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## Catalytic insertion of nitrenes into B–H bonds†

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Organic compounds with boron–nitrogen bonds are widely used as fluorescent sensors and semiconducting materials. This paper presents a new approach for the formation of B–N bonds *via* catalytic insertion of nitrenes into B–H bonds. The reaction proceeds most selectively for cyclic boranes with a 2-phenylpyridine framework and nitrenes generated *in situ* by the oxidation of sulfonamides and sulfamates. The most effective catalysts for this process are the readily available rhodium and ruthenium carboxylates of [M<sub>2</sub>(OOCR)<sub>4</sub>]X type. Complexes with carboxylate ligands NTTL derived from *S*-*tert*-leucine provide unique chiral products with stereogenic boron atoms. The developed method can be used for the introduction of boron heterocycles into biologically active molecules.

### Introduction

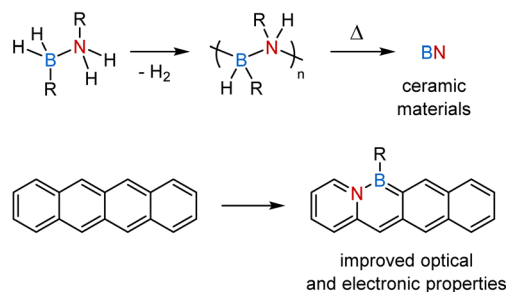
Boron–nitrogen bonds are isoelectronic to ubiquitous carbon–carbon bonds, but due to charge polarization and higher reactivity, they can be even more useful for a variety of applications.<sup>1,2</sup> For example, while alkanes remain relatively inert, their aminoborane analogues RH<sub>2</sub>B–NH<sub>2</sub>R can undergo facile catalytic dehydrogenation, giving polymers that serve as precursors for boron nitride ceramics (Scheme 1a).<sup>3,4</sup> Introduction of B–N fragments in polycyclic molecules remarkably enhances charge transport and other properties of organic optoelectronic materials.<sup>5–9</sup>

Despite the potential utility of compounds with covalent B–N bonds, the methods for their synthesis are essentially confined to two approaches. The first one relies on the direct reaction between boranes R<sub>2</sub>BH and amines R<sub>2</sub>NH to give R<sub>2</sub>B–NR<sub>2</sub> *via* hydrogen evolution, which is mostly used for strongly acidic heterocyclic amines. A more general strategy uses the reaction of boron halides R<sub>2</sub>BHal with nucleophilic amines. However, it has notably restricted functional group tolerance because of the high reactivity and hydrolytic instability of boron halides. Therefore, the development of new, selective methods for the formation of B–N bonds is highly desirable.

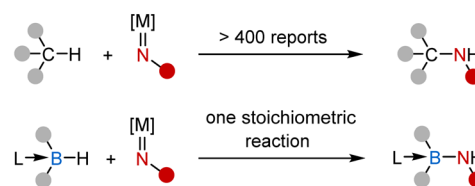
One of the powerful methods for the construction of C–N bonds in complex organic molecules is based on catalytic

reactions of nitrenes (Scheme 1b).<sup>10,11</sup> In recent years, there has been a significant progress in the asymmetric insertion of nitrenes into C–H bonds, sparking the development of new

#### a) Applications of boron-nitrogen compounds



#### b) Nitrene insertion reactions



#### c) This work



- new method for B–N bond formation
- late-stage boron labeling
- chiral-at-boron amidoboranes
- 30+ examples, up to 91:9 er

Scheme 1 Research background and design of this study.

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catalysts and synthetic pathways for the synthesis of valuable chiral amines.<sup>12</sup> Surprisingly, the analogous insertion of nitrenes into much more reactive B–H bonds has remained essentially unexplored.<sup>13–15</sup>

Herein, we report the first detailed investigation of this reaction, which provides a new method for the construction of B–N bonds (Scheme 1c). Due to the high nucleophilicity of boranes, they can react under mild conditions with electrophilic nitrenes generated *in situ* from the corresponding sulfonamides and sulfamates. Insertion of nitrenes into prochiral boranes with the 2-aryl-pyridine framework in the presence of chiral rhodium and ruthenium carboxylates gives access to unique compounds with stereogenic boron atoms. Notably, this nitrene insertion is the only method for the asymmetric formation of covalent B–N bonds.<sup>16,17</sup>

## Results and discussion

### Reaction optimization

We started our investigation by testing the reactions of the common nitrene precursor PhI=NTs with various borane adducts L–BH<sub>3</sub> (**1**) (Table 1). Rh<sub>2</sub>esp<sub>2</sub> catalyst (esp = tetramethyl-1,3-benzenedipropionate) was employed as a natural choice, known for its exceptional robustness in nitrene chemistry, in contrast to other dirhodium(II,II) carboxylates like Rh<sub>2</sub>(OAc)<sub>4</sub> (ref. 18 and 19) The reaction of PhI=NTs with the electron-rich carbene–borane **1a** in the presence of Rh<sub>2</sub>(esp)<sub>2</sub> (2 mol%) immediately gave a mixture of two insertion products – mono-

(**2a**) and bis-amide (**3a**) (entry 1). However, further attempts to enhance the selectivity for the formation of **2a** by reducing the loading of the nitrene precursor and lowering the temperature were unsuccessful. When the sterically hindered borane adduct **1b** bearing two 2,6-diisopropyl-phenyl substituents was used instead of **1a**, no conversion of the borane was observed, despite the prompt full consumption of the starting nitrene precursor. Similarly, the reactions of PhI=NTs with triethylamine and tributyl-phosphine boranes **1c** and **1d** did not provide the desired products, possibly because of the lower nucleophilicity attributed to the higher strength of B–H bonds.<sup>20,21</sup> To our delight, the pyridine–borane complex **1e** afforded the desired mono-amide **2e** with exceptionally high selectivity (entry 5), although we were unable to isolate it in pure form because of its low stability. Interestingly, nitrenes reacted faster with NHC–borane **1a** than pyridine–borane **1e**, while the opposite was observed for the carbene insertion reactions.<sup>20</sup>

