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Formal Carbon Insertion of *N*-Tosylhydrazone into B–B and B–Si Bonds: *gem*-Diborylation and *gem*-Silylborylation of sp^3 Carbon

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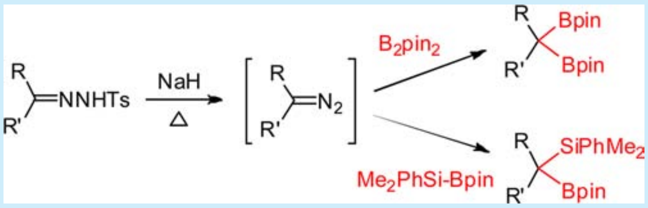
Supporting Information

ABSTRACT: A convenient method is developed to synthesize 1,1-diboronates from the corresponding *N*-tosylhydrazones. This method is also applicable to synthesize 1-silyl-1-boron compounds. Meanwhile, derivatization and consecutive Pd-catalyzed cross-coupling reactions with 1,1-boronates were explored, demonstrating the synthetic potential of 1,1-diboronates.

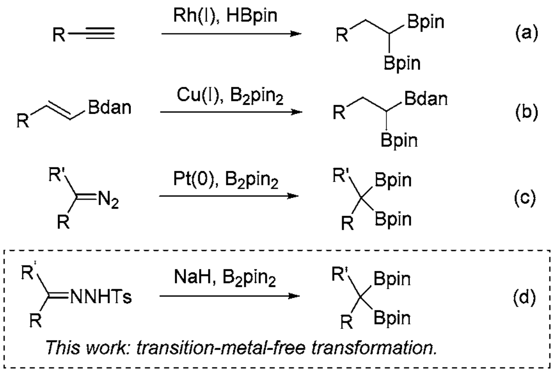


Dimetalated organic compounds have attracted considerable attention due to their unique reactivities.[1] In particular, 1,1-diborylalkanes are highly valuable synthetic building blocks because multiple transformations, including C–C bond formations through Suzuki–Miyaura couplings, are possible from these diboryl reagents. Compared to the widely used Suzuki–Miyaura couplings with vinyl- and arylboron reagents, the coupling reactions with alkylboron compounds are less common, since these reactions suffered some difficulties such as protodeboronation, slow transmetalation, and β-H elimination.[2] Interestingly, 1,1-diboron compounds are quite reactive in Pd-catalyzed cross-coupling reactions with various electrophiles.[3] In 2011, Shibata and co-workers reported a novel coupling reaction of 1,1-diborylalkanes with aryl bromides.[3a] An interesting feature of this coupling is that the reaction is highly chemoselective, with only one boronate moiety participating in the cross-coupling and the remaining boronate moiety keeps intact. Hall and co-workers in the same year reported coupling reactions of chiral 1,1-diboron compounds with aryl and vinyl bromides.[3b]

In contrast to monoboronate alkanes, the Pd-catalyzed cross-coupling of 1,1-diborylalkanes occurs efficiently under mild conditions, indicating that the adjacent boron atom in 1,1-diborylalkanes can facilitate the coupling reaction. Furthermore, the diverse reactivity of C–B bonds provides various transformations with 1,1-diboron compounds. For example, under suitable conditions consecutive cross-coupling of the 1,1-diboron compound with two different aryl bromides can be achieved, constituting a unique method to generate two C–C bonds on a carbon center.[3b,e] 1,1-Diborylalkanes have also been used in the lithiation/nucleophilic addition reaction to ketones for the synthesis of alkenyl boronates, which can be further converted to tetrasubstituted olefins through Suzuki–Miyaura cross-couplings.[4]

Although 1,1-diborylalkanes have shown promising reactivities, the methods to access this type of unique dimetalated organic compounds are still limited.[1a,5] Rh(I)-catalyzed diborylation of alkynes represents an efficient method to synthesize 1,1-diboronates (Scheme 1a).[6] Cu(I)-Catalyzed enantioselective hydroboration of alkenylboron compounds has also been achieved (Scheme 1b).[3b,f] Besides, Srebnik and co-workers reported that Pt(0)-catalyzed diborylation of diazo compounds with B$_2$pin$_2$ afforded 1,1-diborylalkanes (Scheme 1c).[7] However, these methods still suffer from drawbacks such as limited substrate scope and the requirement of expensive transition-metal catalysts. Herein, we communicate a practical method for the synthesis of 1,1-diborylalkanes through the reaction of *N*-tosylhydrazones with B$_2$pin$_2$ under transition-metal-free conditions (Scheme 1d). The reaction can also be extended to the synthesis of 1-boryl-1-silylalkanes. Besides, we explored the sequential coupling reactions with 1,1-diborylalkanes.

