

## Zinc-Mediated Carbene Insertion to C–Cl Bonds of Chloromethanes and Isolable Zinc(II) Isocyanide Adducts

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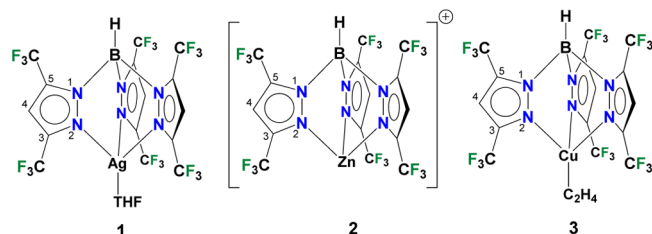
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## S Supporting Information

**ABSTRACT:** The zinc adduct  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}\}^+$ , which was generated from  $[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{ZnEt}$  and  $[\text{Ph}_3\text{C}]\{\text{B}[3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3]_4\}$ , catalyzes the activation of C–halogen bonds of chloromethanes via carbene insertion. Ethyl diazoacetate serves as the carbene precursor. The presence of  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}\}^+$  in the reaction mixture was confirmed by obtaining  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}(\text{CN}^t\text{Bu})_3\}^+$  using  $\text{CN}^t\text{Bu}$  as a trapping agent.  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}(\text{CN}^t\text{Bu})_3\}^+$  loses one zinc-bound  $\text{CN}^t\text{Bu}$  easily to produce five-coordinate  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}(\text{CN}^t\text{Bu})_2\}^+$ .

Processes that facilitate the functionalization of C–Cl bonds are of significant interest<sup>1</sup> because they allow the conversion of relatively cheap and widely available substrates like alkyl chlorides (especially compared to bromo and iodo analogues) to more valuable organic compounds and may even provide a route to deal with environmentally troublesome halogenated products (like hydrochlorofluorocarbons).<sup>2</sup> Activation of unfunctionalized C–Cl bonds, however, is a challenging task because of their high bond strength.<sup>3–5</sup>

In 2003, we reported a novel silver-catalyzed carbene insertion route for the functionalization of C–Cl and C–Br bonds of halomethanes using commercially available ethyl diazoacetate (EDA) as the carbene source.<sup>6,7</sup> This reaction involves the formation of a new  $\text{sp}^3\text{--sp}^3$  C–C bond while retaining the halide on the product. The silver adduct (e.g., **1** in Figure 1) supported by highly fluorinated tris(pyrazolyl)borate ligand  $[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]^-$  serves as the catalyst.<sup>8</sup> High Lewis acidity at the metal site is a key factor for the success of C–halogen bond activation in these reactions. Others have studied this silver-mediated process and provided insight into the mechanism speculated in the original communication.<sup>9</sup>  $[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]^-$



**Figure 1.** Complexes used in the present catalysis process: **1**, **2** (used as its  $\{\text{B}[3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3]_4\}^-$  salt), and  $[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Cu}(\text{C}_2\text{H}_4)$  (**3**).

$(\text{CF}_3)_2\text{Pz})_3]\text{Ag}(\text{THF})$  (**1**; THF = tetrahydrofuran) is also an excellent catalyst for the functionalization of unactivated hydrocarbons.<sup>7,10</sup> Here we present an interesting new development in this field and describe the use of an earth-abundant 3d block metal, in particular a zinc catalyst,  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}\}^+$  (**2**), in the functionalization of chloromethanes via carbene insertion.

The catalyst  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{Zn}\}^+$  (containing a  $\{\text{B}[3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3]_4\}^-$  counterion) used in this work was generated in situ by treating the catalyst precursor  $[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{ZnEt}^{11}$  with triphenylmethyl tetrakis[3,5-bis(trifluoromethyl)phenyl]borate  $[\text{Ph}_3\text{C}]\{\text{B}[3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3]_4\}^{12}$  in a 1:1 molar ratio at 60 °C. In a typical process, a mixture of 1 equiv of  $[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz})_3]\text{ZnEt}$  and  $[\text{Ph}_3\text{C}]\{\text{B}[3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3]_4\}$  was placed in 1 mL of alkyl chloride (substrate and also the solvent) and treated with 20 equiv of EDA, which is the carbene precursor. After the mixture was maintained at 60 °C for 1 h, the resulting products were analyzed using several methods. To our delight, the reaction involving chloroform produced ethyl 2,3,3-trichloropropionate (**4**), which is the product of the insertion of carbene  $:\text{CHCO}_2\text{Et}$  into a C–Cl bond, in 59% yield (Table 1). A further increase in the reaction time did not lead to a significant improvement in the yield. When the catalyst/EDA molar ratio was changed to 1:50, a decrease in the product yield was observed, while changing the

