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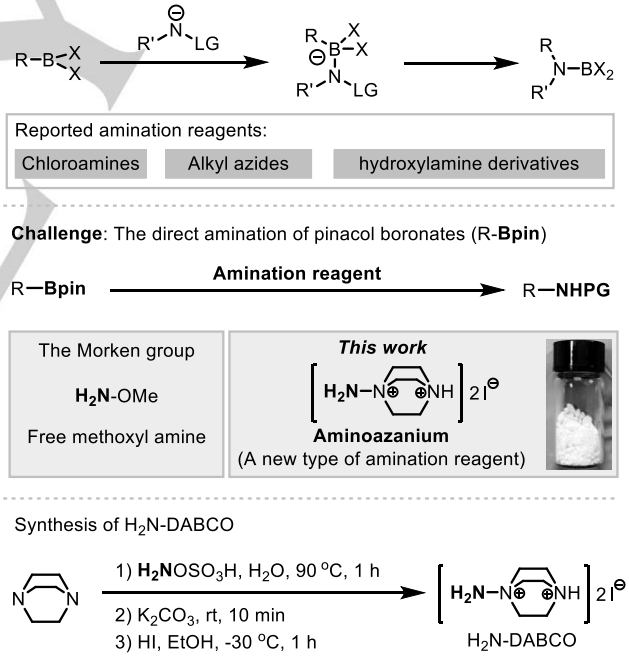
Aminoazanium of DABCO: A General and Practical Amination Reagent for Alkyl and Aryl Pinacol Boronates

Xingxing Liu,[+] Qing Zhu,[+] Du Chen, Lu Wang, Liqun Jin,* and Chao Liu*

Abstract: The aminoazanium of DABCO was firstly developed as a general and practical amination reagent for the direct amination of alkyl and aryl pinacol boronates. This compound is stable and practical for operation. Various primary, secondary and tertiary alkyl-Bpin and aryl-Bpin were well aminated to their corresponding amine derivatives. The amination is stereospecific. The anti-Markovnikov hydroamination of olefins was easily achieved via catalytic hydroboration with HBpin followed by in-situ amination using this newly developed amination reagent H_2N-DABCO. Moreover, the combination of 1,2-diboration of olefins using B_2pin_2 with this amination process achieved the unprecedented 1,2-diamination of olefins to synthesize various 1,2-diamine derivatives. The amination protocol was also successfully extended to aryl pinacol boronates.

Organoboron compounds are useful reagents in chemical sciences, majorly originated from their readily transformable ability in tremendous molecule constructions.[1] Among various transformations of organoboron compounds, the aminations of C-B bond with amphiphilic nitrogen sources through 1,2-metalate rearrangements are highly valuable processes for the synthesis of amines, as those aminations are generally metal-free and stereospecific which are particularly attractive for pharmaceutical amine synthesis. The reactivity of such transformation is strongly dependent on the nature of the boron center, as the reaction was generally initiated by the interaction of the amphiphilic nitrogen with the sp^2-boron center. Early studies achieved the amination of electrophilic borane derivatives including dichloroboranes, difluoroboranes, trialkylboranes by using chloroamines, alkyl azides or hydroxylamine derivatives as the amphiphilic nitrogen sources.[2] Recently, the aminations of arylboronic acids have been succeeded by using benzylic azides and various hydroxylamine derivatives.[3] Along with the development of organoboron chemistry, pinacol organoboronates (R-Bpin) have attracted great attention in current synthetic community, due to their broad applications and easy-handling performance. Although these pinacol boronates have been widely used in various transformations, their amination is still challenging.[4] To achieve the amination of boronic esters, their in-situ conversion to more electrophilic dialkylborinates or dichloroboranes followed by amination with hydroxylamine derivatives or azides has been demonstrated to be a solution.[5] Aiming at efficient synthesis called for direct amination protocols for pinacol boronates. To date, the Morken group has provided the only solution by using freshly-prepared free methoxylamine (H_2N-OMe) as the amination reagent.[6] Obviously, the development of practical and general amination reagent for the direct amination of pinacol boronates is still highly demanding. Herein, we reported that an aminoazanium of DABCO can be efficiently served as a novel amination reagent for the direct amination of pinacol boronates. Moreover, this aminoazanium is a stable solid and can be conveniently obtained from the direct amination of DABCO using H_2NOSO_3H, followed by neutralization with K_2CO_3 and further treatment with HI (Scheme 1).[7] Its structure was confirmed by x-ray analysis and NMR analysis, and it could be stored for months with readily in usage.[8]



Scheme 1. Amination of organoboron compounds with amphiphilic nitrogen sources.

