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$Cu(ClO_4)_2$-Mediated Arene C−H Bond Halogenations of Azacalixaromatics Using Alkali Metal Halides as Halogen Sources

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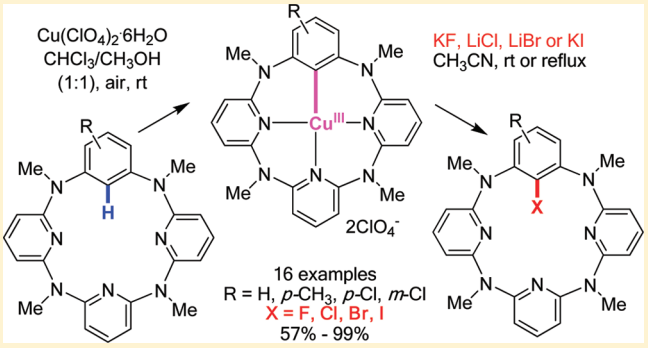
Supporting Information

ABSTRACT: Regiospecific halogenation of azacalix[1]arene[3]pyridines at the lower rim position of the benzene ring was achieved from their cross-coupling reaction with cost-effective alkali metal halides through the $Cu(ClO_4)_2$-mediated aerobic aryl C−H activation, which gave structurally well-defined aryl-Cu(III) intermediates, and a subsequent C−X bond formation reaction under very mild conditions.



INTRODUCTION

Aryl halides are one of the most important classes of organic compounds. They occur widely, for example, as natural products, synthetic pharmaceuticals and agrochemicals, and functional materials. They also serve as the most frequently used and versatile intermediates in organic synthesis. Among many synthetic methods,[1−10] aromatic electrophilic halogenation reaction using halogens in the presence of a Lewis acid or using other positive halogen (X^+) sources is a frequently employed method. The Sandmeyer reaction provides another important yet indirect route to aryl halides from arenes through the reaction of diazonium salts with CuX (X = Cl, Br).[1] These methods suffer from drawbacks such as a narrow substrate scope, harsh reaction conditions, and poor selectivity. In general, fluoroarenes are more difficult to access compared to other haloarenes.[2−8] Aromatic electrophilic fluorination reaction, for instance, generally requires very harsh conditions,[3] while Baltz−Schiemann reaction involves diazotization of an aromatic amine in the presence of tetrafluoroboric acid.[4] Nucleophilic substitution reaction using KF[5] or CuF_2[6] is limited to electron-deficient haloarene reactants. In a very recent report, Buchwald[7] detailed the formation of aryl fluorides from Pd-catalyzed cross-coupling reaction of aryl triflates with CsF at 80−130 °C.

Transition-metal-promoted and -catalyzed aryl C−H bond activations and functionalizations have attracted increasing interest in recent years.[9] They are also emerging as an attractive methodology for the preparation of haloarenes. Sanford[10] reported in 2004 the selective halogenation of benzo[*h*]quinoline through Pd(II)/Pd(IV)-catalyzed oxidative C−H bond transformation using NCS and NBS. Shi[11] later achieved $Pd(OAc)_2$-catalyzed *ortho*-halogenation of acetanilide with CuX_2 (X = Cl, Br), and Yu[12] succeeded in *ortho*-fluorination of triflamide-protected benzylamines with F^+ reagents such as *N*-fluoro-2,4,6-trimethylpyridinium triflate. Due to the lower cost and less toxicity compared to noble metal species, copper salts show advantages in promoting the C−H functionalizations. Yu[13] reported in 2006 that $Cu(OAc)_2$ catalyzes nicely the oxidative halogenation of aryl C−H bonds of 2-arylpyridines using dioxygen as an oxidant at an elevated temperature. In the presence of CuX_2, LiX, and molecular oxygen, electron-rich aromatic C−H bonds are chlorinated and brominated,[14] while CuF_2 has been reported to fluorinate benzene directly at 450−550 °C.[15] Apparently, efficient, mild, and environmentally benign processes using cost-effective halide sources are highly desirable for the synthesis of all types of aryl halides.

