Efficient One-Pot Synthesis of 1-Aryl 1,2,3-Triazoles from Aryl Halides and Terminal Alkynes in the Presence of Sodium Azide

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Abstract: An efficient one-pot synthesis of 1-aryl 1,2,3-triazoles from aryl bromides/iodides and terminal alkynes in the presence of sodium azide is described. In the case of aryl iodides, the reactions proceeded at room temperature. The reactions normally gave high yields.

Key words: 1,2,3-triazoles, one-pot, copper, 1,3-dipolar cycloaddition, catalyst

1,2,3-Triazoles have found widespread use in pharmaceuticals and agrochemicals.[1] The discovery[2] of Cu(I)-catalyzed 1,3-dipolar cycloaddition of azides and terminal alkynes has further triggered the use of 1,2,3-triazoles in bioconjungation, drug discovery,[3] materials science[4] and combinatorial chemistry.[5]

In one of our ongoing medicinal chemistry projects, we need a convenient and efficient method for the preparation of 1-aryl 1,2,3-triazoles. Recently, for concerns about the safety of working with low molecular weight organic azides and convenience, several groups have developed one-pot procedures to prepare 1,2,3-triazoles from in situ generated organic azides and terminal alkynes.[6] One such method,[6c] developed by Fokin et al, for the preparation of 1-aryl 1,2,3-triazoles from the aryl iodides, sodium azide, and terminal alkynes, attracted our attention. In this method, the Cu(I)-catalyzed azidonation of aryl halides[7] and the 1,3-dipolar cycloaddition between aryl azides and alkynes were elegantly combined into a one-pot procedure, which tolerates a wide variety of functional groups. The method, however, suffers even at 65 °C from long reaction times, supposedly due to the slow azidonation of aryl iodide. Moreover, it is limited to the use of the aryl iodides. This is unfortunate because many more aryl bromides are commercially available. We have published an efficient method for the preparation of aryl azides from the corresponding aryl halides.[8] We felt that our method could further be developed into an efficient one-pot procedure to prepare 1-aryl 1,2,3-triazoles from aryl halides via in situ formation of aryl azides. Herein, we report this one-pot synthesis of 1-aryl 1,2,3-triazoles.

To begin with, we examined whether our catalyst system for azidonation of aryl halides has a catalytic effect on the 1,3-dipolar addition between aryl azides and terminal alkynes. The reaction between 4-azido-2-methylaniline and ethynylbenzene was chosen as a prototype reaction (Figure 1). The reactions were performed with 4-azido-2-methylaniline (1 equiv), ethynylbenzene (1 equiv), CuI (0.1 equiv), sodium ascorbate, and ligand **A** (*trans*-*N*,*N*′-dimethyl-1,2-cyclohexanediamine) at room temperature under an argon atmosphere. The conversions were determined by ^{1}H NMR after quenching the reactions at various times.

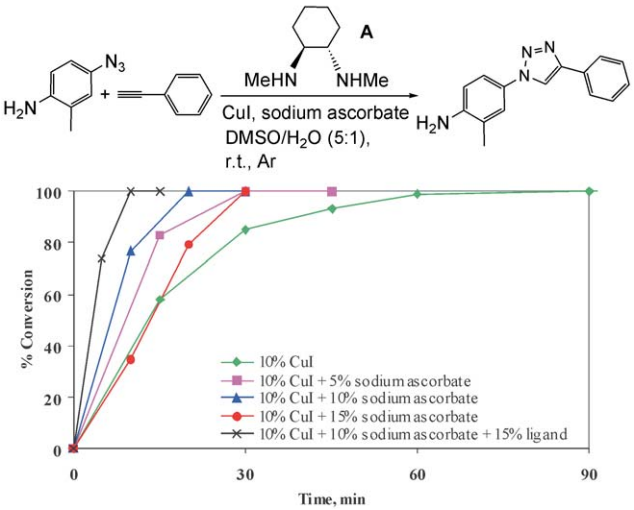

Figure 1 The effect of sodium ascorbate and ligand **A** on the Cu(I)-catalyzed 1,3-dipolar cycloaddition

No conversion was observed within 90 minutes in the absence of CuI, suggesting that Cu(I) is essential for this transformation. As shown in Figure 1, an increase in the amount of sodium ascorbate from 10 mol% to 15 mol% caused a slight decrease in the reaction rate. The same phenomenon was previously observed by using tris(carboxyethyl)phosphine (TCEP) as a reducing agent.[9] The reactions both in the presence and in the absence of ligand **A** had more or less the same reaction rate. These results suggest that ligand **A** does not have a negative effect on the reaction. This is important information, because ligand **A** plays a crucial role in the azidonation of aryl halides.[8] Note that the reaction conditions for the 1,3-dipolar cycloaddition are clearly different from the previous ones that require acetonitrile as co-solvent and at least one equivalent of a nitrogen base, such as 2,6-lutidine,

