Rhodium-catalyzed insertion of nitrenes into B–H bonds

Nikita M. Ankudinov,[a,*] Nikita V. Alexeev,[a,b] Evgeniya S. Podyacheva,[a,c] Denis A. Chusov,[a,c] Konstantin A. Lyssenko,[b,c] Dmitry S. Perekalin[a,c,*]

[a] A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 Vavilova str., Moscow 119334, Russia.

[b] Lomonosov Moscow State University, Leninskie gory 1 bld. 3, Moscow 119991, Russia.

[c] National Research University Higher School of Economics, 7 Vavilova str., Moscow 117312, Russia.

ABSTRACT: The paper presents a new method for the formation of B-N bond by the catalytic insertion of nitrenes into organic boranes. The reaction proceeds most selectively for cyclic boranes with 2-phenylpyridine framework and nitrenes generated *in situ* by oxidation sulfonamides and sulfamates. The most effective catalysts for the process are rhodium and ruthenium carboxylates of $[M_2(OOCR)_4]X$ type. Complexes with NTTL ligands derived from S-*tert*-leucine provide chiral products with stereogenic boron atoms. The developed approach can be useful for the introduction of boron heterocycles into functional materials and biologically active molecules.

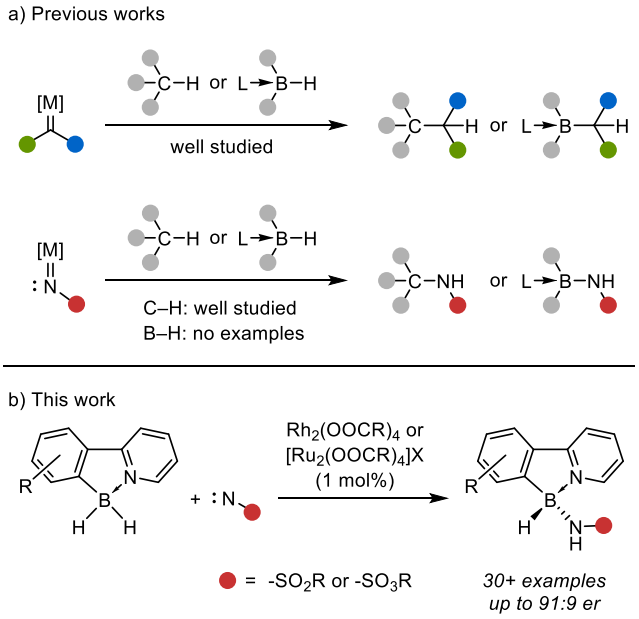
INTRODUCTION

Metal-catalyzed insertion of carbenes into C-H bonds is a powerful method for the construction of complex organic molecules (Scheme 1).[1,2] It is widely employed for the synthesis of natural compounds and late-stage functionalization of biologically active molecules. Due to the development of various catalysts (most notably rhodium carboxylates and copper bis(oxazoline) complexes), such insertion reactions can be carried out with high regio- and enantioselectivity to obtain valuable chiral products. About a decade ago, this approach has been extended to carbene insertion into B-H bonds of L-BH_3 adducts, which provided useful chiral boranes that are inaccessible by other methods, such as hydroboration or direct borylation.[3–8] Moreover, unique compounds with stereogenic boron centers have been obtained this way.[9]

Like carbenes, nitrenes are highly reactive species that can undergo similar metal-catalyzed reactions.[10] In recent years, there has been significant interest in the asymmetric insertion of nitrenes into C-H bonds, sparking the development of new catalysts and synthetic pathways for the synthesis of valuable chiral amines.[11] However, similar insertion of nitrenes into B-H bonds has remained completely unknown, to the best of our knowledge.[12,13]

Herein, we report a first investigation of a such reaction, which provides a new method for the construction of B–N bonds (Scheme 1). Due to the high nucleophilicity of boranes, they react under mild conditions with electrophilic nitrenes generated *in situ* from the corresponding sulfonamides and sulfamates. Insertion of nitrenes into prochiral boranes with 2-aryl-pyridine framework in the presence of chiral rhodium and ruthenium carboxylates gives access to rare compounds with stereogenic boron centers.

Scheme 1. Metal-catalyzed insertion of carbene and nitrenes into C–H and B–H bonds.

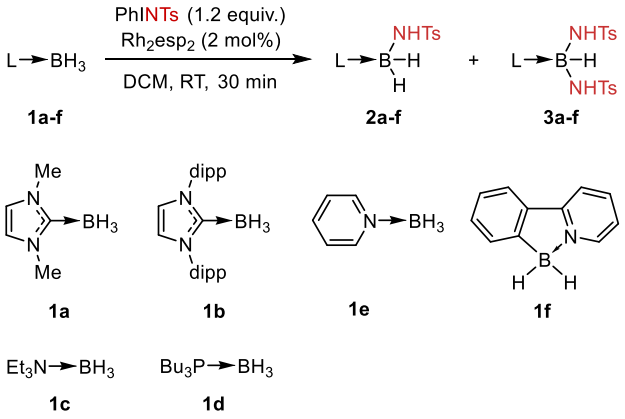


RESULTS AND DISCUSSION

Reaction Optimization. We started our investigation by exploring the reactivity of the common nitrene precursor PhI=NTs with various borane adducts L-BH_3 (**1**) (Table 1). Rh_2esp_2 catalyst was employed as a natural choice, known for its exceptional robustness in nitrene chemistry, in contrast to other dirhodium(II,II) carboxylates like $Rh_2(OAc)_4$[14,15]

The reaction of PhI=NTs with the highly nucleophilic 1,3-dimethylimidazoyl-2-ylidene borane (**1a**) in the presence of $Rh_2(esp)_2$ (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 **1a** 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-diisopropylphenyl substituents was used instead of **1a**, no insertion products were observed, despite the prompt full conversion of the starting nitrene precursor. Similarly, the reactions of PhI=NTs with triethylamine- and tributylphosphine boranes **1c** and **1d** did not provide any desired products, possibly because of the lower nucleophilicity attributed to the higher B–H BDE values.[16,17] To our delight, the pyridine-borane complex **1e** gave the desired mono-amide **2e** with exceptionally high selectivity (entry 5), although we were unable to isolate it in pure form because of its instability. Interestingly, nitrenes reacted faster with NHC-borane **1a** than pyridine-borane **1e**, while the opposite was observed for the carbene insertion reactions.[16]

Table 1. Insertion of nitrene derived from PhI=NTs into various B–H bonds.



entry	SM	conv (%)[a]	yield **2** (%)[a]	yield **3** (%)[a]
1	**1a**	87	24	30
2	**1b**	< 5	< 5	< 5
3	**1c**	14	< 5	< 5
4	**1d**	9	< 5	< 5
5	**1e**	52	50	< 5
6	**1f**	77	69	< 5

[a] Conversion of the starting boranes and yields of the products were estimated by ^{1}H NMR spectra of the crude mixtures using 1,3,5-tribromobenzene as the internal standard.