Heterocalixaromatics, or heteroatom-bridged calixaromatics, are a new generation of macrocyclic host molecules that have gained considerably growing attention recently in the study of supramolecular chemistry.[16] Being different from the methylene linkage in the conventional calixarenes,[17] heteroatoms such as nitrogen can adopt sp^2 and sp^3 electronic configurations to form considerably varied conjugation systems with their adjacent aromatic rings, producing macrocycles of unique conformational structures and of fine-tunable sizes.[18] Furthermore, introduction of heteroatoms into the bridging positions leads to the regulation of binding ability of aromatic rings of macrocyclic hosts.[19] For example, tetraazacalix[4]pyridines exhibit enhanced interactions with transition-metal ions[19a−c] and

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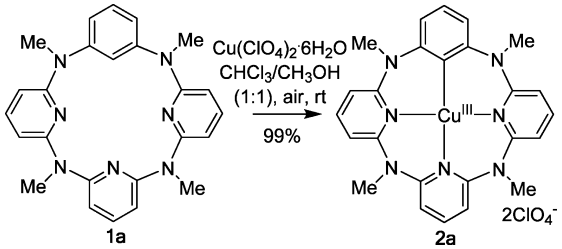
hydrogen-bond donors,[19f] whereas tetraoxacalix[2]arene[2]triazines form complexes with halides via anion−π interactions.[19g−i]

To fabricate tailor-made macrocyclic hosts for targeting molecular recognition and self-assembly, regiospecific chemical manipulations on the parent macrocyclic ring of heterocalixaromatics appear challenging but promising.[16,20] We[21] have recently discovered the highly efficient arene C−H bond activation of azacalix[1]arene[3]pyridine **1a** by $Cu(ClO_4)_2$ under very mild aerobic conditions, which affords a stable and structurally well-defined aryl-Cu(III) complex **2a** (Scheme 1).

Scheme 1. $Cu(ClO_4)_2$-Mediated Aryl C−H Activation

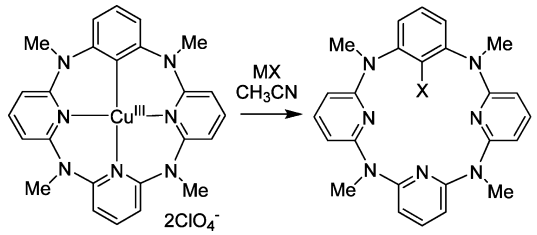


The resulting aryl-Cu(III) complex is able to react with a variety of nucleophiles in acetonitrile to introduce diverse functionalities regiospecifically on the lower rim position of macrocyclic molecules.[21,22] To continue our effort on the development of practical synthesis of functionalized heterocalixaromatics, the reactions of aryl-Cu(III) complexes with the cheapest alkali metal halides, including fluoride, were studied. We report herein a powerful enabling method for the construction of aromatic C−F, C−Cl, C−Br, and C−I bonds.

RESULTS AND DISCUSSION

Previously, we[21] have shown the reaction of **2a** with tetrabutylammonium halides in acetonitrile. Although the formation of C−Cl, C−Br, and C−I bonds is efficient, the use of anhydrous tetrabutylammonium halides as halogen sources is problematic because they are expensive, highly hygroscopic, and inevitably generate nitrogenous waste. Among all metal salts, alkali metal halides are widely available, easy to handle, and inexpensive. To initiate our current study, we first examined the alkali metal halides as halide sources in the reaction. To our delight, most of the cheap alkali metal halides tested acted as effective reactants to halogenate the benzene ring. As compiled in Table 1, for example, LiCl reacted with **2a** in acetonitrile to form chlorobenzene derivative **3a** in a high yield within 10 min at ambient temperature (entry 1, Table 1). Almost quantitative yield of **3a** was obtained from the interaction of **2a** with KCl in 1 h (entry 3, Table 1). No chlorination reaction was observed when NaCl was applied because of the insolubility of table salt in reaction media (entry 2, Table 1). All bromination reactions employing LiBr, NaBr, and KBr as the bromide source proceeded very rapidly at room temperature, yielding the desired product **4a** in excellent yields (entries 4−6, Table 1). The cheapest alkali metal iodides, such as NaI and KI, reacted equally efficiently with **2a** under mild conditions to afford nearly a quantitative yield of iodinated azacalix[1]arene[3]pyridine **5a** (entries 7 and 8, Table 1).The method was readily extended to the preparation of a number of halogenated azacalix[1]arene[3]pyridines. Using LiCl, LiBr, and NaI as halogen sources, aryl-Cu(III) complexes **2b−d** derived from azacalix[1]arene[3]pyridines bearing an electron-donating methyl group or an electron-withdrawing chloro substituent at either *para* or *meta* position were transformed very efficiently into the corresponding C−Cl, C−Br, and C−I bond forming products **3c,d**, **4c,d**, and **5c,d**, respectively, in very good to excellent yields (Figure 1).

