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Synthesis of 5-Substituted 1*H*-Tetrazoles by the Copper-Catalyzed [3+2] Cycloaddition of Nitriles and Trimethylsilyl Azide

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Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday

Abstract: The copper-catalyzed [3+2] cycloaddition between various nitriles and trimethylsilyl azide in DMF/MeOH produced the corresponding 5-substituted 1*H*-tetrazoles in good to high yields. It was proposed that the reaction proceeds through the formation in situ of a copper azide species and subsequent [3+2] cycloaddition with the nitriles. Furthermore, we found that a copper and triethylamine combined catalyst also promoted the cycloaddition of nitriles and trimethylsilyl azide to afford the 5-substituted 1*H*-tetrazoles at relatively low reaction temperatures. The copper azide species would be formed by reaction of the copper catalyst with $Et_3N{\cdot}HN_3$ generated in situ.

Keywords: copper · cycloaddition · homogeneous catalysis · nitriles · tetrazoles

Introduction

1*H*-Tetrazoles are an important class of heterocycles and exhibit a wide range of applications in medicinal chemistry and the materials sciences. For example, tetrazoles are regarded as isosteres of the carboxylic acid functionality in medicinal chemistry; they are applied in the materials sciences and in chemical industry as propellants, explosives, and in photography, and play an important role as ligands in coordination chemistry.[1]

Owing to their potential usefulness, synthetic methods for tetrazoles have been intensively developed, and new preparative methods have appeared.[2] The [3+2] cycloaddition of nitriles with inorganic azides is known as one of the most conventional methods for the synthesis of 5-substituted 1*H*-tetrazoles. Recently, Sharpless and co-workers reported an innovative and safe procedure for the preparation of 5-substituted 1*H*-tetrazoles from the corresponding nitriles and NaN_3 in the presence of a stoichiometric amount or 50 mol% of Zn^{II} salts.[3] Pizzo and co-workers reported an efficient method for the synthesis of tetrazoles by the reaction of nitriles with $TMSN_3$ (TMS = trimethylsilyl) with 50 mol% of tetra-*n*-butylammonium fluoride (TBAF) as catalyst.[4] More recently, Lakshmi Kantam et al. efficiently synthesized tetrazoles by the reaction of nitriles with NaN_3 with nanocrystalline ZnO or zinc hydroxyapatite as the catalyst at 120–130 °C.[5] The development of a catalytic, environmentally friendly, and efficient synthetic method for tetrazoles still remains an active research area.

Previously, we developed Pd- and bimetallic Pd–Cu-catalyzed three-component coupling (TCC) reactions for the regiocontrolled synthesis of various 2- and 1-allyltriazoles as well as fully substituted diallyltriazoles by employing activated alkynes with electron-withdrawing groups or nonactivated terminal alkynes, allyl carbonate, and $TMSN_3$ (Scheme 1, Equations (1)–(4)).[6] We also reported a TCC reaction for the regiocontrolled synthesis of 2-allyltetrazoles with a variety of nitriles, allyl carbonate, and $TMSN_3$ [Eq. (5)].[7] Later, we developed two facile deallylation protocols of the allylated products for a preparation of N-unsubstituted tetrazoles and triazoles: direct deallylation with [$NiCl_2$(dppe)] catalyst combined with a stoichiometric amount of *t*BuMgCl, and a stepwise deallylation through consecutive reactions of a Ru-catalyzed isomerization followed by ozonolysis (Scheme 2).[8] We also explored catalytic, direct, and general synthetic protocols for these heterocycles. The synthesis of N-unsubstituted 1,2,3-triazoles was

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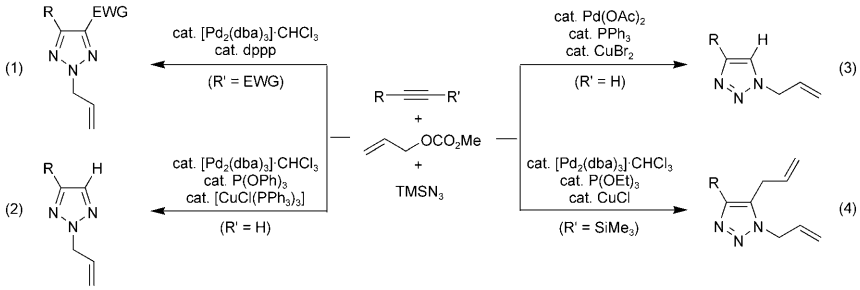
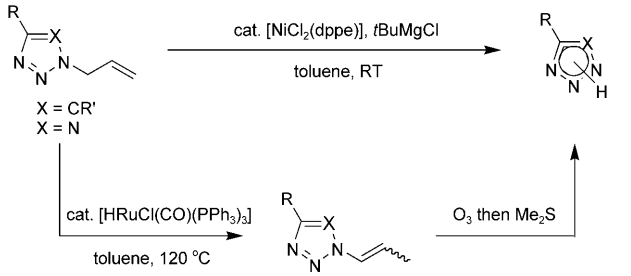
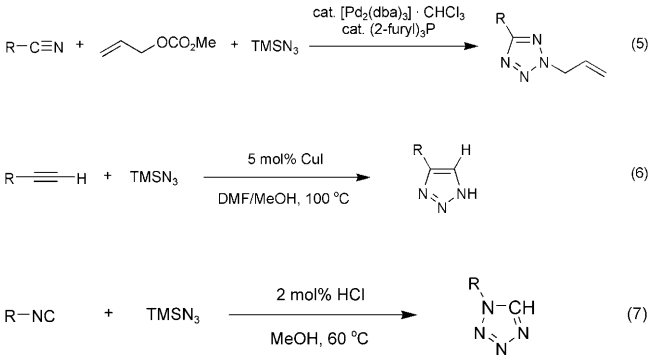


