCH_2Cl$ + *n*-BuLi	0	47	

[a] Yields of alcohol after oxidation with alkaline H_2O_2; GC analyses of the alcohols were carried out on 5% Carbowax 1540 on Chromosorb W (12 ft × $^1/_8$ in.) column. Each alcohol was identified by GC coinjection with an authentic sample. [b] Explosive.

was inconvenient. We then found that we could achieve complete transfer by bringing the reaction mixture in THF to the reflux temperature (65 °C) and maintaining it there generally for 1.5 h. In two cases, 2-(1-norbornyl)-1,3-dioxaborinane and 2-(3-isopinocampheyl)-1,3-dioxaborinane, complete transfer required 5 h at 65 °C. However, in the case of thexyl boronate, refluxing over a longer period did not improve the yield. Evidently in this case, the intermediate encounters difficulty in converting the hindered ester to the desired ate complex.

For our preliminary study, 2-(1-hexyl)-1,3-dioxaborinane was chosen. A slurry of (dichloromethyl)lithium ($LiCHCl_2$) in freshly distilled tetrahydrofuran (THF) was prepared[11] at −100 °C, and the boronic ester was added dropwise, maintaining the temperature at −100 °C. After the addition, the reaction mixture became clear. It was then stirred at −100 °C for 0.5 h, warmed to room temperature, and then refluxed at 65 °C for 1.5 h. The ^{11}B NMR spectrum of the reaction mixture showed cleanly one peak at δ +27 due to the formation of α-chloro boronic ester. This was then reduced[13] in situ with KIPBH at 25 °C for 1 h. The ^{11}B NMR spectrum of the reaction mixture showed the formation of boronic ester (δ +30) and triisopropoxyborane (δ +18) and the presence of an impurity, potassium tetraisopropoxyborane (δ +1), which was originally present in the commercial KIPBH solution. The mixture was then oxidized with alkaline H_2O_2, and the resulting alcohol was identified by GC analysis using *n*-hexadecane as an internal standard. The same procedure was repeated for 2-(3-hexyl)-1,3-dioxaborinane (Table I).

(Dichloromethyl)lithium was generated[18] by reacting CH_2Cl_2 with LDA at −78 °C in the presence of 2-(1-hexyl)-1,3-dioxaborinane and 2-(3-hexyl)-1,3-dioxaborinane. To a cooled mixture of dichloromethane and boronic ester in THF at −78 °C, a freshly prepared solution of lithium diisopropylamide was added dropwise at −78 °C, and the reaction mixture was allowed to stir at −78 °C for 0.5 h. It was then warmed to room temperature and refluxed at 65 °C for 1.5 h. The completion of migration was monitored by ^{11}B NMR (δ +27). The α-chloro boronic ester was reduced with KIPBH at 25 °C, and the resulting boronic ester was oxidized with alkaline H_2O_2 and analyzed by GC using *n*-hexadecane as an internal standard (Table I).

(Dichloromethyl)lithium ($LiCHCl_2$) was also generated in situ by reacting CH_2Cl_2 with preformed LDA at 0 °C. To an ice-cooled solution (ice–salt bath) of CH_2Cl_2 and boronic ester in THF, a freshly prepared solution of LDA was added dropwise at 0 °C. The reaction mixture was then stirred at 0 °C for 0.5 h, whereupon the reaction mixture turned dark due to decomposition of the small excess (10%) of $LiCHCl_2$. The reaction mixture was then refluxed at 65 °C for 1.5 h. The ^{11}B NMR spectrum of the reaction mixture revealed the formation of α-chloro boronic ester (δ +27), which was then reduced in situ with KIPBH. The resulting boronate ester (δ +30) was oxidized with alkaline H_2O_2, and the resulting alcohol was analyzed by GC using *n*-hexadecane as an internal standard. The results are summarized in Table II. In the case of 2-(1-norbornyl)-1,3-dioxaborinane and (3-isopinocampheyl)-1,3-dioxaborinane, complete transfer required 5 h. Increasing the reflux period from 1.5 to 5 h improved the yields of the homologated product. However, in the case of thexyl boronate, increasing the reflux period even up to 24 h did not show any improvement in the yield of the homologation product.