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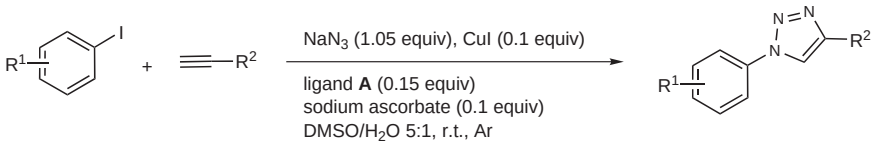
triethylamine, diisopropylethylamine, DBU or pyridine, when CuI is used as catalyst.[2a,10] The reason might be that complexation with acetonitrile and a base prevents oxidation of Cu(I) to Cu(II).[11] Sodium ascorbate has the same stabilizing effect as we observed in the azidonation of aryl halides.

Since our previous[8] and present results clearly proved that the catalytic system is effective for both the azidonation and the 1,3-dipolar cycloaddition, a two-step one-pot preparation of 1-aryl 1,2,3-triazoles from the corresponding aryl halides seemed to be possible. The following one-pot experiments were carried out with an aryl iodide (1 equiv), a terminal alkyne (1 equiv), NaN_3 (1 equiv), CuI (0.1 equiv), sodium ascorbate (0.1 equiv), and ligand **A** (0.15 equiv) in DMSO–H_2O (5:1) at room temperature. The products were normally obtained by simple filtration. As can be seen in Table 1, a variety of functional groups on aryl iodides, as well as on terminal alkynes were tolerated in this one-pot reaction. But, entry 3 is a noticeable exception. In this reaction, not only the desired product (38%), but also a by-product, 4-unsubstituted compound, was obtained. This indicates that the trimethylsilyl group is quite unstable under reaction conditions. Surprisingly, in contrast to the azidonation, which was sluggish, the reaction proceeded smoothly with 4-iodobenzonitrile (Table 1, entry 10). The strong electron-withdrawing nitro group on the aryl iodide was well tolerated (Table 1, entry 15). Reaction with aryl iodide bearing an amino group in *ortho* position was sluggish, indicating that the reaction is sensitive to sterically hindered aryl halides (Table 1, entry 11). This steric effect was further confirmed by a comparison between azidonation of 2-iodotoluene and 4-iodotoluene (Scheme 1). When the 4-iodotoluene was subjected to the azidonation, the reaction went to completion in 15 minutes, giving 91% yield. In comparison, the azidonation of 2-iodotoluene gave only 63% yield after 150 minutes.[12] Aryl alkynes bearing both electron-withdrawing groups, such as trifluoromethyl and nitrile (Table 1, entry 8 and 10), and electron-donating groups, such as ether, hydroxy and aniline (Table 1, entry 5, 11 and 15) underwent the 1,3-dipolar cycloaddition.

Table 1 1-Aryl 1,2,3-Triazoles from Aryl Iodides via in situ Generated Aryl Azides