Scheme 1. Pd- and bimetallic Pd–Cu-catalyzed TCC reaction for the synthesis of various allyl tetrazoles and allyl triazoles. dba = dibenzylideneacetone, dppp = 1,3-bis(diphenylphosphanyl)propane, EWG = electron-withdrawing group.



Scheme 2. Deallylation protocols for various allyl tetrazoles and allyl triazoles. dppe = 1,2-bis(diphenylphosphanyl)ethane.

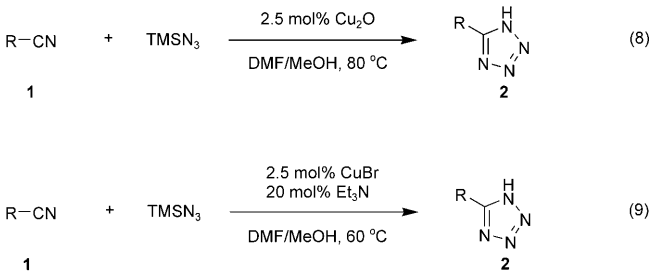
achieved by CuI-catalyzed [3+2] cycloaddition of nonactivated terminal alkynes and trimethylsilyl azide in *N*,*N*-dimethylformamide (DMF)/MeOH [Eq. (6)],[9] and the acid-catalyzed synthesis of 1-substituted tetrazoles was accomplished by the [3+2] cycloaddition of isonitriles with trimethylsilyl azide in MeOH [Eq. (7)].[10]



Abstract in Japanese:

銅触媒の存在下、DMF/MeOH 混合溶媒中ニトリル化合物とトリメチルシリルアジドの [3+2] 環化反応により5位に置換基を有するテトラゾールが高収率で得られることを見いだした。また、銅触媒と触媒量のトリエチルアミンを用いるとさらに低い温度で本反応が進行することを見いだした。本反応は二トリル基質と系内で生成した銅アジドの [3+2] 環化付加反応により進行するものと考えられる。

Encouraged by the success of the catalytic synthesis of 5-substituted 1,2,3-triazoles and 1-substituted tetrazoles, we used nitriles instead of alkynes or isocyanides as partners of the cycloaddition. The corresponding 5-substituted 1*H*-tetrazoles **2** were obtained in good to high yields through the reaction of nitriles **1** with $TMSN_3$ in the presence of Cu_2O catalyst in DMF/MeOH at 80 °C [Eq. (8)].[11] Furthermore, we found that the combined catalyst of CuBr and triethylamine also promoted the [3+2] cycloaddition reaction of nitriles and trimethylsilyl azide at relatively low reaction temperatures [Eq. (9)]. Herein, we report a detailed investigation of these catalytic synthetic methods.



Results and Discussion

Copper Oxide Catalyzed Synthesis of 5-Substituted 1*H*-Tetrazoles from Nitriles and Trimethylsilyl Azide

In the cycloaddition reaction between *p*-methoxybenzonitrile (**1a**) and $TMSN_3$, we investigated the effect of solvents and metal catalysts on the formation of tetrazole **2a** (Table 1). Among the solvents tested (with 2.5 mol% Cu_2O), DMSO and DMF gave low yields of **2a**, but the yield was dramatically improved by using a 9:1 mixture of DMF and MeOH (Table 1, entries 1–3).[9,10,12] Other protic solvents such as *i*PrOH and H_2O were also effective (Table 1, entries 4 and 5) although the yield was dramatically decreased by using a mixture of HCl and DMF (Table 1, entry 6). We next investigated the effect of metal catalysts. Among the copper catalysts tested, Cu_2O gave the best result at 80 °C (Table 1, entry 3); CuBr exhibited high catalytic activity, although a higher reaction temperature was needed (Table 1, entry 7). Other copper catalysts such as CuCl, CuI, $CuCl_2$, $CuBr_2$, CuO, and CuOAc gave lower yields of **2a** (Table 1, entries 8–13). The reaction without copper catalyst gave a low yield (Table 1, entry 14). Other metal catalysts such as AuCl and $ZnBr_2$ were less effective (Table 1, entries 15 and 16).

