

Nitrene Insertion into Aromatic and Benzylic C–H Bonds Catalyzed by Copper Complexes of Fluorinated Bis- and Tris(pyrazolyl)borates

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Abstract: Fluorinated bis- and tris(pyrazolyl)boratocopper complexes catalyze the nitrene insertion to C-H bonds of aromatic hydrocarbons efficiently producing amination products in good to excellent yields at room temperature. Imidoiodanes, PhI=NTs (Ts = p-toluenesulfonyl) and PhI=NNs (Ns = p-nitrophenylsulfonyl) serve as the nitrene source. The bis(pyrazolyl)borate catalyst [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NCMe) with PhI=NNs produced the arene C-H functionalized product of mesitylene in 87% yield with only trace amounts of benzylic C-H insertion. The use of $[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]Cu(NCMe)$ that has an even weakly donating pyrazolate generated the arene C–H insertion product exclusively. The tris(pyrazolyl)borate complex [HB(3,5-(CF₃)₂Pz)₃]Cu(NCMe), in contrast, generated the benzylic amination product from mesitylene and PhI=NNs in 82% yield with only very minor amounts of arene C-H functionalization. DFT calculations suggest that Cu-nitrene moiety generated from [HB(3,5-(CF₃)₂Pz)₃]Cu(NCMe) and PhI=NNs activates the benzylic C–H bond of mesitylene via a hydrogen atom abstraction (HAA) followed by a radical rebound (RR) pathway, whereas the functionalization of sp² C–H bonds of mesitylene by $[H_2B(3.5-(CF_3)_2Pz)_2]Cu(NNs)$ ensues possibly via a nitrene addition to the arene core.

Introduction: Arylamine motifs are widespread in natural products, agrochemicals, functional materials and pharmaceuticals,^[1-4] as well as in supporting ligands utilized in metal coordination chemistry.^[5-7] Consequently, efficient methods for the synthesis of arylamines are of significant value. Classical route to arylamines involves nitration under strongly acidic conditions followed by a reductive hydrogenation step.^[1, 8] Ullmann reported a copper mediated route to arylamines via a cross coupling of aryl halides with amines in 1903.^[9, 10] More efficient, cross-coupling chemistry catalyzed by palladium leading to $C(sp^2)$ -N bond construction was reported by the Buchwald^[11] and Hartwig^[12] groups in the early 1990s. These latter cross-coupling methods and other modifications such as copper mediated Chan-Lam aminations,^[13-16] however require pre-functionalized arenes (typically possessing halide, triflate, boronic acid groups, *etc.*).

Catalytic methods for the direct functionalization of inert arene C–H bonds leading to C(sp²)-N moieties have advantages over classical nitration/hydrogenation pathways or currently preferred cross-coupling chemistry in terms of step-efficiency and environmental considerations.^[2, 3, 17-19] Considering their fundamental importance and synthetic value, significant effort has been devoted to the development of such direct arene C–H amination chemistry resulting in several important findings.^[2, 17, 19-21] Intramolecular C–H amination processes, and those that rely on the use of directing groups or involve activated C–H bonds are more common.^[22-25] In contrast, intermolecular, arene C–H functionalization chemistry of simple arenes such as benzene, mesitylene, *etc.*, is particularly challenging.^[17, 26] Nevertheless, advances have been made in recent years to generate arylamines via the functionalization of C–H bonds of simple arenes.^[27-30]

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Table 1. C–H functionalization of benzene and mesitylene at room temperature using PhI=NTs(Ts = p-toluenesulfonyl) or PhI=NNs (Ns = p-nitrophenylsulfonyl) as the nitrene source



	Yield from	Yields from eq. 2 with		Arene substrate/	Ref
Catalyst	eq. 1 with	mesitylene		PhI=NR	
	benzene				
	C(sp ²)-H	C(sp ²)-H	C(sp ³)-H		
$[HB(3,4,5-Br_3Pz)_3]Cu(NCMe)$	40%	0%	>95%	substrate used as the	[31, 32]
	$\mathbf{R} = \mathbf{T}\mathbf{s}$	$\mathbf{R} = \mathbf{T}\mathbf{s}$	$\mathbf{R} = \mathbf{T}\mathbf{s}$	solvent	
AuCl ₃	<5%	90%	< 5%	8:1 in CH ₂ Cl ₂	[33]
	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$		
{[HC(3,5-	45%	81%	<5%	20-33 vol%	[34]
$(Me)_2Pz)_3]Fe(NCMe)_3\}(BF_4)_2$	$\mathbf{R} = \mathbf{T}\mathbf{s}$	$\mathbf{R} = \mathbf{Ts}$	$\mathbf{R} = \mathbf{T}\mathbf{s}$	substrate in CH ₂ Cl ₂	