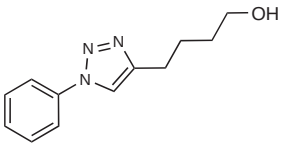
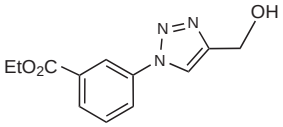
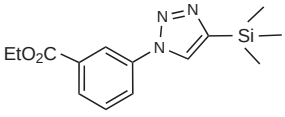
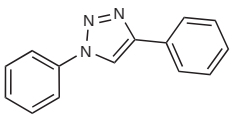
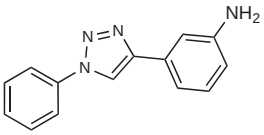
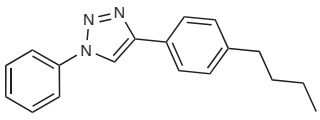
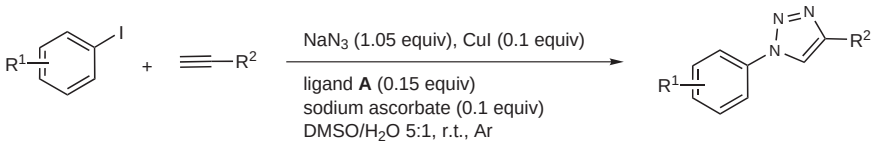
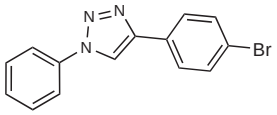
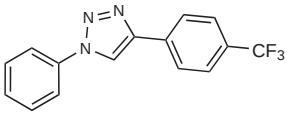
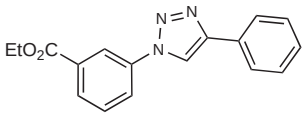
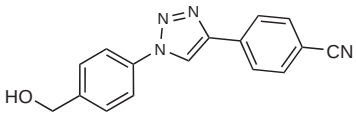
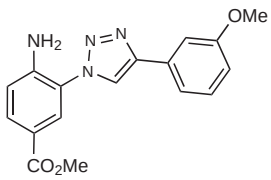
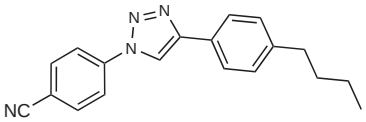
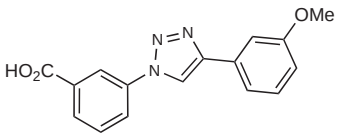
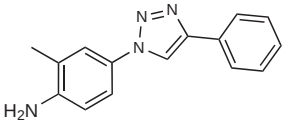
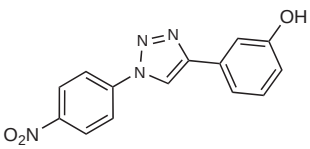
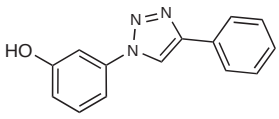
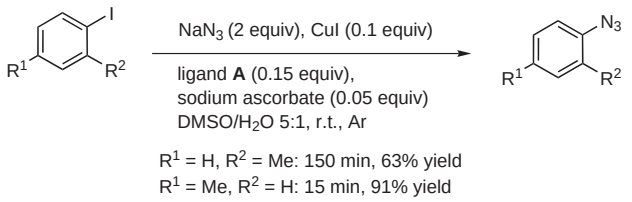
Entry	Product	Time (min)	Yield (%)[a]
1		90	99
2		90	83
3[b]		overnight	38
4		90	76
5		90	94
6		90	84

Table 1 1-Aryl 1,2,3-Triazoles from Aryl Iodides via in situ Generated Aryl Azides (continued)



Entry	Product	Time (min)	Yield (%)[a]
7		90	77
8		90	86
9		90	88
10		90	88
11		overnight	43
12		60	89
13[c,d]		90	54
14		90	68
15		60	97
16		60	97

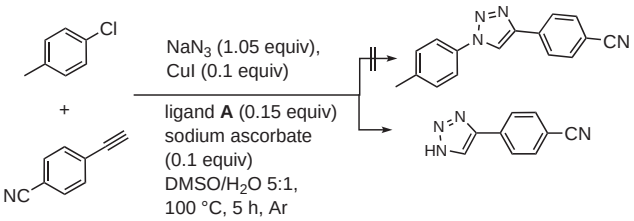
[a] Isolated yield.
[b] The procedure is a slight different from the general one-pot procedure for Table 1, because of the volatile ethynyltrimethylsilane (see experimental section).
[c] NaOH (1 equiv) was used.
[d] Some product might be lost during work-up.



Scheme 1 Azidonation of iodotoluenes

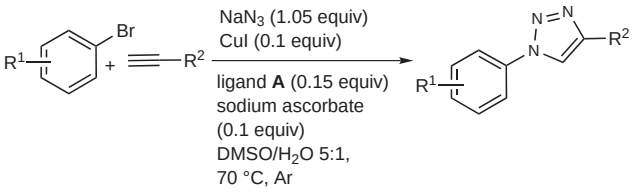
The one-pot reaction was also extended to the use of aryl bromides (Table 2). However, at room temperature, the reaction turned out to be very slow and needed several days to be complete. Gratifyingly, as the temperature was raised to 70 °C, the reactions went to completion within two hours except for the reaction for entry 1, which required 12 hours. Again, a variety of functional groups were compatible with the reaction. The reactions generally gave good to excellent yields.

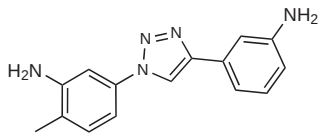
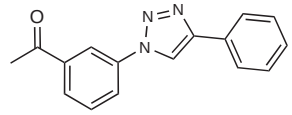
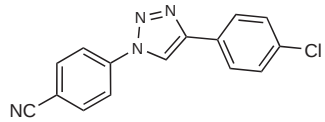
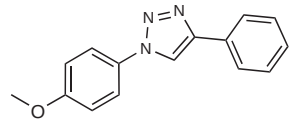
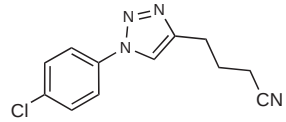
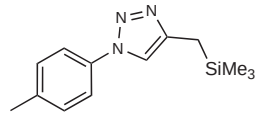
We wondered whether this one-pot procedure could be used for aryl chlorides. As we tried this reaction, we observed that sodium azide and ethynyl benzonitrile underwent [3+2] cycloaddition and an N-unsubstituted 1,2,3-triazole instead of a 1-aryl 1,2,3-triazole, was produced,[13] suggesting that the reactivity of aryl chlorides were insufficient for this type of reaction under the present reaction conditions (Scheme 2).



