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C-O Functionalization of α-Oxyboronates: A Deoxygenative *gem*-Diborylation and *gem*-Silylborylation of Aldehydes and Ketones

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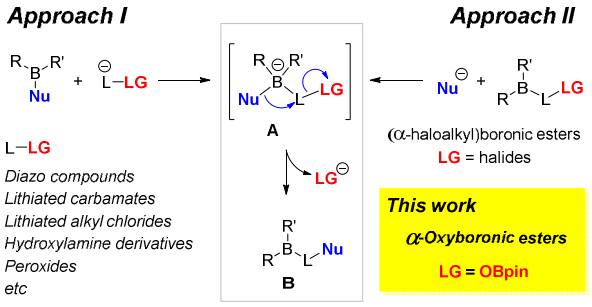
Supporting Information Placeholder

ABSTRACT: A deoxygenative *gem*-diborylation and *gem*-silylborylation of aldehydes and ketones is described. The key for the success of this transformation is the base-promoted C-O bond borylation or silylation of the generated α-oxyboronates. Experimental and theoretical studies exhibit that the C-O bond functionalization proceeds via an intramolecular five-membered transition-state (**9-ts**) boryl migration followed by a 1,2-metallate rearrangement with OBpin as a leaving group. The transformation occurs with an inversion on the carbon center. Direct conversion of aldehydes and ketones to *gem*-diboron compounds was achieved by combining copper catalysis with this base-promoted C-OBpin borylation. Various aldehydes and ketones were deoxygenatively *gem*-diborylated. *gem*-Silylborylation of aldehydes and ketones were achieved by a stepwise operation, in which B_2pin_2 initially react with those carbonyls followed by a silylation with Bpin-$SiMe_2Ph$.

INTRODUCTION

Organoboron compounds are powerful reagents in chemical sciences.[1] Among various boron-involved organic transformations, the tetracoordinated boron-mediated 1,2-metallate rearrangement is one of the most versatile strategies for constructing many complex molecules, and efforts are continually devoted in this area.[2] The key for such transformation is the formation of a four-coordinated boron species **A** with a migrating group (**Nu**) and a leaving group (**LG**) bound to a linker group (**L**) (Scheme 1). Up to date, Approach I dominates the formation of species **A**, in which a tricoordinated boron species interacts with a nucleophilic **L**-**LG**. Many classic transformations follow this approach,[2d] such as the oxidation of organoboranes with peroxides,[3] amination with hydroxylamine derivatives,[4] homologation with diazo compounds,[2c] lithiated carbamates,[2a,5] and lithiated alkyl chlorides,[2e] *etc*. In the other approach (Approach II), an amphoteric nucleophile attacks to the tricoordinated boron center (RR'B-L-LG) to form **A** (Scheme 1). The latter approach mainly relies on the reaction of (α-haloalkyl)boronic esters (LG = halides).[2e,2f,6] Those (α-haloalkyl)boronic esters have been applied in plentiful of synthetic strategies.[2b,7] However, other α-functionalized boronic esters, especially α-oxyboronic esters (*O*-type leaving group) have not been disclosed in such approach to date. The α-oxyboronic esters are conveniently accessed via the catalytic borylation of widely available aldehydes or ketones, including the enantioselective version of borylation.[8] synthetic application of such type of compounds, however, still remains limited.[8b,8g,9] Therefore, applying α-oxyboronic esters in Approach II would not only significantly diversify such boron chemistry but also expand the application of α-oxyboronic esters in synthetic chemistry.

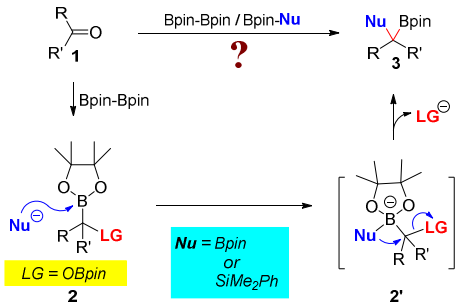
Scheme 1. Approaches for Tetracoordinated Boron Species in Boron-Mediated 1,2-Metallate Rearrangements



α-OBpin (or OH) boronates are usually produced from the borylation of aldehydes and ketones.[8] It has been demonstrated that the boryl group could activate its *gem*-chemical bond.[10] As a result, the α-C-O bond is activated in α-OBpin boronates, and the OBpin group may act as a leaving group. If an amphoteric boryl or silyl nucleophile could be introduced on the *B*pin-C group of **2**, a B-*B*-C or Si-*B*-C intermediate **2'** might be formed (Scheme 2). The 1,2-metallate rearrangement *gem*-diborylation and *gem*-silylborylation with OBpin as the leaving group then might be achieved to form the *gem*-diboryl or *gem*-silylboryl compounds (Scheme 2). It is noteworthy to emphasize the migrating ability of boryl or silyl group in intermediate **2'**. To our knowledge, the 1,2-metallate rearrangement of such type of intermediates has been demonstrated (Approach I type), either with OCb as the leaving group in the *gem*-silylborylation of lithiated carbamates by Aggarwal *et al*,[11] or with N_2 as the leaving group in the *gem*-diborylation or *gem*-silylborylation of *N*-tosylhydrazone by Wang *et al*,[12] or with halide as the leaving