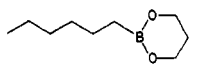
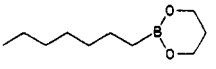
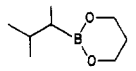
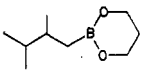
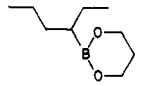
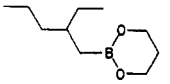
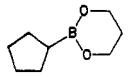
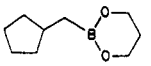
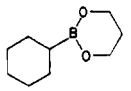
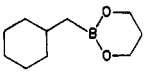
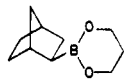
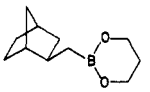
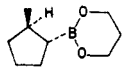
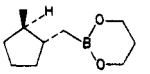
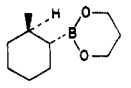
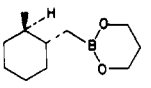
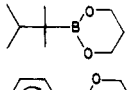
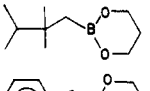
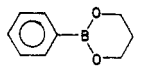
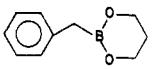
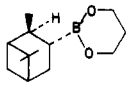
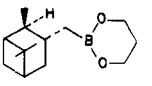
The in situ generation of (dichloromethyl)lithium ($LiCHCl_2$) was attempted by reacting a mixture of CH_2Cl_2 and boronic ester with alkyllithiums, such as *n*-BuLi, *sec*-BuLi, and *t*-BuLi, in THF at −78 °C. It was found that *sec*-BuLi was preferable for the in situ generation of $LiCHCl_2$ at −78 °C. To a solution of CH_2Cl_2 and boronic ester cooled to −78 °C was added *sec*-BuLi in cyclohexane dropwise. This was then stirred at −78 °C for 0.5 h, warmed rapidly to 65 °C, and then refluxed at 65 °C for 1.5 h. The reaction mixture turned dark. The ^{11}B NMR spectrum of the reaction mixture showed the formation of α-chloro boronate ester (δ +27), which was further reduced in situ with KIPBH at 25 °C and oxidized with alkaline H_2O_2, and the resulting alcohol was analyzed by GC using *n*-hexadecane as an internal standard.

The in situ generation of $LiCHCl_2$ at 0 °C was attempted by reacting CH_2Cl_2 and *sec*-BuLi in the presence of boronic ester in THF. Unfortunately there was no formation of α-chloro boronic ester, as is evident by the ^{11}B NMR spectrum. The yield of the homologated product was in the range of 6–10%. The fast reaction of *sec*-BuLi with THF at 0 °C may interfere. The in situ generation of $LiCHCl_2$ was attempted with CH_2Cl_2 and *sec*-BuLi at 0 °C in the presence of boronic ester in diethyl ether and cyclohexane, but no significant success could be achieved.

(Chloromethyl)lithium ($LiCH_2Cl$) was generated in situ at −78 °C by reacting ICH_2Cl with *n*-BuLi in the presence of boronate ester in THF.[2] The reaction mixture was allowed to stir at −78 °C for 0.5 h and then refluxed at 65 °C for 1.5 h. The completion of reaction was monitored by ^{11}B NMR. The yield of the homologated product was indirectly ascertained by oxidizing with alkaline H_2O_2 and analyzing the alcohol by GC analysis (Table I). The in situ generation of $LiCH_2Cl$ was attempted as well by reacting ICH_2Cl with *n*-BuLi in THF at 0 °C. The reaction was violent and explosive.

$LiCH_2Cl$ was also generated in situ by reacting bromochloromethane ($BrCH_2Cl$)[19] with *n*-BuLi in the presence

Table II. One-Carbon Homologation of Organyl-1,3-dioxaborinanes with CH_2Cl_2/LDA at 0 °C and $BrCH_2Cl$/*n*-BuLi at −78 °C

boronic ester	homologated product	yield,[b] %	
		CH_2Cl_2/LDA at 0 °C	$BrCH_2Cl$/*n*-BuLi at −78 °C
		93 (86)	91
		88	
		90	89
		88	89
		89	90
		87	91
		89	90
		90	91
		40	38
		88 (80)	
		83	84

[a] Yields of alcohol after oxidation with alkaline H_2O_2. [b] GC analyses of the alcohols were carried out on 5% Carbowax 1540 on Chromosorb W (12 ft × $^1/_8$ in.) column and SP-2100 on Chromosorb W (12 ft × $^1/_8$ in.) column. Each alcohol was identified by GC coinjection with an authentic sample. The yield in parentheses refers to the isolated yield of the boronic ester.