The results of the [3+2] cycloaddition reaction of various nitriles **1** with $TMSN_3$ are summarized in Table 2. The reac-

Table 1. Effect of catalyst and solvent on the formation of tetrazole **2a** from **1a**.[a]

Entry	Catalyst	Solvent (ratio)	Yield [%][b]
1	Cu_2O[c]	DMSO	30
2	Cu_2O[c]	DMF	46
3	Cu_2O[c]	MeOH/DMF (1:9)	95 (84)[d]
4	Cu_2O[c]	*i*PrOH/DMF (1:9)	77
5	Cu_2O[c]	H_2O/DMF (1:9)	86
6	Cu_2O[c]	HCl/DMF (1:9)	32
7	CuBr	MeOH/DMF (1:9)	(85)
8	CuCl	MeOH/DMF (1:9)	(67)
9	CuI	MeOH/DMF (1:9)	69
10	$CuCl_2$	MeOH/DMF (1:9)	64
11	$CuBr_2$	MeOH/DMF (1:9)	72
12	CuO	MeOH/DMF (1:9)	78
13	CuOAc	MeOH/DMF (1:9)	62
14	none	MeOH/DMF (1:9)	34
15	AuCl	MeOH/DMF (1:9)	(16)
16	$ZnBr_2$	MeOH/DMF (1:9)	32

[a] The reaction of **1a** with $TMSN_3$ (1.5 equiv) was carried out in the presence of 5 mol% catalyst at 100 °C for 24 h. [b] Yield determined by ^1H NMR spectroscopy with dibromomethane as an internal standard. Yield of isolated product is shown in parentheses. [c] 2.5 mol% catalyst was used. [d] 2.5 mol% Cu_2O was used at 80 °C for 12 h. DMSO = dimethyl sulfoxide.

Table 2. Copper-catalyzed synthesis of 5-substituted 1*H*-tetrazoles **2**.[a]

Entry	R	**1**	*t* [h]	**2**	Yield [%][b]
1	*p*-MeO-C_6H_4	**1a**	12	**2a**	84
2	*p*-Me-C_6H_3	**1b**	12	**2b**	79
3	*p*-NO_2-C_6H_4	**1c**	12	**2c**	96
4	3,5-$(NO_2)_2$-C_6H_4	**1d**	12	**2d**	91
5	*p*-HO-C_6H_4	**1e**	12	**2e**	87
6	2-naphthyl	**1f**	12	**2f**	92
7	2-(*p*-tolyl)-C_6H_4	**1g**	24	**2g**	50[c]
8	benzyl	**1h**	24	**2h**	66
9	*n*-butyl	**1i**	24	**2i**	55
10	*tert*-butyl	**1j**	24	**2j**	36

[a] The reaction of **1** with $TMSN_3$ (1.5 equiv) was carried out in the presence of 2.5 mol% Cu_2O at 80 °C. [b] Yield of isolated product. [c] The reaction was carried out in the presence of 10 mol% Cu_2O at 120 °C.

tions of the aryl nitriles **1a** and **1b**, which bear an electron-donating group at the *para* position of the aromatic ring, with trimethylsilyl azide were carried out in a mixture of MeOH and DMF (1:9) at 80 °C in the presence of 2.5 mol% Cu_2O. The reactions were complete in 12 h to afford the corresponding tetrazoles **2a** and **2b** in 84 and 79% yield, respectively (Table 1, entries 1 and 2). The nitriles **1c** and **1d**, which have an electron-withdrawing NO_2 group at the *para* or *meta* position, produced the corresponding tetrazoles **2c** and **2d** in excellent yield (Table 1, entries 3 and 4). Nitrile **1e**, which contains an unprotected hydroxy group at the *para* position, also gave the product tetrazole **2e** in high yield (Table 1, entry 5). Another aryl nitrile, 2-cyanonaphthalene (**1f**), also reacted without any problems to give the corresponding tetrazole **2f** in a high 92% yield (Table 1, entry 6). The reaction of sterically hindered *ortho*-substituted aryl nitrile **1g** afforded the desired tetrazole **2g** in 50% yield, although a prolonged reaction time, higher temperature, and a larger amount of catalyst were required (Table 1, entry 7). It is now clear that the tetrazole-forming reaction tolerates a wide range of functional groups, and the [3+2] cycloaddition proceeds well irrespective of the position and electronic nature of the substituents on the aromatic ring. Next, we investigated the reactivity of the alkyl nitriles **1h–j**. The reaction of benzylnitrile (**1h**), valeronitrile (**1i**), and sterically bulky pivalonitrile (**1j**) furnished the desired tetrazoles **2h–j** in good to moderate yields, although longer reaction times were needed (Table 1, entries 8–10).