Scheme 2

Table 2 1-Aryl 1,2,3-Triazoles Prepared from Aryl Bromides via in situ Generated Aryl Azides



Entry	Product	Time (min)	Yield (%)[a]
1		overnight	98
2		120	89
3		120	89
4		120	74
5		120	83
6[b]		60	77

[a] Isolated yield.

[b] The procedure is slightly different from the general one-pot procedure for Table 2, because of the volatile trimethyl(propargyl)silane (see experimental section).

In summary, we have developed a mild and efficient one-pot procedure for the preparation of 1-aryl 1,2,3-triazoles from the corresponding aryl halides and terminal alkynes in the presence of sodium azide. This method has some advantages – fast reaction and low temperature – over the known method.[6c] Moreover, aryl bromides can be also used in this procedure. We found that 10 mol% of sodium ascorbate can efficiently stabilize the Cu(I) source. Our method opens a way to conveniently prepare a large array of 1-aryl 1,2,3-triazoles under mild conditions.

General One-Pot Procedure for Table 1

Aryl iodide (2 mmol), NaN_3 (2.1 mmol), alkyne (2 mmol), sodium ascorbate (0.2 mmol), CuI (0.2 mmol), ligand **A** (0.3 mmol), and DMSO–H_2O (5:1, 6 mL) were introduced into a two-necked round-bottom flask equipped with a stirring bar. After it was degassed, and then introduced under an argon atmosphere, the reaction mixture was stirred at r.t. and the progress of the reaction was followed by TLC. A precipitate was usually formed during the reaction. When the starting material was completely consumed, or when the progress of the reaction had stopped, H_2O was poured into the crude mixture, and the obtained mixture was cooled down on an ice bath. The precipitate was isolated by filtration, washed with H_2O, and dried in vacuo, giving the desired product. In some cases, chromatography was necessary (vide infra).

General One-Pot Procedure for Table 2

Aryl bromide (2 mmol), NaN_3 (2.1 mmol), alkyne (2 mmol), sodium ascorbate (0.2 mmol), CuI (0.2 mmol), ligand **A** (0.3 mmol), and 6 mL DMSO–H_2O (5:1) were introduced into a two-necked round-bottom flask equipped with a stirring bar. After it was degassed, and then introduced under an argon atmosphere, the reaction mixture was stirred at 70 °C and the progress of the reaction was followed by TLC. When the starting material was completely consumed, or when the progress of the reaction had stopped, H_2O was poured into the crude mixture, and the obtained mixture was cooled down on an ice bath. The formed precipitate was isolated by filtration, washed with H_2O, and dried in vacuo, to obtain the desired product.

4-{1-Phenyl-[1,2,3]triazol-4-yl}butan-1-ol (Table 1, entry 1)
Yield 99%; yellow oil; R_f = 0.23 (PE–EtOAc, 1:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (s, 1 H), 7.71 (dt, *J* = 7.3, 1.1 Hz, 2 H), 7.50 (tt, *J* = 7.3, 1.1 Hz, 2 H), 7.41 (tt, *J* = 7.3, 1.1 Hz, 1 H), 3.70 (t, *J* = 6.1 Hz, 2 H), 2.84 (t, *J* = 7.3 Hz, 2 H), 2.11 (br s, 1 H), 1.91–1.79 (m, 2 H), 1.75–1.63 (m, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 149.2, 137.5, 130.1, 128.9, 120.8, 119.4, 62.8, 41.4, 32.5, 25.7.

MS (ES+): *m/z* (%) = 218 (57) [M + H^+], 240 (100) [M + Na^+].

3-{4-Hydroxymethyl-[1,2,3]triazol-1-yl}benzoic Acid Ethyl Ester (Table 1, entry 2)
Yield 83%; yellow solid; mp 135–137 °C; R_f = 0.24 (PE–EtOAc, 1:3).