group in the *gem*-silylborylation of lithiated alkyl halides by Shimizu *et al.*[13] Therefore, it is possible to realize the hypothesis shown in Scheme 2. Herein, we demonstrate the first borylation and silylation of α-oxyboronic esters, accordingly achieving a deoxygenative *gem*-diborylation and *gem*-silylborylation of aldehydes and ketones (Scheme 2), in which various *gem*-diboryl and *gem*-silylboryl compounds were synthesized. These *gem*-bimetallic compounds have attracted increasing attentions in synthetic applications, due to their potential for selective mono- or di-functionalization.[10c,14] Synthetically, in addition to those reported methods including borylation of diazoalkanes,[15] deprotonation/alkylation of 1,1-diborylmethane,[16] and borylation of terminal alkynes,[17] *N*-tosylhydrodrazones,[12a] *gem*-dihaloalkanes,[18] alkenylboron,[19] benzylic alkanes,[10a,20] the direct deoxygenative *gem*-diborylation of carbonyls would provide an intriguing alternative for the practical and diverse synthesis of *gem*-bis(boronates).

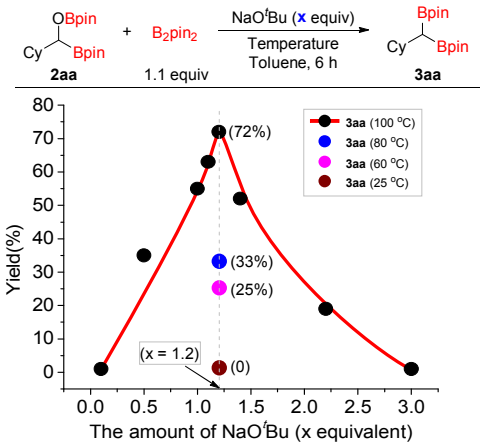
Scheme 2. Deoxygenative *gem*-Diborylation and *gem*-Silylborylation of Aldehydes and Ketones



RESULTS AND DISCUSSION

Borylation of α-OBpin boronic esters. According to the hypothesis shown in Scheme 2, the key challenge would be the introduction of a boryl group to the α-OBpin boronates **2** followed by an 1,2-metallate rearrangement to form the final product **3**, as the addition of B_2pin_2 to aldehydes has been shown to easily take place under NHC-Cu catalytic system at ambient temperature (NHC = *N*-Heterocyclic Carbene).[8] The transformation of **2** (LG = OBpin) to **3** has thus far been elusive. For that reason, in our initial attempt, we focused on realizing this essential step. **2aa** was prepared from cyclohexanecarbaldehyde (**1aa**) by using the reported copper catalytic system.[8e] Moreover, alkali metal alkoxides have been extensively used to activate B_2pin_2 in many borylative transformations. During our investigation, we noticed that 1.2 equivalents of NaO^{t}Bu in toluene at 100 °C was sufficient for converting **2aa** with B_2pin_2 (1.1 equiv) to the desired *gem*-diboryl compound **3aa** (Scheme 3). The amount of NaO^{t}Bu and the reaction temperature were found to be crucial for this transformation. Catalytic amounts of NaO^{t}Bu (10 mol%) resulted in trace amount of the desired **3aa** formation. Along with the increase of NaO^{t}Bu, the yield of **3aa** increased accordingly. When 1.2 equivalents of NaO^{t}Bu was used, the yield of **3aa** reached maximum at 72% (x = 1.2). Further increasing the amount of NaO^{t}Bu resulted in quick decrease of **3aa**. When 3.0 equivalents of NaO^{t}Bu were used, only less than 5% of **3aa** was observed together with remaining of **2aa** (observed as α-OH boronate **2ea**, 75%) and B_2pin_2 (70%), indicating that excess amount of NaO^{t}Bu is detrimental to the conversion of **2aa** to **3aa**. Lowering the reaction temperature to 80 °C or 60 °C resulted in low yields of **3aa**. No **3aa** was observed at 25 °C.

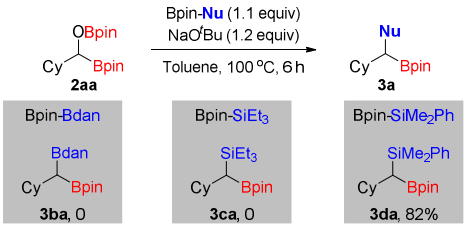
Scheme 3. The Effect of NaO^{t}Bu Amount and Temperature [a]



[a] Reaction conditions: **2aa** (0.2 mmol), B_2pin_2 (0.22 mmol), toluene (1.0 mL), NaO^{t}Bu (0.2x mmol), 6 hours. [b] Yields were determined by GC analysis with biphenyl as an internal standard. Cy = cyclohexyl.

The above results evinced that the introduction of a nucleophilic Bpin group is realizable with OBpin as a leaving group. This promising result encouraged us to further test other nucleophilic boryl or silyl groups for the synthesis of *gem*-diboryl compounds with two different boryl groups or *gem*-silylboryl compounds. Consequently, Bpin-Bdan, Bpin-$SiEt_3$ and Bpin-$SiMe_2Ph$ were applied to react with **2aa** (Scheme 4).[21] As a result, the lower nucleophilic Bpin-Bdan[22] and the less reactive Bpin-$SiEt_3$[23] failed to give any desired product **3ba** or **3ca**, while Bpin-$SiMe_2Ph$ afforded the desired *gem*-silylboronate **3da** in 82% isolated yield, indicating Bpin-$SiMe_2Ph$ is an approapriate reagent for the synthesis of *gem*-silylboryl compounds.

