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Note

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A Tandem Reaction of 1-Copper(I) Alkynes for the Synthesis of 1,4,5-Trisubstituted 5-Chloro-1,2,3-Triazoles

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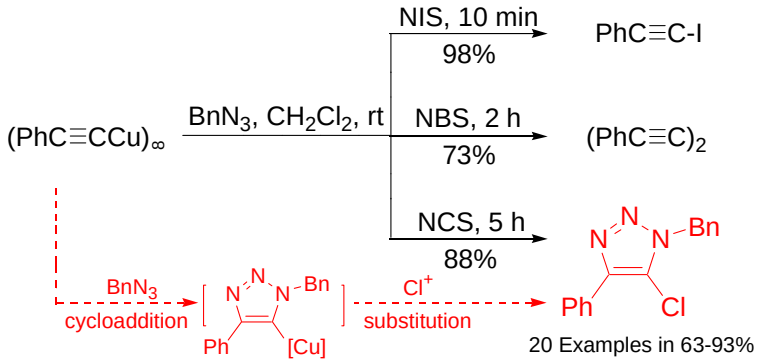
Graphic Abstract

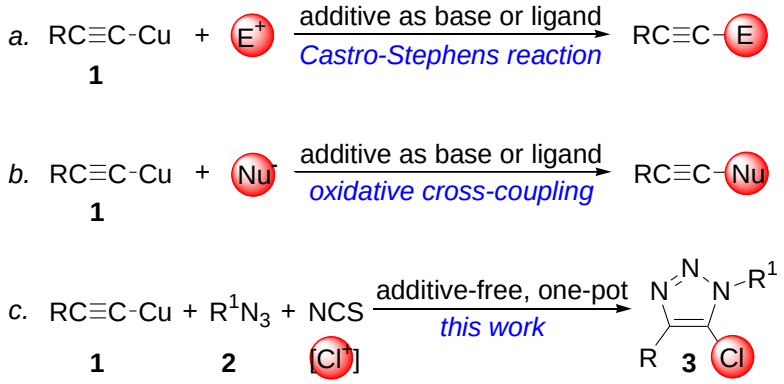


Abstract

A novel tandem reaction of 1-copper(I) alkynes with azides (cycloaddition) and then NCS (electrophilic substitution) was developed as an efficient method for the synthesis of 1,4,5-trisubstituted 5-chloro-1,2,3-triazoles. The method offers a rare example that a tandem reaction of an organometallic substrate does not involve in the reactivity of the metal-carbon bond in the first step.

The isolated 1-copper(I) alkynes (**1**) are believed to have the polymeric complex structure as $(RC{\equiv}CCu)_n$, in which the acetylene bond serves as a ligand without any exogenous ligand.[1] For example, the detailed structures of *t*-BuC≡CCu and PhC≡CCu can be drawn as $(t\text{-BuC}{\equiv}CCu)_{20}$ and $(PhC{\equiv}CCu)_{\infty}$, respectively.[2] Most 1-copper(I) alkynes (**1**) can be simply prepared and isolated as insoluble crystalline solids with extremely chemical stability. Therefore, their structures are poorly understood and their reactions in organic synthesis are shortly studied to date. As shown in Scheme 1, their most important application was in Castro-Stephens reaction, where the Cu(I)-C bond was substituted by various electrophiles (*a*).[3] Recently, a new application of them was reported by Evano, in which the Cu(I)-C bond was substituted by nucleophiles through an oxidative cross-coupling mechanism (*b*).[4] Herein, we report that 1-copper(I) alkynes (**1**) can also carry out a novel tandem reaction with azides (**2**) (cycloaddition) and then NCS (electrophilic substitution), where the reactivity of Cu(I)-C bond was not involved in the first step to give 1,4,5-trisubstituted 5-chloro-1,2,3-triazoles (**3**) as the final products (*c*).

Scheme 1



Recently, 1,4,5-trisubstituted 1,2,3-triazoles were reported to have important applications in organic synthesis, biology and material sciences.[5–9] Prominent among them are 1,4,5-trisubstituted 5-halo-1,2,3-triazoles (**3-5**)[6–9] because they can be used as both product and precursor (Figure 1). However, they can not be prepared by the normal CuAAC reaction (copper-catalyzed azide-alkyne cycloaddition) in which only terminal alkynes are used as substrates and 1,4-disubstituted 1,2,3-triazoles are produced.[1a,10]