The structures **2a–j** were assigned by ^1H and ^{13}C NMR spectroscopy as well as mass spectrometry. Besides these spectral structural determinations, the structure of **2a** was unambiguously confirmed by X-ray crystal-structure analysis (Figure 1).[13] The crystal-structure analysis indicates that **2a** has two conformations, $\mathbf{2a_1}$ and $\mathbf{2a_2}$, in the crystal state with a 1:1 ratio, which are derived from the different orientations of the methoxy group with respect to the hydrogen atom on N1 or N4.

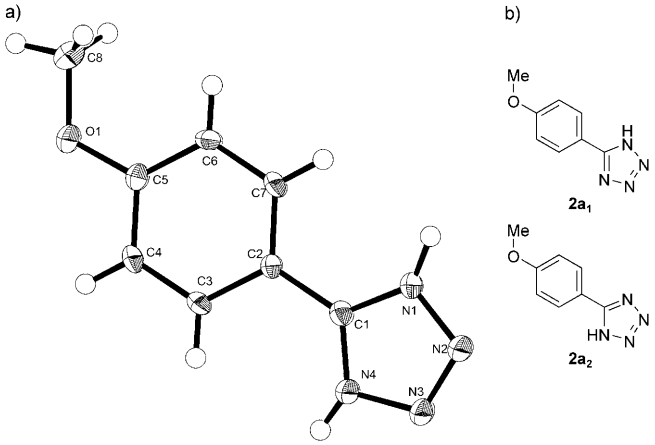
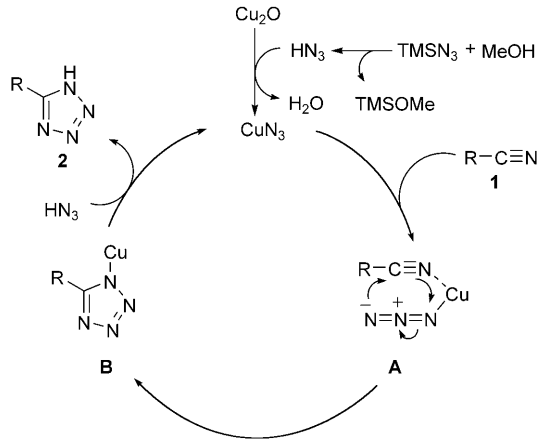


Figure 1. ORTEP drawing and structures of **2a**.

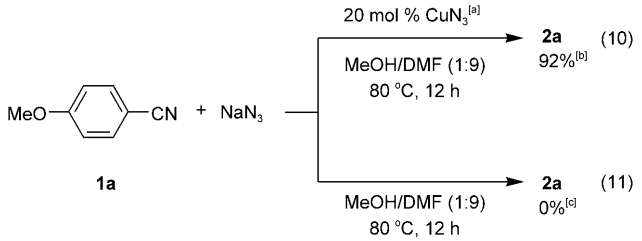
A plausible mechanism for the [3+2] cycloaddition is shown in Scheme 3. Initially, Cu_2O reacts with HN_3 to pro-



Scheme 3. Plausible mechanism for the copper-catalyzed formation of 5-substituted 1*H*-tetrazoles **2**.

duce the CuN_3 catalytic species; HN_3 is formed in situ by the reaction of $TMSN_3$ with MeOH.[14] The [3+2] cycloaddition between the C–N bond of nitrile **1** and CuN_3 takes place readily to form the intermediate **B**; precoordination of the nitrogen atom of the CN group of **1** with copper azide to form complex **A** would accelerate this cyclization step.[15] Protonolysis of the intermediate **B** by HN_3 affords the 5-substituted 1*H*-tetrazole **2** and the copper azide catalyst.

To obtain support for the proposed mechanism, the following experiments were carried out. The reaction of **1a** (1 equiv) with NaN_3 (1.5 equiv) in the presence of 20 mol% of CuN_3, which was generated in situ from NaN_3 (0.2 equiv) and CuI (0.2 equiv),[16] in MeOH/DMF (1:9) gave the corresponding tetrazole **2a** in 92% yield, based on CuI (Scheme 4, [Eq. (10)]), as determined by NMR spectroscopy.[17] On the other hand, the reaction of **1a** with NaN_3 in MeOH/DMF (1:9) did not proceed at all in the absence of the in situ CuN_3 catalyst, and the starting material **1a** was recovered in 89% yield (Scheme 4, [Eq. (11)]). These results clearly indicate that 1) CuN_3 is a key catalytic species that enables the [3+2] cycloaddition with **1a** to produce **B**, 2) **B** undergoes protonolysis with MeOH to give **2a**, and 3) the [3+2] cycloaddition of **1a** with NaN_3 does not take place.



