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Selective synthesis of boron-substituted enynes *via* a one-pot diboration/protodeboration sequence†

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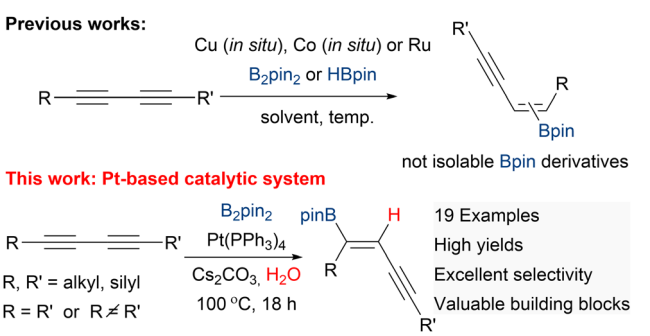
An efficient and facile one-pot protocol to access enynylboronates *via* a Pt-catalyzed diboration/protodeboration strategy has been developed. The reaction is suitable for various silylsubstituted symmetrical and unsymmetrical 1,3-diynes, leading to π-conjugated organoboron compounds with excellent regio- and stereoselectivity.

Organoboron compounds, especially those containing an unsaturated C-C skeleton, such as alkenyl, dienyl or enynyl boronates, are some of the most important and versatile building blocks in modern chemistry.[1–3] They are widely applied in academia and industry for the preparation of biologically active or natural compounds[4,5] and advanced specific-task materials.[6,7] Additionally, low toxicity, high stability and reactivity in certain reaction conditions often make them the first-choice molecules in the formation of new C–C or C–X (X = heteroatom) bonds.[8,9]

Borylation of 1,3-diynes is the simplest but non-trivial way to access enynylboronates. The presence of two triple C–C bonds with different reactivity (for unsymmetrical 1,3-diynes) entails the possibility of the appearance of several different regio- and stereoisomers or overreduction of C≡C bonds.[10] Thus, the selective and efficient synthesis of enynylboronates is a challenging synthetic task. In contrast to the well-established synthesis of alkenyl[11–13] or dienyl boronates,[14,15] the formation of enynylboronates is limited to a few examples.

Several different approaches, such as organocatalytic,[16] radical[17] and TM-catalyzed borylations,[18–22] were applied to access enynylboronates. However, the latter is the most developed. Cu catalysis has emerged as one of the most popular tools to install boron across π-unsaturated C–C bond scaffolds (Scheme 1). In 2015, Li *et al.* used bis(pinacolato)diboron in a protoboration reaction catalyzed by a copper catalyst that was generated *in situ*.[18] A similar approach was applied by Ganesh, who used a mixed diboron reagent.[19] Recently, Santos *et al.* reported the selective synthesis of (*Z*)-1,3-enynes *via* the hydrolysis of borylenyne intermediates.[20] All the described protocols utilized multicomponent catalytic systems that were generated *in situ* or strictly maintained reaction conditions. The regiodivergent Co-catalyzed hydroboration of 1,3-diynes was reported by Ge.[21] However, similarly to copper-based transformations, active catalytic species were generated *in situ*. Our group presented for the first time the hydroboration of symmetrical aryl-substituted 1,3-diynes with the application of molecular ruthenium catalysts.[22] In almost all the examples described above where enynylboronates were isolated, pinacolborane moieties had to be converted to more stable derivatives such as aminoboranes or trifluoroborate salts due to the limited stability of enynyl pinacolboranes to classical silica-based chromatography and boron is attached to an internal carbon bond. The synthesis of a regioisomer with the boryl group at the external C_{sp^2} carbon is more challenging and is limited only to three examples.[18,19,21]

The lack of a simple protocol with a defined molecular catalyst in which enynyl pinacolboronates could be isolated without the necessity of their transformation to more stable derivatives and the small number of papers focused on the enynylboronates with a boron group in the external position



Scheme 1 TM-catalyzed synthesis of enynyl boronates.