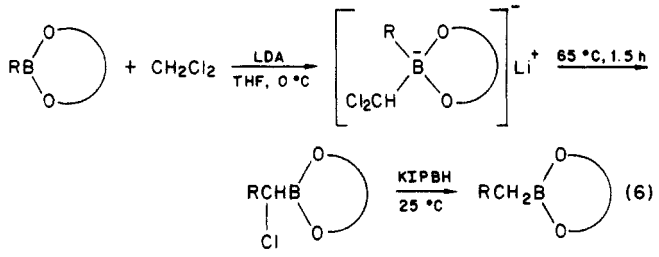
of a boronate ester in THF at −78 °C. Alkyllithiums, such as *n*-BuLi, *sec*-BuLi and *t*-BuLi, were tried; *n*-BuLi proved preferable for the in situ generation of $LiCH_2Cl$. The reaction mixture was stirred at −78 °C for 0.5 h, then warmed rapidly to room temperature, and refluxed at 65 °C for 1.5 h. The completion of the reaction was monitored by ^{11}B NMR, and the yield of the homologated product was ascertained by oxidizing with alkaline H_2O_2, followed by GC analysis for the resulting alcohol (Table I).

In situ generation of $LiCH_2Cl$ was attempted at 0 °C by treating $BrCH_2Cl$ with *n*-BuLi in THF. Although the reaction was not violent, the yield of the homologated product was only 47%. No significant improvement could be achieved by performing the reaction in diethyl ether or *n*-hexane instead of THF.

On the basis of these experiments, we selected two methods for the one-carbon homologation of boronic esters from the point of view of ease of operation, yield, and the cost involved. These are (i) in situ generation of $LiCHCl_2$ by reacting CH_2Cl_2 and LDA at 0 °C in the presence of a boronate ester and (ii) in situ generation of $LiCH_2Cl$ by reacting $BrCH_2Cl$ with *n*-BuLi at −78 °C in the presence of boronate ester, followed by reflux at 65 °C to achieve migration of the organyl moiety. We prefer the $BrCH_2Cl$ over the ICH_2Cl procedure because of its greater economy (ICH_2Cl is presently quite expensive). To establish the generality of these procedures, we decided to vary the organyl moiety in the boronic ester. Accordingly, it was established that all of the 1,3-dioxaborinanes examined with various organic groups attached to boron, including primary, secondary, cyclic, bicyclic, and aryl, can be homologated to the desired boronic esters in excellent yields (Table II).

To an ice-cooled solution of 2-(1-hexyl)-1,3-dioxaborinane and dichloromethane in THF was added dropwise a freshly prepared solution of LDA in THF at 0 °C, and the reaction mixture was stirred at 0 °C for 0.5 h. The reaction mixture turned dark in color. It was then refluxed at 65 °C for 1.5 h. The ^{11}B NMR spectrum of the reaction mixture revealed the formation of 2-(1-chloro-1-heptyl)-1,3-dioxaborinane (δ +27). The intermediate α-chloro boronic ester was reduced in situ by adding a slight excess of KIPBH at 0 °C. The ^{11}B NMR spectrum of an aliquot of the reaction mixture showed the clean formation of 2-(1-heptyl)-1,3-dioxaborinane (δ +30), triisopropoxyborane (δ +18), and potassium tetraisopropoxyborate (δ +1) as an impurity present in the commercial KIPBH. Evaporation of the solvent afforded the crude one-carbon homologated boronic ester (eq 6). The crude 2-(1-heptyl)-1,3-dioxaborinane containing triisopropoxyborane as the byproduct was treated with water to remove the triisopropoxyborane, and the *n*-heptylboronic acid thus obtained was reesterified with 1,3-propanediol.[15] Distil-

(15) Brown, H. C.; Bhat, N. G.; Somayaji, V. *Organometallics* **1983**, *2*, 1311.



