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Unusual Electronic Effects of Ancillary Ligands on the Perfluoroalkylation of Aryl Iodides and Bromides Mediated by Copper(I) Pentafluoroethyl Complexes of Substituted Bipyridines

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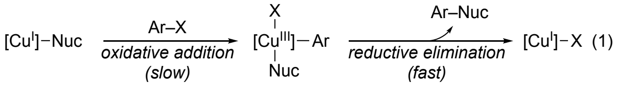
ABSTRACT: Several perfluoroalkylcopper compounds have been reported previously that serve as reagents or catalysts for the perfluoroalkylation of aryl halides. However, the relationships between the reactivity of such complexes and the electronic properties of the ancillary ligands are unknown, and such relationships are not well-known in general for copper complexes that mediate or catalyze cross coupling. We report the synthesis and characterization of a series of pentafluoroethylcopper(I) complexes ligated by bipyridine ligands possessing varied electronic properties. In contrast to the limited existing data on the reactivity of $L_2Cu(I)–X$ complexes bearing amine and pyridine-type ligands in Ullmann-type aminations with aryl halides, the reactions of aryl halides with pentafluoroethylcopper(I) complexes bearing systematically varied bipyridine ligands were faster for complexes bearing less electron-donating bipyridines than for complexes bearing more electron-donating bipyridines. Analysis of the rates of reaction and the relative populations of the neutral complexes $[(R_2bpy)CuC_2F_5]$ and ionic complexes $[(R_2bpy)_2Cu][Cu(C_2F_5)_2]$ formed by these reagents in solution suggests that this effect of electronics on the reaction rate results from an unusual trend of faster oxidative addition of aryl halides to $[(R_2bpy)CuC_2F_5]$ complexes containing less electron-donating R_2bpy ligands than to those containing more electron-donating R_2bpy ligands.

Introduction

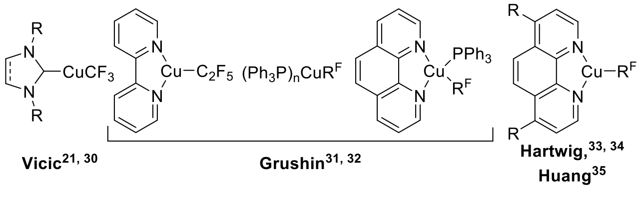
The relationship between the properties of the ancillary ligands and the reactivity of complexes of these ligands in elementary reactions must be understood to select or design catalysts for valuable transformations. While the properties of phosphines and their influence on reactivity have been studied extensively,[1-13] the properties of nitrogen-based ligands and their influence on reactions of organometallic complexes are less studied.[14-15] One class of reactions that is sensitive to the electronic properties of ancillary ligands is oxidative addition. Often, oxidative addition is faster for more electron-rich complexes,[4-7, 14, 16-17] but exceptions to this trend are known, and one such exception of the reactions of three-coordinate Ir(I)–X complexes with C–H and N–H bonds was recently studied in detail.[18]

Previous studies of the mechanism of Cu(I)-based cross coupling reactions of aryl halides have provided strong evidence that oxidative addition of an aryl halide to a Cu(I) complex to form a formal Cu(III) intermediate is rate-limiting and is followed by facile reductive elimination to furnish the coupled product (eq 1).[17, 19-27] Thus, one would expect electron-donating ancillary ligands to increase the electron density at the metal center and facilitate the rate-limiting oxidative addition.[28] Consistent with this hypothesis, our group previously reported that reactions of aryl halides with copper(I) amidate and imidate complexes were faster for complexes ligated by more electron-donating *bis*-amine ligands than those ligated by less electron-donating ligands based on phenanthroline or pyridine structures or ligandless systems.[17] These data suggest that complexes of more electron-rich ligands react faster, but amine and pyridine ligands differ in more than just their electron-donating abilities. Consistent with this trend, Taillefer showed that the yields of a Cu-catalyzed arylation of phenols correlated positively with the electron-donating properties of ancillary bipyridine ligands,[29] but many factors besides reaction rate can affect the yield of a catalytic reaction. Thus, the scope of the trend of the electronic properties on the reactivity of Cu(I) complexes has been assessed in only a cursory fashion and has not been studied for reactions of perfluoroalkyl copper complexes.



$$[Cu^I]–Nuc \xrightarrow[\text{oxidative addition (slow)}]{Ar–X} \overset{X}{\underset{Nuc}{[Cu^{III}]}}–Ar \xrightarrow[\text{reductive elimination (fast)}]{Ar–Nuc} [Cu^I]–X \quad (1)$$