^{1}H NMR (300 MHz, DMSO): δ = 8.82 (s, 1 H), 8.43 (t, *J* = 1.9 Hz, 1 H), 8.20 (ddd, *J* = 0.8, 1.9, 8.0 Hz, 1 H), 8.04 (dt, *J* = 0.8, 8.0 Hz, 1 H), 7.76 (t, *J* = 8.0 Hz, 1 H), 5.35 (t, *J* = 5.4 Hz, 1 H), 4.64 (d, *J* = 5.4 Hz, 2 H), 4.40 (q, *J* = 6.9 Hz, 2 H), 1.37 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 169.7, 149.7, 136.9, 131.5, 130.5, 128.8, 124.3, 121.2, 120.0, 61.2, 54.9, 14.0.

HRMS (EI+): *m/z* [M^+] calcd for $C_{12}H_{13}N_3O_3$: 247.0957; found: 247.0965.

3-{4-Trimethylsilanyl-[1,2,3]triazol-1-yl}benzoic Acid Ethyl Ester (Table 1, entry 3) and 3-[1,2,3]triazol-1-yl-benzoic Acid Ethyl Ester (By-product)
Ethyl 3-iodobenzoate (552 mg, 2.0 mmol), ligand **A** (43 mg, 0.3 mmol), sodium ascorbate (40 mg, 0.2 mmol), and NaN_3 (130 mg, 2.0 mmol) were taken up in DMSO–H_2O (5:1, 6 mL) and degassed with argon. Then, CuI (39 mg, 0.2 mmol) and ethynyltrimethylsilane (295 mg, 3 mmol) were added at r.t. The reaction solution was stirred at the same temperature under an argon atmosphere overnight. Then the solution was poured into H_2O and extracted with EtOAc. The combined organic phases were concentrated in vacuo together with silica gel. The residue was purified by chromatography (PE–EtOAc, 4:1 → EtOAc), giving a desired compound as a colorless oil (220 mg, 38%) and a by-product as a white solid (70 mg, 16%).

Data for the desired compound:

R_f = 0.64 (PE–EtOAc, 1:1).

^{1}H NMR (300 MHz, DMSO): δ = 8.33 (t, *J* = 1.9 Hz, 1 H), 8.10 (dt, *J* = 1.5, 7.6 Hz, 1 H), 8.04 (ddd, *J* = 1.0, 3.3, 8.0 Hz, 1 H), 8.02 (s, 1 H), 7.61 (t, *J* = 8.0 Hz, 1 H), 4.44 (q, *J* = 7.2 Hz, 2 H), 1.43 (t, *J* = 7.2 Hz, 3 H), 0.40 (s, 9 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 165.4, 147.8, 137.2, 132.2, 129.9, 129.4, 127.1, 125.1, 121.3, 61.6, 14.3, –1.1.

HRMS (EI+): *m/z* [M^+] calcd for $C_{14}H_{19}N_3O_2Si$: 289.1247; found: 289.1234.

Data for the by-product:

Mp 81–83 °C; R_f = 0.50 (PE–EtOAc, 1:1).

^{1}H NMR (300 MHz, DMSO): δ = 8.96 (d, *J* = 1.2 Hz, 1 H), 8.43 (dd, *J* = 1.2, 2.3 Hz, 1 H), 8.20 (ddd, *J* = 1.2, 2.3, 7.7 Hz, 1 H), 8.05 (dt, *J* = 1.2, 7.7 Hz, 1 H), 8.01 (d, *J* = 1.2 Hz, 1 H), 7.76 (t, *J* = 7.7 Hz, 1 H), 4.37 (q, *J* = 6.9 Hz, 2 H), 1.35 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 165.2, 137.3, 135.0, 131.9, 130.9, 129.3, 125.0, 123.8, 120.7, 61.7, 14.5.

HRMS (EI+): *m/z* [M^+] calcd for $C_{11}H_{11}N_3O_2$: 217.0851; found: 217.0863.

4-(4-Butyl-phenyl)-1-phenyl-[1,2,3]triazole (Table 1, entry 6)
Yield 84%; pale yellow solid; mp 118–121 °C; R_f = 0.16 (PE–EtOAc, 10:1).

^{1}H NMR (300 MHz, DMSO): δ = 9.25 (s, 1 H), 7.96 (d, *J* = 8.0 Hz, 2 H), 7.86 (d, *J* = 8.0 Hz, 2 H), 7.64 (t, *J* = 7.3 Hz, 2 H), 7.51 (t, *J* = 7.3 Hz, 1 H), 7.31 (d, *J* = 7.3 Hz, 2 H), 2.62 (t, *J* = 7.6 Hz, 2 H), 1.59 (quin, *J* = 7.6 Hz, 2 H), 1.32 (hex, *J* = 7.6 Hz, 2 H), 0.91 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 147.4, 142.4, 136.6, 129.8, 128.8, 128.6, 127.7, 125.2, 119.9, 119.1, 34.5, 32.9, 21.7, 13.7.

