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Catalytic C–S, C–Se, and C–P Cross-Coupling Reactions Mediated by a Cu^{I}/Cu^{III} Redox Cycle

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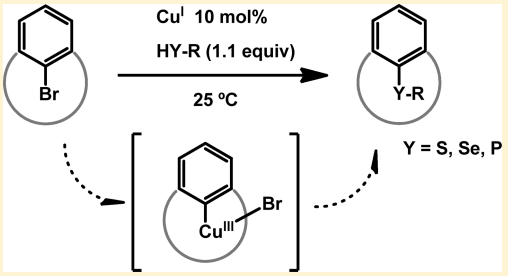
Supporting Information

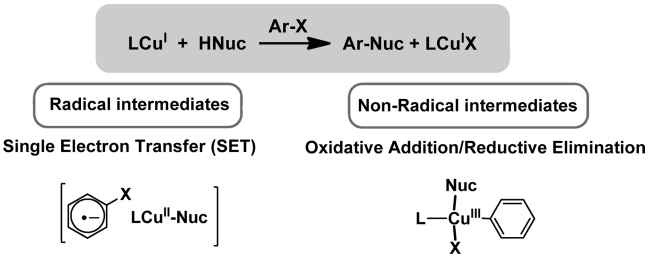
ABSTRACT: A well-defined macrocyclic aryl-Cu^{III} complex (**1**) readily reacts with a series of R–SH, Ar–SH, Ar–SeH, and $(RO)_2(O)$–PH (R = alkyl) nucleophiles to quantitatively afford the corresponding aryl alkyl thioethers, biaryl thioethers, biaryl selenide, and aryl dialkyl phosphonates, respectively. Competition experiments using bifunctional substrates revealed the important impact of lower pK_a values in order to discriminate between functional groups, although other influencing parameters such as steric effects have been identified. The catalytic version of these reactions is achieved using aryl bromide and aryl chloride model substrates, affording C–S, C–Se, and C–P coupling compounds in excellent to moderate yields. Low-temperature UV–vis and NMR monitoring of the reactions of complex **1** with a variety of nucleophiles support the formation of a ground-state **1**–nucleophile adduct. A mechanistic proposal for reaction of **1** with S-nucleophiles involving key nucleophile deprotonation and aryl-nucleophile reductive elimination steps is finally described.



INTRODUCTION

Copper-catalyzed cross-coupling reactions for the formation of aryl–heteroatom bonds is currently a hot topic, due to the importance of developing new sustainable synthetic tools for these transformations and finding new methodologies beyond those based on palladium.[1,2] For the past 10 years many copper-mediated or -catalyzed procedures have been developed for C_{aryl}–N and C_{aryl}–O bond formation, usually starting from aryl halide substrates,[3−5] although direct arene C–H functionalization methodologies have been acquiring more relevance in the recent years.[6−9] Less abundant is the number of publications devoted to copper-catalyzed C_{sp^2}–S and C_{sp^2}–Se bond formation for the synthesis of biaryl thioether, aryl alkyl thioether, alkenyl thioether, and alkenyl selenoether subunits,[1,2,10−12] important in pharmaceutical scaffolds, and a few examples of C_{aryl}–Se or C_{aryl}–P bond formation[13−18] and $C_{alkenyl}$–S,[19,20] $C_{alkenyl}$–Se,[21] or $C_{alkenyl}$–P[22] bond formation have been reported. The vast majority of copper-based cross-coupling methodologies rely on the optimization of the experimental conditions upon the selection of a given auxiliary ligand. Importantly, a clear understanding of the mechanistic details of these transformations could help in the rational design of new methodologies for copper-catalyzed C–heteroatom bond forming reactions.[23−27] However, the use of insoluble bases and the highly concentrated reaction mixtures usually preclude mechanistic studies such as spectroscopic monitoring; thus, several proposals have been made mostly on the basis of a small amount of experimental evidence and extensive computational studies. The most often invoked mechanistic pathways are (a) radical-based single-electron transfer (SET) involving a Cu^{I}/Cu^{II} redox pair and (b) an oxidative addition/reductive elimination process involving a Cu^{I}/Cu^{III} redox catalytic cycle (Scheme 1).[24,25] Furthermore, conclusions based on computational studies have to be interpreted carefully, because conflicting results have been reported depending on the DFT functional or basis set employed.[24,25] A very limited number of publications have also dealt with mass spectrometry monitoring under catalytic conditions and some information has been extracted, although the aryl halide activation step remains obscure.[28] Therefore, it is imperative to develop new systems from which an experimental mechanistic understanding could be extracted. Recently we have reported a family of well-defined aryl–Cu^{III}–halide species that proved competent in C_{aryl}–N,[29,30] C_{aryl}–O,[31,32]

