Article

Stereoselective Synthesis of Trisubstituted Alkenes via Cobalt-Catalyzed Double Dehydrogenative Borylations of 1-Alkenes

Huanan Wen, Lei Zhang, Suzhen Zhu, Guixia Liu, and Zheng Huang

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.7b02104 • Publication Date (Web): 11 Aug 2017

Stereoselective Synthesis of Trisubstituted Alkenes via Cobalt-Catalyzed Double Dehydrogenative Borylations of 1-Alkenes

Huanan Wen, Lei Zhang, Suzhen Zhu, Guixia Liu and Zheng Huang*

[†]State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China.

ABSTRACT: A highly selective cobalt-catalyzed single and double dehydrogenative borylations (DHBs) of terminal alkenes have been developed for the synthesis of *trans*-monoborylalkenes and diborylalkenes, respectively. While the cobalt-catalyzed double DHBs of aryl 1-alkenes with 2 equiv of bis(pinacolato)diboron (B_2pin_2) in the presence of 1 equiv of CsF in DMF produce 1,1-diborylalkenes selectively, the double DHBs with alkyl 1-alkenes generate *cis*-1,2-diborylalkenes in a selective manner. The 1,1-diborylalkene products are further applied to stepwise and stereospecific cross-couplings with aryl halides to create trisubstituted alkenes, including triaryl alkenes.

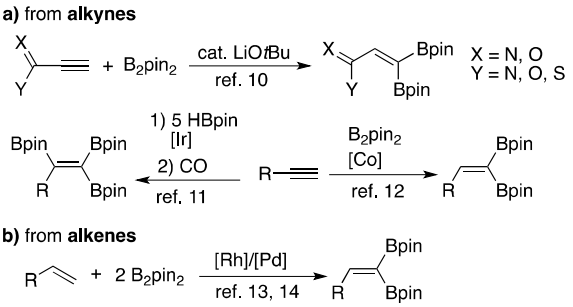
INTRODUCTION

Vinyl boronic acids and boronates are versatile synthetic intermediates due to their reasonable stability, low toxicity and wide applications in C–C and C–heteroatom bond-forming reactions.[1] Among them, 1,1-diborylalkenes bearing two geminal boronate moieties are of particular synthetic interest because they are useful building blocks for diverse synthesis of polysubstituted alkenes, which are prevalent motifs occurring in bioactive compounds and π-conjugated materials.[2] Stereodefined triaryl alkenes (TAAs), for example, have shown interesting biological activities[3] and novel optical properties.[4]

While many methods are available for the synthesis of monoborylalkenes, there are limited approaches to 1,1-diborylalkenes.[1c,5,6] Traditional routes to the latter involve the use of reactive lithium reagents, which may pose a challenge in reactions with sensitive functional groups.[7-9] Recently, several catalytic methods have been developed for the synthesis of 1,1-diborylalkenes using alkynes as the starting materials (Scheme 1a). In 2015, Sawamura and Ohmiya reported the preparation of 1,1-diborylalkenes by LiO*t*Bu-catalyzed reactions of propiolates, propiolamides, and 2-ethynylazoles with B_2pin_2.[10] Ozerov disclosed an Ir-catalyzed synthesis of 1,1,2-triborylalkenes from a two-step reaction of terminal alkynes with HBpin.[11] More recently, Chirik developed a Co-catalyzed 1,1-diboration of terminal alkynes. While very effective for aliphatic alkynes, the reactions with aryl alkynes gave moderate yields due to the homodimerization of alkynes to enynes.[12]

The synthesis of 1,1-diborylalkenes from simple alkenes is of great interest because of the wide accessibility and high stability of the substrates. During their successful development of Rh-catalyzed single dehydrogenative borylation (DHB) of alkenes with B_2pin_2 to yield monoborylalkenes, Marder and Lin found that the reaction of 4-vinyl anisole with 2 equiv of B_2pin_2 at 80 °C after 4-5 days formed 1,1-diborylalkene as the major product, along with *trans*-monoborylalkene as the minor product (Scheme 1b).[13] More recently, a more general route to 1,1-diborylalkenes from 1-alkenes was disclosed by the group of Iwasawa using a pincer Pd catalyst.[6a,6b] Although this Pd catalysis represents a remarkable advance, the development of a catalyst system based on inexpensive, sustainable, and environmentally begin base-metal, such as cobalt, is desirable.

Scheme 1. Known Catalytic Methods for Synthesis of 1,1-Diborylalkenes.



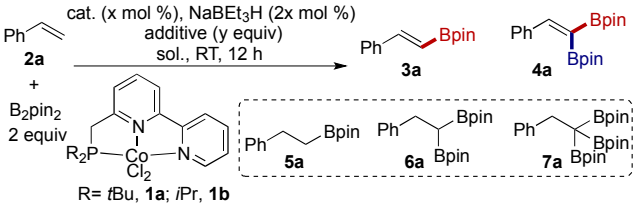
Driven by our interest in developing base-metal catalysis for alkene functionalizations,[14] very recently we reported the synthesis of 1,1,1-tris(boronates) from vinylarene and B_2pin_2 through a Co-catalyzed tandem sequence comprising the double DHBs and the hydroboration of resulting 1,1-diborylalkenes with HBpin generated in situ.[15] Here we report that a combination of a bipyridyl-phosphine (PNN)-Co catalyst with CsF in DMF is effective for selective double DHBs of terminal vinylarenes with B_2pin_2, producing 1,1-diborylalkenes that can be utilized as building blocks for the construction of a diverse range of stereodefined trisubstituted alkenes, including TAAs. Furthermore, selective synthesis of

trans-monoborylalkenes has also been achieved by Co-catalyzed single DHB of vinylarenes under slightly modified conditions. When terminal alkyl alkenes are used as the substrates, the Co-catalyzed double DHBs form *cis*-1,2-diborylalkenes with high stereoselectivity.