Our group have been focusing on the development of new methodology for the synthesis and transformation of organoboron compounds,[9] most of which were obtained as pinacol boronates. Our interests in the direct amination of those less Lewis acidity pinacol boronates promoted us to explore new method for the challenge. It is known that pinacol boronates generally contain weakly electrophilic boron center surrounded by hindered methyl groups. Meanwhile, the amination usually

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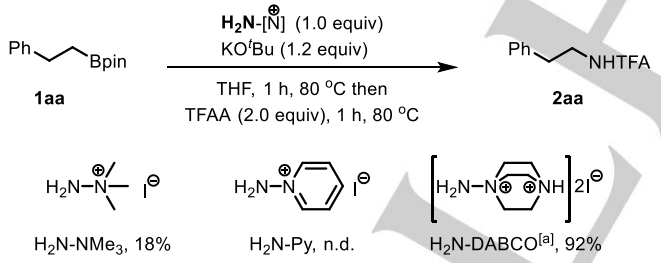
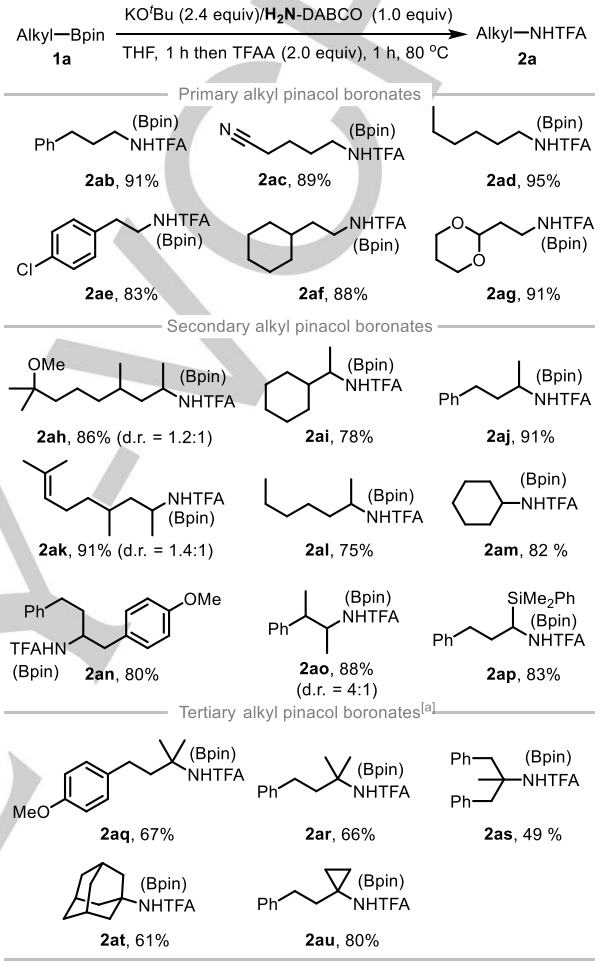
requires the formation of dative B-N bond between the amphiphilic amination reagent and boron center (Scheme 1). Due to the small B and N atoms, the formation of dative B-N bond is strongly sensitive to steric hindrance, which might be the nature of the challenge in the amination of pinacol boronates. On the other hand, the deprotonation of N-H from the amphiphilic amination reagents may enhance the B-N bond so as to overcome the steric-effect. However, the deprotonation may cause the decomposition of amination reagents prior to the amination process. Therefore, a mild yet reactive N-LG bond may be an ideal solution. We assumed that the N-N bond would be an appropriate option. Initially, three typical aminoazaniums (H_2N-NR_3^+) were tested for the direct amination of alkyl pinacol boronate **1aa** as the model substrate by using KO^{t}Bu as the base and THF as the solvent (Scheme 2). The reaction was carried out at 80 °C for 1h. After the completion of the reaction, TFAA was added to capture the resulted amine to *in situ* generate its corresponding TFA-amide **2aa** for the purpose of convenient isolation. H_2N-NMe_3^+ gave 18% of the desired **2aa**. We realized that the potential methyl migration of H_2N-NMe_3^+ in the presence of base might be detrimental to the amination.[10] In the case of aminopyridium (H_2N-Py), although its derivatives have been used as amination reagent under photocatalysis,[11] no **2aa** was detected by using H_2N-Py as the amination reagent and the starting boronic ester **1aa** kept intact in this transformation, which might be ascribed to the anion resonance of aminopyridium in the presence of base. Then, the aminoazanium of DABCO (H_2N-DABCO) was synthesized and subjected to this amination. To our delight, the desired TAF-amide **2aa** was obtained in 92% yield. Comparably, the H_2N-DABCO has a relatively stable DABCO skeleton to ensure the amino transferring without the break of DABCO unit.