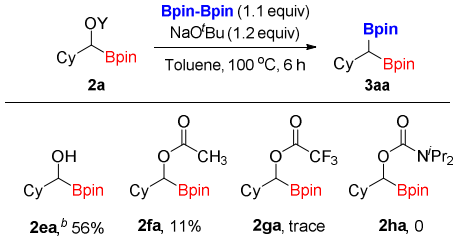
Scheme 4. Reaction of 2aa with Different Boryl or Silyl Nucleophiles



Furthermore, different OY group of **2a** was screened to investigate the reactivity of different leaving groups (Scheme 5). When Y = H (**2ea**), the hydroxyl group was successfully substituted by boryl group to generate **3aa** in 56% yield under the reaction condition of B_2pin_2/NaO^{t}Bu system.[24] It is rather interesting to find that when the OH group was protected by $COCH_3$ (Ac, **2fa**), the yield of the desired borylation product **3aa** dropped to 11%. When the OH group was protected by $COCF_3$ (TFA, **2ga**) group or CON^{i}Pr$_2$ (Cb, **2ha**) group, only trace or none of **3aa** was observed. Generally, OAc, OTFA and OCb are known as better leaving groups than free OH group. However, in our study the OH substrate **2ea** afforded the best yield of **3aa**. These interesting results encouraged us to further investigate the mechanism of this alkoxide-

promoted C-OBpin bond borylation and silylation before expanding the substrate scope.

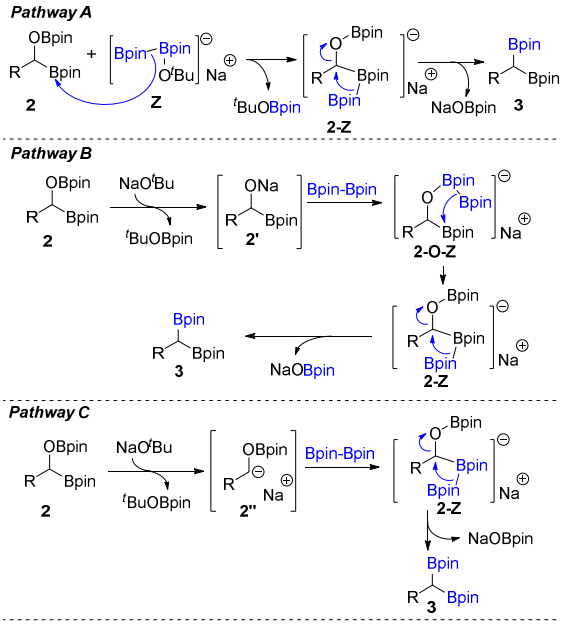
Scheme 5. Reactivity of Different *O*-Type Leaving Groups [a]



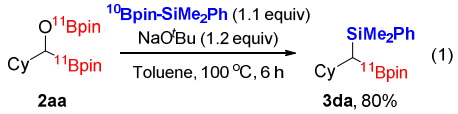
[a] Reaction conditions: **2a** (0.2 mmol), B_2pin_2 (0.22 mmol), toluene (2.0 mL), NaO^{t}Bu (0.24 mmol), 100 °C, 6 hours. Yields were determined by GC analysis with biphenyl as an internal standard. [b] 0.9 equivalents of NaO^{t}Bu was used.

Mechanistic study for the borylation of α-OBpin boronic esters. Three possible reaction pathways were proposed based on the initially possible interaction of NaO^{t}Bu with three types of Bpin group (*Bpin*-B, *Bpin*-O and *Bpin*-C) in the reaction mixture (Scheme 6). The activation of B_2pin_2 (*Bpin*-B) with alkoxide has been previously proven to generate an adduct **Z** which could provide a nucleophilic Bpin group.[25] Accordingly, **Z** may transfer its boryl group to **2** to form an 'ate' complex **2-Z** followed by 1,2-metallate rearrangement with OBpin as leaving group, generating the desired product **3** (Scheme 6, Pathway A). Furthermore, the reaction between **2** and NaO^{t}Bu may occur via two possible routes. First, the *Bpin*-O group exchanges with NaO^{t}Bu to generate **2'** followed by the reaction with B_2pin_2 to afford an adduct **2-O-Z**. An intramolecular transfer of the boryl Bpin group also generate **2-Z**, which undergoes a similar process as Pathway A to generate **3** (Pathway B). It is also possible that NaO^{t}Bu interacts with the *Bpin*-C group of **2** to generate a carbanion **2"** followed by the reaction with B_2pin_2 to afford **2-Z**, then to generate **3** (Pathway C).

Scheme 6. Proposed Reaction Pathways



To verify these possible mechanisms, a ^{10}B-labeling experiment was initially carried out. The synthesized ^{10}Bpin-$SiMe_2Ph$ was applied to react with **2aa** in the presence of 1.2 equivalents of NaO^{t}Bu (eq. 1). As a result, no ^{10}B-labeled **3da** was observed. The normal **3da** was isolated in an 80% yield. From those three pathways discussed above, A and B would result in non-^{10}B-labeled **3da** (with silyl as the migration group), while Pathway C will generate ^{10}B-labeled **3da**. Thus, Pathway C was ruled out.