Chart 1. Discrete perfluoroalkylcopper(I) complexes



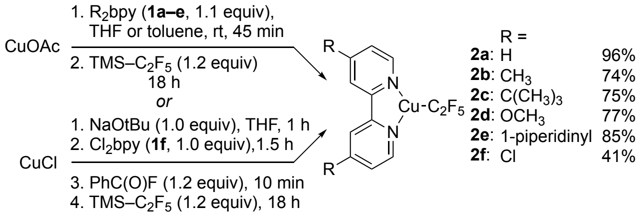
Several discrete perfluoroalkyl complexes of copper(I) bearing ancillary dative ligands, including *N*-heterocyclic carbenes,[21, 30] 1,10-phenanthrolines (phen),[31-35] 2,2'-bipyridine (bpy),[32] and triphenylphosphine[31-32] have been isolated (Chart 1), but studies on the effects of the properties of these ligands on Cu-mediated perfluoroalkylation of aryl halides have not been reported. Several groups have reported that the inclusion of an ancillary ligand (usually phen) in the Cu-catalyzed perfluoroalkylation of aryl iodides is vital to achieve catalytic turnover at moderate reaction temperatures,[28, 35-38] but others have developed Cu-catalyzed reactions that occur in the absence of ancillary ligands at similar temperatures.[39-40] In addition, Grushin and co-workers even reported that addition of phenanthroline, pyridine, and phosphine ligands to “ligandless” $CuCF_3$ diminished the reactivity of this reagent.[41] Thus, the effect of the ancillary ligand on the reactivity of Cu-based perfluoroalkylation reactions is particularly ambiguous.

We report the synthesis of a series of pentafluoroethylcopper(I) complexes containing bipyridine (bpy) ligands with varied electronic properties that react with aryl halides to form perfluoroalkyl arenes. We have measured the effects of the electronic properties of these bpy ligands on the speciation of perfluoroalkylcopper(I) complexes between neutral and ionic forms, the effect of these properties on the rates of the reaction of these complexes with aryl halides, and the effect of the ligand on selectivity. Combined, these data suggest that the reactions of the aryl halides with perfluoroalkylcopper complexes bearing less electron-donating bpy ligands are faster than with those containing more electron-donating bpy ligands. These data contrast the common effects of electronic properties on the rate of oxidative addition of aryl halides.

Results and Discussion

Our investigations began with the preparation of a series of pentafluoroethylcopper(I) complexes ligated by 4,4’-homodisubstituted derivatives of 2,2’-bipyridine (**1a–f**, Scheme 1). Complexes **2a–e** containing electron-donating groups on the bpy scaffold were prepared in good yields by treating a mixture of ligands **1a–e** and anhydrous copper(I) acetate in THF or toluene with trimethyl(pentafluoroethyl)silane (TMS–C_2F_5). While we were unable to prepare complexes containing bpy ligands with strongly electron-withdrawing groups by this procedure, we did prepare $(Cl_2bpy)CuC_2F_5$ by treating CuO*t*Bu generated *in situ* with dichlorobipyridine **1f**, followed by benzoyl fluoride[42] and then TMS–C_2F_5.

Scheme 1. Preparation of $(R_2bpy)CuC_2F_5$ complexes



Consistent with previous reports of perfluoroalkylcopper(I) complexes,[31-35, 42-43] the ^{19}F NMR spectra of complexes **2a–f** in DMF solution all consisted of four resonances, two corresponding to the ethyl group in the neutral $[(R_2bpy)CuC_2F_5]$ form and two to those in the ionic $[(R_2bpy)_2Cu][Cu(C_2F_5)_2]$ form (eq 2). The equilibrium between the neutral and ionic species was reached within 5 min at 65 °C and remained unchanged at different total concentrations of perfluoroalkylcopper species, suggesting that the ionic components exist as solvent-separated ions as opposed to a tight ion pair[17] (see the supporting information). While more electron-donating ligands might be expected to stabilize the cationic $[(R_2bpy)_2Cu]^+$ species more effectively than would more electron-poor ligands, the equilibria of compounds **2a–f** instead generally favored the neutral $[(R_2bpy)CuC_2F_5]$ form more strongly for complexes of more electron-donating R_2bpy than for those of less electron-donating R_2bpy ligands (*K*, Table 1). Indeed, at 65 °C, the system containing the most electron-donating ligand 4,4’-di(1-piperidinyl)-2,2’-bipyridine (**1e**) comprised a 9:91 ratio of the ionic to neutral forms, while the system containing the least electron-donating ligand 4,4’-dichloro-2,2’-bipyridine (**1f**) comprised a 30:70 ratio. A similar trend was observed at 90 °C. A Hammett plot of the equilibrium constants governing the relative populations of the two forms displayed a loose positive correlation (ρ ≈ 1.3) with the σ_p[44] values of the substituents on the bpy ligands (Figure 1).

