Mechanism Study of Copper-Mediated One-Pot Reductive Amination of Aryl Halides Using Trimethylsilyl Azide

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Supporting Information



ABSTRACT: Reaction mechanisms of the copper-mediated amination of aryl halides with trimethylsilyl azide (TMSN₃) were analyzed on the basis of the time-course study using reaction monitoring FT-IR, trapping an intermediary aryl azide by the Huisgen reaction, and the analysis of the generated N₂ gas during the reaction. This amination would proceed through multiple pathways via aryl radicals and copper(I) azide.

INTRODUCTION

Primary aromatic amines are widely used as intermediates of pharmaceuticals, agrochemicals, dyes, and polymers in the chemical industry.¹ Effective synthetic methods for primary aromatic amines based on the palladium- or copper-catalyzed cross-coupling reactions between aryl halides and ammonia or ammonium salts have been developed in less than a decade.^{2,3} Recently, we have found that the use of trimethylsilyl azide (TMSN₃) instead of an ammonia equivalent for the cross-coupling also afforded the corresponding primary amine as the sole product (Scheme 1),^{4,5} although Ma and Liang independently reported the aryl azide synthesis under similar copper-catalyzed conditions using NaN₃.⁶

Scheme 1. Copper-Mediated Reductive Amination of a Variety of Aryl Halides with TMSN₃

Ar V 🔟 TMSN. –	Cu (2.0 equiv) 2-aminoethanol (2.5 equiv)	Ar-NH-
$AI - X + IWSIN_3 =$	DMA, 95 °C, Ar	$A_1 - M_{12}$
X = Br, I, Cl (2.0 equiv)	,,	

Molander et al. found that primary amines were fairly frequently and substrate-dependently obtained instead of azides during the copper-catalyzed aromatic azidation reaction using aryl halides and NaN₃.⁷ Several syntheses of primary aromatic amines using NaN₃ have been reported^{8–10} almost at the same time as our communication⁴ after Molander's pioneering but unintended consequences;⁷ only two reports provided possible reaction mechanisms. Alami et al. speculated that a Cu powder-promoted amination of 3-bromoquinolines or 3-bromocoumarines proceeded through the formation of the corresponding

aryl azide and subsequent removal of N_2 to generate a nitrene intermediate (Scheme 2). Although the formation of the aryl

Scheme 2. Alami's Copper-Catalyzed Amination of Aryl Halides



azide intermediate was confirmed by its Huisgen type reaction with 4-ethynylanisole, no evidence for the nitrene generation was indicated.^{9c} Ramana et al. proposed that the aromatic nucleophilic substitution of electron-deficient aryl halides with NaN₃ would take place using CuSO₄, L-proline, and sodium ascorbate, giving the corresponding aryl azide (Scheme 3), which could be reduced to the amine in situ, based on the fact that 2-fluoro-4-iodonitrobenzene underwent the amination at the more electron-withdrawing but thermodynamically stable fluorine group rather than at the iodine group.^{9d} Both of these aminations are considered to proceed via the formation of the

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Scheme 3. Ramana's Copper-Catalyzed Amination of Aryl Halides



aryl azide as an intermediate, but a real reducing reagent and hydrogen source were not identified.

In our previous paper⁵ on the aromatic amination of aryl halides using TMSN₃, Cu powder, and 2-aminoethanol in *N*,*N*-dimethylacetamide (DMA), we concluded that (1) 2-aminoethanol would work as a major hydrogen source because the amination quantitatively proceeded even without a solvent, (2) DMA could be a minor hydrogen donor due to the 23% generation of ethyl 4-aminobenzoate from the corresponding aryl bromide and TMSN₃ even without 2-aminoethanol, and (3) the reaction would be involved in a single-electron transfer process because of the strong suppression of the reaction by the addition of a single-electron scavenger (TCNQ or TCNE). An advanced reaction mechanistic study of the copper–mediated reductive amination of aryl halides and TMSN₃ in the presence of 2-aminoethanol using FT-IR and reaction monitoring FT-IR will now be reported.