Since only the pyridine–borane selectively yielded the mono-insertion product, we decided to enhance its stability by employing the chelated 2-phenylpyridine borane **1f**.<sup>22</sup> Indeed, the reaction of **1f** with PhI=NTs also gave only the mono-amide **2f**, which, unlike pyridine derivative **2e**, can be isolated and purified by standard column chromatography without decomposition. Later inspection revealed that **2f** only slowly decomposes upon standing in air in CDCl<sub>3</sub> solution (*ca.* 5% decomposition over 3 days at 20 °C) and can be stored indefinitely as a solid in a freezer. The obtained NHC-amidoboranes **2a** and **3a** are even more stable and show no decomposition after one week in solution at ambient temperature in air. We were able to confirm the structures of **2a**, **3a**, and **2f** by X-ray diffraction analysis; the structure of **2a** is shown in Fig. 1.

Before proceeding with the investigation of the reaction scope, we explored the activity of other catalysts, which have previously been used in the nitrene insertion reactions, such as Co(TPP) (TPP = tetraphenylporphyrin), [Cu(MeCN)<sub>4</sub>]<sup>+</sup>, and [Au(PPh<sub>3</sub>)]<sup>+</sup>.<sup>12</sup> These complexes also provided the desired product **2f**, albeit in significantly lower yields than Rh<sub>2</sub>(esp)<sub>2</sub> (see the ESI†). At the same time, we were pleased to find out that in the case of the Rh<sub>2</sub>(esp)<sub>2</sub> catalyst, the nitrene precursor PhI=NTs can be generated *in situ* from tosylamide and PhIO oxidant, despite the presence of the potentially oxidizable borane **1f**. The resulting mixture provides **2f** in 54% yield, which is only slightly

Table 1 Catalytic insertion of nitrene derived from PhI=NTs into various B–H bonds

| Entry | Borane    | Conv. <sup>a,b</sup> (%) | Yield <b>2</b> <sup>a</sup> (%) | Yield <b>3</b> <sup>a</sup> (%) |
|-------|-----------|--------------------------|---------------------------------|---------------------------------|
| 1     | <b>1a</b> | 88                       | 24                              | 30                              |
| 2     | <b>1b</b> | <5                       | <5                              | <5                              |
| 3     | <b>1c</b> | 14                       | <5                              | <5                              |
| 4     | <b>1d</b> | 9                        | <5                              | <5                              |
| 5     | <b>1e</b> | 52                       | 50                              | <5                              |
| 6     | <b>1f</b> | 77                       | 69                              | <5                              |

<sup>a</sup> Conversion of the starting boranes and yields of the products were estimated by <sup>1</sup>H NMR spectra of the crude mixtures using 1,3,5-tribromobenzene as the internal standard. <sup>b</sup> Unaccounted amounts of the reacted boranes probably correspond to the formation of polymeric insoluble materials.