Scheme 4. Formation of **2a** by the reaction of **1a** with NaN_3.[a] CuN_3 was prepared by mixing NaN_3 with CuI in DMF at room temperature for 30 min. [b] Yield based on CuI determined by ^{1}H NMR spectroscopy with dibromomethane as an internal standard. [c] **1a** was recovered in 89% yield.

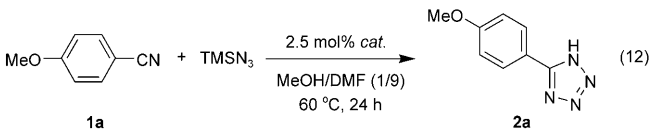
Copper Bromide and Triethylamine-Catalyzed Synthesis of 5-Substituted 1*H*-Tetrazoles from Nitriles and Trimethylsilyl Azide

When a lower reaction temperature such as 60 °C was used in the Cu_2O-catalyzed reaction of **1a** with $TMSN_3$ in MeOH/DMF, **2a** was obtained in only 9% yield [Eq. (12)] (Table 3, entry 1 vs. Table 1, entry 3). It was reported that $Et_3N{\cdot}HN_3$ can be formed by mixing Et_3N with $TMSN_3$ and MeOH.[18] Koguro et al. also reported a facile method for tetrazole synthesis with nitriles and NaN_3 in the presence of a stoichiometric amount of $Et_3N{\cdot}HCl$.[2d] They proposed that the reaction would proceed through cycloaddition between nitriles with $Et_3N{\cdot}HN_3$, which is generated in situ by the reaction of NaN_3 and $Et_3N{\cdot}HCl$. Inspired by their report,[2d] we examined the reaction of **1a** and $TMSN_3$ in the presence of 2.5 mol% of Cu_2O and 20 mol% of Et_3N. As expected, **2a** was obtained in 59% yield at 60 °C (Table 3, entry 2). The reaction without the combined catalyst did not afford any products (Table 3, entry 3). The reaction of **1a** with $TMSN_3$ in the presence of Et_3N alone gave a low yield of **2a** (Table 3, entry 4). This result indicates that Et_3N alone cannot act as a catalyst for the tetrazole-forming reaction. Further investigation of other copper catalysts revealed that the yield of **2a** was dramatically increased in the presence of 2.5 mol% of CuBr (instead of Cu_2O) and 20 mol% of Et_3N (Table 3, entry 5), and that $[CuCl(PPh_3)_3]$ also exhibited high catalytic activity (Table 3, entry 6).

Table 3. Effect of triethylamine on the formation of tetrazole **2a** from **1a**.[a]

Entry	Catalyst	Additive	Yield [%][b]
1	Cu_2O	none	9
2	Cu_2O	Et_3N	59
3	none	none	0
4	none	Et_3N	27
5	CuBr	Et_3N	96 (83)
6	$[CuCl(PPh_3)_3]$	Et_3N	89

[a] The reaction of **1a** with $TMSN_3$ (1.5 equiv) was carried out in the presence of 2.5 mol% copper catalyst and 20 mol% Et_3N at 60 °C for 24 h. [b] Yield determined by ^{1}H NMR spectroscopy with dibromomethane as an internal standard. Yield of isolated product is shown in parentheses.



With the optimized combined-catalyst conditions in hand, we investigated the cycloaddition reaction with the selected nitriles **1g–i** (Table 4). The reaction of sterically hindered *ortho*-substituted aryl nitrile **1g** with $TMSN_3$ was carried out in the presence of 2.5 mol% CuBr and 40 mol% Et_3N in MeOH/DMF (1:9) to afford the corresponding tetrazole **2g** in 44% yield, although higher temperature and prolonged reaction time were needed (Table 4, entry 2). The alkyl nitriles **1h** and **1i** furnished the desired tetrazoles **2h** and **2i** in 75 and 41% yield, respectively, with 2.5 mol% of CuBr and 20 mol% of Et_3N at 60 °C (Table 4, entries 3 and 4).

