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Copper(I)-Catalyzed Aerobic Oxidative Azide–Alkene Cycloaddition: An Efficient Synthesis of Substituted 1,2,3-Triazoles

Donala Janreddy,[a] Veerababurao Kavala,[a] Chun-Wei Kuo,[a] Wen-Chang Chen,[a] Chintakunta Ramesh,[a] Trimurtulu Kotipalli,[a] Ting-Shen Kuo,[a] Mei-Ling Chen,[a] Chiu-Hui He,[a] and Ching-Fa Yao[a,*]

[a] Department of Chemistry, National Taiwan Normal University, 88, Sec. 4, Tingchow Road, Taipei, Taiwan 116, R.O.C.
E-mail: cheyaocf@ntnu.edu.tw

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Abstract: A novel, copper(I)-promoted azide–alkene aerobic oxidative cycloaddition protocol was developed for the regioselective synthesis of 1,4-disubstituted/1,4,5-trisubstituted 1,2,3-triazoles by using azides and electron-deficient olefins under an oxygen atmosphere.

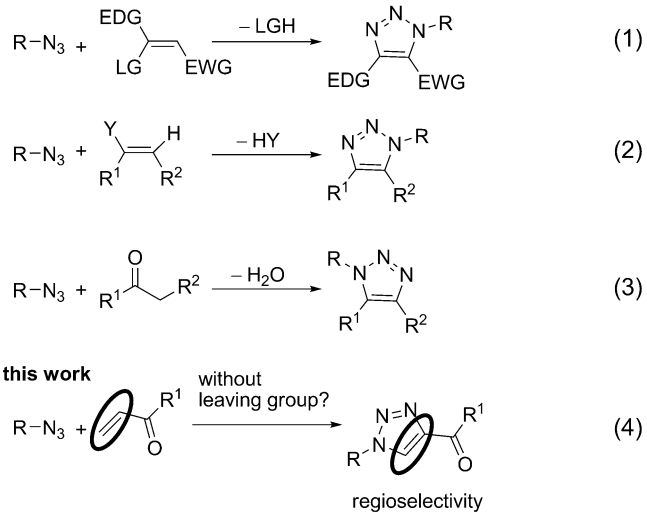
Keywords: aerobic oxidation; azide–alkene cycloaddition; copper catalysis; 1,2,3-triazoles

Introduction

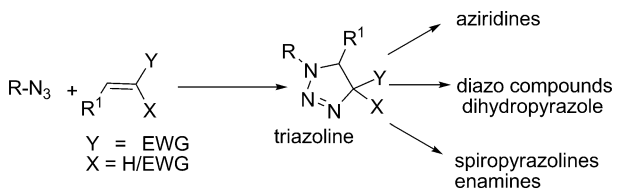
The 1,2,3-triazole motif occupies a special place in heterocyclic chemistry, and is featured in a large number of bioactive molecules[1] as well as substances used in medicinal chemistry[2] and other research fields.[3] Among the various 1,2,3-triazoles, 1,4-disubstituted/1,4,5-trisubstituted 1,2,3-triazole derivatives have found broad applications in different areas such as bioconjugations, polymers, pesticides, pharmaceuticals and surface science.[4] The most general method for the synthesis of 1,2,3-triazoles is the Huisgen 1,3-dipolar cycloaddition reactions between azide and alkyne.[5] However, because of high activation energies and poor regioselectivity, the Huisgen 1,3-dipolar cycloaddition has limited utilization in general synthesis. Concurrently, the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition of azide–alkyne (CuAAC, often referred as click chemistry[6]) has been exposed and became one of the most familiar and efficient approaches to the synthesis of substituted 1,2,3-triazoles, but is generally restricted to terminal alkynes.