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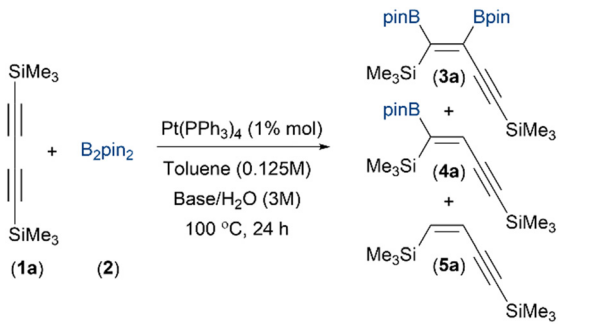
prompted us to develop an easy and efficient method to access isolable enynyl pinacolboranes. Based on our experience in borylfunctionalization of 1,3-diynes[22,23] and the susceptibility of the electrophilic boron center to react with nucleophiles,[24] we envisioned a synthesis of enynyl pinacolboronates *via* a selective one-pot diboration/base-promoted protodeboration sequence of symmetrical and unsymmetrical 1,3-diynes. Our goal was to develop a simple and accessible protocol for synthetic chemists with the application of commercially available starting materials.

To verify our hypothesis, we examined how 1,4-bis(trimethylsilyl)buta-1,3-diyne (**1a**, 1 equiv.) reacts with B_2pin_2 (**2**, 1.1 equiv.) in the presence of a $Pt(PPh_3)_4$ (1 mol%) catalyst and various bases in aqueous solution (3 M). The model reaction in the presence of hydroxides (NaOH and KOH) gave poor conversion of (**1a**) and the formation of a fully protodeboronated product (**5a**) (Table 1, entries 1 and 2). The presence of a strong base such as KOH or NaOH could cause the partial decomposition of (**2**) before the diboration step, which resulted in low diyne conversion. In the next step of base screening, we applied KF and CsF as sources of nucleophilic F^- anion, which is also known to be active in the deboronation process.[25] For both salts, the conversions of **1a** were significantly higher than for hydroxides. However, a mixture of the diboration product (**3a**) and the desired monoboryl substituted enyne (**4a**) was observed (Table 1, entries 3 and 4). Subsequently, we examined three alkali carbonates: Na_2CO_3, K_2CO_3 and Cs_2CO_3. The application of Na_2CO_3 gave only a product (**4a**) with one boryl moiety. However, the conversion of the **1a** substrate was low (Table 1, entry 5). Slightly better consumption of **1a** was observed when a stronger base such as K_2CO_3 was used. Nevertheless, a significant loss of selectivity was observed (Table 1, entry 6). The best results were obtained when Cs_2CO_3 was applied. Under unoptimized reaction conditions, a product (**4a**) with very high selectivity was formed (**3a**/**4a** = 3/97) (Table 1, entry 7). The lack of an undesired product (**5a**) and high conversion of **1a** prompted us to tune the reaction conditions with the application of Cs_2CO_3. A slight excess of B_2pin_2 (1.2 equiv.) towards **1a** was sufficient to complete the conversion of diyne and led exclusively to a monoboryl functionalized enyne (**4a**) with the boron atom attached to the carbon atom adjacent to the silicon atom (Table 1, entry 8). It was proved that complete conversion of diyne took place within 18 h (Table 1, entry 9). A shorter reaction time (16 h) or lower temperature (80 °C) ensured very high but not complete conversion of **1a** (Table 1, entries 10 and 11). To exclude a based-promoted domino borylation/protodeborylation sequence,[24] we performed a model reaction without the Pt catalyst. In the absence of Pt catalysts, we did not observe any traces of products (**3a–5a**) (Table 1, entry 12). On the other hand, the absence of Cs_2CO_3 led to the diboration product, which remains in line with our previous work (Table 1, entry 13).[23] Thus, optimization studies strongly suggest that the synthesis of the monoboryl functionalized enyne (**4a**) proceeds in the biphasic solvent system *via* a diboration/protodeboration sequence.