$$2\ (R_2bpy)CuCF_2CF_3 \underset{65\ ^\circ C}{\overset{K}{\rightleftharpoons}} [(R_2bpy)_2Cu]^+[Cu(CF_2CF_3)_2]^- \qquad (2)$$

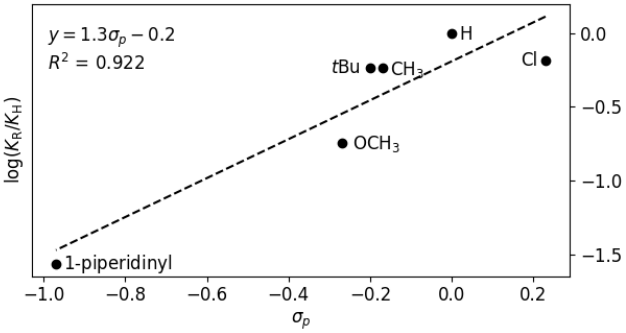
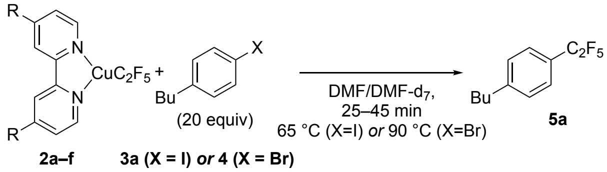


Figure 1. Hammett plot of the equilibrium constants governing the relative populations of neutral and ionic forms of **2a–e** at 65 °C[45]

To assess the effect of the electronic properties of the bpy ligand on perfluoroalkylation reactions with aryl halides, complexes **2a–f** were treated with excess 1-butyl-4-iodobenzene (**3a**) or 1-bromo-4-butylbenzene (**4**) in DMF at 65 °C or 90 °C, respectively (eq 3). The formation of pentafluoroethyl arene **5a** was followed by ^{19}F NMR spectroscopy, and rate constants for these reactions were determined from first-order exponential fits (Table 1, k_{obs}^{I}) or initial rates (k_{init}^{Br}) of the formation of **5a**. These data provide the surprising result that reactions of aryl iodide **3a** with complexes containing the less electron-donating bpy ligands were generally faster than those containing the more electron-donating bpy ligands, with dichlorobipyridine complex **2f** reacting ~4 times faster than di(piperidinyl)bipyridine complex **2e**. A Hammett plot of these rate constants *vs* σ_p revealed a small but positive correlation (ρ ≈ 0.5, Figure 2a).



2a–f **3a (X = I)** *or* **4 (X = Br)** **5a** (3)

Reactions of **2a–f** with aryl bromide **4** at 90 °C proceeded much more slowly than reactions with aryl iodides **3** and in lower yields, complicating analysis of the full reaction profiles. However, the initial rates of reaction, determined from linear fits of the first 5–10% formation of **5a** (Table 1, k_{init}^{Br}), followed the same trend of electronic effects on reaction rates as was observed for reactions with aryl iodides **3** (ρ ≈ 0.4, Figure 2b).

Table 1. Equilibrium constants for complexes 2a–f in DMF and rate constants for the pentafluoroethylation of aryl halides 3a and 4 by reaction with complexes 2a–2f

Complex	R	K (65 °C)^{a}	k_{obs}^{I} (± 0.2×10^{-3} s^{-1})^{b}	k_{corr}^{I} (± 0.3×10^{-3} M^{-1}·s^{-1})^{b,d}	K (90 °C)^{a}	k_{init}^{Br} (± 0.2×10^{-6} M·s^{-1})^{c}	k_{corr}^{Br} (± 0.5×10^{-5} M^{-1}·s^{-1})^{c,e}
2a	H	2.8×10^{-1}	3.2	6.3	1.9×10^{-1}	2.9	11
2b	CH$_3$	1.6×10^{-1}	2.6	4.8	1.4×10^{-1}	2.4	8.3
2c	*t*Bu	1.6×10^{-1}	2.2	4.0	1.4×10^{-1}	2.6	9.1
2d	OCH$_3$	5.1×10^{-2}	2.5	3.7	4.8×10^{-2}	2.7	7.7
2e	1-piperidinyl	7.7×10^{-3}	1.2	1.4	8.1×10^{-3}	1.5	3.6
2f	Cl	1.8×10^{-1}	4.7	8.8	7.8×10^{-2}	5.4	17

