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A Simple, Convenient, General Procedure for the Synthesis of 2-Alkyn-1-ylboronates

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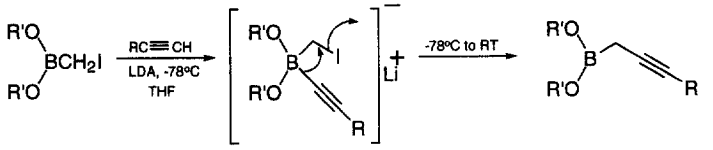
Abstract: *Representative 2-alkyn-1-ylboronates have been synthesized in good to excellent yields using the reaction of the newly available diisopropyl iodomethylboronate with alkynyllithiums generated in situ. Comparable yields are obtained from both acyclic and cyclic boronates. However, 2-(iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane gave superior yields with a wide variety of alkynyllithiums. This procedure offers a simple and convenient alternative route to existing methodologies in terms of the milder reaction condition and the ease of the operation.*

Allyl-, allenyl-, and propargylboranes have proven to be highly versatile reagents for asymmetric organic synthesis.[1] These classes of reagents occupy an important position in organic syntheses due to the high stereoselectivities exhibited in their reactions with carbonyl compounds. Among these reagents, propargylboronates have received relatively little attention, presumably due to the lack of a general method for their preparation.[2] Favre and Gaudemar reported that the direct methods of synthesis, using propargyl metal reagents, such as the Grignard, had serious problems arising from the concurrent formation of an isomeric mixture of allenyl- and propargylboronates.[3] Corey and coworkers have reported a simple propargylboron reagent preparation based on an organotin intermediate.[4] Recently, we have communicated a general synthesis of 2-alkyn-1-ylboronates in excellent isomeric purity *via* one carbon homologation of the 1-alkynylboronates.[5] In view of the importance of these compounds, we undertook a study to develop a new general methodology for the preparation of "higher" propargylboronates. In this communication, we now report a highly simple, convenient, general synthesis of higher propargylboronates in excellent isomeric purity, starting from iodomethylboronates and alkynyllithiums.

Our strategy is based on the simple assumption that the reaction of alkynyllithiums (generated *in situ* from the corresponding alkynes and LDA) with dialkyl iodomethylboronates would produce an "ate" complex identical to the one formed in our previously reported procedure.[5] Likewise, this "ate" complex would then be expected to rearrange to the corresponding propargylboronates (Scheme 1).

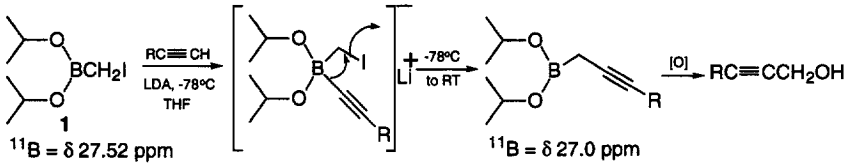


Scheme 1

For this study, we examined both acyclic and cyclic boronates for comparative study, since cyclic boronates appear to be relatively more stable than their acyclic analogs during rearrangement.[6] The rearrangement of the "ate" complex intermediate is faster for the cyclic boronates. Also, iodomethylboronates were selected because it was evident from the literature that the "ate" complex derived from alkynylboronate and $LiCH_2I$ gives results superior to those achieved with $LiCH_2Br$ and $LiCH_2Cl$.[7] During the preparation of boronic ester substituted Δ^2-isoxazolines, Wallace and Zong achieved an improved chemical yield of homologated product when $LiCH_2I$ was generated from CH_2I_2 and MeLi, instead of *n*-BuLi. Previously, diisopropyl iodo-

methylboronate was prepared from triisopropyl borate and *in situ* generated $LiCH_2I$ using *n*-BuLi in only 70% chemical yield.[9] The use of MeLi significantly improved the chemical yield of diisopropyl iodomethylboronate (>90%).[10]

Diisopropyl iodomethylboronate (**1**) (^{11}B NMR at 27.5 ppm) is reacted with *in situ* generated alkynyllithium at -78 °C in THF (Scheme 2). The capture of alkynyllithium is almost instantaneous leading to the formation of the intermediate "ate" complex (^{11}B NMR at -1.0 to +3.0 ppm), which then slowly rearranges to the propargylboronate. The progress of the reaction can easily be monitored with ^{11}B NMR by the disappearance of the "ate" complex peak at δ 0.0 ppm and the appearance of the product propargylboronate peak at δ 27.0 ppm. These higher propargylboronates could not be isolated and characterized due to their instability. Therefore, these propargylboronates were oxidized to propargyl alcohols with alkaline H_2O_2 and characterized spectroscopically. The results obtained with representative alkynyllithiums are summarized in Table 1.