RESULTS AND DISCUSSION

Optimization Studies. To produce vinylboronates in a selective manner, the Co catalyst system must fulfill the following requirements: (1) the hydroboration of alkene or borylalkene, which can occur rapidly using the (PNN)Co catalyst as shown in our previous works,[14c,15] must be entirely inhibited; (2) the catalyst system should enable a clear discrimination between the single DHB and the double DHBs events.

Table 1. Condition Optimizations for Selective Double DHBs or Single DHB of Styrene with B_2pin_2[α]



Entry	cat. (x)	additive (y)	sol.	yield (%)[b]		
				3a	**4a**	**5a**/(**6a**+**7a**)
1	**1a** (2)	EtOH (1)	tol	32	52	8/5
2	**1a** (2)	DIPA[c] (1)	tol	24	40	5/1
3	**1a** (2)	Thiocresol (1)	tol	2	6	0/0
4	**1a** (2)	MesBr[d] (1)	tol	1	77	12/11
5	**1a** (2)	CsF (1)	tol	81	5	14/1
6	**1a** (2)	CsF (1)	DMF	5	87	1/<1
7	**1a** (3)	CsF (1)	DMF	<1	96	3/<1
8	**1b** (3)	CsF (1)	DMF	6	47	14/25
9	**1a** (3)	none	DMF	19	0	<1/0
10	**1a** (3)	KF (1)	DMF	65	0	0/0
11	**1a** (3)	LiF (1)	DMF	42	0	2/<1
12	**1a** (3)	CsCl (1)	DMF	36	0	<1/0
13	**1a** (3)	CsF (0.7)	DMF	59	36	<1/<1
14	**1a** (3)	CsF (0.4)	DMF	91	1	<1/0
15	**1a** (3)	CsF (0.2)	DMF	33	0	<1/0

[a]Reaction conditions: on 0.5 mmol scale and used 2 mL solvent at 25 °C; [b]Yields were determined by GC with mesitylene as an internal standard. [c]2,6-Diisopropylaniline. [d]Mesityl bromide.

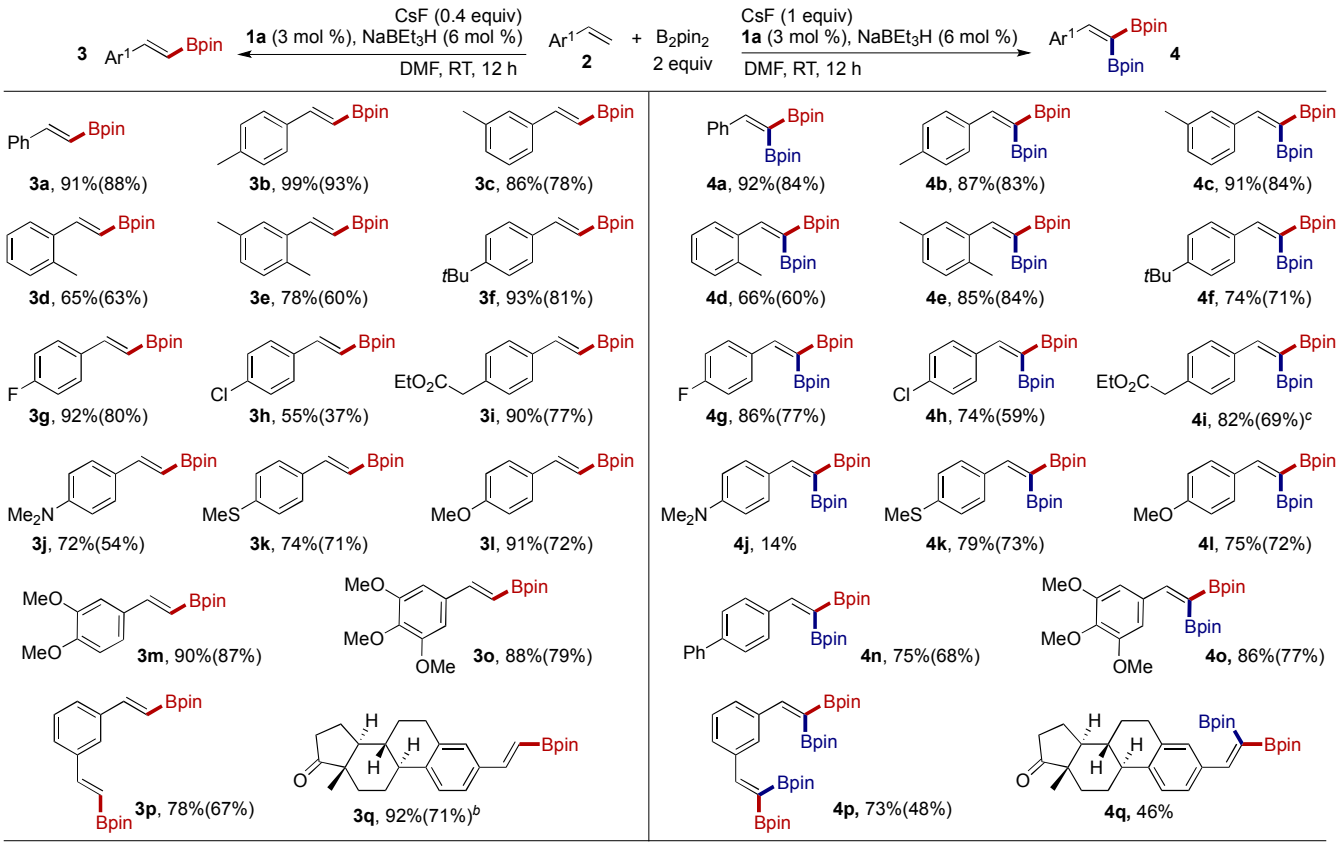
Initial efforts focused on the search for an additive that can suppress the hydroboration, but has no adverse effect on the DHB process. Considering the successful dehydrocouplings of alcohols, amines, and thiols with HBpin,[16] such reagents were tested as the HBpin scavenger. In the presence of 1 equiv of ethanol or 2,6-diisopropylaniline (DIPA), the reaction of styrene (**2a**) with B_2pin_2 (2 equiv) in toluene at rt using the Co catalyst generated in situ from **1a** (2 mol %) and $NaBEt_3H$ (4 mol %),[17] mainly formed the double DHBs product **4a** and the single DHB product **3a**, with minimal yields of the hydroboration by-products (**5a**, **6a** and **7a**) (entries 1 and 2, Table 1). Unfortunately, the addition of 1 equiv of *p*-thiolcresol inhibited the catalysis (entry 3). In our previous attempt to synthesize 1,1,1-tris(boronates) from 4-bromostyrene, a decent amount of the corresponding 1,1-diborylalkene was detected.[15] Given this observation, mesityl bromide (1 equiv) was used as an additive. The run gave 77% **3a**, but substantial amounts of the hydroboration products resulted (entry 4). Preforming the reaction with 1 equiv CsF in toluene was somewhat selective for the formation of monoborylalkene **3a** (81%) (entry 5). Gratifyingly, switching the solvent from toluene to DMF for an enhanced solubility of CsF resulted in the formation of 87% **4a** (entry 6). A slight increasing of the catalyst loading (3 mol %) provided the desired product **4a** in 96% yield (entry 7). Switching the precatalyst **1a** to the *i*Pr-substituted variant **1b** gave poor selectivity (47% **4a**, 6% **3a**, and 14% **5a**，entry 8). A control experiment without CsF gave only 19% **3a** (entry 9). The reactions with other inorganic additives, KF, LiF and CsCl, afforded moderate yields of **3a**; in none case was **4a** observed (entries 10-12). In addition, reducing the loading of CsF from 1.0 to 0.7 equiv decreased the yield of **4a** from 96% to 36%, with 59% **3a** (entry 13 vs 7). Significantly, the reaction with 0.4 equiv of CsF is highly selective for the formation of the single DHB product (91% **3a**, entry 14). A further decreasing of the loading of CsF, however, had a detrimental effect on the yield of **3a** (entry 15).