Alternatively, 1,2,3-triazole derivatives could also be achieved from the 1,3-dipolar cycloaddition of azides onto alkenes bearing the leaving group[7] [or azides with push-pull alkene with a leaving group (LG)] [Scheme 1, Eqs. (1) and (2)] and azides with α-functionalized ketones/carbonyl compounds/1,3-diketone/β-dicarbonyl compounds [Scheme 1, Eq. (3)].[8] Moreover, the reaction of organic azides with electron-deficient olefins proceed *via* 1,3-dipolar cycloaddition to form unstable regioisomeric triazolines, which produce different products depending upon the conditions employed (Scheme 2).[9]

Johnston et al. reported that the Brønsted-acid promoted addition of azides on activated olefins (methyl vinyl ketone) delivers the corresponding aziridines *via* triazoline intermediates, whereas active ester derivatives bearing a Lewis basic oxygen [such as methyl acryloyl(benzyl)carbamates] readily participate in a tandem process to deliver oxazolidinedione com-



Scheme 1. Previous reports on substituted 1,2,3-triazoles from activated alkenes.



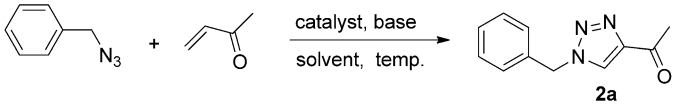
Scheme 2. Previous reports on the reaction of electron-deficient olefins with azides.

pounds.[10] In the mean time, Finney et al. reported that the reaction of vinyl acetate with azides in the presence of trimethyl or triethyl orthoformate at high temperature produced unstable triazoline intermediates, furthermore, they undergo elimination of an acetate group in the presence of acid or base to afford the corresponding triazoles.[11] In addition, recently, some groups reported on the regioselective synthesis of substituted 1,2,3-triazole derivatives from chalcones and azides.[12] However, to the best of our knowledge, the synthesis of 1,4-disubstituted 1,2,3-triazoles *via* oxidative cycloaddition of azides to electron-deficient terminal olefins has not been reported in the literature. Recently, we became interested in developing newer strategies for the construction of variety of heterocyclic compounds *via* transition metal catalysis.[13] In continuation to our interest on this topic, we wanted to investigate the oxidative cycloaddition of azides to electron-deficient olefins for the synthesis of 1,4-disubstituted 1,2,3-triazole derivatives.

Results and Discussion

To pursue our objective, we initially subjected methyl vinyl ketone to reaction with benzyl azide in the presence of copper iodide in THF solvent at room temperature for 12 h. Under these conditions, we obtained a trace amount of the desired 1,4-disubstituted 1,2,3-triazole (**2a**) (Table 1, entry 1). Next, we con-

Table 1. Optimization of the reaction conditions for **2a**.



2a

Entry[a]	Catalyst	Base	Solvent	Temp. [°C]	Time [h]	NMR Yield[b] [%]
1	CuI (5/10 mol%)	-	THF	60	24(12)	15 (trace)
2	CuI (10 mol%)	K_2CO_3	THF	60	24	40 (25)
3	CuBr (10 mol%)	K_2CO_3	THF	60	24	30 (trace)
4	CuCl (10 mol%)	K_2CO_3	THF	60	24	35 (trace)
5	CuI (10 mol%)	Et_3N	THF	60	24	50
6	CuI (10 mol%)	DABCO	THF	60	24	46
7	CuI (10 mol%)	DBU	THF	r.t.	24	42
8	CuI (10 mol%)	pyridine	THF	60	24	37
9	CuI (10 mol%)	DIPEA	THF	60	24	57
10	CuI (10 mol%)	DIPEA	DMSO	60	24	50
11	CuI (10 mol%)	DIPEA	DMF	60	24	52
12	CuI (10 mol%)	DIPEA	1,4-dioxane	60	20	60
13	CuI (10 mol%)	DIPEA	CH_3CN	60	24	35
14	CuI (10 mol%)	DIPEA	toluene	60	24	45
15	CuI (10 mol%)	DIPEA	benzene	60	24	33
16	CuI (10 mol%)	DIPEA	1,4-dioxane	80	15	65
17	CuI (20 mol%)	DIPEA	1,4-dioxane	80	12	76
18[c]	CuI (10 mol%)	DIPEA	1,4-dioxane	80	12	12
19[d]	CuI (10 mol%)	DIPEA	1,4-dioxane	80	8	75
20[d]	**CuI (20 mol%)**	**DIPEA**	**1,4-dioxane**	**80**	**4**	**95**
21[d]	-	DIPEA	1,4-dioxane	80	24	trace
22[d]	-	-	1,4-dioxane	80	24	11