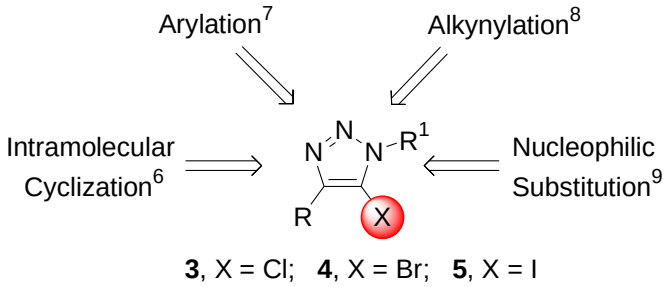
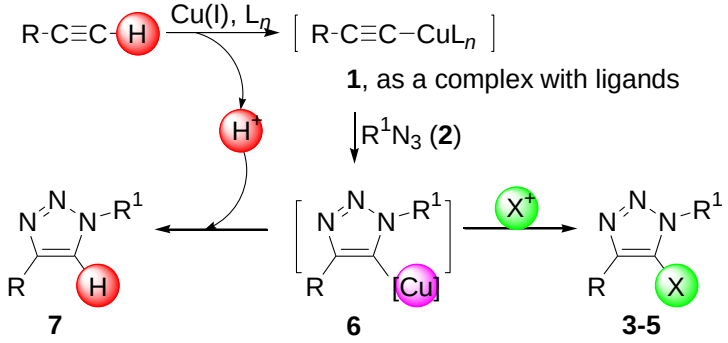


Figure 1. The synthetic applications of 1,4,5-trisubstituted 5-halo-1,2,3-triazoles

Many efforts have been made to develop the methods for the synthesis of 1,4,5-trisubstituted 5-halo-1,2,3-triazoles (**3**-**5**). As shown in Scheme 2, an early method was to simply add an electrophile X^+ (X = Cl, Br and I) into a normal CuAAC reaction, by which the intermediate 5-copper(I) 1,2,3-triazole (**6**)[8a,8c,11] was trapped *in situ* by X^+. Unfortunately, this method usually gave a mixture containing both the desired product and the byproduct 1,4-disubstituted 1,2,3-triazole (**7**) due to a competitive protonation of H^+. In some cases, the byproduct **7** was even the major product depending upon the structure of the substrate. This drawback was unavoidable because this H^+ came from the terminal alkyne, which was the required substrate for a normal CuAAC reaction.

Scheme 2



To overcome the drawbacks caused by terminal alkynes, 1-bromo-alkynes (**8**) were wisely introduced as the substrates (Figure 2).[9b] Under the modified CuAAC conditions, 1,4,5-trisubstituted 5-bromo-1,2,3-triazoles (**4**) were produced smoothly by the cycloaddition of **8** and **2**. Later, 1-iodo-alkynes (**9**) were proved to be the most suitable substrates for the synthesis of 1,4,5-trisubstituted 5-iodo-1,2,3-triazoles (**5**).[6,7b,12] Recently, 1-alumino-alkynes (**10**) were reported to be versatile substrates

for the synthesis of various 1,4,5-trisubstituted 1,2,3-triazoles including the products **3-5**.[13] But, there are two drawbacks to this otherwise efficient method caused by the highly active Al-C bonds in both **10** and its reaction intermediates 5-alumino-1,2,3-triazoles (**11**). First, this method has to be performed under anhydrous conditions because Al-C bonds are sensitive to moisture. Second, the method has to be proceeded in two steps because these two Al-C bonds do not have chemoselectivity to the electrophile X^+.

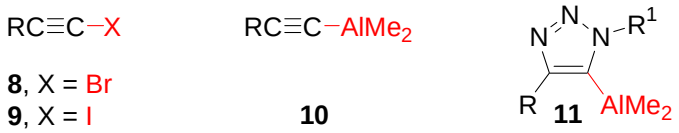
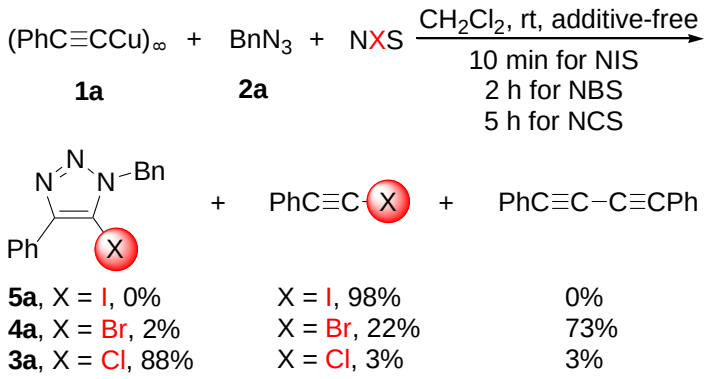


Figure 2. The structures of **8-11**.