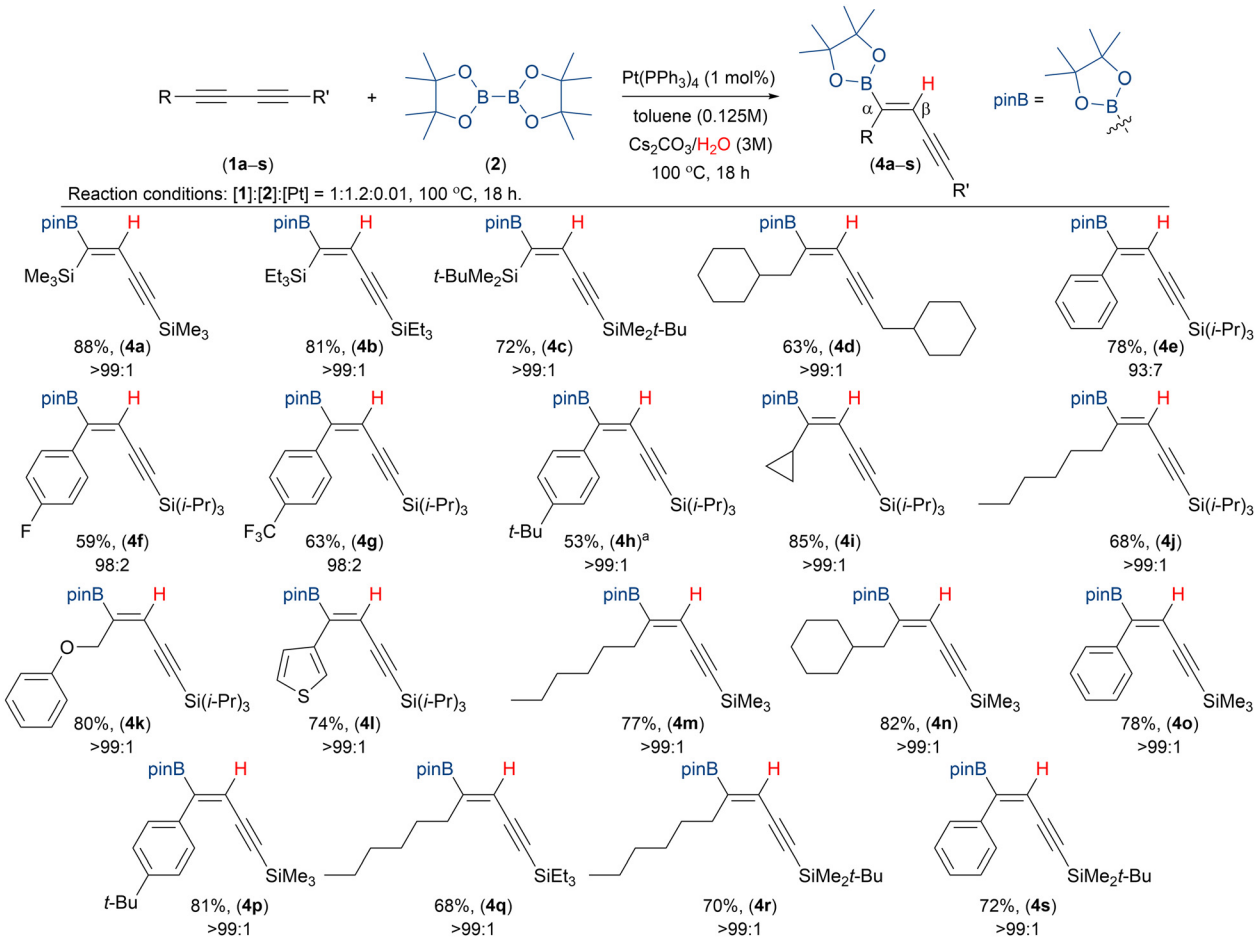
Table 1 Optimization of the reaction conditions



Entry	Base	Conv. of **1a** [%][a]	Selectivity **3a**/**4a**/**5a**[b]
1	NaOH	40	0/10/90
2	KOH	16	0/0/100
3	KF	55	82/18/0
4	CsF	64	50/50/0
5	Na_2CO_3	21	0/100/0
6	K_2CO_3	41	37/63/0
7	Cs_2CO_3	90	3/97/0
8[c]	Cs_2CO_3	100	0/100/0
9[cd]	**Cs_2CO_3**	**100**	**0/100/0**
10[ce]	Cs_2CO_3	98	0/100/0
11[cf]	Cs_2CO_3	94	0/100/0
12[g]	Cs_2CO_3	0	nd
13	-	100	100/0/0