$^{a}K = [[Cu(C_2F_5)_2]^-]^2/[(R_2bpy)CuC_2F_5]^2$; relative concentrations determined by ^{19}F NMR spectroscopy in DMF at the specified temperature. ^{b}Reaction conditions: **2** (0.0500 M) and aryl iodide **3a** (1.00 M) in 5:1 DMF:DMF-d$_7$ at 65 °C for 45 min; k_{obs}^{I} derived from exponential fit of formation of **5a**. ^{c}Reaction conditions: **2** (0.0500 M) and aryl bromide **4** (1.00 M) in 5:1 DMF:DMF-d$_7$ at 90 °C for 30 min; k_{init}^{Br} determined from linear fit of formation of **5a**. $^{d}k_{corr} = k_{obs}(1 + 2\sqrt{K})/[\mathbf{3a}]_0$ $^{e}k_{corr} = k_{obs}(1 + 2\sqrt{K})/[\mathbf{2}]_0[\mathbf{4}]_0$ (see the supporting information for derivations)

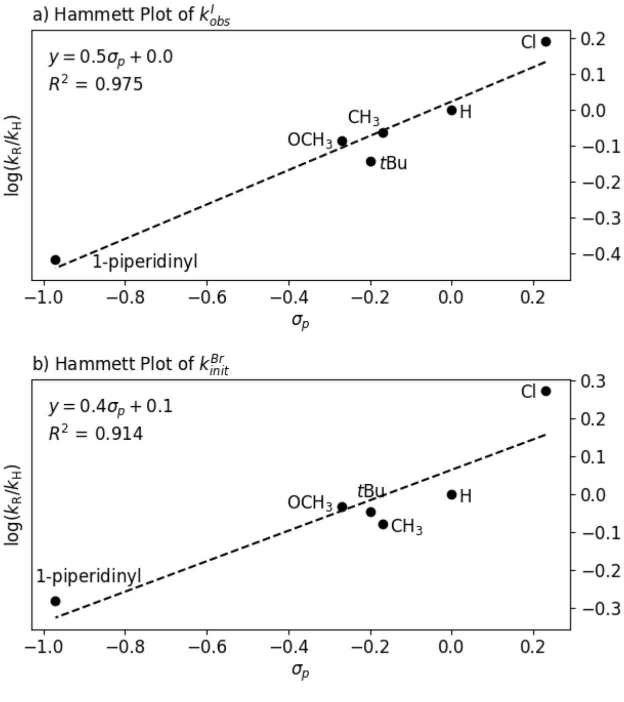
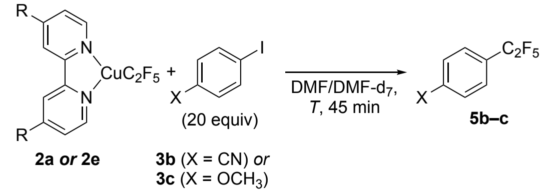


Figure 2. Hammett plots (*vs* σ$_p$) of a) k_{obs}^{I} for the pentafluoroethylation of aryl iodide **3a** by reaction with complexes **2a-f** and b) k_{init}^{Br} for the pentafluoroethylation of aryl bromide **4** by reaction with complexes **2a-f**[45]

The results in Table 2 show the effect of varying the electronic properties of the aryl iodide on the rate of the reaction with pentafluoroethylcopper complexes **2a** and **2e** (eq 4). Reactions of electron-neutral and electron-rich complexes **2a** and **2e** with electron-poor aryl iodide 4-iodobenzonitrile (**3b**) occurred more readily than those with more electron-rich 4-butyl iodobenzene (**3a**) or 4-iodoanisole (**3c**), proceeding at 27 °C at rates that were similar to those of reactions of the same complexes with **3a** or **3c** at the higher temperature of 65 °C. This trend is in agreement with the trend in the rates of reaction of electronically varied aryl halides with "ligandless" CuCF$_3$,[26] wherein more electron-poor aryl iodides reacted more quickly than more electron-rich iodides, and is consistent with commonly-observed effects of the electronic nature of the aryl halide on rate-limiting oxidative addition.[26, 46] However, the effect of the bpy ligand on the reactions of complexes **2a** and **2e** with aryl iodides **3b** and **3c** remained the same as those for reactions with **3a**: reactions of the more electron-poor complex **2a** proceeded more rapidly than reactions involving more electron-rich complex **2e**. Thus, the unusual electronic effects of the ancillary ligand on the rate of the reaction between the perfluoroalkyl copper complex and the aryl halide are not compensated by a balancing trend in electronic effects of the aryl halide.

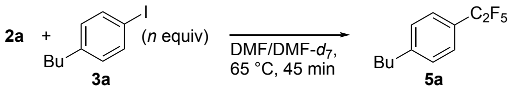


(4)

Table 2. Rate constants for the reaction of electron-neutral and electron-rich complexes 2a and 2e with electronically varied aryl iodides (eq 4).