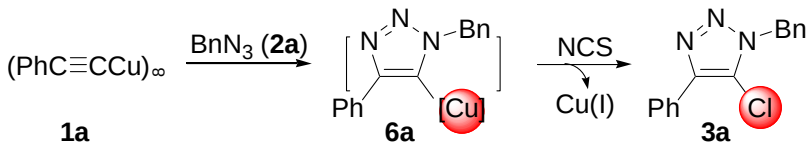
In our recent CuAAC project, 1-copper(I) alkynes (**1**) were used often as substrates and intermediates in the synthesis of 1,4-disubstituted 1,2,3-triazoles.[14] Interestingly, we found that they were perfectly stable to air and moisture, but were still never used for the synthesis of 1,4,5-trisubstituted 5-halo-1,2,3-triazoles (**3-5**). Thus, we were encouraged to develop an easy method for the synthesis of **3-5** by using 1-copper(I) alkynes (**1**) as substrates. Unfortunately, the primary experimental results indicated that only a complicated mixture was produced when the solution of 1-copper(I) phenylethyne (**1a**) and benzyl azide (**2a**) in CH_2Cl_2 was treated by NXS (X = Cl, Br or I) in the presence of an additive (as base or ligand), such as Et_3N, DIPEA, pyridine or 1,10-phenanthroline. However, the same reactions gave a group of interesting results under the additive-free conditions. As shown in Scheme 3, 1-iodo-phenylethyne was obtained in 98% yield as a single product after **1a**, **2a** and NIS were mixed together in CH_2Cl_2 for 10 minutes. By replacement of NIS with NBS, the same reaction offered a mixture of **3a** (2%), 1-bromo-phenylethyne (22%) and 1,4-diphenylbutadiyne (73%). To our delight, the desired **3a** was obtained in 88% yield as a major product when NCS served as an electrophile.

Scheme 3



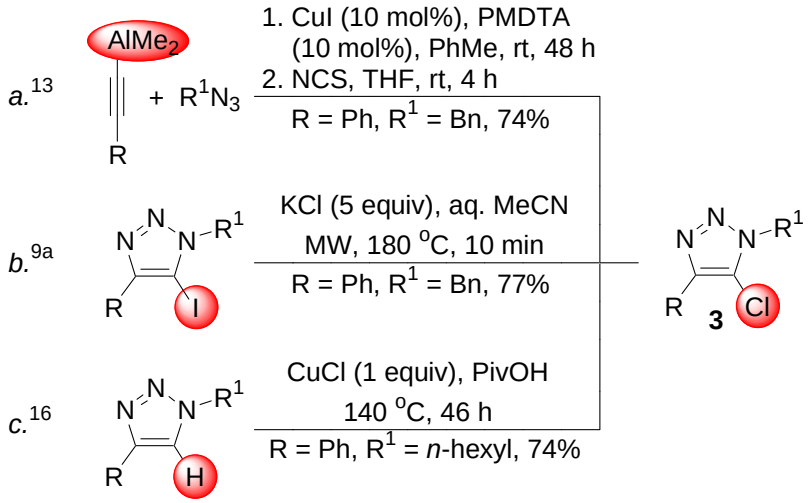
The results in Scheme 3 clearly indicate that the reaction products strongly depend upon the properties of NXS. For example, NIS is a strong electrophile and therefore it undergoes a fast electrophilic substitution with **1a** to yield 1-iodo-phenylethyne as a unique product. However, NBS as a moderate electrophile reacts slowly with **1a** to initially yield some of 1-bromo-phenylethyne. Then, the produced 1-bromo-phenylethyne further reacts with unreacted **1a** to form 1,4-diphenylbutadiyne as a major product by Castro-Stephens reaction. But, the conditional experiments showed that the electrophilic substitution between **1a** and NCS underwent very slowly under the same conditions (< 10% of **1a** was consumed in 5 h) because NCS was the weakest electrophile compared to NIS and NBS. Thus, a CuAAC reaction between **1a** and **2a** occurs preferentially to give **6a** as an intermediate due to the "click reaction" having a high thermodynamic driving force (Scheme 4).[15] Then, the intermediate **6a** is trapped by NCS to give **3a**. This result indicates that the Cu(I)-C bond of **1a** has much lower reactivity than that of **6a** because **1a** is a polymeric complex. This result also offers a rare example whereby a tandem reaction of an organometallic substrate does not involve in the reactivity of the metal-carbon bond in the first step.

