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Copper-Catalyzed Cross-Dehydrogenative N^2-Coupling of *NH*-1,2,3-Triazoles with *N,N* -Dialkylamides: *N*-Amidoalkylation of *NH*-1,2,3-Triazoles

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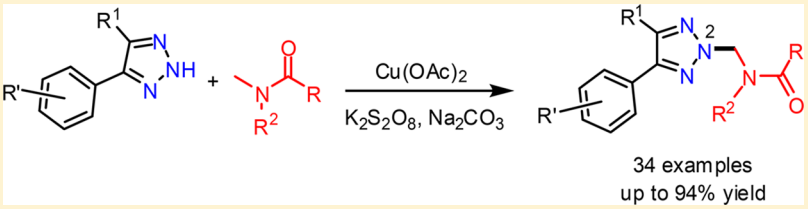
Supporting Information



ABSTRACT: An efficient copper-catalyzed C−N bond formation by N−H/C−H cross-dehydrogenative coupling (CDC) between *NH*-1,2,3-triazoles and *N,N*-dialkylamides has been developed. The method provided *N*-amidoalkylated 1,2,3-triazoles with moderate to high yields, and the reactions showed high N^2-selectivities when 4,5-disubstituted *NH*-1,2,3-triazoles served as the substrates.

INTRODUCTION

Cross-dehydrogenative coupling (CDC) reactions have emerged as powerful tools for organic synthesis because of their high atom- and step-economical characteristics[1] and have also been widely applied in the functionalization of heterocyclic compounds in recent years.[2] *N*-Alkylamines and alkylamides are good reaction partners for the CDC reactions. For example, DMF (*N,N*-dimethylformamide), which is widely recognized as a common solvent, can also be employed as a cheap, readily available reaction partner in CDC reactions.[3] Moreover, the CDC reaction of DMF is a straightforward method to introduce an amide group into a molecule. Indeed, some heterocyclic molecules with an amide group have been found to show a range of interesting biological activities.[4]

1,2,3-Triazoles have become important building blocks in organic chemistry in the past few years. They have received considerable attention and have shown many applications in medicinal chemistry,[5] material chemistry,[6] synthetic organic chemistry,[7] and other fields.[8] Most 1,2,3-triazoles are obtained by reactions of organic azides with other partners, such as click reactions of organic azides with alkynes,[9] multicomponent reactions of organic azides with activated carbonyl compounds,[10] and condensation reactions of organic azides with activated alkenes.[11] More recently, new azide-free strategies have also been developed.[12] These methods usually produce the N^1- or $N^{1'}$-substituted 1,2,3-triazoles, but are not suitable for producing N^2-substituted 1,2,3-triazoles. N^2-substituted 1,2,3-triazoles were obtained mostly via post-*N*-functionalization of *NH*-1,2,3-triazoles with different reaction partners, including alkyl halides, alcohols, alkynes, and alkenes.[13] Still, advances for the synthesis of diverse N^2-substituted 1,2,3-triazole were desirable.

In continuation of our research for the synthesis of new 1,2,3-triazole-related heterocyclic compounds,[14] herein, we report a copper-catalyzed N−H/C−H cross-dehydrogenative coupling of *NH*-1,2,3-triazoles with different amides. By tuning the substituents, the reactions gave N^2-coupling products with high yield.

RESULTS AND DISCUSSION

4-Methyl-5-phenyl-2*H*-1,2,3-triazole (**1a**) and DMF (*N,N*-dimethylformamide) were chosen as model substrates for the initial condition screening. The results are shown in Table 1. We proposed that methyl and phenyl groups could block the N^1- and $N^{1'}$-coupling sites, which might lead to high N^2-coupling selectivity.

First, the reaction was performed in the presence of **1a** (0.3 mmol) and CuCl (0.06 mmol, 0.2 equiv) in 3 mL of DMF as the solvent with air as the oxidant at 110 °C. After 5 h there was no reaction at all. When CuCl was changed to $CuCl_2$, it gave the same result (Table 1, entries 1 and 2). However, when TBHP (*tert*-butyl hydroperoxide), a common oxidant, was used instead of air, after 5 h we found that the desired **3a** was formed in 54% yield (entry 3). Inspired by this, other common copper salts were examined, which showed that $Cu(OAc)_2$ gave the best result (entries 4−10). Furthermore, other inexpensive iron salts were tested, including $FeCl_2$ and $FeCl_3$ (entries 11 and 12); however, their catalytic efficiency was inferior to that of

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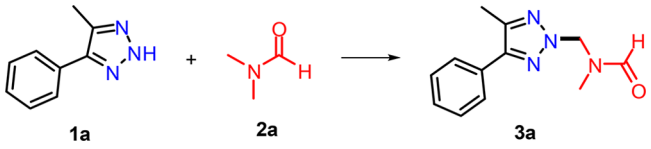
Table 1. Optimization of the Reaction Conditions[a]

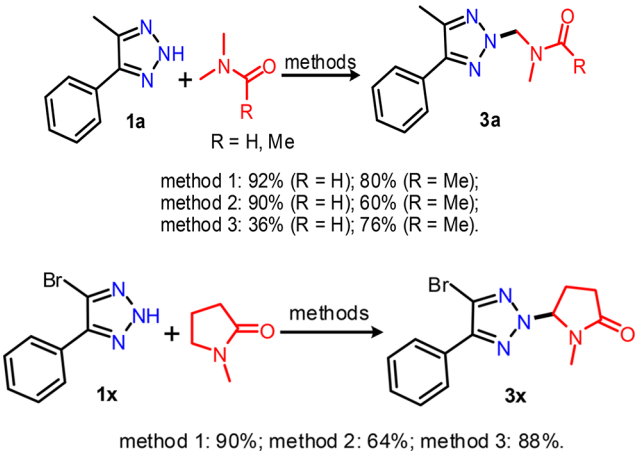


entry	catalyst	oxidant	additive	conversion[b]	yield[c] (%)
1	CuCl	air	none	0	0
2	$CuCl_2$	air	none	0	0
3	CuCl	TBHP	none	60	54
4	CuBr	TBHP	none	69	61
5	$CuCl_2$	TBHP	none	65	59
6	$CuBr_2$	TBHP	none	75	68
7	CuO	TBHP	none	64	59
8	$Cu(NO_3)_2$	TBHP	none	48	43
9	$CuSO_4$	TBHP	none	55	51
10	$Cu(OAc)_2$	TBHP	none	85	76
11	$FeCl_2$	TBHP	none	30	23
12	$FeCl_3$	TBHP	none	35	32
13	$Cu(OAc)_2$	TBHP	Na_2CO_3	100	88
14	$Cu(OAc)_2$	TBHP	K_2CO_3	93	82
15	$Cu(OAc)_2$	TBHP	NaOAc	78	69
16	$Cu(OAc)_2$	TBHP	DBU	85	75
17	$Cu(OAc)_2$	DTBP	Na_2CO_3	<5	trace
18	$Cu(OAc)_2$	H_2O_2	Na_2CO_3	<5	trace
19	$Cu(OAc)_2$	$K_2S_2O_8$	Na_2CO_3	100	92
20	$Cu(OAc)_2$	BPO	Na_2CO_3	<5	trace
21	$Cu(OAc)_2$	DDQ	Na_2CO_3	<5	trace
22[d]	$Cu(OAc)_2$	$K_2S_2O_8$	Na_2CO_3	60	53
23		$K_2S_2O_8$	Na_2CO_3	100	90

[a]Reaction conditions: **1a** (0.3 mmol, 47.7 mg), **2a** (3 mL as solvent), oxidant (0.6 mmol, 2.0 equiv, 162.2 mg), Na_2CO_3 (0.33 mmol, 1.1 equiv, 35.0 mg), catalyst (0.06 mmol, 0.2 equiv, 12.0 mg), 110 °C, 8 h. [b]Based on **1a**. [c]Isolated yields. [d]Temperature of 80 °C.