Table 1. Chlorination, Bromination, and Iodination of Ar−Cu(III) Complex 2a with Alkali Halides[a]



2a **3a**, X = Cl; **4a**, X = Br; **5a**, X = I

entry	MX	equiv	temp (°C)	time	product	X	yield (%)[b]
1	LiCl	1	rt	10 min	**3a**	Cl	87
2	NaCl	1	rt	>30 min	**3a**	Cl	
3	KCl	1	rt	60 min	**3a**	Cl	99
4	LiBr	1	rt	<1 min	**4a**	Br	97
5	NaBr	1	rt	8 min	**4a**	Br	90
6	KBr	1	rt	18 min	**4a**	Br	95
7	NaI	1	rt	<1 min	**5a**	I	92
8	KI	1	rt	2 h	**5a**	I	99

[a]A mixture of **2a** (0.1 mmol) and MX (0.1 mmol) was reacted in acetonitrile. [b]Isolated yield.

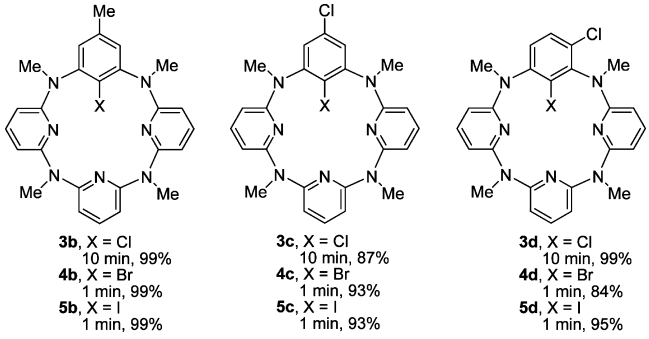


Figure 1. Halogenated azacalix[1]arene[3]pyridines **3−5** synthesized.

Encouraged by the facile C−X bond formation from the reaction between alkali metal halides and aryl-Cu(III) species **2a−d** under very mild conditions, we then investigated the coupling reaction of aryl-Cu(III) complexes with alkali metal fluorides. As indicated by the results in Table 2, both LiF and NaF appeared inert. No reaction was observed even with the use of a large excess amount of fluoride salt at an elevated temperature (entries 1 and 2, Table 2). When 1 equiv of KF was used, the reaction also did not take place at room temperature (entry 3, Table 2). Pleasingly, when the reaction was executed in refluxing acetonitrile, the desired C−F bond forming product **6a** was isolated in 42% yield (entry 4, Table 2). The chemical yield of **6a** was then improved to 56 and 57% when 2 equiv of KF was refluxed with **2a** in acetonitrile for 1 and 3 h, respectively (entries 5 and 6, Table 2). It should be noted that further increasing the ratio of KF over **2a** did not lead to higher chemical yields (entries 7 and 8, Table 2). It was also found that CsF was not as effective as KF in fluorinating