Scheme 1. Relevant Mechanistic Proposals for Copper-Catalyzed Cross-Coupling (Ullmann-Type) Reactions



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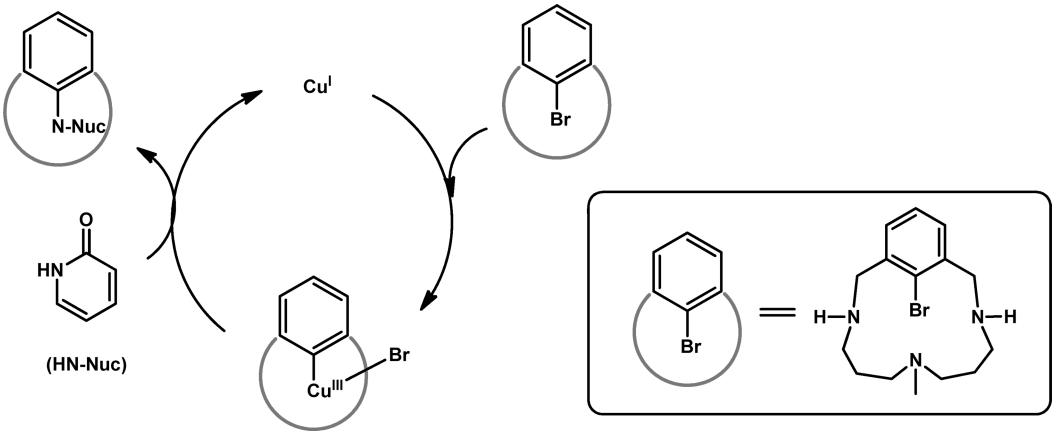
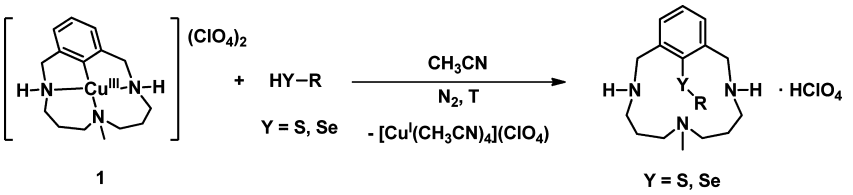
Scheme 2. Copper-Catalyzed C−N Cross-Coupling Reaction Using Model Aryl Halide Substrates, with the Direct Spectroscopic Observation of Aryl−Cu^{III}−Br Intermediate Species



Scheme 3. Reaction of Aryl−Cu^{III} Complex 1 with Sulfur and Selenium Nucleophiles Resulting in C−S and C−Se Reductive Elimination Products



and C_{aryl}−halide[33] bond forming reactions. The isolated aryl−Cu^{III} species react at room temperature with amides, phenols, and carboxylic acids to undergo reductive elimination, affording the corresponding cross-coupling products and Cu^{I}. Importantly, aryl halide model substrates and catalytic amounts of Cu^{I} in the presence of a given nitrogen or oxygen nucleophile engage in a catalytic reaction to quantitatively produce the cross-coupling product with the intermediacy of aryl−Cu^{III}−X species (Scheme 2), which is formed by aryl halide oxidative addition at Cu^{I}.[29] Important mechanistic information has been gained with the latter systems, since those constitute the first unequivocal experimental evidence of the Cu^{I}/Cu^{III} catalytic cycle in Ullmann-type reactions,[29,31] in which the oxidative addition occurs rapidly and the halide to nucleophile exchange or the reductive elimination is rate-limiting.

In the present work we expand the study of the reactivity of the well-defined macrocyclic aryl−Cu^{III} species with S, Se, and P nucleophiles, and experimental proof is given for the catalytic version of these transformations with the intermediacy of aryl−Cu^{III}−X species. Aromatic and aliphatic thiols, benzeneselenol, and H-phosphonate diesters are the nucleophiles used, and the pK_a dependence of the nucleophile reactivity is discussed in detail.

RESULTS AND DISCUSSION

We selected the well-defined aryl−Cu^{III} complex **1** as the starting point, to test its ability to react with different sulfur, selenium, and phosphorus nucleophiles and to afford the corresponding C_{aryl}−heteroatom coupled products.[8,34] We followed a general procedure that consists of mixing complex **1** and the nucleophile (0.9−1.5 equiv) in deuterated acetonitrile under mild temperatures (25−50 °C) and monitoring the reaction by ^{1}H NMR spectroscopy.