Scheme 4



To further confirm the hypothesized pathway in Scheme 4, the cycloaddition of 1-chloro-phenylethyne (PhC≡C-Cl) and **2a** was tested in the presence of one equivalent of CuCl (CH_2Cl_2, rt, 5 h). As was expected, no any desired product **3a** was obtained and PhC≡C-Cl was confirmed to be not an intermediate in the conversion of **1a** to **3a**. Thus far, we discovered a novel tandem reaction method for the synthesis of 1,4,5-trisubstituted 5-chloro-1,2,3-triazoles (**3**). Since the synthesis of **3** was the most difficult task among the isomers **3-5** and there were only three chemoselective procedures (*a-c*, Scheme 5)[9a,13,16] for this purpose in literature to date, therefore this mild and convenient tandem reaction method may be a valuable addition.

Scheme 5



Since the product **3a** was produced under extremely simple conditions, only the solvent needs to be optimized. As shown in Table 1, the solvents have a significant effect on the yield of **3a** and MeOH gave the lowest yield (entry 1). Interestingly, halo-containing solvents, such as $CHCl_3$, $ClCH_2CH_2Cl$ and CH_2Cl_2 (entries 5-7), were all good solvents and CH_2Cl_2 gave the best results (entry 7). The reaction concentrations did not have comparable effect on the reaction (entries 7-9). Finally, the entry 7 was assigned as our standard conditions.

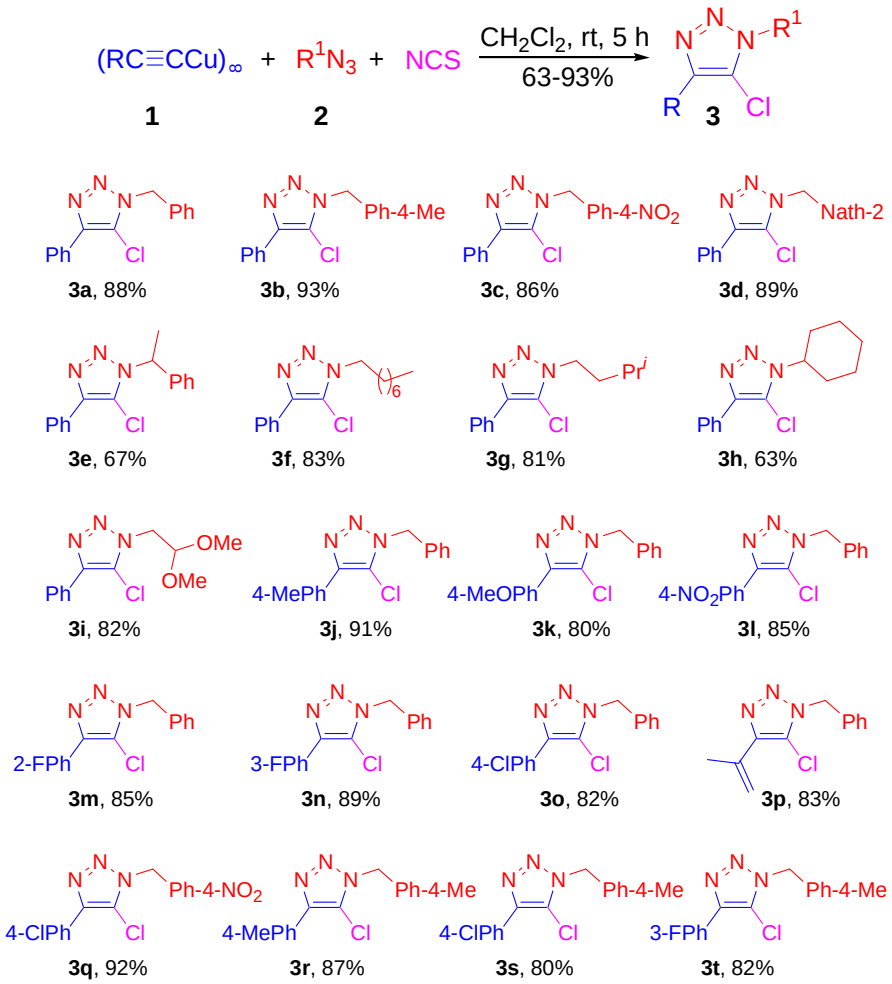
Table 1. The effect of solvent on the reaction[a]

Entry	Solvent	Concentration of **1a** (mmol/mL)	Yield of **3a** (%)[b]
1	MeOH	0.5/1	32
2	MeCN	0.5/1	53
3	Toluene	0.5/1	57
4	THF	0.5/1	70
5	$CHCl_3$	0.5/1	76
6	$ClCH_2CH_2Cl$	0.5/1	84
7	CH_2Cl_2	0.5/1	88
8	CH_2Cl_2	0.5/2	83
9	CH_2Cl_2	0.5/4	85

[a]The mixture of **1a** (0.5 mmol), **2a** (0.6 mmol) and NCS (0.6 mmol) in solvent was stirred in a stoppered tube at room temperature for 5 h. [b]The isolated yields.