We then utilized Density functional theory (DFT) calculation to further reveal Pathways A and B (Pathway C has also been revealed for comparison, see details in the supporting information). Density function M11-L with a standard 6-311+G(d) basis set were employed in the calculation. It can be derived from Scheme 6 that **2-Z** is the same intermediate for all these three pathways. As shown in Figure 1, the free energy of α-OBpin boronate **2** was set to the relative zero value. In Pathway A, the interaction of *tert*-butoxide with B_2pin_2 generates intermediate **Z**.[25-26] Then a direct transfer of a boryl Bpin to **2** takes place via a transition state **4-ts** to afford the intermediate **2-Z**. The computed activation free energy for this step is 60.4 kcal/mol, indicating that Pathway A is less possible. In pathway B, the coordination of *tert*-butoxide to **2-Z** reversibly affords a boronate intermediate **6** via the transition state **5-ts** with a barrier of 16.1 kcal/mol. The following dissociation of ^{t}BuOBpin from **6** could occur via transition state **7-ts**. In this case, a three-membered spiro-boronate intermediate **2'** was generated. The free energy span of this step is 23.7 kcal/mol. Subsequently, intermediate **2'** could readily react with B_2pin_2 by the cleavage of the three-membered ring to give a more stable boronate intermediate **2-O-Z** via transition state **8-ts**. The energy barrier of this step is only 5.6 kcal/mol. Then, the intermediate **2-Z** is formed irreversibly by a concerted boryl transfer via a five-membered ring type transition state **9-ts** with an energy barrier of 14.0 kcal/mol.[27] The computational results implied that the dissociation of ^{t}BuOBpin from intermediate **6** via transition state **7-ts** is the rate-determining step in pathway B. The calculated apparent activation free energy is 23.7 kcal/mol, indicating that this transformation could take place under mild conditions through Pathway B (Comparably, the calculated apparent activation free energy of Pathway C is 29.4 kcal/mol, which is 5.7 kcal/mol higher than that of Pathway B, see details in the supporting information). Later on, the generation of *gem*-diboron product **3** from intermediate **2-Z** was also studied theoretically. A concerted boron-shift and C-O bond cleavage transition state is located as **14-ts**. In geometry information of transition state **14-ts**, the bond lengths of B1-B2, B2-C, and C-O are 1.91, 2.21, and 2.21 Å, respectively, indicating that when the B2-C bond is forming, the B1-B2 and C-O bonds are partly broken. The angle of B2-C-O is 160.6°, which reveals an intramolecular nucleophilic substitution from the back of C-O bond (See details in the supporting information). The calculated activation free energy of this step is 20.6 kcal/mol, suggesting a facile process. The calculated highest occupied molecular orbital (HOMO) of intermediate **2-Z** (Figure 1) showed that this orbital majorly located between the B-B bond, further demonstrating the nucleophilicity of the migrating boron atom. Therefore, the subsequent nucleophilic substitution would occur. Overall,

the DFT calculations exhibit that Pathway B is the most plausible pathway for the borylation of α-OBpin boronate.

Moreover, Pathway B could explain why α-OH boronate **2ea** is reactive in the borylation process (Scheme 5), as the deprotonation of **2ea** with NaO^{t}Bu would generate **2'** followed by a facile generation of **2-O-Z**. When the OH group was protected (**2fa**, **2ga**, **2ha**), the generation of **2-O-Z** was blocked as a result to shut the borylation down. The OAc (**2fa**) substrate afforded 11% of the desired **3aa** might due to the trans-esterification of **2fa** with NaO^{t}Bu to release intermediate **2'** to initiate the reaction. Therefore, both theoretical studies and experimental results support Pathway B as the reaction mechanism for the borylation of α-OBpin boronates.

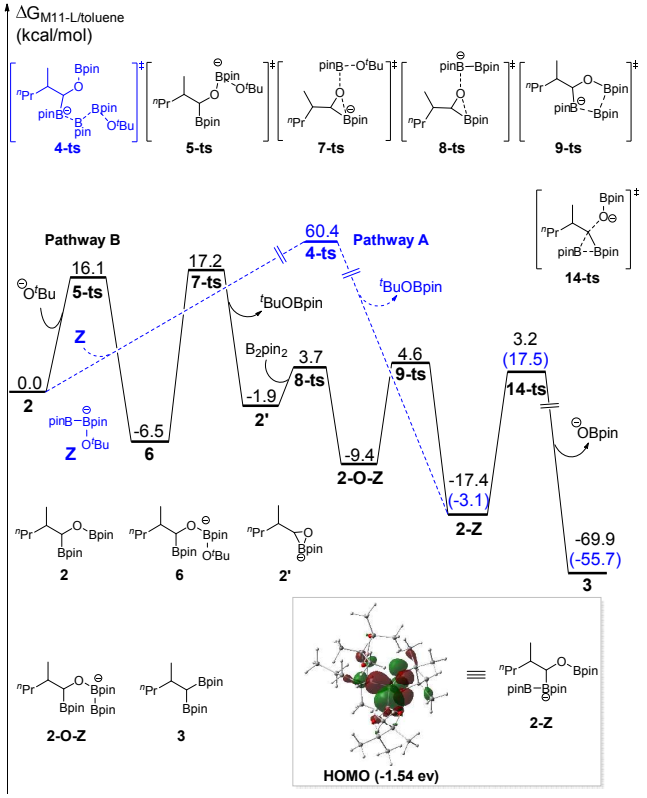
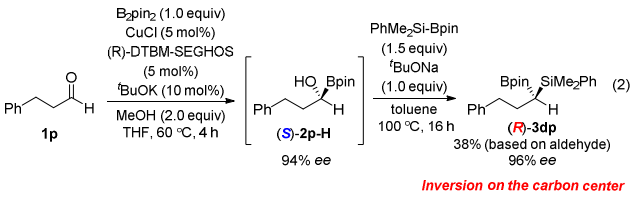


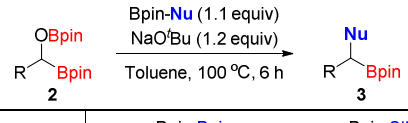
Figure 1. Free energy profiles of Pathways A and B. Energy values are given in kcal/mol and represent the relative free energies that were calculated using the M11-L method in toluene. Energy values of **2-Z** to **3** in Pathway A are in parentheses.