Scheme 1. Synthesis of 1,1-Diboronates



N-Tosylhydrazones can be easily prepared from the corresponding ketones or aldehydes. They have been known to generate diazoalkanes upon treatment with base (Bamford–Stevens reaction),[8] and more recently they have been

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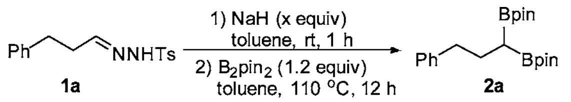
extensively explored in transition-metal-catalyzed cross-coupling reactions.[9] We have previously reported a metal-free monoborylation reaction of *N*-tosylhydrazones with B_2pin_2.[10] In the mechanistic study, we found that 1,1-diboronates could be effectively formed by thermal reaction of *N*-tosylhydrazone sodium salt with B_2pin_2. In addition, 1,1-diboronate was found stable in the absence of base or a proton source. Encouraged by these initial results, we further improved the preparative procedure by using sodium hydride (NaH, 60%, dispersed in mineral oil) as the base to generate tosylhydrazone sodium salt *in situ*. The advantage of NaH as the base in this reaction is that the proton removed from *N*-tosylhydrazone vanishes from the reaction system with the release of H_2, thus avoiding protodeboronation of the 1,1-diboronate product. Since the reaction is sensitive to the quantity of base, the loading of NaH has been optimized (Scheme 2). It was found that optimal results could be obtained with 1.2 equiv of NaH.

Scheme 2. Reaction Optimization[a]



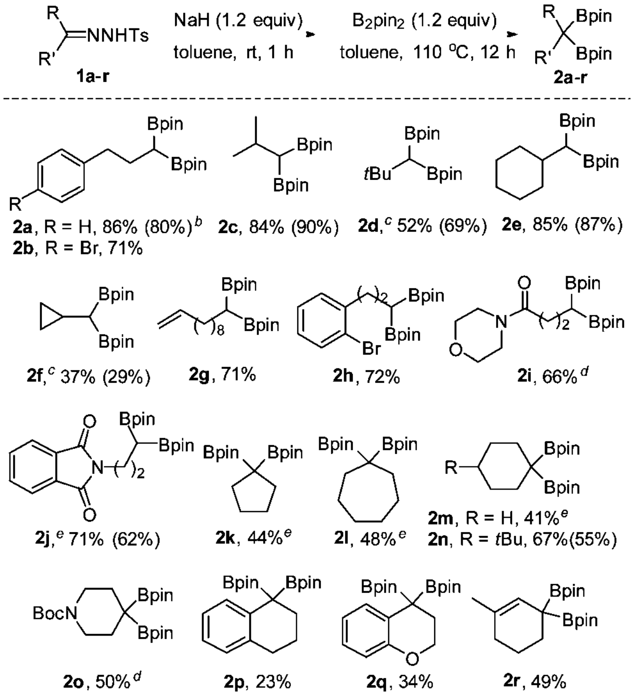
NaH (x equiv)	x = 1.05	1.1	1.2	1.3	1.5
2a, yield	69%	80%	86%	74%	67%

[a]Reaction conditions: *N*-tosylhydrazone (1 mmol), NaH (*x* mmol), B_2pin_2 (1.2 mmol), toluene (10 mL). Product was isolated by silica gel chromatography.

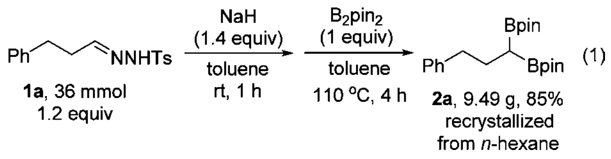
A series of *N*-tosylhydrazones were then applied to the optimized reaction conditions (Scheme 3). For the *N*-tosylhydrazones derived from aldehydes, when the R group is a bulky substituent such as *i*Pr (**2c**), the yield is also good. However, if the R group is a very bulky group such as *t*Bu (**2d**), the yield is diminished. The reaction conditions tolerate *N*-tosylhydrazones bearing halogen, vinyl, and amido substituents (**2b**, **2h**, **2g**, **2i**, **2j**). The *N*-tosylhydrazones derived from aryl and alkenyl aldehydes were also reactive, but the isolated yield was low due to severe side reactions and instability of the products. For the *N*-tosylhydrazones derived from ketones, the reactivity was relatively low due to the steric hindrance and poor solubility. Therefore, a polar solvent such as dioxane and phase transfer catalyst BTMAC (benzyltrimethyl-ammoniun chloride) were applied to enhance the solubility and the conversion of the tosylhydrazone salt to the coressponding diazo compound;[11] however, the yields were moderate in these cases (**2k**–**r**). For **2n**, a slightly improved yield was obtained because of its good solubility. However, for the *N*-tosylhydrazones derived from linear ketones, the yield was quite low.