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**.[18] 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 significant decomposition. Later inspection revealed that **2f** slowly decomposes upon standing in air in $CDCl_3$ solution (ca. 5% decomposition over 3 days at 20 °C), but can be stored indefinitely as a solid in a freezer. The obtained NHC-amidoboranes **2a** and **3a** are even more stable, showing 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 analysis; the structure of **2a** is shown in Figure 1.

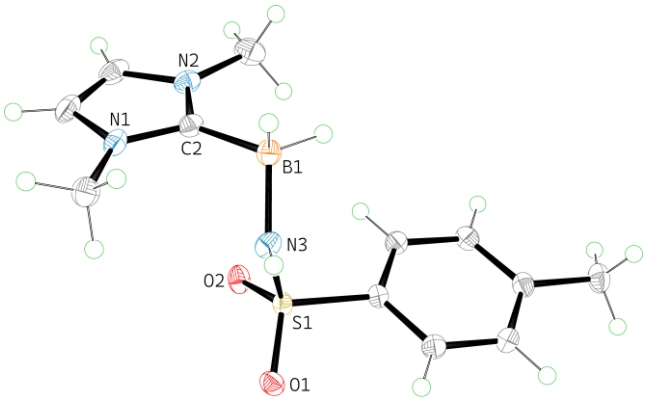


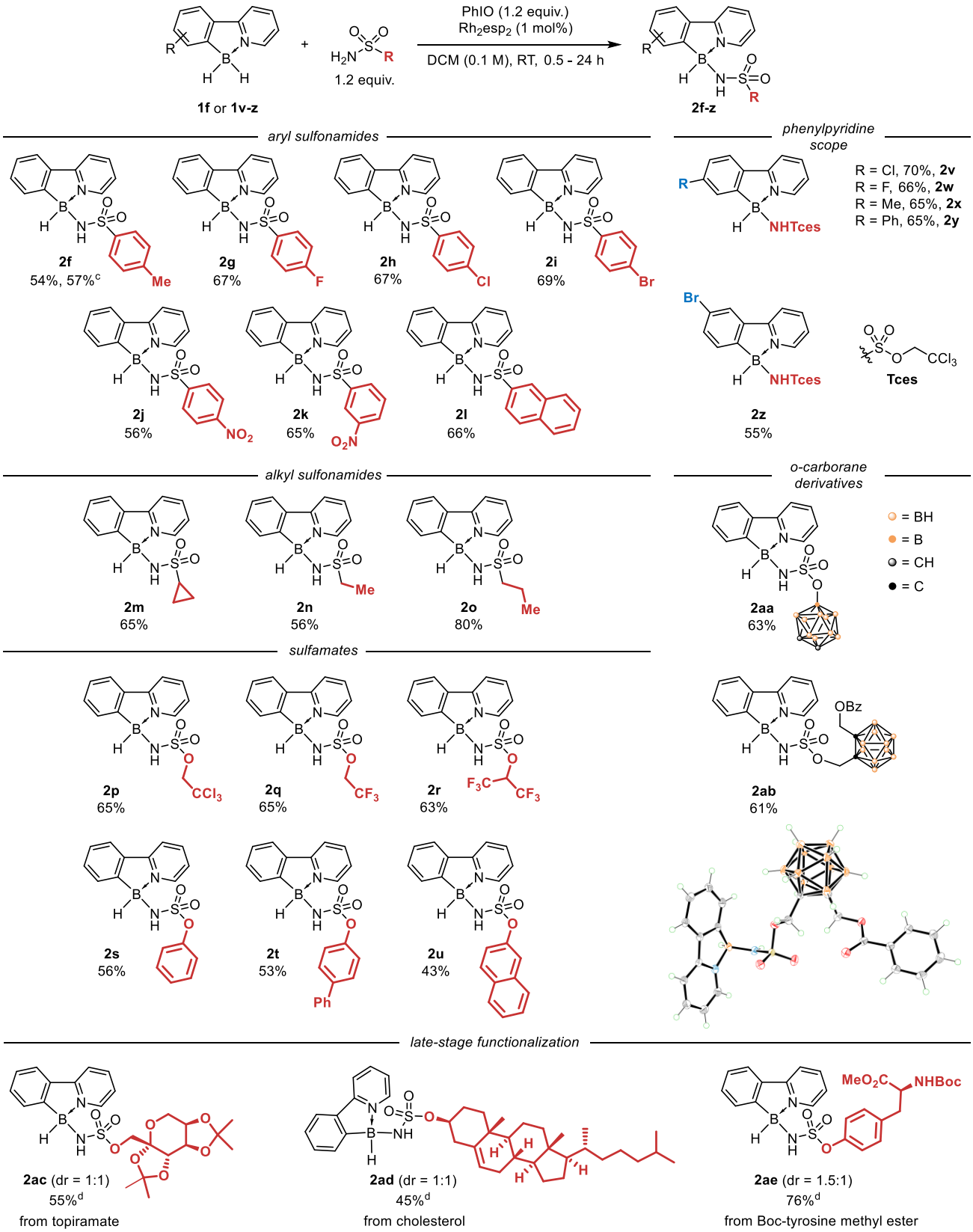
Figure 1. X-ray structure of **2a**. Atoms are shown as 50% thermal ellipsoids. Selected distances [Å]: B1–C2 1.612(2), B1–N3 1.553(2).

Before proceeding with 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), $[Cu(MeCN)_4]^+$, and $[Au(PPh_3)]^+$.[11] These complexes also provided the desired product **2f**, albeit in significantly lower yields than $Rh_2(esp)_2$ (see SI). At the same time, we were pleased to find out that in the case of $Rh_2(esp)_2$ catalyst, the nitrene precursor PhI=NTs can be generated *in situ* from tosylamide and PhIO oxidant, despite the presence of borane **1f**. The resulting mixture provides **2f** in 54% yield, which is only slightly lower compared to the reaction with the preformed iodinane.

