JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 30 Mar 2018

Just Accepted

ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Copper(I)-catalyzed synthesis of 1,4-disubstituted 1,2,3-triazoles from azidoformates and aryl terminal alkynes

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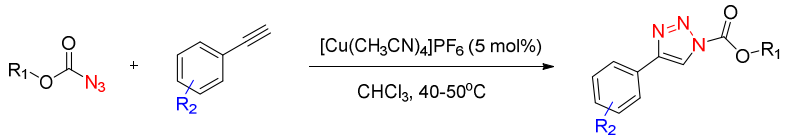
ABSTRACT

The copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction has been extensively studied and widely applied in organic synthesis. However, the formation of 1,2,3-triazoles with electron-deficient azide has been a challenging problem. In this report, we have demonstrated the formation of regioselective 1,4-disubstituted 1,2,3-triazoles from various types of aryl terminal alkynes and azidoformates, which are electron-deficient azides, using a commercialized $[Cu(CH_3CN)_4]PF_6$ copper(I) catalyst under mild conditions.



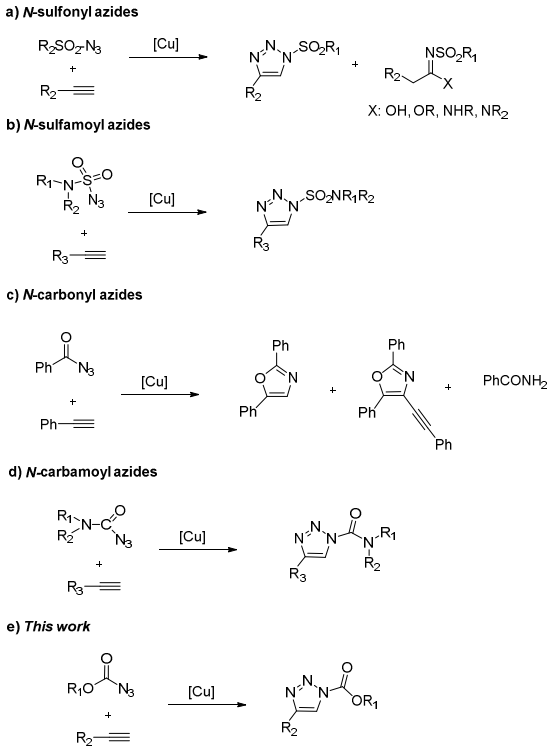
Due to the discovery of the copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction, the "click" reaction,[1] the synthesis process for 1,2,3-triazoles has been significantly advanced. The classical thermal Huisgen cycloaddition[2] proceeds very slowly even at high temperatures, and produces a 1,4- and 1,5-disubstituted 1,2,3-triazoles mixture. In 2002, the group of Medal[3] and Sharpless[4] discovered the copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction. In CuAAC, 1,2,3-triazole are formed with a copper(I) salt catalyst,[3,4] which improves both the selectivity and the reaction rate. Synthesis of 1,2,3-triazoles has been conducted in a wide range of organic solvents, including water and at room temperature. Although these heterocycles do not take place naturally, the 1,2,3-triazoles have various biological activities.[5] The CuAAC reaction has found valuable applications in a variety of fields.[6]

Most CuAAC reactions are limited to alkyl or aryl azides. It is usually hard for an electron-deficient azide to react with terminal alkynes to produce a triazole ring in the presence of copper catalysts. To date, only a few research groups have reported the 1,2,3-triazole formation with electron-deficient azides such as *N*-sulfonyl, *N*-sulfamoyl, and *N*-carbamoyl azides (Scheme 1).[7-12]

When *N*-sulfonyl azides react with terminal alkynes in the presence of copper catalysts, they not only form acyclic N-containing compounds such as amidine, but they also form triazole rings. *N*-Sulfonyl triazoles may then undergo a ring-opening process via the ketenimine species occurring due to the loss of nitrogen gas from the *N*-sulfonyl triazolyl copper intermediate.[7]

Next, *N*-sulfamoyl triazoles are obtained when *N*-sulfamoyl azides react with terminal alkynes under the specific copper catalyst thiophene-2-carboxylate, i.e., Libeskind's reagent,[8] resulting in yields ranging from 82% to 95%.[9]