Reaction conditions: [**1a**] : [**2**] : [$Pt(PPh_3)_4$] = 1 : 1.1 : 0.01, toluene (0.125 M), $base_{aq}$. (3 M), 100 °C, 24 h. [a] Determined by GC and GC-MS analyses. [b] Determined by GC-MS and ^1H NMR analyses. [c] 1.2 equiv. of (**2**) was used. [d] 18 h. [e] 16 h. [f] 80 °C. [g] Without $Pt(PPh_3)_4$.

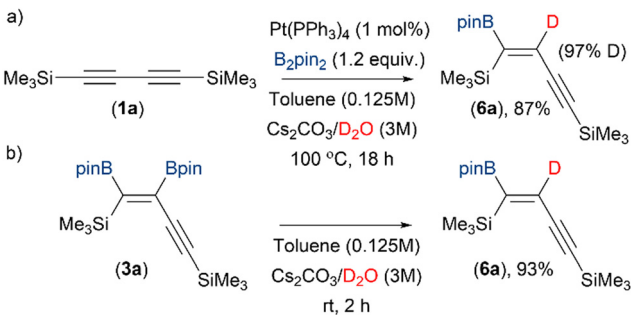
Under optimized reaction conditions, we examined several symmetrical and unsymmetrical 1,3-diynes (**1a–s**) (Scheme 2). Similar to the $–SiMe_3$ group, the symmetrical diynes with $–SiEt_3$ (**1b**) or $SiMe_2t$-Bu (**1c**) substituents could also be efficiently applied to access monoboryl functionalized enynes (**4b–c**) with excellent isolated yields. The application of alkyl-substituted diyne (**1d**) gave the desired product (**4d**) exclusively, with a satisfactory isolation yield. However, the application of symmetrical diynes with highly steric substituents such as $–Si(i\text{-}Pr)_3$ or aryl moieties gave target products with low conversion of diyne and excellent reaction selectivity (for $–Si(i\text{-}Pr)_3$) or with good conversion of diyne and poor selectivity for aryl-substituted diynes (see ESI†). Subsequently, we applied much more challenging unsymmetrical-1,3-diynes (**1e–s**). Based on the good results of the borylation of symmetrically silyl-substituted diynes, we synthesized several unsymmetrical diynes with one silyl moiety attached to C_{sp}. The presence of the silyl group in the substrate's structure enables further functionalization of the product obtained and influences its high reaction selectivity since silyl moieties work as directing groups in borylation reactions.[18,23] Under the optimized reaction conditions, several diynes with the $–Si(i\text{-}Pr)_3$ group on one side and various substituents on the other, such as aryl (**1e–h**), *c*-alkyl (**1i**), *n*-alkyl (**1j**), phenoxy (**1k**) and thienyl (**1l**), were transformed to monoborylated enynes (**4e–l**) with excellent selectivity and high isolation yields. Similar to the bulky $–Si(i\text{-}Pr)_3$ substituent, smaller $–SiMe_3$, $–SiEt_3$ and $–SiMe_2t$-Bu moieties also efficiently worked as a directing group for the borylation of diyne, tolerating both aryl and alkyl substituents (**4m–s**). The regio- and stereoselectivity of the developed process was confirmed *via* selective 1D NOESY and $^1H–^{13}C$ HMBC NMR for representative symmetrical and



Scheme 2 Scope of borylation of symmetrical and unsymmetrical 1,3-diynes *via* a diboration/protodeboration sequence. The ratio between α-boryl and β-boryl substituted products based on ^{1}H NMR is presented. [a]1.5 Equiv. of (**2**) was used.

unsymmetrical substituted products (**4b**) and (**4i**) (see ESI†). For both products, the NOE effect was only observed between an alkenyl proton and pinacol protons, which strongly suggests that the boron atom is attached to the external C_{sp^2} carbon. Due to moderate or low stability towards silica-based chromatography, all products were purified from the post reaction mixture by condensation on a cold-finger trap (see ESI†). Among the 19 monoborylated enynes, 18 of them are new and fully characterized compounds.