Substrate Scope of Co-Catalyzed Double DHBs and Single DHB of Vinylarenes. Next we evaluated the scope and limitation of our protocol for the synthesis of gem-diborylalkenes and *trans*-monoborylalkenes (Table 2). In the presence of 1 equiv of CsF, the Co catalyst derived from **1a** is effective for double DHBs of various aryl alkenes. The gem-diborylalkenes products are moisture- and air-stable, and can be purified by flash chromatography. A range of functional groups, such as halide (**4g**, **4h**), ester (**4i**), thioether (**4k**), ether (**4l**, **4o**), and ketone (**4q**), can be tolerated. An exception was the *para*-Me_2N-substituted styrene that gave only 14% **4j**, but 67% of the monoboryl **3j**. Me-substituents at the *ortho* positions are tolerated as demonstrated by the isolation of **4d** and **4e** in good yields. Double DHBs of two double bonds in 1,3-divinylbenzene occurred smoothly to form the tetraboryl **4p**. The estrone-derived diborylalkene **4q** was obtained in a moderate yield.

Noteworthily, simple modification of the reaction conditions by using 0.4 equiv of CsF led to the formation of the corresponding *trans*-monoborylalkenes (**3**) in excellent selectivity (Table 2). Most single DHB reactions of aryl alkenes proceeded with high yields, although a few products resulted in moderate isolated yields due to decomposition during the purification by column chromatography.

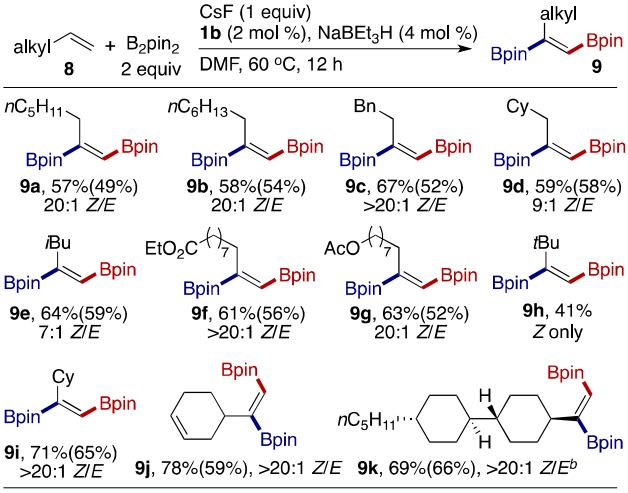
Substrate Scope of Co-Catalyzed Double DHBs of Alkyl Alkenes. Compared to the DHB reactions of aryl alkenes, the DHB reactions of aliphatic alkenes are more challenging, partly due to competing alkene isomerization. With the precatalyst **1a**, initial attempts employing the conditions applied for double DHBs of aryl alkenes have been unsuccessful for the double DHBs of alkyl alkenes. Gratifyingly, the substitution of the precatalyst **1a** for the less

Table 2. Cobalt-Catalyzed Selective Double DHBs or Single DHB of Various Aryl Alkenes[a]



[a]Conditions: on 0.5 mmol scale and used 2 mL DMF; Yields were determined by ^{1}H NMR and values in parentheses are isolated yields. [b]The reaction time was 24 h. [c]Performed at 40 °C.