HRMS (EI+): *m/z* [M^+] calcd for $C_{18}H_{19}N_3$: 277.1529; found: 277.1577.

1-Phenyl-4-(4-trifluoromethylphenyl)-[1,2,3]triazole (Table 1, entry 8)
Yield 86%; pale yellow solid; mp 224–228 °C; R_f = 0.14 (PE–EtOAc, 10:1)

^{1}H NMR (300 MHz, DMSO): δ = 9.49 (s, 1 H), 8.18 (d, *J* = 8.0 Hz, 2 H), 7.97 (dd, *J* = 7.3, 1.2 Hz, 2 H), 7.88 (d, *J* = 8.0 Hz, 2 H), 7.66 (t, *J* = 7.3 Hz, 2 H), 7.54 (tt, *J* = 7.3, 1.2 Hz, 1 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 145.8, 136.4, 134.2, 133.3, 129.9 (2 C), 128.3 (q, *J* = 31 Hz), 125.9 (q, *J* = 3 Hz, 2 C), 125.8 (2 C), 124.1 (q, *J* = 271 Hz), 120.9, 120.1 (2 C).

HRMS (EI+): *m/z* [M^+] calcd for $C_{15}H_{10}F_3N_3$: 289.0827; found: 289.0830.

4-{1-(4-Hydroxymethylphenyl)-[1,2,3]triazol-4-yl}benzonitrile (Table 1, entry 10)
Yield 88%; orange solid; mp 222–224 °C; R_f = 0.04 (PE–EtOAc, 3:1).

^{1}H NMR (300 MHz, DMSO): δ = 9.47 (s, 1 H), 8.14 (d, *J* = 8.8 Hz, 2 H), 7.98 (d, *J* = 8.4 Hz, 2 H) 7.90 (d, *J* = 8.4 Hz, 2 H), 7.57 (d, *J* = 8.8 Hz, 2 H), 5.37 (t, *J* = 5.4 Hz, 1 H), 4.60 (d, *J* = 5.4 Hz, 1 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 146.0, 144.0, 139.2, 135.4, 133.4, 128.0, 126.2, 121.7, 120.3, 119.1, 110.8, 62.6.

HRMS (EI+): *m/z* [M^+] calcd for $C_{16}H_{12}N_4O$: 276.1011; found: 276.1031.

4-Amino-3-{4-(3-methoxyphenyl)-[1,2,3]triazol-1-yl}benzoic Acid Methyl Ester (Table 1, entry 11)
Purified by flash chromatography (PE–EtOAc, 10:1 → 3:1).

Yield 43%; off-white solid; mp 128–130 °C; R_f = 0.11 (PE–EtOAc, 1:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 8.00 (d, *J* = 1.9 Hz, 1 H), 7.90 (dd, *J* = 8.4, 1.9 Hz, 1 H), 7.51 (t, *J* = 2.3 Hz, 1 H), 7.44 (d, *J* = 7.7 Hz, 1 H), 7.36 (t, *J* = 7.7 Hz, 1 H), 6.93 (dm, *J* = 7.6 Hz, 1 H), 6.88 (d, *J* = 8.4 Hz, 1 H), 5.15 (br s, 2 H), 3.89 (s, 6 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 166.1, 160.2, 147.7, 144.9, 131.4, 131.2, 130.1, 125.6, 121.8, 120.2, 119.6, 118.3, 116.8, 114.8, 110.9, 55.4, 52.0.

HRMS (EI+): *m/z* [M^+] calcd for $C_{17}H_{16}N_4O_3$: 324.1222; found: 324.1187.

4-{4-(4-Butylphenyl)-[1,2,3]triazol-1-yl}benzonitrile (Table 1, entry 12)
Yield 88%; orange solid; mp 144–149 °C; R_f = 0.37 (PE–EtOAc, 1:3).

^{1}H NMR (300 MHz, DMSO): δ = 9.39 (s, 1 H), 8.20 (d, *J* = 8.6 Hz, 2 H), 8.13 (d, *J* = 8.6 Hz, 2 H), 7.85 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 2.62 (t, *J* = 7.3 Hz, 2 H), 1.59 (quin, *J* = 7.3 Hz, 2 H), 1.32 (hex, *J* = 7.3 Hz, 2 H), 0.91 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 147.8, 142.7, 139.5, 134.2, 128.8, 127.2, 125.3, 120.2, 119.2, 118.0, 110.9, 34.5, 32.9, 21.7, 13.7.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{19}H_{18}N_4$: 302.1531; found: 302.1541.

