Silver(I) Scorpionate Mediated Insertion of Carbenes into Aliphatic C−H Bonds

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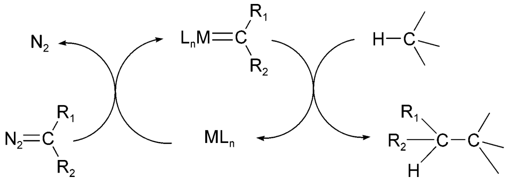
Summary: Silver(I) adducts featuring highly fluorinated tris(pyrazolyl)borate, [HB(3,5-(CF$_3$)$_2$Pz)$_3$]$^-$, catalyze the carbene insertion into carbon−hydrogen bonds of cyclic and acyclic hydrocarbons at room temperature. These silver complexes are more effective than related copper catalysts such as [HB(3,5-(CF$_3$)$_2$Pz)$_3$]Cu(THF) for hydrocarbon activation via this route.

Methods that allow the activation of unfunctionalized carbon−hydrogen bonds are of significant importance, because such processes would enable the utilization of readily available hydrocarbon feedstocks as precursors for the synthesis of more complex organic compounds.[1−4] However, despite many efforts, only a handful of catalytic processes are presently available for the functionalization of aliphatic C−H bonds.[1−7] One of the most promising routes among these has been C−H bond activation via a metal-mediated carbene insertion process (Scheme 1).[5,7]

Activation of relatively inert aliphatic C−H bonds via this route requires a metallocarbenoid species with high electrophilic character at the carbon.[5,7,8] Diazo compounds, in particular those with electron-withdrawing substituents (R_1 and R_2 in Scheme 1) such as carbonyl groups, serve as excellent carbene sources. Metal complexes featuring good σ-acceptor and weak π-donor metal ions (M in Scheme 1) and weakly coordinating ligands (L) function well as catalysts, since they provide the necessary ingredients to generate a sufficiently electrophilic carbenoid species that inserts smoothly into C−H bonds. Rhodium(II) and copper(I) complexes (e.g., rhodium(II) carboxylates, carboxamidates, and phosphates and copper(I) adducts of tris(pyrazolyl)borates) are the most effective catalysts for this process.[5,7,9−12] Here we describe a silver(I)-mediated process that inserts carbenes into aliphatic C−H bonds at room temperature. It is also noteworthy that homogeneous catalytic processes mediated by silver(I) are relatively rare. There is a report describing the use of silver complexes in C−H insertion reactions.[13] It involves the use of metal salt/ligand combinations such as $AgSbF_6$ and bis(oxazolidine) to catalyze the intramolecular C−H activation chemistry of a L-menthyl phenyldiazoacetate derivative. Recent reports of other types of silver(I)-catalyzed processes include carbon−halogen bond activation,[14] aziridination,[15] silacyclopropanation,[16] α-hydroxylation reactions,[17] cycloadditions,[18] and propargylic amine synthesis.[19] This is in spite of the fact that heterogeneous silver-catalyzed olefin epoxidation is one of the most important and thoroughly investigated industrial processes.[20]

Scheme 1. Metal-Mediated Carbene Insertion into C−H Bonds



For a number of years, we have been interested in the chemistry of metal complexes with weakly coordinating, highly fluorinated tris(pyrazolyl)borate ligands (scorpionates).[21,22] During our investigation of silver(I) complexes bearing one such ligand, [HB(3,5-(CF$_3$)$_2$Pz)$_3$]$^-$ (**1**), with diazo reagents, we discovered that [HB(3,5-

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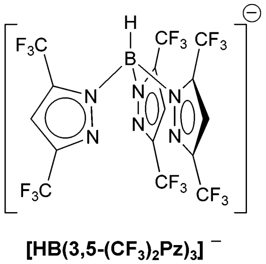
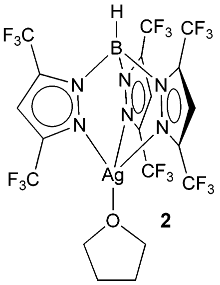
$(CF_3)_2Pz)_3]Ag(THF)$ (**2**)[23] catalyzes carbene insertions into aliphatic C−H bonds under remarkably mild conditions.