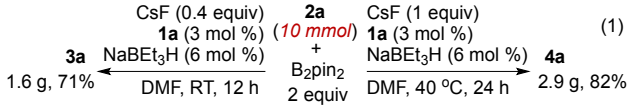
Table 3. Cobalt-catalyzed Double DHBs of Various Alkyl Alkenes[a]



[a]Conditions: On 0.5 mmol scale and used 2 mL DMF, Yields were determined by ^{1}H NMR and values in parentheses are isolated yields. [b]Used 5.0 mol % of **1b** and 10 mol % $NaBEt_3H$ and the reaction time was 24 h.

sterically hindered **1b** led to selective formation of *cis*-1,2-diborylalkenes (Table 3). The substrate scope is not limited to 1-alkenes bearing branches (**8h-k**) that can prevent undesired isomerization. The challenging linear α-olefins, including 1-octene and 1-nonene, undergo double DHBs to give 1,2-diborylalkenes with satisfactory selectivity (**9a-g**). Ester functionalities are tolerated as shown by the isolation of **9f** and **9g** in useful yields. Comparison of the outcomes of the double DHB reactions with aryl alkenes and alkyl alkenes shows different selectivity (1,1- versus 1,2-diborylalkens), which is tentatively attributed to the inverted regioselectivity of the insertion of the monoborylalkene intermediates into the Co–B bond.[15] The formation of *cis*-1,2-diborylalkene products is consistent with the results obtained by Pd-catalyzed double DHBs of alkyl alkenes.[6a,6b]

We have also developed procedures for large scale synthesis. While the monoboryl **3a** could be isolated in 71% yield (1.6 g) from 10 mmol of **2a** using the standard single DHB conditions (rt, 12 h), the gram scale preparation of 1,1-diborylalkene **6a** required an elevated temperature (40 °C) and a longer reaction time (24 h) in order to gain a high isolated yield (82%, 2.9 g, eq 1).[18]

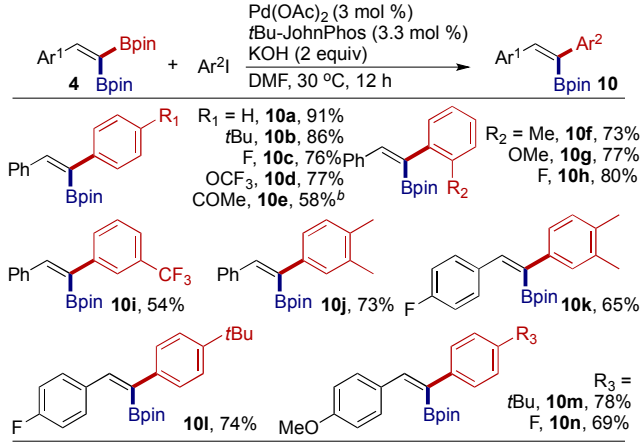


(1)

Substrate Scope of Pd-Catalyzed Stepwise Cross-Coupling of 1,1-Diboryl-1-alkenes. With a broad array of 1,1-diborylalkenes in hand, we sought to develop stepwise Suzuki-Miyaura cross-couplings for stereodefined synthesis of TAAs. Althoug several approaches, such as Wittig-type carbonyl olefinations,[19] catalytic hydroarylations of alkynes,[4d,20] and cross-couplings of 1,1-dihaloalkenes with organometallic nucleophiles,[21] are known for the synthesis of TAAs, few methods offer a stereocontrol for the construction of TAAs with three different aryl substituents.[4a,21a,22] Note that Shimizu and Hiyama have reported Pd-catalyzed consecutive couplings of 1,1-arylalkyl-2,2-diborylalkenes with aryl iodides to form tetrasubstituted alkenes,[2b] yet the trisubstituted type was not disclosed.

The use of aryl iodides as the coupling reagents was responsible for the success of selective single arylation of **4**. The couplings using the Pd catalyst of *t*Bu-JohnPhos and KOH as the base occurred under mild conditions (30 °C), allowing the introduction of the aryl group, Ar^2, exclusively at the position *trans* to the Ar^1 group regardless of the nature of substituents on the *para*, *meta*, and *ortho* positions of Ar^1 (Table 4). The *cis* or double arylation products were not observed. In contrast, the reaction with an aryl bromide required a higher reaction temperature (80 °C), and led to both of the single and double arylation products (see Supporting Information for details). A number of functional groups, including the acetyl group (**10e**), were compatible with the catalyst. Most of the *trans*-1,2-diaryl-substituted monoborylalkene products **10** could be obtained in good-to-high isolated yields.