Complex	R	X (in ArI)	T (°C)	k_{obs}^{I} (± 0.2×10^{-3} s^{-1})
2a	H	CN	27	3.1
2a	H	Bu	65	3.2
2a	H	OCH$_3$	65	3.1
2e	1-piperidinyl	CN	27	1.8
2e	1-piperidinyl	Bu	65	1.2
2e	1-piperidinyl	OCH$_3$	65	1.3

Reaction conditions: **2** (0.0500 M) and **3b** or **3c** (1.00 M) in 5:1 DMF:DMF-d$_7$ at the specified temperature for 45 min



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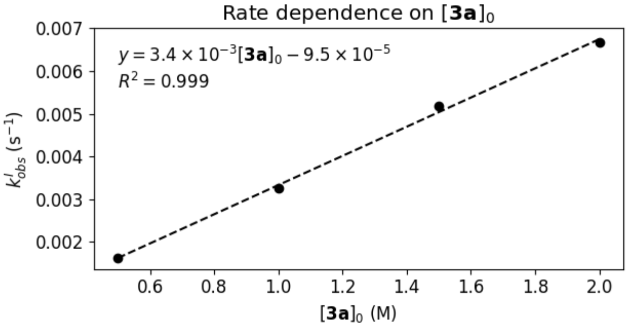


Figure 3. Dependence of the rate of the reaction of **2a** with **3a** on the initial concentration of **3a** ([**3a**]$_0$). Reaction conditions: **2a** (0.0500 M) and aryl iodide **3a** (0.500–2.00 M, *n* = 10–40) in 5:1 DMF:DMF-d$_7$ at 65 °C for 45 min

The rates of reaction of **2a** with varying concentrations of aryl iodide **3a** revealed the reaction order in aryl halide. The rates of the reactions of **2a** in the presence of 0.500, 1.00, 1.50, and 2.00 M **3a** (eq 5) displayed a strong linear correlation with the initial concentration of **3a** ([**3a**]$_0$), implying that the reaction is first-order in in aryl iodide (Figure 3). Combined with the first-order behavior in the concentration of complexes **2** (revealed by the first-order exponential fits of product formation in reactions with a large excess of **3a**), these findings are consistent with rate-limiting oxidative addition of aryl halide to complexes **2**.

Because the neutral form of perfluoroalkylcopper species, not the ionic form, is known to be the component that reacts with aryl halides,[21, 47] it is necessary to account for the equilibrium between these forms of the CuC_2F_5 reagents to determine the effect of the bpy ligands on the rate of reaction of $[(R_2bpy)CuC_2F_5]$ with aryl halides **3a** and **4**. Given the first-order dependence of the rate on both **2** and the aryl halide, the rate constants k_{corr} obtained after correcting k_{obs}^{I} and k_{init}^{Br} for the relative equilibrium population of the $[(R_2bpy)CuC_2F_5]$ species are given by eq 6 and eq 7, respectively (see the supporting information for detailed derivations). The values for k_{corr} are given in Table 1.

$$k^{I}_{corr} = \frac{(1+2\sqrt{K})k^{I}_{obs}}{[3]_0} \quad (6) \qquad k^{Br}_{corr} = \frac{(1+2\sqrt{K})k^{Br}_{init}}{[2]_0[4]_0} \quad (7)$$

Hammett plots of k_{corr} *vs* σ_p for the reactions with aryl iodide **3a** and bromide **4** (Figure 4) provided positive correlations between the rate constants and σ_p that were more linear than those obtained from the raw rate constants k_{obs}^{I} and k_{init}^{Br}. The substituent effects on k_{corr} were also slightly stronger than on k_{obs}^{I} and k_{init}^{Br} ($\rho \approx 0.7$ for k_{corr}^{I} and $\rho \approx 0.5$ for k_{corr}^{Br}). Assuming rate-limiting oxidative addition of the aryl halides to the neutral $[(R_2bpy)CuC_2F_5]$ complex (*vide supra*), this result suggests that oxidative addition is faster to the complexes of *less* electron-donating bpy ligands than to complexes of *more* electron-donating bpy ligands. This trend is the opposite of what is observed most commonly for oxidative addition to a metal center.[4-7, 14, 16]

An alternative hypothesis to account for this trend of ligand electronic effects on the rate of the reaction of aryl halides with$[(R_2bpy)CuC_2F_5]$ is that the bpy ligand initially dissociates from the Cu center to generate a small amount of free "CuC_2F_5" (**6**), which then reacts more rapidly with the aryl halide than the ligated species (eq 8). Because more electron-rich σ-donor ligands generally bind more strongly to metal centers, complexes of more electron-rich bpy ligands would generate smaller quantities of free CuC_2F_5 than complexes of more electron-poor ligands. Moreover, Mikami and Grushin have both shown that solutions of "ligandless" CuC_2F_5 in DMF react with aryl iodides and bromides at temperatures similar to or lower than those in this work to form pentafluoroethyl arenes.[43, 48] Thus, a "ligandless" complex, instead of $[(R_2bpy)CuC_2F_5]$, could be the species that reacts with aryl halides during our studies.

