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Reactions of N--Halosuccinimides with 1,1-Bimetallics Based on Zirconocene and Boronic Esters: A New Synthesis of α-Haloboronic Esters

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Abstract: *Rapid hydrozirconation of alkenyl boronic esters by zirconocene hydrochloride, followed by addition of N-halosuccinimides leads to the corresponding α-halo boronic esters in high yields.*

Hydrozirconation of unsaturated hydrocarbons has been shown to be useful for the preparation of organozirconium compounds. The latter have a number of unique properties enabling them to be used as highly reactive reagents in organic synthesis[1] and as effective catalysts for organic reactions and polymerizations of olefins.[2]

Boronic esters are very useful intermediates in organic synthesis and have been intensely studied.[3] Recently we have reported the preparation and selective cleavage reactions of boron-zirconium 1,1-bimetallics based on trialkylboranes.[4] Later we prepared boron-zirconium 1,1-bimetallics based on boronic esters. These are much more stable and more practically useful.[5] In our continuing studies on the synthesis and utility of boron-zirconium bimetallic reagents, we have now found that the selective cleavage of the carbon-zirconium bond in 1,1-bimetallics based on zirconocene and boronic esters by N-halosuccinimides provides α-haloboronic esters in excellent chemical yields and with complete regioselectivity to provide a very useful class of boron intermediates for organic synthesis.[6](eq 1)

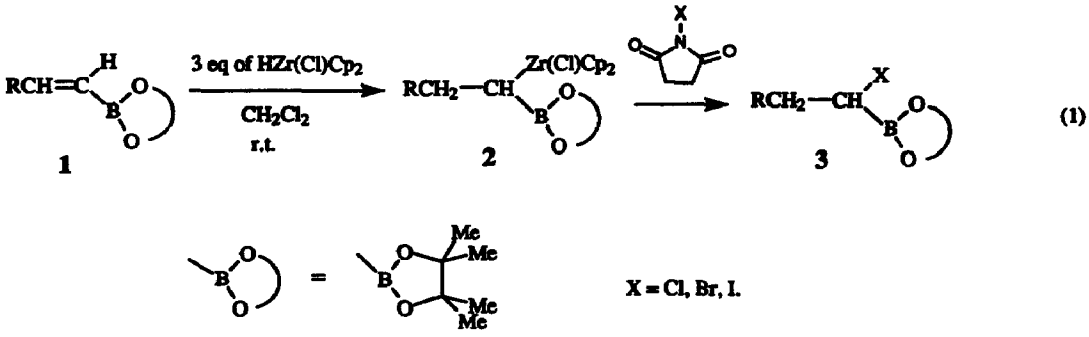
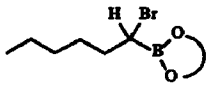
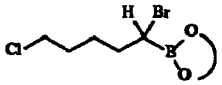
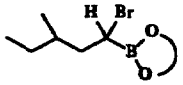
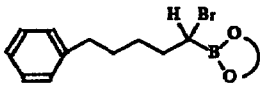
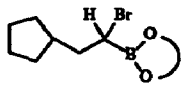
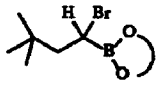
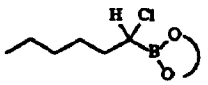
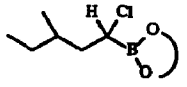
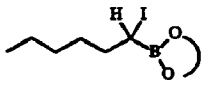


Table I. Preparation of α–Haloboronic Esters 3 by Selective Cleavage of Bimetallics 2.

Entry	R in Alkenyl Boronate, 1	Cleavage Reagent	Cleavage Reaction Time, min	Cleavage Reaction Time, min		^{1}H NMR δ(ppm) of α-H	Yield[a] %
1	n-butyl	NBS	10		3a	3.30(t)	98
2	3-chloropropyl	NBS	10		3b	3.30(t)	97
3	1-methylpropyl	NBS	15		3c	3.39(m)	92
4	3-phenylpropyl	NBS	15		3d	3.32(t)	97
5	cyclopentyl	NBS	15		3e	3.33(t)	99
6	t-butyl	NBS	60		3f	3.40(dd)	83
7	n-butyl	NCS	90		3g	3.41(t)	94
8	1-methylpropyl	NCS	90		3h	3.48(m)	84
9	n-butyl	NIS	10		3i	3.21(t)	91
10	n-butyl	Br_2	10		3a	3.30(t)	92
11	n-butyl	I_2	10		3i	3.21(t)	89

[a]Crude yields, percent based on alkenylboronic esters. The purities of crude products were >95% according to GC analysis. Satisfactory spectral data (IR, ^{1}H- and ^{13}C-NMR, MS) were obtained for all products.

