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Efficient one-pot synthesis of dan-substituted organo- and silyl-boron compounds†

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Direct, transition metal-free B(dan)-installation into organic frameworks has been developed. Heteroaryl-H bonds were transformable into the respective heteroaryl-B(dan) bonds through deprotonation. The resulting heteroaryl-B(dan) compounds, which are otherwise difficult to access, can undergo the direct Suzuki-Miyaura coupling. The method was demonstrated to apply to a silicon nucleophile, giving Lewis acidity-diminished stable silyl-B (dan) and -B(aam) in one pot.

Installation of a naphthalene-1,8-diaminato (dan) substituent on boron centers significantly diminishes the boron-Lewis acidity,¹ thus providing transmetalation-resistant properties to the respective organoboron compounds [R-B(dan)] that are conventionally synthesized by dehydration condensation of organoboronic acids [R-B(OH)₂] and 1,8-diaminonaphthalene (danH₂) (Scheme 1A).² The characteristic feature has been utilized for the boron-masking strategy in the iterative Suzuki-Miyaura coupling (SMC),² where the B(dan) moieties remain intact during the cross-coupling event at Lewis acidic B(OH)₂ or pinacol boronates [B(pin)]. On the other hand, we have disclosed that the B(dan) moieties can be activated toward transmetalation by treatment with t-BuOK, leading to the direct SMC of aryl-^{3,4} and cyclopropyl-B(dan).⁵ In addition to the inactive/active flexible properties in the SMC depending on bases, dan-installation also endows organoboron compounds with air- and water-resistant properties: protodeborylation is substantially suppressed with 2-pyridyl-B(dan),^{3,6} and PhMe₂Si-B(dan)⁷ becomes stable in air, while their B(OH)₂/B (pin) counterparts usually suffer from serious decomposition under these conditions.^{8,9} In this regard, the development of a direct method of synthesizing dan-substituted organoboron compounds,¹⁰ especially heteroaryl ones that are often unstable in their Lewis acidic -B(OH)₂ forms,¹¹ would be an

important subject, since it could open the way to synthetic transformations with heteroaryl-B(dan). We have previously reported on a reaction of Grignard reagents with H-B(dan) that directly produces various R-B(dan) including 2-pyridyland 2-thienyl-B(dan) under transition metal-free conditions (Scheme 1B);⁶ however, this reaction requires organic bromides (R-Br for preparing R-MgBr) and pre-prepared H-B (dan), which would leave something to be desired.¹² Hence, our attention was focused on the use of borates $[R-B(OR')_3]$, one of the most common intermediates in the synthesis of organoboronic acid derivatives, generated from readily accessible $B(OR')_3$ and carbon nucleophiles (R-M, M = Li, MgX) for their direct conversion to R-B(dan). Here we disclose an improved approach to prepare R-B(dan) by using only commercially available reagents, wherein deprotonation of R-H moieties is also usable for generating the requisite carbon nucleophiles (Scheme 1C).

We first conducted a reaction (5 mmol scale) of 5-pyrazolyl lithium, prepared readily by deprotonation of 1-methyl-1*H*-pyr-



Scheme 1 Transition metal-free synthesis of Ar–B(dan).

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azole (1a), with triethylborate $[B(OEt)_3]$; subsequent treatment of the resulting pyrazoylborate $[5-pyrazolyl-B(OEt)_3^-]$ with 1,8diaminonaphthalene and acetic acid, in a similar way to the direct transformation of trialkyl borates $[R-B(OR')_3]$ into pinacol boronates [R-B(pin)],¹³ provided 5-pyrazolyl-B(dan) (2a) in 88% yield (Scheme 2).¹⁴ Because the one-pot direct conversion of a heteroaryl-H bond into a heteroaryl-B(dan) bond can be carried out under non-aqueous conditions, 5-thiazolyl-B(dan) (2b and 2c) could also be synthesized, avoiding the intermediary formation of their protodeborylation-prone $B(OH)_2$ counterparts.^{11b} An acidic C-H moiety of furan (1d) or thiophene (1e) was also convertible into the respective C-B (dan) (2d: 75% and 2e: 70%), and 4,4-dimethyl-2-phenyl-2-oxazoline (1f) and 1,3-dimethoxybenzene (1g) could participate in the reaction via directed ortho metalation. Owing to the diminished boron Lewis acidity, all the heteroaryl-B(dan) and other products mentioned below exhibit sufficient stability under ambient conditions, allowing for their isolation by column chromatography. The use of 1,1'-dilithioferrocene generated by dual deprotonation of ferrocene (1h) resulted in the formation of 1,1'-B(dan)-substituted ferrocene (2h) in 59% yield, and the procedure was also applicable to phenylacetylene (1i) or 1,3dithiane (1j), giving phenylethynyl-B(dan) (2i) or 1,3-dithian-2yl–B(dan) (2j) as air/water-stable compounds.¹⁵