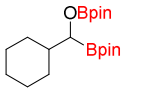
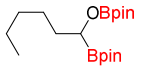
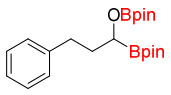
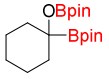
According to the transformation of intermediate **2-Z** to the final product **3** in Pathway B, the boryl group attacks the carbon center from the back side and will result in an inversion on the carbon center. In order to testify the inversion process (eq. 2), an enantioenriched α-OH boronate (*S*)-**2p-H** (94% *ee* of the corresponding silyl protected product) was synthesized from aldehyde **1p** according to the Ito procedure[9a] and subjected to the silylation with Bpin-SiMe$_2$Ph to confirm the inversion process (eq. 2). Since (*S*)-**2p-H** is unstable to be purified by column chromatography over silica gel, we used it only after a fast filtration through a silica plug followed by removing the solvent (See details in the supporting information). The obtained (*S*)-**2p-H** was subjected to the silylation with PhMe$_2$Ph-Bpin in the presence of NaO^{t}Bu. Consequently, we observed the desired (*R*)-**3dp** in 38% yield (based on aldehyde **1p**) with 96% *ee* (The absolute configuration was confirmed by comparing with the reported result[11]), indicating an inversion on the carbon center and the silylation indeed took place with a stereospecific manner. The stereochemical course further confirms the proposed transformation of **2-Z** to the final product **3**.



Selected substrate scope for the borylation and silylation of α-OBpin boronic esters. With the insightful understanding of this transformation, several α-OBpin boronic esters **2** were synthesized and were subjected to react with B$_2$pin$_2$ or Bpin-SiMe$_2$Ph (Table 1).[28] Compounds **2** generated from aldehydes, such as **2aa**, **2al**, and **2ap** were successfully borylated with B$_2$pin$_2$ and silylated with Bpin-SiMe$_2$Ph in the presence of NaO^{t}Bu. The corresponding *gem*-diboryl compounds **3aa**, **3af** and **3ag**, *gem*-silylboryl compounds **3da**, **3df** and **3dg** were obtained in good to excellent yields. Those products are stable for isolation. Compound **2kg** generated from cyclohexanone afforded its corresponding *gem*-diboryl compound **3kg** and *gem*-silylboryl compound **3dg** in 51% and 56% yields, respectively.

Table 1. Borylation and Silylation of α-OBpin Boronic Esters 2 [a]



2	Bpin-Bpin	Bpin-SiMe$_2$Ph
 **2aa**	**3aa**, 60%	**3da**, 82%
 **2al**	**3al**, 61%	**3dl**, 75%[b]
 **2ap**	**3ap**, 59%	**3dp**, 50%
 **2kg**	**3kg**, 51%	**3dg**, 56%[b]

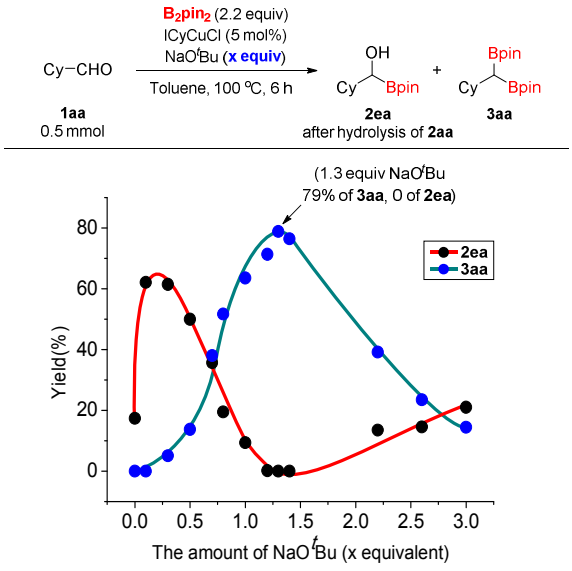
[a] Reaction conditions: **2** (0.3 mmol), B$_2$pin$_2$ (0.33 mmol) or Bpin-SiMe$_2$Ph (0.33 mmol), toluene (2.0 mL), NaO^{t}Bu (0.36 mmol), 100 °C, 6 hours. Isolated yields. [b] 0.5 mmol scale in 2.0 mL toluene.

Exploring the direct deoxygenative *gem*-diborylation of aldehyde and ketones. Compounds **2** are usually not easy to isolate and suffer from instability in air, which makes the method impractical for the synthesis of *gem*-diboryl or *gem*-silylboryl compounds. Directly utilizing aldehydes or ketones would be more straightforward and practical. Inspired by the pioneering work on NHC-Cu catalyzed addition

of B_2pin_2 to aldehydes or ketones,[8b,8e,8f] our next effort is to explore the integrated use of Cu catalytic system with the above base-promoted C-OBpin borylation to figure out the direct *gem*-diborylation of aldehydes and ketones.