RESULTS AND DISCUSSION

The azido peak at 2129 cm^{-1} of TMSN₃ in DMA [Figure 1, spectrum (a)] was shifted to 2012 cm^{-1} by the addition of 2-



Figure 1. IR spectra in DMA of (a) TMSN $_3$; (b) TMSN $_3$ and 2-aminoethanol; (c) TMSN $_3$ and TBAF.

aminoethanol [spectrum (b)]. This peak shift would be attributed to the partial liberation of the N_3^- ion together with the formation of TMSO(CH₂)₂N⁺H₃ because of the observed similar peak at 2010 cm⁻¹ by the addition of *n*-tetrabutylammonium fluoride (TBAF) to the TMSN₃ solution in DMA, partially generating N_3^- with TBA⁺ and TMSF [spectrum (c)].¹¹

Real-time infrared (IR) analysis of the copper-mediated aromatic amination using a reaction-monitoring FT-IR spectrometer was carried out to obtain insight into the reaction process. When TMSN₃ was treated with Cu (1.0 equiv) and 2aminoethanol (1.25 equiv) in heated DMA (95 °C) in the absence of the aromatic halide as a substrate, a peak at 2013 cm⁻¹ derived from TMSN₃ was time-dependently shifted to 2057 cm⁻¹ over a 1 h period. The newly generated single broad peak was attributed to the formation of copper(I) azide (CuN₃), which was consistent with the adsorption indicated in the literature (Figure 2).^{12,13} A similar time-course of the IR





Figure 2. Time-course study using reaction monitoring FT-IR of the reaction of Cu powder, $TMSN_{3}$, and 2-aminoethanol in DMA at 95 °C for 1 h.

spectrum was observed for 0.5 h in the presence of ethyl 4bromobenzoate (1); during the copper-mediated amination of 1 with TMSN₃ and 2-aminoethanol in DMA at 95 °C, the peak intensity at 2012 cm⁻¹ gradually decreased, and the peak intensity at 2058 cm⁻¹ increased. The peak at 2058 cm⁻¹ then slowly decreased from 0.5 to 1 h, and no change was observed in the spectrum after 1 h (Figure 3). This result would correspond to the fact that the amination was almost completed



Figure 3. Time-course study using reaction monitoring FT-IR of the amination of ethyl 4-bromobenzoate with $TMSN_3$ in the presence of Cu powder and 2-aminoethanol in DMA at 95 °C for 1 h.

within 1 h. Furthermore, the peak⁵ at 2126 cm⁻¹ for the aryl azide (ethyl 4-azidobenzoate) was never detected in the IR study (Figure 3) during the reaction. These results suggest that the amination of ethyl 4-bromobenzoate (1) with TMSN₃ would mainly proceed without the formation of the ethyl 4-azidobenzoate intermediate (3), although the azide itself could be gradually reduced to the corresponding aniline (2) under the present amination conditions over a 5 h period (Scheme 4).



A further investigation to acquire the aryl azide as a possible intermediate, which could not be detected by the reaction monitoring FT-IR (Figure 3), through use of the Huisgen cycloaddition by the addition of ethynylbenzene (4) to the reaction mixture of ethyl 4-bromobenzoate (1) and TMSN₃ using copper and 2-aminoethanol was carried out (Scheme 5).

Scheme 5. Confirmation of Generated Ethyl 4-Azidobenzoate during the Amination of Ethyl 4-Bromobenzoate and TMSN₃ Using the Huisgen Cyclization



Although ethyl 4-aminobenzoate (2), the copper-mediated amination product, was obtained as the major product (73%), formation of the 1,2,3-triazole derivative (5) could also be detected, but in a low yield (12%) (Scheme 5). Two possible reaction pathways toward 5 would be considered through (1) the Huisgen cycloaddition¹⁴ of ethynylbenzene (4) with ethyl 4-azidobenzoate, or (2) Ullmann type reaction between 1 and 4-phenyl-*1H*-1,2,3-triazole (6), which could be first generated by the Huisgen cycloaddition between 1 and TMSN₃. Since the Ullmann-type reaction scarcely proceeded under the reaction conditions (3%, Scheme 6), 5 should be obtained via the formation of ethyl 4-azidobenzoate. Therefore, the formation of aryl azide would be involved in the present copper-mediated amination processes.¹⁵