3-{4-(3-Methoxyphenyl)-[1,2,3]triazol-1-yl}benzoic Acid (Table 1, entry 13)

The reaction mixture was acidified to pH 1 with 4 M HCl before cooling down on ice-bath.

Yield 54%; off-white solid; mp 219–220 °C; R_f = 0.07 (PE–EtOAc, 1:3 + 1% AcOH).

^{1}H NMR (500 MHz, DMSO, 60 °C): δ = 13.4 (br s, 1 H), 9.18 (s, 1 H), 8.44 (br s, 1 H), 8.09 (d, *J* = 6.1 Hz, 1 H), 7.94 (br s, 2 H), 7.54 (s, 1 H), 7.51 (br s, 1 H), 7.38 (t, *J* = 7.9 Hz, 1 H), 6.94 (dd, *J* = 8.2, 1.8 Hz, 1 H), 3.86 (s, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 159.7, 147.4, 131.4, 130.1, 123.7, 119.9, 117.6, 114.0, 110.5, 55.1. Not all signals were observed on the NMR time scale due to the slow internal rotation.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{16}H_{13}N_3O_3$: 295.0957; found: 295.0937.

2-Methyl-4-{4-phenyl-[1,2,3]triazol-1-yl}phenylamine (Table 1, entry 14)

Purified by flash chromatography (PE–EtOAc, 3:1 → 1:3).

Yield 68%; off-white solid; mp 153–155 °C; R_f = 0.08 (PE–EtOAc, 3:1).

^{1}H NMR (300 MHz, DMSO): δ = 9.02 (s, 1 H), 7.93 (d, *J* = 6.9 Hz, 2 H), 7.53–7.43 (m, 3 H), 7.43 (dd, *J* = 8.4, 2.7 Hz, 1 H), 7.36 (tt, *J* = 6.9, 1.2 Hz, 1 H), 6.77 (d, *J* = 8.4 Hz, 1 H), 5.28 (s, 2 H), 2.17 (s, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 147.3, 146.6, 130.6, 128.8, 127.8, 126.0, 125.1, 122.1, 121.7, 119.1, 118.9, 113.7, 17.4.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{15}H_{14}N_4$: 250.1218; found: 250.1222.

3-{1-(4-Nitrophenyl)-[1,2,3]triazol-4-yl}phenol (Table 1, entry 15)

Yield 97%; brown solid; mp 239–243 °C; R_f = 0.09 (PE–EtOAc, 3:1).

^{1}H NMR (500 MHz, DMSO, 80 °C): δ = 9.12 (s, 1 H), 9.05 (br s, 1 H), 8.41 (d, *J* = 9.2 Hz, 2 H), 8.21 (d, *J* = 9.2 Hz, 2 H), 7.39 (s, 1 H), 7.34 (d, *J* = 7.6 Hz, 1 H), 7.28 (d, *J* = 7.6 Hz, 1 H), 6.80 (d, *J* = 7.63 Hz, 1 H).

^{13}C NMR (75.4 MHz, DMSO, 80 °C): δ = 158.8, 149.2, 148.1, 142.0, 132.1, 130.7, 126.1, 121.8, 120.6, 117.7, 116.7, 113.9.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{14}H_{10}N_4O_3$: 282.0753; found: 282.0757.

3-{4-Phenyl-[1,2,3]triazol-1-yl}phenol (Table 1, entry 16)

Yield 97%; pale green solid; mp 227–231 °C; R_f = 0.14 (PE–EtOAc, 3:1).

^{1}H NMR (300 MHz, DMSO): δ = 10.07 (br s, 1 H), 9.25 (s, 1 H), 7.98 (d, *J* = 7.6 Hz, 2 H), 7.58–7.19 (m, 6 H), 6.91 (br s, 1 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 147.1, 130.8 (br), 130.2, 128.9, 128.1, 125.3, 119.5, 110.5 (br). Not all signals were observed on the NMR time scale due to the slow internal rotation.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{14}H_{11}N_3O$: 237.0902; found: 237.0896.

5-{4-(3-Aminophenyl)-[1,2,3]triazol-1-yl}-2-methylphenylamine (Table 2, entry 1)

Yield 98%; pale green solid; mp 177–181 °C; R_f = 0.20 (PE–EtOAc, 1:3).

^{1}H NMR (300 MHz, DMSO): δ = 8.92 (s, 1 H), 7.24–7.19 (m, 2 H), 7.11 (t, *J* = 7.7 Hz, 1 H), 7.10 (d, *J* = 8.0 Hz, 1 H), 7.04 (dm, *J* = 7.7 Hz, 1 H), 6.95 (dd, *J* = 8.0, 2.3 Hz, 1 H), 6.58 (dm, *J* = 7.7 Hz, 1 H), 5.28 (s, 2 H), 5.18 (s, 2 H), 2.12 (s, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 148.9, 147.7, 147.6, 135.5, 130.8, 130.6, 129.3, 121.5, 118.7, 113.7, 113.2, 110.5, 107.0, 104.9, 17.0.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{15}H_{15}N_5$: 265.1327; found: 265.1318.