Pérez and his co-workers developed a well-defined copper-based catalytic system, $[CuTpm^{*,Br}(CH_3CN)]BF_4$ ($Tpm^{*,Br}$=tris(3,5-dimethyl-4-bromo-pyrazolyl)methane), which promotes the exclusive synthesis of *N*-sulfonyl triazoles in high yields under mild conditions.[10] When this catalyst was used for the formation of *N*-carbonyl triazoles from *N*-carbonyl azides, two types of oxazole derivatives were unexpectedly formed, instead of the expected triazole rings.[11] One was a 2,5-disubstituted oxazole, and the other was a trisubstituted oxazole. In further studies, they solely investigated the synthesis of 2,5-disubstituted oxazole derivatives in presence of the $[CuTpa^*]PF_6$ (Tpa=tris(pyrazolylmethyl)amine).[12] Based on experimental data and mechanistic studies, this catalytic system was a more active and selective. The intermediate nitrene copper species was formed via the loss of nitrogen gas.[13] They also observed the formation of *N*-carbamoyl triazoles from *N*-carbamoyl azides and terminal alkynes in the presence of $[CuTpa^*]PF_6$. That is because the N-C(O)-N moiety delocalizes the electronic density. The loss of nitrogen gas and the formation of the copper-nitrene intermediate are interrupted because of the conjugation effect.[14] In our study, we achieved direct formation of regioselective 1,4-disubstituted 1,2,3-triazoles from various azidoformates and aryl terminal alkynes using the commercialized copper(I) catalyst, $[Cu(CH_3CN)_4]PF_6$, under mild conditions. This is the first report in the literature of the reaction between electron-deficient aryl azidoformates and aryl terminal alkynes.[15]

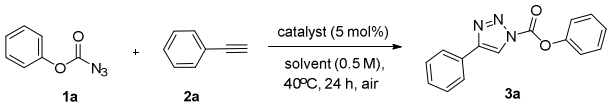


Scheme 1. Developed synthetic methods using electron-deficient azide for cycloaddition

There is a potential reaction pathway like as aryl or alkyl azides. This pathway forms the copper-acetylide intermediate that leads to the formation of the triazolyl-cuprate intermediate in equilibrium with the diazoimino species. Because of the electron-withdrawing nature of the group attached to the N_3 moiety, the diazo derivative loses N_2 with concomitant formation of acyclic products. Therefore we consider the electronic characteristics of the azidoformate. We hypothesized that the lone electron pair of the O within the N-C(O)-O bond would help increase the electron density due to conjugation effect. To explore this, we investigated the reaction of 1,2,3-triazole with phenyl azidoformate (**1a**) and phenyl acetylene (**2a**) (Table 1). We first performed the synthesis of 1,2,3-triazole **3a** without the copper catalyst, and did not obtained the product (Table 1, entry 1). The same synthesis with various commercialized copper catalysts were then tested (Table1, entries 2-10). As expected from the reactivity according to oxidation states of Cu(I) and Cu(II), the reaction proceeded only in the presence of the copper(I) catalysts. The copper(II) catalysts such as $CuSO_4 \cdot 5H_2O$, $Cu(OAc)_2$ and $Cu(OSO_2CF_3)_2$ were inefficient (Table 1, entries 3-5). Other copper catalysts, such as CuI, CuOAc, $[Cu(phen)(PPh_3)_2]NO_3 \cdot ½CH_2Cl_2$, and $[Cu(PPh)_3]Br$ were less effective (Table 1, entries 6, 8, and 9). For the synthesis of 1,2,3-triazole from electron-deficient azide, we primarily used halogenated solvents. In our experiments, chloroform showed the highest yields. With other solvents, such as 1,2-dichloroethane (DCE), **3a** was obtained in just an 8% yield (Table 1, entry 11). The conversion of 3a is lower at room temperature than at 40 ^oC (Table 1, entry 12). Overall, the [3+2] cycloaddition reaction of **1a** (1.0 mmol) and **2a** (1.0 mmol) showed the best yield (92%) using the $[Cu(CH_3CN)_4]PF_6$ (5 mol%) catalyst in $CHCl_3$ (2.0 mL) in

open air at 40 °C for 24 h (Table 1, entry 10).