Reactivity of Thiophenols and Alkanethiols in C−S Bond Formation Reactions. The aryl−Cu^{III} complex **1** reacts smoothly with HS nucleophiles in acetonitrile at room temperature to form quantitatively the corresponding C−S reductive elimination product (Scheme 3). Since both reactants and products are diamagnetic species, containing either low-spin Cu^{III} or Cu^{I} metal ions, the reaction can be directly monitored by ^{1}H NMR spectroscopy. Reaction occurs easily at room temperature using aromatic and aliphatic thiols (Table 1).

The reaction of complex **1** with thiophenols at room temperature is significantly faster (<10 min) than that with aliphatic thiols (1.5−3 h to reach completion, as determined by NMR monitoring) to yield the corresponding diaryl thioethers and aryl alkyl thioethers, respectively, suggesting that the reaction rate is pK_a dependent (Table 1).[31,35] It is worth pointing out that 1-butanethiol takes about 1.5 h to reach completion, whereas 2-methyl-2-propanethiol requires about 3 h despite the similar pK_a values, indicating that steric effects also influence the reaction rate (see mechanistic discussion below). Kinetic studies for the reaction of complex **1** with thiol nucleophiles were precluded due to the abundant precipitation of Cu^{I}−sulfide compounds upon reaction of the excess thiol with the Cu^{I} formed during the course of the reaction.[36,37]

Reactivity of Benzeneselenol in C−Se Bond Forming Reactions. Complex **1** reacts with benzeneselenol in acetonitrile at room temperature to afford the C−Se coupling product quantitatively (Scheme 3). The reaction proceeds very rapidly (approximately 1 min), and 1.5 equiv of benzeneselenol is needed to displace the reaction to the complete formation of the biaryl selenide product (Table 1, entry 8). The coupling product has been characterized by NMR spectroscopy, including the experimental evidence on the formation of the C−Se bond by observing a new ^{77}Se NMR signal at −150.7

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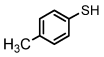
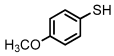
Table 1. C_{aryl}–S and C_{aryl}–Se Coupling Product Yields from the Reaction of 1 with Thiophenols, Aliphatic Thiols, and Benzeneselenol[a]

Entry	HY-R	pKa (DMSO)	% yield[b]
1		10.3	100
2		10.3-11.2	100
3		11.2	100
4		9.0[c]	100
5		17.0	100
6		17.9	100
7		-	100
8		7.1	100[d]

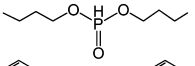
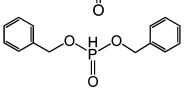
[a]General conditions: [**1**] = 12 mM, [HS-R] = 12.5 mM, CD_3CN in 0.7 mL of CD_3CN at 25 °C. [b]Calculated by ^1H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. [c]pK_a(DMSO) value for 4-bromothiophenol (the 4-chlorothiophenol pK_a value is not tabulated; a value close to that of the 4-bromo species is expected).[35] [d]Conditions: [**1**] = 12 mM, [HSe-Ph] = 18 mM, reaction time <1 min.

ppm in the ^1H–^{77}Se HMBC spectrum,[38] taking benzeneselenol itself (0 ppm) as the reference.[39]

Reactivity of H-phosphonate Diesters in C–P Bond Forming Reactions. To further investigate the scope of reactions in which Cu^I/Cu^{III} redox cycles could be implicated, we turned our attention to copper-catalyzed C–P bond forming reactions. The combination of aryl–Cu^{III} complex **1** with H-phosphonate diesters in acetonitrile at 50 °C afforded the corresponding aryl dialkyl phosphonate products in moderate to excellent yields (Scheme 4 and Table 2).

Reaction with H-phosphonate dimethyl ester (Table 2, entry 1) is complete after 1.5 h, affording excellent yields of the corresponding aryl–P coupling product. Similarly, the coupling product from the reaction of **1** and H-phosphonate dibenzyl ester is formed quantitatively after 2 h (Table 2, entry 3). However, in both cases, partial dealkylation and phosphite–oxide alkylation of the nucleophile occurs (see the Supporting Information). This phenomenon has been already reported in the literature,[16] and a much faster decomposition of the nucleophile itself under the reaction conditions is found in the case of H-phosphonate dibenzyl ester. On the other hand, a 48% yield of the coupling product was obtained when H-phosphonate dibutyl ester was used as nucleophile (Table 2, entry 2). In this case, a lower reactivity of the nucleophile is

Table 2. Reaction of Aryl–Cu^{III} Complex 1 with H-phosphonate Diesters To Yield the Corresponding C–P Coupling Product[a]