$Cu(OAc)_2$. Therefore, $Cu(OAc)_2$ was chosen as the catalyst for all further reactions. Interestingly, it was found that the addition of a base could promote the reaction, and Na_2CO_3 gave a better result (entries 13−16). In addition, other different oxidants were also investigated, including DTBP (di-*tert*-butyl peroxide), H_2O_2, BPO (benzoyl peroxide), and DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) (entries 17−21), and they failed to promote the reaction. However, when $K_2S_2O_8$ was chosen as the oxidant, the yield of **3a** rose to 92%, which also revealed high N^2-selectivity.[15] In addition, a relatively lower conversion and yield were detected with a reaction temperature of 80 °C (entry 22). If the reaction was run without copper catalyst (entry 23),[16] a satisfactory result was also obtained; the isolated yield of **3a** was up to 90%. To establish the best reaction conditions, comparisons of different methods have also been made (Scheme 1). When DMF served as a reactant, the yield of the TBHP/TBAI (tetrabutylammonium iodide) protocol was only 36%, much lower than those of the Cu or Cu-free protocols. When DMA or NMP served as the substrate for the coupling reaction under copper-free reaction conditions, the yields were inferior to those of the Cu-catalyzed reactions, while when TBHP/TBAI was used instead of Cu or Cu-free reaction conditions, the yields of **3a** and **3x** were up to 76% and 88%, which were similar to those of the Cu-catalyzed protocol. However, the colors of the Cu-free reaction system or TBHP/TBAI protocol were darker than those of the Cu-catalyzed reaction system generally. We suspected that the polymerization of the imine cation intermediates was easier under copper-free conditions. Thus, $Cu(OAc)_2/K_2S_2O_8/Na_2CO_3$ at 110 °C was chosen as the optimal reaction condition.

Scheme 1. Comparisons of the Reaction Conditions[a]



[a]Reaction conditions: **1a** and **1x** (200 mg, 1 equiv), solvent (10 mL); isolated yields. Method 1: $Cu(OAc)_2$ (0.2 equiv), $K_2S_2O_8$ (2 equiv), Na_2CO_3 (1.1 equiv), 110 °C. Method 2: $K_2S_2O_8$ (2 equiv), Na_2CO_3 (1.1 equiv), 110 °C. Method 3: TBHP (3 equiv), TBAI (0.1 equiv), 110 °C.

Then we set out to study the scope and limitation of this conversion with different *NH*-1,2,3-triazoles and amides (Scheme 2). In general, the reactions all performed well; the corresponding N^2-substituted products were less polar than other isomers. First, 4-Me (or Br)-5-Ar-disubstituted *NH*-1,2,3-triazoles were checked due to the potentially high N^2-regioselectivities. In fact, the Me group and Br atom could indeed block the N^1 reaction sites. In all cases, the N^2-substituted product was formed predominantly. The structure of **3q** was identified by X-ray single-crystal analysis.[17]

Then other 4,5-disubstituted *NH*-1,2,3-triazoles, such as 4,5-diaryl-1,2,3-triazoles **3aa**−**3ac** and 4-benzoyl-5-phenyl-1,2,3-triazoles **3y** and **3z**, were suitable for this reaction and showed high N^2-regioselectivities. At the same time, both electron-donating functional groups, such as methoxy or methyl substituents, and electron-withdrawing groups, such as halogenated moieties in the aryl ring, were compatible with this transformation. The yield of N^2-coupling product was up to 94%. However, when the 1*H*-1,2,3-triazole and 4-ethyl-5-methyl-1,2,3-triazole were tested, the reactions gave complex mixtures and the products were hard to identify.

At the same time, commercially available amide solvents, such as DMF and DMA, were suitable reaction partners to couple with *NH*-1,2,3-triazoles, although the reactions with DMA need more time to give the full conversion. However, some side reactions or decomposition of the products could occur over an extended reaction time, which resulted in the loss of isolated yields. Furthermore, *N*-methyl-2-pyrrolidinone (NMP) was also a suitable substrate, which gave the N^2-coupling products with high yield. It should be pointed out that the reactions could be finished in 30 min under standard reaction conditions. However, *N*,*N*-dimethylaniline, piperidine-1-carbaldehyde, *N*,*N*-diethylformamide, and *N*,*N*-dimethylbenzamide cannot react in this reaction system.

To further investigate the reaction substrate scope, we tested 4-aryl-substituted *NH*-1,2,3-triazoles (Table 2). The reactions also performed well. The corresponding N^2-coupling product

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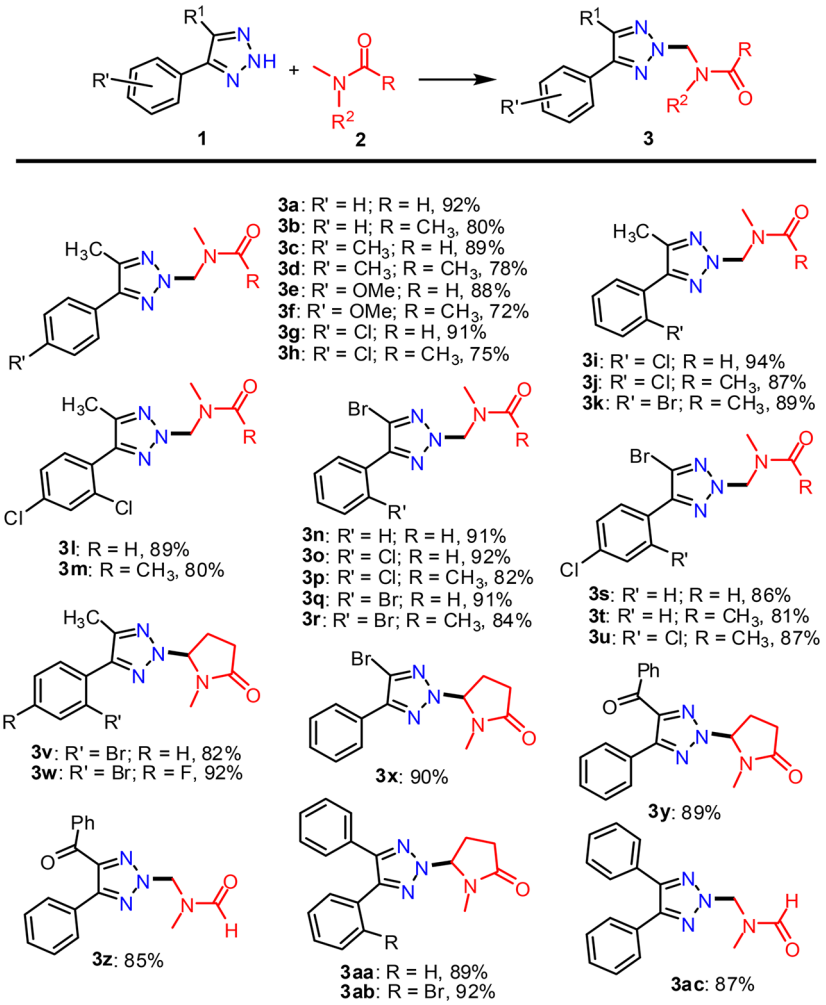
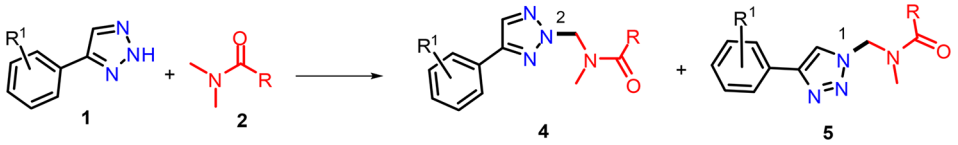
Scheme 2. Substrate Scope for the Synthesis of N^2-Amidoalkylated 1,2,3-Triazoles[a]



[a]Reaction conditions: **1** (0.3 mmol), **2** (3 mL as solvent), $Cu(OAc)_2$ (0.06 mmol), $K_2S_2O_8$ (0.6 mmol) and Na_2CO_3 (0.33 mmol), reaction temperature 110 °C.