Among the various options for direct C–H aminations, transition-metal-catalyzed formal nitrene insertion to arene C(sp²)-H bonds represents one of the powerful and attractive strategies to obtain molecules with C(sp²)-N bonds.^[2, 17] Imidoiodanes such as PhI=NTs (Ts = *p*-toluenesulfonyl) are the most common nitrene source.^[35, 36] In 2003, Perez *et al.* demonstrated the functionalization of C(sp²)-H bonds of benzene (used in excess as the solvent) using a copper tris(pyrazolyl)borate [HB(3,4,5-Br₃Pz)₃]Cu(NCMe) catalyst and PhI=NTs as the nitrene source (Table 1).^[31, 32] The use of toluene or mesitylene, however, leads to reactions occurring solely at

the benzylic positions. Sadighi *et al.* reported the use of copper(I) supported by a 2,9-diarylphenanthroline to catalyze nitrene transfer to the C–H bonds of electron rich arenes such as 1,3dimethyoxybenzene, but this catalyst is ineffective for benzene.^[37] He and co-workers described the use of an AuCl₃ catalyst and PhI=NNs (Ns = *p*-nitrophenylsulfonyl) to achieve arene amination of mesitylene with remarkable arene C–H selectivity (Table 1).^[33] Although arene C–H amination of tri- or more methyl substituted benzenes works well, less substituted benzenes including benzene itself gave less than 5% of nitrene insertion products while substrates with activated benzylic C–H bonds have produced varying amounts of C(sp²)-H and C(sp³)-H functionalizations. The Fe(II) catalyst {[HC(3,5-(Me)₂Pz)₃]Fe(NCMe)₃}(BF4)₂ reported by Jensen and Liang displays notably high aromatic to benzylic C–H amination selectivity (Table 1).^[34] Overall, despite these and other important findings, there is still room for improvements in direct, intermolecular, arene C–H functionalization via nitrene insertion with respect to substrate scope, chemoselectivity, product yields, milder conditions, and arene/N-source ratio.



Figure 1. Fluorinated tris- and bis-(pyrazolyl)borate copper complexes

An area of activity in our laboratory concerns nitrene and carbene transfer chemistry of coinage metal ions supported by highly fluorinated ligands. For example, in 2002 we reported that

copper(I) adducts such as [HB(3,5-(CF₃)₂Pz)₃]Cu(C₂H₄) (Figure 1, 1) are competent aziridination catalysts, readily converting a variety of olefins into the corresponding *N*-tosyl aziridines with PhI=NTs.^[38] The copper and silver complexes supported by fluorinated tris(pyrazolyl)borates are also excellent catalysts for functionalizing C–H and C-Cl bonds of alkanes via carbene transfer.^[39-41] Given the current interest and importance, we set out to probe the utility of tris(pyrazolyl)borato copper complexes such as 2 and related bis(pyrazolyl)borates **3**^[42] and **4** as catalysts for C–H aminations of aromatic hydrocarbons. As reported below, we found a remarkable difference in chemistry between the bis- and tris(pyrazolyl)borate ligand supported catalysts, and notably high yields of amination products even with low substrate/nitrene source ratios. Results from a computational study of this process are also presented.

Results and discussion:

Details of the synthesis of $[HB(3,5-(CF_3)_2Pz)_3]Cu(NCMe)$ (2)^[43] and $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NCMe)$ (3)^[42] catalysts utilized in this work have been reported elsewhere (Figure 1). The related fluorinated bis(pyrazolyl)borate copper complex $[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]Cu(NCMe)$ (4) possessing NO₂ groups at the pyrazolyl ring 4-positions was prepared in an analogous manner to that of 3 using 3,5-(CF₃)₂-4-(NO₂)PzH^[44] and KBH₄ and CuOTf. X-ray crystal structure analysis shows that it is a 3-coordinate copper complex (Figure 2) with a trigonal planar copper site. The bis(pyrazolyl)borate ligand adopts a typical boat conformation.^[45, 46]