As shown in Scheme 6, this novel method was general and efficient for the molecular diversity. Under the standard conditions, 1-copper(I) alkynes (**1**), azides (**2**) and NCS reacted smoothly to give the

Scheme 6



corresponding 1,4,5-trisubstituted 5-chloro-1,2,3-trizoles (**3a-3t**) in satisfactory yields. By fixing 1-copper(I) phenylethyne (**1a**), all tested azides were suitable substrates (see: the products **3a-3i**) and the azides bearing bulky groups gave relatively low yields (see: the products **3e** and **3h**). By fixing benzyl azide (**2a**), no apparent difference was observed for all tested 1-copper(I) alkynes, no matter which electron-donating-groups (see: the products **3j-3k**) or electron-withdrawing-groups (see: the product **3l**) are on the arylethynes.

In conclusion, a novel tandem reaction method was established for the preparation of 1,4,5-trisubstituted 5-chloro-1,2,3-triazoles by directly using the isolated 1-copper(I) alkynes as substrates. The method shows noteworthy importance because it proceeds under mild conditions and its products are expected to have important medicinal properties.

Experimental Section

The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$. TMS was used as an internal reference and *J* values are given in Hz. 1-Copper(I) alkynes (**1**) were prepared according to the procedure reported in reference.[3c]

A Typical Procedure for the Preparation of 1-Benzyl-4-phenyl-5-chloro-1,2,3-triazole (3a). To a suspension of 1-copper(I) phenylethyne (**1a**, 82 mg, 0.5 mmol) and benzyl azide (**2a**, 80 mg, 0.6 mmol) in CH_2Cl_2 (1 mL) was added NCS (80 mg, 0.6 mmol). The resultant mixture was stirred at room temperature for 5 h and then passed through a column chromatography [silica gel, 10% EtOAc in petroleum ether (60–90 ^{o}C)] to give 119 mg (88%) of product **3a** as a white solid, mp 60–62 ^{o}C (lit.[13] mp 58–60 °C). IR (KBr) *v* 3063, 3035, 2952, 1606 cm^{-1}; ^{1}H NMR δ 7.97–7.91 (m, 2H), 7.45–7.26 (m, 8H), 5.52 (s, 2H); ^{13}C NMR δ 141.8, 133.7, 129.2, 128.8 (2C), 128.6 (2C), 128.5, 128.4, 127.7 (2C), 126.2 (2C), 121.6, 51.9; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{12}ClN_3$, $[M + H]^+$ 270.0793; found 270.0792.

The similar procedure was used for the preparation of products **3b-3t**.

1-(4-Methylbenzyl)-4-phenyl-5-chloro-1,2,3-triazole (3b). White solid, 132 mg (93%), mp 83–85 ^{o}C; IR (KBr) *v* 3028, 2984, 1611 cm^{-1}; ^{1}H NMR δ 7.96 (d, *J* = 7. 92 Hz, 2H), 7.44–7.31 (m, 3H), 7.21–7.12 (m, 4H), 5.49 (s, 2H), 2.30 (s, 3H); ^{13}C NMR δ 141.8, 138.4, 130.8, 129.5 (2C), 129.2, 128.5 (2C), 128.4, 127.7 (2C), 126.2 (2C), 121.5, 51.8, 21.0; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{14}ClN_3$, $[M + H]^+$ 284.0949; found 284.0950.

1-(4-Nitrobenzyl)-4-phenyl-5-chloro-1,2,3-triazole (3c). White solid, 135 mg (86%), mp 123–125 ^{o}C; IR (KBr) *v* 3079, 2953, 2851, 1606 cm^{-1}; ^{1}H NMR δ 8.24–8.14 (m, 2H), 7.99–7.90 (m, 2H), 7.52–7.33 (m, 5H), 5.67 (s, 2H); ^{13}C NMR δ 147.9, 142.1, 140.6, 128.8, 128.7 (3C), 128.5 (2C), 126.1 (2C), 124.1 (2C), 121.7, 50.9; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{11}ClN_4O_2$, $[M + H]^+$ 315.0643; found 315.0642.