Table 4. Synthesis of 5-substituted 1*H*-tetrazoles **2** catalyzed by CuBr and Et_3N.[a]

Entry	R	1	*t* [h]	2	Yield [%][b]
1	*p*-MeO-C_6H_4	**1a**	24	**2a**	83
2	2-(*p*-tolyl)-C_6H_4	**1g**	36	**2g**	44[c]
3	benzyl	**1h**	24	**2h**	75
4	*n*-butyl	**1i**	24	**2i**	41

[a] The reaction of **1** with $TMSN_3$ (1.5 equiv) was carried out in the presence of 2.5 mol% CuBr catalyst and 20 mol% Et_3N at 60 °C for 24 h. [b] Yield of isolated product. [c] The reaction of **1g** and $TMSN_3$ (2 equiv) was carried out in the presence of 2.5 mol% CuBr and 40 mol% Et_3N at 100 °C.

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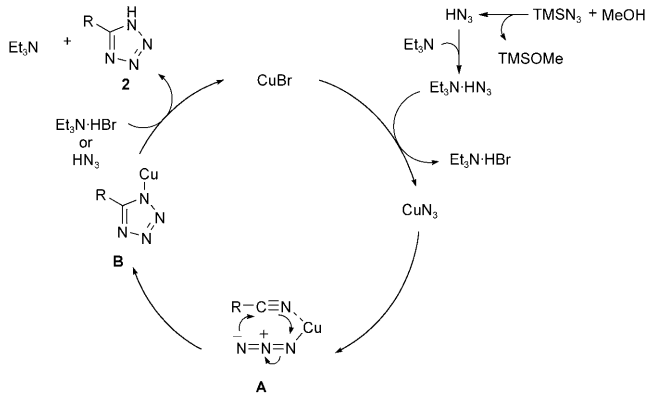
A proposed mechanism for the formation of tetrazole **2** with the copper and Et_3N combined catalyst is shown in Scheme 5. Initially, $Et_3N{\cdot}HN_3$ salt is formed in situ by the reaction of Et_3N, $TMSN_3$, and MeOH. Subsequently, CuBr catalyst reacts with $Et_3N{\cdot}HN_3$ to produce the CuN_3 catalytic species and $Et_3N{\cdot}HBr$. The [3+2] cycloaddition between CuN_3 and nitrile **1** affords the Cu–tetrazole complex **B** via formation of the complex **A**. Protonolysis of the intermediate **B** by $Et_3N{\cdot}HBr$ or HN_3 produces the desired product **2** along with the regenerated CuBr or CuN_3 and Et_3N catalyst.



Scheme 5. Plausible mechanism for the formation of **2** catalyzed by copper and triethylamine.

The above results further support the intervention of CuN_3 species in the catalytic cycle and indicate that 1) the ease of exchange between CuBr catalyst and the $Et_3N{\cdot}HN_3$ formed in situ to produce the CuN_3 species, and 2) the ease of protonolysis of the Cu–tetrazole complex **B** by $Et_3N{\cdot}HBr$ to regenerate the copper catalyst, are two important factors for accelerating the catalytic cycloaddition reaction.

Conclusions

We are now in a position to synthesize the 5-substituted tetrazole **2** with a wide range of substituents in good to high yields through the efficient and convenient copper-catalyzed [3+2] cycloaddition reaction between nitriles **1** and trimethylsilyl azide. Furthermore, we have demonstrated that a copper and triethylamine combined catalyst also promotes the cycloaddition reaction at relatively low reaction temperatures. The reactions most likely proceed through the formation in situ of a copper azide catalytic species, followed by a successive [3+2] cycloaddition with the nitrile.

Experimental Section

General

^1H and ^{13}C NMR spectra were recorded on a JEOL JNM AL 400-MHz spectrometer. ^1H NMR spectra are reported as follows: chemical shifts (δ) in ppm downfield from tetramethylsilane as an internal standard, multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz), integration. ^{13}C NMR chemical shifts (δ) are reported in ppm relative to the central line of the triplet for [D$_6$]DMSO at 3.50 ppm. IR spectra were recorded on a SHIMADZU FTIR-8200A spectrometer; absorptions are reported in cm^{-1}. High-resolution mass spectra were obtained on a HITACHI M-2500S spectrometer. X-ray crystallographic data were obtained on a Rigaku/MSC Saturn diffractometer with a Cu CCD device. Column chromatography was carried out with silica gel 60 N (spherical, neutral, 40–100 μm, KANTO Chemical Co.). Analytical thin-layer chromatography (TLC) was performed on 0.2-mm precoated plates with Kieselgel 60 F_{254} (Merck). Anhydrous DMF (WAKO), methanol (WAKO), triethylamine (WAKO), trimethylsilyl azide (TCI), Cu_2O (Aldrich), and CuBr (Aldrich) were purchased and used as received. All other compounds are commercially available. Elemental analysis was performed on a CHN CORDER MT-6.