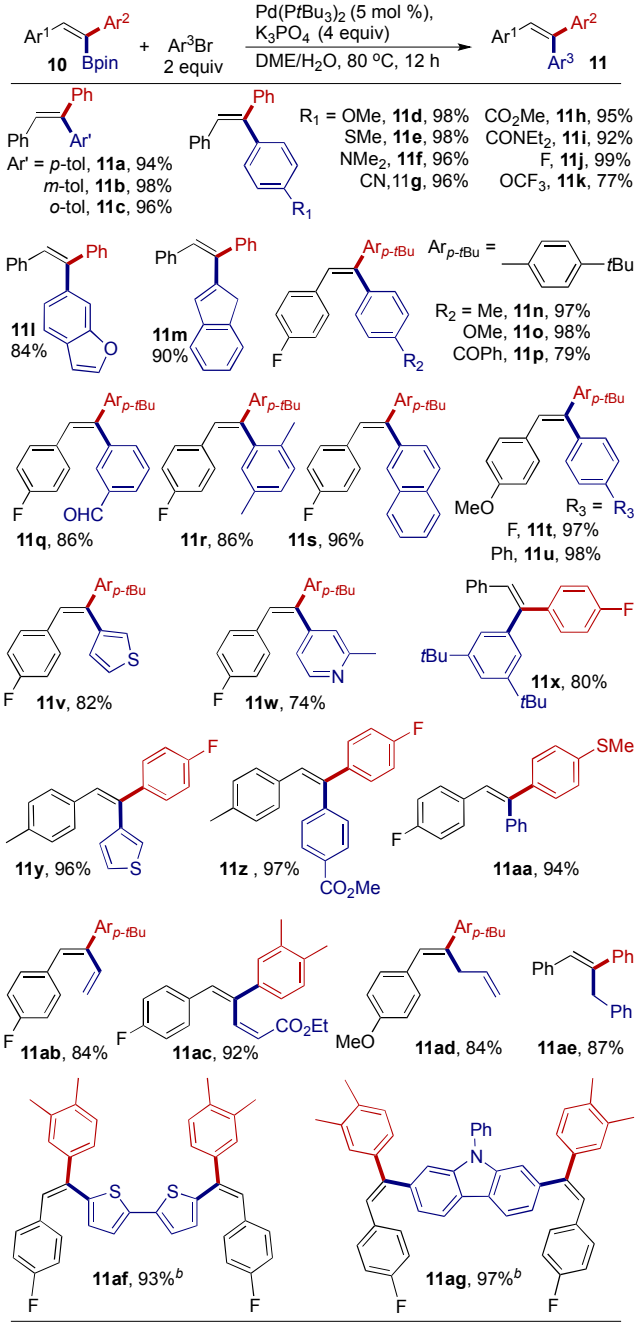
Table 4. Synthesis of Stereodefined *trans*-1,2-Diaryl-1-borylalkenes via Cross-Couplings of 4 with Aryl Iodides.[a]



[a]Conditions: on 0.2 mmol scale. Yields shown are of isolated products. [b]Used 1 equiv of KOH.

Next we developed a procedure for the installation of the second aryl group (Ar^3) to complete the synthesis of TAAs. Using $Pd(PtBu_3)_2$ as the catalyst and K_3PO_4 as the base, the couplings of **10** with various aryl bromides proceeded at 80 °C, furnishing the desired products **11** in high yields (Table 5). The alkene geometry was effectively preserved in all cases. A wide range of reactive functionalities, including the formyl (**11q**), ketone (**11p**), cyanide (**11g**) groups, were tolerated. Noteworthily, the TAA product with a *para*-MeS substituent (**11aa**) can be readily oxidized to the sulfonyl derivative,

Table 5. Stereoselective Synthesis of Triaryl Alkenes via Cross-Couplings of 10 with Aryl Bromides.[a]

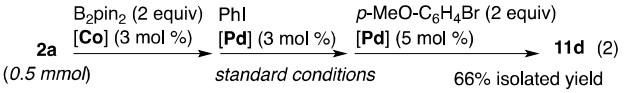


[a]Conditions: on 0.1 mmol scale. Yields shown are of isolated products. [b]Used 0.1 mmol ArBr and 0.2 mmol **10k**.

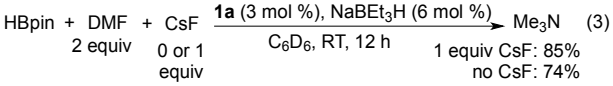
which is a novel inhibitor of the cyclooxygenase-2 isozyme.[19a] Thiophenyl (**11v**, **11y**, **11af**) and pyridyl (**11w**) bromides were suitable coupling reagents. In addition, allyl (**11ad**), benzyl (**11ae**), and vinyl (**11m**, **11ab**, **11ac**) bromides gave high yields and high selectivities for the desired trisubstituted alkenes. The coupling with ethyl (*Z*)-3-bromoacrylate produced 1,3,4-trisubstitued *cis,trans*-1,3-butadiene (**11ac**) as the single stereoisomer. Finally, two extended π-systems, **11af** and **11ag**,

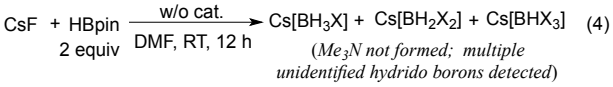
were obtained in high isolated yields, demonstrating the utility of diborylalkenes in the synthesis of conjugated materials. Thus, the synthetic scheme provides a general route to stereospecific trisubstituted alkenes, including those bearing three different substituents (**11n-11ag**). Some products bearing reactive functionalities (for examples, **11p**, **11q**, **11ac**) would be difficut to access by the couplings of 1,1-dihaloalkenes with Grignard or zinc reagents.[21a]

Importantly for the user, the transformation of the simple terminal alkenes to TTAs can be performed in a one-pot, three-step fashion without the requirement for isolation of the intermediates. For example, the sequence comprising the Co-catalyzed double DHBs of **2a** and Pd-catalyzed arylations with iodobenzene and 4-bromoanisole gave **11d** in 66% overall yield (eq 2).

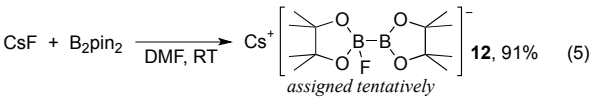


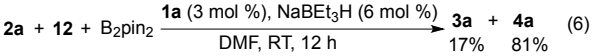
Mechanistic Studies. To probe the role of DMF and CsF in the double DHBs process, stoichiometric experiments were carried out. Treatment of HBpin with DMF (2 equiv) and the Co catalyst in C_6D_6 resulted in the reduction of DMF, giving 85% or 74% yield of Me_3N in the reaction with (1 equiv) or without CsF, respectively (eq 3). Treatment of HBpin with CsF in DMF, but without the Co catalyst, led to a rapid decomposition of HBpin to form multiple unidentified hydrido boron compounds; however, no Me_3N was detected in this reaction, suggesting the reduction of DMF with HBpin occurs under the Co catalysis (eq 4). Though the identity of these hydrido boron compounds is not known definitively, comparison of the ^{1}H-coupled and ^{1}H-decoupled ^{11}B NMR data of the reaction mixture with those of previously reported hydrido boron compouds[23] implies the formation of cesium boron trihydride, dihydride, and monohydride species (see spectral data in the Supporting Information) (eq 4).[24] Note that HBpin remains intact in DMF in the absence of the Co catalyst and CsF. All together, these results imply that DMF can inhibit the undesired hydroboration by consuming HBpin derived from the Co-catalyzed DHBs. While CsF does react with HBpin, the addition of CsF is not required for suppressing the hydroboration, which is in accord with the lack of the hydroboration products in the control without CsF (entry 9, Table 1).