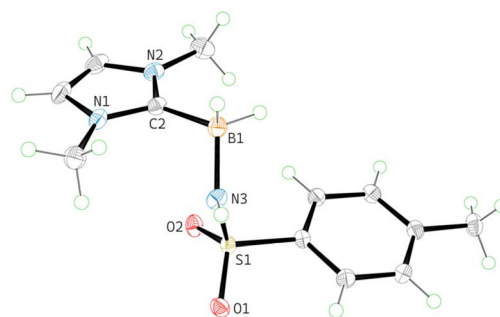


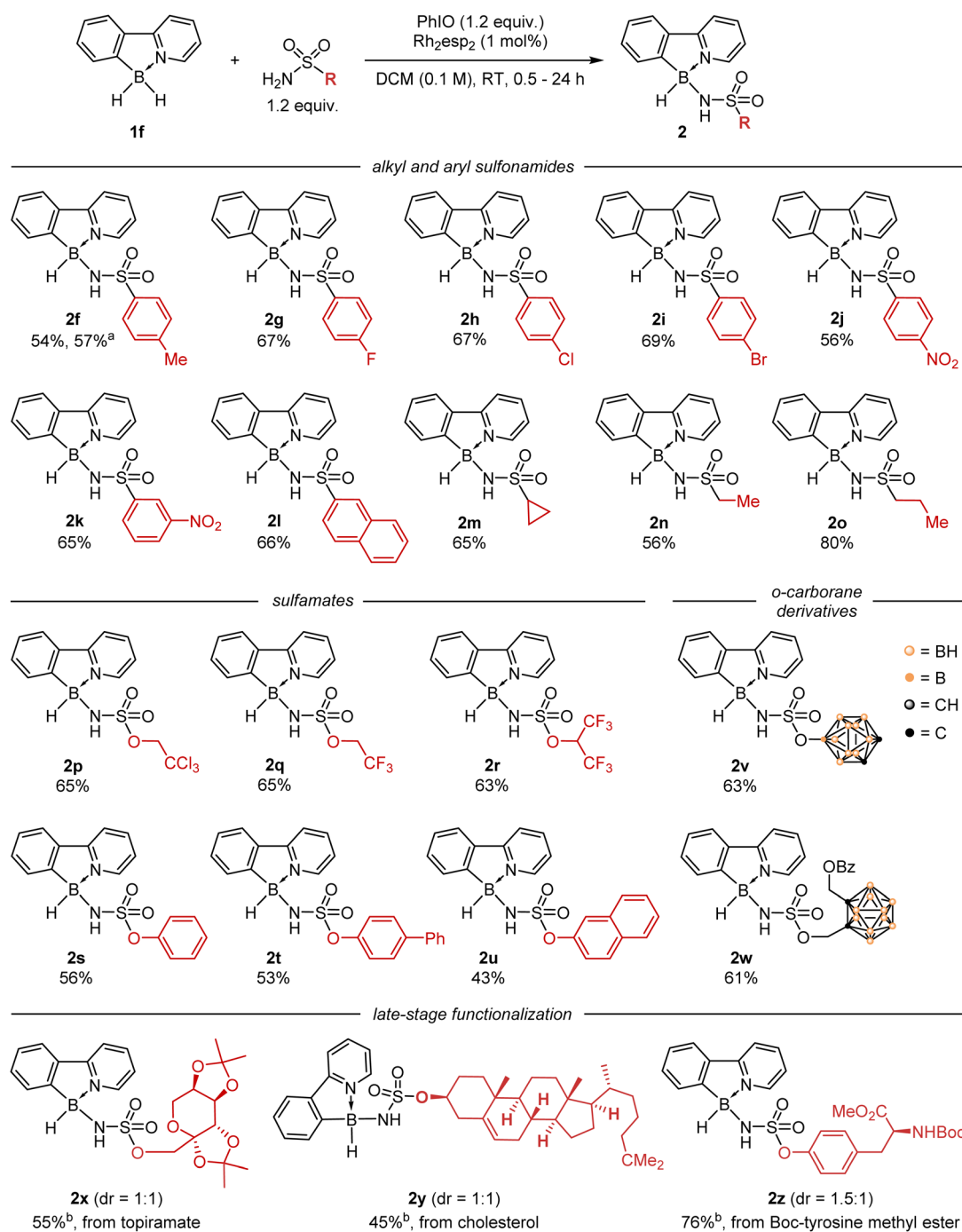
Fig. 1 X-ray structure of **2a**. Atoms are shown as 50% thermal ellipsoids. BH<sub>2</sub> and NH hydrogens were located from the Fourier density synthesis. Selected distances [Å]: B1–C2 1.612(2), B1–N3 1.553(2).



lower than that obtained by the reaction with the preformed iodane. The control experiments showed that borane **1f** does not react with  $\text{TsNH}_2$  or  $\text{PhIO}$  alone, while its reaction with  $\text{TsN}=\text{IPh}$  in the absence of a catalyst proceeded slowly and unselectively (only *ca.* 30% of **2f** was formed, see the ESI†).

### Scope and limitations

With the optimized conditions in hand, we explored the reactivity of various substituted nitrenes in the B–H insertion reaction (Scheme 2). Aryl sulfonamides reacted similarly to  $\text{TsNH}_2$ , giving the desired insertion products **2g–l** in *ca.* 55–65% yields, regardless of the presence of electron-rich (**2i**, Ar = naphthyl) or electron-poor (**2j**, Ar = *p*-nitrophenyl) groups. Even more electron-rich alkyl sulfonamides also reacted smoothly and gave



**Scheme 2** Catalytic insertion of nitrenes derived from sulfonamides and sulfonates into 2-phenylpyridine–borane **1f**. Reaction conditions: **1f** (0.2 mmol), sulfonamide or sulfonate (0.24 mmol),  $\text{PhIO}$  (0.24 mmol),  $\text{Rh}_2\text{esp}_2$  (1 mol%), DCM (2 ml), RT, 0.5 to 24 h. Isolated yields are given. <sup>a</sup> Performed on a 6 mmol scale. <sup>b</sup> Performed on a 0.1 mmol scale.

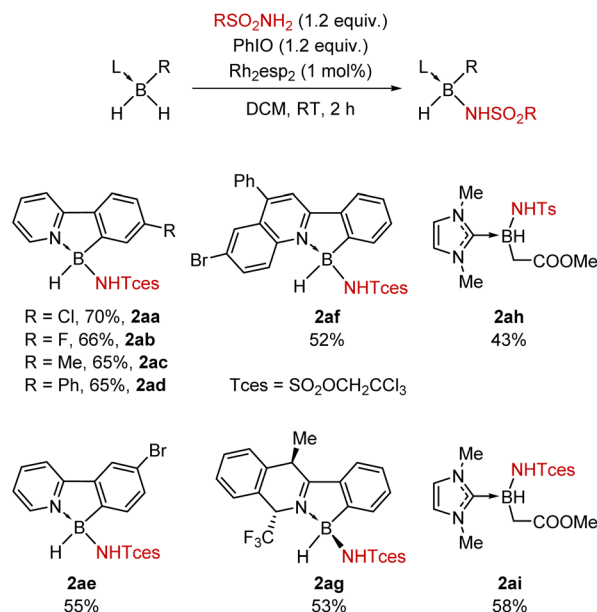


products **2m–o**, although the reaction time for these substrates had to be extended up to 24 hours (aryl sulfamides usually reacted within 1 hour).