To demonstrate the practical applicability, in several cases we have carried out the reactions in gram scales (**2a**, **c**–**f**, **j**, **n**). As shown in Scheme 3, the isolated yields were also satisfactory. Furthermore, for the synthesis of 1,1-diboronate **2a**, we have considered isolating the product by recrystallization. The initial trial of purifying the product by recrystallization failed because of cocrystallization of the 1,1-diboronate products with the remaining B_2pin_2. This problem can be solved by simply inverting the molar ratio of *N*-tosylhydrazone to B_2pin_2 and in this way the 1,1-diboronate **2a** could be obtained in good yield by recrystallization from hexane (eq 1).

Scheme 3. Reactions of Tosylhydrazones with B_2pin_2[a]



[a]Reaction conditions: *N*-tosylhydrazone (1 mmol), NaH (1.2 mmol), B_2pin_2 (1.2 mmol), toluene (10 mL). The products were isolated by silica gel column chromatography. [b]The yields described in parentheses refer to the reactions carried out in 10 mmol scale. [c]The reaction was carried out at 90 °C. [d]Dioxane was used as the solvent. [e]Dioxane was used as the solvent, and 10 mol % of BTMAC was added.

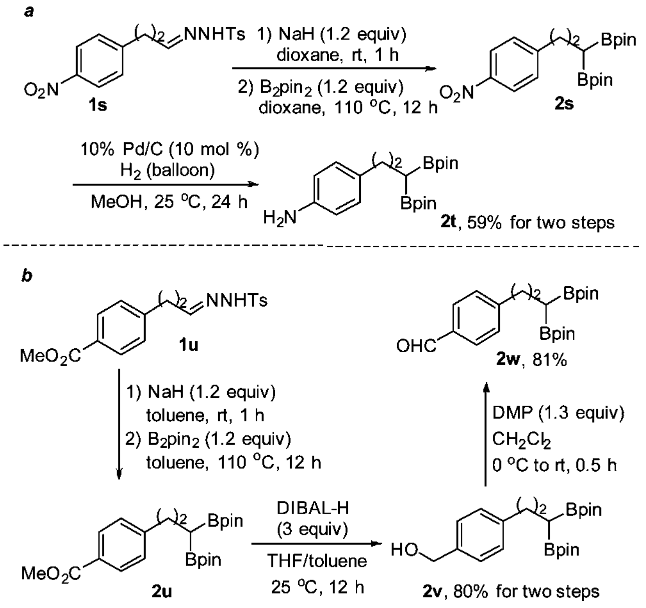


The 1,1-diboronates are quite stable under various reaction conditions, which benefit further functionalization of these compounds. For example, the 1,1-diboronate bearing nitro group (**2s**) could be reduced to the corresponding amine (**2t**) in moderate yield (Scheme 4a). Likewise, the 1,1-diboronate bearing ester group (**2u**) could be reduced to the corresponding alcohol (**2v**) using DIBAL-H as the reductant. Upon Dess-Martin oxidation, a 1,1-diboronate bearing aldehyde moiety (**2w**) could be obtained (Scheme 4b). Both an aryl amine and aldehyde are useful building blocks in organic synthesis.

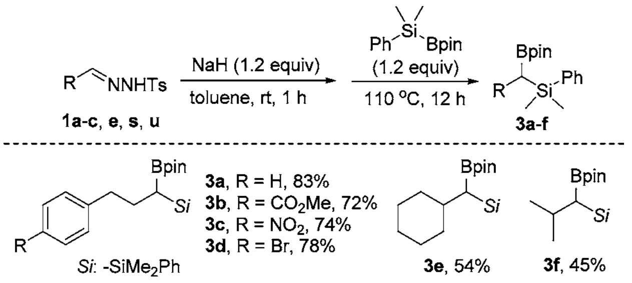
Interestingly, under the same reaction conditions but with a silylborane reagent as the substrate, 1-silyl-1-boryl compounds could also be obtained in moderate to high yields with good functional group compatibility (Scheme 5).[12,13] In this case, the silyl group migrated instead of the boron group.[10b] However, as shown by the diminished yields of **3e** and **3f**, the reaction was affected by steric hindrance.