Figure 2. Molecular structure of bis(pyrazolyl)borate copper complex [H₂B(3,5-(CF₃)₂-4-(NO₂)Pz)₂]Cu(NCMe) (**4**). Selected distances (Å) and angles (°): Cu-N2 2.040(3), Cu-N5 2.020(3), Cu-N7 1.865(3), N7-C11 1.102(5), N1-B 1.582(5), N4-B 1.586(5), B•••Cu 2.92, N5-Cu-N2 91.98(11), N7-Cu-N2 129.28(14), N7-Cu-N5 138.72(14), C11-N7-Cu 178.1(4)

In contrast to tris(pyrazolyl)borates, coordination chemistry and in particular, catalytic properties of bis(pyrazolyl)borato metal complexes have received notably less attention.^[41, 46, 47] We began our work by testing the prowess of bis(pyrazolyl)borato copper(I) adduct, $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NCMe)$ (3) in C–H amination chemistry using benzene as the substrate and PhI=NTs as the nitrene source. Dichloromethane was chosen as the solvent. At room temperature, the reaction involving 5 mol% of catalyst 3 and 1:5 molar ratio of PhI=NTs to benzene produced the arene C–H amination product in 44% isolated yield (Table 2, entry 1) and the remaining 56% is TsNH₂ and unidentified products. This is comparable to yields observed with $[HB(3,4,5-Br_3Pz)_3]Cu(NCMe)$ and $\{[HC(3,5-(Me)_2Pz)_3]Fe(NCMe)_3\}(BF_4)_2$ but involves much lower

substrate loadings (Table 1). When we changed the nitrene source to PhI=NNs, the benzene aminated product yield improved significantly to 68% (Table 2, entry 2) and the remaining 32% is NsNH₂ and unidentified products. This result involving benzene substrate indicates that PhI=NNs is a better nitrene source than PhI=NTs for the arene C-H amination. We also managed to improve the C–H amination yield further to 76% by using $[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]Cu(NCMe)$ (4) catalyst that has an even more weakly donating supporting ligand (Table 2, entry 3). Comparison of entries 2 and 4 shows that the tris(pyrazolyl)borate complex $[HB(3,5-(CF_3)_2Pz)_3]Cu(NCMe)$ (2) gives PhNHNs only in 41% yield even with PhI=NNs as the nitrene source, indicating that the related bis(pyrazolyl)borate complex 3 is a better catalyst for this reaction. Note also that AuCl₃ with this imidoiodane failed to activate benzene (Table 1). The need for excess substrates to achieve decent yields is a common issue with hydrocarbon amination chemistry.^[2, 29] Entry 5 shows that catalyst 3 can produce reasonable yields (52%) of the nitrene insertion product even when the aminating agent and benzene is used in an equimolar amounts, which is very rare.^[2]

We then tested the C–H amination chemistry of mesitylene using PhI=NNs as the nitrene source (room temperature reactions with 5:1 arene:nitrogen source) and catalysts **2-4**. The chemistry mediated by tris(pyrazolyl)borate complex **2** produced benzylic amination product in 82% isolated yield with very minor arene C–H functionalization products (Table 2, entry 4). The use of PhI=NTs gave slightly lower yield, but still showing high selectivity for benzylic C–H activation (entry 6). The [HB(3,4,5-Br₃Pz)₃]Cu(NCMe) catalyst of Perez *et al.*^[32] displayed similar behavior with mesitylene (Table 1). The bis(pyrazolyl)borate catalyst **3** with PhI=NNs, in contrast produced the arene C–H functionalized product (87% isolated yield, entry 2) with only trace amounts of benzylic C–H insertion. The use of **4** instead of **3**, generated the arene C–H

insertion product exclusively and at notable yields of 90% (entry 3). This result is similar to the outcome reported with AuCl₃ but involves a catalyst containing an earth abundant copper.^[33] It is also possible to produce arene C–H insertion products in respectable 72% yield (entry 5) using equimolar amounts of mesitylene and PhI=NNs. In this case, we also observed benzylic amination products in about 8% yield.

Table 2. C–H functionalization of benzene and mesitylene at room temperature using PhI=NTs (Ts = *p*-toluenesulfonyl) or PhI=NNs (Ns = *p*-nitrophenylsulfonyl) as the nitrene source and catalysts [HB(3,5-(CF₃)₂Pz)₃]Cu(NCMe) (**2**), [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NCMe) (**3**), [H₂B(3,5-(CF₃)₂-4-(NO₂)Pz)₂]Cu(NCMe) (**4**). All the reactions were performed at room temperature and the yields reported below are isolated yields after separation and purification by column chromatography. The yields of the minor products (<10% yields) were estimated from NMR data of the crude reaction mixture.