Scheme 2. Initial attempts. **1aa** (0.25 mmol), amphiphilic nitrogen sources (0.25 mmol), KO^{t}Bu (0.3 mmol), THF (3 mL), 80 °C, 1 h, then TFAA (0.5 mmol), 80 °C, 1 h; [a] KO^{t}Bu (0.6 mmol); Yields based on isolated products.

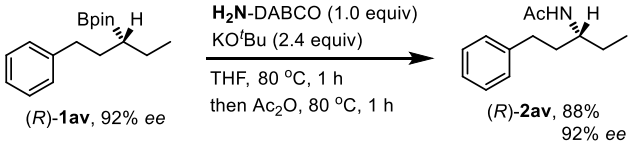
The promising result promoted us to further evaluate the scope of this amination (Scheme 3). The amination was effective to various primary, secondary and tertiary alkyl pinacol boronates. Alkyl-CN (**2ac**), Ar-Cl (**2ae**), and acetyl (**2ag**) groups were well tolerated and the corresponding products were obtained in excellent yields. Secondary alkyl pinacol boronates generally afforded excellent yields (**2ah**-**2ap**) in which methoxyl (**2ah**, **2an**) and alkenyl group (**2ak**) were kept intact. For secondary alkyl-Bpin **1ah**, **1ak** and **1ao**, the dr values of the starting materials were identical with their amination products, demonstrating a stereospecific manner of this amination process.

Interestingly, the *gem*-borylsilylalkane was well aminated to give its corresponding α-silyl amine **2ap**. Those tertiary alkyl pinacol boronates generally provided good yields in this amination reaction (**2aq**-**2au**). Adamantyl (**2at**) and cyclopropyl (**2au**) pinacol boronates proceeded well to give the desired products.



Scheme 3. Substrate scope of the amination. Reaction conditions: Reaction conditions: **1a** (0.25 mmol), H_2N-DABCO (0.25 mmol), KO^{t}Bu (0.6 mmol), THF (3 mL), 80 °C, 1 h, then TFAA (0.5 mmol), 80 °C, 1 h; [a] KO^{t}Bu (0.88 mmol), 100 °C; Yields based on isolated products.

To confirm the stereospecific transformation of 1,2-metalate rearrangement for this amination process, an enantioenriched secondary alkyl pinacol boronate (*R*)-**1av** (92% *ee*) was subjected to this amination process (Scheme 4).[12] As a result, the desired amination product (*R*)-**2av** in 92% *ee* was isolated. This complete retention further demonstrated a 1,2-metalate rearrangement process of this amination.