[a] All the reactions were carried out under the following conditions, benzyl azide (1.0 mmol), methyl vinyl ketone (3.0 mmol) and base (1.5 mmol) under an air condenser.
[b] Yields determined by ^1H NMR (CH_2Br_2 as internal standard). Time and yield given in parentheses refer to reactions conducted at room temperature.
[c] Under a nitrogen atmosphere (N_2).
[d] Under an oxygen atmosphere (O_2).

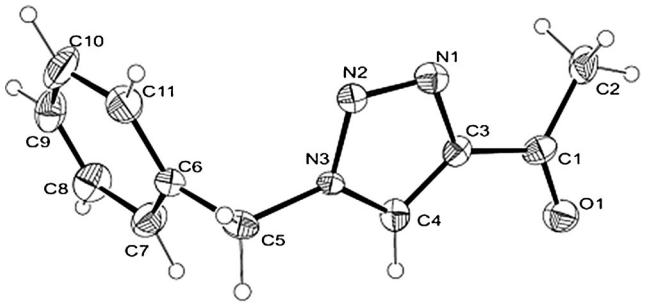
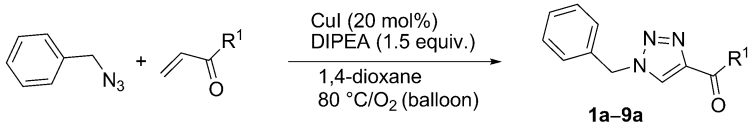


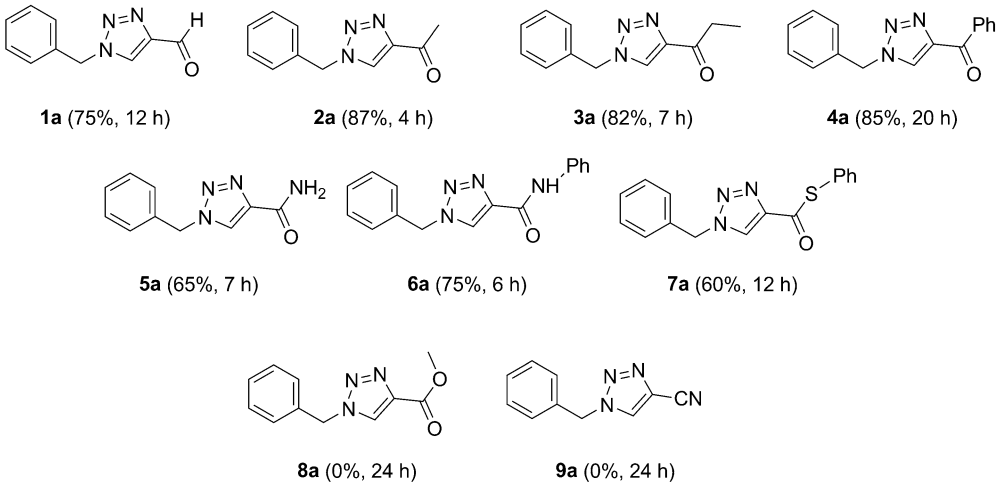
Figure 1. ORTEP diagram of the single crystal X-ray diffraction structure of **2a**.[18]