Table 2. 4-Aryl-Substituted *NH*-1,2,3-Triazoles as the Substrate[a]



entry	R^1	R	**4** yield[b] (%)	**5** yield[b] (%)
1	H	H	64 (**4a**)	18 (**5a**)
2	H	CH_3	50 (**4b**)	25 (**5b**)
3	4-CH_3	CH_3	59 (**4c**)	21 (**5c**)
4	4-OMe	CH_3	47 (**4d**)	27 (**5d**)
5	2-Br	CH_3	57 (**4e**)	20 (**5e**)

[a]Reaction conditions: **1** (0.3 mmol), **2** (3 mL as solvent), $Cu(OAc)_2$ (0.06 mmol), $K_2S_2O_8$ (0.6 mmol), and Na_2CO_3 (0.33 mmol), 110 °C. [b]Isolated yields.

was the major product generally. However, the regioselectivities were not very high; other N^1-products were also obtained.[18] The lower regioselectivities were similar to the results for the alkylation, arylation, and alkenylation of 4-aryl-1,2,3-triazoles.[13]

To identify the structures of *N*-amidoalkylated 1,2,3-triazoles, a gram-scale experiment[19] was done to obtain the N^1-coupling regioisomer (**3q′**) of **3q**. The structure was also confirmed by X-ray single-crystal analysis.[17] The obtained crystal structures of the two regioisomers **3q** and **3q′** were beneficial in determining the methods for the determination of the N^2-regioisomers for other reactions.

According to the ^{13}C NMR spectra of **3q** and **3q′**, there were significant differences between the CH_2 groups (which linked to 1,2,3-triazole) of the N^1 (**3q′**) and N^2 (**3q**) isomers. The chemical shifts of the CH_2 group for the N^2-isomer were 67.8 and 61.5 ppm (for two conformers), which were located at

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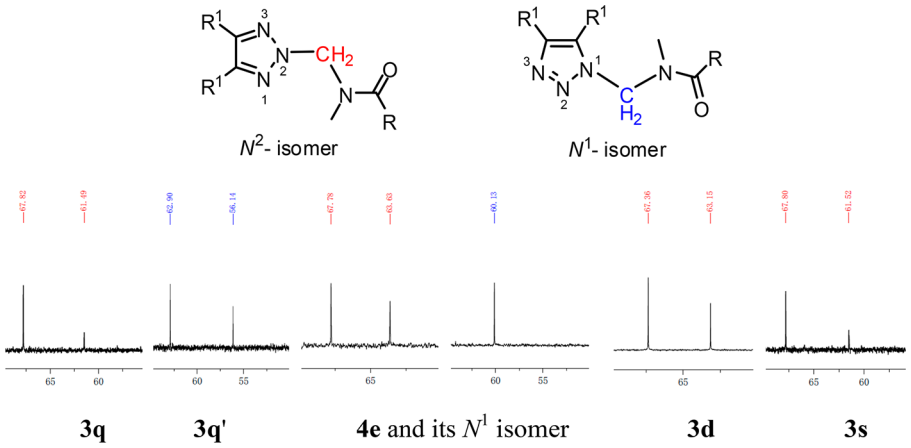
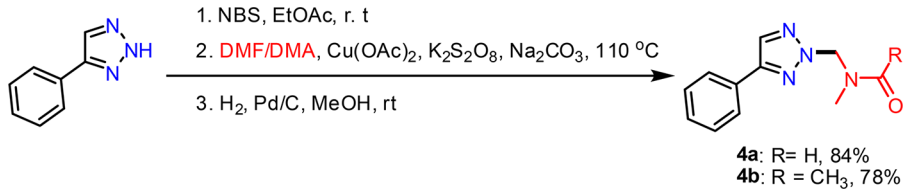


Figure 1. Analysis of ^{13}C NMR spectra.

Scheme 3. Alternative Synthesis of N^2-Amidoalkylated 4-Aryl-1,2,3-triazoles

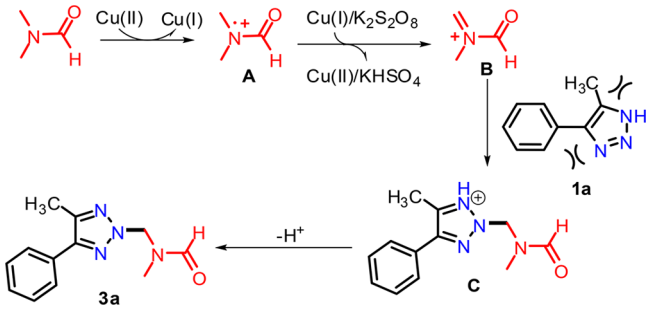


lower field than those of the N^1-isomer (62.9 and 56.1 ppm, for two conformers). Also, the corresponding ^{13}C NMR spectra of two regioisomeric products for 4-aryl-substituted 1,2,3-triaoles gave the same information, for example, **4e** and its N^1-isomer (**5e**). The chemical shifts of the CH_2 group for **4e** were located at 67.8 and 63.6 ppm. By contrast, the NMR spectra for **5e** showed one conformer, and the ^{13}C NMR chemical shift for the CH_2 group was 60.1 ppm, which was located at higher field. For other DMF or DMA coupling products, the corresponding N^2-isomers gave higher ^{13}C NMR chemical shifts for the CH_2 group, which were located at about 67 and 62 ppm (two conformers), for example, **3d** and **3s**, while the N^1-isomer gave lower chemical shifts. Moreover, some N^1-isomers only gave one conformer signal (Figure 1). Indeed, the N^1- and N^2-isomers of other triazoles and benzotriaoles showed similar results.[13,20] As for the coupling reactions with NMP, it was found that the reactions gave only N^2-coupling products because of a big steric hindrance.

To selectively synthesize 2,4-disubstituted 1,2,3-triazoles, a stepwise reaction strategy was developed. As shown in Scheme 2, the 4-phenyltriazole was first reacted with NBS (*N*-bromosuccinimide) to introduce a Br atom on the triazole ring[14b,21] and then reacted with DMF or DMA. The corresponding N^2-amidoalkylated bromotriazoles were further reduced under catalytic hydrogenation conditions (H_2, Pd/C) to give the 2-amidoalkylated 4-phenyl-1,2,3-triazoles in higher overall yields. This method provides a highly selective synthesis of 2-amidoalkylated 4-aryl-1,2,3-triazoles (Scheme 3).