Table 1. Optimization of the reaction conditions[a]



Entry	Catalyst	Solvent	Yield[b]
1	none	$CHCl_3$	trace
2[c]	$CuSO_4 \cdot 5H_2O$	$CHCl_3$	trace
3	$CuSO_4 \cdot 5H_2O$	$CHCl_3$	NR
4	$Cu(OAc)_2$	$CHCl_3$	NR
5	$Cu(OSO_2CF_3)_2$	$CHCl_3$	NR
6	CuI	$CHCl_3$	3
7	CuOAc	$CHCl_3$	trace
8	$[Cu(phen)(PPh_3)_2]NO_3 \cdot \frac{1}{2}CH_2Cl_2$	$CHCl_3$	11
9	$[Cu(PPh)_3]Br$	$CHCl_3$	54
10	$[Cu(CH_3CN)_4]PF_6$	$CHCl_3$	92
11	$[Cu(CH_3CN)_4]PF_6$	DCE	8
12[d]	$[Cu(CH_3CN)_4]PF_6$	$CHCl_3$	4

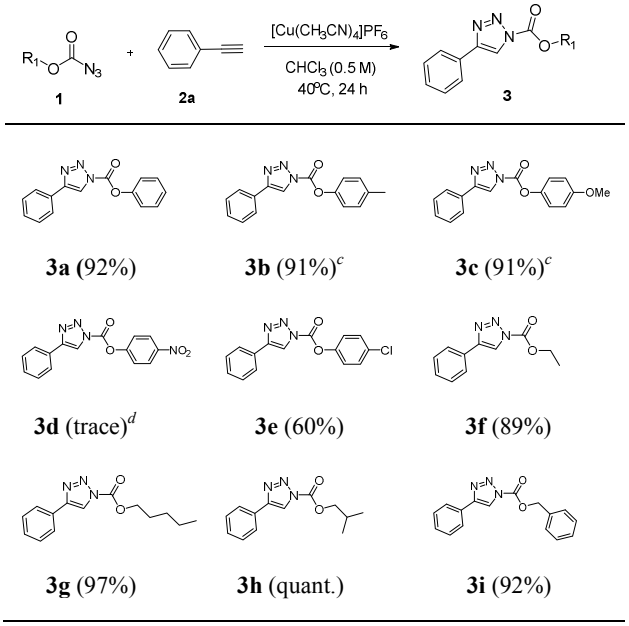
[a] *Reaction conditions*: **1a** (1mmol, 1.0 equiv.), **2a** (1 mmol, 1.0 equiv.), catalyst (5 mol%), 40 °C, 24 h in chloroform (2.0 mL, 0.5 M) under aerobic condition. [b] Yields were determined after the deprotection of carbamate moiety; NR = No Reaction. [c] Na ascorbate (10 mol%) was added. [d] This reaction was performed at room temperature.

The structure of **3a**[16] and its configuration were determined using X-ray crystal structure analysis (see ESI), and the structure of **3g** was confirmed by a 1D ^{1}H selective NOESY spectrum (included in ESI). In addition, the ^{1}H NMR spectrum of **3a** exhibited a sharp singlet peak at 8.54 ppm, which is the characteristic peak of the hydrogen at position 5 in 1,4-disubstituted 1,2,3-triazoles (see ESI for more details).

Efficient conversion of **3a** was observed with 5 mol% of $[Cu(CH_3CN)_4]PF_6$. Therefore, the scope of the copper(I)-catalyzed [3+2] cycloaddition reaction with various azidoformates **1** and terminal alkynes **2** was studied using the established optimized reaction conditions (Table 1, entry 10). All results are shown in Scheme 2. The substrates **1a-i** (Scheme 2; representing the azidoformate functional groups of phenyl **1a**, electron-donating **1b** and **1c**, electron-withdrawing **1d** and **1e**, and aliphatic **1f-i**) resulted in the corresponding 1,2,3-triazoles **3a-i** in relatively high yields except **1d**. In the case of **1d**, a strong electron-withdrawing nitro group, formation of the 1,2,3-triazole

proved difficult. This is likely due to a similar mechanism as observed in previous reports using *N*-carbonyl azides.[11]

