

# Estimated Rate Constants for Hydrogen Abstraction from N-Heterocyclic Carbene–Borane Complexes by an Alkyl Radical<sup>†</sup>

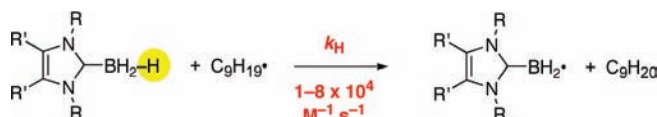
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## ABSTRACT



Rate constants for hydrogen abstraction by a nonyl radical from 20 complexes of N-heterocyclic carbenes and boranes (NHC–boranes) have been determined by the pyridine-2-thioneoxycarbonyl (PTOC) competition kinetic method at a single concentration point. The rate constants range from  $<1 \times 10^4$  to  $8 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ . They show little dependence on the electronic properties of the carbene core, but there is a trend for increasing rate constants with decreasing size of the carbene N-substituents. Two promising new reagents with small N-substituents (R = Me) have been identified.

Interest in complexes of N-heterocyclic carbenes and main group elements is rapidly increasing.<sup>1</sup> Carbene–borane complexes (NHC–boranes) are an emerging class of reagents with potential applications in radical,<sup>2</sup> ionic,<sup>3a–c</sup> and orga-

nometallic reactions.<sup>3d</sup> Much of the early work has focused on the prototypical complex 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene borane **1** (hereafter called dipp-Imd-BH<sub>3</sub>). In a representative radical reaction (Scheme 1), reduction of xanthate **2** with 2 equiv of **1** (80 °C, 2 equiv of AIBN, 10 h) provided the reduced product **4** in 64% along with dithiocarbonate borane complex **3**.<sup>2b</sup>

Mechanistic studies of the xanthate deoxygenation with **1** support a standard two-step radical-chain reaction for this new type of Barton–McCombie reaction<sup>4</sup> in which **1** plays the role of radical hydrogen atom donor (eq 1) and its derived

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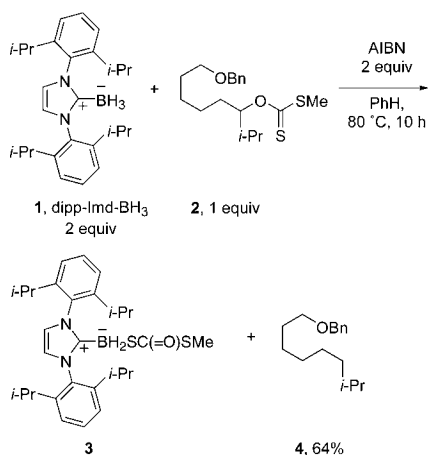
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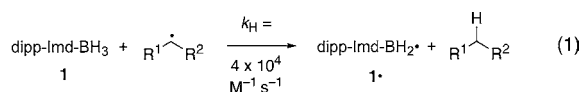
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**Scheme 1.** Typical Xanthate Reduction by *dipp*-Imd-BH<sub>3</sub> **1**<sup>a</sup>



<sup>a</sup> Formal charges are shown in this scheme only.

NHC–boryl radical (*dipp*-Imd-BH<sub>2</sub><sup>•</sup>, **1**<sup>•</sup>) adds back to the xanthate to propagate the chain. In a careful series of kinetic experiments, the rate constant for the hydrogen abstraction reaction of a secondary cyclobutylcarbinyl radical probe with **1** was measured as  $k_H = 4 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$  (eq 1).<sup>2b</sup> This rate constant is in an interesting regime; it is lower than rate constants of other popular hydrogen donors like tributyltin hydride (Bu<sub>3</sub>SnH) or tris(trimethylsilyl)silane (TTMSH) but higher than rate constant of reagents like triethylsilane that do not propagate radical chains efficiently.<sup>5</sup>



Substituent effects on the radical hydrogen donor ability of the NHC–boranes are of fundamental interest because the derived NHC–boryl radicals are a new class of boron-centered radicals. In addition, benefits of such knowledge could be reaped in synthesis. For example, 2 equiv or more of both **1** and AIBN were needed to obtain optimal yields in reductions of xanthates. This might be because the rate constant for hydrogen transfer from **1** is on the low end of the hydrogen-donor scale.<sup>6</sup> NHC–boranes that are better hydrogen donors might be better reagents in practice.

We have accumulated dozens of carbene boranes over the last 2 years, and we decided to survey a subset of these as potential radical hydrogen atom donors by measuring rate constants for reactions with an alkyl radical. With so many substrates, the usual method of conducting radical probe experiments at multiple concentrations<sup>7</sup> was deemed to be too time-consuming. Instead, for ease of both conducting

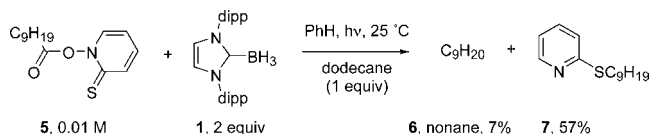
(5) Chatgililoglu, C.; Newcomb, M. In *Advances in Organometallic Chemistry*; West, R., Hill, A. F., Eds.; Academic Press: San Diego, 1999; Vol. 44, pp 67–112.