Scheme 6. Ullmann-Type Amination of Ethyl 4-Bromobenzoate (1) and 4-Phenyl-1*H*-1,2,3-triazole (6)



During the course of the present amination using $TMSN_{3}$, the release of N₂ gas is indispensable. The N₂ gas generated in the test tube during the amination was analyzed by gas chromatography (Table 1). N_2 (15%) from a test tube filled with only Ar was detected as a background because the internal gas in the test tube was collected by the water substitution method, and the dissolved N2 in H2O was easily contaminated (entry 1). When the gas in the test tube containing ethyl 4bromobenzoate, TMSN₃, Cu powder, 2-aminoethanol, and DMA was measured just after the air was replaced with Ar, 18% N₂ was detected, indicating that nearly no N₂ generation took place (entry 2). The ratio of N₂ gas was increased to 60% during the early stage of the reaction (0.25 h) (entry 3). Moreover, even without ethyl 4-bromobenzoate (1), 38% N₂ was detected after 0.25 h. Therefore, a part of the present amination would proceed through the removal of N2 from copper azide before its coupling reaction with the aryl halide (entries 2 vs 4). The aryl amine (2) would be mainly generated before the formation of aryl azide (3, Scheme 4), since 3 was

Table 1. Analysis of Nitrogen Gas Generated during the Amination Using Ethyl 4-Bromobenzoate (1) and TMSN₃

	Br Cu (+ TMSNa —	2.0 equiv) ninoethanol (2.5 eq	uiv)
EtO ₂ C	1 10013	DMA, Ar, 95 °C	EtO ₂ C
1	(2.0 equiv)		2
entry	time (h)	N ₂ (%)	Ar (%)
1	background	15 ^a	80
2	0	18	74
3	0.25	60	32
4^b	0.25	38	55

^aThe measured N_2 should be contaminated by the dissolved N_2 in H_2O during the water-substituted method for the internal gas collection in a test tube. ^bWithout ethyl 4-bromobenzoate.

not detected during the reaction by the IR study despite its non-short-lived nature (Scheme 4).

A possible reaction mechanism of the present amination is depicted in Scheme 7. We assumed that an aryl anion radical would form by a single-electron transfer from Cu powder to an aromatic ring of the haloarene and undergo the elimination of a halide ion (X⁻) to generate the corresponding aryl radical.¹⁶ At the same time, copper(I) azide would be produced together with the trimethylsilyl (TMS)-protected 2-aminoethanol from TMSN₃ and 2-aminoethanol. Copper(I) azide would then be subjected to either a removal of N₂ gas to form copper(I) complex (A)^{17,18} or an oxidative insertion of the aryl radical to afford the aryl copper(II) azide complex (B). The aryl copper(II) complex (C)^{17,18} would be generated by the oxidative coupling of the aryl radical with the copper(I) complex (A) or by the removal of N₂ from the aryl copper(II) azide complex (B), and subsequent elimination of copper species would afford the desired primary aromatic amine (E). The intermediate (B) would convert to the corresponding aryl

Scheme 7. Proposed Reaction Mechanism

azide (**D**) by the reductive elimination of the Cu(0) species,¹⁹ which would be gradually reduced to the primary aromatic amine (**E**) (Scheme 4).

CONCLUSION

In conclusion, we proposed reaction mechanisms for the copper-mediated amination of aryl halides with TMSN₃ by IR study and Huisgen reaction combined with the analysis of the generated N₂ gas during the reaction. Aromatic amines would be generated through multiple pathways via aryl radicals and copper(I) azide. Although the formation of aryl azide as an intermediate was confirmed, the amination would rather proceed through an aryl copper(II)–amine complex (C, Scheme 7) based on the significant N₂ release during the early stage of the reaction.

EXPERIMENTAL SECTION

General Experimental. All reagents were obtained from commercial sources and used without further purification. Chemical shifts of NMR spectra are expressed in parts per million (ppm) based on an internal standard (¹H NMR: δ = 7.26 ppm and ¹³C NMR: δ = 77.0 ppm for CDCl₃). The ESI mass spectra were taken by a TOF instrument. Gas composition was analyzed by gas chromatography equipped with a thermal conductivity detector and a carbon molecular sieve (60/80 mesh)-packed column (4.5 m, 3.2 mm, i.d., SUS).