(6)

lation of the residue gave pure 2-(1-heptyl)-1,3-dioxaborinane in excellent yield. Similarly, 2-(benzyl)-1,3-dioxaborinane was also prepared in high yield. Since these organylboronic esters have been isolated and characterized in our laboratory,[3,13] we decided to determine the yields and purities of the homologated boronic esters by GC analysis of the alcohols produced following oxidation. The results are summarized in Table II.

Similarly, the one-carbon homologation of 2-(1-hexyl)-1,3-dioxaborinane was achieved by the use of (chloromethyl)lithium ($LiCH_2Cl$) generated in situ by reacting $BrCH_2Cl$ with *n*-BuLi in THF at −78 °C. To a solution of boronic ester, CH_2Cl_2, and $BrCH_2Cl$ at −78 °C was added *n*-BuLi dropwise, and the reaction mixture was allowed to stir at −78 °C for 0.5 h. Next, it was rapidly warmed to room temperature and refluxed at 65 °C for 1.5 h. The completion of the reaction was monitored by ^{11}B NMR (δ +30). Evaporation of the solvent furnished crude one-carbon homologated boronate ester, which was further purified by distillation in vacuo. Similarly, 2-benzyl-1,3-dioxaborinane was also prepared and isolated in excellent yield. To establish the generality of the procedure, the yields and purities of homologated boronic esters were determined by oxidation and GC analysis of the alcohols produced (Table II).

It should be pointed out that the in situ generation of $LiCHCl_2$ from CH_2Cl_2 and *sec*-BuLi offers especial promise for the Matteson asymmetric synthesis.[11,12] However, we did not attempt to test its utility in that synthesis.

Conclusion

The present homologation procedures make it possible to achieve one-carbon homologation of organylboronic esters by a simple, efficient, and convenient procedure. This sequence is attractive for economical synthesis on a large scale of the homologated boronic acids and esters not available by simple, direct hydroboration.

Experimental Section

All operations were carried out under a nitrogen atmosphere with oven-dried glassware.[20] ^{11}B NMR spectra were recorded on a Varian FT-80A instrument, and the chemical shifts are in δ relative to $EE{\cdot}BF_3$, with chemical shifts downfield from $EE{\cdot}BF_3$ as positive. ^1H NMR spectra were recorded on a Varian T-60 (60 MHz) spectrometer, and the chemical shifts are in δ relative to Me_4Si. IR spectra were recorded on a Perkin-Elmer 1420 ratio recording spectrophotometer. The GC analyses were carried out on a Varian 1200 research chromatograph and Hewlett-Packard 5890A gas chromatograph equipped with a flame ionization detector (columns 12 ft × $^1/_8$ in. packed with 5% Carbowax 1540 on Chromosorb W, AW DMCS and 5% SP-2100 on Chromosorb W, AW, DMCS).

Materials. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl prior to use. Anhydrous diethyl ether was purchased from Mallinckrodt, Inc., and was used directly. Dichloromethane, bromochloromethane, and chloroiodomethane were distilled over P_2O_5 and stored over 4-Å molecular sieves. Diisopropylamine was distilled over calcium hydride. Butyllithium (Alfa) in hexane was estimated to be 2.3 M. *sec*-BuLi and *t*-BuLi were purchased from Aldrich Chemical Co. and estimated prior to use. Potassium triisopropoxyborohydride (KIPBH, 1.0 M) in THF was purchased from Aldrich Chemical Co.