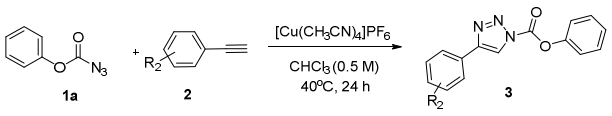
Scheme 2. Scope study for azidoformates[a,b]

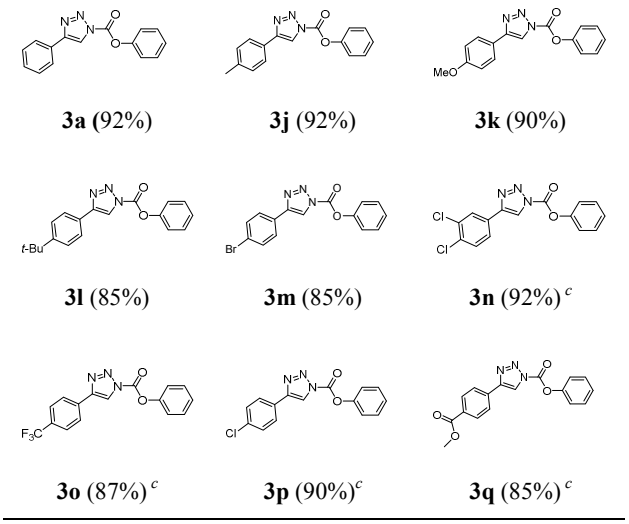


[a] *Reaction conditions*: **1** (1 mmol, 1.0 equiv.), **2a** (1 mmol, 1.0 equiv.), catalyst (5 mol%), 40 °C, 24 h in $CHCl_3$ (2.0 mL, 0.5 M). [b] Yields were determined after the deprotection of carbamate moiety. [c] This reaction was performed at 50 °C. [d] Compounds **3d** could not be isolated because of the extremely low conversion.

The reactions involving various aryl terminal alkynes also produced high yields (Scheme 3). The yield of 1,2,3-triazole products **3n-q** from electron-withdrawing terminal alkynes was relatively lower than the other compounds. Therefore, the reaction was kept at 50 °C until the starting material disappeared. At this temperature, most of the terminal alkynes had good reactivity and high yield for the synthesis of 1,2,3-triazoles. The 1,2,3-triazole products **3a-q** were unstable, so it was difficult to isolate them through column chromatography. The reaction yields were determined after the deprotection of carbamate moiety (Scheme 4). For the structural analysis of the desired products, the crude products were purified by recrystallization with chloroform and hexane.

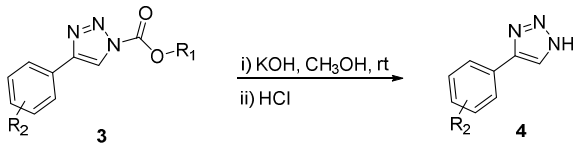
Scheme 3. Scope study for terminal alkynes[a,b]





[a] Reaction conditions: **1a** (1 mmol, 1.0 equiv.), **2** (1 mmol, 1.0 equiv.), catalyst (5 mol%), 40 °C, 24 h in $CHCl_3$ (2.0 mL, 0.5 M). [b] Yields were determined after the deprotection of carbamate moiety. [c] This reaction was performed at 50 °C.

Scheme 4. Deprotection of carbamate moiety



In conclusion, we have demonstrated the formation of regioselective 1,4-disubstituted 1,2,3-triazoles from various types of aryl terminal alkynes and azidoformates, which are electron-deficient azides, using a commercialized $[Cu(CH_3CN)_4]PF_6$ copper(I) catalyst under mild conditions. This methodology can be used to synthesize a range of bioactive triazole derivatives with electron-deficient groups.

■ EXPERIMENTAL SECTION

General information.

All reagents and catalysts were purchased from commercial sources (Sigma Aldrich, TCI) and used without any further purification, unless specifically mentioned. ^{1}H and ^{13}C NMR were recorded on a Bruker 400 MHz instrument using $CDCl_3$ as a NMR solvent. Infrared spectroscopic data were obtained using a Bruker FT-IR spectrometer. HRMS analyses with EI-double focusing or FAB-double focusing mode (JMS-700) were performed at the Daegu center of Korea Basic Science Institute. X-ray measurements were taken on a Rigaku R-AXIS RAPID diffractometer using graphite monochromated Mo-Ka radiation.