**Table 1.** Catalysis Data<sup>a</sup>

| catalyst | catalyst/EDA | substrate                | product | NY % <sup>b</sup> | GY % <sup>c</sup> | IY % <sup>d</sup> |
|----------|--------------|--------------------------|---------|-------------------|-------------------|-------------------|
| 2        | 1:20         | $\text{CHCl}_3$          | 4       | 59                | 67                | 32                |
| 2        | 1:50         | $\text{CHCl}_3$          | 4       | 23                | 21                | 16                |
| 2        | 1:10         | $\text{CHCl}_3$          | 4       | 68                | 76                | 53                |
| 2        | 1:20         | $\text{CH}_2\text{Cl}_2$ | 5       | 20                | 22                |                   |
| 2        | 1:20         | $\text{CCl}_4$           | 6       | 64                |                   |                   |
| 1        | 1:20         | $\text{CHCl}_3$          | 4       | 78                | 75                |                   |
| 3        | 1:20         | $\text{CHCl}_3$          | 4       | 0                 | 0                 |                   |

<sup>a</sup>All of the reactions were carried at 60 °C for 1 h. Yields are based on an average of at least two runs. <sup>b</sup>Yield based on the integration of <sup>1</sup>H NMR signals. <sup>c</sup>Yield based on gas chromatography (GC) analysis. <sup>d</sup>Yield based on isolated products. Note: The isolated product yields are lower than the NMR (or GC) yields because of the loss of volatile products during the workup.

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[catalyst]/[EDA] ratio to 1:10 improves the yield (Table 1). This can be explained on the basis of the increased number of catalytically active species per substrate molecules in the latter case. Similarly, dichloromethane and tetrachloromethane were also converted into ethyl 2,3-dichloropropionate (**5**) and ethyl 2,3,3,3-tetrachloropropionate, respectively, in 20% and 64% yield (Table 1). The yields of products **4–6** follow the relative C–Cl bond energies of the starting alkyl halide substrates.<sup>4</sup> The rest of EDA in these reactions remained mostly unreacted (see Table S1 in the Supporting Information, SI). When *n*-BuCl was used as a substrate under similar reaction conditions, no C–Cl insertion product was observed. Instead, C–H insertion products (15%) and ethyl 2-chloroacetate (which results from HCl elimination from *n*-BuCl and addition to carbene :CHCO<sub>2</sub>Et) were found in the reaction mixture. The rest of EDA remained essentially unreacted, with a small amount ending up as (~3%) carbene dimers.

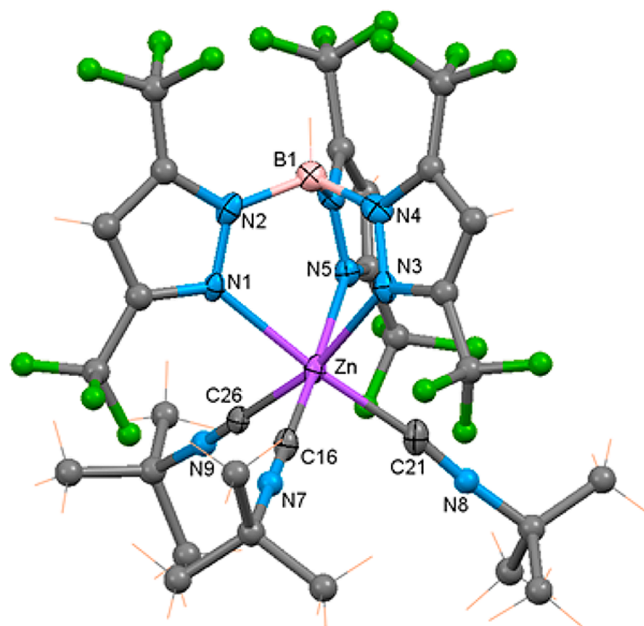
Generation of the zinc cation from [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]ZnEt is a key step for which a strong hydride abstracting agent, [Ph<sub>3</sub>C]{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>}, was used.<sup>12</sup> It reacts with [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]ZnEt, producing {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn}<sup>+</sup> as its {B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>}<sup>−</sup> salt with liberation of an ethylene molecule. When [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]ZnEt was used alone, no catalytic activity was observed under various conditions, indicating the need for generation of {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn}<sup>+</sup>. The elevated temperature (60 °C) is necessary for this reaction. When the same reaction was carried at room temperature, no notable product formation was observed because of the sluggish generation of catalytically active cationic zinc species. Other zinc compounds such as Zn(OTf)<sub>2</sub>, Et<sub>2</sub>Zn,<sup>13</sup> or the combination of Et<sub>2</sub>Zn and [Ph<sub>3</sub>C]{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>} or just [Ph<sub>3</sub>C]{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>} with 20 equiv of EDA in chloroform at 60 °C did not produce any measurable amounts of **4**.