Scope and Limitations. With the optimized conditions in hand, we explored the reactivity of various substituted nitrenes in B–H insertion reaction (Scheme 2). Aryl sulfonamides reacted similarly to $TsNH_2$, giving the desired insertion products **2g-l** in ca. 55-65% yields, regardless of the presence of electron-rich (**2l**, Ar = naphthyl) or electron-poor (**2j**, Ar = p-nitrophenyl) groups. Even more electron-rich alkyl sulfonamides also reacted smoothly and gave products **2m-o**, although the reaction time for these substrates had to be extended up to 24 hours (aryl sulfonamides usually reached full conversion within an hour).

Then we explored the reactivity of the more electron-deficient sulfamates $ROSO_2NH_2$. The classic trichloroethyl sulfamate ($TcesNH_2$)[19] reacted with **1f** much faster than $TsNH_2$, 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 compared to sulfonamide insertion products **2f-o**, and notable decomposition was observed upon standing in solution in air for 24 hours.

Scheme 2. Catalytic insertion of nitrenes derived from sulfonamides and sulfonates into 2-phenylpyridine-boranes.



[a] Reaction conditions: borane derivative **1f** or **1v-z** (0.2 mmol), sulfonamide or sulfonate (0.24 mmol), PhIO (0.24 mmol), Rh_2esp_2 (1 mol%), DCM (2 ml), RT, 0.5 to 24 h. [b] Isolated yields. [c] Performed on a 6 mmol scale. [d] Performed on a 0.1 mmol scale.

The introduction of substituents into the phenylpyridine framework does not influence the reactivity of the starting borane adduct, so the corresponding insertion products **2v-z** were obtained in good yields (55-70%). Given the rising interest in carboranes as unique structural pharmacophores for drug design,[20,21] we also carried out the reaction with two carborane sulfamate derivatives, which gave the target products **2aa** and **2ab** in ca. 60% yields. It is noteworthy, that intramolecular insertion of nitrene into less electron-rich B–H bonds of carborane core was not observed, although similar reactions are known in the literature.[13] 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 (**2ac**, topiramate derivative), secondary (**2ad**, cholesterol derivative), and aryl sulfamates (**2ae**, tyrosine derivative) reacted smoothly with **1f** to give the desired products. This approach may find an application for boron labeling of biologically active molecules.

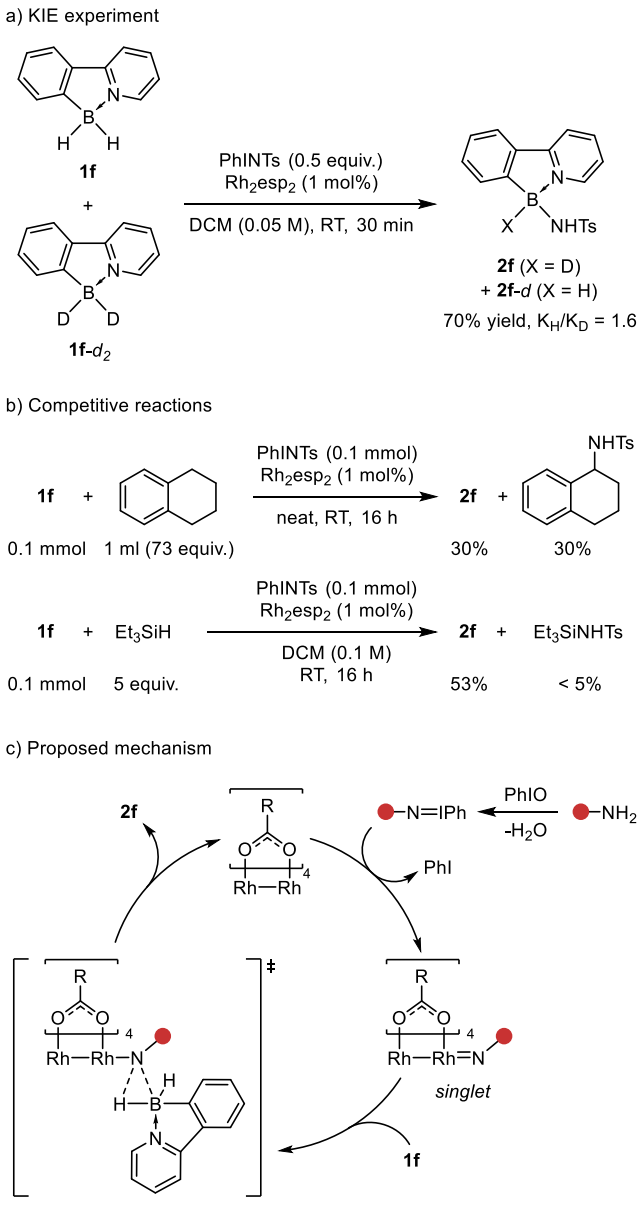
Nitrenes have been previously generated from carbamates in the presence of $Rh_2(OAc)_4$ and $PhI(OAc)_2$,[22] so we also briefly investigated their applicability for the insertion into B–H bonds. While regular carbamates such as $BocNH_2$ did not cause any conversion of the borane **1f** under our conditions, the activated trichloroethyl carbamate ($TrocNH_2$) quickly reacted, giving the insertion product. However, we could not isolate it in pure form apparently due to its instability.

Overall, the reaction scope demonstrates that borane **1f** can react with a variety of nitrene precursors. This is markedly different from the catalytic nitrene insertion into C–H bonds, which usually require some specific nitrene precursors such as $TcesNH_2$. These results are consistent with the fact that B–H bonds are, in general, much more reactive than C–H bonds.[16]

In order to describe the observed reactivity patterns, we performed some mechanistic studies. The competitive reaction of **1f** and **1f**-d_2 with PhI=NTs provided a mixture of products in a 1.6:1 ratio, regardless of the conversion of starting materials (Scheme 3, a). This kinetic isotopic effect (KIE) is similar to the one previously observed for Rh-catalyzed carbene insertion into B–H bonds (KIE=1.5)[6] and somewhat lower than the one obtained for the Rh-catalyzed nitrene insertion into C–H bonds (KIE=2.6).[23] This is consistent with the highly reactive nature of borane adducts and demonstrates that nitrene insertion into B–H bond is unlikely to be a rate-determining step.