Then we explored the reactivity of the more electron-deficient sulfamates  $\text{ROSO}_2\text{NH}_2$ . The classic trichloroethyl sulfamate ( $\text{TcesNH}_2$ )<sup>23</sup> reacted with **1f** much faster than  $\text{TsNH}_2$ , reaching the full conversion within a few minutes and giving the corresponding product **2p** in 65% yield. Other polyhalogenated alkyl sulfamates, as well as aryl sulfamates, provided the expected products **2q–u** in comparable yields. It should be noted that the resulting compounds are somewhat less stable than sulfonamide insertion products **2f–o**, and some decomposition was observed upon standing in solution in air for 24 hours. Given the interest in carboranes as unique structural pharmacophores for drug design,<sup>24,25</sup> we also carried out the reaction with two carborane sulfamate derivatives, which gave the target products **2v** and **2w** in *ca.* 60% yields. It is noteworthy that intramolecular insertion of nitrene into less electron-rich B–H bonds of the carborane core was not observed, although similar reactions are known in the literature.<sup>14</sup> Finally, we examined the possibility of using the developed strategy for the late-stage functionalization of sulfamates derived from natural compounds. It was found that primary (**2x**, topiramate derivative), secondary (**2y**, cholesterol derivative), and aryl sulfamates (**2z**, tyrosine derivative) reacted smoothly with **1f** to give the desired products. This approach may be useful for boron labelling of biologically active molecules.

Overall, this scope demonstrates that borane **1f** can react with a variety of nitrene precursors. This situation is markedly different from the catalytic nitrene insertion into C–H bonds, which usually require some specific nitrene precursors such as  $\text{TcesNH}_2$ . These results are consistent with the fact that B–H bonds are, in general, much more reactive than C–H bonds.<sup>20</sup> However, nitrenes with low electrophilicity seem to be not suitable for selective B–H insertion. Thus, no reaction occurs upon heating **1f** with benzyl azide at 60 °C, while heating with tosyl azide converts only 50% of the borane into **2f** after 120 h. The use of the rhodium catalyst  $\text{Rh}_2\text{esp}_2$  did not improve the rate and apparently decreased the selectivity of this reaction. No conversion of **1f** was observed in the reaction with 3-phenyl-1,4,2-dioxazolone-5 in the presence of the  $[\text{Cp}^*\text{RhCl}_2]/\text{NaBAR}_4$  catalyst<sup>26</sup> as well as in the reaction with  $\text{BocNH}_2$  and  $\text{PhI}(\text{OAc})_2$  in the presence of  $\text{Rh}_2\text{esp}_2$ .<sup>27</sup> The activated trichloroethyl carbamate  $\text{TrocNH}_2$  quickly reacted with **1f** under similar conditions, however we could not isolate the corresponding insertion product in the pure form due to its low stability.

We further expanded the scope of accessible products by varying the structure of starting boranes (Scheme 3). The introduction of substituents into the phenylpyridine framework did not hamper the insertion of nitrene generated from  $\text{TcesNH}_2$  and the corresponding products **2aa–ae** were obtained in good yields (55–70%). The reaction also proceeded well for the quinoline and dihydroisoquinoline derivatives giving the amidoboranes **2af** and **2ag**. As noted above, NHC–borane **1a** reacts with  $\text{PhI}=\text{NTs}$  giving a mixture of mono- and bis-insertion products. However, when **1a** was first modified by the insertion of methyl diazoacetate into the B–H bond,<sup>28,29</sup>



**Scheme 3** Catalytic insertion of nitrenes into various boranes. Reaction conditions: borane (0.2 mmol),  $\text{TsNH}_2$  or  $\text{TcesNH}_2$  (0.24 mmol),  $\text{PhIO}$  (0.24 mmol),  $\text{Rh}_2\text{esp}_2$  (1 mol%), DCM (2 ml). Isolated yields are given.

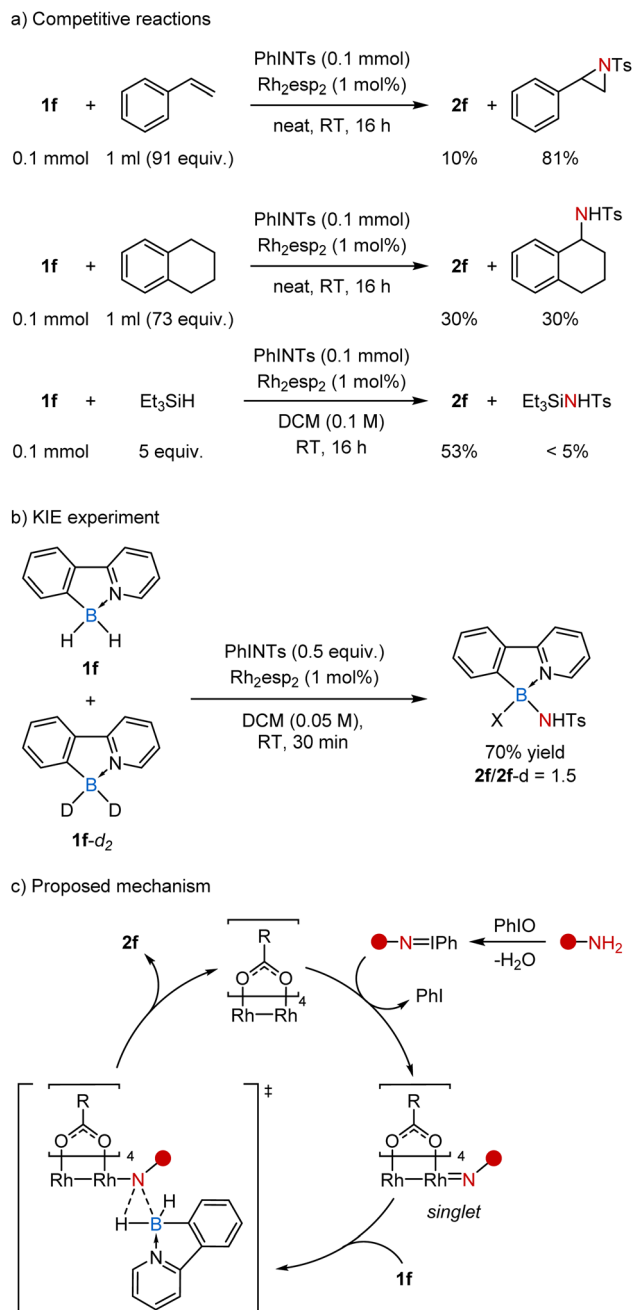
further insertion of nitrenes proceeded smoothly and gave the amides **2ah** and **2ai** in 43% and 58% yields.

