Hydroboration of Terminal Alkynes Catalysed by Sodium Triethylborohydride

Anna M. Maj[a,b], Piotr Pawluć[b,c,], Maciej Zaranek[b,c,]*

a Faculty of Chemical Technology and Engineering, University of Technology and Life Sciences in Bydgoszcz, Seminaryjna St. 3, 85-326 Bydgoszcz, Poland
b Centre for Advanced Technologies, Adam Mickiewicz University, Uniwersytetu Poznańskiego St. 10, 61-614 Poznań, Poland
c Faculty of Chemistry, Adam Mickiewicz University, Uniwersytetu Poznańskiego St. 8, 61-614 Poznań, Poland
** m.zaranek@amu.edu.pl*

Abstract. Sodium triethylborohydride - commonly used as a reducing agent for hydroboration catalysts based on the first-row transition metal complexes with tridentate ligands, has been found a highly selective catalyst for hydroboration of terminal alkynes. Hydroboration of aromatic and aliphatic alkynes with pinacolborane in the presence of 10 mol% of $NaHBEt_3$ proceeded in a highly selective manner to give (*E*)-vinylboronate esters with high yields, whereas ethynylsilanes seem to be less reactive in this process.

Keywords: hydroboration, alkynes, transition-metal-free, borohydrides

Introduction

Vinylboronates play a pivotal role in modern organic synthesis as essential synthons in selective carbon−carbon or carbon−heteroatom bond formation reactions which are important especially in the pharmaceutical, agrochemical and cosmetic industries. [1] Catalytic hydroboration of alkynes with hydroborates is a powerful tool for generating vinylboronates (Scheme 1) and this transformation usually occurs via *syn*-addition of a B–H moiety to yield (*E*)-vinylboronate esters.[2] Recently, a new generation of catalysts for selective alkyne hydroboration was reported. They were based on earth-abundant first- row transition metal complexes with tridentate nitrogen-containing ligands and have attracted considerable attention. [3]·[4] These bench-stable precatalysts required activation, usually using alkali metal trialkylborohydrides, to achieve high catalytic activity. [3]
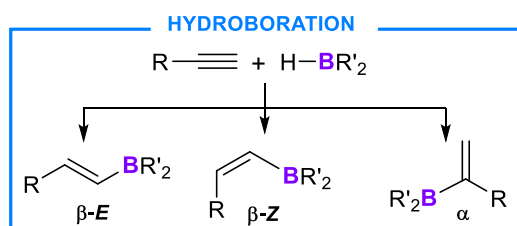
Scheme 1. Theoretically possible products of hydroboration of terminal alkynes.

Hydroboration of terminal and internal alkynes has been also successful using transition metal-free, boron-containing catalysts (e.g. $B(C_6F_5)_3$, borenium cations, $HB(C_6F_5)_2$, tris[3,5-bis(trifluoromethyl)phenyl]borane, tris(2,4,6-trifluorophenyl)borane, $H_3B \cdot THF$) [5]·[6]·[7]·[8]·[9]·[10]

however, to the best of our knowledge, there is only a single report on the use of commercially available sodium triethylborohydride in this process.[9] NaHBEt$_3$ has been demonstrated by Thomas and co-workers to catalyse hydroboration of phenylacetylene with pinacolborane to give (*E*)-styryl boronic ester in 45% yield.[9]

We have already reported that NaHBEt$_3$ can be used as a selective catalyst for dehydrogenative silylation of alkynes with hydrosilanes [11] and Markovnikov-selective hydrosilylation of alkenes.[12]·[13] Given the preliminary report from the Thomas group and the mechanistic similarity of hydrosilylation and hydroboration reactions, we decided to study in more detail the reactivity of terminal alkynes and pinacolborane in the presence of alkali metal triethylborohydrides in order to examine the impact of these commonly used reductants on the course of the hydroboration process.

Methods

General remarks

All reactions were performed in an oven-dried glassware under the argon atmosphere. Solvents were dried by distillation over sodium/benzophenone. Alkynes and pinacolborane were used as supplied and degassed prior to use. Alkali metal trialkylborohydrides were commercially available as 1M solutions in toluene or THF and used as received. Gas chromatography was performed on a Bruker Scion 436-GC with a TCD detector. GC-MS analyses were performed on a Bruker Scion 436-GC a Scion SQ-MS mass spectrometry detector. NMR analyses were performed on a Bruker Fourier 300 spectrometer and referenced to the solvent residual peak.