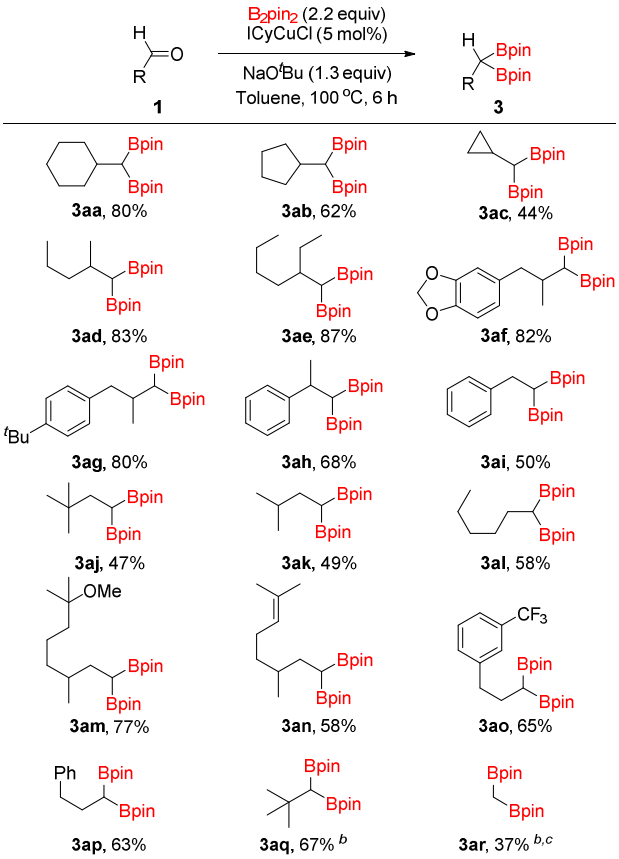
With cyclohexanecarbaldehyde **1aa** and B_2pin_2 (2.2 equiv) as substrates, the amount of NaO^{t}Bu was investigated in toluene at 100 °C (Scheme 7) by using ICyCuCl as the catalyst (ICy = 1,3-dicyclohexylimidazol-2-ylidene, the optimizations of other reaction parameters were listed in the supporting information). As **2aa** is easily hydrolyzed to give **2ea** during aqueous workup, the amount of **2ea** was quantified instead of **2aa**. It can be seen from Scheme 7 that less than 20% of **2ea** was obtained and no **3aa** was observed in the absence of NaO^{t}Bu. When 10 mol% of NaO^{t}Bu was added, there was still no observation of **3aa**, while the yield of **2ea** increased to over 60%. This may due to the generation of more active catalyst ICyCuO^{t}Bu from ICyCuCl and NaO^{t}Bu, for the addition of B_2pin_2 to aldehyde carbonyl.[8f] Whereafter, along with the increase of NaO^{t}Bu, the yield of **2ea** decreased together with the yield of **3aa** increased. When 1.3 equivalents of NaO^{t}Bu was applied, the yield of **3aa** maximized at 79% without any observation of **2ea**. These results are consistent with the previous study on the conversion of **2aa** to **3aa**, indicating that **2aa** is the intermediate for the *gem*-diborylation of **1aa** to **3aa**. Interestingly, further increasing the amount of NaO^{t}Bu resulted in a quick decrease of **3aa** with the re-observation of **2ea**. To rationalize this phenomenon, mechanistic study (Pathway B in Scheme 6) exhibited that the exchange between α-OBpin boronate **2** and one equivalent of NaO^{t}Bu will generate **2'** which is also an alkoxide analog. Excess NaO^{t}Bu will compete with **2'** to interact with B_2pin_2. This may slow down the conversion of **2'** to **2-O-Z**. Furthermore, even if **2-O-Z** is formed, the coordination of excess amount of *tert*-butoxide to either C-*Bpin* or the migrating Bpin group may block the migration step. Hence, excess amount of NaO^{t}Bu is detrimental to the conversion of **2aa** to **3aa**. Finally, a single-operation *gem*-diborylation of aldehyde with B_2pin_2 was achieved under copper catalysis in the presence of 1.3 equivalents of NaO^{t}Bu.

Scheme 7. The Effect of NaO^{t}Bu for the Conversion of Aldehyde



Substrate scope of deoxygenative *gem*-diborylation of aldehydes and ketones. Following the standard condition, a series of aliphatic aldehydes were examined in this transformation (Table 2). The R group of **1** can be various secondary alkyl groups, including cyclopentyl, cyclopropyl and *i*-pentyl, all affording the corresponding products **3ab**-**3ah** in moderate to excellent isolated yields. Especially, lily aldehyde and helional were well *gem*-diborylated to generate their corresponding products **3af** and **3ag** in high yields. Both 2-phenylpropionaldehyde and phenylacetaldehyde were shown to be suitable substrates and the desired product **3ah** and **3ai** were obtained in 68% and 50% yields, respectively. Simple long chain aliphatic aldehydes proceeded smoothly and gave the corresponding *gem*-diboron compound in a moderate yields (**3aj**-**3al**). 7-Methoxy-3,7-dimethyl-octanal afforded the corresponding product **3am** in a 77% isolated yield. *gem*-Diborylation product **3an** of citronellal was isolated in 58% yield, indicating that the olefinic bond could be tolerated. Aromatic trifluoromethyl group could also kept intact (**3ao**). When R is a bulky ^{t}Bu group, the reaction became sluggish and a prolonged reaction time was required to reach a good yield for pivalaldehyde (**3aq**). It was interesting to find that paraformaldehyde $(CH_2O)_n$ also worked under the reaction condition and afforded the desired product **3ar** albeit in a relatively low yield (37%).