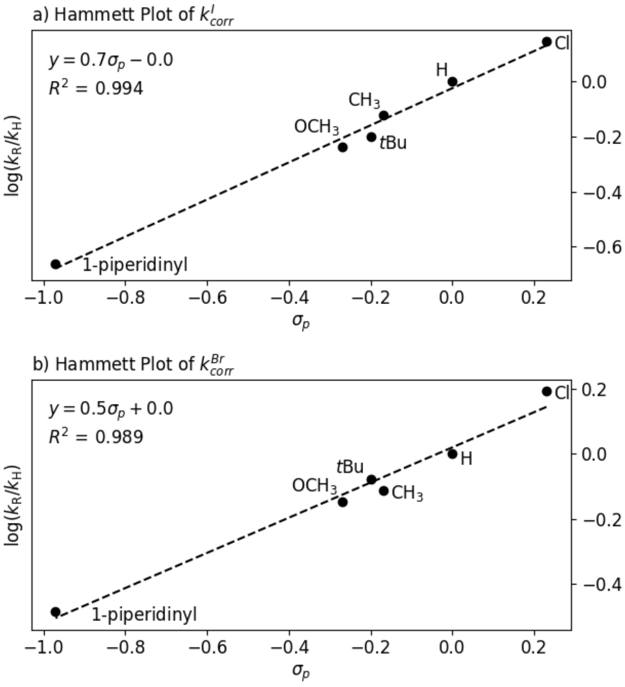


Figure 4. Hammett plots (*vs* σ_p) of equilibrium-adjusted rate constants k_{corr} for the pentafluoroethylation of a) **3a** and b) **4** by reaction with complexes **2a-f**[45]

$$[(R_2bpy)CuC_2F_5] \xrightarrow[R_2bpy]{} \underset{\mathbf{6}}{\text{"}CuC_2F_5\text{"}} \xrightarrow[CuX]{ArX} ArC_2F_5 \quad (8)$$

To evaluate this hypothesis, a solution of "ligandless" CuC_2F_5 (**6**) in DMF was prepared by treatment of a solution of $K(DMF)[Cu(O\mathit{t}Bu)_2]$[49] in DMF with ethyl pentafluoropropionate, followed by neutralization with $3HF{\cdot}NEt_3$.[48] The formation of pentafluoroethyl arene **5a** by reaction of **6** with excess aryl iodide **3a** at 65 °C was monitored by ^{19}F NMR spectroscopy and was found to occur with a rate constant of 9.7×10^{-4} s^{-1}. While this value is similar to the rate constant of reactions of **3a** with piperidinyl-substituted **2e** ($k_{obs}^{I} = 1.4\times10^{-3}$ s^{-1}), which is the slowest-reacting of complexes **2a–f**, reactions of **2a–d** and **2f** with **3a** proceeded at least 2.5 times faster than the reactions of "ligandless" CuC_2F_5 reagent **6** with **3a** (Table 1, k_{obs}^{I}). This result shows that "ligandless" CuC_2F_5 is not kinetically competent to be an intermediate in the reactions of complexes **2a–d** and **2f** with aryl halides.

To assess the potential reactivity through the "ligandless" complex **6** further, we conducted a competition experiment, whereby complexes **2a**, **2e**, or **6** were allowed to react with an equimolar mixture of 2- and 4-iodotoluene (**3d** and **3e**, Scheme 2). The ratio of pentafluoroethyl toluene products **5d**:**5e** formed from the reactions with **2a** and **2e** (44:56 and 39:61, respectively) were different from that with ligandless **6** (68:32), implying that the steric environment of the Cu center that reacts with the aryl halide starting from **2a** and **2e** is different from that starting from **6**,[50] and is, therefore, not the "ligandless" copper complex.