Entry	Catalyst	Yield from eq. 1 with benzene	Amination yields from eq. 2 with mesitylene		Arene substrate/
		C(sp ²)-H	C(sp ²)-H	C(sp ³)-H	PhI=NR
1	[H ₂ B(3,5-	44			5:1
	$(CF_3)_2Pz)_2]Cu(NCMe)$ (3)	$\mathbf{R} = \mathbf{Ts}$			in CH ₂ Cl ₂
2	[H ₂ B(3,5-	68	87%	<3%	5:1
	$(CF_3)_2Pz)_2]Cu(NCMe)$ (3)	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	in CH ₂ Cl ₂

3	[H ₂ B(3,5-(CF ₃) ₂ -4-	76	90%	< 1%	5:1
	$(NO_2)Pz)_2]Cu(NCMe)$ (4)	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{Ns}$	in CH ₂ Cl ₂
4	[HB(3,5-	41	< 5%	82%	5:1
	$(CF_3)_2Pz)_3]Cu(NCMe)$ (2)	$\mathbf{R} = \mathbf{Ns}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	in CH ₂ Cl ₂
5	[H ₂ B(3,5-	52	72%	8%	1:1
	$(CF_3)_2Pz)_2]Cu(NCMe)$ (3)	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	$\mathbf{R} = \mathbf{N}\mathbf{s}$	in CH ₂ Cl ₂
6	[HB(3,5-	36	< 5%	75%	5:1
	$(CF_3)_2Pz)_3]Cu(NCMe)$ (2)	$\mathbf{R} = \mathbf{Ts}$	$\mathbf{R} = \mathbf{T}\mathbf{s}$	$\mathbf{R} = \mathbf{T}\mathbf{s}$	in CH ₂ Cl ₂

Encouraged by these results, we have examined the amination of several other aromatic hydrocarbons using 5 mol% of the bis(pyrazolyl)borato copper catalysts 3 and 4 (Table 3) in CH₂Cl₂. Toluene and ethylbenzene substrates used in this work represent less electron rich and less crowded arenes relative to mesitylene. Ethylbenzene, however, has secondary benzylic C–H bonds, which are typically relatively more active than primary.^[48] Products from the toluene reaction show that the reaction is less chemoselective, and the nitrene insertions take place at both arene and benzylic C–H sites, with slight preference for benzylic sites (Table 3, entries 1, 2). The 3 and 4 catalyzed nitrene transfer to ethyl benzene occurs exclusively at benzylic sites with no detectable arene C–H amination products (Table 3, entries 3, 4). The 1,3,5-triisopropylbenzene substrate, which contains both active benzylic C-H bonds and electron-rich, yet crowded arene core, displays reactivity at both arene and benzylic C–H sites, with slightly more preference for nitrene insertions at benzylic positions. The 1,3,5-triethylbenzene substrate, displays significantly more selective amination at arene C-H sites and with only minor amounts of benzylic C-H insertion, which is very different from the outcome involving ethylbenzene substrate noted above. All four substrates listed on Table 3 generate higher amination product yields with the catalyst 4 relative to that of **3**.

The bis(pyrazolyl)borate copper catalysts **3** and **4** show a unique reactivity profile compared to the previously utilized $[HB(3,4,5-Br_3Pz)_3]Cu(NCMe)$,^[32] { $[HC(3,5-Br_3Pz)_3]Cu(NCMe)$,^{[32}