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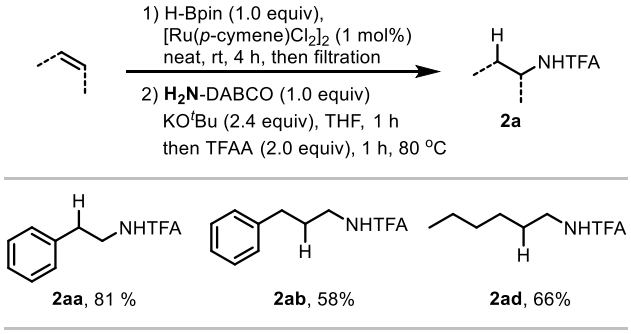
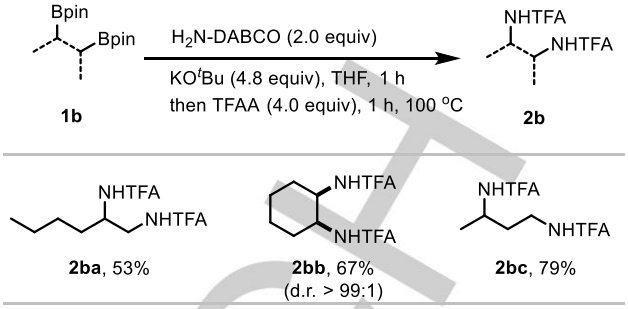
Scheme 4. Stereo-retention experiment.

It is known that the transition-metal-catalyzed hydroboration of olefins with HBpin has been well studied to generate various alkyl pinacol boronates. Three typical olefins were subjected to the hydroboration under Ru-catalysis (Scheme 5).[13] The following in-situ amination with H_2N-DABCO achieved the overall hydroamination of these olefins in moderate to good yields (**2aa**, **2ab**, **2ad**).



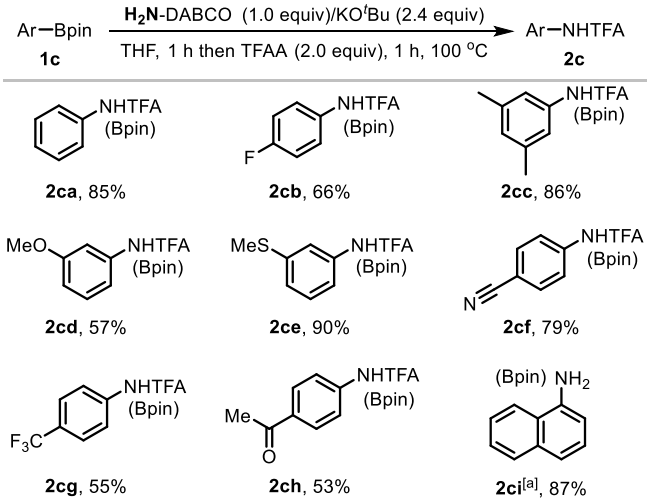
Scheme 5. Olefin hydroamination via hydroboration/amination experiments. Reaction conditions: 1) Olefin (0.5 mmol), HBpin (0.5 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (1 mol%), neat, rt, 4 h; 2) H_2N-DABCO (0.5 mmol), KO^{t}Bu (1.2 mmol), THF (3 mL), 80 °C, 1 h, then TFAA (1 mmol), 80 °C, 1 h; Yields based on isolated products.

Next, the 1,2-diboration of olefin with B_2pin_2 has been reported as an efficient method for the synthesis of 1,2-diborylalkanes.[14] We assumed that the in-situ amination of both C-B bonds might afford 1,2-diamino compounds which are important skelotons. Indeed, the 1,2-diborylalkanes could be obtained throught the simple transition-metal-free diboration of olefins.[14c] Moreover, the 1,3-diborylalkanes could be obtained through copper-catalyzed borylation protocol.[15] Then, three selected diborylalkanes were subjected to the di-amination using H_2N-DABCO, which successfully afforded their corresponding 1,2-diamination and 1,3-diamination products in good yields (Scheme 6). In the case of cyclohexene, the *syn*-diaminocyclohexane **2bb** was obtained in good yield with high selectivity (d.r. > 99:1). To our knowledge, this is the first example of 1,2-diamination of pinacol boronates, providing an efficient diborylation/amination protocal for the synthesis of 1,2-diamine derivatives.