The alkenylboronic esters **1** were obtained by the hydroboration of various alkynes with dibromoborane-methyl sulfide complex in methylene chloride (0° to 25 °C) followed by the conversion of the intermediate dibromoboronic esters to the corresponding alkenylboronic acids (NaOH, ice, AcOEt, 0 °C) and esterification with pinacol (1.2 equiv., $MgSO_4$, 1:1 ether:hexanes, 25 °C).[5] Hydrozirconation of the alkenyl boronic esters **1** with 3 equiv of Schwartz's reagent, $Cp_2Zr(H)Cl$, (except for t-butylvinylboronic esters which required 4 equiv of Schwartz's reagent at 40 °C) in methylene chloride afforded a clear yellow solution of the 1,1-bimetallics **2** . The 1,1-bimetallics **2** were isolated and their structures were characterized by IR, NMR and elemental analysis, and the specific regioselectivity in hydrozirconation step was determined.[5] Addition of a N-halosuccinimide (1.2 equiv) in situ resulted in the disappearance of the original yellow color. After the cleavage reactions were completed (monitored by ^1H NMR), removal of methylene chloride, and extraction with hexanes from the reaction mixture provided the crude oily α-halo boronic esters **3** in high yields.[7] GC analysis showed that the purities of the crude products were very high and over 95%. Therefore no further purification was required for the crude products. The results are summarized in Table I. The reaction is highly general and works equally well for the preparation of chloro, bromo and iodo derivatives. Reaction times are somewhat longer with NCS .

α-Haloboronic esters have also been obtained by hydrogen halide additions to alkenyl boronic esters or borane additions to 1-alkenyl halides. But the regioselectivities of these additions are not always satisfactory in either way. For instance, the hydroboration of 1-chloro-1-butene with BH_3 gave an 85:15 mixture of α- and β-addition of boron moiety.[8] To our knowledge, regioselective additions to vinyl halides by dibromoborane or catecholborane which might provide convenient conversions to boronic esters has not been reported whereas dipropyl vinylboronate with hydrogen iodide gave a 60:40 ratio of α- and β-iodoboronic esters.[9] In contrast to those results, our novel method for preparation of α-haloboronic esters from alkenyl boronic esters has obvious advantages which include regiospecific selectivity and conversion to α-chloro, bromo, iodoboronic esters by corresponding N-halosuccinimides in a one-pot reaction.

In addition to above results, we found that the cleavage of carbon-zirconium bond in a sample of 1,1-bimetallics **2** by bromine in methylene chloride (1M solution) or iodine (neat) afforded the same effect. After a similar work-up procedure as with N-halosuccinimides, the α-bromo or iodoboronic ester was achieved. The results were listed in Table I (Entry 10, 11). However because of ease of handling, we prefer to use the N–halosuccinimides

In conclusion, a new and facile synthetic method for α-haloboronic esters is described which relies on cleavage of carbon-zirconium bond in the readily available boron-zirconium-1,1-bimetallics. According to this procedure, α-chloro, bromo and iodoboronic esters are easily obtained with excellent regioselectivity in high yields.

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spectrometer and to the U.S. Department of Education for a cost-sharing grant for the purchase of a GC/MS/DS instrument used in this work.

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7. Typical procedure. **Preparation of pinacol 1-bromohexylboronate:** A suspension of $Cp_2ZrCl(H)$ (0.420g, 1.63mmol) in dry methylene chloride (3.2ml) was stirred at ambient temperature under an atmosphere of argon. A 1.1 ml of 0.5 M solution of pinacol 1-hexenyl boronate (0.55mmol) in methylene chloride was then added. The reaction mixture was stirred for 40 min, and became a clear green-yellow solution. Addition of N-bromosuccinimide (1.17g, 0.66mmol) in situ led to the discharge of the color of the solution. After pumping off the methylene chloride, hexanes (3x10ml) was added to extract the reaction mixture. Evaporation of the solvent from the filtrate afforded the colorless oil of pinacol 1-bromohexylboronic ester (0.156g, 98%). ^1H NMR (400 MHz, CDCl3): 3.30(1H, t), 1.91-1.84(2H, m), 1.50-1.43(1H, m), 1.40-1.21(17H, m), 0.87(3H, t); ^{13}C NMR (100.6 MHz, CDCl3): 84.1, 34.0, 31.2, 28.4, 24.5, 24.4, 22.4, 13.9. IR (neat): 2981, 2950, 2885, 1715, 1622, 1438, 1345, 1252, 1159, 1129, 1005, 974, 850, 727. MS (EI) (m/z, relative intensive): 292(M^+, 0.48), 290(0.48).
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