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(Me)₂Pz)₃]Fe(NCMe)₃}(BF₄)₂.^[34] and AuCl₃ catalysts in arene hydrocarbon amination.^[33] For comparison, with toluene, [HB(3,4,5-Br₃Pz)₃]Cu(NCMe) catalyst^[32] produces exclusive benzylic aminations while $\{[HC(3,5-(Me)_2Pz)_3]Fe(NCMe)_3\}(BF_4)_2$ shows a large preference for arene C-H amination.^[34] Catalysts **3** and **4** functionalize both arene and benzylic C–H sites of tolunene. with slight preference for benzylic sites. The nitrene transfer to ethylbenzene catalyzed by 3 and 4 occurs exclusively at benzylic sites with no detectable arene C-H amination products while $\{[HC(3,5-(Me)_2Pz)_3]Fe(NCMe)_3\}(BF_4)_2$ in contrast, produces near equal amounts of arene and benzylic C–H amination products. The results from the **3** or **4** catalyzed reactions involving 1,3,5triethyl or triisopropylbenzene are similar to the outcome reported with AuCl₃ catalyst.^[33] However, AuCl₃ does not show any significant arene C-H bond functionalization with benzene or less substituted benzenes. Catalysts 3 and 4 are also effective at significantly lower substrate $[HB(3,4,5-Br_3Pz)_3]Cu(NCMe)^{[32]}$ loadings compared to and {[HC(3,5- $(Me)_2Pz_3$ [Fe(NCMe)₃ (BF₄)₂.^[34] For example, the substrate (arene) has been used as the reaction medium or at 20-30 vol% in CH₂Cl₂ with the latter two catalysts (Table 1), whereas the catalyst **3** afforded high yields of the nitrene insertion products at 5:1 substrate:nitrene source ratio (Tables 2 and 3).

Table 3. C–H functionalization of aromatic hydrocarbons at room temperature using PhI=NNs (Ns = *p*-nitrophenylsulfonyl) as the nitrene source and catalysts $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NCMe)$ (**3**), $[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]Cu(NCMe)$ (**4**) (using 5:1 molar ratio of arene:PhI=NNs and 5% catalysts in CH₂Cl₂). All the reactions were performed at room temperature and the yields reported below are isolated yields after separation and purification by column chromatography. The yield of the minor products of <10% yields were estimated from NMR data of the crude reaction mixture.



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7	$[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NCMe)$ (3)	68%	10%	
8	$[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]Cu(NCMe)$ (4)	75%	<5%	

The results summarized in Tables 2 and 3 suggest several important steric and electronic factors in play in terms of the selectivity of nitrene insertions mediated by **2**, **3** and **4** to aromatic hydrocarbons that relies on a delicate balance between supporting ligand, C–H bond energy, electron density at the arene core, and steric crowding at nitrene insertion sites. The difference in selectivity displayed by tris(pyrazolyl)borate **2** and bis(pyrazolyl)borate **3** is particularly interesting. In order to better understand the nitrene insertion process, a computational study was undertaken to further elucidate the mechanism, especially the selectivity of C–H amination. Many of the results of the present work parallel the study by Hou *et al.*,^[49] so the points most salient to the present experiments are summarized herein, with additional details in the Supporting Information.

In a 2015 computational study, Hou *et al.* reported that C–H amination of benzene via nitrene addition is more favored than sp² C–H bond activation by hydrogen atom abstraction (HAA) followed by radical rebound (RR) when studying a tris(pyrazolyl)borate Cu(I) catalyst [HB(3,4,5-Br₃Pz)₃]Cu(NCMe) utilized by Pérez and co-workers.^[31, 32, 49] Herein, the free barriers calculated for nitrene addition to functionalize an sp² C–H bond of mesitylene are similar in comparison to the HAA/RR pathway for benzylic amination of mesitylene by [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NNs) and [HB(3,5-(CF₃)₂Pz)₃]Cu(NNs) active species. The DFT calculations with the B3LYP functional indicate a triplet ground state for both of these nitrenes. The calculated singlet-triplet splitting is ~13 kcal mol⁻¹ for both the bis(pyrazolyl)borate and tris(pyrazolyl)borate models. Note also that the generation of copper-nitrenes in these processes have been proposed,^[50] and observed experimentally with related bis(pyrazolyl)methane systems with pendent

heteroarenes.^[51] Significant spin density is found on both the nitrene nitrogen and the copper, suggesting a mix of Cu(II)-imidyl and Cu(I)-nitrene character. For $[HB(3,5-(CF_3)_2Pz)_3]Cu(NNs)$, the spin density (via Mulliken population analyses) is 1.4 e^- on nitrene N and 0.31 e^- on Cu, whereas for $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NNs)$, the spin densities are 0.91 e^- on nitrene N and 0.36 e^- on Cu, with the rest of the spin density located on the two oxygens of the Ns group. The Cu-N(Ns) bond length in $[HB(3,5-(CF_3)_2Pz)_3]Cu(NNs)$ is 1.78 Å and in $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NNs)$ is 1.77 Å.