Scheme 2

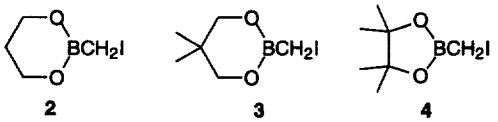
Table 1. Reaction of Diisopropyl Iodomethylboronate with Representative *in situ* Generated Alkynyllithiums[a]

$RC{\equiv}CCH_2B(O^iPr)_2$ (R)	Time (h)	Yields of $RC{\equiv}CCH_2OH$ Following H_2O_2 Oxidation (%)[b, c, d]	Yields of Side Product Based on ^{11}B NMR (%)
n-Butyl	2.0	65	15
n-Octyl	3.0	66	14
tert-Butyl	2.5	80	06
Isobutyl	2.0	63	17
3-Chloropropyl	3.5	80	14
2-(CH_2CH_2O)pyran	3.0	62	19
(Triisopropyl)silyl	22.0	53	19
Cyclopentyl	1.5	64	16

[a]1.20 eq. of the reagent is used. [b]Yields based on the ^1H NMR analyses of the alcohols produced by the oxidation of the propargylboronates with alkaline hydrogen peroxide using biphenyl as an internal standard. [c]Isolated yields were 3-5% lower than their NMR yields. [d]All the new alcohols were characterized by IR, ^1H, ^{13}C, and Mass (both low and high resolution) spectroscopy.

This methodology appears to be highly general, accommodating alkynes bearing representative functional groups. It is important to note that the generation of the "ate" complex at 0 °C, instead of, at -78 °C, had little or no effect on the chemical yields of the propargylboronates, while greatly simplifying the experimental procedure. Formation of the "ate" complex was quantitative, with the moderately lower yields of the products due to the parallel formation of a side product (^{11}B NMR at δ 17.5 ppm).[11] The side product appears to build up by the destruction of main product, propargylboronates. In another experiment, an alkynyllithium was generated separately at -78 °C and added to the boronate to form the "ate" complex, hoping to avoid any parallel reactions, such as, the possible coordination of LDA with boronate. Unfortunately, the experimental result showed no improvement in the chemical yield.

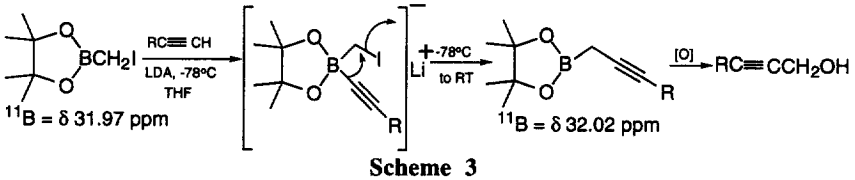
In order to improve the chemical yields of the various propargylboronates and simultaneously suppress the formation of the undesired side products, we prepared various cyclic iodomethylboronates for this study. Three cyclic iodomethylboronates, 2-(iodomethyl)-1,3,2-dioxaborinane (**2**), 2-(iodomethyl)-1,3,2-dioxa-5,5-dimethylborinane (**3**), and 2-(iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane (**4**), were prepared by transesterification of diisopropyl iodomethylboronate (**1**) with the corresponding diols in dry pentane in almost quantitative yields.



2 **3** **4**

The "ate" complexes derived from 2-(iodomethyl)-1,3,2-dioxaborinane and alkynyllithiums rearrange to propargylboronates at 0 °C much faster than the corresponding acyclic diisopropyl iodomethylboronate. Interestingly, the formation of side product was suppressed considerably, but not completely. Only 5-6% of the side product (^{11}B NMR at δ 17.5 ppm) could be observed after 1.5h. To ensure the quantitative capture of boronate with alkynyllithiums, LDA was added at -78 °C and the ^{11}B NMR spectrum was recorded immediately. After 0.5 h, ^{11}B NMR spectrum showed the complete absence of the starting boronate (^{11}B NMR at δ 28.5 ppm). 2-(Iodomethyl)-1,3,2-dioxa-5,5-dimethylborinane also gave results similar to those in the case of 2-(iodomethyl)-1,3,2-dioxaborolane. In this case also, the formation of the side product (5-6%) could not be completely suppressed. The rearrangement of the "ate" complex was slightly faster than its unsubstituted analog. The chemical yields were also comparable to those of the unsubstituted analog.

The best results were obtained with 2-(iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane (Scheme 3). The "ate" complex derived from 2-(iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane rearranged slightly faster than the "ate" complex derived from 2-(iodomethyl)-1,3,2-dioxa-5,5-dimethylborinane. The formation of side product was completely suppressed. It is interesting to note that the pinacol propargylboronate derived from *n*-decynyllithium showed no significant deterioration (<2%) even after 24 h at room temperature.



Scheme 3

Table 2. Reaction of 2-Iodomethyl-1,3,2-dioxa-4,4,5,5-tetramethylborolane with Representative *in situ* Generated Alkynyllithiums[a]

$RC{\equiv}CCH_2B[OCH_2C(CH_3)_2\text{-}]_2$ (R)	Time (h)	Yields of $RC{\equiv}CCH_2OH$ Following H_2O_2 Oxidation (%)[b]
n-Octyl	1.5	72
3-Chloropropyl	2.0	74
2-(CH_2CH_2O)pyran	2.5	76
(Triisopropyl)silyl	2.5	71

[a] 1.25 eq. of the reagent is used. [b] Yields based on the ^{1}H NMR analyses of the alcohols produced by the oxidation of the propargylboronates with alkaline hydrogen peroxide using biphenyl as an internal standard.