1-{4-(4-Phenyl-[1,2,3]triazol-1-yl)-phenyl}ethanone (Table 2, entry 2)

Yield 89%; off-white solid; mp 141–143 °C; R_f = 0.17 (PE–EtOAc, 3:1).

^{1}H NMR (300 MHz, DMSO): δ = 9.45 (s, 1 H), 8.46 (t, *J* = 1.9 Hz, 1 H), 8.25 (dm, *J* = 8.0 Hz, 1 H), 8.09 (dm, *J* = 8.0 Hz, 1 H), 7.98 (td, *J* = 7.7, 1.5 Hz, 2 H), 7.80 (t, *J* = 8.0 Hz, 1 H), 7.52 (td, *J* = 7.7, 1.5 Hz, 2 H), 7.40 (tt, *J* = 7.7, 1.5 Hz, 1 H), 2.70 (s, 3 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 197.0, 147.4, 138.2, 136.9, 130.4, 130.1, 128.9, 128.2, 128.2, 125.3, 124.2, 119.7, 119.0, 26.9.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{16}H_{13}N_3O$: 263.1059; found: 263.1078.

4-{4-(4-Chlorophenyl)-[1,2,3]triazol-1-yl}benzonitrile (Table 2, entry 3)

Yield 89%; yellow solid; mp 188–190 °C; R_f = 0.28 (PE–EtOAc, 3:1).

^{1}H NMR (300 MHz, DMSO): δ = 9.48 (s, 1 H), 8.18 (d, *J* = 9.2 Hz, 2 H), 8.13 (d, *J* = 9.2 Hz, 2 H), 7.95 (d, *J* = 8.4 Hz, 2 H), 7.58 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 146.9, 139.8, 134.7, 133.3, 129.5, 129.1, 127.4, 120.7, 120.5, 118.4, 111.5.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{15}H_9ClN_4$: 280.0516; found: 280.0501.

4-{1-(4-Chlorophenyl)-[1,2,3]triazol-4-yl}butyronitrile (Table 2, entry 5)

Yield 83%; off-white solid; mp 70–72 °C; R_f = 0.51 (PE–EtOAc, 1:3).

^{1}H NMR (300 MHz, DMSO): δ = 8.67 (s, 1 H), 7.92 (d, *J* = 8.8 Hz, 2 H), 7.66 (d, *J* = 8.8 Hz, 2 H), 2.83 (t, *J* = 7.3 Hz, 2 H), 2.61 (t, *J* = 7.3 Hz, 2 H), 1.98 (p, *J* = 7.3 Hz, 2 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 146.6, 135.5, 132.6, 129.7, 121.4, 120.6, 120.3, 24.5, 23.9, 15.7.

HRMS (EI+): *m/z* [M$^+$] calcd for $C_{12}H_{11}ClN_4$: 246.0672; found: 246.0650.

1-*p*-Tolyl-4-trimethylsilanylmethyl-[1,2,3]triazole (Table 2, entry 6)

4-Bromotoluene (342 mg, 2.0 mmol), ligand **A** (43 mg, 0.3 mmol), sodium ascorbate (40 mg, 0.2 mmol), and NaN_3 (130 mg, 2.0 mmol) were taken up in DMSO–H_2O (5:1, 6 mL) and degassed with argon. Then, CuI (39 mg, 0.2 mmol) was added. After the mixture was heated to 70 °C, trimethyl(propargyl)silane (purity: 85%, 396 mg, 3 mmol) was added. The reaction solution was stirred at the same temperature for 1 h. Then the solution was poured into H_2O and extracted with CH_2Cl_2. The combined organic phases were concentrated in vacuo together with silica gel. The residue was purified by

chromatography (PE–EtOAc, 3:1), giving the title compound as a white solid (372 mg, 77%); mp 89–90 °C.

R_f = 0.52 (PE–EtOAc, 3:1).

^{1}H NMR (300 MHz, DMSO): δ = 8.28 (s, 1 H), 7.74 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 8.4 Hz, 2 H), 2.32 (s, 3 H), 2.07 (s, 2 H), 0.04 (s, 9 H).

^{13}C NMR (75.4 MHz, DMSO): δ = 145.9, 138.0, 135.0, 130.5, 119.9, 119.1, 20.9, 14.9, 1.3.

MS (ES+): *m/z* (%) = 246 (100) [M + H$^+$].

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