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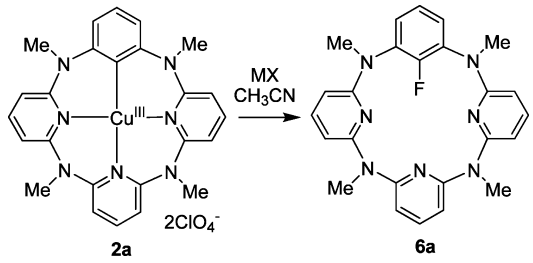
Table 2. Fluorination of Aryl-Cu(III) Complex 2a[a]



2a **6a**

entry	MF	equiv	temp (°C)	time (h)	yield of **6a** (%)[b]
1	LiF	5	82	3	
2	NaF	5	82	3	
3	KF	1	rt	10	
4	KF	1	82	3	42
5	KF	2	82	1	56
6	KF	2	82	3	57
7	KF	3	82	1	49
8	KF	5	82	3	50
9	CsF	3	82	3	25
10	CsF	5	82	3	35

[a]A mixture of **2a** (0.1 mmol) and MF was refluxed in acetonitrile. [b]Isolated yield.

the benzene ring of **2a** (entries 9 and 10). Under optimized conditions using KF as a fluoride source, azacalix[1]arene[3]-pyridine−Cu(III) complexes underwent fluorination reaction to afford fluoro-substituted azacalixaromatics in moderate yields (Figure 2).

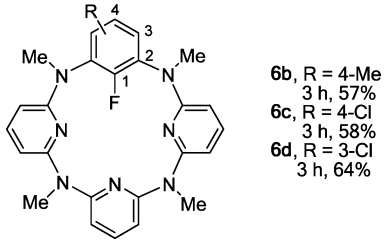
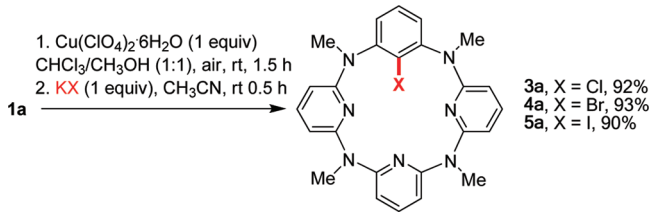


Figure 2. Fluorinated azacalix[1]arene[3]pyridines **6** synthesized.

The extraordinary efficiency in the formation of all types of carbon−halogen bonds using widely available and cost-effective alkali metal halides is most probably due to the unique reactivity of high valent copper ion toward halides and the consecutive facile reductive elimination reaction. The acetonitrile solvent may also play an important role in facilitating the rapid transformation as it dissolves reactants and forms an energetically stable complex with the Cu(I) ion which is expelled by the reductive elimination step.

The synthesis of regiospecifically halogenated azacalix[1]-arene[3]pyridines does not necessarily require the isolation and purification of an aryl-Cu(III) intermediate. To demonstrate the practical copper-mediated synthesis of functionalized macrocyclic compounds, we performed a very convenient one-pot preparation of **3a**, **4a**, and **5a** simply by reacting at ambient temperature a mixture of **1a** and $Cu(ClO_4)_2·6H_2O$ in chloroform and methanol (1:1) in an open vial for 1.5 h followed by adding a KX salt and acetonitrile. After the resulting mixture was stirred at room temperature for another 0.5 h, the target products were then formed in excellent yields (Scheme 2).

Scheme 2. One-Pot Synthesis of 3a, 4a, and 5a



Last but not least, halogenations of aryl-Cu(III) intermediates with metal halides led to the formation of Cu(I) salt. This has been evidenced nicely by the observations of the color change of the reaction solution from brown to colorless and of the formation of white precipitates. Recrystallization of precipitates in acetonitrile gave single crystals of $Cu(I)(CH_3CN)_4ClO_4$ (see Supporting Information).

CONCLUSION

In summary, we have shown a highly efficient and practical method for the construction of all types of C−X bonds from the reaction of aryl-Cu(III) complexes with widely available and the cheapest alkali metal halides under very mild conditions. The practical synthesis of the C−X bond has also been demonstrated with a one-pot reaction starting with the $Cu(ClO_4)_2$-mediated aryl C−H bond activation followed by a C−X bond formation. The method provides a straightforward synthetic route to regiospecifically halogenated azacalix[1]arene[3]pyridines, which are the springboard to diverse functional macrocyclic host molecules. The insight into the reactivity of aryl-Cu(III) species toward various nucleophiles may open a new avenue to the design of copper-mediated and -catalyzed reactions.