1-(2-Naphthylmethyl)-4-phenyl-5-chloro-1,2,3-triazole (3d). White solid, 142 mg (89%), mp 95–97 ^{o}C; IR (KBr) *v* 3055, 1601 cm^{-1}; ^{1}H NMR δ 7.98–7.96 (m, 2H), 7.82–7.74 (m, 4H), 7.50–7.32 (m, 6H), 5.69 (s, 2H); ^{13}C NMR δ 142.0, 133.0 (2C), 131.1, 129.2, 128.9, 128.6 (2C), 128.5, 127.9, 127.7, 127.0, 126.5 (2C), 126.2 (2C), 125.0, 121.7, 52.2; HRMS (ESI-TOF) (*m/z*): calcd for $C_{19}H_{14}ClN_3$, $[M + H]^+$ 320.0949; found 320.0951.

1-(1-Ethylbenzyl)-4-phenyl-5-chloro-1,2,3-triazole (3e). White solid, 95 mg (67%), mp 88–90 ^{o}C; IR (KBr) *v* 3063, 3032, 2990, 1607 cm^{-1}; ^{1}H NMR δ 7.98–7.95 (m, 2H), 7.47–7.24 (m, 8H), 5.71 (q, *J* = 6.87 Hz, 1H), 2.07 (d, *J* = 6.87 Hz, 3H); ^{13}C NMR δ 141.8, 139.5, 129.3, 128.8 (2C), 128.5 (2C), 128.3, 128.2, 126.3 (4C), 121.4, 58.9, 21.3; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{14}ClN_3$, $[M + H]^+$ 284.0949; found 284.0948.

1-Octyl-4-phenyl-5-chloro-1,2,3-triazole (3f). Yellow oil, 121 mg (83%); IR (KBr) *v* 3062, 3033, 2956, 2855, 1608 cm^{-1}; ^{1}H NMR δ 8.00–7.96 (m, 2H), 7.48–7.26 (m, 3H), 4.35 (t, *J* = 7.20 Hz, 2H),

1.98–1.91 (m, 2H), 1.34–1.27 (m, 10H), 0.88 (t, J = 7. 20 Hz, 3H); ^{13}C NMR δ 141.5, 129.4, 128.6 (2C), 128.3, 126.2 (2C), 121.3, 48.4, 31.6, 29.3, 29.0, 28.9, 26.3, 22.5, 14.0; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{22}ClN_3$, $[M + H]^+$ 292.1575; found 292.1577.

1-(3-Methylbutyl)-4-phenyl-5-chloro-1,2,3-triazole (3g). Yellow oil, 101 mg (81%); IR (KBr) *v* 3062, 2958, 2871, 1608 cm^{-1}; ^{1}H NMR δ 7.99–7.96 (m, 2H), 7.48–7.33 (m, 3H), 4.36 (t, J = 7.56 Hz, 2H), 1.86–1.78 (m, 2H), 1.70–1.61 (m, 1H), 0.99 (d, J = 6.51Hz, 6H); ^{13}C NMR δ 141.5, 129.3, 128.5 (2C), 128.3, 126.2 (2C), 121.2, 46.7, 37.9, 25.4, 22.1 (2C); HRMS (ESI-TOF) (*m/z*): calcd for $C_{13}H_{16}ClN_3$, $[M + H]^+$ 250.1106; found 250.1107.

1-Cyclohexyl-4-phenyl-5-chloro-1,2,3-triazole (3h). Green solid, 82 mg (63%), mp 100–102 ^{o}C; IR (KBr) *v* 3074, 2931, 2855, 1611 cm^{-1}; ^{1}H NMR δ 7.99–7.93 (m, 2H), 7.48–7.34 (m, 3H), 4.41–4.31 (m, 1H), 2.14–1.95 (m, 6H), 1.79–1.74 (m, 1H), 1.51–1.26 (m, 3H); ^{13}C NMR δ 141.4, 129.6, 128.6 (2C), 128.3, 126.4 (2C), 120.6, 58.6, 32.3 (2C), 25.3 (2C), 25.0; HRMS (ESI-TOF) (*m/z*): calcd for $C_{14}H_{16}ClN_3$, $[M + H]^+$ 262.1106; found 262.1104.

1-(2,2-Dimethoxylethyl)-4-phenyl-5-chloro-1,2,3-triazole (3i). Colorless oil, 110 mg (82%); IR (KBr) *v* 3061, 3029, 2959, 2836, 1608 cm^{-1}; ^{1}H NMR δ 8.00–7.97 (m, 2H), 7.48–7.27 (m, 3H), 4.87 (t, J = 5.52 Hz, 1H), 4.46 (d, J = 5.52 Hz, 2H), 3.40 (s, 6H); ^{13}C NMR δ 141.3, 129.2, 128.5 (2C), 128.3, 126.2 (2C), 122.3, 101.8, 54.5 (2C), 49.2; HRMS (ESI-TOF) (*m/z*): calcd for $C_{12}H_{14}ClN_3O_2$, $[M + H]^+$ 268.0847; found 268.0848.