Table 2. Deoxygenative *gem*-Diborylation of Aldehydes [a]

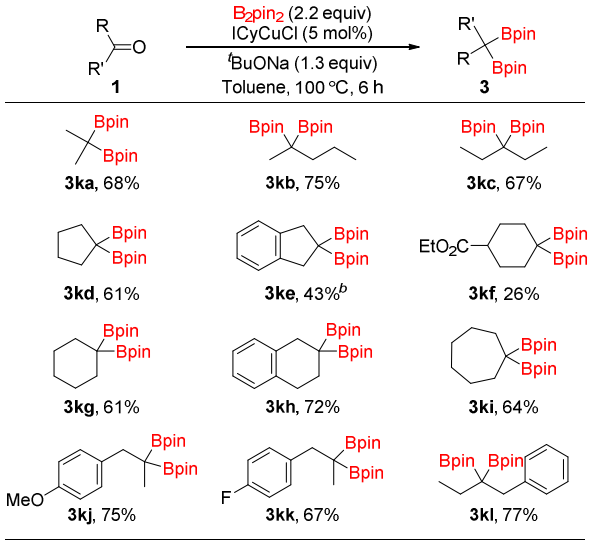


[a] Reaction conditions: **1** (0.5 mmol), B_2pin_2 (1.1 mmol), ICyCuCl (0.025 mmol), NaO^{t}Bu (0.65 mmol), toluene (2.0 mL), 100 °C, 6 hours. Isolated yields. [b] 24 hours. [c] paraformaldehyde was used.

Next, deoxygenative *gem*-diborylation of ketones was also examined under the standard condition (Table 3). Acetone, 2-pentanone and 3-pentanone were well *gem*-diborylated to

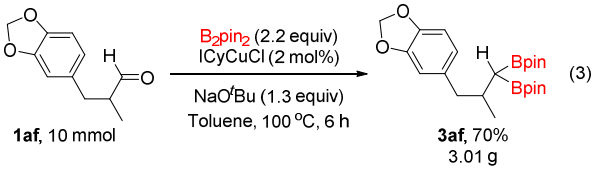
afford their products **3ka**-**3kc** in good yields. Cyclic ketones with five-membered ring, six-membered ring and seven-membered ring were all suitable for this deoxygenative *gem*-diborylation and gave their corresponding products **3kd**-**3ki** in moderate to good yields. Arylacetones were also applied and the aromatic methoxyl and C-F groups were well tolerated (**3kj**, **3kk**). Benzyl ethyl ketone afforded the desired product **3kl** in a 77% yield.

Table 3. Deoxygenative *gem*-Diborylation of Ketones [a]

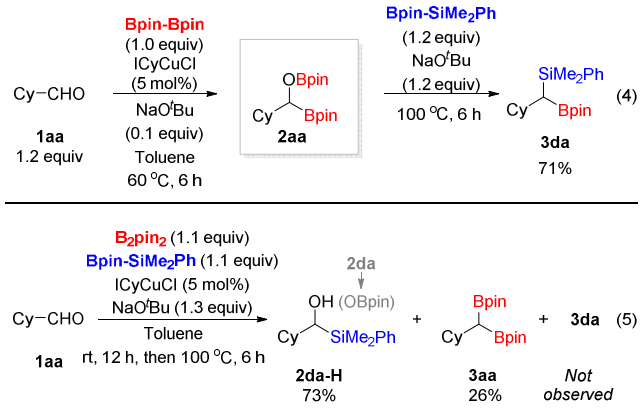


[a] Reaction conditions: **1** (0.5 mmol), B_2pin_2 (1.1 mmol), ICyCuCl (0.025 mmol), NaO^tBu (0.65 mmol), toluene (2.0 mL), 100 °C, 6 hours. Isolated yields. [b] 1.0 mmol scale in 2.0 mL toluene.

To demonstrate the practicability of this transformation, a 10 mmol scale reaction was carried out using helional (**1af**) as substrate while lowering the catalyst loading to 2 mol% (eq. 3). Subsequently, 3.01 grams (70% yield) of the desired product **3af** was isolated, indicating the possibility to scale up this procedure.