We then conducted competitive experiments to compare the reactivity of the borane adduct **1f** with other substrates (Scheme 3, b). Thus, the reaction **1f** with PhI=NTs in neat 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 and tetralin (1:73) and the number of potentially reactive hydrogen atoms, 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 PhI=NTs in the presence of triethylsilane revealed that B–H bond is at least 50 times more reactive than Si–H bond.

Scheme 3. Mechanistic studies.

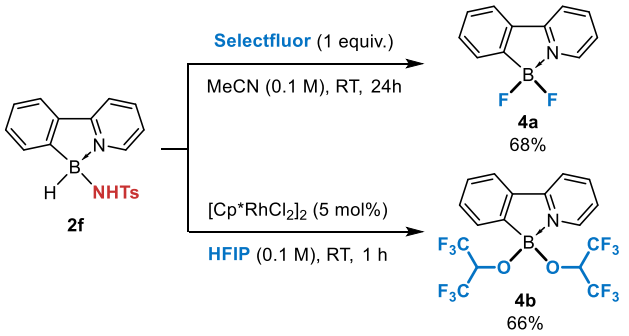


These data suggest that the reaction follows the classical mechanism, similar to the one proposed for the well-studied C–H insertion reactions (Scheme 3, c).[24] Initially, amide reacts with PhIO to form the imino-iodane. We assume this to be the rate-determining step, based on the low kinetic isotopic effect and the fact that the reaction proceeds almost immediately if the preformed PhI=NTs nitrene precursor was employed. Next, the imino-iodane forms dirhodium singlet nitrene species, which then reacts with nucleophilic borane in a concerted fashion.

We investigated further transformation of the synthesized amidoboranes (Scheme 4). The electrophilic fluorination[25] of **2f** with Selectfluor unexpectedly led to the cleavage of B–N bond and formation of the difluoride **4a**.[26] Similarly the reaction of **2f** with HFIP in the presence of the catalytic amount of $[Cp^*RhCl_2]_2$ gave the dialkoxy-substituted product **4b**. Both **4a** and **4b** can be synthesized

in even higher yields from the starting borane **1f**. We also tried to react **2f** with a simple carbene source such as ethyldiazoacetate in the presence of $[Cu(MeCN)_4]PF_6$. However, despite of the large excess of the diazo compound (5 equiv.) the conversion of **2f** was relatively low, and we could not isolate the pure insertion product. Apparently, the amidoboranes **2** are much weaker hydride donors than the starting borane **1f**. At the same time, B–N bond in these compounds is rather labile, so it is easily cleaved in further transformations. In order to get more insight on the stability of **2f** we heated it at 100 °C in dry toluene for 3 days. The formation of at least 5 different decomposition products was observed by ^{1}H and ^{11}B, but **2f** still remained the major component in the mixture.

Scheme 4. Reactions of amidoboranes.

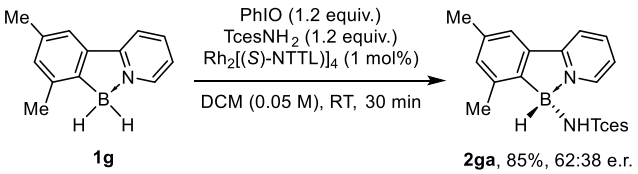


Asymmetric Insertion. The cyclic amidoboranes **2** obtained in this work contain a stereogenic boron atom with four different substituents. While chiral stereogenic boron compounds sporadically appeared in the literature, the protocols for their synthesis were unknown until very recently.[27,28] In particular, Yu and Song et al. proposed an elegant approach for the construction of enantiomerically pure boron compounds via asymmetric insertion of carbene into 2-arylpyridine boranes **1**.[9,29] Therefore we assumed that similar nitrene insertion can afford the chiral amidoboranes.

We have strategically chosen the dimethyl-substituted prochiral borane **1g** (Scheme 5) as a starting material over the unsubstituted **1f** for two reasons. Firstly, two methyl groups make the benzene ring sterically more different from the pyridine ring, which was expected to provide better asymmetric induction. Secondly, *ortho*-substituent can prevent potential racemization of the stereogenic boron center via the dissociation of B–N bond and the rotation of BHNHTs group. With our preliminary DFT calculations we expected the insertion product **2f** to have racemization barrier close to 25 kcal mol^{-1}, which is 3-9 kcal mol^{-1} lower than the arylpyridine borane derivatives reported previously.[30]

Since rhodium carboxylates were shown to be the most effective catalysts for the nitrene B–H insertion, we proceeded with the screening of different chiral paddlewheel Rh(II,II) complexes. To our surprise, among 12 tested catalysts, only one, namely $Rh_2[(S)\text{-NTTL}]_4$, gave the insertion product **2ga** with notable enantioselectivity 62:38 er (Scheme 5).

Scheme 5. Initial attempts for asymmetric insertion.

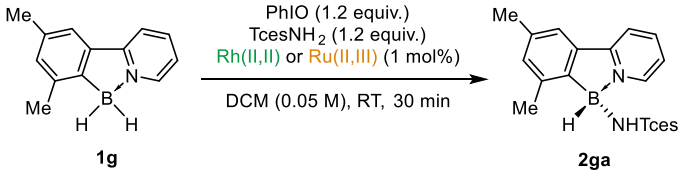


We continued catalyst screening by varying the substituents in the naphthalimide core of the NTTL ligand (Table 2). Previously Davies group has demonstrated that rhodium complexes with bromo-substituted TPCP ligand can be easily modified by the classic Suzuki–Miyaura reaction.[29] We expanded this approach for NTTL complexes. Thus, fourfold cross-coupling reactions between $Rh_2[(S)\text{-4-Br-NTTL}]_4$ and various boronic acids gave a series of aryl-substituted $Rh_2[(S)\text{-4-Ar-NTTL}]_4$ complexes in good yields (see SI). Among those, simple phenyl-substituted catalyst $Rh_2[(S)\text{-4-Ph-NTTL}]_4$ 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, specifically lowering the temperature to −30 °C and changing the solvent to chlorobenzene, allowed us to synthesize **2ga** in 91% yield and decent 82:18 er (entry 7).