On the basis of the experimental results and existing literature,[2,22] a postulated mechanism for this transformation has been put forward (Scheme 3). The initiation step is proposed to be a single electron transfer between Cu(II) and DMF to produce radical cation **A**. Next, the successive hydrogen atom abstraction from the radical cation A with the aid of $Cu(I)/K_2S_2O_8$ forms the iminium ion **B**, which is selectively attacked by the N^2-site of triazole **1a** to form the intermediate **C**. Then a proton is lost to form the product **3a**. A base is added to neutralize the formed acid and further improve the reaction conversion (Scheme 4).

Scheme 4. Plausible Mechanism for Oxidative N^2-Coupling



CONCLUSION

In conclusion, we report here a copper-catalyzed oxidative cross-dehydrogenative C−H/N−H coupling reaction between *N,N*-dialkylamides and *NH*-1,2,3-triazoles. This method can give *N*-amidoalkylated 1,2,3-triazoles with high efficiency. By tuning the substituents on the *NH*-1,2,3-triazoles, the N^2-amidoalkylated 1,2,3-triazoles can be obtained in high selectivity and yield.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial sources and used without further purification. ^1H NMR spectra were determined on 400 and 600 MHz spectrometers as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (δ), and the signals are reported as s (singlet), d (doublet), t (triplet), m (multiplet), and dd (doublet of doublets), and coupling constants (J) are given in hertz. ^{13}C NMR spectra were recorded at 100 and 150 MHz in $CDCl_3$ solution. Chemical shifts as are referenced to $CDCl_3$ (δ = 7.26 ppm for ^1H and δ = 77.0 ppm for ^{13}C NMR) as the internal

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standard. High-resolution mass spectrometry (HRMS) was performed with a Fourier-transform mass spectrometer by electrospray ionization and a time-of-flight mass spectrometer by electrospray ionization. TLC was performed on silica gel coated glass slides. All solvents were dried before use. 4-Phenyltriazoles and 4-methyl-5-phenyl-2*H*-1,2,3-triazoles were prepared according to the literature procedure.[14a]

Typical Experimental Procedure: Synthesis of Br-Substituted 1,2,3-Triazole. To a solution of 4-phenyltriazole (500 mg, 3.45 mmol) in EtOAc (10 mL) was added NBS (920 mg, 5.18 mmol) at room temperature. The reaction was checked by TLC. After the completion of the reaction, the mixture was poured into water, extracted by ethyl acetate, washed with NaCl(aq), and dried with anhydrous Na_2SO_4, then the solvent was removed under reduced pressure to obtain a yellow solid, and the crude product was purified by column chromatography [silica gel, PE−EtOAc (10:1 to 5:10)] to give **1n** as a white solid (90%, 694 mg).

Typical Experimental Procedure: Synthesis of *N*-Amidoalkylated 1,2,3-Triazoles. A 50 mL round-bottom flask equipped with a magnetic stir bar was charged with 4-methyl-5-phenyl-2*H*-1,2,3-triazole (47.7 mg, 0.3 mmol), DMF (3 mL as the solvent), $K_2S_2O_8$ (162.3 mg, 0.6 mmol), Na_2CO_3 (35 mg, 0.33 mmol), and $Cu(OAc)_2$ (12 mg, 0.05 mmol). The mixture was then stirred at 110 °C in air for 0.5−6 h (TLC monitoring) and poured into H_2O (20 mL). The pH was adjusted to neutral using 10% HCl, and the mixture was extracted with EtOAc (3 × 20 mL). Next the organic phase was evaporated under vacuum, and the crude product was purified by column chromatography [silica gel, PE−EtOAc (10:1 to 2:1)] to give **3a** as a white solid (89%, 61 mg).

Procedure for the Synthesis of 4a or 4b. To a solution of 4-phenyltriazole (200 mg, 1.38 mmol) in EtOAc (4 mL) was added NBS (367.8 mg, 2.07 mmol) at room temperature. The reaction was checked by TLC. The workup procedure was the same as for the synthesis of Br-substituted 1,2,3-triazoles. The obtained crude yellow solid can be used for the next step without further purification. The yellow solid reacted with DMF or DMA (4 mL) to obtain the N^2-amidoalkylated 4-bromotriazoles (see the section "Typical Experimental Procedure: Synthesis of N-Amidoalkylated 1,2,3-Triazoles"), and then the N^2-amidoalkylated 4-bromotriazoles and 10% Pd/C in methanol (8 mL) were stirred under atmospheric H_2 in a 50 mL Schlenk bottle for 2 h. Then triethylamine (3 mmol) was added to the mixture. After being stirred for 10 min, the mixture was filtered by diatomite. The filtrate was diluted with ethyl acetate (20 mL) and washed with water (20 mL). Then the organic phase was evaporated under vacuum, and the crude product was purified by column chromatography [silica gel, PE−EtOAc (10:1 to 2:1)] to give product **4a** (82%, 333 mg) or **4b** (78%, 332 mg).

4-Bromo-5-phenyl-2*H*-1,2,3-triazole (1n). White solid (90%, 694 mg). Mp: 142−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.91 (s, 1H), 7.52−7.49 (m, 1H), 7.47 (d, J = 4.0 Hz, 1H), 7.46−7.42 (m, 1H), 3.52 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 129.2, 128.7, 127.4. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_8H_6BrN_3$ 223.9818, found 223.9817.

4-Bromo-5-(2-chlorophenyl)-2*H*-1,2,3-triazole (1o). White solid (88%, 633 mg). Mp: 81−82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.52 (m, 1H), 7.50−7.47 (m, 1H), 7.45−7.41 (m, 1H), 7.40−7.36 (m, 1H), 3.53 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.9, 131.8, 130.9, 130.2, 127.1, 126.8, 123.2. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_8H_6BrClN_3$ 257.9428, found 257.9427.

4-Bromo-5-(2-bromophenyl)-2*H*-1,2,3-triazole (1q). White solid (85%, 575 mg). Mp: 92−93 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.4 Hz, 1H), 7.46−7.31 (m, 3H), 3.53 (d, J = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.2, 131.8, 131.0, 127.3, 123.5. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_8H_6Br_2N_3$ 301.89230, found 301.89246.

4-Bromo-5-(4-chlorophenyl)-2*H*-1,2,3-triazole (1s). White solid (92%, 662 mg). Mp: 192−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 2.0 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 3.50 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.0, 128.7. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_8H_6BrClN_3$ 257.9428, found 257.9426.

4-Bromo-5-(2,4-dichlorophenyl)-2*H*-1,2,3-triazole (1u). White solid (90%, 616 mg). Mp: 148−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 2.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.38−7.36 (m, 1H), 3.51 (d, J = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 134.8, 132.9, 130.1, 127.3. ESI-MS: m/z 290.9 [M]$^+$. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_8H_6BrCl_2N_3$ 291.9038, found 291.9034.

***N*-Methyl-*N*-((4-methyl-5-phenyl-2*H*-1,2,3-triazol-2-yl)methyl)formamide (3a).** White solid (92%, 132 mg). Mp: 60−62 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.34 (s, 0.73H), 8.01 (s, 0.25H), 7.56 (t, J = 7.8 Hz, 2H), 7.31 (t, J = 7.2 Hz, 2H), 7.24 (t, J = 7.2 Hz, 1H), 5.71 (s, 0.49H), 5.53 (s, 1.59H), 2.87 (s, 0.7H), 2.80 (s, 2.16H), 2.35 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.8, 162.6, 146.0, 145.5, 142.2, 141.8, 130.4, 130.3, 128.4, 128.0, 127.8, 126.9, 66.4, 60.1, 33.3, 29.1, 11.5. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{12}H_{15}N_4O$ 231.1240, found 231.1235.