The boronic esters were prepared by the hydroboration of alkenes with dibromoborane–dimethyl sulfide, followed by alcoholysis.[15] Phenyl 1,3-dioxaborinane was prepared by the procedure reported in the literature.[16] (3-Isopinocampheyl)-1,3-dioxaborinane was prepared[3] by the direct alcoholysis of monoisopinocampheylborane (generated from $IpcBH_2{\cdot}TMED$ adduct).[17]

Homologation of 2-(1-Hexyl)-1,3-dioxaborinane. The one-carbon homologation of 2-(1-hexyl)-1,3-dioxaborinane to 2-(1-heptyl)-1,3-dioxaborinane using CH_2Cl_2 and LDA at 0 °C is representative. Freshly prepared lithium diisopropylamide (24 mmol) was added dropwise to a mixture of dichloromethane (1.55 mL, 24 mmol) and 2-(1-hexyl)-1,3-dioxaborinane (3.4 g, 20 mmol) in THF (24 mL) at 0 °C (an internal temperature of 0 °C with a cooling bath at −5 °C; ice–salt bath). The reaction mixture was allowed to stir at 0 °C for 0.5 h. It was then rapidly warmed to room temperature and refluxed at 65 °C for 1.5 h. The ^{11}B NMR spectrum of the reaction mixture revealed the formation of 2-(1-chloro-1-heptyl)-1,3-dioxaborinane (δ +27). The intermediate α-chloroboronic ester was reduced without isolating with KIPBH (22 mL, 22 mmol) at 25 °C for 0.5 h, as indicated by the ^{11}B NMR analysis (δ +30). The solvent was removed at reduced pressure (14 torr), and the residue thus obtained was stirred with water (20 mL) for 1 h to hydrolyze triisopropoxyborane and the product. The reaction mixture was extracted with ether (5 × 20 mL), washed twice with water, and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded the crude *n*-heptylboronic acid, which was reesterified with 1,3-propanediol[15] and distilled under high vacuum.

2-(1-Heptyl)-1,3-dioxaborinane: 86% yield; bp 74 °C (2 torr); ^1H NMR ($CDCl_3$) δ 0.38–1.6 (m, 15 H), 1.9 (q, J = 6 Hz, 2 H), 3.93 (t, J = 6 Hz, 4 H).

Homologation of 2-Phenyl-1,3-dioxaborinane. To an ice-cooled mixture of 2-phenyl-1,3-dioxaborinane (2.43 g, 15 mmol) and dichloromethane (1.16 mL, 18 mmol) in THF (20 mL) was added freshly prepared LDA (18 mmol) dropwise over a period of 15 min. The reaction mixture was allowed to stir at 0 °C for 0.5 h. It was then rapidly warmed to room temperature and refluxed at 65 °C for 1.5 h to complete the rearrangement of the borate complex. The intermediate α-chloro boronic ester (δ +27) was reduced with KIPBH (16.5 mL, 16.5 mmol) at 25 °C in 0.5 h, as revealed by the ^{11}B NMR analysis (δ +30). The solvent was removed at reduced pressure, and the product was hydrolyzed with water (15 mL). The aqueous solution was extracted with ether (5 × 20 mL), washed with water (2 × 20 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent furnished the crude benzylboronic acid, which was reesterified with 1,3-propanediol[15] and purified by distillation.

2-(Benzyl)-1,3-dioxaborinane: 80% yield; bp 75 °C (0.4 torr); ^1H NMR ($CDCl_3$) δ 1.86 (q, J = 6 Hz, 2 H), 2.2 (s, 2 H), 3.93 (t, J = 6 Hz, 4 H), 7.16 (m, 5 H).

Homologation of 2-(1-Hexyl)-1,3-dioxaborinane to 2-(1-Heptyl)-1,3-dioxaborinane. The following procedure using $BrCH_2Cl$ and *n*-BuLi at −78 °C is representative. A solution of 2-(1-hexyl)-1,3-dioxaborinane (0.85 g, 5 mmol) and bromochloromethane (0.46 mL, 7 mmol) in THF (5 mL) was cooled to −78 °C (dry ice–acetone bath). To this was added chilled *n*-BuLi (3.05 mL, 2.3 mmol in hexane, 7 mmol) dropwise from the side of the flask, maintaining the temperature at −78 °C in an atmosphere of nitrogen gas. The reaction mixture was stirred at −78 °C for 0.5 h and then rapidly brought to room temperature. To this was added *n*-hexadecane (2 mmol) as an internal standard. The reaction mixture was refluxed at 65 °C for 1.5 h, cooled to room temperature, and oxidized with alkaline hydrogen peroxide. The aqueous layer was saturated with potassium carbonate and