In attempt to enhance enantioselectivity we decided to replace rhodium carboxylates with their ruthenium analogs $[Ru_2(OOCR)_4]X$. Recently, Matsunaga group has shown that these complexes can outperform classic rhodium carboxylates in terms of robustness and stereoselectivity.[31,32] We explored the catalytic activity of several ruthenium carboxylates bearing NTTL-ligands and found that they reacted slower than rhodium analogs, but somewhat more selectively (Table 2, entries 8-10). It is interesting to note that there is no direct succession of the substituent effects in the NTTL core upon the transition from rhodium to ruthenium complexes. For instance, 4-phenyl-substituted rhodium complex showed the highest enantioselectivity, which was not the case for diruthenium analogs. We then briefly investigated the role of the counter-ion X in $[Ru_2(OOCR)_4]X$ complexes, since Davies et al. recently have shown that such a replacement may significantly influence selectivity.[33] However, in our case changing X from BAr^F to Cl, N_3, or NO_3 had only little effect (Table 2, entries 11-13). On the other hand, further optimizations of reaction temperature and solvent allowed us to obtain the target amidoborane **2ga** in 81% yield and with 83:17 er using simple $[Ru_2((S)\text{-NTTL})_4]Cl$ catalyst (Table 2, entry 14).

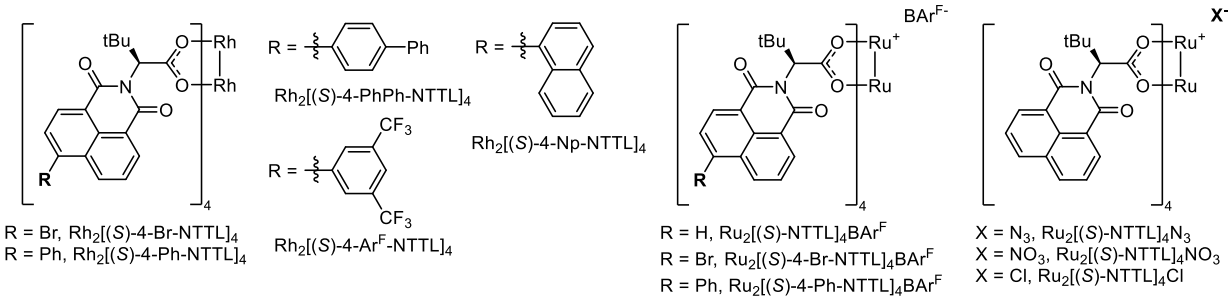
We then explored the substituent effects in the phenyl ring of phenylpyridine boranes **1g-j** on the enantioselectivity (Scheme 6). In contrast to our expectation, the introduction of bulky ^{t}Bu group in *ortho*-position to the boron atom (**2ab**) had no positive effect on selectivity and only decreased the overall yield, apparently, because of the excessive steric repulsion. We were also surprised to see 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.

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



entry	catalyst	yield, %[a]	er[b]	entry	catalyst	yield, %[a]	er[b]
1	Rh_2[(*S*)-NTTL]$_4$	85	62:38	8	Ru_2[(*S*)-NTTL]$_4BAr^F$	71	70:30
2	Rh_2[(*S*)-4-Br-NTTL]$_4$	78	59:41	9	Ru_2[(*S*)-4-Br-NTTL]$_4BAr^F$	60	68:32
3	Rh_2[(*S*)-4-Ph-NTTL]$_4$	77	67:33	10	Ru_2[(*S*)-4-Ph-NTTL]$_4BAr^F$	44	60:40
4	Rh_2[(*S*)-4-PhPh-NTTL]$_4$	69	66:34	11	Ru_2[(*S*)-NTTL]$_4N_3$	69	71:29
5	Rh_2[(*S*)-4-Np-NTTL]$_4$	64	65:35	12	Ru_2[(*S*)-NTTL]$_4NO_3$	63	72:28
6	Rh_2[(*S*)-4-Ar^F-NTTL]$_4$	71	55:45	13	Ru_2[(*S*)-NTTL]$_4$Cl	63	72:28
7	Rh_2[(*S*)-4-Ph-NTTL]$_4$[c]	91	82:18	14	Ru_2[(*S*)-NTTL]$_4$Cl[d]	81	83:17

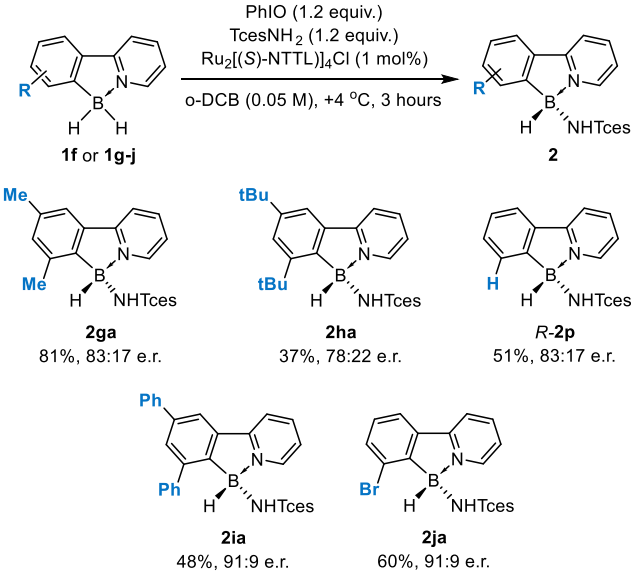
[a] Isolated yields are given. [b] Determined by chiral HPLC. [c] PhCl as a solvent, -30 °C for 24 hours. [d] o-DCB as a solvent, +4 °C for 6 hours.



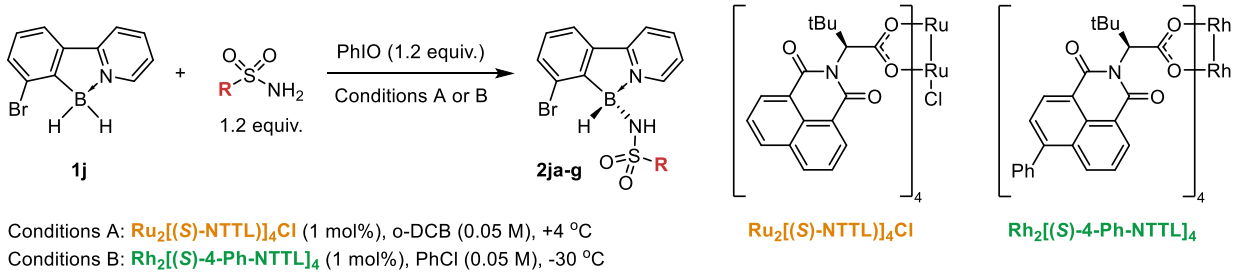
Finally, we explored the asymmetric insertion of different nitrenes into the bromo-substituted borane **1j** using [Ru_2((*S*)-NTTL)$_4$]Cl catalyst (Scheme 7). Two factors were found to be necessary to achieve high yield and stereoselectivity under the optimized conditions: 1) high electrophilicity of the nitrene species (for high yields), and 2) the presence of -OCH_2- moiety next to the sulfur (for high stereoselectivity). Thus, electron-deficient sulfamates, such as $CF_3CH_2OSO_2NH_2$, $C_3F_7CH_2OSO_2NH_2$, and $C_6F_5CH_2OSO_2NH_2$, which were previously found to be effective nitrene precursors,[34,35] 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 hexafluoroisopropyl sulfamate gave almost racemic product **2jf**, indicating the importance of the -OCH_2- group. We also investigated the catalytic activity of the rhodium complex Rh_2[(*S*)-4-Ph-NTTL]$_4$, but it gave products **2ja-je** with generally 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 *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.