EXPERIMENTAL SECTION

General Procedure for the Reaction between 2 and Halides. *Method A (For the Reaction with Halides except for Fluoride):* A mixture of the copper(III) complex **2** (0.1 mmol) and LiCl (1.0 equiv), LiBr (1.0 equiv), or NaI (1.0 equiv) in CH_3CN (3 mL) was stirred at room temperature. When the initial dark brown color faded away or changed into orange, the reaction mixture was quenched with aqueous ammonia solution and extracted with dichloromethane. The combined extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. The residue was chromatographed on a silica gel column to give pure products **3**, **4**, or **5**.

Method B (For the Reaction with Fluoride): To the solution of the copper(III) complex **2** (0.1 mmol) in acetonitrile (6 mL) was added KF (0.2 mmol, 2.0 equiv). After being refluxed for 3 h, the reaction mixture was quenched with aqueous ammonia solution and extracted with dichloromethane. The combined extracts were washed with brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. The residue was chromatographed on a silica gel column to give pure products **6**.

General Procedure for the One-Pot Halogenation Reaction: Azacalix[1]arene[3]pyridine **1a** (42.3 mg, 0.1 mmol) and $Cu(ClO_4)_2·6H_2O$ (35 mg, 0.1 mmol) were dissolved in a mixture of chloroform (1 mL) and methanol (1 mL) in an open vial. After being stirred under aerobic conditions for 1.5 h, acetonitrile (2 mL) and KCl, KBr, or KI (0.1 mmol) were added. The reaction went to completion after another 0.5 h. Aqueous ammonia (5 mL) was added, and the mixture was extracted with dichloromethane (3 × 5 mL). The combined organic layer was washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated, and the residue was chromatographed on a silica gel column eluted with a mixture of petroleum ether, ethyl acetate, and dichloromethane (10:1:2) to give pure product **3a**, **4a**, or **5a**.

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All products, which are white solids, were well characterized. For the spectroscopic data of compounds **3a**, **4a**, and **5a**, please see ref 21. Characterization data for new compounds are listed as follows.

3b: mp 202−203 °C; IR (KBr) ν 1575 (s), 1475 (s), 1415 (s), 1274 (w), 1153 (m), 769 (m), 713 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (t, J = 8.1 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H), 6.74 (s, 2H), 6.63 (d, J = 7.8 Hz, 2H), 6.04 (d, J = 8.1 Hz, 2H), 6.00 (d, J = 8.1 Hz, 2H), 3.24 (s, 6H), 3.12 (s, 6H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 158.8, 157.0, 145.5, 139.0, 136.4, 136.1, 130.9, 129.6, 120.8, 95.4, 94.3, 37.3, 36.3, 20.9; MS (CI) m/z 472.1 [M + H]$^+$. Anal. Calcd for $C_{26}H_{26}ClN_7$: C, 66.16; H, 5.55; N, 20.77. Found: C, 66.09; H, 5.63; N 20.50.

3c: mp 233−234 °C; IR (KBr) ν 1578 (s), 1563 (s), 1476 (s), 1418 (m), 1276 (w), 1155 (m), 771 (m), 717 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 8.1 Hz, 2H), 6.92 (s, 2H), 6.67 (d, J = 7.8 Hz, 2H), 6.07 (d, J = 8.1 Hz, 2H), 5.99 (d, J = 8.1 Hz, 2H), 3.25 (s, 6H), 3.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 158.7, 156.8, 146.8, 139.2, 137.2, 133.2, 131.1, 129.5, 120.9, 95.9, 94.3, 37.0, 36.3; MS (CI) m/z 492.1 [M + H]$^+$. Anal. Calcd for $C_{25}H_{23}Cl_2N_7$: C, 60.98; H, 4.71; N, 19.90. Found: C, 60.82; H, 4.74; N, 19.60.