Entry	Nucleophile	(equiv.)	T (°C)	Reaction time	% yield[b]
1		(1.1)	50	1.5 h	95
2		(2)	50	18 h	48
3		(0.9)	50	2 h	95[c]

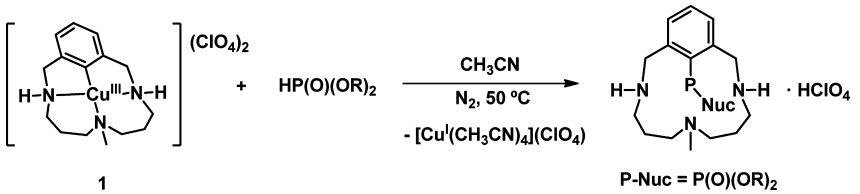
[a]General conditions: [**1**] = 12 mM, [HS-Nuc] = 11–24 mM, CD_3CN. [b]Calculated by ^1H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. [c]With respect to limiting nucleophile.

observed but the formed product does not undergo the aforementioned decomposition pathway.

Competition Experiments Using Bifunctional Substrates. Given the excellent yields obtained for the cross-coupling reactions with the S, Se, and P nucleophiles tested, we decided to undertake competition experiments to evaluate the reactivity of **1** with substrates bearing two distinct nucleophile moieties capable of undergoing cross-coupling (Scheme 5), and in particular we selected bifunctional substrates combining (a) aromatic thiol and alcohol groups (Table 3, entry 1), (b) aromatic carboxylic acid and thiol groups (Table 3, entry 2), and (c) aliphatic carboxylic acid and thiol groups (Table 3, entries 3 and 4).

The aryl–Cu^{III} complex **1** reacts readily with 4-mercaptophenol to yield quantitative cross-coupling with the thiol moiety (Table 3, entry 1); thus, no reactivity is observed with the alcohol moiety. In this substrate, the disparate pK_a(DMSO) values (18.0 for phenol and 10.3 for thiophenol) are presumed to be the most important parameter favoring reactivity toward the most acidic thiol moiety. On the other hand, reaction with 4-mercaptobenzoic acid affords the C–S coupling product in a low 45% yield (Table 3, entry 2). The other approximately 50% of product corresponds to the C–O coupling, which precipitates out of the solution due to the formation of insoluble Cu–sulfide species (see IR characterization in the Supporting Information). In this case, the very similar pK_a(DMSO) values (11.0 for benzoic acid and 10.3 for thiophenol) allow for a competitive reactivity, affording almost equimolar amounts of C–S and C–O coupling products. Finally, we compared the reactivity between aliphatic carboxylic acid or thiol moieties in the same molecule, and we selected 3-mercaptopropanoic acid and 11-mercaptoundecanoic acid as bifunctional nucleophiles (Table 3, entries 3 and 4, respectively). These competition experiments show that 3-mercaptopropanoic acid affords better yields (75% in C–S coupling product) than 11-mercaptoundecanoic acid (51% of

Scheme 4. Reaction of Aryl–Cu^{III} Complex 1 with Selenium and Phosphorus Nucleophiles Resulting in C–Se or C–P Bond Coupling



1

P-Nuc = P(O)(OR)$_2$

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Scheme 5. Reaction of Aryl−Cu^{III} Complex 1 with Thiols in Presence of Other Functional Groups

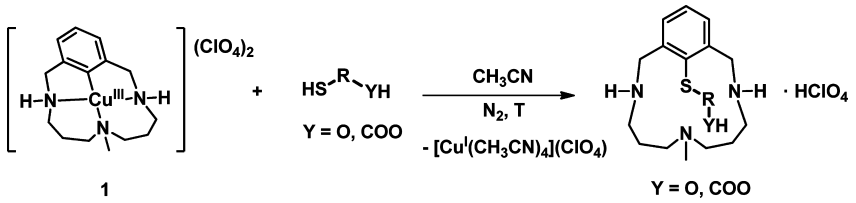
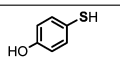
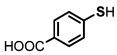
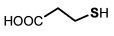
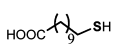


Table 3. Aryl-S-Nuc Product Yields from the Reaction of 1 with Bifunctional Substrates[a]

Entry	HY-R-SH	C-S / C-O % yield[b]
1		100 / 0
2		45 / 55
3		75 / 25
4		51 / 43 [c]

[a]General conditions: [1] = 12 mM, [HS-Nuc] = 12.5 mM, CD_3CN in 0.7 mL CD_3CN at room temperature. [b]Calculated by ^1H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. [c]6% of intramolecular C−N reductive elimination product.[33]