IR Spectra in DMA (Figure 1). IR spectra of reagents in DMA were directly measured. The samples were prepared as follows: (a) TMSN₃ (66.4 μ L, 500 μ mol) was dissolved in DMA (500 μ L); (b) TMSN₃ (66.4 μ L, 500 μ mol) and 2-aminoethanol (37.4 μ L, 625 μ mol) were dissolved in DMA (500 μ L); (c) TMSN₃ (66.4 μ L, 500 μ mol) and TBAF·3H₂O (197 mg, 625 μ mol) were dissolved in DMA (500 μ L).

Time-Course Study Using Reaction Monitoring FT-IR for the Reaction of Copper Powder, TMSN₃, and 2-Aminoethanol in DMA at 95 °C for 1 h (Figure 2). A mixture of copper powder (127 mg, 2.00 mmol), 2-aminoethanol (150 μ L, 2.50 mmol), and TMSN₃ (265 μ L, 2.00 mmol) in DMA (2 mL) in a 10 mL two-neck flask was



stirred under an Ar atmosphere (balloon) at 95 $^{\circ}\text{C}$, and the IR peak of the mixture was monitored vs time.

Time-Course Study Using Reaction Monitoring FT-IR for the Amination of Ethyl 4-Bromobenzoate with TMSN₃ in the Presence of Copper Powder and 2-Aminoethanol in DMA at 95 °C for 1 h (Figure 3). A mixture of ethyl 4-bromobenzoate (1) (160 μ L, 1.00 mmol), copper powder (127 mg, 2.00 mmol), 2-aminoethanol (150 μ L, 2.50 mmol), and TMSN₃ (265 μ L, 2.00 mmol) in DMA (2 mL) in a 10 mL two-neck flask was stirred under an Ar atmosphere (balloon) at 95 °C, and the IR peak of the mixture was monitored vs time.

Reduction of Ethyl 4-Azidobenzoate (Scheme 4). A mixture of ethyl 4-azidobenzoate (3) (65.9 mg, 500 μ mol), copper powder (63.5 mg, 1.00 mmol), and 2-aminoethanol (74.9 µL, 1.25 mmol) in DMA (1 mL) in a 15 mL test tube was stirred under an Ar atmosphere (balloon) at 95 °C using an organic synthesizer. After the complete consumption of ethyl 4-bromobenzoate was confirmed by TLC analyses (n-hexane/EtOAc, 2:1), the mixture was diluted with EtOAc (10 mL) and then filtered through a Celite pad. The pad was successively washed with EtOAc (20 mL), H₂O (25 mL), and concd aq ammonia solution (5 mL). After the two layers were separated, the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO4, filtered, and concentrated under reduced pressure. The residue was dissolved in $CDCl_3$, and the ratio of 3 and ethyl 4-aminobenzoate (2) was determined by the ¹H NMR analysis. The ¹H NMR spectral data is shown below for the experiment for Scheme 5.

Confirmation of Generated Ethyl 4-Azidobenzoate during the Amination of Ethyl 4-Bromobenzoate and TMSN₃ Using Huisgen Cyclization (Scheme 5). A mixture of ethyl 4bromobenzoate (1) (80.1 μ L, 500 μ mol), ethynylbenzene (4) (54.9 µL, 500 µmol), copper powder (63.5 mg, 1.00 mmol), 2-aminoethanol (74.9 µL, 1.25 mmol), and TMSN₃ (133 µL, 1.00 mmol) in DMA (1 mL) in a 15 mL test tube was stirred under an Ar atmosphere (balloon) at 95 °C using an organic synthesizer. After the complete consumption of ethyl 4-bromobenzoate was confirmed by TLC analyses (n-hexane/EtOAc, 2:1), the mixture was diluted with EtOAc (10 mL) and then filtered through a Celite pad. The pad was successively washed with EtOAc (20 mL), H₂O (25 mL), and a concd aq ammonia solution (5 mL). After the two layers were separated, the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography with n-hexane/EtOAc $(5:1 \rightarrow 2:1)$ as the eluent.