General Procedure for Azidoformate from Chloroformate (1a-1i)[17a]

Chloroformate (20 mmol, 1.0 equimolar) was added to a well-stirred suspension of NaN_3 (1.2 equimolar) in acetone (40 mL) at room temperature. After the reaction finished, the mixture was then poured into a celite pad. The filtrate was collected and concentrated by rotary evaporation to isolate the product. In case of the synthesis of 4-chlorophenyl azidoformate, the reaction was carried out with THF as the solvent.

Phenyl azidoformate (**1a**).[17b] Colorless oil; yield: 2.52 g (77%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (t, J = 8.0 Hz, 2H), 7.27 (t, J = 7.8 Hz, 1H), 7.18 (d, J = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 150.6, 129.6, 126.6, 120.8; IR (neat): 2157, 1734, 1492, 1196, 953, 731 cm^{-1}.

p-Tolyl azidoformate (**1b**).[17c] Colorless oil; yield: 3.46 g (98%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, J = 8.2 Hz, 2H), 7.05 (t, J = 8.6 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 148.5, 136.4, 130.1, 120.6, 20.8; IR (neat): 2154, 1737, 1505, 1216, 1188, 737 cm^{-1}.

4-Methoxyphenyl azidoformate (**1c**).[17d] Colorless oil; yield: 3.55 g (92%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, J = 9.2 Hz, 2H), 6.89 (d, J = 9.1 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 156.7, 144.2, 121.8, 114.5, 55.5; IR (neat): 2152, 1736, 1504, 1238, 1195, 737 cm^{-1}.

4-Nitrophenyl azidoformate (**1d**).[17e] White solid; yield: 1.25 g (30%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 9.2 Hz, 2H), 7.40 (d, J = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 154.8, 145.8, 125.4, 121.9; IR (neat): 2170, 1736, 1522, 1470, 1209, 858, 743 cm^{-1}.

4-Chlorophenyl azidoformate (**1e**).[17c] White solid; yield: 786 mg (20%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 9.0 Hz, 2H), 7.13 (d, J = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 149.0, 132.1, 129.7, 122.3; IR (neat): 2156, 1736, 1486, 1208, 1084, 828, 735 cm^{-1}.

Ethyl azidoformate (**1f**).[17f] Colorless oil; yield: 1.45 g (63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.28 (q, J = 7.2 Hz, 2H), 1.33 (t, J =7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 64.7, 14.1; IR (neat): 2133, 1725, 1368, 1219, 1021, 751 cm^{-1}.

Amyl azidoformate (**1g**).[17g] Colorless oil; yield: 3.08 g (98%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21 (t, *J* = 6.7 Hz, 2H), 1.69 (quint, *J* = 7.0 Hz, 2H), 1.37-1.32 (m, 4H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 69.0, 28.3, 27.9, 22.4, 14.1; IR (neat): 2133, 1727, 1219, 751 cm^{-1}.

Isobutyl azidoformate (**1h**).[17a] Colorless oil; yield: 2.81 g (98%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.00 (d, *J* = 6.7 Hz, 2H), 2.00 (n, *J* = 6.7Hz, 1H), 0.96 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 74.5, 27.7, 18.8; cm^{-1}; IR (neat): 2136, 1726, 1221, 993, 752 cm^{-1}.

Benzyl azidoformate (**1i**).[17h] Colorless oil; yield: 3.44 g (97%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (s, 2H), 5.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 134.4, 128.9, 128.7, 128.6, 70.1; IR (neat): 2137, 1723, 1219, 958, 745, 695 cm^{-1}.

General Procedure for [3+2] Cycloaddtion of Alkyne and Azidoformate (3a-3q)

The catalyst (18.6 mg, 0.05 mmol, 5 mol%) and azidoformate (1.0 mmol) were dissolved in Chloroform (2.0 mL) in 10 mL round-bottom flask. The alkyne (1.0 mmol) was added to the solution. The reaction mixture was stirred at 40-50 °C for 24h until the starting material disappeared. The reaction crude was extracted with dichloromethane and distilled-water. After drying over $MgSO_4$, the mixture was poured into a celite pad. The solvent was evaporated under reduced pressure. For the structural analysis of the desired products **3**, the crude products were purified by recrystallization with chloroform and hexane.

Phenyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3a**). White solid; yield: 244 mg (92%); m.p. 121-123 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 7.94 (d, *J* = 7.0 Hz, 2H), 7.53-7.47 (m, 4H), 7.45-7.37 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 148.4, 146.5, 130.2, 129.4, 129.3, 129.1, 127.5, 126.4, 121.1, 119.6; IR (neat): 3156, 1780, 1424, 1263, 1210, 742, 686 cm^{-1}; HRMS(EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{15}H_{11}N_3O_2$ 265.0851; found 265.0849.

p-Tolyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3b**). White solid; yield: 254 mg (91%); m.p. 139-140 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.93 (d, *J* = 6.8 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.41 (td, *J* = 7.3, 1.2 Hz, 1H), 7.29-7.22(m, 4H), 2.40(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 147.9, 146.4, 137.2, 130.4, 129.2, 129.1, 128.9, 126.2, 120.6, 119.4; IR (neat): 3148, 3064, 2920, 1775, 1423, 1230, 1002, 766 cm^{-1}; HRMS(EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{16}H_{13}N_3O_2$ 279.1008; found 279.1006.

4-Methoxyphenyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3c**). White solid; yield: 269 mg (91%); m.p. 152.7-153 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (s, 1H), 7.92 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.0 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 9.1 Hz, 2H), 6,98 (d, *J* = 9.1 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 148.2, 146.6, 143.5, 129.2, 129.1, 128.9, 126.2, 121.8, 119.4, 114.8, 55.7; IR (neat): 3148, 2931, 1771, 1505, 1419, 1178, 994, 769 cm^{-1}; HRMS(EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{16}H_{13}N_3O_3$ 295.0957; found 295.0959.

4-Chlorophenyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3e**). White solid; yield: 180 mg (60%); m.p. 122-123.8 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (s, 1H), 7.93 (d, *J* = 7.0 Hz, 2H), 7.51-7.40 (m, 5H), 7.33 (d, *J* = 8.9 Hz,

2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 148.3, 146.0, 132.9, 130.0, 129.3, 129.0, 128.7, 126.2, 122.3, 119.3; IR (neat): 3150, 3077, 1777, 1428, 1260, 1070, 743 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{15}H_{10}ClN_3O_2$ 299.0462; found 299.0465.

Ethyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3f**). White solid; yield: 193 mg (89%); m.p. 86.1-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, 1H), 7.89 (d, *J* = 7.0 Hz, 2H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 4.65 (q, *J* = 7.2 Hz, 2H), 1.54 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1, 147.8, 129.3, 129.3, 129.2, 126.4, 119.3, 66.2, 14.4; IR (neat): 3155, 2984, 1759, 1455, 1270, 1003, 762 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{11}H_{11}N_3O_2$ 217.0851; found 217.0853.

Pentyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3g**). White solid; yield: 252 mg (97%); m.p. 59.8-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.89 (d, *J* = 7.0 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 4.57 (t, *J* = 6.8 Hz, 2H), 1.89 (qunit, *J* = 6.8 Hz, 2H), 1.50-1.36 (m, 4H), 0.94 (t, *J* = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.0, 147.9, 129.3, 129.2, 127.0, 126.3, 119.3, 70.1, 28.3, 27.9, 22.4, 14.1; IR (neat): 3155, 2969, 1753, 1427, 1271, 1002, 761 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{14}H_{17}N_3O_2$ 259.1321; found 259.1320.

Isobutyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3h**). White solid; yield: 245 mg (Quant.); m.p. 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.90 (d, *J* = 7.7 Hz, 2H), 7.49-7.38 (m, 3H), 4.36 (d, *J* = 6.8 Hz, 2H), 2.22 (n, *J* = 6.8 Hz, 1H), 1.08 (d, *J* = 6.7, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.8, 129.1, 129.0, 129.0, 126.1, 126.1, 119.0, 75.4, 27.8, 18.9; IR (neat): 3152, 2973, 1764, 1426, 1225, 1002, 759 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{13}H_{15}N_3O_2$ 245.1164; found 245.1165.