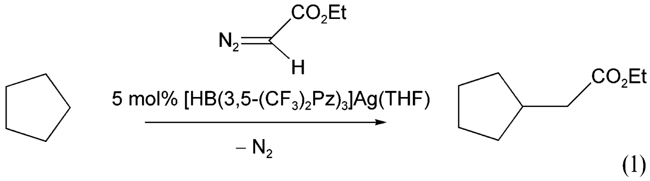
$[HB(3,5-(CF_3)_2Pz)_3]^-$

1

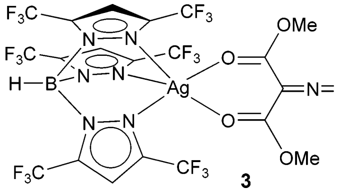


2

For example, we were able to synthesize ethyl 2-cyclopentylacetate in 88% yield using a mixture of cyclopentane, ethyl diazoacetate (EDA) as a carbene source, and 5 mol % $[HB(3,5-(CF_3)_2Pz)_3]Ag(THF)$ as the catalyst (eq 1). The reaction presumably proceeds with the formation of a transient metal carbene intermediate.[24] The removal of a carbene moiety from the N_2 part of EDA was evident from the rapid evolution of nitrogen. In contrast to EDA, the reaction of $[HB(3,5-(CF_3)_2Pz)_3]Ag(THF)$ with $N_2C(CO_2Me)$ (dimethyl diazomalonate, which is a relatively more stable diazo reagent) at room temperature afforded the thermally stable, Ag−O-bonded $[HB(3,5-(CF_3)_2Pz)_3]Ag[OC(OMe)]_2CN_2$ (**3**).[25]



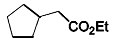
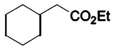
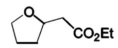
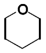
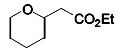
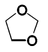
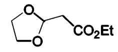
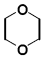
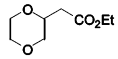
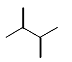
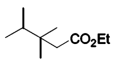
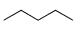
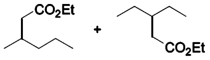
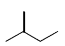
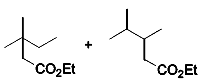
(1)



3

Silver-catalyzed carbene insertions are not limited to C−H bonds of cyclic hydrocarbons such as cyclopentane and cyclohexane. As shown in Table 1, a variety of linear and branched hydrocarbons can also be used as substrates.[26] Data from Table 1, entries 7, 8, and, in particular, 9, suggest the tertiary ≈ secondary ≫ primary order of regioselectivity for insertion into C−H bonds. The tertiary and secondary C−H bond activation product ratios for 2-methylbutane reflect the relative number of hydrogen atoms.

Table 1. $[HB(3,5-(CF_3)_2Pz)_3]Ag(THF)$-Catalyzed Carbene Insertion into C−H Bonds

Entry	Substrate	Products	Yield (%)[a]
1			88[b]
2			88[b]
3			24[c] only
4			41[d] only
5			0
6			0
7			85[b]
8		 81 : 19	81[b]
9		 35 : 65	87[b]

[a] These *isolated* yields are based on the average of at least two experiments and on the amount of EDA used. The product distribution was observed by ^1H NMR spectroscopy. [b] The carbene fragments of the remaining EDA end up as the carbene dimerization products diethyl fumarate and diethyl maleate. [c] Nearly equal amounts of dimers and unreacted EDA were found in the product mixture. [d] The product mixture contains 40% dimers and 6% EDA. Unreacted EDA was obtained from entries 5 and 6.

The C−H bond activation chemistry reported by Perez et al. using $[HB(3,4,5-Br_3Pz)_3]Cu$ catalyst provides useful data for a comparison, since it involves a related coinage metal ion and a scorpionate ligand.[11] Yields for cyclohexane substrate involving the copper(I)-catalyzed process (90%; using 1.0 mmol of EDA, 0.05 mmol of catalyst, 30 mL of substrate) is comparable to that of silver(I) (88%; using 1.0 mmol of EDA, 0.05 mmol of catalyst, 6.5 mL of substrate). However, the silver(I) complex appears to be a more effective carbene insertion catalyst for the open chain hydrocarbon compounds (e.g., Table 1, entry 7 with 85% for $[HB(3,5-(CF_3)_2Pz)_3]Ag$ vs 56% for $[HB(3,4,5-Br_3Pz)_3]Cu$ and entry 8 with 81% for $[HB(3,5-(CF_3)_2Pz)_3]Ag$ vs 50% for $[HB(3,4,5-Br_3Pz)_3]Cu$). We note that $[HB(3,5-(CF_3)_2Pz)_3]^-$ is a more strongly electron withdrawing ligand than $[HB(3,4,5-Br_3Pz)_3]^-$. This is apparent from the carbonyl stretching frequency data of $[HB(3,5-(CF_3)_2Pz)_3]CuCO$ (ν_{CO} 2137 cm^{-1}) and $[HB(3,4,5-Br_3Pz)_3]CuCO$ (ν_{CO} 2110 cm^{-1}).[11,27] Furthermore, Ag(I) is also a much weaker π-donor metal ion.[23]