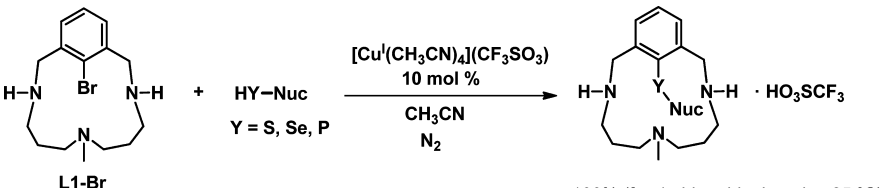
C−S coupling), despite the similarity of pK_a(DMSO) values for the SH and OH moieties, respectively (17 for 1-butanethiol and 12.6 for acetic acid). This noticeable difference in yields indicates that at least one additional, as yet unidentified factor in addition to the pK_a is also contributing to the reaction. A possible explanation might consist of the fact that the shorter chain spacer between functional groups allows the nucleophile to interact in a proper way through both the carboxylic acid and the thiol moieties of the molecule, leaving the molecule oriented to favor the C−S coupling. In contrast, when the alkyl chain is larger (11-mercaptoundecanoic acid, Table 3, entry 4), the yield remains at 50%.

Catalytic C−S, C−Se, and C−P Bond Formation Involving an Aryl−Cu^{III} Complex. The catalytic coupling of thiophenols, alkanethiols, selenols, and dialkyl phosphites was achieved by using the model aryl bromide **L1-Br** substrate in the presence of catalytic amounts of Cu^I salt (Scheme 6). A 1.1 equiv amount of both 4-chlorothiophenol and 1-butanethiol undergo quantitative catalytic cross-coupling with the aryl bromide **L1-Br** to afford the corresponding diaryl thioether and aryl alkyl thioether products in the presence of 10 mol % of $[Cu^I(CH_3CN)_4](CF_3SO_3)$ at room temperature under a nitrogen atmosphere.

In the case of the catalytic insertion of 4-chlorothiophenol, the loading of the Cu^I source was lowered to 0.5 mol %, still with quantitative yields. Furthermore, when the aryl chloride substrate **L1-Cl** was used, an 85% yield of the C−S coupling product could be obtained with 1 mol % of Cu^I. On the other hand, catalysis employing Se nucleophiles and P nucleophiles proved to be more challenging. It was necessary to increase the amount of benzeneselenol to 2 equiv to afford the corresponding diaryl selenide product in 72% yield. For H-phosphonate dimethyl ester the desired coupling was achieved in 46% yield upon heating to 50 °C and employing up to 2 equiv of substrate. In all cases slow addition of the substrate proved to increase the yields of the catalytic reaction either by preventing the precipitation of the Cu^I salt with thiolates and selenolates or by minimizing the dimethyl phosphite decomposition. As expected, when these reactions were monitored by UV−visible spectroscopy, the oxidative addition product aryl−Cu^{III}−Br ($\mathbf{2_{Br}}$) was observed as a steady-state intermediate (see the Supporting Information for details).[29]

Mechanistic Insights: Identification of aryl−Cu^{III}···HS−R Adducts. The detailed mechanism of the interaction of **1** with the HX−Nuc (X = S, Se, P) nucleophiles is still not completely understood, although a clear parallelism can be made with the reactivity of **1** with carboxylic acids and phenols.[31] In this regard, we investigated the possibility of trapping adduct species between **1** and the R−SH nucleophile, as was previously observed for carboxylic acids and the most acidic phenol derivatives.[31] To test this hypothesis, low-temperature UV−visible studies were conducted using substoichiometric amounts of the nucleophile to prevent precipitation of copper(I)−sulfide species. When the reaction of complex **1** with 1-butanethiol (*n*Bu-SH), 4-methoxythiophenol, and benzeneselenol was monitored, clear changes in the UV−vis spectra were observed (see Figure 1). The corresponding ^1H NMR monitoring for the reactions with 1-butanethiol and 4-methoxythiophenol revealed the formation of transient species that we assign to an adduct between **1** and the thiol nucleophile (see Figures S51−S53 in the Supporting Information). Signals that appears within the first 5 min of reaction are assigned to the adduct species, which show a clear

Scheme 6. Catalytic C−S, C−Se, and C−P Cross-Coupling Reactions



100% (for 4-chlorothiophenol at 25 °C)
100% (for 1-butanethiol at 25 °C)
72% (for C_6H_5-SeH at 25 °C)
46% (for $HP(O)(OCH_3)_2$ at 50 °C)