Scheme 2. Competition reactions of pentafluoroethyl complexes with aryl iodides 7a and **7b**

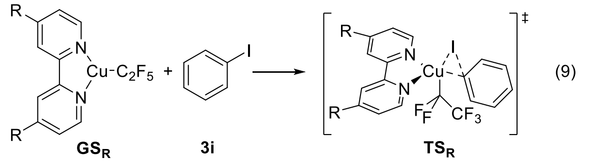
	5d		5e
2a	44%	:	56%
2a + 2 bpy	40%	:	60%
2a + 15 bpy	39%	:	61%
2e	39%	:	61%
2e + 2 pip$_2$bpy	37%	:	63%
2e + 15 pip$_2$bpy	37%	:	63%
6	68%	:	32%

Finally, the possibility of reactions of **2a–f** through the ligandless complex was assessed by measuring the rate of reaction of **2a** with **3a** in the presence of 2 equiv added bpy. The rates of reaction in the presence and absence of added ligand were indistinguishable (k_{obs}^{I} = 3.0×10^{-3} s^{-1} with 2 equiv of added bpy *vs* 3.2×10^{-3} s^{-1} without), implying that the overall effect of a pathway involving reaction with the ligandless species must be minor and that the electronic effect of the ligand on the rate of reaction is not due to dissociation of R$_2$bpy from [(R$_2$bpy)CuC$_2$F$_5$] prior to reaction with the aryl halide.

Table 3. Computed energies of activation for the oxidative addition of iodobenzene to [(R$_2$bpy)CuC$_2$F$_5$]

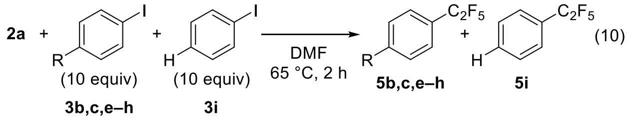
R	σ_p	$\Delta G_{calc}^{\ddagger}$ (kcal/mol)	$\Delta H_{calc}^{\ddagger}$ (kcal/mol)	$\Delta S_{calc}^{\ddagger}$ (cal/mol·K)
N(CH$_3$)$_2$	–0.83	24.5	9.5	–41
OCH$_3$ (**2d**)	–0.27	23.9	9.4	–40
H (**2a**)	0	23.9	8.8	–42
Cl (**2f**)	0.23	25.0	8.3	–46
CN	0.66	26.1	7.5	–52

See the supporting information for computational details



These experimental results were consistent with DFT calculations (see the supporting information for computational details). The computed free energy barriers of concerted oxidative addition of unsubstituted iodobenzene (**3f**) to the neutral forms of **2a**, **2d**, and **2f** ($\Delta G_{calc}^{\ddagger}$ = 24–25 kcal/mol; Table 3; eq 9) were similar in magnitude to those determined experimentally from k_{obs}^{I} ($\Delta G_{expt}^{\ddagger}$ = 23–24 kcal/mol). However, no clear trend was observed between the computed free energies of activation and the σ_p values of the substituents on the bpy ligand (Table 3). Nevertheless, a clear trend was observed between the *enthalpies* of activation $\Delta H_{calc}^{\ddagger}$ and the σ_p values of the substituents on the bpy ligand, and this trend was consistent with the trend observed experimentally; the enthalpies of activation for oxidative addition of iodobenzene to complexes of the more electron-poor bpy ligands were computed be lower than those to complexes of the more electron-rich ligands. These calculated values for $\Delta H_{calc}^{\ddagger}$ are significantly lower than those for $\Delta G_{calc}^{\ddagger}$, highlighting a large entropic contribution to $\Delta G_{calc}^{\ddagger}$ ($\Delta S_{calc}^{\ddagger}$ = –40 – –52 cal/mol·K), which has been measured experimentally[46] and calculated previously for other reactions of copper complexes with aryl halides.[17, 23] The observation of a trend in $\Delta H_{calc}^{\ddagger}$ but not in $\Delta G_{calc}^{\ddagger}$ likely results from the large uncertainties introduced in implicit solvation models and calculated entropies.[51] These calculations, therefore, support our hypothesis that the effect of the ancillary ligand on the experimental rates is due to modulation of the barrier to the rate-limiting elementary step of oxidative addition.

The observed trends in the rates of reaction of complexes **2** with aryl halides and in $\Delta H_{calc}^{\ddagger}$ could be explained by an accumulation of negative charge around the Cu center during the oxidative addition step, which would be stabilized by more electron-poor ligands. Indeed, the natural atomic charges on the Cu centers determined through natural population analysis[52] of the optimized transition state structures **TS$_R$** in all cases decreased relative to those of the **GS$_R$** structures (Δq_{Cu} = –0.02 – –0.04), although all of the net charges were positive (q_{Cu} = +0.44 – +0.56; see Tables S5–S6 in the supporting information for a list of natural atomic charges of specific atoms and fragments of the computed structures). Such a decrease in charge could result from the aryl halide attacking an electrophilic Cu center during the oxidative addition step. In such a pathway, more electron-rich aryl halides would be expected to react more quickly with compounds **2** than electron-poor aryl iodides due to better stabilization of a partial positive charge on the arene.