Figure 3. Calculated Gibbs free energy map of arene H-atom abstraction (HAA), blue, and nitrene addition, black, by $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NNs)$. Reported free energies are in kcal mol⁻¹.

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Arene and benzylic C-H activation of mesitylene was investigated. The HAA/RR [H₂B(3,5mechanism evaluated for both $[HB(3,5-(CF_3)_2Pz)_3]Cu(NNs)$ was and (CF₃)₂Pz)₂]Cu(NNs) catalyzed C-H amination, Figure 3. The optimized HAA TS structures show an elongated benzylic C-H bond and arene C-H bond. With [HB(3,5-(CF₃)₂Pz)₃]Cu(NNs), the C-H bond is stretched from 1.09 to 1.38 Å for arene HAA ($N \cdots H \cdots C$ angle = 175°) and from 1.10 to 1.28 Å for benzylic HAA (N···H···C angle = 168°). With [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NNs), the C–H bond is stretched from 1.10 to 1.37 Å for arene HAA ($N \cdots H \cdots C$ angle = 178°) and from 1.09 to 1.24 Å for benzylic HAA (N···H···C angle = 175°). For the HAA C–H activation step, calculated free energy barriers show that benzylic C-H activation is more favored than arene C-H activation for both tris- and bis(pyrazolyl)borato-Cu(NNs): 22.8 kcal mol⁻¹ vs. 35.5 kcal mol⁻¹ for [HB(3,5-(CF₃)₂Pz)₃]Cu(NNs) and 13.5 kcal mol⁻¹ vs. 27.0 kcal mol⁻¹ for [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NNs) (see Supporting Information). This difference is expected due to the breaking of the stronger arene C–H bond^[48] and the unfavorable formation of arene radical upon the loss of aromaticity. Additionally, for mesitylene, one expects an additional steric advantage for activation at a benzylic versus an arene C-H bond. The formation of the organic radical and Cu[NH(Ns)] after the arene HAA transition state is endergonic by 18 - 20 kcal mol⁻¹ for both tris- and bis(pyrazolyl)borato-Cu(NNs), while it is only marginally exergonic (4 - 6 kcal mol⁻¹) for benzylic HAA. These calculations suggest that this Cu-nitrene moiety is more likely to activate the benzylic than arene C-H bond of mesitylene if operating via an HAA/RR pathway due to the sterically more accessible and weaker benzylic C–H bond, which clearly contrasts experimental selectivity observed in the case of bis(pyrazolyl)borate systems. Inspired by the work of Hou *et al.* the direct C-N bond formation or nitrene addition pathway for [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NNs) was examined next due to the observed high arene C-H selectivity. The optimized transition state suggests a step-

wise nitrene addition followed by proton transfer rather than a concerted nitrene insertion, as was proposed by Hou *et al.*^[49] This result agrees with previous experiment-theory research on nitrene two-step aziridination using substituted styrenes as substrate studies.^[52, 53] The nitrene addition pathway has a lower barrier than arene sp² HAA (17.0 vs. 27.0 kcal mol⁻¹), suggesting it is the preferred route for functionalization of the mesitylene sp² C–H bonds. NBO analysis shows that nitrene addition leads to an amido-copper intermediate as illustrated in Figure 3, with a Cu(I) – $N^{-}(Ns)(Mes^{+})$ configuration. The barrier of nitrene addition TS for the [HB(3,5-(CF_3)_2Pz)_3]Cu is calculated to be 35.1 kcal mol⁻¹ higher than the reactants. It is surmised that the steric bulk of the κ^3 -[HB(3,5-(CF_3)_2Pz)_3]Cu coordination and the energetic expense of a reduced coordination to κ^2 -[HB(3,5-(CF₃)₂Pz)₃]Cu linkage isomer thwart this pathway. The optimized structure of the nitrene addition TS shows that geometry distortion of the complex is required for the mesitylene to fit into the activation site, which could cause the high barrier. One of the Cu-N^{Pz} is elongated from 2.01 to 2.72 Å, hence moving from κ^3 towards κ^2 coordination of the tris(pyrazolyl)borate supporting ligand. Benzylic HAA may not be the favored pathway in the experiments with [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NNs) even though it has a slightly lower calculated barrier than that of nitrene addition (13.5 vs. 17.0 kcal mol⁻¹) perhaps because the benzylic HAA is reversible or that the mesitylene radical might be trapped in the solvent cage. In both cases, the rate of HAA could be greatly limited and make RR the rate limiting step even though benzylic C–H bond is weaker.