***N*-Methyl-*N*-((4-methyl-5-phenyl-2*H*-1,2,3-triazol-2-yl)methyl)acetamide (3b).** Light yellow oil (80%, 123 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (t, J = 7.8 Hz, 2H), 7.42 (q, J = 7.8 Hz, 2H), 7.36−7.33 (m, 1H), 5.87 (s, 0.87H), 5.71 (s, 1.25H), 3.08 (s, 1.23H), 3.03 (s, 1.82H), 2.46 (s, 3H), 2.43 (s, 1.85H), 2.13 (s, 1.24H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.2, 145.8, 145.5, 142.0, 141.7, 130.8, 130.6, 128.5, 128.1, 127.9, 127.1, 67.3, 63.1, 35.1, 33.0, 21.7, 11.7. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_4O$ 245.1397, found 245.1398.

***N*-Methyl-*N*-((4-methyl-5-(*p*-tolyl)-2*H*-1,2,3-triazol-2-yl)methyl)formamide (3c).** Light yellow solid (89%, 125 mg). Mp: 66−68 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.43 (d, J = 8.4 Hz, 0.64H), 8.11 (d, J = 9.0 Hz, 0.22H), 7.61−7.45 (m, 2H), 7.28−7.15 (m, 2H), 5.80 (d, J = 9.0 Hz, 0.48H), 5.61 (d, J = 9.0 Hz, 1.53H), 2.99−2.95 (m, 0.7H), 2.92−2.87 (m, 2.12H), 2.45−2.39 (m, 3H), 2.38−2.30 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.9, 162.7, 146.3, 145.8, 142.2, 141.8, 138.0, 129.2, 127.5, 126.9, 66.5, 60.2, 33.4, 29.3, 21.1, 11.6. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_4O$ 245.1397, found 245.1400.

***N*-Methyl-*N*-((4-methyl-5-(*p*-tolyl)-2*H*-1,2,3-triazol-2-yl)methyl)acetamide (3d).** Colorless oil (78%, 116 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.61−7.52 (m, 2H), 7.25 (t, J = 8.4 Hz, 2H), 5.89 (s, 0.8H), 5.73 (s, 1.21H), 3.10 (s, 1.20H), 3.05 (s, 1.77H), 2.47 (s, 3H), 2.45 (s, 1.76H), 2.39 (d, J = 4.8 Hz, 3H), 2.16 (s, 1.14H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.4, 171.3, 146.0, 145.7, 141.9, 141.7, 138.1, 137.9, 129.3, 128.1, 127.8, 127.1, 67.4, 63.2, 35.1, 33.2, 29.7, 21.8, 21.3, 11.8. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{14}H_{19}N_4O$ 259.1553, found 259.1558.

***N*-((4-(4-Methoxyphenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylformamide (3e).** Light yellow oil (88%, 120 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.45 (s, 0.72H), 8.13 (s, 0.24H), 7.67−7.48 (m, 2H), 7.06−6.85 (m, 2H), 5.81 (s, 0.52H), 5.63 (s, 1.59H), 3.82 (d, J = 3.6 Hz, 3H), 2.99 (s, 0.69H), 2.92 (s, 2.10H), 2.44 (d, J = 1.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.0, 162.7, 159.5, 146.2, 145.7, 142.0, 141.7, 128.4, 123.0, 114.0, 66.6, 60.3, 55.2, 33.5, 29.4, 11.7. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_4O_2$ 261.1346, found 261.1340.

***N*-((4-(4-Methoxyphenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylacetamide (3f).** Light yellow oil (72%, 104 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.60 (t, J = 8.4 Hz, 2H), 6.96 (t, J = 7.8 Hz, 2H), 5.87 (s, 0.79H), 5.71 (s, 1.17H), 3.83 (d, J = 3.7 Hz, 3H), 3.09 (s, 1.11H), 3.04 (s, 1.61H), 2.44 (d, J = 3.0 Hz, 4.79H), 2.15 (s, 1.2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 159.6, 159.4, 145.8, 145. 5, 141.6, 141.4, 128. 5, 123.5, 123.2, 114.1, 67.3, 63.1, 55.3, 35.1, 33.1, 21.8, 11.7. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{14}H_{19}N_4O_2$ 275.1503, found 275.1501.

***N*-((4-(4-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylformamide (3g).** Light yellow solid (91%, 124 mg). Mp: 74−76 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.45 (s, 0.73H), 8.14 (s, 0.23H), 7.60 (t, J = 7.8 Hz, 2H), 7.38 (t, J = 8.4 Hz, 2H), 5.82 (s, 0.5H), 5.65 (s, 1.5H), 3.01 (s, 0.77H), 2.91 (s, 2.23H), 2.44 (s, 3H). ^{13}C NMR (150 MHz, CDCl3): δ 163.0, 162. 8, 145.3, 144.8, 142.4, 142.1, 134.2, 134.0, 129.2, 129.2, 129.0, 128.9, 128.8, 128.3,

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66.8, 60.4, 33.6, 29. 5, 11.8. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{14}ClN_4O$ 265.0851, found 265.0844.

***N*-((4-(4-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3h).** Light yellow oil (75%, 108 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62 (t, J = 8.4 Hz, 2H), 7.43−7.36 (m, 2H), 5.87 (s, 0.93H), 5.73 (s, 1.22H), 3.11 (s, 1.27H), 3.04 (s, 1.7H), 2.46 (s, 3H), 2.44 (s, 1.67H), 2.15 (s, 1.32H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 144.9, 144.5, 142.0, 141.8, 134.2, 133.9, 129.4, 129.2, 128.8, 128.4, 67.5, 63.3, 35.3, 33.2, 21.8, 11.8. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{13}H_{16}ClN_4O$ 279.1007, found 279.1012.

***N*-((4-(2-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylformamide (3i).** Light yellow oil (94%, 129 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.42 (s, 0.70H), 8.12 (s, 0.23H), 7.44 (d, J = 7.8 Hz, 1H), 7.35−7.25 (m, 3H), 5.83 (d, J = 1.2 Hz, 0.54H), 5.66 (d, J = 1.2 Hz, 1.59H), 2.97 (d, J = 1.2 Hz, 0.78H), 2.90 (d, J = 1.2 Hz, 2.22H), 2.22 (d, J = 1.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.9, 162.7, 145.2, 144.7, 144.3, 143.9, 133.7, 131.6, 130.2, 130.0, 129.8, 129.7, 129.6, 129.3, 126.7, 126.6, 66.7, 60.4, 33.4, 29.4, 10.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{14}ClN_4O$ 265.0851, found 265.0844.

***N*-((4-(2-Chlorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3j).** Light yellow oil (87%, 125 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.50−7.44 (m, 1H), 7.38−7.29(m, 3H), 5.91 (s, 0.87H), 5.76 (s, 1.21H), 3.09 (s, 1.2H), 3.05 (s, 1.68H), 2.43 (s, 1.73H), 2.26 (s, 3H), 2.16 (s, 1.26H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.4, 144.8, 144.5, 144.0, 143.7, 133.8, 131.8, 131.7, 130.1, 130.1, 130.0, 129.9, 129.8, 129.6, 126.7, 67.5, 63.3, 35.1, 33.2, 21.8, 10.8. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{13}H_{16}ClN_4O$ 279.1007, found 279.1004.