1-Benzyl-4-(4-methylphenyl)-5-chloro-1,2,3-triazole (3j). White solid, 129 mg (91%), mp 76–78 ^{o}C; IR (KBr) *v* 3065, 2951, 2871, 1645 cm^{-1}; ^{1}H NMR δ 7.84 (d, J = 8.25 Hz, 2H), 7.34–7.18 (m, 7H), 5.49 (s, 2H), 2.34 (s, 3H); ^{13}C NMR δ 141.9, 138.2, 133.8, 129.2 (2C), 128.8 (2C), 128.4, 127.6 (2C), 126.3, 126.0 (2C), 121.1, 51.8, 21.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{14}ClN_3$, $[M + H]^+$ 284.0949; found 284.0947.

1-Benzyl-4-(4-methoxyphenyl)-5-chloro-1,2,3-triazole (3k). White solid, 120 mg (80%), mp 61–62 °C. IR (KBr) *v* 3063, 3033, 2940, 2836, 1612 cm^{-1}; ^1H NMR δ 7.91–7.87 (m, 2H), 7.37–7.24 (m, 5H), 6.99–6.94 (m, 2H), 5.52 (s, 2H), 3.81 (s, 3H); ^{13}C NMR δ 159.7, 141.8, 133.8, 128.8 (2C), 128.5, 127.7 (2C), 127.5 (2C), 121.8, 120.7, 114.0 (2C), 55.2, 51.9; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{14}ClN_3O$, $[M + H]^+$ 300.0898; found 300.0901.

1-Benzyl-4-(4-nitrophenyl)-5-chloro-1,2,3-triazole (3l). Yellow solid, 134 mg (85%); mp 130–132 °C. IR (KBr) *v* 3033, 1599 cm^{-1}; ^1H NMR δ 8.30 (d, J = 8.25 Hz, 2H), 8.18 (d, J = 8.25 Hz, 2H), 7.40–7.32 (m, 5H), 5.61 (s, 2H); ^{13}C NMR δ 147.4, 139.9, 135.5, 133.3, 129.1 (2C), 128.8, 127.9 (2C), 126.6 (2C), 124.0 (2C), 123.2, 52.3; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{11}ClN_4O_2$, $[M + H]^+$ 315.0643; found 315.0644.

1-Benzyl-4-(2-flourophenyl)-5-chloro-1,2,3-triazole (3m). Colorless oil, 122 mg (85%); IR (KBr) *v* 3066, 3034, 2951, 2855, 1582 cm^{-1}; ^1H NMR δ 7.70–7.64 (m, 1H), 7.41–7.28 (m, 6H), 7.24–7.12 (m, 2H), 5.56 (s, 2H); ^{13}C NMR δ 159.5 (d, J = 249.0 Hz), 138.7, 133.7, 130.7 (d, J = 2.9 Hz, 2C), 128.9 (2C), 128.5, 127.8 (2C), 124.2 (d, J = 2.8 Hz), 124.0, 117.1 (d, J = 14.3 Hz), 115.9 (d, J = 21.5 Hz), 52.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{11}ClFN_3$, $[M + H]^+$ 288.0698; found 288.0700.

1-Benzyl-4-(3-flourophenyl)-5-chloro-1,2,3-triazole (3n). White solid, 128 mg (89%), mp 64–66 °C; IR (KBr) *v* 3079, 3035, 2925, 1617 cm^{-1}; ^1H NMR δ 7.77–7.67 (m, 2H), 7.43–7.24 (m, 6H), 7.08–7.01 (m, 1H), 5.56 (s, 2H); ^{13}C NMR δ 162.8 (d, J = 243.8 Hz), 140.8, 133.6, 131.3 (d, J = 8.6 Hz), 130.3 (d, J = 7.9 Hz), 128.9 (2C), 128.6, 127.8 (2C), 122.0, 121.7, 115.3 (d, J = 20.8 Hz), 113.1 (d, J = 23.0 Hz), 52.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{11}ClFN_3$, $[M + H]^+$ 288.0698; found 288.0701.

1-Benzyl-4-(4-chlorophenyl)-5-chloro-1,2,3-triazole (3o). White solid, 125 mg (82%), mp 124–126 °C; IR (KBr) *v* 3066, 3034, 2933, 1603 cm^{-1}; ^1H NMR δ 7.92–7.89 (m, 2H), 7.42–7.31 (m, 7H), 5.56 (s, 2H); ^{13}C NMR δ 141.0, 134.4, 133.6, 129.0 (2C), 128.9 (2C), 128.7, 127.8 (3C), 127.5 (2C), 121.7, 52.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{11}Cl_2N_3$, $[M + H]^+$ 304.0403; found 304.0402.