We have also performed an isotope labelling experiment using a 1:1 mesitylene and mesitylene-d¹² mixture with PhI=NNs using $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NCMe)$ (3) catalyst, as described by He *et al* for a similar AuCl₃ mediated process.^[33] Product analysis indicated the formation of MesNHNs and d¹¹-MesNHNs in a 1:1 ratio, suggesting that the C-H functionlization step might not be the rate determining step.

In summary, we have described efficient nitrene insertion into aromatic and benzylic C–H bonds catalyzed by highly fluorinated bis- and tris(pyrazolyl)boratocopper complexes, producing amination products in good to excellent yields. We have also found that bis(pyrazolyl)borate ligand supported catalyst **3** is a better catalyst than the tris(pyrazolyl) version **2** for the arene C-H amination reaction. We have also shown that PhI=NNs acts as a better nitrene source than its analog PhI=NTs for the arene C-H amination. The tris- and bis(pyrazolyl)borate ligand supported catalysts **2** and **3** show remarkable difference in, and opposite selectivity towards benzylic vs aromatic C–H aminations with mesitylene. We have also demonstrated that it is possible to achieve reasonable yields of nitrene insertion products using equimolar amounts of aminating agent and the aromatic substrate. This work also highlight the value of less explored bis(pyrazolyl)borate ligand support in the Scorpionate family.^[46]

Experimental Section:

General Considerations. All manipulations were conducted in a N₂ atmosphere using standard Schlenk techniques, unless noted otherwise. Toluene was freshly distilled from sodium and benzophenone prior to use. The CH₃CN and CH₂Cl₂ were freshly distilled over CaH₂. Glassware was oven-dried at 150°C overnight. All reagents were purchased from commercial vendors. *N*-tosyl phenyliodinane (PhI=NTs)^[54] and *N*-nosyl phenyliodinane (PhI=NNs) were synthesized according to known methods.^[55] Temperatures mentioned refer to the external oil bath temperature. All additions and manipulations were done under a dry N₂ atmosphere. Column chromatography was done using 230-400 mesh silica gel in open air. Preparative TLC was done using commercial silica plates with UV absorbance. NMR spectra were recorded at 25°C on a JEOL Eclipse 500 spectrometer (¹H, 500.16 MHz; ¹³C, 125.77 MHz; ¹⁹F, 470.62 MHz). Proton

and carbon chemical shifts are reported in parts per million versus Me₄Si. ¹⁹F NMR chemical shifts were referenced relative to external CFCl₃. Elemental analyses were performed using a Perkin-Elmer Model 2400 CHN analyzer. The 4-nitro-3,5-bis(trifluoromethyl)pyrazole,^[44], [HB(3,5-(CF₃)₂Pz)₃]Cu(NCMe) (**2**)^[43] and [H₂B(3,5-(CF₃)₂Pz)₂]Cu(NCMe) (**3**)^[42] were prepared by published methods.

Synthesis of [H₂B(3,5-(CF₃)₂-4-(NO₂)Pz)₂]K. 4-nitro-3,5-bis(trifluoromethyl)pyrazole (500 mg, 2.0 mmol) in toluene (10 mL) was added at room temperature to KBH₄ (60 mg, 0.96 mmol) in 10 mL of toluene. The reaction mixture was heated to ca. 115-120 °C with stirring and kept at that temperature for 20 h. After cooling, the mixture was filtered through Celite and the toluene was removed under reduced pressure to obtain [H₂B(3,5-(CF₃)₂-4-(NO₂)Pz)₂]K as a white solid, 90% yield. ¹H NMR (acetone-*d*₆): δ 3.66 (v br, B-H, 2H) ppm. ¹³C{¹H}NMR (acetone-*d*₆): δ 118.8 (q, ¹*J*_{CF} = 269 Hz, CF₃), 120.1 (q, ¹*J*_{CF} = 268 Hz, CF₃), 132.5 (q, ²*J*_{CF} = 38 Hz, *C*CF₃), 135.2 (q, ²*J*_{CF} = 36 Hz, *C*CF₃) ppm; ¹⁹F NMR (acetone-*d*₆): δ -58.9, -62.7 ppm. Anal. Calcd for C₁₀H₂BF₁₂KN₆O₄: C, 21.92; H, 0.37; N, 15.33. Found: C, 21.87; H, 0.38; N, 15.32.