3d: mp 166−167 °C; IR (KBr) ν 1580 (s), 1562 (s), 1473 (s), 1420 (s), 1155 (w), 769 (w), 719 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.70 (d, J = 7.5 Hz, 1H), 6.60 (d, J = 7.8 Hz, 1H), 6.07 (d, J = 7.8 Hz, 1H), 6.06 (d, J = 8.1 Hz, 1H), 6.00 (d, J = 7.8 Hz, 1H), 5.99 (d, J = 7.8 Hz, 1H), 3.24 (s, 6H), 3.11 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 158.9, 158.8, 156.8, 155.8, 144.5, 143.0, 139.21, 139.17, 137.5, 136.5, 133.9, 129.8, 127.3, 120.9, 120.7, 95.9, 95.7, 94.2, 93.9, 37.0, 36.25, 36.15, 35.6; MS (CI) m/z 492.1 [M + H]$^+$. Anal. Calcd for $C_{25}H_{23}Cl_2N_7$: C, 60.98; H, 4.71; N, 19.90. Found: C, 60.78; H, 4.81; N, 19.51.

4b: mp 224−225 °C; IR (KBr) ν 1583 (s), 1475 (s), 1416 (m), 1275 (w), 1152 (w), 767 (w), 713 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H), 6.72 (s, 2H), 6.61 (d, J = 7.8 Hz, 2H), 6.03 (d, J = 7.8 Hz, 2H), 5.98 (d, J = 8.1 Hz, 2H), 3.24 (s, 6H), 3.11 (s, 6H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 158.8, 156.9, 147.3, 139.0, 137.1, 136.4, 129.7, 123.6, 120.8, 95.2, 94.2, 37.2, 36.3, 20.9; MS (CI) m/z 516.1 [M + H]$^+$. Anal. Calcd for $C_{26}H_{26}BrN_7$: C, 60.47; H, 5.07; N, 18.99. Found: C, 60.43; H, 5.10; N, 18.73.

4c: mp 218−219 °C; IR (KBr) ν 1586 (s), 1564 (s), 1472 (s), 1422 (s), 1277 (w), 1152 (m), 769 (m), 720 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (t, J = 8.1 Hz, 1H), 7.42 (t, J = 8.1 Hz, 2H), 6.90 (sz, 2H), 6.66 (d, J = 7.8 Hz, 2H), 6.06 (d, J = 7.8 Hz, 2H), 5.98 (d, J = 8.1 Hz, 2H), 3.25 (s, 6H), 3.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 158.7, 156.6, 148.5, 139.2, 137.2, 132.1, 129.5, 126.0, 120.9, 95.8, 94.2, 36.9, 36.2; MS (CI) m/z 538.1 [M + H]$^+$. Anal. Calcd for $C_{25}H_{23}BrClN_7$: C, 55.93; H, 4.32; N, 18.26. Found: C, 55.94; H, 4.33; N, 18.07.

4d: mp 187−188 °C; IR (KBr) ν 1580 (s), 1561 (s), 1474 (s), 1420 (s), 1154 (w), 770 (w), 717 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (t, J = 8.1 Hz, 1H), 7.41 (t, J = 8.1 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H), 6.70 (dd, J_1 = 7.5 Hz, J_2 = 7.5 Hz, 1H), 6.60 (d, J = 7.5 Hz, 1H), 6.07 (d, J = 8.1 Hz, 1H), 6.05 (d, J = 8.1 Hz, 1H), 5.99 (d, J = 7.8 Hz, 1H), 5.98 (d, J = 7.8 Hz, 1H), 3.25 (s, 6H), 3.11 (s, 3H), 3.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 158.8, 158.74, 158.71, 156.6, 155.7, 146.2, 144.5, 139.2, 137.5, 133.8, 129.8, 129.4, 128.2, 120.9, 120.7, 95.8, 95.6, 94.1, 93.8, 37.0, 36.2, 36.1, 35.5; MS (CI) m/z 538.0 [M + H]$^+$. Anal. Calcd for $C_{25}H_{23}BrClN_7$: C, 55.93; H, 4.32; N, 18.26. Found: C, 55.76; H, 4.26; N, 18.03.