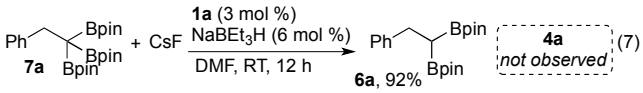


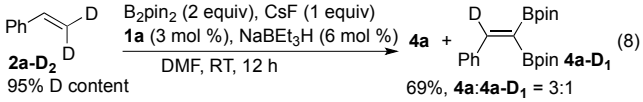
On the other hand, CsF has an important effect on promoting the DHBs (entry 7 vs 8, Table 1). The reaction of CsF with 1 equiv of B_2pin_2 in DMF formed a putative anionic fluoride diboron adduct, $Cs[B_2pin_2F]$ **12**, in 91% yield (eq 5). This compound exhibits very low solubility in common organic solvents, but was fully characterized by combustion analysis and solid-state ^{11}B{^{1}H}, ^{19}F, ^{13}C{^{1}H}, and ^{1}H NMR spectroscopies (see spectral data in the Supporting Information). Similar fluoride diboron adducts $[n\text{Bu}_4\text{N}][B_2pin_2F]$ and $[Me_4N][B_2pin_2F]$ have been reported by Marder and colleagues, and the structure of $[Me_4N][B_2pin_2F]$ was confirmed by X-ray diffraction analysis.[25] Note that the ^{11}B{^{1}H} (both solid-state and simulation), ^{19}F, ^{13}C{^{1}H} NMR data of **12** are very similar with those of $[n\text{Bu}_4\text{N}][B_2pin_2F]$ and $[Me_4N][B_2pin_2F]$,[25] suggesting that **12** is likely an anionic fluoride adduct. Treatment of the isolated **12** with **2a** and B_2pin_2 in a 1:1:1 ratio under the catalytic conditions formed 17% **3a** and 81% **4a** (eq 6). The data suggest that the diboron adduct **12** is likely an active source of boryl species in the double DHBs process.[24d]



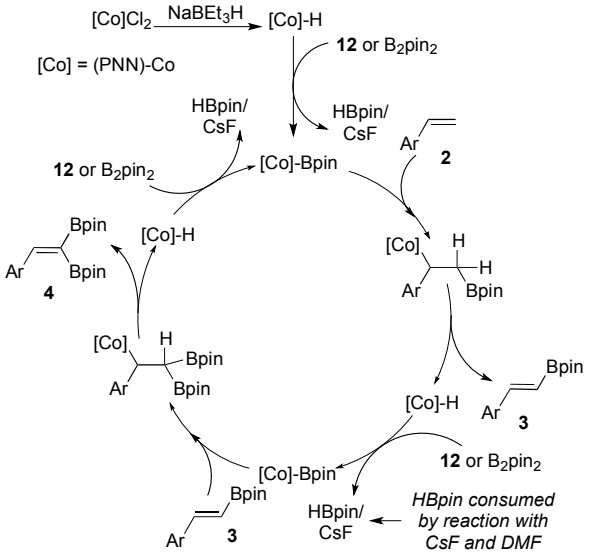


To test the possibility of the formation of 1,1-diborylalkenes via CsF-mediated dehydroboration of 1,1,1-tris(boronates), **7a** was submitted to the reaction with CsF in DMF under the standard catalytic conditions. The product observed in this reaction was the protodeboronation product **6a** (92% yield, eq 7),[26] instead of **4a**. Moreover, a deuterium labeling experiment was performed using styrene-β,β-D_2 **2a-D$_2$** as the substrate. The reaction gave **4a** and **4a-D$_1$** in a 3:1 ratio (eq 8), indicating that the competing 1,2-insertion of vinylarene or monoborylalkene into a Co−D bond occurs during catalysis. These data, combined with the mechanistic insights obtained in our earlier studies on the Co-catalyzed synthesis of tris(boronates),[15] are consistent with a pathway of Co-catalyzed double DHBs. Following the 2,1-insertion insertion of vinyarene **2** into the Co−B bond, β-H elimination gives monoborylalkene **3**, which undergoes the second DHB to form 1,1-diborylalkene **4** (Scheme 2).





Scheme 2. Proposed Mechanism.



CONCLUSIONS

In summary, we have developed a controlled, dehydrogenative borylation(s) approach (double versus single DHB) for selective synthesis of 1,1-diborylalkenes and *trans*-monoborylalkenes from aryl alkenes. On the contrary, the double DHBs of alkyl alkenes yield *cis*-1,2-diborylalkenes with high stereoselectivity. The boronate groups introduced in the diboryl products offer flexible synthetic manipulations as demonstrated by the stepwise Suzuki cross-couplings of 1,1-diborylalkenes, allowing a convenient, stereoselective synthesis of trisubstituted alkenes, such as triaryl alkenes, utilizing simple to access starting materials, 1-alkenes.