ducted the reaction by the addition of K_2CO_3 as base. Under these conditions, the reaction produced a slightly improved yield of the desired product (entry 2). To screen the catalysts, we performed the reaction with other copper catalysts like CuBr and CuCl, respectively. However, there was no marked improvement in the reaction was observed (entries 3 and 4). Furthermore, we screened the reaction with various bases like triethylamine (Et_3N), 1,4-diazabicyclo-[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), pyridine and *N*,*N*-diisopropylethylamine (DIPEA) (entries 5–9). Among the bases tested in this reaction, DIPEA gave the best yield of the product (entry 9). Next, we examined different solvents for this reaction, although polar solvents like DMSO and DMF are equally efficient for this reaction (entries 10 and 11), 1,4-dioxane turned out to be the best solvent for this reaction and produced the corresponding triazole derivative in good yield (entry 12). Further improvement of the yield was observed, when the reaction was conducted in the presence of 20 mol% of CuI at 80 °C in 1,4-dioxane solvent (entry 17). Moreover, it is reported in the literature that the aromatization process proceeds smoothly under copper catalysis in the presence of molecular oxygen.[14] Hence, we performed the reaction in the presence of molecular oxygen (entry 20). To our delight, the reaction furnished the desired 1,4-disubstituted 1,2,3-triazole product (**2a)** in excellent yield. In all these reactions, we utilized 3.0 equiv. of methyl vinyl ketone. We also conducted the reactions using lower amounts of methyl vinyl ketone (1.5 equiv., 2 equiv. and 2.5 equiv.). The reactions produced compartively low yields of desired product.This might be due to the polymerization of some amount of methyl vinyl ketone in the presence of copper iodide.[15] The structure of the 1,4-disubstituted 1,2,3-triazole product (**2a**) was well characterized using all spectroscopic techniques and confirmed by ^{1}H NMR, ^{13}C NMR, LR-MS, HR-MS and a single crystal X-ray analysis (Figure 1).

After the optimization of the reaction conditions, different azides and electron-deficient olefins were used to evaluate the reaction scope. In this regard, we first examined the reaction with a variety of electron-deficient olefins. As illustrated in Table 2, the reac-

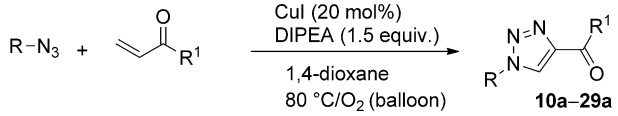
Table 2. Substituted triazole formation from benzyl azide and various electron-deficient olefins.[a,b]