***N*-((4-(2-Bromophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3k).** White solid (89%, 121 mg). Mp: 122−124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70−7.66 (m, 1H), 7.40−7.29 (m, 3H), 5.93 (s, 1H), 5.78 (s, 1.18H), 3.10 (s, 1.27H), 3.07 (s, 1.78H), 2.45 (s, 1.8H), 2.27 (s, 3H), 2.18 (s, 1.2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 146.34, 143.8, 133.1, 132.2, 131.5, 130.3, 127.3, 123.9, 67.8, 63.3, 35.0, 33.2, 21.8, 10.8. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{13}H_{16}BrN_4O$ 323.0502, found 323.0504.

***N*-((4-(2,4-Dichlorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylformamide (3l).** Light yellow oil (89%, 116 mg).^{1}H NMR (600 MHz, $CDCl_3$): δ 8.39 (s, 0.65H), 8.09 (s, 0.21H), 7.45−7.41(m, 1H), 7.27−7.20 (m, 2H), 5.79 (d, J = 1.2 Hz, 0.54H), 5.63 (d, J = 1.2 Hz, 1.54H), 2.95 (d, J = 1.2 Hz, 0.77H), 2.87 (d, J = 1.2 Hz, 2.18H), 2.18 (d, J = 1.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.9, 162.7, 144.2, 143.9, 143.7, 135.4, 135.3, 134.4, 132.4, 129.6, 128.2, 128.0, 127.0, 66.8, 60.5, 33.5, 29.4, 10.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{13}Cl_2N_4O$ 299.0461, found 299.0465.

***N*-((4-(2,4-dichlorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3m).** Light yellow oil (80%, 110 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 (d, J = 9.0 Hz, 1H), 7.35−7.27 (m, 2H), 5.90 (s, 0.82H), 5.76 (s, 1.05H), 3.10 (s, 1.32H), 3.05 (s, 1.73H), 2.43 (s, 1.68H), 2.25 (s, 3H), 2.16 (s, 1.3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.4, 143.9, 143.6, 135.5, 135.3, 134.6, 132.6, 132.5, 129.8, 128.6, 128.3, 127.1, 67.6, 63.4, 35.2, 33.2, 21.8, 10.8. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{13}H_{15}Cl_2N_4O$ 313.0617, found 313.0624.

***N*-((4-Bromo-5-phenyl-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylformamide (3n).** Light yellow solid (91%, 118 mg). Mp: 68−70 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.46 (s, 0.73H), 8.16 (s, 0.27H), 7.90 (d, J = 7.2 Hz, 2H), 7.48−7.40 (m, 3H), 5.87 (s, 0.61H), 5.70 (s, 1.66H), 3.05 (s, 0.86H), 2.95 (s, 2.25H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.9, 146.8, 146.3, 129.2, 129.0, 128.7, 128.6, 128.5, 128.3, 127.3, 121.4, 121.0, 67.6, 61.3, 33.7, 29.6. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{11}H_{12}BrN_4O$ 295.0189, found 295.0186.

***N*-((4-Bromo-5-(2-chlorophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylformamide (3o).** White semisolid (92%, 117 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (s, 0.73H), 8.19 (s, 0.29H), 7.55−7.49 (m, 1H), 7.45−7.34 (m, 3H), 5.92 (s, 0.62H), 5.76 (s, 1.48H), 3.08 (s, 0.83H), 2.99 (s, 2.2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 146.5, 134.0, 131.8, 130.9, 130.1, 127.4, 126.7, 124.4, 124.0, 67.8, 61.5, 33.9, 29.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{11}H_{11}BrClN_4O$ 328.9799, found 328.9800.

***N*-((4-Bromo-5-(2-chlorophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3p).** Colorless oil (82%, 109 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.49 (m, 1H), 7.46−7.32 (m, 3H), 5.96 (s, 1H), 5.83 (s, 1.07H), 3.16 (s, 1.52H), 3.08 (s, 1.62H), 2.44 (s, 1.62H), 2.19 (s, 1.49H).^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 171.2, 146.0, 145.7, 134.0, 131.9, 131.7, 130.8, 130.7, 130.1, 130.0, 127.9, 127.5, 126.7, 126.6, 123.9, 123.5, 68.5, 64.4, 35.4, 33.3, 21.7, 21.6. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{13}BrClN_4O$ 342.9956, found 342.9962.

***N*-((4-Bromo-5-(2-bromophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylformamide (3q).** White solid (91%, 112 mg). Mp: 78−80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 0.75H), 8.19 (s, 0.28H), 7.71 (d, J = 7.2 Hz, 1H), 7.46−7.30 (m, 3H), 5.93 (s, 0.6H), 5.76 (s, 1.54H), 3.08 (s, 0.88H), 2.99 (s, 2.27H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 147.8, 133.2, 131.9, 131.1, 129.4, 127.3, 124.3, 123.7, 67.8, 29.6. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{11}H_{11}Br_2N_4O$ 372.9294, found 372.9290.

***N*-((4-Bromo-5-(2-bromophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3r).** Colorless oil (84%, 108 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75−7.65 (m, 1H), 7.43−7.38 (m, 2H), 7.37−7.30 (m, 1H), 5.97 (s, 1H), 5.84 (s, 1.11H), 3.15 (s, 1.51H), 3.08 (s, 1.65H), 2.44 (s, 1.66H), 2.19 (s, 1.52H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 171.4, 147.3, 146.9, 133.2, 131.9, 130.9, 129.89, 129.6, 127.2, 123.9, 123.6, 123.4, 77.3, 68.5, 64.4, 35.4, 33.3, 29.5, 21.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{13}Br_2N_4O$ 386.9451, found 386.9449.

***N*-((4-Bromo-5-(4-chlorophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylformamide (3s).** White solid (86%, 110 mg). Mp: 65−66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 0.71H), 8.18 (s, 0.28H), 7.94−7.81 (m, 2H), 7.49−7.37 (m, 2H), 5.88 (s, 0.59H), 5.72 (s, 1.46H), 3.08 (s, 0.88H), 2.97 (s, 2.16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 145.9, 145.4, 135.3, 128.9, 128.6, 126.9, 121.5, 121.0, 67.8, 61.5, 33.8, 29.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{11}H_{11}BrClN_4O$ 328.9799, found 328.9797.

***N*-((4-Bromo-5-(4-chlorophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3t).** White solid (81%, 108 mg). Mp: 89−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98−7.76 (m, 2H), 7.53−7.33 (m, 2H), 5.92 (s, 1H), 5.80 (s, 1H), 3.16 (s, 1.47H), 3.06 (s, 1.46H), 2.44 (s, 1.5H), 2.18 (s, 1.53H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 171.2, 145.5, 145.0, 135.3, 135.0, 128.7, 127.3, 127.0, 121.0, 120.6, 68.5, 64.5, 35.6, 33.3, 21.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{13}BrClN_4O$ 342.9956, found 342.9959.

***N*-((4-Bromo-5-(2,4-dichlorophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylacetamide (3u).** Colorless oil (87%, 112 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, J = 7.2, 1.6 Hz, 1H), 7.40−7.32 (m, 2H), 5.95 (s, 1H), 5.83 (s, 1H), 3.16 (s, 1.5H), 3.07 (s, 1.5H), 2.43 (s, 1.5H), 2.19 (s, 1.5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 171.2, 145.0, 144.7, 136.3, 136.1, 134.9, 132. 6, 130.0, 127.1, 126.5, 126.1, 123.9, 123.5, 68.6, 64.6, 35.5, 33.3, 21.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{12}H_{12}BrCl_2N_4O$ 376.9566, found 376.9561.