1-Benzyl-4-isopropenyl-5-chloro-1,2,3-triazole (3p). Colorless oil, 97 mg (83%); IR (KBr) *v* 3065, 3034, 2980, 2953, 1635 cm^{-1}; ^1H NMR δ 7.37–7.26 (m, 5H), 5.70 (s, 1H), 5.49 (s, 2H), 5.24(s, 1H), 2.23 (s, 3H); ^{13}C NMR δ 142.6, 133.8, 133.3, 128.8 (2C), 128.4, 127.7 (2C), 121.5, 114.5, 51.8, 21.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{12}H_{12}ClN_3$, $[M + H]^+$ 234.0793; found 234.0795.

1-(4-Nitrobenzyl)-4-(4-chlorophenyl)-5-chloro-1,2,3-triazole (3q). Yellow solid, 161 mg (92%), mp 134–136 ^oC; IR (KBr) *v* 2925, 2852, 1603 cm^{-1}; ^1H NMR δ 8.23 (d, J = 8.94 Hz, 2H), 7.96–7.88 (m, 2H), 7.53–7.40 (m, 4H), 5.68 (s, 2H); ^{13}C NMR δ 148.0, 141.2, 140.4, 134.6, 128.9 (2C), 128.6 (2C), 127.4 (2C), 127.3, 124.2 (2C), 121.8, 51.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{15}H_{10}Cl_2N_4O_2$, $[M + H]^+$ 349.0254; found 349.0253.

1-(4-Methylbenzyl)-4-(4-methylphenyl)-5-chloro-1,2,3-triazole (3r). White solid, 130 mg (87%), mp 52–54 ^oC; IR (KBr) *v* 3023, 2920, 2856, 1649 cm^{-1}; ^1H NMR δ 7.84 (d, J = 8.25 Hz, 2H), 7.24–7.08 (m, 6H), 5.47 (s, 2H), 2.35 (s, 3H), 2.30 (s, 3H); ^{13}C NMR δ 141.9, 138.3, 138.2, 130.8, 129.5 (2C), 129.2 (2C), 127.7 (2C), 126.4, 126.1 (2C), 121.1, 51.7, 21.2, 21.0; HRMS (ESI-TOF) (*m/z*): calcd for $C_{17}H_{16}ClN_3$, $[M + H]^+$ 298.1106; found 298.1107.

1-(4-Methylbenzyl)-4-(4-chlorophenyl)-5-chloro-1,2,3-triazole (3s). White solid, 127 mg (80%), mp 83–85 ^oC; IR (KBr) *v* 3025, 2920, 1608 cm^{-1}; ^1H NMR δ 7.93–7.87 (m, 2H), 7.42–7.37 (m, 2H), 7.23–7.13 (m, 4H), 5.50 (s, 2H), 2.32 (s, 3H); ^{13}C NMR δ 140.9, 138.5, 134.3, 130.6, 129.6 (2C), 128.8 (2C), 127.8 (2C), 127.4 (2C), 124.9, 121.6, 51.9, 21.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{13}Cl_2N_3$, $[M + H]^+$ 318.0559; found 318.0561.

1-(4-Methylbenzyl)-4-(3-fluorophenyl)-5-chloro-1,2,3-triazole (3t). White solid, 124 mg (82%), mp 98–100 ^oC; IR (KBr) *v* 3026, 2956, 2855, 1617 cm^{-1}; ^1H NMR δ 7.77–7.67 (m, 2H), 7.43–7.36 (m, 1H), 7.25–7.14 (m, 4H), 7.08–7.02 (m, 1H), 5.52 (s, 2H), 2.33 (s, 3H); ^{13}C NMR δ 162.9 (d, J = 243.8 Hz), 140.8, 138.6, 131.4 (d, J = 8.6 Hz), 130.6, 130.3 (d, J = 8.6 Hz), 129.6 (2C), 127.8 (2C), 121.9,

121.8, 115.3 (d, J = 21.5 Hz), 113.1 (d, J = 23.7 Hz), 52.0, 21.1; HRMS (ESI-TOF) (*m/z*): calcd for $C_{16}H_{13}ClFN_3$, $[M + H]^+$ 302.0855; found 302.0856.

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Supporting Information Available. ^1H and ^{13}C NMR spectra for products **3a-3t**. This material is available free of charge via the Internet at http://pubs.acs.org.

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