Ethyl 4-aminobenzoate (2):^{3a} 73% (60.0 mg, 363 μ mol) as a pale yellow solid; mp 92–94 °C; IR (ATR) ν_{max} 3416, 3340, 3218, 2983, 2899, 1678, 1631, 1592, 1511, 1473, 1440, 1366, 1309, 1272, 1169, 1122, 1023, 844, 770, 699, 638, 501 cm⁻¹; ¹H NMR (400 MHz) δ 7.85 (d, *J* = 7.9 Hz, 2H), 6.62 (d, *J* = 7.9 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.13 (br s, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz) δ 166.8, 150.9, 131.5, 119.9, 113.8, 60.3, 14.4; MS (EI) *m/z* 165 (M⁺, 44), 137 (15), 120 (100), 92 (21), 65 (17); HRMS (ESI) calcd for C₉H₁₁NO₂ (M⁺) 165.07898, found 165.07823.

Ethyl 4-(4-phenyl-1H-1,2,3-triazol-yl)benzoate (5):²⁰ 12% (17.9 mg, 61.0 μmol) as a white solid; mp 178–180 °C; IR (ATR) ν_{max} 3120, 3098, 2984, 2933, 1707, 1605, 1519, 1456, 1435, 1408, 1364, 1313, 1273, 1226, 1177, 1103, 1037, 1020, 992, 851, 820, 773, 763, 694 cm⁻¹; ¹H NMR (500 MHz) δ 8.27 (s, 1H), 8.22 (d, *J* = 8.8 Hz, 2H), 7.89–7.92 (m, 4H), 7.46 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 4.42 (q, *J* = 7.3 Hz, 2H), 1.43 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (125 MHz) δ 165.4, 148.7, 139.9, 131.3, 130.5, 129.8, 128.9, 128.6, 125.8, 119.7 117.3, 61.4, 14.3; MS (ESI) *m*/*z* 293 (M⁺, 2), 265 (100), 237 (89), 220 (22), 207 (23), 192 (65), 165 (37), 116 (52), 89 (46), 76 (26), 65 (11); HRMS (ESI) calcd for C₁₇H₁₅N₃O₂ [(M + Na)⁺] 316.10620, found 316.10547.

Ullmann-Type Amination of Ethyl 4-Bromobenzoate and 4-Phenyl-1*H*-1,2,3-triazole (6) (Scheme 6). A mixture of ethyl 4bromobenzoate (1) (55.6 μ L, 347 μ mol), 4-phenyl-1*H*-1,2,3-triazole (6)²¹ (50.4 mg, 347 μ mol), copper powder (44.1 mg, 694 μ mol), and 2-aminoethanol (52.0 µL, 868 µmol) in DMA (700 µL) in a 15 mL test tube was stirred under an Ar atmosphere (balloon) at 95 °C using an organic synthesizer. After the complete consumption of ethyl 4-bromobenzoate was confirmed by TLC analyses (*n*-hexane/EtOAc, 2:1), the mixture was diluted with EtOAc (10 mL) and then filtered through a Celite pad. The pad was successively washed with EtOAc (20 mL), H₂O (25 mL), and a concd aq ammonia solution (5 mL). After the two layers were separated, the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography with *n*-hexane/EtOAc (5:1 → 2:1 → 1:1) as the eluent to afford ethyl 4-(4-phenyl-1H-1,2,3-triazol-1-yl)benzoate (5) as a white solid in 3% yield (3.4 mg, 11.5 µmol). The spectra data are shown for the experiment for Scheme 5.

Analysis of Nitrogen Gas Generation during the Amination Using Ethyl 4-Bromobenzoate and TMSN₃ (Table 1). A mixture of ethyl 4-bromobenzoate (1) (80.1 μ L, 500 μ mol), copper powder (63.5 mg, 1.00 mmol), 2-aminoethanol (74.9 μ L, 1.25 mmol), and TMSN₃ (133 μ L, 1.00 mmol) in DMA (1 mL) in a 15 mL test tube was stirred under an Ar atmosphere at 95 °C using an organic synthesizer. After the reaction, the gas in the test tube was collected over water and analyzed by gas chromatography. Helium was used as the carrier gas at the flow rate of 40 mL/min. The injector and detector temperatures were both 150 °C. The column temperature was 40 °C.