Syntheses

Representative procedure for the Cu_2O-catalyzed synthesis of **2**: Trimethylsilyl azide (0.1 mL, 0.75 mmol) was added to a solution of Cu_2O (1.8 mg, 0.0125 mmol) and *p*-methoxybenzonitrile (**1a**; 66.6 mg, 0.5 mmol) in DMF and MeOH (9:1, 1 mL, 0.5 M) in a pressure vial. The reaction mixture was stirred at room temperature for 10 min and then heated at 80 °C for 12 h. After consumption of **1a**, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed with HCl (1 N), dried with anhydrous Na_2SO_4, and concentrated. NaOH (0.25 N) was added to the residue, and the resulting mixture was stirred for 30 min at room temperature. The mixture was washed with ethyl acetate, and then concentrated HCl was added until the pH of the aqueous layer became 1. The aqueous layer was extracted with ethyl acetate (×3), and the combined organic layers were washed with HCl (1 N). The organic layer was dried over anhydrous Na_2SO_4 and concentrated. Tetrazole **2a** was obtained as a white solid in 84 % yield (73.7 mg).

Representative procedure for the CuBr-and-triethylamine-catalyzed synthesis of **2**: Trimethylsilyl azide (0.1 mL, 0.75 mmol) was added to a solution of CuBr (1.8 mg, 0.0125 mmol), Et_3N (14 μL, 0.1 mmol), and **1a** (66.6 mg, 0.5 mmol) in DMF and MeOH (9:1, 1 mL, 0.5 M) in a pressure vial. The reaction mixture was stirred at room temperature for 10 min and then heated at 60 °C for 24 h. A workup procedure similar to that for the Cu_2O-catalyzed reaction was used, and tetrazole **2a** was obtained in 83 % yield (73 mg).

Experimental Data

2a: 5-(4-Methoxyphenyl)-1*H*-tetrazole: White solid; m.p.: 231–233 °C; IR (KBr): $\tilde{\nu}$ = 3200–2300 (br), 1298, 1184, 1035, 750 cm^{-1}; ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 3.83 (s, 3H), 7.14 (d, J = 9.0 Hz, 2H), 7.96 ppm (d, J = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 55.4, 114.7, 116.2, 128.5, 154.6, 161.3 ppm; HRMS (ESI): *m*/*z* calcd for $C_8H_7N_4O$: 175.0625 [M−H]$^-$; found: 175.0622; elemental analysis: calcd (%) for $C_8H_8N_4O$: C 54.53, H 4.58, N 31.81; found: C 54.60, H 4.83, N 32.06.

2b: 5-(4-Methylphenyl)-1*H*-tetrazole: White solid; m.p.: 248–249 °C; IR (KBr): $\tilde{\nu}$ = 3100–2200 (br), 1614, 1569, 1504, 1163, 1055, 1028, 823, 744 cm^{-1}; ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 2.47 (s, 3H), 7.49 (d, J = 8.0 Hz, 2H), 8.00 ppm (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 21.0, 121.2, 126.8, 129.8, 141.0, 155.0 ppm; HRMS (ESI): *m*/*z* calcd for $C_8H_7N_4$: 159.0676 [M−H]$^-$; found: 159.0675; elemental analysis: calcd (%) for $C_8H_8N_4$: C 59.98, H 5.03, N 34.99; found: C 59.86, H 5.21, N 35.12.

2c: 5-(4-Nitrophenyl)-1*H*-tetrazole: White solid; m.p.: 219–220 °C; IR (KBr): $\tilde{\nu}$ = 3500–2400 (br), 1604, 1531, 1488, 1338, 1311, 993, 867, 854 cm^{-1}; ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 8.29 (d, J = 9.0 Hz, 2H), 8.44 ppm (d, J = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 124.6, 128.3, 130.7, 148.8, 155.6 ppm; HRMS (ESI): *m*/*z* calcd for $C_7H_4N_5O_2$: 190.0370 [M−H]$^-$; found: 190.0371; elemental analysis: calcd (%) for $C_7H_5N_5O_2$: C 43.98, H 2.64, N 36.64; found: C 44.08, H 2.79, N 36.91.

2d: 5-(3,5-Dinitrophenyl)-1*H*-tetrazole: Yellow solid; m.p.: 178–179 °C; IR (KBr): $\tilde{\nu}$ = 3200–2400 (br), 3097, 1535, 1342, 1082, 921, 754, 729 cm^{-1};

^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=8.95 (dd, J=2.0, 2.0 Hz, 1H), 9.14 ppm (d, J=2.0 Hz, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 120.0, 126.6, 127.9, 148.6, 154.7 ppm; HRMS (ESI): m/z calcd for $C_7H_3N_6O_4$: 235.0221 [M−H]$^-$; found: 235.0221; elemental analysis: calcd (%) for $C_7H_4N_6O_4$: C 35.60, H 1.71, N 35.59; found: C 35.66, H 1.98, N 35.69.