In conclusion, a simple, convenient general procedure for the preparation of higher propargylboronates in good to excellent chemical yields with excellent isomeric purity has been developed. This new methodology avoids the necessity of making individual cyclic and acyclic boronates. The mildness of the procedure and the ability to run the reaction at ambient conditions make it a simple and convenient alternative route. Even an acid sensitive group, e.g., acetal, which would be difficult to accommodate using previously developed methodology, has been accommodated. The formation of the undesired side product, which could not be avoided in the earlier procedure[5], has been supressed. Pinacol propargylboronates have been found to be the most stable ones amongst cyclic and acyclic analogs.

Our preliminary result has shown that the propargylboronate derived from 2-(iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane and *n*-decynyllithium reacts with benzaldehyde at room temperature which upon oxidative workup gives an α-allenic alcohol, 4-hydroxy-3-octyl-4-phenyl-1,2-butadiene in 60% chemical yield. We also plan to synthesize chiral propargyl-boronates using this methodology and study the enantioselective addition of aldehydes. This research work is in progress and will be reported in due course.

A Representative Procedure for the Reaction of 2-(Iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane with Alkynyllithium: LDA (1.7 mL, 2.5 mmol) was added slowly to a stirring solution of 2-(iodomethyl)-1,3,2-dioxa-4,4,5,5-tetramethylborolane (0.536 g, 3 mmol), and *n*-decyne (0.45 mL, 2.5 mmol) in THF (5 mL), cooled to -78 °C under nitrogen atmosphere. The mixture was stirred at -78 °C for 0.5-1.0 h, the cold bath was then removed and the contents were allowed to warm to rt without stirring for 1.5 h. The boronate was then oxidized with alkaline hydrogen peroxide according to the usual procedure.[12] After adding biphenyl (0.0385 g, 0.25 mmol) and saturating the aqueous layer with anhydrous K_2CO_3, the propargyl alcohol was extracted with EE (3 x 30 mL), dried over anhydrous K_2CO_3, and concentrated. The crude product was analysed by ^1H NMR spectroscopy. The alcohol was purified by column chromatography on silica gel and the chemical yield of the isolated product was also determined.

Acknowledgment. The financial support from Office of Naval Research is gratefully acknowledged.

References and Notes:

1. Brown, H. C.; Ramachandran. P. V. In *Advances in Asymmetric Synthesis*; Hassner, A. ; Ed.; JAI Press: Greenwich, CT, 1995; Vol. 1, p. 147.
2. Favre, E.; Gaudemer, M. *J. Organomet. Chem.* **1974**, 297, 305.
3. (a) Epsztein, R. In *Comprehensive Carbanion Chemistry*; Buncel, E.; Durst, T.; Eds.; Elsevier: Amsterdam, 1984; Part B. (b) Favre, E.; Gaudemar, M. *Bull. Soc. Chim., Fr.* **1968**, 3724. (c) Brown, H. C.; Khire, U. R. *Tetrahedron Lett.* **1993**, *34*, 15.
4. Corey, E. J.; Yu, C-M.; Lee, D-H. *J. Am. Chem. Soc.* **1990**, *112*, 878.
5. Soundararajan, R.; Li, G.; Brown, H. C. *Tetrahedron Lett.* **1994**, *35*, 8961.
6. Soundararajan, R.; Li, G.; Brown, H. C. *Tetrahedron Lett.* **1994**, *35*, 8957.
7. Rangaishenvi, M. V.; Singaram, B.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 3286.
8. Wallace, R. H.; Zong, K. K. *Tetrahedron Lett.* **1992**, *33*, 6941.
9. Soundararajan, R.; Li, G.; Brown, H. C. *J. Org. Chem.* **1996**, *61*, 100.
10. Coupling of triisopropyl borate with $LiCH_2I$, generated from CH_2I_2 and *n*-BuLi gave diisopropyl iodomethylboronate in 70% yield. Formation of side product *n*-BuI (bp 130-131 °C) and unreacted starting borate always contaminated the product during fractional distillation. The use of MeLi in place of *n*-BuLi not only improves the chemical yield (>90%) of the diisopropyl iodomethylboronate but also makes the purification step easier. MeLi procedure produces MeI which, being a very low boiling liquid (bp 41-43 °C) makes the fractional distillation simpler.
11. Previous communication has ruled out the presence of either tricoordinated borates or any allenic intermediate from the 1,3-rearrangement of the initially formed 2-alkyn-1-ylboronates (See Ref. 5).
12. Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. In *Organic Syntheses via Boranes*, John Wiley and Sons, New York (1975).

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