The C–Cl bond activation chemistry of CHCl<sub>3</sub> was probed under comparable conditions using the well-established silver catalyst **1**<sup>6</sup> for comparison. Results show that the silver adduct **1** (which is a neutral complex and a 4d metal-based catalyst) is still the better catalyst compared to the zinc catalyst **2** (Table 1). However, the copper(I) catalyst **3** (Figure 1) produced only carbene dimers (100% consumption of EDA) under similar conditions, indicating its inability to mediate the halogen activation process.<sup>14</sup>

The zinc(II)-mediated process is likely to proceed via a metal–carbene intermediate, which results from the reaction between EDA and {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn}<sup>+</sup> with the loss of N<sub>2</sub> (see the SI for the proposed mechanism).<sup>9</sup> Chloroalkanes then bind to the electrophilic metallacarbene carbon center via a chlorine atom, forming a ylide, which after additional steps generates products of formal carbene insertion into C–Cl bonds, releasing the zinc(II) catalyst. These reaction mixtures containing the {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn}<sup>+</sup> catalyst produced [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]ZnCl (from CHCl<sub>3</sub> and CH<sub>2</sub>Cl<sub>2</sub> solutions) in about 85% yield (with respect to the amount of [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]ZnEt used) upon standing. This compound might have resulted from the migration of a chloride ion to the metal center (rather than to the metallacarbene carbon)<sup>9</sup> or from the direct reaction of {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn}<sup>+</sup> with a chlorinated solvent and likely represents a termination step of the catalytic reaction. We have also prepared [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]ZnCl from an independent route (see the SI) and employed it in the same catalytic reaction with [Ph<sub>3</sub>C]{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>}. It was

found to be catalytically inactive for C–Cl bond activation, suggesting that it could indeed be a termination product.

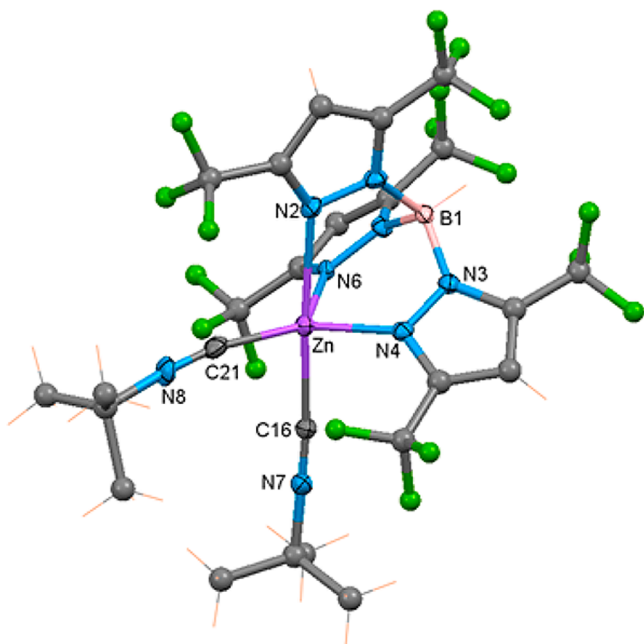
In order to confirm generation of {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn}<sup>+</sup>, we performed a trapping reaction using *tert*-butyl isocyanide instead of EDA in dichloromethane. We were able to isolate a zinc(II) isocyanide adduct, {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn(CN<sup>*t*</sup>Bu)<sub>3</sub>}{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>}, in good yield. It was characterized using several methods including X-ray crystallography (Figure 2). Such structurally authenticated zinc(II) isocyanide