2e: 5-(4-Hydroxyphenyl)-1*H*-tetrazole: White solid; m.p.: 234–235 °C; IR (KBr): $\tilde{\nu}$=3600–3200 (br), 1616, 1515, 1471, 1282, 1247, 1080, 995, 842 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=6.49 (d, J=8.5 Hz, 2H), 7.84 (d, J=8.5 Hz, 2H), 10.15 ppm (br s, 1H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 114.6, 116.2, 128.7, 154.8, 160.0 ppm; HRMS (ESI): m/z calcd for $C_7H_5N_4O$: 161.0469 [M−H]$^-$; found: 161.0468.

2f: 5-(2-Naphthyl)-1*H*-tetrazole: White solid; m.p.: 205–206 °C; IR (KBr): $\tilde{\nu}$=3200–2200 (br), 3060, 1566, 1417, 1249, 1085, 1020, 825, 759 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=7.59–7.68 (m, 2H), 7.98–8.18 (m, 4H), 8.65 ppm (s, 1H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 121.5, 123.5, 126.9, 127.1, 127.7, 127.7, 128.5, 129.1, 132.5, 133.8, 171.8 ppm; HRMS (ESI): m/z calcd for $C_{11}H_7N_4$: 195.0676 [M−H]$^-$; found: 195.0676; elemental analysis: calcd (%) for $C_{11}H_8N_4$: C 67.33, H 4.11, N 28.56; found: C 67.03, H 4.36, N 28.71.

2g: 5-(2-(4′-methyl)biphenyl)-1*H*-tetrazole: White solid; m.p.: 149–151 °C; IR (KBr): $\tilde{\nu}$=3200–2300 (br), 1600, 1568, 1483, 1446, 1398, 1245, 1159, 825, 756 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=2.28 (s, 3H), 6.95 (d, J=8.0 Hz, 2H), 7.10 (d, J=8.0 Hz, 2H), 7.48–7.58 (m, 2H), 7.59–7.70 ppm (m, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 20.7, 123.1, 127.4, 128.5, 128.8, 130.4, 130.5, 131.0, 136.2, 136.6, 141.3, 154.2 ppm; HRMS (ESI): m/z calcd for $C_{14}H_{11}N_4$: 235.0989 [M−H]$^-$; found: 235.0989.

2h: 5-Benzyl-1*H*-tetrazole: White solid; m.p.: 123–124 °C; IR (KBr): $\tilde{\nu}$= 3300–2200 (br), 1533, 1494, 1458, 1251, 1074, 734, 711 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=4.27 (s, 2H), 7.21–7.36 ppm (m, 5H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 28.9, 126.9, 128.5, 128.6, 135.8, 155.1 ppm; HRMS (ESI): m/z calcd for $C_8H_7N_4$: [M−H]$^-$ 159.0676; found: 159.0675; elemental analysis: calcd (%) for $C_8H_8N_4$: C 59.98, H 5.03, N 34.99; found: C 60.00, H 5.13, N 35.09.

2i: 5-*n*-Butyl-1*H*-tetrazole: White solid; m.p.: 40–42 °C; IR (KBr): $\tilde{\nu}$= 3100–2300 (br), 2960, 2877, 1583, 1550, 1467, 1261, 1109, 1045 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=0.88 (t, J=7.5 Hz, 3H), 1.30 (sext, J=7.5 Hz, 2H), 1.66 (q, J=7.5 Hz, 2H), 2.85 ppm (t, J=7.5 Hz, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 13.5, 21.5, 22.4, 29.1, 155.6 ppm; elemental analysis: calcd (%) for $C_5H_{10}N_4$: C 47.59, H 7.99, N 44.42; found: C 47.60, H 7.95, N 44.48.

2j: 5-*tert*-Butyl-1*H*-tetrazole: Colorless oil; IR (KBr): $\tilde{\nu}$=3300–2300 (br), 2981, 2869, 1560, 1467, 1398, 1377, 1265, 1218, 1045 cm^{-1}; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ=1.36 ppm (s, 9H); ^{13}C NMR (100 MHz, [D$_6$]DMSO): 28.9, 30.3, 163.2 ppm; HRMS (ESI): m/z calcd for $C_{10}H_{19}N_8$: 251.1738 [2M−H]$^-$; found: 251.1739; elemental analysis: calcd (%) for $C_5H_{10}N_4$: C 47.59, H 7.99, N 44.42; found: C 47.71, H 7.92, N 44.43.

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[13] CCDC-684836 (**2a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

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