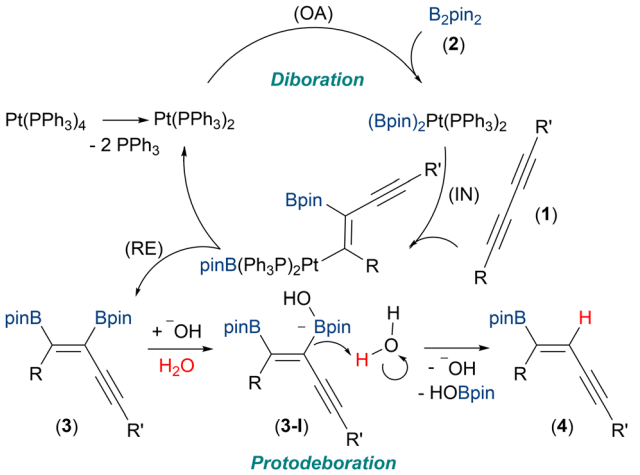
In the next step of our research, we performed deuterium labelling studies by replacing H_2O with D_2O in the model reaction of **1a** with **2** (Scheme 3a). The reaction yielded a deuterium substituted product (**6a**) with comparable efficiency to an H_2O solution with 97% D-incorporation. The same product (**6a**) could be obtained *via* protodeboration of bisborylfunctionalized enyne (**3a**) (Scheme 3b). Based on the deuteration and optimization studies (Table 1, entries 12 and 13), we proposed the catalytic cycle of the developed process. In the first step, the selective diboration of diyne (**1**) occurs *via* oxidative addition (OA) of B_2pin_2 (**2**) to Pt(0) species, followed by the insertion of (IN) diyne into the Pt–B bond. The reductive elimination (RE) gives the diborylfuncionalized enyne.[23] Subsequently, the hydroxide



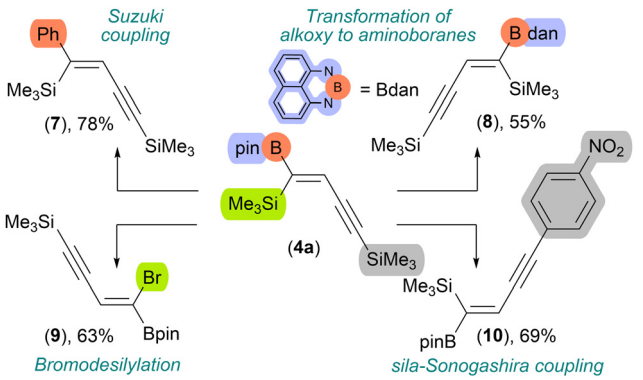
Scheme 3 Deuterium labelling studies for (a) diboration/protodeboration and (b) protodeboration reactions.

anion formed during Cs_2CO_3 hydrolysis attacks the internal boryl group of (**3**) to form a boronate anion (**3–I**). The protodeborylation of (**3–I**) results in the formation of the desired product (**4**). The ^{11}B NMR analysis of the aqueous phase indicates the presence of a $pinB(OH)_2^-$ anion (δ = 4.47 ppm), which supports the proposed mechanism (see ESI†) (Scheme 4).[25]

The presence of unsaturated C=C and C≡C bonds, and boryl and silyl moieties makes the monoborylated enynes



Scheme 4 Proposed mechanism of the diboration/protodeboration sequence.



Scheme 5 Functionalization of **4a** *via* catalytic and non-catalytic methods.

extremely attractive compounds for further functionalization. This was proved by using **4a** as a starting building block in four reactions (Scheme 5). The Suzuki coupling of **4a** with iodobenzene yielded product 7 with full conversion of **4a** and high isolation yield. Moreover, **4a** was also susceptible to the transformation of acid pinacol ester to aminoborane (**8**). Interestingly, we found that each of the $-SiMe_3$ groups attached to the C_{sp} or C_{sp^2} carbons can be selectively modified *via* sila-Sonogashira coupling (**9**) or bromodesilylation (**10**).