### Mechanistic studies

To get a deeper understanding of the reaction, we performed several mechanistic studies (Scheme 4). In particular, the competitive reaction **1f** with  $\text{PhI}=\text{NTs}$  in neat styrene (91 equiv.) gave mostly the corresponding aziridine (81%) along with only minor amounts of **2f** (10%) due to low conversion of **1f** (14%). At the same time, a similar reaction in tetralin, which is a common substrate for nitrene insertion, led to the products of amination of B–H and C–H bonds in a 1 : 1 ratio. Considering the ratio of the starting borane to tetralin (1 : 73) and the number of potentially reactive hydrogen atoms, the B–H bond in **1f** appears to be *ca.* 150 times more reactive than the benzylic C–H bond. Similarly, the competitive reaction of **1f** with  $\text{PhI}=\text{NTs}$  in the presence of triethylsilane revealed that the B–H bond is at least 50 times more reactive than the Si–H bond.

The competitive reaction of **1f** and its deuterated analog **1f-d<sub>2</sub>** with  $\text{PhI}=\text{NTs}$  provided a mixture of products **2f** and **2f-d** in a 1.5 : 1 ratio, regardless of the conversion of starting materials (Scheme 4b). This kinetic isotopic effect (KIE) is similar to that previously observed for Rh-catalyzed carbene insertion into B–H bonds (KIE = 1.5)<sup>30</sup> and somewhat lower than the one obtained for the Rh-catalyzed nitrene insertion into C–H bonds (KIE = 2.6).<sup>31</sup> It is generally assumed that KIE values lower than 3 indicate a concerted insertion mechanism involving metal complexes with singlet nitrenes.<sup>32</sup> Thus, the reaction appears to follow the classical mechanism, similar to the one proposed for the well-studied C–H insertion reactions (Scheme 4c).<sup>33</sup> Initially, amide reacts with  $\text{PhIO}$  to form the imino-iodane. Next it





Scheme 4 Mechanistic studies.

coordinates with the rhodium catalyst, releases PhI, and forms a singlet nitrene complex. Finally, this electrophilic complex reacts with the nucleophilic borane in a concerted fashion to form the desired B–N bond.

### Asymmetric insertion

The cyclic amidoboranes **2** obtained in this work contain a stereogenic boron atom with four different substituents. While chiral stereogenic boron compounds sporadically appeared in the literature, the protocols for their synthesis have not been developed until very recently.<sup>16,34</sup> Within the last decade, M.-H. Xu *et al.*,<sup>35–37</sup> S.-F. Zhu *et al.*,<sup>38–40</sup> and several other

groups<sup>41,42</sup> demonstrated that rhodium and copper-catalyzed insertion of carbenes into B–H bonds can produce boranes with stereogenic carbon atoms. More recently, Yu and Song *et al.* used a similar reaction of 2-arylpiperidine boranes to synthesize compounds with stereogenic boron atoms<sup>43,44</sup> (see also a related work on NHC–boranes).<sup>45</sup> Therefore, we assumed that similar nitrene insertion can afford the chiral amidoboranes.

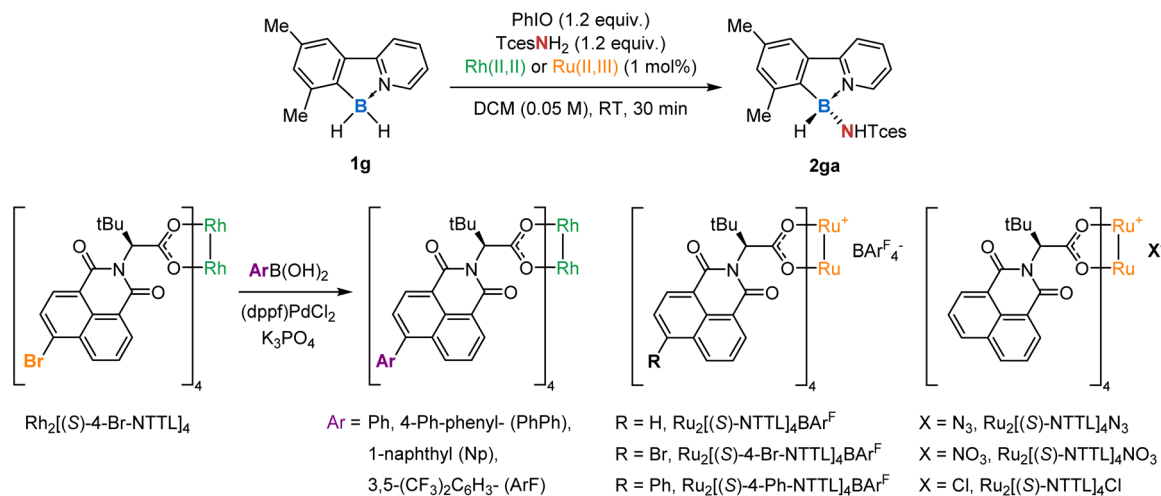
For our study, we strategically chose the dimethyl-substituted prochiral borane **1g** (Table 2) as the starting material over the unsubstituted **1f** for two reasons. First, the presence of two methyl groups makes the benzene ring sterically more different from the pyridine ring, which was expected to provide better asymmetric induction. Second, *ortho*-substituents can prevent potential racemization of the stereogenic boron center *via* the dissociation of the B–Py bond and the rotation of the BHNHTs group.<sup>46</sup>