Scheme 6. Scope of 2-phenylpyridines.

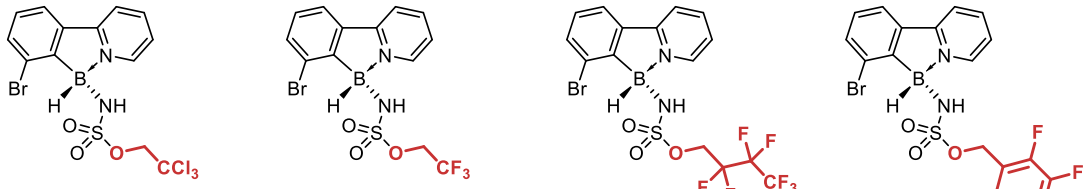


Scheme 7. Scope of the nitrene insertion products.



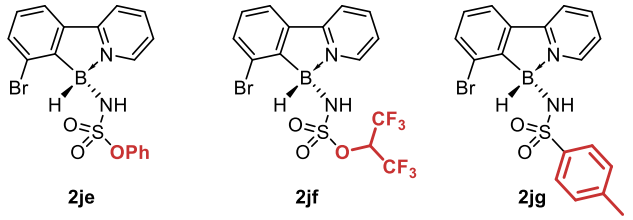
Conditions A: $Ru_2[(S)\text{-NTTL})]_4Cl$ (1 mol%), o-DCB (0.05 M), +4 °C
Conditions B: $Rh_2[(S)\text{-4-Ph-NTTL}]_4$ (1 mol%), PhCl (0.05 M), -30 °C

primary sulfamates

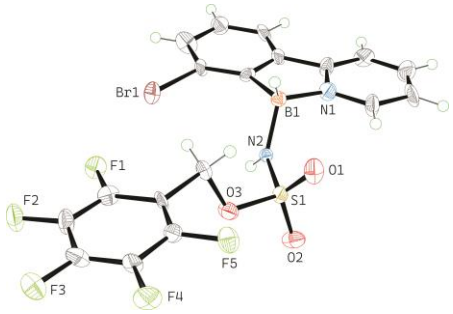


	2ja	2jb	2jc	2jd
with [Ru]:	60%, 91:9 e.r. 6 hours	66%, 91:9 e.r. 48 hours	68%, 90:10 e.r. 48 hours	74%, 89:11 e.r. 72 hours
with [Rh]:	89%, 89:11 e.r. 48 hours	88%, 71:29 e.r. 7 days	78%, 77:23 e.r. 5 days	68%, 80:20 e.r. 14 days

other substrates



	2je	2jf	2jg
with [Ru]:	24%, 62:38 e.r. 24 hours	41%, 54:46 e.r. 24 hours	48%, 53:47 e.r. 48 hours
with [Rh]:	84%, 62:38 e.r. 10 days		



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 are 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 proper chiral catalyst. This looked like a rather simple task, since many different rhodium carboxylates were introduced since the pioneering works of Davies and Doyle.[36,37] How wrong we were here. Only $M_2[NTTL]_4X$ (M = Rh or 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. Thanks 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 pre-formed bromo-substituted complexes $M[(S)\text{-4-Br-NTTL}]_4$. 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.[38,39] Significant progress has been made to address this issue in

the recent works of Davies and Sigman groups.[40–43] However, the proposed descriptor models are still unintuitive and computationally expensive.

Following Matsunaga et al.[31] we confirmed that ruthenium carboxylates can be used as a more selective alternatives for the classic rhodium analogs despite their significantly lower catalytic 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 material chemistry and biochemistry. Further efforts may be focused on the improvement of 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.

ASSOCIATED CONTENT

Experimental procedures, mechanistic experiments, NMR spectra, HPLC traces, and crystallographic data can be found in the Supporting Information.

AUTHOR INFORMATION

Corresponding Author

Nikita M. Ankudinov - A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Email: nickankudinov@gmail.com
Dmitry S. Perekalin - A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Email: dsp@ineos.ac.ru

ACKNOWLEDGMENT

This work was supported by the Russian Science Foundation (grant no. 23-13-00345). Analytical data were collected using the equipment of the Center for molecular composition studies of INEOS RAS with financial support from the Ministry of Science and Higher Education of the Russian Federation (contract no. 075-03-2023-642). X-ray data was collected using the equipment (Bruker D8 QUEST) provided by the Lomonosov Moscow State University.

REFERENCES

(1) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic Carbene Insertion into C–H Bonds. *Chem. Rev.* **2010**, *110*, 704–724.

(2) He, Y.; Huang, Z.; Wu, K.; Ma, J.; Zhou, Y.-G.; Yu, Z. Recent Advances in Transition-Metal-Catalyzed Carbene Insertion to C–H Bonds. *Chem. Soc. Rev.* **2022**, *51*, 2759–2852.

(3) Li, X.; Curran, D. P. Insertion of Reactive Rhodium Carbenes into Boron–Hydrogen Bonds of Stable N-Heterocyclic Carbene Boranes. *J. Am. Chem. Soc.* **2013**, *135*, 12076–12081.

(4) Cheng, Q.; Zhu, S.; Zhang, Y.; Xie, X.; Zhou, Q. Copper-Catalyzed B–H Bond Insertion Reaction: A Highly Efficient and Enantioselective C–B Bond-Forming Reaction with Amine–Borane and Phosphine–Borane Adducts. *J. Am. Chem. Soc.* **2013**, *135*, 14094–14097.