For entry 1: Without the addition of any reagents, air inside the test tube (15 mL) was replaced with Ar, and then the gas inside the test tube was immediately collected over water.

For entry 2: Ethyl 4-bromobenzoate (1), copper powder, 2aminoethanol, $TMSN_3$, and DMA were placed in the test tube, and the air inside the test tube was replaced with Ar. The gas inside the test tube was then collected over water.

For entry 3: The reaction mixture was stirred at 95 $^\circ$ C for 0.25 h, and then the gas inside the test tube was collected over water.

For entry 4: The reaction mixture was carried out in the absence of ethyl 4-bromobenzoate (1). After the mixture was stirred for 0.25 h, the gas inside the test tube was collected over water.

ASSOCIATED CONTENT

Supporting Information

¹H and ¹³C NMR spectra of compounds (2 and 5), IR spectra of tetrabutylammonium azide and compound (3), IR spectra of the time-course study using reaction monitoring FT-IR for the reaction of 3 in the presence of copper powder and 2-aminoethanol, and IR spectra of the time-course study using reaction monitoring FT-IR for the reaction of ethyl 4-bromobenzoate (1) with copper powder, and 2-aminoethanol in DMA in the presence of ethynylbenzene (4). 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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(12) If the azide species was copper(II) azide $[Cu(N_3)_2]$, several strong absorptions woud be observed between $2050-2150 \text{ cm}^{-1}$ in the IR spectrum. On the other hand, only a single strong peak should be observed at 2024 cm⁻¹ together with a shoulder peak at 2070 cm⁻¹, if copper(I) azide (CuN₃) formed; see: Dehnicke, K. Z. Anorg. Allg. Chem. **1974**, 409, 311–319.

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(17) For the generation of copper nitrene species from copper reagents and azides and their application for the organic synthesis, see: (a) Gephart, R. T, III; Warren, T. H. Organometallics 2012, 31, 7728-7752. (b) Badiel, Y. M.; Krishnaswamy, A.; Melzer, M. M.; Warren, T. H. J. Am. Chem. Soc. 2006, 128, 15056-15057. (c) Badiei, Y. M.; Dinescu, A.; Dai, X.; Palomino, R. M.; Heinenmann, F. W.; Cundari, T. R.; Warren, T. H. Angew. Chem. 2008, 120, 10109-10112; Angew. Chem., Int. Ed. 2008, 47, 9961-9964. (d) Wiese, S.; Badiei, Y. M.; Gephart, R. T.; Mossin, S.; Varonka, M. S.; Melzer, M. M.; Meyer, K.; Cundari, T. R.; Warren, T. H. Angew. Chem. 2010, 122, 9034-9039; Angew. Chem., Int. Ed. 2010, 49, 8850-8855. (e) Gephart, R. T., III; Huang, D. L.; Aguila, M. J. B.; Schmidt, G.; Shahu, A.; Warren, T. H. Angew. Chem. 2012, 124, 6594-6598; Angew. Chem., Int. Ed. 2012, 51, 6488-6492. (f) Aguila, M. J. B.; Badiei, Y. M.; Warren, T. H. J. Am. Chem. Soc. 2013, 135, 9399-9408. (g) Han, H.; Park, S. B.; Kim, S. K.; Chang, S. J. Org. Chem. 2008, 73, 2862-2870.

(18) Qu and co-workers demonstrated that copper–nitrogen bonds of diamine-ligated copper (I) nitrene complexes, $[(N \cdots N)Cu-N-R]$, show single-bonded character in some cases, e.g., when the substituent R is methyl group, from density functional theory analysis. Meng, Q.; Wang, F.; Qu, X.; Zhou, J.; Li, M. *THEOCHEM* **2007**, *815*, 111–118 For more studies on the structure of copper nitrene species, see ref 17a and references cited therein.

(19) The recovery of Cu(0) species would explain the fact that the amount of copper could be reduced to 0.5 equiv for the amination of ethyl 4-bromobenzoate (1) without a significant loss of the reaction efficiency (94%) as mentioned in our previous paper; see ref 5.

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