Since rhodium carboxylates were shown to be the most effective catalysts for the nitrene B–H insertion, we tested the selectivity of different chiral paddlewheel Rh(II,II) complexes in the reaction of **1g** with TcesNH<sub>2</sub> and PhIO. However, among 12 tested catalysts only one, namely Rh<sub>2</sub>[(*S*)-NTTL]<sub>4</sub>, gave the insertion product **2ga** with notable enantioselectivity 62 : 38 er. We continued catalyst screening by varying the substituents in the naphthalimide core of the NTTL ligand (Table 2). Previously, the Davies group has demonstrated that rhodium complexes with a bromo-substituted TPCP ligand can be easily modified by the classic Suzuki–Miyaura reaction.<sup>29</sup> We expanded this approach to NTTL complexes. Thus, fourfold cross-coupling reactions between Rh<sub>2</sub>[(*S*)-4-Br-NTTL]<sub>4</sub> and various boronic acids gave a series of aryl-substituted Rh<sub>2</sub>[(*S*)-4-Ar-NTTL]<sub>4</sub> complexes in good yields. Among those, the simple phenyl-substituted catalyst Rh<sub>2</sub>[(*S*)-4-Ph-NTTL]<sub>4</sub> was found to be the most effective and gave the desired insertion product **2ga** with 67 : 33 er (Table 2, entry 3). Subsequent optimization of the reaction conditions, in particular, lowering the temperature to –30 °C and changing the solvent to chlorobenzene, allowed us to synthesize **2ga** in 91% yield and with a decent 82 : 18 er (entry 7).

In an attempt to enhance the enantioselectivity we decided to replace rhodium carboxylates with their ruthenium analogs [Ru<sub>2</sub>(OOCR)<sub>4</sub>]X. Recently, the Matsunaga group has shown that these complexes can outperform classic rhodium carboxylates in terms of robustness and stereoselectivity.<sup>47,48</sup> We explored the catalytic activity of several ruthenium carboxylates bearing NTTL-ligands and found that they reacted more slowly than rhodium analogs, but somewhat more selectively (Table 2, entries 8–10). Interestingly, there was no direct succession of the substituent effects in the NTTL core upon the transition from rhodium to ruthenium complexes. For instance, the 4-phenyl-substituted rhodium complex showed the highest enantioselectivity, which was not the case for ruthenium analogs. We briefly investigated the role of the counter-ion X in [Ru<sub>2</sub>(OOCR)<sub>4</sub>]X complexes, since Davies *et al.* recently have shown that it may significantly influence selectivity.<sup>49</sup> However, in our case changing X from BAr<sup>F</sup> to Cl, N<sub>3</sub>, or NO<sub>3</sub> had only little effect (entries 11–13). On the other hand, lowering the reaction



Table 2 Catalyst screening for the asymmetric B–H insertion reaction



| Entry | Catalyst  | Yield <sup>a</sup> , % | er <sup>b</sup> | Entry | Catalyst   | Yield <sup>a</sup> , % | er <sup>b</sup> |
|-------|---|------------------------|-----------------|-------|--|------------------------|-----------------|
| 1     | $\text{Rh}_2[(S)\text{-}NTTL]_4$                      | 85                     | 62 : 38         | 8     | $\text{Ru}_2[(S)\text{-}NTTL]_4\text{BAR}^F$             | 71                     | 70 : 30         |
| 2     | $\text{Rh}_2[(S)\text{-}4\text{-Br-NTTL}]_4$          | 78                     | 59 : 41         | 9     | $\text{Ru}_2[(S)\text{-}4\text{-Br-NTTL}]_4\text{BAR}^F$ | 60                     | 68 : 32         |
| 3     | $\text{Rh}_2[(S)\text{-}4\text{-Ph-NTTL}]_4$          | 77                     | 67 : 33         | 10    | $\text{Ru}_2[(S)\text{-}4\text{-Ph-NTTL}]_4\text{BAR}^F$ | 44                     | 60 : 40         |
| 4     | $\text{Rh}_2[(S)\text{-}4\text{-PhPh-NTTL}]_4$        | 69                     | 66 : 34         | 11    | $\text{Ru}_2[(S)\text{-}NTTL]_4\text{N}_3$               | 69                     | 71 : 29         |
| 5     | $\text{Rh}_2[(S)\text{-}4\text{-Np-NTTL}]_4$          | 64                     | 65 : 35         | 12    | $\text{Ru}_2[(S)\text{-}NTTL]_4\text{NO}_3$              | 63                     | 72 : 28         |
| 6     | $\text{Rh}_2[(S)\text{-}4\text{-Ar}^F\text{-NTTL}]_4$ | 71                     | 55 : 45         | 13    | $\text{Ru}_2[(S)\text{-}NTTL]_4\text{Cl}$                | 63                     | 72 : 28         |
| 7     | $\text{Rh}_2[(S)\text{-}4\text{-Ph-NTTL}]_4^c$        | 91                     | 82 : 18         | 14    | $\text{Ru}_2[(S)\text{-}NTTL]_4\text{Cl}^d$              | 81                     | 83 : 17         |