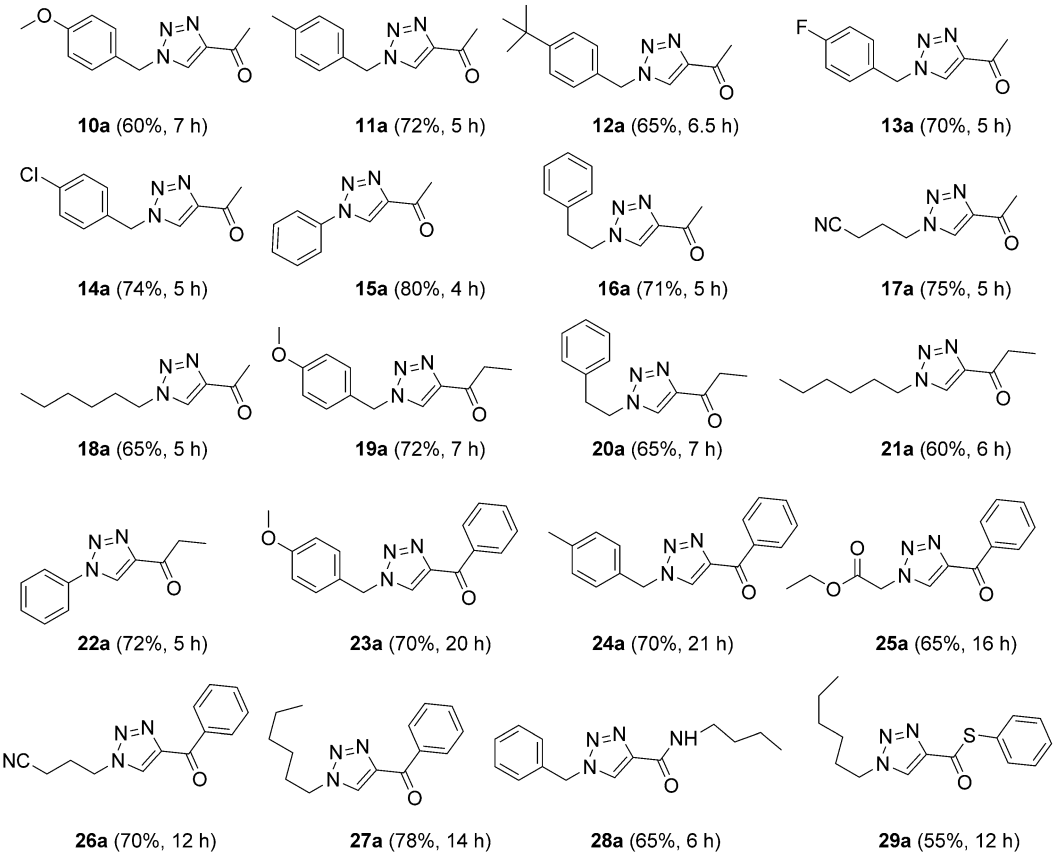




[a] All the reactions were conducted on a 2-mmol scale.
[b] Isolated yields.
[c] Reaction became messy.

Table 3. Substrate scope of the reaction with various azides and electron-deficient terminal olefins.[a,b]



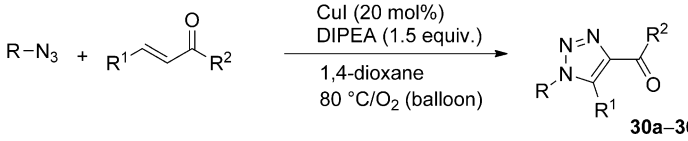


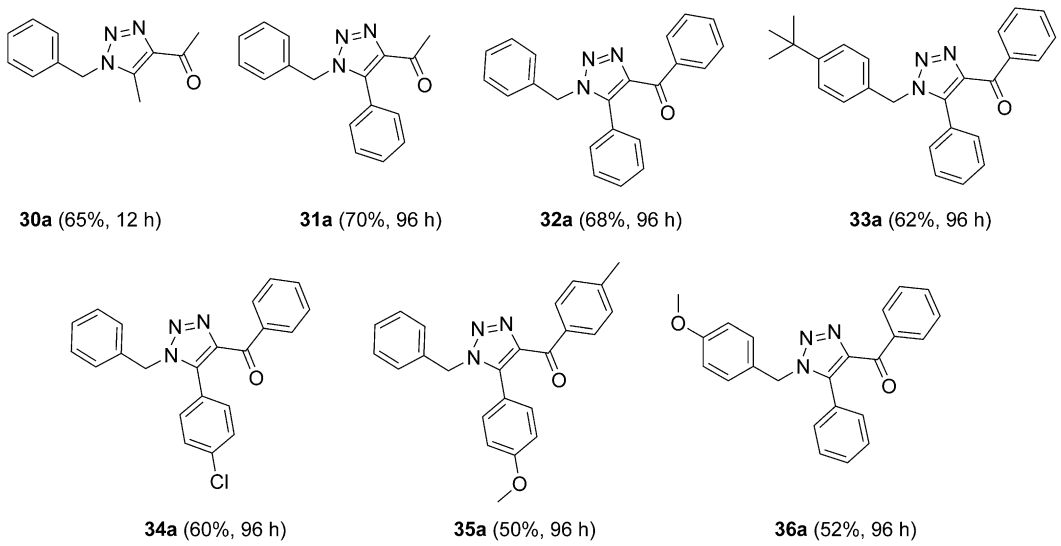
[a] All the reactions were conducted on a 2-mmol scale.
[b] Isolated yields.