(16) Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316.
(17) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *J. Org. Chem.* **1982**, *47*, 5074.
(18) Brown, H. C.; Singh, S. M. *Organometallics* **1986**, *5*, 994.
(19) The in situ generation of (chloromethyl)lithium from bromochloromethane and lithium dispersion in the presence of carbonyl compounds, with variable yields, was reported earlier: Cainelli, G.; Umani Ronchi, A.; Bertini, F.; Graselli, P.; Zubiani, G. *Tetrahedron Lett.* **1971**, 6109.
(20) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, 1975.

extracted with ether. The ether layer was analyzed by GC on a 5% Carbowax 1540 on Chromosorb W AW DMCS column: yield, 91%.

Homologation of 2-(1-Hexyl)-1,3-dioxaborinane Using CH_2Cl_2 and *sec*-BuLi. A solution of 2-(1-hexyl)-1,3-dioxaborinane (0.85 g, 5 mmol) and CH_2Cl_2 (0.45 mL, 7 mmol) in THF (5 mL) was cooled to −78 °C (dry ice–acetone bath). To this was added chilled *sec*-BuLi (5 mL, 7 mmol, 1.4 M solution in cyclohexane) dropwise from a syringe (bringing the tip of the syringe needle very close to the surface of the cold solution), and the reaction mixture was stirred at −78 °C for 0.5 h. It was then rapidly brought to room temperature and refluxed at 65 °C for 1.5 h. The ^{11}B NMR spectrum of the reaction mixture revealed the formation of 2-(1-chloro-1-heptyl)-1,3-dioxaborinane (δ +27). The intermediate α-chloroboronic ester was reduced without isolating with KIPBH (7 mL, 7 mmol, 1 M solution in THF) at 25 °C for 0.5 h, as indicated by the ^{11}B NMR analysis (δ +30). This was then oxidized with alkaline H_2O_2, and the oxidation product was analyzed by GC: yield; 86%.

Characterization of the Homologated Products by Oxidation. The other boronic esters homologated (Table II) were not isolated, but characterized by oxidation with alkaline hydrogen peroxide. The alcohols produced were characterized by GC examination and the yield established by analysis of the alcohols (Table II).

Acknowledgment. Financial support from the National Science Foundation (Grant CHE 8414171) is gratefully acknowledged.

Registry No. $LiCHCl_2$, 2146-67-0; CH_2Cl_2, 75-09-2; $BrCH_2Cl$, 74-97-5; ICH_2Cl, 593-71-5; 2-(1-heptyl)-1,3-dioxaboronane, 101031-41-8; 2-(benzyl)-1,3-dioxaboronane, 62930-28-3; 2-(3-hexyl)-1,3-dioxaboronane, 86290-28-0; 2-(2,3-dimethyl-1-butyl)-1,3-dioxaboronane, 98303-39-0; 2-(cyclopentylmethyl)-1,3-dioxaboronane, 101031-43-0; 2-(cyclohexylmethyl)-1,3-dioxaboronane, 102746-89-4; 2-((2-bicyclo[2.2.1]heptyl)methyl)-1,3-dioxaboronane, 102746-90-7; 2-((*trans*-2-methylcyclopentyl)-methyl)-1,3-dioxaboronane, 98303-41-4; 2-((*trans*-2-methylcyclohexyl)methyl)-1,3-dioxaboronane, 98303-42-5; 2-(2,2,3-trimethyl-1-butyl)-1,3-dioxaboronane, 101031-44-1; 2-[((1α,2α,3β,5α)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl)methyl]-1,3-dioxaboronane, 102849-29-6; 2-(1-hexyl)-1,3-dioxaboronane, 86290-24-6; 2-(phenyl)-1,3-dioxaboronane, 4406-77-3; 2-(3-methyl-2-butyl)-1,3-dioxaboronane, 98303-38-9; 2-(cyclopentyl)-1,3-dioxaboronane, 30169-74-5; 2-(2-bicylco[2.2.1]-heptyl)-1,3-dioxaboronane, 102746-91-8; 2-(cyclohexyl)-1,3-dioxaboronane, 30169-75-6; 2-(*trans*-2-methylcyclopentyl)-1,3-dioxaboronane, 86290-31-5; 2-(*trans*-2-methylcyclohexyl)-1,3-dioxaboronane, 98392-60-0; 2-(2,3-dimethyl-2-butyl)-1,3-dioxaboronane, 63689-74-7; 2-((1α,2α,3β,5α)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl)-1,3-dioxaboronane, 102849-30-9; 2-(1-chloro-1-heptyl)-1,3-dioxaboronane, 102746-92-9; 2-(α-chlorobenzyl)-1,3-dioxaboronane, 102746-93-0.

