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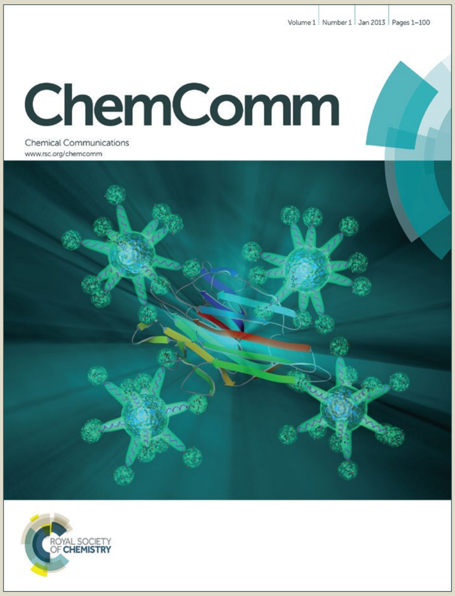

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Catalyst-Free Dehydrocoupling of Amines, Alcohols, and Thiols with Pinacol Borane and 9-Borabicyclononane (9-BBN)

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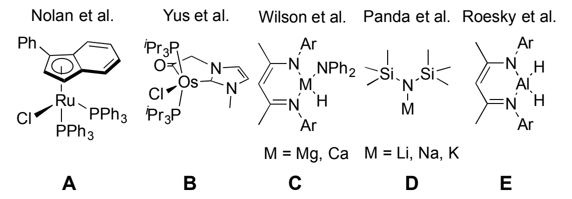
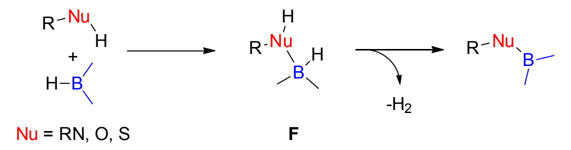
Contrary to recent reports, the dehydrocoupling of pinacol borane and 9-borabicyclononane with a variety of amines, alcohols and thiols can be achieved under mild conditions without catalyst. This process involves the formation of Lewis acid-base adducts featuring a hydridic B–H in close proximity to an acidic Nu–H.

In 2013 Nolan and coworkers[1] described the dehydrocoupling reaction of pinacol and catechol boranes with thiols catalyzed by the ruthenium complex **A** (Fig. 1). More recently, the catalytic dehydrogenative coupling of amines and/or alcohols with 9-borabicyclononane (9-BBN) and/or pinacol borane have been reported using catalysts based on osmium **B**,[2] alkali earth metals **C**,[3] alkali metals **D**,[4] and aluminum **E**.[5] The osmium complex **B** is postulated to utilize metal-ligand cooperativity to activate pinacol borane. The other catalysts (**C**-**E**) are proposed to proceed through metal amido, alkoxide or sulfide intermediates, which readily react with the Lewis acidic hydridoboranes. Subsequent hydride transfer to the corresponding metal yields the highly reactive metal hydride that can deprotonate another equivalent of Nu–H (E = RN, O, S) to close the cycle. Interestingly, these results seem to exclude that pinacol borane and 9-BBN are sufficiently Lewis acidic to form adducts of type **F** shown in Scheme 1. These adducts would feature hydridic B–H bonds in close proximity to acidic Nu–H bonds, and therefore should release H_2 without the need for a catalyst.

Fig. 1. Reported catalysts for the dehydrocoupling of amines, alcohols and thiols with pinacol borane, catechol borane and/or 9-BBN.



Scheme 1. Proposed catalyst-free dehydrocoupling pathway through Lewis acid-base adducts **F**.



Indeed, although numerous catalysts have been reported to promote the dehydrogenation of several amine-borane adducts, including ammonia-borane (NH_3-BH_3), it has also been shown that catalyst-free dehydrogenative processes can occur under thermal conditions.[6] Herein we report the facile catalyst-free dehydrocoupling of amines, alcohols, and thiols with pinacol borane and 9-BBN.[7]

We began our investigation using a stoichiometric mixture of aniline and pinacol borane[8] (0.4 mmol) in 0.4 mL of C_6D_6 (Table 1, Entry 1). After 4 h at room temperature, 60% conversion into **1a** was observed, with no byproducts detected. The influence of the solvent (Entries 1-4) and of the concentration (Entries 5-8) on the rate of the reaction were tested. The best results were found in the absence of solvent.[9] In this case, bubbling of H_2 stopped after 15 minutes at room temperature, and after another 10 minutes the solution solidified. Dissolving this solid in acetonitrile led to nearly quantitative formation of **1a**, the only impurities being traces of pinBOH and aniline.