5b: mp 244−245 °C; IR (KBr) ν 1582 (s), 1563 (s), 1474 (s), 1414 (m), 1280 (w), 1154 (w), 764 (w), 713 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (t, J = 7.8 Hz, 2H), 7.17 (t, J = 7.8 Hz, 1H), 6.68 (s, 2H), 6.59 (d, J = 7.8 Hz, 2H), 6.04 (d, J = 7.8 Hz, 2H), 5.98 (d, J = 8.1 Hz, 2H), 3.24 (s, 6H), 3.10 (s, 6H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 158.8, 156.6, 151.2, 139.1, 138.6, 136.4, 128.7, 120.7, 104.2, 95.2, 94.3, 37.3, 36.3, 20.9; MS (CI) m/z 564.1 [M + H]$^+$. Anal. Calcd for $C_{26}H_{26}IN_7$: C, 55.42; H, 4.65; N, 17.40. Found: C, 55.50; H, 4.72; N, 17.10.

5c: mp 239−240 °C; IR (KBr) ν 1578 (s), 1562 (s), 1466 (s), 1422 (s), 1276 (w), 1160 (m), 767 (m), 723 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (t, J = 8.1 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 6.85 (sz, 2H), 6.64 (d, J = 7.5 Hz, 2H), 6.06 (d, J = 7.8 Hz, 2H), 5.98 (d, J = 8.1 Hz, 2H), 3.25 (s, 6H), 3.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 158.6, 156.4, 152.4, 139.2, 137.1, 133.7, 128.4, 120.8, 106.8, 95.7, 94.3, 37.0, 36.2; MS (CI) m/z 584.0 [M + H]$^+$. Anal. Calcd for $C_{25}H_{23}ClIN_7$: C, 51.43; H, 3.97; N, 16.79. Found: C, 51.39; H, 4.04; N, 16.52.

5d: mp 204−205 °C; IR (KBr) ν 1581 (s), 1561 (s), 1472 (s), 1419 (s), 1155 (w), 770 (w), 717 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (t, J = 8.4 Hz, 1H), 7.43 (t, J = 8.1 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.68 (d, J = 7.5 Hz, 1H), 6.58 (d, J = 7.5 Hz, 1H), 6.08 (d, J = 7.8 Hz, 1H), 6.06 (d, J = 8.1 Hz, 1H), 5.99 (d, J = 8.1 Hz, 1H), 5.98 (d, J = 8.1 Hz, 1H), 3.25 (s, 6H), 3.11 (s, 3H), 3.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 158.8, 158.6, 156.4, 155.5, 150.1, 147.8, 139.24, 139.20, 137.5, 132.4, 129.5, 129.0, 120.8, 120.6, 110.8, 95.8, 95.5, 94.2, 93.9, 37.1, 36.2, 36.1, 35.4; MS (CI) m/z 584.0 [M + H]$^+$. Anal. Calcd for $C_{25}H_{23}ClIN_7$: C, 51.43; H, 3.97; N, 16.79. Found: C, 51.21; H, 4.03; N, 16.46.

6a: mp 249−250 °C; IR (KBr) ν 2897 (w), 1578 (s), 1478 (s), 1420 (s), 1367 (m), 1278 (m), 1155 (m), 767 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (t, J = 7.8 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 6.85−6.84 (m, 3H), 6.60 (d, J = 7.5 Hz, 2H), 6.06 (d, J = 8.7 Hz, 2H), 6.02 (d, J = 8.7 Hz, 2H), 3.23 (s, 6H), 3.13 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 158.95, 158.1, 157.4, 154.8, 139.0, 137.4, 135.9, 135.7, 128.74, 128.72, 123.15, 123.09, 120.5, 96.0, 94.95, 38.10, 38.08, 36.4; MS (ESI) m/z 442.3 [M + H]$^+$, 464.2 [M + Na]$^+$, 480.2 [M + K]$^+$. Anal. Calcd for $C_{25}H_{24}FN_7$: C, 68.01; H, 5.48; N, 22.21. Found: C, 68.06; H, 5.55; N, 22.12.