Organic bromides (**1k–1q**) were naturally usable as starting materials (Scheme 3), and thus 2-fluorophenyl–B(dan) (**2k**), 2-pyridyl–B(dan) (**2l**) and 2,2'-B(dan)-substituted 1,1'-binaphthyl (**2m**) were produced through lithium–bromine exchange. In addition, various aryl–B(dan) (**2n–2p**)¹⁶ and alkyl–B(dan) (**2q** and **2r**¹⁷) could be synthesized with the respective Grignard reagents.¹⁸ A carbon nucleophile used for B(dan)-installation was also available by lithium–tin exchange of 2,5-bis(tributyl-



Scheme 2 Synthesis of R–B(dan) from R–H.





stannyl)thiophene (1s) to afford a 63% yield of 2s bearing B(dan) and $SnBu_3$ functionalities on the thiophene ring (Scheme 4).

It should be noted that the present method could also be applied to capturing a silicon nucleophile: air-resistant PhMe₂Si–B(dan) (**2t**) became straightforwardly accessible in 40% yield by treating PhMe₂SiLi with B(OEt)₃ (Scheme 5),^{19,20} while the previous multistep method⁷ required the use of air/ water-sensitive reagents and intermediates [BCl₃, (i-Pr₂N)₂BCl and PhMe₂Si–B(Ni-Pr₂)₂]. A new air-resistant silylborane bearing an anthranilamide substituent on the boron center [PhMe₂Si–B(aam) (**2u**)] was generated by extending the direct synthesis, although the yield was relatively low.²¹ According to the previous procedure using PhMe₂Si–B(Ni-Pr₂)₂, the yield was improved to 65%.

To gain insight into the reaction pathway, we carried out ¹¹B NMR experiments using *n*-BuLi as a carbon nucleophile (Fig. 1). Treatment of $B(OEt)_3$ (18.3 ppm, Fig. 1A) with *n*-BuLi resulted in the generation of an upfield-shifted species (3.0 ppm, Fig. 1B), being in a typical chemical shift range of a tetracoordinate borate.²² The resulting borate [*n*-Bu-B(OEt)₃⁻] remained unchanged upon mixing with 1,8-diaminonaphtha-



Scheme 4 B(dan)-installation via lithium-tin exchange.

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Scheme 5 Synthesis of PhMe₂Si-B(dan) and -B(aam).



Fig. 1 ¹¹B NMR experiments on the reaction pathway.

lene (Fig. 1C), while further addition of acetic acid led to the formation of *n*-Bu–B(dan) (2v) with complete disappearance of the borate (Fig. 1D).²³ These results imply that dan-installation on the boron center does not occur at the tetracoordinate borate stage; the intermediary formed neutral species $[R-B(OEt)_2]$ *via* protonation of the borates would immediately undergo ligand exchange to afford R–B(dan) (Scheme 6).

Finally, the synthetic utility of heteroaryl–B(dan) was demonstrated by the direct SMC: treatment of **2a** with 4-bromoanisole and $Ba(OH)_2$ under Pd–dppf catalysis³ quantitatively provided the coupling product (**3a**), which verifies the protodeborylation-resistant yet enough reactive property of the C–B(dan) bond (Scheme 7). Furthermore, chemoselective



Scheme 6 Proposed reaction pathway.



Scheme 7 Direct SMC of heteroaryl-B(dan).

cross-coupling at the $SnBu_3$ moiety of **2s** gave a 95% yield of **3b**, whose thienyl–B(dan) bond was then coupled with 4-(tri-fluoromethyl)bromobenzene efficiently under the $Ba(OH)_2$ conditions.

Conclusions

We have developed a one-pot direct method for installing the B(dan) moiety without the intermediary formation of sometimes unstable organoboronic acids. The present transition metal-free method is superior to our previous H–B(dan) one⁶ in that organolithium reagents directly generated by deprotonation are usable as carbon nucleophiles;¹² diverse R–B(dan) (R = heteroaryl, aryl, alkynyl, alkyl) endowed with air/waterresistant characters have become accessible in good yields. Moreover, the method was demonstrated to apply to a silicon nucleophile to lead to the direct synthesis of PhMe₂Si–B(dan) and –B(aam). Further studies on the synthetic utilization of the resulting R–B(dan) especially for catalytic carbon–carbon bond-forming reactions are in progress.

Author contributions

K.T. and H.Y. conceived the concept and wrote the manuscript. K.T. conducted most of the experiments and data collection. Y. I. synthesized **2u** according to the previous method. K.N. performed the X-ray crystal structure analysis of **2u**. M.N. provided advice for the research. H.Y. directed the project. All authors have approved the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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