(6) Additionally, *dipp*-Imd-BH<sub>2</sub><sup>•</sup> proved to be a persistent radical, which might suggest that its radical–molecule reactions with xanthates could also be slow. See ref 2d.

experiments and analyzing results, we opted for single-point comparisons in the reaction with a simple PTOC ester 2-thioxopyridin-1(2*H*)-yl decanoate (**5**).<sup>8</sup>

Scheme 2 shows the results of a typical kinetic experiment. A solution of the pyridine-2-thioneoxycarbonyl (PTOC, **5**),

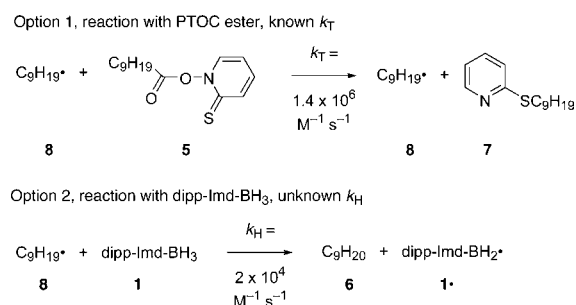
**Scheme 2.** Results of a Typical Single-Point Kinetic Experiment with PTOC Ester **5** and Hydrogen Donor *dipp*-Imd-BH<sub>3</sub> (**1**)



*dipp*-Imd-BH<sub>3</sub> (**1**), and dodecane (internal standard) in benzene was irradiated with a sunlamp for 5 min. TLC analysis verified that the PTOC ester **5** was consumed. Then the yields of the nonane **6** (7%) and 2-nonylthiopyridine (**7**) (57%) were determined by GC analysis of the crude product against the internal standard.

Similar experiments were conducted for the other NHC–borane complexes. Kinetic experiments were conducted in duplicate with good reproducibility. Additional details are provided in the Supporting Information.

Figure 1 shows the mechanistic framework for analysis of the results. Nonyl radical **8** generated from PTOC ester **5**