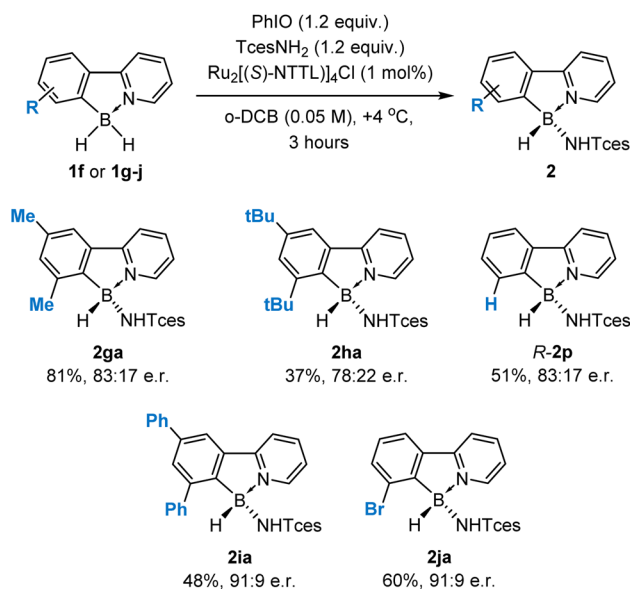
<sup>a</sup> Isolated yields are given. <sup>b</sup> Determined by chiral HPLC. <sup>c</sup> PhCl as a solvent,  $-30^\circ\text{C}$  for 24 hours. <sup>d</sup> *o*-DCB as a solvent,  $+4^\circ\text{C}$  for 6 hours.

temperature to  $+4^\circ\text{C}$  and changing the solvent to *o*- $\text{C}_6\text{H}_4\text{Cl}_2$  allowed us to obtain the target amidoborane **2ga** in 81% yield and with 83 : 17 er using the simple  $[\text{Ru}_2[(S)\text{-}NTTL]_4]\text{Cl}$  catalyst (entry 14). Noteworthy, the control experiment revealed that borane **1f** can react with highly electrophilic  $\text{TcesNH}_2$  and  $\text{PhIO}$  even in the absence of the rhodium or ruthenium catalysts and this side-process can diminish the selectivity at  $20^\circ\text{C}$ .

We then explored the scope of this asymmetric reaction and the effects of substituent in the phenyl ring of phenylpyridine boranes **1g–j** on the enantioselectivity (Scheme 5). In contrast to our expectation, the introduction of the bulky *t*Bu group in the *ortho*-position to the boron atom (**2ha**) had no positive effect on selectivity and only decreased the overall yield, apparently, because of the excessive steric repulsion. We were also surprised to find that the unsubstituted borane **1f** undergoes nitrene insertion with decent enantioselectivity, giving the product *R*-**2m** with 83 : 17 er. Both phenyl and bromo-substituted boranes were converted into the target products with good enantioselectivities 91 : 9 er.

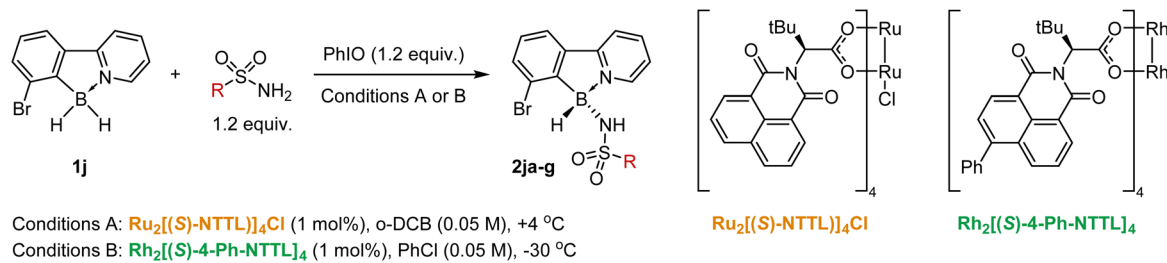
Finally, we explored the asymmetric insertion of different nitrenes into the bromo-substituted borane **1j** using the  $[\text{Ru}_2[(S)\text{-}NTTL]_4]\text{Cl}$  catalyst (Scheme 6). Two factors were found to be necessary to achieve high efficiency under the optimized conditions: (1) high electrophilicity of the nitrene species (for high yields), and (2) the presence of  $-\text{OCH}_2-$  moiety next to the sulfur (for high stereoselectivity). Thus, electron-deficient sulfamates, such as  $\text{CF}_3\text{CH}_2\text{OSO}_2\text{NH}_2$ ,  $\text{C}_3\text{F}_7\text{CH}_2\text{OSO}_2\text{NH}_2$ , and

$\text{C}_6\text{F}_5\text{CH}_2\text{OSO}_2\text{NH}_2$ , which were previously found to be effective nitrene precursors,<sup>50,51</sup> gave the desired products **2jb–jd** in 60–70% yields with about 90 : 10 er. Other sulfamates and sulfonamides gave amidoborane products **2je–jg** with much lower enantioselectivity. In particular, electron-deficient

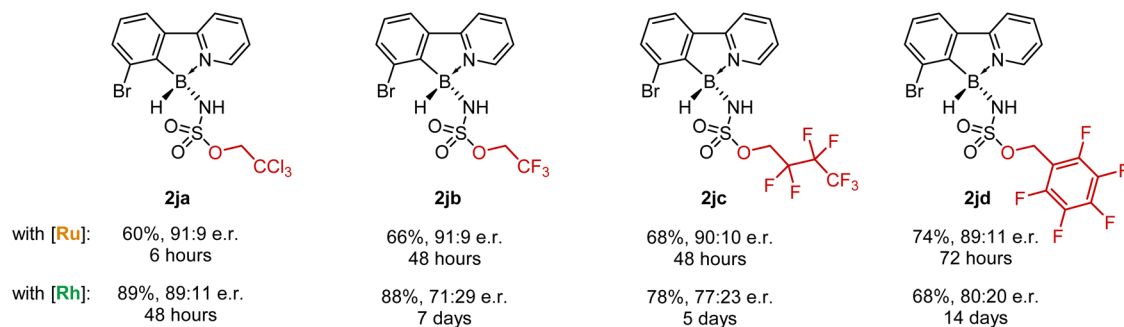


Scheme 5 Scope of 2-phenylpyridines.