### General procedure of NaHBEt$_3$-catalysed hydroboration

1.0 mmol of alkyne, 0.1 mL of decane and 1.1 mmol of pinacolborane, were placed in previously evacuated Schlenk bomb flask fitted with a plug valve. A reference sample was taken. Next, 0.1 mL of 1M solution of NaHBEt$_3$ (0.1 mmol) in toluene was added, reaction vessel was closed and heated at 60 °C with stirring. After specified time, reaction mixture was cooled down to the room temperature and analysed using GC and GC-MS. Products of hydroboration were isolated by extraction with 1 mL of DCM followed by column chromatography of concentrated extract (SiO$_2$, hexane/Et$_2$O, 98:2).

Identification of selected hydroboration products
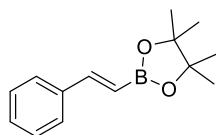
(E)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane:
^{1}H NMR (300MHz, CDCl$_3$): δ [ppm] 1.25 (s, 12H), 6.10 (d, 1H, *J*= 18.43 Hz), 7.24 (m, 4H), 7.40 (m, 2H); **^{13}C NMR** (75 MHz, CDCl$_3$): δ [ppm] 24.99, 55.34, 83.22, 113.90, 128.38, 130.30, 133.50, 148.94, 159.66; **^{11}B NMR** (128 MHz, CDCl$_3$): δ [ppm] 30.11; **MS** (EI, 70 eV): m/z (%)*:*183 (100), 105 (20), 184 (16), 181 (16)
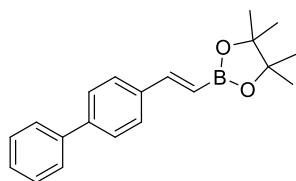

(E)-2-(2-([1,1'-biphenyl]-4-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:
^{1}H NMR (300MHz, CDCl$_3$): δ [ppm] 1.35 (s, 12H), 6.25 (d, 1H, *J*= 18.42 Hz), 7.38 (m, 2H), 7.45 (m, 1H), 7.61 (m, 6H); **^{13}C NMR** (75 MHz, CDCl$_3$): δ [ppm] 144.45, 135.84, 135.69, 133.14, 129.84 129.71, 128.30, 128.05, 127.84, 125.05, 27.09, 16.63; **MS** (EI, 70 eV): m/z (%):183 (100), 105 (20), 184 (16), 181 (16)
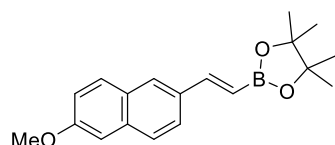
(E)-2-(2-(6-methoxynaphthalen-2-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:

¹H NMR (300MHz, CDCl₃): δ [ppm] 1.36 (s, 12H), 3.95 (s, 3H), 6.25 (d, 1H, *J*= 18.39 Hz), 7.14 (m, 2H), 7.56 (d, 1H), 7.74 (m, 4H); **¹³C NMR** (75 MHz, CDCl₃): δ [ppm] 24.84, 55.35, 83.32, 105.88, 119.02, 124.04, 127.09, 127.86, 128.82, 129.95, 132.98, 135.01, 149.66, 158.14; **¹¹B NMR** (128 MHz, CDCl₃): δ [ppm] 30.33; **MS** (EI, 70 eV): m/z (%): 183 (100), 105 (20), 184 (16), 181 (16)
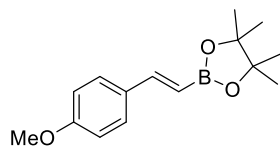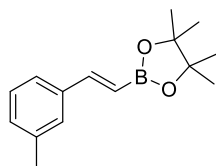
(E)-2-(4-methoxystyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:

¹H NMR (300MHz, CDCl₃): δ [ppm] 1.33 (s, 12H), 3.84 (s, 3H), 6.06 (d, 1H, *J*= 15.00 Hz), 6.89 (d, 2H), 7.42 (d, 2H); **¹³C NMR** (75 MHz, CDCl₃): δ [ppm] 24.99, 55.34, 83.22, 113.90, 128.38, 130.30, 133.50, 148.94, 159.66; **MS** (EI, 70 eV): m/z (%): 183 (100), 105 (20), 184 (16), 181 (16)
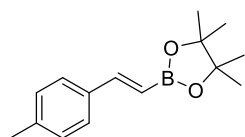
(E)-4,4,5,5-tetramethyl-2-(4-methylstyryl)-1,3,2-dioxaborolane:

¹H NMR (300MHz, CDCl₃): δ [ppm] 1.34 (s, 12H), 2.37 (s, 3H), 6.14 (d, 1H, *J*= 18.47 Hz), 7.16 (m, 2H), 7.40 (m, 2H); **¹³C NMR** (75 MHz, CDCl₃): δ [ppm] 144.45, 135.84, 135.69, 133.14, 129.84 129.71, 128.30, 128.05, 127.84, 125.05, 27.09, 16.63; **MS** (EI, 70 eV): m/z (%):183 (100), 105 (20), 184 (16), 181 (16)

(E)-4,4,5,5-tetramethyl-2-(3-methylstyryl)-1,3,2-dioxaborolane:

¹H NMR (300MHz, CDCl₃): δ [ppm] 1.34 (s, 12H), 2.37 (s, 3H), 6.18 (d, 1H, *J*= 18.43 Hz), 7.13 (m, 1H), 7.28 (m, 3H), 7.47 (m, 1H); **¹³C NMR** (75 MHz, CDCl₃): δ [ppm] 21.40, 24.94, 83.31, 124.24, 127.78, 128.45, 129.70, 137.60, 138.24, 149.67; **¹¹B NMR** (128 MHz, CDCl₃): δ [ppm] 30.29; **MS** (EI, 70 eV): m/z (%): 183 (100), 105 (20), 184 (16), 181 (16)

Results and discussion

We began our study with hydroboration of phenylacetylene (**1**) with 1.1 eq. of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (pinacolborane, HBpin) using sodium triethylborohydride as a catalyst and without any additional solvent. It has to be noted, however, that all the borohydrides were supplied and used as 1M solutions in either toluene or THF. The results of the reaction conditions screening are presented in Table 1.

A portion of 10 mol % of NaHBEt₃ (1M in toluene) applied in the model reaction led to 71% conversion of 1 after 1 h at 60 °C, and yielded exclusively monoborylated linear (*E*)-alkenyl boronate ester **2** (entry 7). The prolonged reaction time of 24 h gave higher conversion of **1** (93%, entry 6). Increasing the reaction temperature to 80 °C resulted in complete conversion of **1** within 1h affording product **2** with as high *anti*-Markovnikov regioselectivity as previously (>99%, entry 5). Decreasing the catalyst loading to 5 mol% of NaHBEt₃ resulted in a decrease in reactivity: after 1h at 80 °C, only 87% conversion of **1** was observed (entry 4). The reactions carried out with an addition of solvents, such as toluene, THF or dioxane, led to lower conversions of **1** (83-85%) (entries 10-12). Interestingly, two additional experiments performed with 2.2 equivalents of HBpin, with and without addition of toluene, both led to drastic reduction of phenylacetylene conversion and formation of two by-products: the alkyl boronate ester **3** and alkyl bisboronate ester **4** (entries 13-14).

Table 1. Screening of the reaction conditions

Ph–C≡CH (**1**, 1 mmol) + H–Bpin (**H-Bpin**, 1.1 mmol) →[NaHBEt₃] Ph–CH=CH–**B**pin (**2**) + Ph–CH₂CH₂–**B**pin (**3**) + Ph–CH₂CH(**B**pin)₂ (**4**)

#	NaHBEt₃ loading	Solvent added	T [°C]	t [h]	Conversion of 1 [a]	Selectivity [b]
1	0	None	60	24	2%	n/a
2	5 mol%	None	80	24	90%	>99% **2**(E)
3			80	2	90%	>99% **2**(E)
4			80	1	87%	>99% **2**(E)
5	**10 mol%**	**None**	**80**	**1**	**99%**	**>99% 2(E)**
6			60	24	93%	>99% **2**(E)
7			60	1	71%	>99% **2**(E)
8			60	0.5	69%	>99% **2**(E)
9			45	1	51%	>99% **2**(E)
10		Toluene (1 mL)	80	1	85%	>99% **2**(E)
11		THF (1 mL)	80	1	83%	>99% **2**(E)
12		1,4-Dioxane (1 mL)	80	1	84%	>99% **2**(E)
13 [c]		None	80	24	38%	85% **2**(E) / 12% **3** / 3% **4**
14 [c]		Toluene (1 mL)	80	24	57%	73% **2**(E) / 8% **3** / 18% **4**

[a] Determined by GC using 0.1 mL of decane as a reference; [b] Determined by GC-MS and ^{1}H NMR; [c] 1.0 mmol of phenylacetylene and 2.2 mmol of HBpin used.
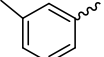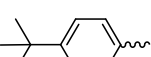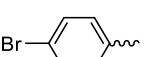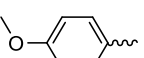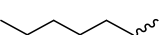
Next, using the optimised reaction conditions as established above (entry 5), we examined the capabilities of other commercially available alkali metal trialkylborohydrides in catalysing hydroboration of phenylacetylene. All of the other borohydrides, i.e. NaHB(*s*-Bu)₃, LiHBEt₃ and KHBEt₃, led to very high *anti*-Markovnikov regioselectivity of 97-99% of the (E) isomer. Nevertheless, NaHBEt₃ turned out to be the most active catalyst, as conversions of **1** reached with the other borohydrides did no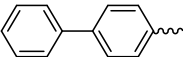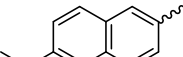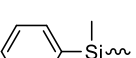t go over 90% for LiHBEt₃ and were even smaller for NaHB(*s*-Bu)₃ (61%) and KHBEt₃ (36%). Moreover, in the case of LiHBEt₃ and KHBEt₃, the GC-MS analysis showed that the alkyl bisboronate ester **4** was present as a by-product in small quantity (<2%).