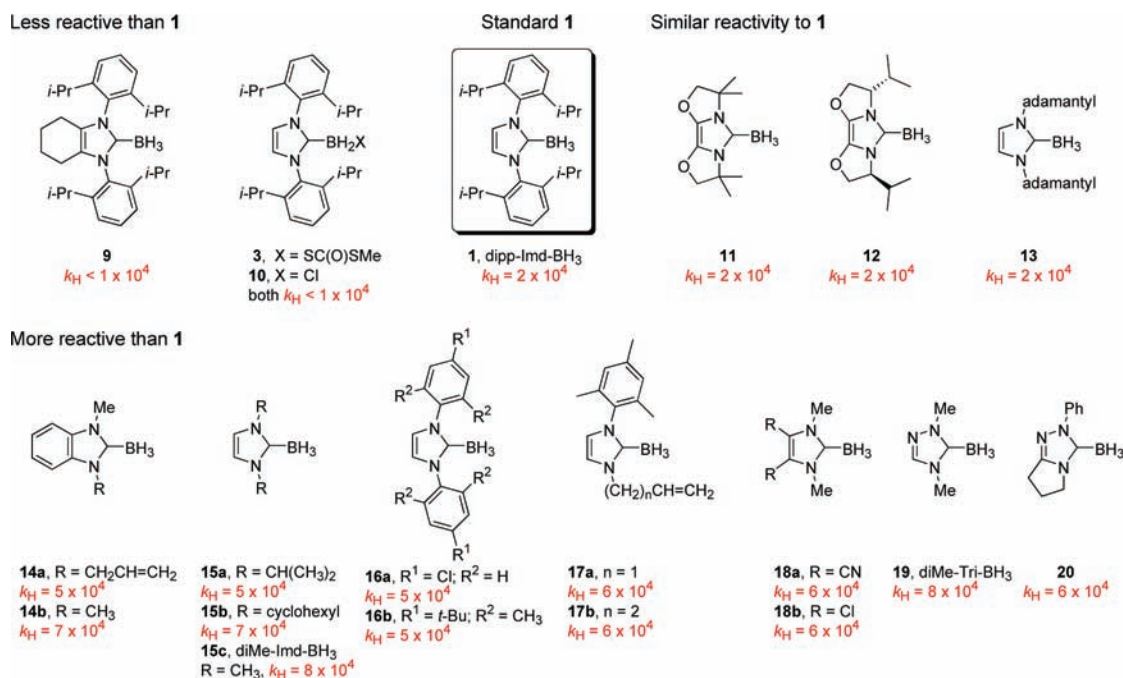


**Figure 1.** Competing options for the nonyl radical **8** with known (option 1) and unknown (option 2) rate constants.

has two competing options. It can react with the starting PTOC ester **5** (so-called “self-trapping”) to provide **7** and another nonyl radical **8** (option 1), or it can react with NHC–borane **1** to provide nonane **6** and NHC–boryl radical **1**<sup>•</sup> (option 2). By analogy to xanthate reactions, we assume that the NHC–boryl radical **1**<sup>•</sup> adds back to the starting PTOC ester **5** to propagate the chain; however, we did not attempt to isolate the expected product from that reaction

(7) (a) Newcomb, M. *Tetrahedron* **1993**, *49*, 1151–1176. (b) Newcomb, M. In *Radicals in Organic Synthesis*, 1st ed.; Renard, P., Sibi, M., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 1, pp 317–336.

(8) (a) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901–3924. (b) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1987**, *28*, 1615–1618.



**Figure 2.** NHC–borane structures and rate constants  $k_H$  ( $M^{-1} s^{-1}$ ) for hydrogen-atom transfer.

(NHC–BH<sub>2</sub>SPy). The rate constant for H-transfer ( $k_H$ ) is then calculated in the usual way from the known rate constant for self-trapping ( $k_T$ )<sup>8b</sup> and the experimentally determined product ratio, which was corrected for background reduction as described in the Supporting Information.

In this way, the rate constant  $k_H$  for the reaction of a primary alkyl radical **8** with **1** was determined to be  $2 \times 10^4 M^{-1} s^{-1}$ . This is two times lower than the more accurately determined rate constant of  $4 \times 10^4 M^{-1} s^{-1}$  for the reaction of a secondary radical with **1**. Since primary alkyl radicals are unlikely to be less reactive than secondary ones, the difference in these numbers is presumably due to experimental error. The yield of reduction product nonane **6** in the experiments with **1** is low (7%), so background correction is a possible source of error.

The background error will become more significant for less reactive boranes, so we decided to use **1** as the cutoff for rate constant estimation. Any boranes that are less reactive than **1** are simply listed with rate constants  $<10^4 M^{-1} s^{-1}$ . To further validate the analysis, we conducted several more control experiments with hydrogen donors that are both less reactive (amine- and phosphine-boranes<sup>9</sup>) and more reactive (Bu<sub>3</sub>SnH and TTMSH<sup>5</sup>) than **1**. The measured rate constants were in reasonable agreement with literature values (see the Supporting Information).

The structures and rate constants for the 20 NHC–boranes studied in this work are collected in Figure 2.

Most of the boranes were prepared by in situ deprotonation of the corresponding salt by base, followed by addition of BH<sub>3</sub>–THF. A few of the complexes have already been

described,<sup>10,11</sup> and complete details for preparation and characterization of the new complexes are contained in the Supporting Information. Crystal structures were solved for **11**, **15a**, and **15b**, and the Supporting Information provides diagrams and data.

Table S1 in the Supporting Information collects the experimental data from which the rate constants in Figure 2 were calculated. We assume that the B–H bonds are the primary source of hydrogen atoms in the reduced products. In support of this assumption, radicals derived from several of the boranes have already been observed by EPR spectroscopy.<sup>2d</sup> The rate constants are not corrected for the number of hydrogen atoms on boron (three for all boranes except **3** and **10**, which have two).

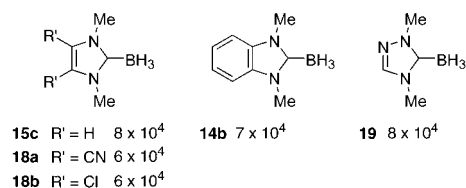
The structures in Figure 2 are collected into three groups depending on whether they are less reactive than **1** ( $k_H < 10^4 M^{-1} s^{-1}$ ), similar in reactivity to **1** ( $k_H 2\text{--}4 \times 10^4 M^{-1} s^{-1}$ ), or more reactive than **1** ( $k_H 4\text{--}8 \times 10^4 M^{-1} s^{-1}$ ). The global impression is that the range of rate constants is small given the diversity of different structures.

Selected comparisons of substrates based on NHC rings and carbene ring substituents are shown in Figure 3. Compare the carbene boranes **15c**, **14b**, and **19** with *N,N*-dimethyl substituents. Despite the variation in carbene core (imidazol-2-ylidene, benzimidazol-2-ylidene, 1,2,4-triazol-3-ylidene), the rate constants are very similar. Analogously, inspection of Figure 2 shows that the carbene boranes with bulky

(10) Complexes **3** (ref 2b), **14b** (ref 2d), **15c** (ref 2d), **16b** (ref 2d), **17a** (ref 2d), **19** (ref 12) and **20** (ref 2a) are described in prior preparative or EPR papers. Compound **12** was described by Lindsay and McArthur during the course of this study (ref 3b).