Benzyl 4-phenyl-1H-1,2,3-triazole-1-carboxylate (**3i**). White solid; yield: 257 mg (92%); m.p. 118-119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (s, 1H), 7.88 (d, *J* = 7.0 Hz, 2H), 7.54-7.51 (m, 2H), 7.48-7.37 (m, 6H), 5.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 147.6, 133.5, 129.4, 129.1, 129.1, 129.0, 129.0, 128.9, 126.2, 119.2, 71.1; IR (neat): 3134, 2974, 1768, 1404, 1210, 1009, 690 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{16}H_{13}N_3O_2$ 279.1008; found 279.1012.

Phenyl 4-(p-tolyl)-1H-1,2,3-triazole-1-carboxylate (**3j**). White solid; yield: 257 mg (92%); m.p. 117.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.50 (t, *J* = 8.4 Hz, 2H), 7.40-7.35 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 148.3, 146.3, 139.3, 130.0, 129.8, 129.8, 127.3, 126.1, 126.1, 120.9, 119.0, 21.4; IR (neat): 3134, 1769, 1405, 1204, 1022, 743 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{16}H_{13}N_3O_2$ 279.1008; found 279.1008.

Phenyl 4-(4-methoxyphenyl)-1H-1,2,3-triazole-1-carboxylate (**3k**). White solid; yield: 266 mg (90%); m.p. 162-163 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.86 (d, *J* = 8.7 Hz, 2H), 7.52-7.48 (m, 2H), 7.40-7.36 (m, 3H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 150.0, 148.1, 146.3, 130.0, 127.6,

127.3, 121.5, 120.9, 118.3, 114.5, 55.4; IR (neat): 3150, 2958, 1777, 1358, 1189, 1112, 994, 752 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{16}H_{13}N_3O_3$ 295.0957; found 295.0959.

Phenyl 4-(4-(tert-butyl)phenyl)-1H-1,2,3-triazole-1-carboxylate (**3l**). Ivory solid; yield: 273 mg (85%); m.p. 112-114 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.52-7.47 (m, 4H), 7.40-7.35 (m, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 150.0, 148.2, 146.3, 130.0, 127.3, 126.1, 126.0, 126.0, 121.0, 119.0, 32.8, 31.3; IR (neat): 3175, 2963, 1760, 1427, 1222, 989, 743 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{19}H_{19}N_3O_2$ 321.1477; found 321.1480.

Phenyl 4-(4-bromophenyl)-1H-1,2,3-triazole-1-carboxylate (**3m**). White solid; yield: 293 mg (85%); m.p. 163-165 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (s, 1H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.53-7.48 (m, 2H), 7.40-7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 147.2, 146.1, 132.3, 130.0, 127.8, 127.7, 127.4, 123.4, 120.9, 119.6; IR (neat): 3148, 1779, 1427, 1259, 811, 741 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{15}H_{10}BrN_3O_2$ 342.9956; found 342.9958.

Phenyl 4-(3,4-dichlorophenyl)-1H-1,2,3-triazole-1-carboxylate (**3n**). White solid; yield: 307 mg (92%); m.p. 137.5-139 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.05 (d, *J*=2.0 Hz, 1H), 7.77 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.57-7.48 (m, 3H), 7.41-7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 149.9, 146.1, 133.5, 133.3, 131.1, 130.0, 128.9, 128.0, 127.5, 125.3, 120.8, 120.0; IR (neat): 3134, 1784, 1426, 1226, 1011, 749 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{15}H_9Cl_2N_3O_2$ 333.0072; found 333.0072.

Phenyl 4-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole-1-carboxylate (**3o**). White solid; yield: 290 mg (87%); m.p. 130-132 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.06 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.54-7.48 (m, 2H), 7.41-7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 146.8, 146.1, 132.3, 131.1 (q, *J* = 32.5 Hz), 130.0, 127.5, 126.5, 126.1 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 270.5 Hz), 120.9, 120.4; IR (neat): 3142, 1785, 1427, 1261, 1123, 1000, 746 cm^{-1}; HRMS (EI-double focusing) *m/z*: $[M]^+$ calcd. for $C_{16}H_{10}F_3N_3O_2$ 333.0725; found 333.0722.