5-(4-(2-Bromophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-1-methylpyrrolidin-2-one (3v). Light yellow oil (82%, 115 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, J = 7.8 Hz, 1H), 7.38 (q, J = 7.2 Hz, 1H), 7.36−7.32 (m, 1H), 7.32−7.27 (m, 1H), 5.98 (m, 1H), 2.97−2.90 (m, 1H), 2.75 (s, 3H), 2.63−2.56 (m, 2H), 2.48 (m, 1H), 2.26 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.1, 146.1, 143.6, 133.0, 131.7, 130.3, 127.2, 123.7, 76.8, 28.9, 27. 4, 24.9, 10.7. HRMS (ESI-FTMS): m/z $[M + H]^+$ calcd for $C_{14}H_{16}BrN_4O$ 335.0502, found 335.0501.

5-(4-(2-Bromo-4-fluorophenyl)-5-methyl-2*H*-1,2,3-triazol-2-yl)-1-methylpyrrolidin-2-one (3w). Colorless oil (92%, 254 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.38 (m, 1H), 7.32−7.25 (m, 1H), 7.12−7.05 (m, 1H), 5.94 (dd, J = 7.2, 2.4 Hz, 1H), 2.97−2.83 (m, 1H), 2.71 (s, 3H), 2.62−2.52 (m, 2H), 2.51−2.41 (m, 1H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 163.7, 161.2, 145.3, 143.7, 132.7, 132.6, 127.93, 127.90, 124.2, 124.1, 120.5, 120.2, 114.7, 114.5, 78.5, 28.9, 27.5, 24.9, 10.7. HRMS (ESI-FTMS): m/z $[M + Na]^+$ calcd for $C_{14}H_{14}BrFN_4NaO$ 375.0227, found 375.0223.

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5-(4-Bromo-5-phenyl-2*H*-1,2,3-triazol-2-yl)-1-methylpyrrolidin-2-one (3x). White solid (90%, 258 mg). Mp: 116−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, J = 8.4, 1.6 Hz, 2H), 7.51−7.38 (m, 3H), 5.99 (dd, J = 7.6, 1.6 Hz, 1H), 2.99−2.85 (m, 1H), 2.78 (s, 3H), 2.68−2.56 (m, 1H), 2.55−2.44 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 146.3, 129.2, 128.63, 128.57, 127.3, 120.9, 79.6, 28.7, 27.7, 25.1. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{13}H_{13}BrN_4NaO$ 343.0165, found 343.0158.

5-(4-Benzoyl-5-phenyl-2*H*-1,2,3-triazol-2-yl)-1-methylpyrrolidin-2-one (3y). White solid (89%, 247 mg). Mp: 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10−7.97 (m, 2H), 7.80 (dd, J = 6.4, 3.2 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.42−7.37 (m, 3H), 6.10 (dd, J = 7.6, 1.6 Hz, 1H), 3.00−2.87 (m, 1H), 2.82 (s, 3H), 2.73−2.62 (m, 1H), 2.62−2.46 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.6, 175.1, 150.2, 142.5, 136.9, 133.5, 130.3, 129.3, 129.1, 128.6, 128.4, 128.3, 79.6, 28.6, 27.8, 25.3. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{20}H_{18}N_4NaO_2$ 369.1322, found 369.1328.

***N*-((4-Benzoyl-5-phenyl-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylformamide (3z).** White solid (85%, 218 mg). Mp: 116−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 8.18 (s, 1H), 7.58−7.52 (m, 4H), 7.39−7.33 (m, 6H), 5.94 (s, 1H), 5.75 (s, 2H), 3.07 (s, 1H), 3.01 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 162.7, 145.8, 145.3, 130.4, 130.2, 128.6, 128.5, 128.42, 128.40, 128.2, 128.1, 67.0, 60.7, 33.6, 29.6. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{18}H_{16}N_4NaO_2$ 343.1166, found 343.1169.

5-(4,5-Diphenyl-2*H*-1,2,3-triazol-2-yl)-1-methylpyrrolidin-2-one (3aa). Light yellow solid (89%, 256 mg). Mp: 92−94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57−7.52 (m, 4H), 7.40−7.35 (m, 6H), 6.06 (dd, J = 6.8, 2.8 Hz, 1H), 3.04−2.93 (m, 1H), 2.83 (s, 3H), 2.68−2.58 (m, 2H), 2.56−2.46 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 145.4, 130.5, 128.59, 128.55, 128.2, 78.9, 28.9, 27.7, 25.2. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{19}H_{18}N_4NaO$ 341.1373, found 341.1379.

5-(4-(2-Bromophenyl)-5-phenyl-2*H*-1,2,3-triazol-2-yl)-1-methylpyrrolidin-2-one (3ab). White solid (92%, 243 mg). Mp: 128−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, J = 8.0, 0.8 Hz, 1H), 7.50−7.41 (m, 2H), 7.43−7.36 (m, 2H), 7.34−7.24 (m, 4H), 6.07 (t, J = 4.8 Hz, 1H), 3.05−2.92 (m, 1H), 2.81 (s, 3H), 2.72−2.60 (m, 2H), 2.56−2.46 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 146.0, 144.5, 133.2, 132.4, 131.8, 130.6, 130.1, 128.54, 128.47, 127.5, 126.8, 124.2, 79.0, 28.9, 27.6, 25.0. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{19}H_{17}BrN_4NaO$ 419.0478, found 419.0483.

***N*-((4,5-Diphenyl-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylformamide (3ac).** White solid (87%, 229 mg). Mp: 105−107 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (s, 1H), 8.17 (s, 1H), 8.03 (dd, J = 16.5, 7.5 Hz, 2H), 7.79−7.76 (m, 2H), 7.59 (d, J = 7.5 Hz, 1H), 7.50−7.43 (m, 2H), 7.43−7.34 (m, 3H), 5.96 (s, 1H), 5.79 (s, 1H), 3.07 (s, 1H), 2.99 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.6,187.5, 162.9, 162.8, 150.4, 150.1, 143.0, 142.6, 136.8, 136.7, 133.6, 133.5, 130.3,130.2, 129.3, 129.2, 129.1, 128.9, 128.6, 128.5, 128.4, 128.32, 128.27, 67.6, 61.3, 33.8, 29.6. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{17}H_{16}N_4NaO$ 315.1206, found 315.1208.

***N*-((4-Bromo-5-(2-bromophenyl)-2*H*-1,2,3-triazol-2-yl)-methyl)-*N*-methylformamide (3q′).** White solid (5%, 61 mg). Mp: 196−198 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 (s, 0.38H), 7.80 (dd, J = 7.8, 1.2 Hz, 0.57H), 7.74 (dd, J = 7.8, 1.2 Hz, 0.37H), 7.55−7.42 (m, 2.54H), 7.29−7.26 (m, 1.16H), 5.77 (d, J = 13.8 Hz, 0.4H), 5.69 (d, J = 4.8 Hz, 0.42H), 5.67 (d, J = 5.4 Hz, 0.56H), 5.62 (d, J = 14.4 Hz, 0.59H), 2.98 (s, 1.20H), 2.79 (s, 1.77H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 161.8, 161.5, 135.6, 135.1, 133.7, 133.2, 132.8, 132.3, 132.0, 131.7, 128.4, 127.9, 126.0, 125.9, 124.4, 124.2, 122.7, 122.4, 62.9, 56.1, 33.4, 29.1. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{11}H_{11}Br_2N_4O$ 372.9294, found 372.9288.