R = CN (**3b**), OCH$_3$ (**3c**), CH$_3$ (**3e**), Cl (**3f**), CF$_3$ (**3g**), COCH$_3$ (**3h**)

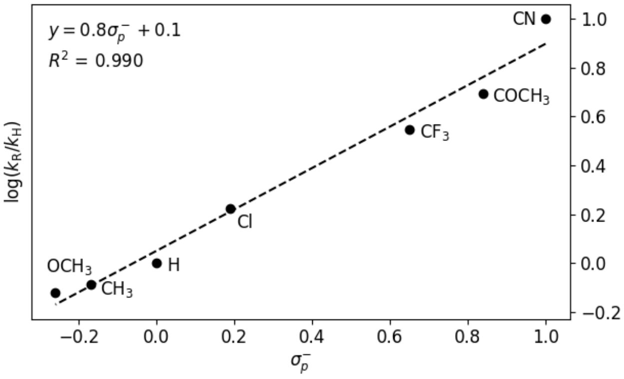


Figure 5. Hammett plot (*vs* σ_p^-) of the rates of reaction of **2a** with *para*-substituted iodobenzenes relative to unsubstituted iodobenzene as determined by competition experiments. See the supporting information for experimental details.

This prediction is inconsistent with the measured rates of reaction of aryl iodides **3a–c** with **2a** and **2e** (*vide supra*). To gain a more detailed view into this electronic effect, we subjected **2a** to reactions with equimolar mixtures of *para*-substituted aryl iodides **3b**, **3c**, or **3e–3h** and unsubstituted iodobenzene (**3i**) at 65 °C (eq 10). The rates of reaction of the substituted iodobenzenes with **2a** were determined relative to **3i** with **2a** by the final ratio of substituted pentafluoroethylarene products **5** to pentafluoroethylbenzene (**5i**; see the supporting information for details). A Hammett plot of these relative rates revealed a strong *positive* correlation with σ_p^-[44] (ρ = 0.8, Figure 5), the opposite of what would be expected for a mechanism in which the copper acts as an electrophile. The positive ρ value suggests a buildup of negative charge on the arene, which is reflected by a decrease in the summed natural atomic charges of the aryl fragment in all $\mathbf{TS_R}$ (Δq_{aryl} = –0.06 – –0.07). This result is consistent with the results of Grushin and co-workers, who found a ρ value of +0.91 for reactions involving substituted aryl iodides with a "ligandless" $CuCF_3$ system when fitting against the σ_p^- parameters of the substituent on the arene.

Despite the aforementioned decrease in positive charge on the Cu center in $\mathbf{TS_R}$, relative to $\mathbf{GS_R}$, the aggregate natural atomic charges of the R_2bpy fragments of the computed structures in all cases were slightly more positive in $\mathbf{TS_R}$ than in $\mathbf{GS_R}$ (Δq_{R2bpy} = +0.02 – +0.03). Such an observation is inconsistent with the hypothesis that the bpy ligand helps to accommodate a buildup of negative charge at the Cu center, although we acknowledge that calculated localized charges (both those on the bpy ligands and those on the Cu centers) may be misleading due to the global nature of the electronic wavefunction. Unfortunately, further analysis of the atomic charges, computed geometries, and the frontier molecular orbitals in the context of so-called "inverted ligand field" measured for the formally Cu(III) complex $Cu(CF_3)_4^{-}$[53-56] revealed no clear trends that might explain the reactivities of complexes **2** with aryl halides. A more detailed theoretical treatment than that presented in this work is needed to elucidate the underlying effect of the bpy ligand on the reactivities of complexes **2** with aryl halides.

Conclusions

In summary, we have prepared a series of $L_2Cu–C_2F_5$ complexes in which L_2 are bpy ligands possessing varied electronic properties and investigated the kinetics of the reactions of these complexes with aryl halides to form pentafluoroethyl arenes. The complexes comprised an equilibrium between the neutral $[(R_2bpy)CuC_2F_5]$ and ionic $[(R_2bpy)_2Cu][Cu(C_2F5)_2]$ forms in DMF solution, which favored the neutral form more heavily for the complexes of more electron-donating bpy ligands than for complexes of less electron-donating bpy ligands. A combination of equilibrium data on this interconversion and kinetic data on the reactions with aryl halides implies that the rate-limiting oxidative addition of aryl halides to the neutral form of these complexes is, in contrast to common effects of ancillary ligands, faster for complexes of less electron-donating ligands than for those of more electron-donating ligands. This effect contrasts with the trend of the electronic effects of ligands on the rate of oxidative addition of aryl halides to amidate complexes ligated by more electron-rich alkylamines *vs* less electron-rich phenanthrolines[17] and highlights the unusual properties of complexes containing perfluoroalkyl ligands.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures, spectral data, computational procedures, and molecular coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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