Synthesis of [H₂B(3,5-(CF₃)₂-4-(NO₂)Pz)₂]Cu(NCMe) (4):

Bis(copper(I) trifluoromethanesulfonate) benzene (147 mg, 0.29 mmol) and $[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]K$ (321 mg, 0.58 mmol) were combined in toluene (15 mL) and stirred for 15 min at room temperature. Dry acetonitrile (0.5 mL) was added to this mixture and the solution was heated to 80 °C. This temperature was maintained for 1 h. The mixture was filtered through Celite and the toluene removed under reduced pressure to obtain $[H_2B(3,5-(CF_3)_2-4-(NO_2)Pz)_2]Cu(NCMe)$ as a white solid, 76% yield. ¹H NMR (CDCl₃): δ 2.33 (s, CH₃, 3H), 3.86 (v br, B-H, 2H) ppm.

¹³C{¹H} NMR (CDCl₃): δ 2.72 (s, CH₃), 115.2 (s, CN), 118.0 (q, ¹*J*_{CF} = 270 Hz, CF₃), 121.0 (q, ¹*J*_{CF} = 269 Hz, CF₃), 132.1 (br s, CNO₂), 133.3 (q, ²*J*_{CF} = 42 Hz, CCF₃), 135.3 (q, ²*J*_{CF} = 39 Hz, CCF₃) ppm. ¹⁹F NMR (CDCl₃): δ -58.0, -61.2 ppm. Anal. Calc. for C₁₂H₅BCuF₁₂N₇O₄: C, 23.49; H, 0.82; N, 15.98. Found: C, 23.41; H, 0.85; N, 15.90.

General Procedure for C–H Amination:

Benzene (0.2 ml, 2.47 mmol, 5.0 equiv.) and *N*-tosyl phenyliodinane (200 mg, 0.49 mmol, 1.0 equiv.) and 4 Å molecular sieves (100 mg) were dissolved in dry CH_2Cl_2 (5 mL). Catalyst $[H_2B(3,5-(CF_3)_2Pz)_2]Cu(NCMe)$ (**3**, 5 mol%) was added, and the resulting mixture was stirred at room temperature under N₂ for 12 h. The greenish solution, was diluted with CH_2Cl_2 and the products were separated using silica gel column chromatography (7:3/hexanes:EtOAc). Yield 44% based on the nitrene source used. Note: The yield of product did not change much when we have used acetonitrile as the solvent. Other experiments were performed via a similar procedure using the applicable catalyst and the arene in a CH_2Cl_2 medium.

X-ray crystallographic data. A suitable crystal covered with a layer of hydrocarbon/Paratone-N oil was selected and mounted on a Cryo-loop. The X-ray intensity data were measured at the room temperature on a Bruker D8 Quest with a Photon 100 CMOS detector equipped with an Oxford Cryosystems 700 series cooler, a Triumph monochromator, and a Mo K α fine-focus sealed tube ($\lambda = 0.71073$ Å). Intensity data were processed using the Bruker Apex3 program suite. Absorption corrections were applied by using SADABS. Initial atomic positions were located by direct methods using XT, and the structures of the compounds were refined by the least-squares method using SHELXL^[56, 57] within Olex2^[58] GUI. All the non-hydrogen atoms were refined

anisotropically. Hydrogen atoms on acetonitrile CH₃ group were included at calculated positions and refined riding on corresponding carbon. The BH₂ hydrogen atoms were located in a Fourier difference synthesis and refined satisfactorily. Oxygen atoms of one of the nitro groups show positional disorder, which was resolved satisfactorily. X-ray structural figures were generated using Olex2. CCDC 1917595 file contains the supplementary crystallographic data. Further details are given in the CIF.

Computational Details: DFT calculations were carried out using Gaussian 16, Revision A.03 package.^[59] Geometry optimization and frequency calculations were performed with B3LYP functional and 6-31+G(d) basis set, which have been proven accurate in previous study of nitrene aziridination catalysts.^[52, 53] The calculated Gibbs free energies are computed in the gas-phase, at 298.15 K and 1.0 atm.

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Supporting Information Available: Tables of selected structural and spectroscopic and computational data, additional figures and details.

Keywords: Catalysis, C-H functionalization, Copper, Nitrene, Pyrazolyl borates

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