Scheme 6. Diamination of 1,2- and 1,3-diborylalkanes. Reaction conditions: 1) **1b** (0.25 mmol), H_2N-DABCO (0.5 mmol), KO^{t}Bu (1.2 mmol), THF (3 mL), 80 °C, 1 h, then TFAA (1.0 mmol), 80 °C, 1 h; Yields based on isolated products.

Along with the development of catalytic borylation, more and more arylboron compounds are initially obtained as aryl pinacol boronates.[16] To achieve their amination is important for the synthesis of aniline derivatives. Up to date, only the Morken's protocol has been succeeded on the amination of aryl pinacol boronates by using free methoxyl amine and only one example has been shown in McCubbin's procedure.[3e, 6a] To our delight, this amination reagent H_2N-DABCO was aslo suitable for the amination of various pinacol arylboronates (Scheme 7). Functional groups, such as C-F (**2cb**), C-OMe (**2cd**), C-SMe (**2ce**), were well tolerated to give their corresponding products. The presence of cyano or carbonyl groups did not affects the amination of these C-B bonds and the desired products **2cf** and **2ch** were obtained in moderate to good yields. Interestingly, the Morken's protocol by using free methoxyl amine failed to aminate *p*-CF_3 substituted phenyl pinacol boronate **1cg**,[6a] while this new amination reagent (H_2N-DABCO) successfully provided the desired amination product **2cg** in 55% yield. In the case of 1-naphthyl-Bpin (**1ci**), the desired free 1-naphthylamine **2ci** was easily isolated in excellent yield without TFA-protection.



Scheme 7. Amination of aryl pinacol boronates. Reaction conditions: **1c** (0.25 mmol), H_2N-DABCO (0.25 mmol), KO^{t}Bu (0.6 mmol), THF (3 mL), 100 °C, 1 h, then TFAA (0.5 mmol), 100 °C, 1 h; [a] Without TFAA quenching; Yields based on isolated products.

In summary, the aminoazanium of DABCO was firstly developed as a general and practical amination reagent for the direct amination of alkyl and aryl pinacol boronates (Alkyl-Bpin and Ar-Bpin). Various primary, secondary and tertiary alkyl-Bpin were well aminated to their amine derivatives. The amination is stereospecific for alkyl pinacol boronates. The anti-Markovnikov hydroamination of olefins was easily achieved via catalytic hydroboration with HBpin followed by in-situ amination using our newly developed reagent H_2N-DABCO. Moreover, the combination of 1,2-diboration of olefins using B_2pin_2 with this amination process achieved the unprecedented 1,2-diamination of olefins to synthesize various 1,2-diamine derivatives. Aryl pinacol boronates were also successfully aminated.

Acknowledgements

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Keywords: Aminoazanium • Amination • Organoboron • Amine • Synthetic methods

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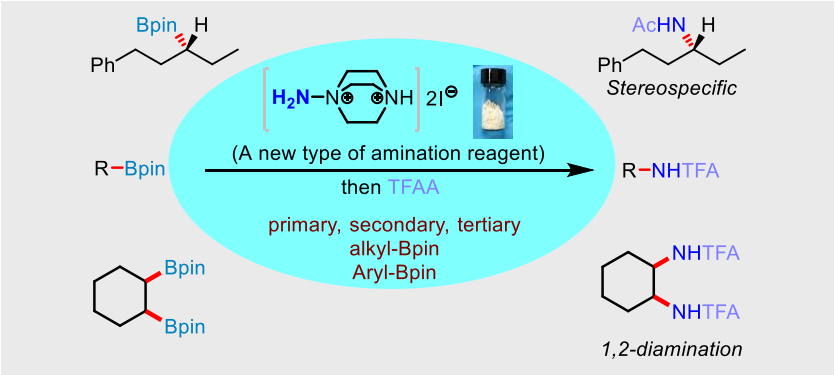

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