Cycloadducts of Arynes with 1,3-Bis(trimethylsilyl)naphtho[1,2-*c*]furan: Formation of Novel Polycyclic Aromatic Derivatives and Related Reactions

Daniel J. Pollart and Bruce Rickborn*

Department of Chemistry, University of California, Santa Barbara, California 93106

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A recently developed procedure for the preparation of trimethylsilylated isobenzofurans and the use of these materials in cycloaddition reactions has been extended to an isonaphthofuran analogue. The 1,3-bis(trimethylsilyl)naphtho[1,2-c]furan (7) has been isolated; its reaction with maleic anhydride at room temperature is rapid and readily reversible as shown by endo to exo cycloadduct interconversion. The failure of 7 to give cycloadduct with 2-butenolide indicates that it is less reactive than the parent naphtho[1,2-c]furan. In situ generation and cycloaddition reactions with various arynes (benzyne, 4-methylbenzyne, 3,4-pyridyne, 9,10-phenanthrolyne, 1,2-naphthalyne, and 2,3-naphthalyne) are described. The three unsymmetrical arynes all give mixtures of cycloadducts indicative of negligible regioselectivity in Diels–Alder reactions with 7; thus, in spite of possible steric hindrance the reaction with 1,2-naphthalyne gives a 1:1 mixture of dibenz[a,h]- and dibenz[a,j]anthracene derivatives. In contrast, the reaction of 1-ethoxy-3-(trimethylsilyl)naphtho[1,2-c]furan (21) with 1,2-naphthalyne exhibits modest regioselectivity, favoring the formation of the dibenz[a,j]anthracene derivative. Various reactions of the cycloadducts are described.

A recently developed procedure[1] allows the one-flask conversion of 1,3-dihydro-1-ethoxyisobenzofuran to 1,3-bis(trimethylsilyl)isobenzofuran, and subsequent cycloaddition with in situ generated arynes, to afford novel polycyclic materials. This paper describes the extension of this methodology to the naphtho[1,2-c]furan (benzo[e]isobenzofuran) system, which has been shown[2] to be accessible through lithium dialkylamide induced 1,4-elimination reactions. We were interested in the feasibility of forming the bis(trimethylsilyl) derivative, its relative reactivity, whether cycloaddition reactions with arynes would occur, and whether these would exhibit regioselectivity.

Results and Discussion

The 1,2-naphthalic anhydride (1) used in this study was prepared by the method of Newman and co-workers.[3] Sodium borohydride reduction of 1 gave a mixture (75%) of the lactones 2 and 3 in nearly equal amounts. This mixture was O-ethylated and then reduced as described previously for the individual lactone isomers[2] to provide a mixture of the acetals 4 and 5 (63%) as outlined in eq 1. Since both 4 and 5 serve as precursors to naphtho[1,2-c]furan (6), this mixture of isomers was used without separation in further applications. Thus, treatment with

(1) (a) Crump, S. L.; Netka, J.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 2746. (b) Netka, J.; Crump, S. L.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 1189. (c) Camenzind, R.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 1914.

(2) Cornejo, J. J.; Ghodsi, S.; Johnson, R. D.; Woodling, R.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 3869.

(3) Newman, M. S.; Dhawan, B.; Hashem, M. M.; Khanna, V. K.; Springer, J. M. *J. Org. Chem.* **1976**, *41*, 3925.

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