The scope of the amine dehydrocoupling reaction with pinacol borane was studied in the absence of solvent, except when amines are solid at room temperature; in these cases 0.151 mL of acetonitrile was used with 0.8 mmol of both reactants (Fig. 2). This reaction can be applied to both aliphatic and aromatic amines with varying degrees of steric and electronic contributions. Due to the high selectivity of the dehydrogenative coupling reaction, products **1a-e** and **1g-r** were obtained in good purity (as can be seen from the NMR

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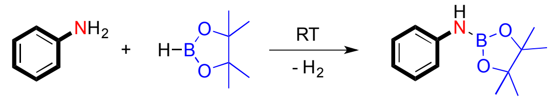
Table 1. Solvent and Concentration Effects on Amine Dehydrocoupling with pinacol borane[a]



Entry	Time (h)	Solvent	Conc. (M)	Conversion (%)[b]
1	4	C_6D_6	0.8	60
2	4	$CDCl_3$	0.8	22
3	4	THF-d_8	0.8	30
4	4	CD_3CN	0.8	75
5	0.5	CD_3CN	0.8	29
6	0.5	CD_3CN	1.3	49
7	0.5	CD_3CN	2.8	85
8	0.5	-	-	94

[a] The reactions were carried out in a J-Young NMR tube at room temperature under an argon atmosphere using a 1:1 mixture (0.40 mmol) of aniline and pinacol borane. [b] Conversion measured by ^1H NMR referencing residual starting aniline.

spectra included in the Supporting Information) by simply removing all volatiles under vacuum.

Interestingly, among all the amines that were considered, 2,6-diisopropylaniline was the only one that appeared to be unreactive even after 24 hours at 120 °C. This prompted us to investigate the mechanism of the dehydrogenative coupling. Monitoring by ^1H NMR spectroscopy the reaction of various amines with pinacol borane does not show the presence of any intermediates. However, in the case of allylamine, the addition of pinacol borane immediately produced a white solid with no hydrogen evolution. The physical state of both starting materials (liquids) suggested that the white solid obtained was the Lewis acid-base adduct **Fg**, which was confirmed by a single crystal X-ray diffraction study (Fig. 3). Upon dissolution of the solid in acetonitrile, ^1H, ^{13}C and ^{11}B NMR analysis initially showed exclusively starting allylamine and free pinacol borane, in agreement with a weak B⋯N interaction. Monitoring the reaction by ^1H NMR, showed complete formation of the dehydrocoupled product **1g** after 24 h (Fig. 4).[10]

These observations confirm that the first step for dehydrocoupling is the reversible formation of **Fg**. To further substantiate this hypothesis, pinacol borane was added to fluorene, which has a comparable Brønsted acidity to that of amines, but (a) lacks the heteroatom coordination ability. No reaction occurred regardless of time and temperature. Similarly, hydrochloric acid failed to react with pinacol borane to form chloropinacolborane. These results highlight the intermediacy of the Lewis adduct in the dehydrocoupling reaction. On the other hand, the stability of **Fg** in the solid state led to the question of whether H_2 elimination is an intra- or intermolecular process. The latter could explain why the dehydrogenative coupling of the very bulky Dipp–NH_2 with pinacolborane did not occur even under elevated temperatures. Indeed, we found that addition of traces of triethylamine[11] allowed for this coupling, the borylated product **1f** being quantitatively formed after 24 hours at 120 °C (Fig. 2). These results suggest that, at least with this sterically hindered substrate, the H_2 elimination is an intermol-

Fig. 2. Substrate scope for the dehydrocoupling of pinacol borane and 9-BBN with amines at room temperature, with conversions measured by ^1H NMR (referencing residual starting amine), and reaction times. [a] 120 °C and 1 mol% NEt_3.

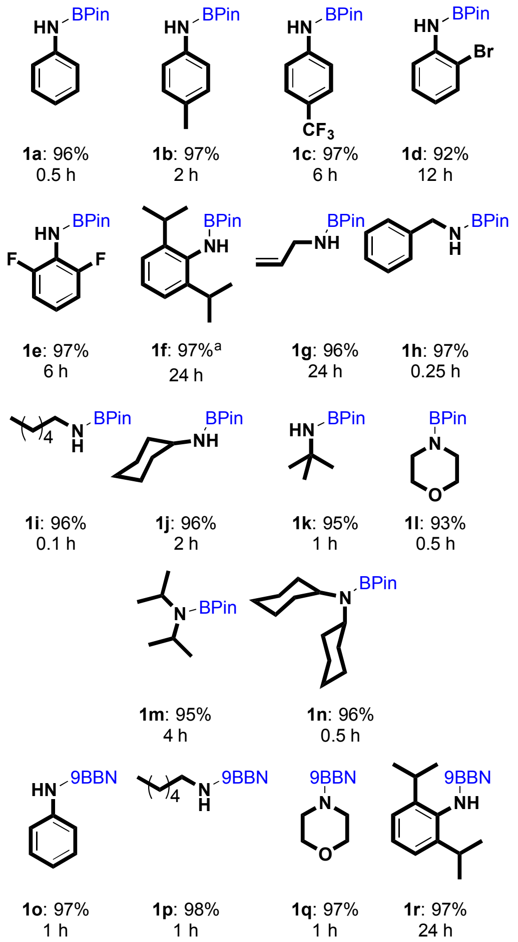


Fig. 3. Solid-state structure of **Fg** at 50% probability thermal ellipsoids (C: grey, N: blue, B: yellow, O: red). Selected bond length: N–B = 1.61(7) Å.