EXPERIMENTAL SECTION

General Procedure for Cobalt-Catalyzed Double DHBs of Various Aryl Alkenes. In an Ar-filled glovebox, a sealed tube (10 mL) was charged with complex **1a** (6.7 mg, 15 μmol, 3.0 mol %), CsF (76.0 mg, 0.5 mmol, 1.0 equiv), and DMF (2 mL). $NaBEt_3H$ (30 μmol, 6 mol %, 1.0 M in THF) was added to the mixture. After stirring for 3 min, **2** (0.5 mmol, 1.0 equiv) and B_2pin_2 (254 mg, 1.0 mmol, 2.0 equiv) were added. The mixture s stirred at room temperature for 12 h, and then quenched by exposing the solution to air. The mixture was filtered through silica gel. H_2O (10 mL) was added to the filtrate and the aqueous phase was extracted with diethyl ether (3x20 mL). The combined organic extracts were washed with H_2O and brine, dried ($MgSO_4$) and concentrated in vacuo. The crude product was dissolved in $CDCl_3$ to obtain ^1H NMR yield, and then purified by flash chromatography on silica with ethyl acetate and petroleum ether (v/v, 1:30 to 1:5) to afford the pure products **4**.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures, full spectroscopic data for all new compounds, and copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: huangzh@sioc.ac.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The National Key R&D Program of China (2015CB856600, 2016YFA0202900), National Natural Science Foundation of China (21422209, 21432011, 21421091, 21572255), and Chinese Academy of Sciences (XDB20000000) support this work.

REFERENCES

(1) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483. (b) Lennox, A. J. J.; Lloyd-Jones, G. C. *Chem. Soc. Rev.* **2014**, *43*, 412-443. (c) Geier, S. J.; Westcott, S. A. *Rev. Inorg. Chem.* **2015**, *35*, 69-79.

(2) (a) Jordan, V. C. *J. Med. Chem.* **2003**, *46*, 883-908. (b) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 12506-12507. (c) Shimizu, M.; Hiyama, T. *Proc. Jpn. Acad. Ser. B* **2008**, *84*, 75-85.

(3) (a) Collins, D. J.; Hobbs, J. J.; Emmens, C. W. *J. Med. Chem.* **1971**, *14*, 952-957. (b) Emmens, C. W. *Reproduction* **1973**, *34*, 23-28. (c) Borgna, J. L.; Coezy, E.; Rochefort, H. *Biochem. Pharmacol*. **1982**, *31*, 3187-3191.

(4) (a) Itami, K.; Ohashi, Y.; Yoshida, J. *J. Org. Chem.* **2005**, *70*, 2778-2792. (b) Yuan, W. Z.; Tan, Y.; Gong, Y.; Lu, P.; Lam, J. W. Y.; Shen, X. Y.; Feng, C.; Sung, H. H. Y.; Lu, Y.; Williams, I. D.; Sun, J. Z.; Zhang, Y.; Tang, B. Z. *Adv. Mater.* **2013**, *25*, 2837-2843. (c) Wen, W.; Shi, Z.; Cao, X.; Xu, N. *Dyes Pigm*. **2016**, *132*, 282-290. (d) Masai, H.; Matsuda, W.; Fujihara, T.; Tsuji, Y.; Terao, J. *J. Org. Chem.* **2017**, *82*, 5449-5455.

(5) Recent reviews on the synthesis of monoborylalkenes: (a) Yun, J. *Asian J. Org. Chem.* **2013**, *2*, 1016-1025. (b) Yoshida, H. *ACS Catal.* **2016**, *6*, 1799-1811. (c) Neeve, E. C.; Geier, S. J.; Mkhalid, I. A. I.; Westcott, S. A.; Marder, T. B. *Chem. Rev.* **2016**, *116*, 9091-9161.

(6) Recent works on the monoborylalkenes via catalytic alkene dehydrogenative borylation: (a) Takaya, J.; Kirai, N.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 12980-12983. (b) Kirai, N.; Iguchi, S.; Ito, T.; Takaya, J.; Iwasawa, N. *Bull. Chem. Soc. Jpn.* **2013**, *86*, 784-799. (c) Sasaki, I.; Doi, H.; Hashimoto, T.; Kikuchi, T.; Ito, H.; Ishiyama, T. *Chem. Commun.* **2013**, *49*, 7546-7548. (d) Brown, A. N.; Zakharov, L. N.; Mikulas, T.; Dixon, D. A.; Liu, S.-Y. *Org. Lett.* **2014**, *16*, 3340-3343. (e) Morimoto, M.; Miura, T.; Murakami, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 12659-12663. (f) Mazzacano, T. J.; Mankad, N. P. *ACS Catal.* **2017**, *7*, 146-149. (g) Wang, C.; Wu, C.; Ge, S. *ACS Catal*. **2016**, *6*, 7585-7589.

(7) Matteson, D. S. *Synthesis* **1975**, 147-158.

(8) (a) Hata, T.; Kitagawa, H.; Masai, H.; Kurahashi, T.; Shimizu, M.; Hiyama, T. *Angew. Chem. Int. Ed.* **2001**, *40*, 790-792. (b) Kurahashi, T.; Hata, T.; Masai, H.; Kitagawa, H.; Shimizu, M.; Hiyama, T. *Tetrahedron* **2002**, *58*, 6381-6385. (c) Shimizu, M.; Shimono, K.; Schelper, M.; Hiyama, T. *Synlett* **2007**, 1969-1971.

(9) (a) Weber, L.; Eickhoff, D.; Halama, J.; Werner, S.; Kahlert, J.; Stammler, H.-G.; Neumann, B. *Eur. J. Inorg. Chem.* **2013**, *2013*, 2608-2614. (b) Hyodo, K.; Suetsugu, M.; Nishihara, Y. *Org. Lett.* **2014**, *16*, 440-443. (c) Ho, H. E.; Asao, N.; Yamamoto, Y.; Jin, T. *Org. Lett.* **2014**, *16*, 4670-4673.

(10) Morinaga, A.; Nagao, K.; Ohmiya, H.; Sawamura, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 15859-15862.