(5) Chen, D.; Zhang, X.; Qi, W.-Y. Y.; Xu, B.; Xu, M.-H. Rhodium(I)-Catalyzed Asymmetric Carbene Insertion into B–H Bonds: Highly Enantioselective Access to Functionalized Organoboranes. *J. Am. Chem. Soc.* **2015**, *137*, 5268–5271.

(6) Pang, Y.; He, Q.; Li, Z.-Q.; Yang, J.-M.; Yu, J.-H.; Zhu, S.-F.; Zhou, Q.-L. Rhodium-Catalyzed B–H Bond Insertion Reactions of Unstabilized Diazo Compounds Generated in situ from Tosylhydrazones. *J. Am. Chem. Soc.* **2018**, *140*, 10663–10668.

(7) Kan, S. B. J.; Huang, X.; Gumulya, Y.; Chen, K.; Arnold, F. H. Genetically Programmed Chiral Organoborane Synthesis. *Nature* **2017**, *552*, 132–136.

(8) Ankudinov, N. M.; Chusov, D. A.; Nelyubina, Y. V; Perekalin, D. S. Synthesis of Rhodium Complexes with Chiral Diene Ligands via Diastereoselective Coordination and Their Application in the Asymmetric Insertion of Diazo Compounds into E–H Bonds. *Angew. Chem. Int. Ed.* **2021**, *60*, 18712–18720.

(9) Zhang, G.; Zhang, Z.; Hou, M.; Cai, X.; Yang, K.; Yu, P.; Song, Q. Construction of Boron-Stereogenic Compounds via Enantioselective Cu-Catalyzed Desymmetric B–H Bond Insertion Reaction. *Nat. Commun.* **2022**, *13*, 1–11.

(10) Davies, H. M. L.; Manning, J. R. Catalytic C–H Functionalization by Metal Carbenoid and Nitrenoid Insertion. *Nature* **2008**, *451*, 417–424.

(11) Ju, M.; Schomaker, J. M. Nitrene Transfer Catalysts for Enantioselective C–N Bond Formation. *Nat. Rev. Chem.* **2021**, *5*, 580–594.

(12) For the related insertion of nitrenes into Si-H bonds see: Rodríguez, A. M.; Pérez-Ruíz, J.; Molina, F.; Poveda, A.; Pérez-Soto, R.; Maseras, F.; Díaz-Requejo, M. M.; Pérez, P. J. Introducing the Catalytic Amination of Silanes via Nitrene Insertion. *J. Am. Chem. Soc.* **2022**, *144*, 10608–10614.

(13) For the related formation of B–N bond via metal-catalyzed activation of carboranes and subsequent amination see: Lyu, H.; Quan, Y.; Xie, Z. Transition Metal Catalyzed Direct Amination of the Cage B(4)–H Bond in o-Carboranes: Synthesis of Tertiary, Secondary, and Primary o-Carboranyl Amines. *J. Am. Chem. Soc.* **2016**, *138*, 12727–12730.

(14) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. Expanding the Scope of C–H Amination through Catalyst Design. *J. Am. Chem. Soc.* **2004**, *126*, 15378–15379.

(15) Zalatan, D. N.; Du Bois, J. Understanding the Differential Performance of Rh2(Esp)2 as a Catalyst for C–H Amination. *J. Am. Chem. Soc.* **2009**, *131*, 7558–7559.

(16) Allen, T. H.; Curran, D. P. Relative Reactivity of Stable Ligated Boranes and a Borohydride Salt in Rhodium(II)-Catalyzed Boron–Hydrogen Insertion Reactions. *J. Org. Chem.* **2016**, *81*, 2094–2098.

(17) Horn, M.; Schappele, L. H.; Lang-Wittkowski, G.; Mayr, H.; Ofial, A. R. Towards a Comprehensive Hydride Donor Ability Scale. *Chem. Eur. J.* **2013**, *19*, 249–263.

(18) Ishida, N.; Moriya, T.; Goya, T.; Murakami, M. Synthesis of Pyridine–Borane Complexes via Electrophilic Aromatic Borylation. *J. Org. Chem.* **2010**, *75*, 8709–8712.

(19) Fiori, K. W.; Du Bois, J. Catalytic Intermolecular Amination of C–H Bonds: Method Development and Mechanistic Insights. *J. Am. Chem. Soc.* **2007**, *129*, 562–568.

(20) Marfavi, A.; Kavianpour, P.; Rendina, L. M. Carboranes in Drug Discovery, Chemical Biology and Molecular Imaging. *Nat. Rev. Chem.* **2022**, *6*, 486–504.

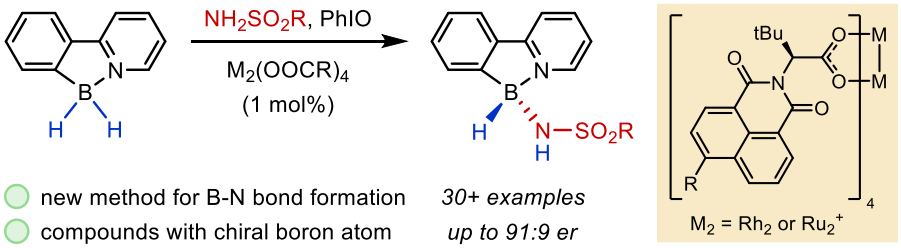
(21) Tse, E. G.; Houston, S. D.; Williams, C. M.; Savage, G. P.; Rendina, L. M.; Hallyburton, I.; Anderson, M.; Sharma, R.; Walker, G. S.; Obach, R. S.; Todd, M. H. Nonclassical Phenyl Bioisosteres as Effective Replacements in a Series of Novel Open-Source Antimalarials. *J. Med. Chem.* **2020**, *63*, 11585–11601.

(22) Zenzola, M.; Doran, R.; Luisi, R.; Bull, J. A. Synthesis of Sulfoximine Carbamates by Rhodium-Catalyzed Nitrene Transfer of Carbamates to Sulfoxides. *J. Org. Chem.* **2015**, *80*, 6391–6399.