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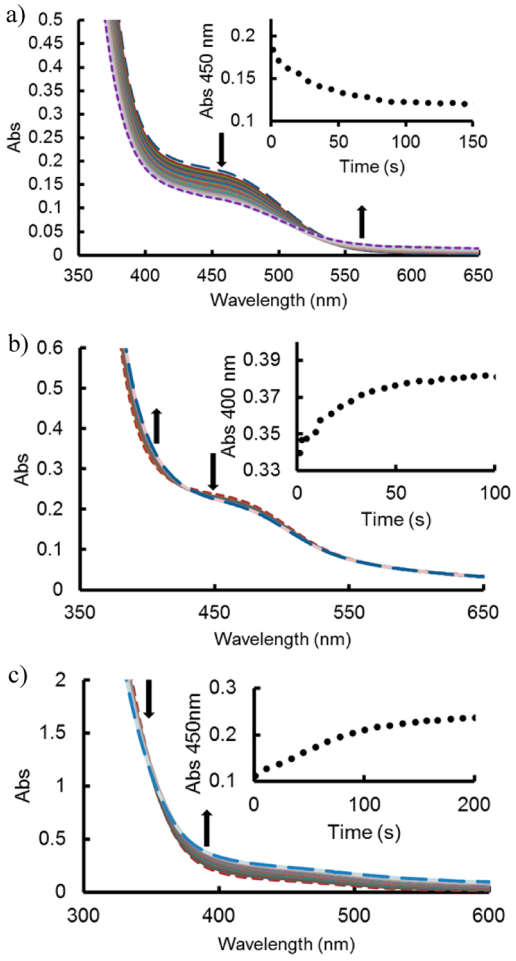


Figure 1. Low-temperature UV−vis monitoring of the reaction of **1** with (a) 1-butanethiol, (b) benzeneselenol, and (c) 4-methoxythiophenol ,showing the formation of an adduct species. Conditions: [**1**] = 0.8 mM, [Nuc] = 0.72 mM, CH_3CN, 0 °C, except for the reaction of 4-methoxythiophenol, which was performed at −35 °C.

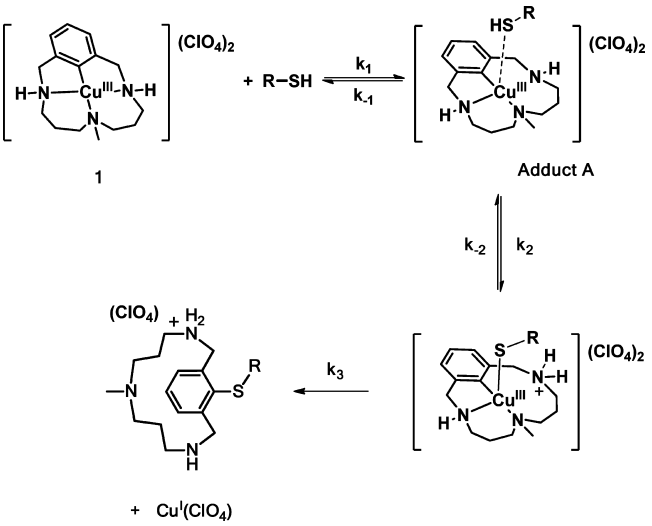
shift upon reaching product formation at the end of the reaction. Especially distinctive are the aromatic and benzylic signals of the adduct species in comparison to the same signals of the starting complex **1** and of the final coupled C−S product.

Therefore, minor but evident changes in the UV−vis (Figure 1) could be correlated with new signals in the ^{1}H NMR (Figures S51−S53 in the Supporting Information) corresponding to what we propose to be the **1**·R−SH adduct. The exact nature of the **1**·R−SH adduct is unclear, but the minor changes in the electronic spectra seem to exclude the direct coordination of the deprotonated nucleophile (thiolate), since strong thiolate to metal charge transfer bands would be expected. On the other hand, when the sterically more demanding 2-methyl-2-propanethiol is used as nucleophile, the reaction proceeds without the formation of any intermediate species even at low temperature.

Since adduct formation could be experimentally observed for 4-methoxythiophenol and 1-butanethiol despite their different pK_a(DMSO) values (11.2 and 17.0, respectively) but it is not observed for 2-methyl-2-propanethiol (pK_a(DMSO) = 17.9), we conclude that in the latter case the steric constraints should destabilize a proper interaction, precluding formation of the adduct species.