In conclusion, an efficient method for the synthesis of monoborylated enynes *via* a one-pot diboration/protodeboration sequence was developed. This protocol is especially usable for silyl substituted symmetrical and unsymmetrical diynes with various functionalities. The alternative isolation method based on the product being condensed on a cold-finger trap allowed several enynyl pincacolboronate derivatives with boron attached to the carbon with a silyl group to be accessed and isolated for the first time. The products showed potential as versatile building blocks in various transformations.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

1 S. J. Geier, C. M. Vogels, J. A. Melanson and S. A. Westcott, *Chem. Soc. Rev.*, 2022, **51**, 8877–8922.
2 J. Pyziak, J. Walkowiak and B. Marciniec, *Chem. – Eur. J.*, 2017, **23**, 3502–3541.
3 A. Whyte, A. Torelli, B. Mirabi, A. Zhang and M. Lautens, *ACS Catal.*, 2020, **10**, 11578–11622.
4 C. Gunawan and M. A. Rizzacasa, *Org. Lett.*, 2010, **12**, 1388–1391.
5 D. Gao and G. A. O'Doherty, *Org. Lett.*, 2010, **12**, 3752–3755.
6 J. Miao, Y. Wang, J. Liu and L. Wang, *Chem. Soc. Rev.*, 2022, **51**, 153–187.
7 F. Jäkle, *Chem. Rev.*, 2010, **110**, 3985–4022.
8 J. Szyling, A. Franczyk, P. Pawluć, B. Marciniec and J. Walkowiak, *Org. Biomol. Chem.*, 2017, **15**, 3207–3215.
9 D. G. Hall, *Boronic acids: preparation and applications in organic synthesis and medicine*, 2005, pp. 1–99.
10 J. Walkowiak, J. Szyling, A. Franczyk and R. L. Melen, *Chem. Soc. Rev.*, 2022, **51**, 869–994.
11 Y. Ping, T. Chang, K. Wang, J. Huo and J. Wang, *Chem. Commun.*, 2019, **55**, 59–62.
12 G.-M. Ho, L. Segura and I. Marek, *Chem. Sci.*, 2020, **11**, 5944–5949.
13 J. Altarejos, A. Valero, R. Manzano and J. Carreras, *Eur. J. Org. Chem.*, 2022, e202200521.
14 L. Mao and S. K. Bose, *Adv. Synth. Catal.*, 2020, **362**, 4174–4188.
15 Y. Zhang, B. Li and S. Y. Liu, *Angew. Chem., Int. Ed.*, 2020, **59**, 15928–15932.
16 S. Jos, C. Szwetkowski, C. Slebodnick, R. Ricker, K. L. Chan, W. C. Chan, U. Radius, Z. Lin, T. B. Marder and W. L. Santos, *Chem. – Eur. J.*, 2022, **28**, e202202349.
17 K. Takahashi, S. J. Geib, K. Maeda, D. P. Curran and T. Taniguchi, *Org. Lett.*, 2021, **23**, 1071–1075.
18 D. Li, Y. E. Kim and J. Yun, *Org. Lett.*, 2015, **17**, 860–863.
19 S. Ghosh, R. Chakrabortty, S. Kumar, A. Das and V. Ganesh, *ACS Catal.*, 2022, **12**, 11660–11666.
20 A. L. Burgio, N. W. Buchbinder and W. L. Santos, *Org. Lett.*, 2023, **25**, 2652–2656.
21 H. L. Sang, C. Wu, G. G. D. Phua and S. Ge, *ACS Catal.*, 2019, **9**, 10109–10114.
22 T. Sokolnicki, J. Szyling, A. Franczyk and J. Walkowiak, *Adv. Synth. Catal.*, 2020, **362**, 177–183.
23 J. Szyling, A. Szymańska, A. Franczyk and J. Walkowiak, *J. Org. Chem.*, 2022, **87**, 10651–10663.
24 Z. Kuang, K. Yang, Y. Zhou and Q. Song, *Chem. Commun.*, 2020, **56**, 6469–6479.
25 S. Nave, R. P. Sonawane, T. G. Elford and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2010, **132**, 17096–17098.