Interestingly, for the C−H bond activation of ether substrates such as THF, $[HB(3,5-(CF_3)_2Pz)_3]Ag(THF)$ is a poor choice compared to the copper(I) catalysts. $[HB(3,4,5-Br_3Pz)_3]Cu$ is a better catalyst for these sub-

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(23) Dias, H. V. R.; Wang, Z.; Jin, W. *Inorg. Chem.* **1997**, *36*, 6205−6215.

(24) Although the possible involvement of a metal carbene intermediate for these types of reactions is widely accepted, without further studies, it is not possible to completely rule out other mechanistic possibilities, such as the involvement of a free carbene.

(25) Dias, H. V. R.; Polach, S. A. *Inorg. Chem.* **2000**, *39*, 4676−4677.

(26) *General procedure for C−H insertion reactions:* reactions were carried out under nitrogen in the absence of light. EDA (114 mg, 1.00 mmol) in the hydrocarbon or ether (5 mL) was added by automatic syringe over 1 h to a stirred solution of the catalyst (0.05 mmol) in the hydrocarbon or ether (1.5 mL). The resulting mixture was stirred overnight at ambient temperature. The solution was concentrated, and the residue was purified by flash chromatography (SiO_2, 9:1 hexanes/Et_2O) to obtain the products.

(27) Dias, H. V. R.; Lu, H.-L. *Inorg. Chem.* **1995**, *34*, 5380−5382. Dias, H. V. R.; Goh, T. K. H. H. *Polyhedron* **2004**, *23*, 273−282.

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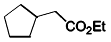
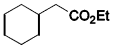
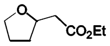
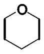
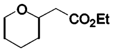
Table 2. [HB(3,5-$(CF_3)_2$Pz)$_3$]Cu(THF)-Catalyzed Carbene Insertion into C−H Bonds

Entry	Substrate	Product	Yield (%)[a]
1			60
2			58
3			73 only
4			75 only

[a] These *isolated* yields are based on the average of at least two experiments and on the amount of EDA used. The material balance is accounted for by the carbene dimerization products diethyl fumarate and diethyl maleate.

strates.[10] It is possible that ether molecules (present in large excess) compete with EDA and coordinate to the silver center of [HB(3,5-$(CF_3)_2$Pz)$_3$]Ag (as observed in structurally characterized **2**),[23] thus preventing silver-mediated decomposition of the EDA and subsequent metallocarbenoid formation.[28] In fact, unreacted EDA can be recovered quantitatively from the reaction mixtures when ethers such as 1,3-dioxalane and 1,4-dioxane are used as the substrate. Our previous work shows that [HB(3,5-$(CF_3)_2$Pz)$_3$]Ag inserts carbenes into C−X (X = Cl, Br) rather than C−H bonds when substrates such as CH_2X_2 and CHX_3 are used.[14]

We have also investigated the activity of the analogous copper(I) complex using [HB(3,5-$(CF_3)_2$Pz)$_3$]Cu(THF)[29] catalyst and several substrates (Table 2). It provides moderate to good yields of C−H insertion products. The yield trends are similar to those of other copper scorpionates and opposite of the silver-catalyzed results: i.e., ethers give a higher yield of insertion products than do hydrocarbons.

In conclusion, we have described an interesting silver(I)-catalyzed aliphatic C−H bond activation process. It involves the insertion of a carbene moiety into a C−H bond, leading to the formation of a new carbon−carbon bond between two sp^3 carbon centers. The silver(I) scorpionate [HB(3,5-$(CF_3)_2$Pz)$_3$]Ag(THF) appears to be a *more effective* catalyst compared to the related copper(I) analogues to activate unfunctionalized C−H bonds of hydrocarbons yet shows *lower activity* toward C−H bonds of ethers. Further investigations into the effects of other ligands, diazo reagents, and reaction conditions on this silver-catalyzed process are currently underway.

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(28) Note that THF has been used as a solvent successfully in a silver-catalyzed intramolecular C−H activation process.[13] It involves a different silver species and a diazo reagent.

(29) Dias, H. V. R.; Lu, H.-L.; Kim, H.-J.; Polach, S. A.; Goh, T. K. H. H.; Browning, R. G.; Lovely, C. J. *Organometallics* **2002**, *21*, 1466−1473.