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SUCCESSFUL APPLICATION OF α-HALOALLYLLITHIUM FOR A SIMPLE, CONVENIENT PREPARATION OF α-HALOALLYLBORONATE ESTER

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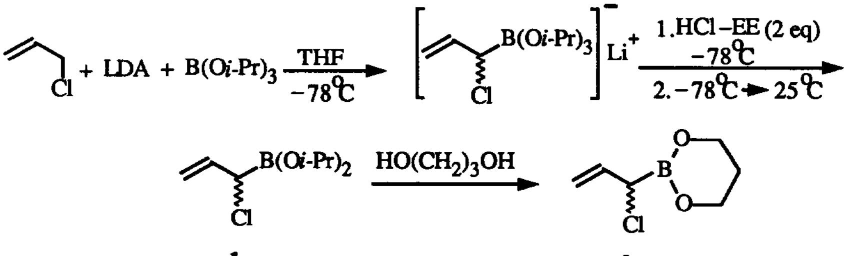
Summary: The first successful application of α-haloallyllithium, $LiCH(X)CH{=}CH_2$, conveniently generated *in situ* from allyl halide and LDA in THF at –78 °C, for reaction with triisopropyl borate to produce the valuable intermediate, α-haloallylboronate ester, is described.

Halogen-substituted carbanions have received considerable attention over the last three decades, especially for evaluating their synthetic potential and their reactivity towards electrophiles.[1] For instance, (dichloromethyl)lithium, $LiCHCl_2$, and (chloromethyl)lithium, $LiCH_2Cl$, conveniently generated in the presence of borate esters at –78°C, have been used extensively for the synthesis of the corresponding haloalkylboronate esters. [2] The simplicity and convenience of this procedure makes it attractive for large scale syntheses.

Halogen-substituted allylic carbanions also constitute an important segment of carbanion chemistry, [3] but unfortunately, have received only limited synthetic attention because of their rapid "self-consumption".[4] Recently, Macdonald *et al* have successfully demonstrated[5] a simple and elegant procedure for the *in situ* generation of α-haloallyllithium, $LiCH(Cl)CH{=}CH_2$, from allyl chloride and LDA in THF at –78 °C, by trapping the intermediate with primary halides, thereby circumventing the problem of "self-consumption". Regretably, the utility of such α-haloallyllithium intermediates has not yet been explored for the valuable transfer reactions of organoboranes. In this letter, we wish to report the facile and direct synthesis of the α-haloallylboronate ester utilizing α-haloallyllithium, $LiCH(Cl)CH{=}CH_2$, with an appropriate borate ester (eq 1).

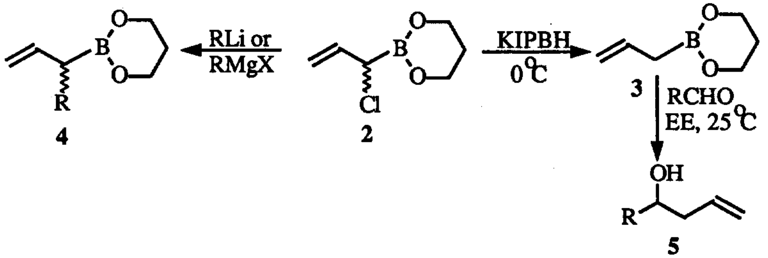


1 2 (1)

Gratifyingly, the reaction of triisopropyl borate with an equiv. of $LiCH(Cl)CH{=}CH_2$, generated *in situ*, followed by the treatment with two equiv. of anh. HCl-EE afforded diisopropyl α-chloroallylboronate **1** in 88% yield. Evidently, the labile α-haloallyllithium generated *in situ* in the presence of triisopropyl borate is captured as soon as it is formed, prior to its self-destruction. The following procedure for the preparation of **1** is representative.

To a cooled solution of triisopropyl borate(23.1 ml, 100 mmol), and allyl chloride(8.15 ml, 110 mmol) in freshly distilled anh. THF(100 ml) at –78 °C was added a solution of preformed LDA in THF(200 ml) [prepared by treating diisopropylamine(15.4 ml, 110 mmol) with *n*-BuLi(47.9 ml of 2.3M solution in hexane) in THF] dropwise by means of a cannula over a period of 0.5h. Stirring was continued at –78 °C for an additional 0.5h. To this solution was added anh. HCl in ether(75.9 ml of 2.9M solution) at –78 °C and the reaction mixture was allowed to warm to 25 °C. The volatiles were pumped off *in vacuo*(20 torr) and the residue extracted with *n*-pentane (3x100 ml). Separation of the pentane portion by filtration under N_2, followed by distillation under reduced pressure, afforded the desired boronate ester **1**: bp 95-96 °C(25 torr), yield(18.0 g, 88%), ^{11}BNMR($CDCl_3$) δ 28 ppm; ^{1}HNMR($CDCl_3$) δ 1.20[d, J=7Hz, 12H, CH(CH_3)], 4.07(m, 1H, CHCl), 4.67(m, 2H), 4.97-5.40(m, 2H, =CH_2), 5.87-6.33(m, 1H). Transesterification of **1** with trimethylene glycol afforded **2** in almost quantitative yield: bp 110-112 °C(20 torr); ^{11}BNMR($CDCl_3$) δ 28.6 ppm; ^{1}HNMR($CDCl_3$) δ 2.03(m, 2H, CH_2), 3.92(m, 2H, CHCl), 4.1(t, J =8Hz, 4H, OCH_2), 5.0-5.4(m, 2H, =CH_2), 5.73-6.36(m, 1H, olefinic). We have also established the successful preparation of **1** at –5 °C by treatment of allyl chloride or bromide with LDA in the presence of triisopropyl borate.

The carbon skeleton of **2** has been confirmed by the hydride transfer reaction using KIPBH,[2e] producing the parent allylboronate ester, **3**. Treatment of the intermediate **2** with RLi or RMgX, gives the corresponding product **4**. These allylic derivatives undergo the usual allylboration of aldehydes to furnish **5** (eq 2).



(2)

It should be pointed out that Matteson *et al* have reported[6] the preparation of such α-haloallylboronate esters *via* the homologation of vinylboronate ester with preformed $LiCHCl_2$ at –100 °C. Hoffmann *et al* have also demonstrated[7] the preparation of α-haloallyl boronate esters *via* the reaction of vinyl Grignard with dichloromethylboronate ester. However, this procedure has the disadvantage of being a multi-step process, but has the advantage of making possible the synthesis of diastereomerically pure α-haloallylboronate ester by an appropriate choice of a chiral auxiliary with C_2 symmetry.

The new synthesis of α-haloallylboronate ester **2** is essentially a simple, one-pot, high yield process, especially convenient for large scale synthesis. Some of the potential applications of these versatile intermediates have been developed[8] in our laboratory and additional exploration of the chemistry is currently underway.[9]

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8. See the following paper in this issue.
9. We wish to thank the National Science Foundation (Grant CHE-8706102) for the financial support of this project.

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