(23) Harvey, M. E.; Musaev, D. G.; Du Bois, J. A Diruthenium Catalyst for Selective, Intramolecular Allylic C–H Amination: Reaction Development and Mechanistic Insight Gained through Experiment and Theory. *J. Am. Chem. Soc.* **2011**, *133*,

17207–17216.
(24) Azek, E.; Khalifa, M.; Bartholoméüs, J.; Ernzerhof, M.; Lebel, H. Rhodium(II)-Catalyzed C–H Aminations Using N-Mesyloxycarbamates: Reaction Pathway and by-Product Formation. *Chem. Sci.* **2019**, *10*, 718–729.
(25) Nerkar, S.; Curran, D. P. Synthesis and Suzuki Reactions of N-Heterocyclic Carbene Difluoro(Aryl)-Boranes. *Org. Lett.* **2015**, *17*, 3394–3397.
(26) Shinde, G. H.; Sundén, H. Boron-Mediated Regioselective Aromatic C–H Functionalization via an Aryl BF_2 Complex. *Chem. Eur. J.* **2023**, *29*, e202203505.
(27) Li, X.; Zhang, G.; Song, Q. Recent Advances in the Construction of Tetracoordinate Boron Compounds. *Chem. Commun.* **2023**, *59*, 3812–3820.
(28) Abdou-Mohamed, A.; Aupic, C.; Fournet, C.; Parrain, J.-L.; Chouraqui, G.; Chuzel, O. Stereoselective Formation of Boron-Stereogenic Organoboron Derivatives. *Chem. Soc. Rev.* **2023**, *52*, 4381–4391.
(29) Zhang, G.; Cai, X.; Jia, J.; Feng, B.; Yang, K.; Song, Q. Cu(I)-Catalyzed Highly Diastereo- and Enantioselective Constructions of Boron/Carbon Vicinal Stereogenic Centers via Insertion Reaction. *ACS Catal.* **2023**, *13*, 9502–9508.
(30) Zu, B.; Guo, Y.; He, C. Catalytic Enantioselective Construction of Chiroptical Boron-Stereogenic Compounds. *J. Am. Chem. Soc.* **2021**, *143*, 16302–16310.
(31) Miyazawa, T.; Suzuki, T.; Kumagai, Y.; Takizawa, K.; Kikuchi, T.; Kato, S.; Onoda, A.; Hayashi, T.; Kamei, Y.; Kamiyama, F.; Anada, M.; Kojima, M.; Yoshino, T.; Matsunaga, S. Chiral Paddle-Wheel Diruthenium Complexes for Asymmetric Catalysis. *Nat. Catal.* **2020**, *3*, 851–858.
(32) Makino, K.; Kumagai, Y.; Yoshino, T.; Kojima, M.; Matsunaga, S. Catalytic Enantioselective Amination of Enol Silyl Ethers Using a Chiral Paddle-Wheel Diruthenium Complex. *Org. Lett.* **2023**, *25*, 3234–3238.
(33) Sailer, J. K.; Sharland, J. C.; Bacsa, J.; Harris, C. F.; Berry, J. F.; Musaev, D. G.; Davies, H. M. L. Diruthenium Tetracarboxylate-Catalyzed Enantioselective Cyclopropanation with Aryldiazoacetates. *Organometallics* **2023**, *42*, 2122–2133.
(34) Fanourakis, A.; Williams, B. D.; Paterson, K. J.; Phipps, R. J. Enantioselective Intermolecular C–H Amination Directed by a Chiral Cation. *J. Am. Chem. Soc.* **2021**, *143*, 10070–10076.
(35) Nasrallah, A.; Boquet, V.; Hecker, A.; Retailleau, P.; Darses, B.; Dauban, P. Catalytic Enantioselective Intermolecular Benzylic C(sp^3)–H Amination. *Angew. Chem. Int. Ed.* **2019**, *58*, 8192–8196.
(36) Doyle, M. P.; Winchester, W. R.; Hoorn, J. A. A.; Lynch, V.; Simonsen, S. H.; Ghosh, R. Dirhodium(II) Tetrakis(Carboxamidates) with Chiral Ligands. Structure and Selectivity in Catalytic Metal-Carbene Transformations. *J. Am. Chem. Soc.* **1993**, *115*, 9968–9978.
(37) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. Asymmetric Cyclopropanations by Rhodium(II) N-(Arylsulfonyl)Prolinate Catalyzed Decomposition of Vinyldiazomethanes in the Presence of Alkenes. Practical Enantioselective Synthesis of the Four Stereoisomers of 2-Phenylcyclopropan-1-Amino Acid. *J. Am. Chem. Soc.* **1996**, *118*, 6897–6907.
(38) Davies, H. M. L.; Morton, D. Guiding Principles for Site Selective and Stereoselective Intermolecular C–H Functionalization by Donor/Acceptor Rhodium Carbenes. *Chem. Soc. Rev.* **2011**, *40*, 1857.
(39) Adly, F. On the Structure of Chiral Dirhodium(II) Carboxylate Catalysts: Stereoselectivity Relevance and Insights. *Catalysts* **2017**, *7*, 347.
(40) Ren, Z.; Musaev, D. G.; Davies, H. M. L. Influence of Aryl Substituents on the Alignment of Ligands in the Dirhodium Tetrakis(1,2,2-Triarylcyclopropane-carboxylate) Catalysts. *ChemCatChem* **2021**, *13*, 174–179.
(41) Cammarota, R. C.; Liu, W.; Bacsa, J.; Davies, H. M. L.; Sigman, M. S. Mechanistically Guided Workflow for Relating Complex Reactive Site Topologies to Catalyst Performance in C–H Functionalization Reactions. *J. Am. Chem. Soc.* **2022**, *144*, 1881–1898.
(42) Boni, Y. T.; Cammarota, R. C.; Liao, K.; Sigman, M. S.; Davies, H. M. L. Leveraging Regio- and Stereoselective C(sp^3)–H Functionalization of Silyl Ethers to Train a Logistic Regression Classification Model for Predicting Site-Selectivity Bias. *J. Am. Chem. Soc.* **2022**, *144*, 15549–15561.
(43) Souza, L. W.; Miller, B. R.; Cammarota, R. C.; Lo, A.; Lopez, I.; Shiue, Y.-S.; Bergstrom, B. D.; Dishman, S. N.; Fettinger, J. C.; Sigman, M. S.; Shaw, J. T. Deconvoluting Nonlinear Catalyst–Substrate Effects in the Intramolecular Dirhodium-Catalyzed C–H Insertion of Donor/Donor Carbenes Using Data Science Tools. *ACS Catal.* **2024**, *14*, 104–115.

Table of Contents artwork



- new method for B-N bond formation
- compounds with chiral boron atom

30+ examples
up to 91:9 er