**Figure 2.** View of the molecular structure of {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn(CN<sup>*t*</sup>Bu)<sub>3</sub>}{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>}. Selected bond lengths (Å) and angles (deg): Zn–N1 = 2.259(7), Zn–N5 = 2.325(7), Zn–N3 = 2.287(7), Zn–C16 = 2.149(10), Zn–C21 = 2.137(10), Zn–C26 = 2.178(10), C21–N8 = 1.175(12), C16–N7 = 1.145(12), C26–N9 = 1.114(11); N1–Zn–N3 = 82.5(3), N1–Zn–N5 = 84.7(2), N3–Zn–N5 = 82.2(2), Zn–C21–N8 = 173.3(9), Zn–C16–N7 = 178.6(9), Zn–C26–N9 = 174.0(8).

adducts are of interest because they could serve as models for intermediates in zinc-catalyzed processes involving isocyanides.<sup>15,16</sup> The six-coordinate zinc atom in this adduct adopts an octahedral geometry, with three isocyanides occupying the *facial* configuration. [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]<sup>−</sup> serves as a typical  $\kappa^3$  ligand.

Interestingly, one of the isocyanide ligands in {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn(CN<sup>*t*</sup>Bu)<sub>3</sub>}{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>} can be removed quite easily under reduced pressure (in fact, one isocyanide coordinates to zinc with a longer Zn–C bond relative to the other two), leading to the formation of a five-coordinate bis(isocyanide) adduct, {[HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]Zn(CN<sup>*t*</sup>Bu)<sub>2</sub>}{B[3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sub>4</sub>}. The X-ray crystal structure of this adduct is illustrated in Figure 3. It has a distorted trigonal-bipyramidal zinc center. The  $\kappa^3$ -bound [HB(3,5-(CF<sub>3</sub>)<sub>2</sub>Pz)<sub>3</sub>]<sup>−</sup> ligand occupies two equatorial and one axial sites, as is evident from two long and one short Zn–N distances. The axial and equatorial Zn–C distances are also very different, 2.204(6) and 2.013(7) Å, respectively. Structurally characterized zinc(II) isocyanide adducts are rare,<sup>15,17</sup> and four-coordinate ZnBr<sub>2</sub>(CN<sup>*t*</sup>Bu)<sub>2</sub> is one such example in the literature. The Zn–C distances of this adduct [2.069(5) and 2.072(4) Å] are close to the average Zn–C



**Figure 3.** View of the molecular structure of  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz)}_3]\text{Zn}(\text{CN}^t\text{Bu})_2\}^+$ . Selected bond lengths (Å) and angles (deg): Zn–N2 = 2.448(5), Zn–N6 = 2.026(5), Zn–N4 = 2.027(5), Zn–C16 = 2.204(6), Zn–C21 = 2.013(7), C21–N8 = 1.156(8), C16–N7 = 1.157(7); N4–Zn–N6 = 97.39(18), N6–Zn–C21 = 132.5(2), N4–Zn–C21 = 128.5(2), N2–Zn–C16 = 174.68(19), Zn–C21–N8 = 168.3(6), Zn–C16–N7 = 173.4(5).

distance of  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz)}_3]\text{Zn}(\text{CN}^t\text{Bu})_2\}^+$  (ave 2.108 Å), although the latter is a five-coordinate zinc system.

Overall, we have discovered a competent zinc catalyst that mediates carbene insertion to aliphatic C–Cl bonds. It is a particularly noteworthy finding involving a cheap 3d metal catalyst.<sup>18–21</sup> The related copper(I) adduct did not catalyze carbene insertion to C–Cl bonds under similar conditions. We have also confirmed the generation of  $\{[\text{HB}(3,5\text{-(CF}_3)_2\text{Pz)}_3]\text{Zn}\}^+$  by stabilizing it using *tert*-butyl isocyanide and obtained two rare and isolable zinc(II) isocyanide complexes. Catalyst improvement and mechanistic studies of this zinc(II)-mediated process, as well as the catalytic activity of other group 12 metals, are presently under investigation in our laboratory.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

Details of the synthesis and characterization and catalysis, proposed mechanism, additional figures and tables, and X-ray crystallographic data in CIF format. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.5b00929.

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### Author Contributions

The manuscript was written through contributions of all authors.

### Notes

The authors declare no competing financial interest.

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