Phenyl 4-(4-chlorophenyl)-1H-1,2,3-triazole-1-carboxylate (**3p**). White solid; yield: 270 mg (90%); m.p. 164.8-165 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.52-7.47 (m, 4H), 7.40-7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 147.1, 146.1, 135.1, 130.0, 129.3, 127.5, 127.4, 121.1, 120.9, 119.5; IR (neat): 3149, 1773, 1420, 1226, 992, 764 cm^{-1}; HRMS(FAB-double focusing) m/z: $[M+H]^+$ calcd. for $C_{15}H_{10}ClN_3O_2$+H 300.0540; found 300.0542.

Phenyl 4-(4-(methoxycarbonyl)phenyl)-1H-1,2,3-triazole-1-carboxylate (**3q**). White solid; yield: 275 mg (85%); m.p. 183-185 °C**;** ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 8,5 Hz, 2H), 7.53-7.49 (m, 2H), 7.41-7.37 (m, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 149.9, 147.2, 133.1, 130.4, 130.0, 127.4, 126.1, 120.9, 120.9, 120.4; IR (neat): 1781, 1429, 1411, 1297, 1110, 1002, 753 cm^{-1}; HRMS(FAB-double focusing) m/z: $[M+H]^+$ calcd. for $C_{17}H_{13}N_3O_4$+H 324.0984; found 324.0986.

General Procedure for 1*H*-1,2,3-Triazoles (4a-4i)

The reaction yields were determined after the deprotection of carbamate moiety. The crude mixture was reacted with KOH in methanol at room temperature overnight and was quenched with HCl aqueous solution to produce the free triazole. Compounds **4** were confirmed according to literature.[18]

4-Phenyl-1H-1,2,3-triazole (**4a**).[18a] White solid; yield: 134 mg (92%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.34 (s, 1H), 7.86 (d, J = 7.1 Hz, 2H), 7.45 (t, J = 7.4 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H).

4-(p-Tolyl)-1H-1,2,3-triazole (**4b**).[18a] White solid; yield: 146 mg (92%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.27 (s, 1H), 7.74 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 2.32 (s, 3H).

4-(4-Methoxyphenyl)-1H-1,2,3-triazole (**4c**).[18a] White solid; yield: 158 mg (90%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.22 (s, 1H), 7.79 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H).

4-(4-(tert-Butyl)phenyl)-1H-1,2,3-triazole (**4d**).[18b] White solid; yield: 171 mg (85%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.25 (s, 1H), 7.76 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 1.29 (s, 9H).

4-(4-Bromophenyl)-1H-1,2,3-triazole (**4e**).[18a] White solid; yield: 190 mg (85%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.40 (s, 1H), 7.83 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H).

4-(3,4-Dichlorophenyl)-1H-1,2,3-triazole (**4f**).[18c] White solid; yield: 197 mg (92%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.51 (s, 1H), 8.12 (d, J = 2.0 Hz, 1H), 7.87 (dd, J = 2.0, 8.4 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H).

4-(4-(Trifluoromethyl)phenyl)-1H-1,2,3-triazole (**4g**).[18d] White solid; yield: 185 mg (87%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.54 (s, 1H), 8.10 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 8.3 Hz, 2H).

4-(4-Chlorophenyl)-1H-1,2,3-triazole (**4h**).[18a] White solid; yield: 162 mg (90%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.39 (s, 1H), 7.89 (d, J = 8.6 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H).

Methyl 4-(1H-1,2,3-triazol-4-yl)benzoate (**4i**).[18a] White solid; yield: 173 mg (85%); ^{1}H NMR (400 MHz, DMSO-d_6+TFA 1 drop): δ 8.51 (s, 1H), 8.05-8.00 (m, 4H), 3.86 (s, 3H).

■ ASSOCIATED CONTENT

Supporting Information

Supporting Information is available free of charge on the ACS Publications website at DOI: X-ray crystal structure of compound **3a**, ^{1}H and ^{13}C NMR spectra of products, and NOE difference experiment for compound **3g**.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGEMENTS

This research was supported by the Basic Science Research Program administered through the National Research Foundation of Korea (NRF), funded by the Ministry of Education (2015R1D1A1A09058536) and by the Korean Ministry of Education through the BK21-Plus Project of the Hanyang University Graduate Program.

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