With all the data presented, a plausible mechanistic proposal for the reactivity of aryl−Cu^{III} species **1** with thiols and selenols is disclosed in Scheme 7. First, the formation of the adduct

Scheme 7. Plausible Mechanism for the C−S Cross-Coupling between 1 and R-SH Nucleophiles



species A, i.e. **1**···HS−R, is proposed to occur, in clear similarity to the reactivity with carboxylic acids.[31] The following step is the rate-limiting deprotonation of the nucleophile by one of the amines in the complex (possibly a lateral secondary amine),[30] and finally C_{aryl}−heteroatom reductive elimination occurs to yield the corresponding coupled product and Cu^I. On the other hand, we cannot rule out the participation of an external base assisting the deprotonation of the nucleophile, as was reported for the carboxylic acid mechanistic proposal.[31] Indeed, R−SeH and $(RO)_2(O)$−PH nucleophiles are thought to react by a similar mechanistic pathway. More mechanistic insights would be reached if kinetic studies were possible, but the unavoidable precipitation of noncharacterized $[Cu^I-S-R]_n$ species, possibly of oligomeric nature, poses a very challenging problem. Nevertheless, the catalytic versions of the C−S, C−Se, and C−P couplings reported herein proceed by an initial **L1-Br** oxidative addition at Cu^I to afford the aryl−Cu^{III}−Br intermediate species, followed by exchange of the axially coordinated halide by the corresponding nucleophile,[33] thus following the proposal in Scheme 7 at this stage.

CONCLUSIONS

We have presented for the first time conclusive evidence of the competence of well-defined aryl−Cu^{III} species in cross-coupling reactions to form new C−S, C−Se, and C−P bonds. Stoichiometric experiments with the aromatic and aliphatic thiol, selenol, and phosphite nucleophiles afforded the quantitative formation of the corresponding C−heteroatom coupling products. Monitoring experiments by UV−vis and NMR along with competitive experiments with bifunctional nucleophiles indicate that the pK_a parameter is a key issue but is not the only parameter that should be be taken into account. The catalytic version of the reaction has been performed with R−SH, R−SeH, and $(RO)_2(O)$−PH nucleophiles in excellent to good yields, and remarkably low catalyst loadings (0.5 mol %) are achieved for 4-chlorothiophenol with the model substrate **L1-Br**. The mechanistic proposal is in line with our

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previous proposal when carboxylic acids and phenols are used as nucleophiles. Therefore, this work demonstrates the viability of the Cu^{I}/Cu^{III} redox cycle for C−S, C−Se, and C−P cross-coupling reactivity in model aryl halide substrates, thus opening the door to future developments of C−heteroatom bond forming reactions catalyzed by copper.

EXPERIMENTAL SECTION

Synthesis and Characterization of Aryl Thioethers and Diaryl Selenide. In an inert-atmosphere glovebox, a sample of the Cu^{III}−aryl complex **1** (21.4 mg, 42 μmol) was dissolved in CD_3CN (1.6 mL) and 0.4 mL of a solution of 1,3,5-trimethoxybenzene was added as an internal standard. A portion of this solution (0.4 mL) was loaded into an NMR tube, and 1.1−1.5 equiv of the corresponding nucleophile was added to the tube (0.3 mL, 29.2−42 mM). Final concentrations: [**1**] = 12 mM and [HNuc] = 12.5−18 mM. The tube was sealed with a screw cap, and the reaction was allowed to proceed at room temperature and monitored by ^{1}H NMR spectroscopy until completion. ^{1}H, ^{13}C, COSY, NOESY, $^{1}H-^{13}C$ HSQC, and $^{1}H-^{77}Se$ HMBC NMR spectra and mass spectrometric analysis were obtained without isolation of the C nucleophile coupling product. Reaction yields were obtained by integration of the ^{1}H NMR spectra of the crude reaction mixtures relative to internal standard.

Synthesis and Characterization of Aryl Dialkyl Phosphonates. In an inert-atmosphere glovebox, a sample of the Cu^{III}−aryl complex **1** (21.4 mg, 42 μmol) was dissolved in CD_3CN (1.6 mL) and 0.4 mL of a solution of 1,3,5-trimethoxybenzene was added as an internal standard. A portion of this solution (0.4 mL), 0.25 mL of CD_3CN, and 0.9−2 equiv of the corresponding dialkyl phosphite nucleophile were added to the tube (0.05 mL, 0.48−0.34 M). Final concentrations: [**1**] = 12 mM and [dialkyl phosphite] = 10.8−24 mM. The tube was sealed with a screw cap, and the reaction was allowed to proceed at 50 °C and monitored by ^{1}H NMR spectroscopy until completion. ^{31}P, ^{1}H, COSY, NOESY, $^{1}H-^{13}C$ HSQC, and ^{13}C NMR spectra and mass spectrometric analysis were obtained without isolation of the C−P coupling product. Reaction yields were obtained by integration of the ^{1}H NMR spectra of the crude reaction mixtures relative to internal standard.