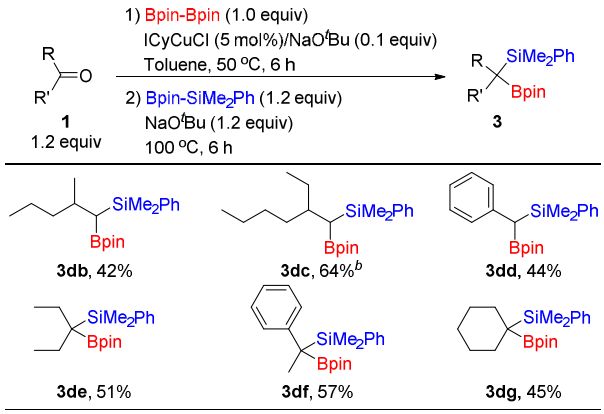


Exploring deoxygenative *gem*-silylborylation of aldehydes and ketones. The silylation of α-OBpin boronic esters with Bpin-$SiMe_2Ph$ in Table 1 encouraged us to further investigate the deoxygenative *gem*-silylborylaton of aldehydes and ketones. Since α-OBpin boronic esters **2** can be generated from aldehydes or ketones with B_2pin_2 and can be silylated with Bpin-$SiMe_2Ph$, the stepwise addition of B_2pin_2 and Bpin-$SiMe_2Ph$ was carried out to achieve deoxygenative *gem*-silylborylation of **1aa** (eq. 4). First, the reaction between **1aa** and Bpin-Bpin proceeded initially in the presence of 5 mol% ICyCuCl and 0.1 equivalents of NaO^tBu in toluene at 60 °C. After 6 hours, 1.2 equivalents of Bpin-$SiMe_2Ph$ and 1.2 equivalents of NaO^tBu were added into the reaction mixture. Then, the reaction was heated at 100 °C for another 6 hours. To our delight, the desired *gem*-silylborylation product **3da** was obtained in 71% yield (eq. 4). The yield was quantified based on B_2pin_2. 1.2 equivalents of **1aa** was used to make sure the full conversion of B_2pin_2 in the first step. We also attempted one-step reaction for this *gem*-silylborylation by initially adding all materials (eq. 5). Unfortunately, no desired **3da** was observed in this case. The α-silyl alcohol **2da-H** was obtained as the major product (73%) together with the observation of **3aa** (26%). **2da-H** was generated from the addition of Bpin-$SiMe_2Ph$ to **1aa**, followed by hydrolysis.[29] The products distribution suggested that Bpin-$SiMe_2Ph$ is more reactive than Bpin-Bpin in the addition to aldehyde **1aa** under the reaction conditions and **2da** could not be converted to the desired *gem*-silylboryl compound **3da** in the presence of B_2pin_2 and NaO^tBu.



Following the above result, several aldehydes and ketones were selected to test the substrate scope under the stepwise strategy (Table 4). Both aliphatic and aromatic aldehydes afforded their corresponding *gem*-silylboryl compounds **3db**-**3dd** in moderate yields. Acyclic and cyclic ketones were silylborylated in moderate yields (**3de**, **3dg**). It is worthy to note that acetophenone was also suitable substrate and gave the desired *gem*-silylboryl compound **3df** in a 57% yield.

Table 4. *gem*-Silylborylation of Aldehydes and Ketones



[a] Reaction conditions: **1** (0.6 mmol), B_2pin_2 (0.5 mmol), ICyCuCl (0.025 mmol), NaO^tBu (0.05 mmol), toluene (2.0 mL), 50 °C, 6 hours, then NaO^tBu (0.6 mmol), Bpin-$SiMe_2Ph$ (0.6 mmol), 100 °C, 6 h. Isolated yields. [b] 1.0 mmol scale in 2.0 mL toluene.

CONCLUSION

In summary, we have demonstrated a deoxygenative *gem*-diborylation and *gem*-silylborylation of aldehydes and ketones for the first time. The key for the success of this transformation is the base-promoted C-O bond borylation or silylation of the generated α-oxyboronates. Experimental and theoretical studies exhibit that the C-O bond functionalization proceeds via an intramolecular five-membered transi-

tion-state boryl migration followed by a 1,2-metallate rearrangement with OBpin as a leaving group. The transformation occurs with an inversion on the carbon center. Direct conversion of aldehydes and ketones to *gem*-diboron compounds was achieved by combining copper catalysis with this base-promoted C-OBpin borylation. Various aldehydes and ketones were deoxygenatively *gem*-diborylated. *gem*-Silylborylation of aldehydes and ketones were achieved by a stepwise operation, in which B_2pin_2 must react with those carbonyls first followed by a silylation with Bpin-$SiMe_2Ph$. Further exploring other nucleophiles in the reaction with α-oxyboronates is currently ongoing in our laboratory.

ASSOCIATED CONTENT

Supporting Information

This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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(21) Other nucleophiles such as PhBpin, hexyl-Bpin and ^{n}BuLi were also tested to react with **2aa**, in which ^{n}BuLi afforded the desired alkylation product in a 33% yield, suggesting that the alkylation of α-OBpin boronates could also be achieved with OBpin as the leaving group. See details in the supporting information.
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(27) The direct attack of boryl group to the carbon center (**2-O-Z**) via a four-membered transition state has been considered by DFT calculation. Although we have tried many times to locate the transition state, no stable structure could be found. The required C-B bond could not be formed when the C-O bond cleaves during the structure optimization, which might due to the less possible four-membered intramolecular attack.
(28) As α-OBpin boronic esters were sensitive to chromatographic purification (see reference 8e), they were isolated by recrystallization from hexane.
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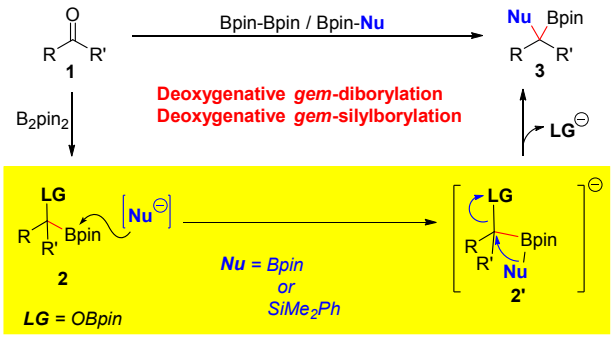
Bpin-Bpin / Bpin-Nu
Deoxygenative gem-diborylation
Deoxygenative gem-silylborylation
B2pin2
LG
Nu = Bpin
or
SiMe2Ph
LG = OBpin
1
2
3
2'