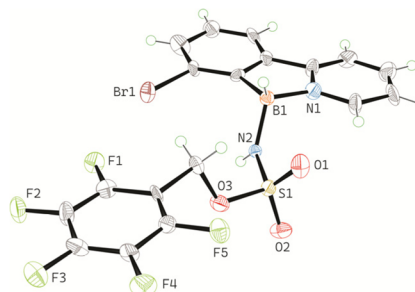
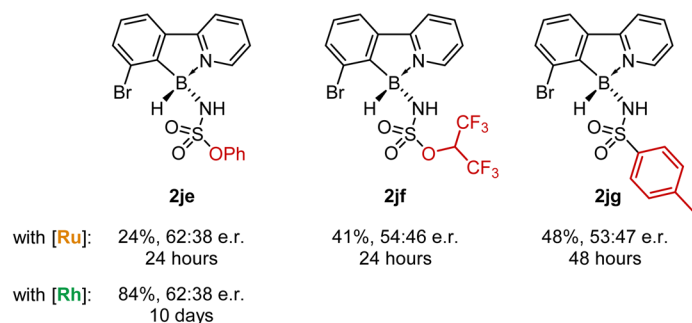




primary sulfamates



other substrates



Scheme 6 Scope of suitable nitrenes and crystal structure of the chiral product 2jd.

hexafluoroisopropyl sulfamate gave almost a racemic product 2jf, indicating the importance of the  $-\text{OCH}_2-$  group. We also investigated the catalytic activity of the rhodium complex  $\text{Rh}_2[(S)\text{-4-Ph-NTTL}]_4$ , but it gave products 2ja–je with lower selectivity.

The absolute configuration of the boron stereocenter (*R*) was established by X-ray diffraction analysis of the product 2jd. Surprisingly, the crystal unit cell contains two independent molecules, the one being the *R*-enantiomer and the other being the superposition of *R*- and *S*-enantiomers with 77% and 23% contributions, respectively. Thus, the overall enantiomeric purity of the crystalline sample closely corresponds to the enantiomeric excess measured in solution by chiral HPLC.

## Conclusions

The initial goal of this project was to explore the reactivity of classical nitrene species with non-classical substrates. Interestingly, the least active C–H bonds are in fact the most studied in nitrene insertion reactions. Undoubtedly, catalytic amination of hydrocarbons is a valuable tool in organic synthesis, but why

more reactive boranes have not been tested? This question haunted our mind for quite some time, because, from a fundamental viewpoint, nothing should interfere with the existence of such a reaction. As we began our project on B–H nitrene insertion reactions, we quickly realized the main problem was not the reactivity, but the stability of the products. After adjusting the surroundings of the boron center, we found the cyclic arylpyridine boranes to be the most suitable substrates. As a result of these studies, the first method for the catalytic insertion of nitrenes into B–H bonds was developed.

Since the resulting cyclic amidoboranes contained a stereogenic boron center, we decided to explore an enantioselective version of this reaction. The only thing to be done was to find a suitable chiral catalyst. This looked like a rather simple task, since many different rhodium carboxylates were introduced since the pioneering studies of Davies and Doyle.<sup>52,53</sup> However, only  $\text{M}_2[\text{NTTL}]_4\text{X}$  ( $\text{M} = \text{Rh}$  or  $\text{Ru}$ ) phthalimide carboxylates were found to be effective in terms of stereoselectivity, allowing for the synthesis of chiral-at-boron products with er up to 91:9. Owing to the exceptionally high stability of dirhodium and diruthenium cores, the structures of the catalysts can be tuned



by the cross-coupling reactions of the preformed bromo-substituted complexes  $M[(S)\text{-}4\text{-Br-NTTL}]_4$ . This approach can certainly be useful for post-modification of other carboxylate complexes. The reasons why only NTTL-bearing catalysts provide reasonable enantioselectivity for nitrene insertion into B–H bonds remain unclear. It is well known that dirhodium(II,II) carboxylates have exceptionally high conformational flexibility. While X-ray analysis of crystals has been previously considered to be helpful for rationalization of the observed selectivity, today it has become clear that one must have information about the three-dimensional shape of the catalyst in solution.<sup>54,55</sup> Significant progress has been made to address this issue in the recent studies of Davies and Sigman groups.<sup>56–59</sup> However, the proposed descriptor models are still unintuitive and computationally expensive.

Following Matsunaga *et al.*,<sup>47</sup> we confirmed that ruthenium carboxylates can be used as more selective alternatives for the classic rhodium catalysts despite their significantly lower activity. The exceedingly high reactivity of dirhodium paddlewheel complexes allows one to replace them with less active analogs and still carry out reactions under mild conditions.

We believe that the proposed method for nitrene insertion in B–H bonds will be useful for the synthesis of new organoboron compounds, which can find application in materials chemistry and biochemistry. Further efforts may be focused on the improvement of the thermal and chemical stability of the resulting amidoboranes. However, the products obtained in this study are already stable enough to be studied in the context of various applications.<sup>60</sup>

## Data availability

All the data supporting this article have been included in the ESI.†

## Author contributions

N. M. A. and D. S. P. – conceptualization; N. M. A. and N. V. A. – investigation (lead); E. S. P., D. A. C., K. A. L., and D. S. P. – investigation (supporting); N. M. A. and D. S. P. – writing original draft.

## Conflicts of interest

There are no conflicts to declare.

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