(11) Lee, C.-I.; Shih, W.-C.; Zhou, J.; Reibenspies, J. H.; Ozerov, O. V. *Angew. Chem., Int. Ed.* **2015**, *54*, 14003-14007.

(12) Krautwald, S.; Bezdek, M. J.; Chirik, P. J. *J. Am. Chem. Soc.* **2017**, *139*, 3868-3875.

(13) (a) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 8863-8869. (b) Coapes, R. B.; Souza, F. E. S.; Thomas, R. L.; Hall, J. J.; Marder, T. B. *Chem. Commun.* **2003**, 614-615. (c) Mkhalid, I. A. I.; Coapes, R. B.; Edes, S. N.; Coventry, D. N.; Souza, F. E. S.; Thomas, R. L.; Hall, J. J.; Bi, S.-W.; Lin, Z.; Marder, T. B. *Dalton Trans.* **2008**, 1055-1064.

(14) (a) Peng, D.; Zhang, Y.; Du, X.; Zhang, L.; Leng, X.; Walter, M. D.; Huang, Z. *J. Am. Chem. Soc.* **2013**, *135*, 19154-19166. (b) Zhang, L.; Peng, D.; Leng, X.; Huang, Z. *Angew. Chem. Int. Ed.* **2013**, *52*, 3676-3680. (c) Zhang, L.; Zuo, Z.; Leng, X.; Huang, Z. *Angew. Chem., Int. Ed.* **2014**, *53*, 2696-2700. (d) Zhang, L.; Zuo, Z.; Wan, X.; Huang, Z. *J. Am. Chem. Soc.* **2014**, *136*, 15501-15504. (e) Du, X.; Zhang, Y.; Peng, D.; Huang, Z. *Angew. Chem. Int. Ed.* **2016**, *55*, 6671-6675. (f) Jia, X.; Huang, Z. *Nat. Chem.* **2016**, *8*, 157-161.

(15) Zhang, L.; Huang, Z. *J. Am. Chem. Soc.* **2015**, *137*, 15600-15603.

(16) Romero, E. A.; Peltier, J. L.; Jazzar, R.; Bertrand, G. *Chem. Commun.* **2016**, *52*, 10563-10565.

(17) $NaBEt_3H$ acts as the the catalyst activator, see: Bouwkamp, M. W.; Bowman, A. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 13340-13341.

(18) Note that CsF has limited solubility in DMF, and the product derived from the reaction of CsF and B_2pin_2 also exhibits very poor solubility in DMF (see the characterization of compound **12** in the Mechanistic Studies section). Thus, the reaction mixture of **2a**, 2 equiv of B_2pin_2, and 1 equiv of CsF on 10 mmol scale contains a large amount of solids, making the stirring of the mixture much more difficult than that on 0.5 mmol scale. Therefore, performing the reaction on a large scale required a higher temperature and a longer reaction time relative to the run on 0.5 mmol scale. In fact, the large scale reaction under standard conditions (at 25 °C for 12h) resulted in the formation of a mixture of diborylalkene (**4a**, 55% GC yield) and monoborylalkene (**3a**, 43% GC yield), while increasing the reaction

temperature (to 40 °C) and prolonging the reaction time (to 24 h) significantly enhanced the yield of **4a**.
(19) (a) Uddin, M. J.; Rao, P. N. P.; McDonald, R.; Knaus, E. E. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 439-442. (b) Huo, C.; He, X.; Chan, T. H. *J. Org. Chem.* **2008**, *73*, 8583-8586.
(20) (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918-9919. (b) Zhang, J.; Shrestha, R.; Hartwig, J. F.; Zhao, P. *Nat. Chem.* **2016**, *8*, 1144-1151.
(21) (a) Minato, A.; Suzuki, K.; Tamao, K. *J. Am. Chem. Soc.* **1987**, *109*, 1257-1258. (b) Shen, W.; Wang, L. *J. Org. Chem,* **1999**, *64*, 8873-8879. (c) Gu, S.; Xu, H.; Zhang, N.; Chen, W. *Chem. Asian J.* **2010**, *5*, 1677-1686. (d) Zhu, Y.; Sun, P.; Yang, H.; Lu, L.; Yan, H.; Creus, M.; Mao, J. *Eur. J. Org. Chem.* **2012**, *2012*, 4831-4837. (e) Dai, W.; Xiao, J.; Jin, G.; Wu, J.; Cao, S. *J. Org. Chem.* **2014**, *79*, 10537-10546.
(22) (a) Itami, K.; Nokami, T.; Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J.-i. *J. Am. Chem. Soc.* **2001**, *123*, 11577-11585. (b) Itami, K.; Mineno, M.; Muraoka, N.; Yoshida, J.-i. *J. Am. Chem. Soc.* **2004**, *126*, 11778-11779.
(23) (a) Brown, H. C.; Nazer, B.; Sikorski, J. A. *Organometallics* **1983**, *2*, 634-637. (b) Query, I. P.; Squier, P. A.; Larson, E. M.; Isley, N. A.; Clark, T. B. *J. Org. Chem.* **2011**, *76*, 6452-6456. (c) Docherty, J. H.; Peng, J.; Dominey, A. P.; Thomas, S. P. *Nat. Chem.* **2017**, *9*, 595-600.
(24) Note that unidentified white solid also precipitated from the solution of the reaction shown in eq 4.
(25) Pietsch, S.; Neeve, E. C.; Apperley, D. C.; Bertermann, R.; Mo, F.; Qiu, D.; Cheung, M. S.; Dang, L.; Wang, J.; Radius, U.; Lin, Z.; Kleeberg , C.; Marder , T. B. *Chem. Eur. J.* **2015**, *21*, 7082-7098.
(26) Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 10581-10584.

For Table of Contents Only