(11) Compound **15a** has been prepared by a different route: Yamaguchi, Y.; Kashiwabara, T.; Ogata, K.; Miura, Y.; Nakamura, Y.; Kobayashi, K.; Ito, T. *Chem. Commun.* **2004**, 2160–2161.

Variation of NHC rings and ring carbon substituents



Variation of NHC ring nitrogen substituents

compd	R	$k_H$
<b>13</b>	adamantyl	$2 \times 10^4$
<b>1</b>	2,6-diisopropylphenyl	$2 \times 10^4$
<b>16a</b>	<i>p</i> -chlorophenyl	$5 \times 10^4$
<b>15a</b>	isopropyl	$5 \times 10^4$
<b>15b</b>	cyclohexyl	$7 \times 10^4$
<b>15c</b>	methyl	$8 \times 10^4$

**Figure 3.** Selected comparisons of rate constants ( $M^{-1} s^{-1}$ ) based on NHC ring (top) and nitrogen substituents (bottom).

N-substituents (**1**, **11–13**) have similar rate constants (about  $2 \times 10^4 M^{-1} s^{-1}$ ). Likewise, the three carbenes **15c**, **18a**, and **18b** with the same carbene core and N-substituents but different substituents on C4 and C5 (H, CN, Cl) of the carbene ring show about the same reactivity (top of Figure 3).

In contrast, the N-substituents play a more significant role. Consider the series of imidazol-2-ylidene boranes with different N-substituents in the lower part of Figure 3. As the size of the pair of N-substituents decreases, the rate constant increases from  $2 \times 10^4$  to  $8 \times 10^4 M^{-1} s^{-1}$ . It can be difficult to change the hydrogen-donating ability of reagents like tin hydrides through substituent effects, so the ability to modulate the reactivity of carbene boranes by changing N-substituents could be advantageous.

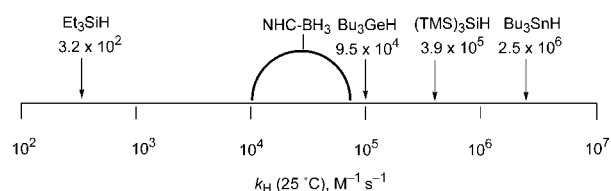
There is limited information in Figure 2 on the effect of boron substituents. However, both boron chloride **10** and boron dithiocarbonate **3** are less reactive than **1**, so it looks like electron-withdrawing substituents may deactivate.

Substrates **17a** and **17b** bearing alkenyl groups (allyl and homoallyl) were originally made to study the potential for cyclization of the derived NHC-boryl radicals. However, in a limited series of preparative experiments with  $Et_3B$  and air (25 °C) or AIBN (80 °C), we did not isolate any apparent cyclized products.

There are important preparative ramifications of the data in Figure 2, both looking backward and looking forward. Looking backward, early work on reductions of xanthates focused on reagents **1** and **20**, and the 1,2,4-triazol-3-ylidene derivative **20** often provided better performance either via superior yield or faster reaction. This can now be understood at least in part because **20** is a better hydrogen donor than

**1**. Looking forward, two complexes stand out as potentially useful reagents, 1,3-dimethylimidazol-2-ylideneborane (**15c**, diMe-Imd-BH<sub>3</sub>) and 2,4-dimethyl-1,2,4-triazol-3-ylideneborane (**19**, diMe-Tri-BH<sub>3</sub>). These complexes are ideal candidates for three reasons: (1) they come from very cheap precursors, (2) they have the lowest molecular weights of all the reagents in Figure 2 (110 and 111 g mol<sup>-1</sup>), and (3) they are the best hydrogen donors ( $8 \times 10^4 M^{-1} s^{-1}$ ). Indeed, preparative experiments in the following paper<sup>12</sup> suggest that these two compounds above may indeed hit the reagent trifecta.

In summary, we have implemented a simple kinetic competition experiment with PTOC esters to measure rate constants for radical hydrogen abstraction from NHC-boranes. Experiments on several substrates are conveniently conducted in parallel, and this has allowed us to provide rate constants for 20 known and new NHC-boranes. The rate constants fall in an interesting range, as summarized in Figure 4. They



**Figure 4.** Scale of rate constants for donations of hydrogen atoms to alkyl radicals.

are lower than those of tin hydrides, tris(trimethylsilyl)silicon hydrides, and germanium hydrides yet still above the threshold for conducting successful radical chain reactions.

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**Supporting Information Available:** Procedures and characterization of all new compounds, details of kinetic experiments, copies of spectra of products, and crystal structures (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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