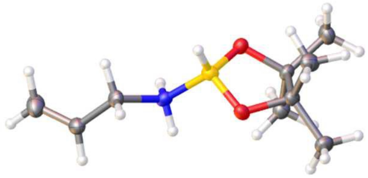
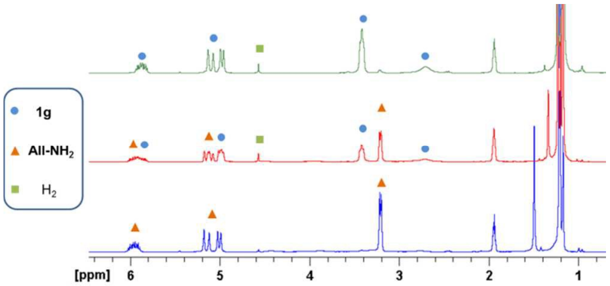


Fig. 4. ^1H NMR spectra of allylamine and pinacol borane in acetonitrile at t_0 (bottom), 12 h (middle), and 24 h (top).



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ecular process.

To extend the scope of the non-catalyzed dehydrocoupling reaction, we then used a broad range of alcohols and phenols as substrates. Under the standard experimental conditions used for amines, we observed quantitative formation of the desired coupling products **2a-k** and **2m-w** within minutes (Fig. 5). Note that here also, traces of triethylamine had to be added when the bulky 2,6-di-*tert*-butylphenol was used (**2l**).

As demonstrated by Roesky and others, the dehydrocoupling of thiols is more challenging than that of amines and alcohols.[5] We found that no reaction occurred between thiols with pinacol borane even at 120 °C for 48 hours. However, addition of 1 mol% of triethylamine allowed a complete conversion into product **3a** and **3b** after 48 h and 96 h, respectively. With 9-BBN, the reaction proceeds at room temperature with dodecane thiol and at 60 °C for 2,6-dimethylthiophenol, without the need for Et_3N.

Fig. 5. Substrate scope for the dehydrocoupling of pinacol and 9-BBN with alcohols and phenols at room temperature with isolated yields. [a]24 h at 120 °C with 1 mol% NEt_3.

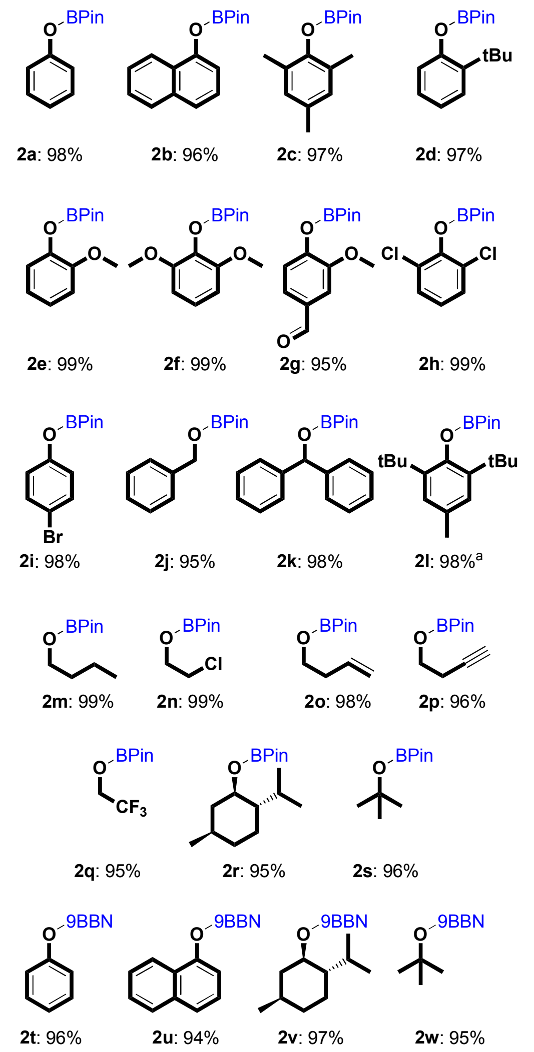
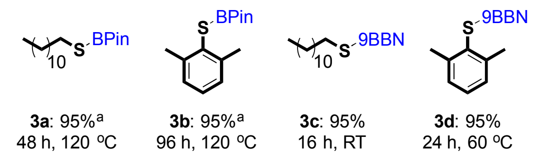


Fig. 6. Substrate scope for the dehydrocoupling of pinacol borane and 9-BBN with thiols with conversions measured by ^1H NMR (referencing residual starting thiol). [a]1 mol% NEt_3.



Herein we have disclosed the first extensive investigation into the non-catalyzed dehydrocoupling of amines, alcohols, and thiols with both pinacol borane and 9-BBN. Among the possible applications of this process is the synthesis of BN containing polymers.[12] In addition, novel uses for these dehydrocoupled products are currently being developed by us and others. For example, Fernandez and coworkers[13] have shown amino- and thio- pinacol boranes to act as convenient sources of E^- with both ynones and Michael acceptors yielding *cis*-1,4-addition products.

Acknowledgements

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