***N*-Methyl-*N*-((4-phenyl-2*H*-1,2,3-triazol-2-yl)methyl)-formamide (4a).** Light yellow solid (64%, 89 mg). Mp: 58−60 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.50 (s, 0.74H), 8.16 (s, 0.26H), 7.90 (d, J = 3.6 Hz, 1H), 7.79 (d, J = 1.2 Hz, 1H), 7.43 (q, J = 7.2 Hz, 2H), 7.38 (d, J = 7.2 Hz, 1H), 5.92 (s, 0.57H), 5.75 (s, 1.4H), 3.02 (s, 0.76H), 2.94 (s, 2.25H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.9, 162.6, 159.8, 148.5, 131.5, 131.2, 127.0, 126.9, 122.0, 114.0, 66.7, 60.3, 54.9, 33.2, 29.1. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{11}H_{12}N_4NaO$ 239.0903, found 239.0900.

***N*-Methyl-*N*-((4-phenyl-2*H*-1,2,3-triazol-2-yl)methyl)-acetamide (4b).** Colorless oil (50%, 76 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.79 (t, J = 7.8 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.37 (s, 1H), 5.97 (s, 0.91H), 5.82 (s, 1.01H), 3.11 (s, 1.42H), 3.05 (s, 1.4H), 2.47 (s, 1.48H), 2.16 (s, 1.46H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.2, 159.9, 159.8, 148.4, 148.0, 131.2, 127.2, 122.5, 122.3, 114.1, 67.5, 63.4, 55.1, 35.1, 33.0, 21.5. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{12}H_{14}N_4NaO$ 253.1060, found 253.1056.

***N*-Methyl-*N*-((4-(*p*-tolyl)-2*H*-1,2,3-triazol-2-yl)methyl)-acetamide (4c).** Light yellow solid (59%, 86 mg). Mp: 84−86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.74−7.58 (m, 2H), 7.30−7.15 (m, 2H), 5.96 (s, 0.89H), 5.82 (s, 0.98H), 3.11 (s, 1.26H), 3.05 (s, 1.31H), 2.47 (s, 1.4H), 2.39 (d, J = 3.2 Hz, 3H), 2.17 (s, 1.32H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.0, 135.4, 133.7, 130.9, 130.1, 129.9, 127.6, 121.9, 67.1, 60.8, 33.6, 29.6. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{13}H_{16}N_4NaO$ 267.1216, found 267.1212.

***N*-((4-(4-Methoxyphenyl)-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylacetamide (4d).** Light yellow solid (47%, 67 mg). Mp: 81−83 °C. ^{1}H NMR (600 MHz, CDCl3): δ 7.81 (s, 1H), 7.71 (t, J = 7.8 Hz, 2H), 6.95 (t, J = 7.8 Hz, 2H), 5.94 (s, 0.85H), 5.79 (s, 1.13H), 3.82 (d, J = 4.2 Hz, 3H), 3.10 (s, 1.29H), 3.04 (s, 1.6H), 2.45 (s, 1.59H), 2.15 (s, 1.26H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.9, 162.6, 148.8, 138.5, 131.9, 129.3, 129.2, 126.6, 125.6, 66.8, 60.4, 33.3, 29.2, 21.0. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{13}H_{16}N_4NaO_2$ 283.1166, found 283.1161.

***N*-((4-(2-Bromophenyl)-2*H*-1,2,3-triazol-2-yl)methyl)-*N*-methylacetamide (4e).** Light yellow solid (57%, 78 mg). Mp: 92−94 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.78−7.64 (m, 2H), 7.40−7.36 (m, 1H), 7.28−7.20 (m, 7.4 Hz, 1H), 5.99 (s, 0.9H), 5.86 (s, 1H), 3.14 (s, 1.38H), 3.07 (s, 1.41H), 2.47 (s, 1.38H), 2.17 (s, 1.37H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 148.7, 148.3, 131.9, 128.8, 128.6, 126.0, 67.8, 63.6, 35.2, 33.2, 21.7. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{12}H_{14}BrN_4O$ 309.0346, found 309.0343.

Mixture of N^1 [*N*-Methyl-*N*-((4-phenyl-1*H*-1,2,3-triazol-1-yl)-methyl)formamide] and $N^{1'}$ [*N*-Methyl-*N*-((5-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)formamide] Products (5a). Yield: 25 mg (18%). Ratio $N^{1'}$:N^1 = 1:3 (based on ^{1}H NMR).

***N*-Methyl-*N*-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-acetamide (5b).** Light yellow oil (25%, 38 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.29 (t, J = 7.8 Hz, 2H), 7.21 (t, J = 7.8 Hz, 1H), 5.72 (s, 2H), 3.03 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.8, 147.9, 130.1, 128.6, 128.0, 125.8, 125.5, 125.4, 120.4, 59.9, 35.6, 21.4. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{12}H_{14}N_4NaO$ 253.1060, found 253.1058.

***N*-Methyl-*N*-((4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)methyl)-acetamide (5c).** Light yellow oil (21%, 31 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.22 (d, J = 7.2 Hz, 2H), 5.84 (s, 2H), 3.16 (s, 3H), 2.36 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.0, 148.3, 138.0, 129.5, 129.4, 127.4, 125.9, 125.8, 125.5, 120.1, 60.0, 35.7, 21.5, 21.2. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{13}H_{16}N_4NaO$ 267.1216, found 267.1215.

***N*-((4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-*N*-methylacetamide (5d).** Light yellow oil (27%, 38 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.75 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 5.83 (s, 2H), 3.83 (s, 3H), 3.16 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.0, 159.6, 148.0, 127.2, 126.9, 122.9, 119.6, 114.2, 114.1, 60.0, 55.2, 35.7, 21.5. HRMS (ESI-FTMS): m/z [M + Na]$^+$ calcd for $C_{13}H_{16}N_4NaO_2$ 283.1166, found 283.1164.

***N*-((4-(2-Bromophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-*N*-methylacetamide (5e).** Light yellow oil (20%, 27 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.10−8.04 (m, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.39 (d, J = 7.2 Hz, 1H), 7.19 (d, J = 0.6 Hz, 1H), 5.89 (s, 2H), 3.20 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.9, 145.8, 133.5, 131.1, 130.5, 129.4, 127.5, 123.9, 121.3, 60.1, 35.8, 21.6. HRMS (ESI-FTMS): m/z [M + H]$^+$ calcd for $C_{12}H_{14}BrN_4O$ 309.0346, found 309.0343.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00752.

^{1}H and ^{13}C NMR spectra of the synthesized compounds (PDF)

Crystallographic data for compound **3q** (CIF)

Crystallographic data for compound **3q′** (CIF)

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Notes

The authors declare no competing financial interest.

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(19) To a solution of 4-bromo-5-(2-bromophenyl)-1*H*-1,2,3-triazole (1 g, 3.3 mmol) in DMF (20 mL) were added $Cu(OAc)_2$ (132 mg, 0.66 mmol), $K_2S_2O_8$ (1.78 g, 6.6 mmol), and Na_2CO_3 (0.38 g, 3.6 mmol). The mixture was stirred at 110 °C for 12 h. The isomer **3q′** was separated by silica gel chromatography from the mixture products in 5% yield.
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