A possible reaction mechanism is shown in Scheme 6. First, from *N*-tosylhydrazone the diazo compound **A** is generated *in situ*. The nucleophilic diazo carbon then reacts with the electron-deficient boron of the B_2pin_2 or $Me_2PhSiBpin$ to form a tetracoordinated boron complex **B**. Subsequently, release of

Scheme 4. Derivatization of 1,1-Diboronates

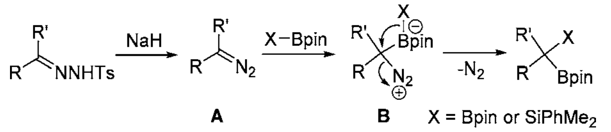


Scheme 5. Reaction of Tosylhydrazones with Silylborane[a]



[a]Reaction conditions: tosylhydrazone (0.5 mmol), NaH (0.6 mmol), B_2pin_2 (0.6 mmol), toluene (5 mL). The products were isolated by silica gel column chromatography.

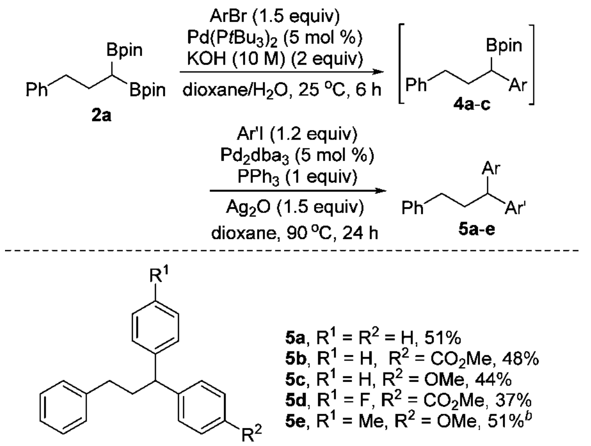
Scheme 6. Possible Reaction Mechanism



dinitrogen occurs with the simultaneous 1,2-shift of the Bpin or $SiPhMe_2$ from boron to carbon to afford the formal B—B or B—Si insertion product, respectively.

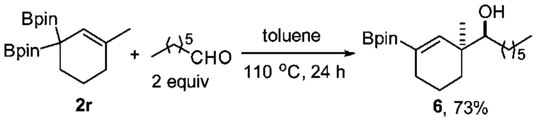
In order to demonstrate the potential of synthetic applications of 1,1-diboronates, we next carried out investigations on the transition-metal-catalyzed coupling reactions of 1,1-diboronates. Based on the previous reports by Shibata[3a] and Crudden,[14] we first explored the stepwise coupling of 1,1-diboron compounds with two aryl halides. By using Shibata's reaction conditions, the 1,1-dibron compound **2a** was coupled with aryl bromides to afford benzyl boronates with $Pd(PtBu_3)_2$ as the catalyst. Upon completion of the reaction, the solvent was removed and the residue was extracted with diethyl ether several times. The combined ethereal extracts were concentrated, and the crude products **4a−c** were submitted to the next coupling with aryl iodides and catalytic Pd_2dba_3 (Crudden's conditions). The two-step coupling afforded diarylmethane derivatives in moderately high yields (Scheme 7).

Scheme 7. Stepwise Coupling Reactions of 1,1-Diboronate 2a with Aryl Bromides and Aryl Iodides[a]



[a]The reaction was carried out in 0.2 mmol scale. The crude product of the first step was extracted with Et_2O before the second step. [b] The reaction time for the second step was prolonged to 48 h.

Furthermore, we applied diboronates **2r** in the allylboration reactions with aldehyde (eq 2).[15] To our delight, the desired product **6** could be obtained with good yield upon heating the reactants in toluene. The vinyl boronate moiety formed in this transformaton may be further functionalized *via* cross-coupling reactions or undergo other functional group transformations.



(2)

In conclusion, we have developed a new method to synthesize 1,1-diboronate and 1-silyl-1-boryl compounds. This method has the following features: (1) the starting material *N*-tosylhydrazones can be easily synthesized from the corresponding carbonyl compounds; (2) the reaction can be easily operated and scaled up and shows wide substrate scope; (3) the reaction is under transition-metal-free conditions. With these features, we expect this reaction will become a general method for the synthesis of 1,1-diboronates. Furthermore, some transformations of the 1,1-diboronates, including stepwise Pd-catalyzed cross-coupling reactions, have been explored, demonstrating the unique reactivity features of 1,1-diboronates. Further explorations of the reactions with 1,1-diboronates are underway in our laboratory, and the results will be reported in due course.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experiment details, spectral data, and ^1H and ^{13}C NMR spectra for products. These materials are available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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