Synthesis and Characterization of Products with Bifunctional Groups. In an inert-atmosphere glovebox, a sample of the Cu^{III}−aryl complex **1** (21.4 mg, 42 μmol) was dissolved in CD_3CN (1.6 mL) and 0.4 mL of a solution of 1,3,5-trimethoxybenzene was added as an internal standard. A portion of this solution (0.4 mL), 0.25 mL of CD_3CN, and 1.1 equiv of the corresponding bifunctional nucleophile were added to the tube (0.3 mL, 0.48−0.34 M). Final concentrations: [**1**] = 12 mM and [Nuc] = 13.2 mM. The tube was sealed with a screw cap, and the reaction was allowed to proceed at room temperature and monitored by ^{1}H NMR spectroscopy until reaction completion. ^{1}H, COSY, NOESY, $^{1}H-^{13}C$ HSQC, $^{1}H-^{13}C$ HMBC, and ^{13}C NMR spectra and mass spectrometric analysis were obtained without isolation of the C−S coupling product. Reaction yields were obtained by integration of the ^{1}H NMR spectra of the crude reaction mixtures relative to 1,3,5-trimethoxybenzene.

General Procedure for Catalytic Experiments. In an inert-atmosphere glovebox, a vial was loaded with 0.5 mL of a 30 mM solution of ligand **L1-X** (X = Cl, Br) in CH_3CN and 0.5−10 mol % of $[Cu^{I}(CH_3CN)_4](CF_3SO_3)$ was added (0.2 mL of a 0.75−7.5 mM stock solution in CH_3CN). The colorless solution became slightly red, indicating that oxidative addition took place, giving the corresponding aryl−Cu^{III}−X (**2**$_X$; X = Cl, Br). Then 2.3 mL of a 7.15−13 mM solution of HS nucleophile in CH_3CN was added dropwise. Final concentrations: [**L1-X**] = 5 mM, [Cu] = 0.05−0.5 mM, and [HY-nucleophile] = 5.5−10 mM. After 24 h of stirring the crude mixture, either at room temperature (for Y = S (thiols) and Se (benzeneselenol)) or at 50 °C (for Y = P (phosphites)), 150 μL of 3 mM trimethoxybenzene in CH_3CN as internal standard was added and the solvent was removed. The sample was redissolved in 0.5 mL of CD_3CN, and NMR yields were obtained by integration of the ^{1}H NMR of the crude reaction mixtures relative to 1,3,5-trimethoxybenzene.

General Procedure for Monitoring Kinetics by UV−Vis Spectroscopy. A UV−visible cuvette equipped with a Teflon stopcock was dried in an oven and cooled under vacuum. Stock solutions of the nitrogen nucleophile (21.6 mM) and the aryl−Cu^{III} complex **1** (4.8 mM) were prepared in dry CH_3CN (2 mL). After the cuvette was back-filled with dry N_2, 0.5 mL of the nucleophile stock solution was added via syringe, and it was diluted with CH_3CN to a total volume of 2.9 mL. The cuvette was inserted into the spectrophotometer, and the temperature was allowed to equilibrate. The reaction was initiated by adding the aryl−Cu^{III} stock solution (0.1 mL) to the cuvette followed by rapid mixing of the combined solutions. Final concentrations: [**1**] = 0.8 mM, [Nuc] = 0.72 mM.

General Procedure for Monitoring Kinetics by NMR Spectroscopy. In an inert-atmosphere glovebox, a stock solution of the aryl−Cu^{III} complex **1** (7 mM) was prepared in CD_3CN (2 mL). A stock solution of the corresponding nucleophile (50.4 mM) in CD_3CN (1 mL) was prepared. Pulse widths and relaxation times were determined by using standard methods. To acquire the kinetic data, 0.4 mL of the complex **1** stock solution was added to a NMR tube, diluted with 0.25 mL of CD_3CN, and sealed with a septum. The sample was placed in the NMR probe and cooled to the corresponding temperature. The reaction was initiated by addition of 50 μL of the nucleophile stock solution to the NMR tube via syringe. The solution was mixed rapidly, and the tube was inserted into the probe to begin data acquisition. Final concentrations: [**1**] = 4 mM, [Nuc] = 3.6 mM.

ASSOCIATED CONTENT

Supporting Information

Text and figures giving details of the syntheses and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

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