Having established the most optimal conditions, we attempted at extending the substrate scope over substituted phenylacetylene derivatives and other aromatic and aliphatic terminal alkynes.

Table 2 summarises the study of the influence of various types of substituents at the ethynyl moiety on its conversion and selectivity towards the desired product. Phenylacetylenes decorated with a methyl substituent located at the aryl group were converted with excellent *anti*-Markovnikov regioselectivity (>99%) to linear (E)-alkenyl pinacol boronic esters. However the conversions after 1h were rather moderate (59-75%). As expected, the steric hindrance influences the reaction rate and 4-ethynyltoluene

reacted faster than 3- and 2-ethynyltoluene (75% vs 61% vs 59% conversion, entries 2-4). When using 4-ethynyltoluene, extending reaction time to 24 h allowed for a nearly complete conversion of the alkyne. Phenylacetylene bearing electron-withdrawing bromo substituent underwent hydroboration by HBpin without any loss of regioselectivity, but with a moderate conversion of only 35% after 1h (entry 6). The phenylacetylene derivatives with either a phenyl (entry 10) or a methoxy (entry 7) group at *para* position did also react much slower, giving only 40% and 68% of conversion, respectively. In both these cases, an extension of the reaction time 24 h increased the conversions to 87% and 99 %, respectively. On the other hand, weakly electron-donating *p-tert*-butyl group did not affect the reactivity of the phenylacetylene derivative (entry 5).

Table 2. Hydroboration of terminal alkynes.

$$R\text{---}\equiv\ +\ \text{H-}\mathbf{B}\text{pin} \xrightarrow[\text{neat, 80}^\circ\text{C}]{\begin{array}{c}\text{Na}\mathbf{H}\mathbf{B}\text{Et}_3\\(10\ \text{mol}\%)\end{array}} R\diagup\hspace{-6pt}\diagdown\mathbf{B}\text{pin}$$

#	R	t	Conv.[a]	Yield [b]
1	(phenyl)	1h	99%	99(86)%
2	(4-methylphenyl)	24h	98%	97(82)%
3	(3-methylphenyl)	1h	61%	60(46)%
4	(2-methylphenyl)	1h	59%	59%
5	(4-tert-butylphenyl)	1h	99%	99%
6	(4-bromophenyl)	1h	35%	34%
7	(4-methoxyphenyl)	24h	99%	99(91)%
8	(cyclohexyl)	1h	82%	81%
9	(n-alkyl)	1h	97%	97%
10	(biphenyl)	24h	87%	87(73)%
11	(methoxynaphthyl)	1h	40%	40(30)%
12	(dimethylphenylsilyl)	1h	53%	42%
13	(triisopropylsilyl)	24h	85%	82%

[a] Determined by GC; [b] GC yield, isolated yields are given in parentheses.

Aliphatic alkynes were also successfully converted into adequate pinacol boronic esters. Similarly, an excellent *anti*-Markovnikov regioselectivity was observed, however, the alkyl substitution had a small negative effect on the catalyst activity, as the conversions were slightly lower. We then turned our attention to ethynylsilanes as another group of substrates whose hydroboration could possibly lead to potent building blocks - (*E*)-1-silyl-2-borylethenes. We carried out hydroboration of ethynyldimethyl(phenyl)silane (entry 12) and ethynyltriisopropylsilane (entry 13) with pinacolborane in the presence of NaHBEt$_3$ (1M in toluene) as a catalyst. As it turned out, hydroboration of ethynylsilanes was not as effective as that of previous alkynes. The reaction with ethynyldimethyl(phenyl)silane resulted in moderate conversion of the substrate giving the corresponding product with only 80% of regioselectivity towards the linear ester. A higher regioselectivity of >99% was observed with the use of ethynyltriisopropylsilane, however, the conversion was sill moderate. Noteworthy, trimethylsilylacetylene did not react at all. Representative examples of hydroboration products were isolated and analysed.

Conclusions

Sodium triethylborohydride turned out to catalyse regioselective hydroboration of aromatic and aliphatic terminal alkynes with pinacolborane. The conditions for this reaction were optimised and applied to synthesis of a group of (*E*)-1-boryl-2-alkyl- and (*E*)-1-boryl-2-arylethenes Although, the catalytic activity of NaHBEt$_3$ can be moderate, alkali metal trialkylborohydrides, which are often used as activators of transition-metal-based catalytic systems, can exert direct influence on the hydroboration pathway. It should be emphasised that each their further use in this role should be preceded by careful consideration of possible influence on actual processes under study.

Acknowledgements

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