6b: mp 210−212 °C; IR (KBr) ν 2901 (w), 1579 (s), 1471 (s), 1417 (s), 1363 (m), 1285 (w), 1133 (m), 771 (s), 718 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (t, J = 7.8 Hz, 2H), 7.21 (t, J = 7.8 Hz, 1H), 6.66 (d, J = 6.9 Hz, 2H), 6.62 (d, J = 7.8 Hz, 2H), 6.06 (d, J = 7.8 Hz, 2H), 6.01 (d, J = 8.1 Hz, 2H), 3.23 (s, 6H), 3.12 (s, 6H), 2.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 159.0, 157.5, 156.0, 152.7, 139.0, 136.5, 135.4, 135.2, 132.11, 132.06, 129.17, 129.15, 120.4, 95.9, 95.0, 38.07, 38.05, 36.4, 20.8; MS (ESI) m/z 456.3 [M + H]$^+$, 478.3 [M + Na]$^+$, 494.2 [M + K]$^+$. Anal. Calcd for $C_{26}H_{26}FN_7$: C, 68.55; H, 5.75; N, 21.52. Found: C, 68.71; H, 5.74; N, 21.34.

6c: mp 223−225 °C; IR (KBr) ν 2900 (s), 1576 (s), 1474 (s), 1415 (s), 1278 (m), 1154 (m), 1132 (m), 770 (m), 716 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (t, J = 7.8 Hz, 1H), 7.40 (t, J = 7.8 Hz, 2H), 6.85 (d, J = 6.0 Hz, 2H), 6.68 (d, J = 7.8 Hz, 2H), 6.08 (d, J = 7.8 Hz, 2H), 6.02 (d, J = 8.1 Hz, 2H), 3.24 (s, 6H), 3.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 158.8, 157.1, 153.8, 139.2, 137.2, 136.74, 136.56, 129.15, 129.14, 127.08, 127.03, 120.6, 96.4, 95.0, 37.74, 37.72, 36.38; MS (ESI) m/z 476.2 [M + H]$^+$, 498.2 [M + Na]$^+$, 514.1 [M + K]$^+$. Anal. Calcd for $C_{25}H_{23}ClFN_7$: C, 63.09; H, 4.87; N, 20.60. Found: C, 63.11; H, 4.99; N, 20.33.

6d: mp 188−190 °C; [1] IR (KBr) ν 2904 (w), 1578 (s), 1474 (s), 1421 (s), 1365 (m), 1276 (m), 1155 (m), 1125 (m), 897 (m), 769 (s), 716 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.26 (t, J = 7.7 Hz, 1H), 6.96 (dd, J_1 = 1.5 Hz, J_2 = 8.7 Hz, 1H), 6.82 (t, J = 7.8 Hz, 1H), 6.71 (d, J = 7.8 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 6.09 (d, J = 7.8 Hz, 1H), 6.08 (d, J = 8.1 Hz, 1H), 6.04 (d, J = 7.8 Hz, 1H), 6.02 (d, J = 8.1 Hz, 1H), 3.25 (s, 6H), 3.13 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.15, 159.12, 158.94, 158.91, 158.83, 157.2, 156.25, 155.8, 139.21, 139.17, 137.65, 134.5, 134.3, 133.7, 133.5, 133.26, 133.23, 129.44, 129.40, 124.0, 123.9, 120.6, 120.4, 96.4, 96.2, 94.9, 94.5, 37.82, 37.80, 36.66, 36.64, 36.4, 36.3; MS (ESI) m/z 476.2 [M + H]$^+$, 498.2 [M + Na]$^+$, 514.1 [M + K]$^+$. Anal. Calcd for $C_{25}H_{23}ClFN_7$: C, 63.09; H, 4.87; N, 20.60. Found: C, 62.99; H, 4.78; N, 20.40.

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■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of products **3**−**6**, X-ray molecular structure of $Cu(I)(CH_3CN)_4ClO_4$ (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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