tions of benzyl azide with α,β-unsaturated aldehyde (acrolein) provided the corresponding triazole derivative in good yield (Table 2, **1a**). It is important to note that the yields of the desired product were high when the α,β-unsaturated ketones like methyl vinyl ketone, ethyl vinyl ketone, and phenyl vinyl ketone were employed as substrates in the reaction with benzyl azide in the present reaction conditions (**2a**–**4a**). Furthermore, when α,β-unsaturated amides were employed as substrates, the reaction provided the corresponding triazole derivatives in moderate to good yields (**5a** and **6a**). The reaction of benzyl azide with an α,β-unsaturated thioester, that is, *S*-phenyl prop-2-enethioate produced the corresponding triazole product in moderate yield (**7a**). On the other hand, the reactions of benzyl azide with methyl/ethyl acrylate and acrylonitrile failed to form the desired 1,4-disubstituted 1,2,3-triazole products (**8a** and **9a**).

Once we had studied the efficacy of our method for the different classes of electron-deficient alkenes and benzyl azide, we decided to establish the versatility of our protocol using different azides. In this regard, we examined the reaction of various structurally diverse azides and electron-deficient alkenes. The results are summarized in Table 3. The reactions of benzyl azides equipped with electron-donating as well as electron-withdrawing groups reacted equally easily with methyl vinyl ketone to produce their corresponding triazole derivatives in moderate to good yields (Table 3, **10a**–**14a**). Interestingly, under the present reaction conditions, the reaction of phenyl azide with methyl vinyl ketone furnished the desired product in good yield (**15a**). Importantly, the reactions of aliphatic azides with methyl vinyl ketone proceeded smoothly to afford the expected 1,4-disubstituted 1,2,3-triazole derivatives in moderate to good yields (**17a** and **18a**). Moreover, more or less similar reactivity was

Table 4. Substrate scope of the reaction with various azides and internal olefins.[a,b]

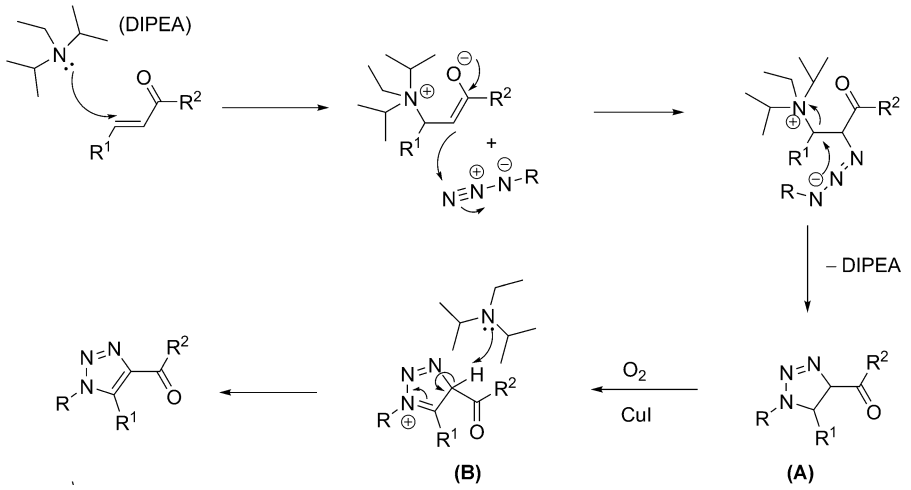




[a] All the reactions were conducted on a 2-mmol scale.
[b] Isolated yields.

observed when ethyl vinyl ketone was used as substrate (**19a**–**22a**). However, when phenyl vinyl ketone was used as substrate, the reaction took a longer time compared with other electron-deficient alkenes (**23a**–**27a**). Notably, the functional groups like ester, cyano and halogen survived under the present reaction conditions.

Finally, to evaluate the scope of the present methodology, we performed the reactions of substituted internal olefins with various substituted azides under the optimal reaction conditions. To our delight, the desired product was obtained in moderate yields in most of the tested reactions. However, the reactions took a longer time (96 h) to produce the corresponding triazole products than did the terminal olefins (Table 4, **31a**–**36a**). The possible reason for the slow reaction might be a steric effect of substituents at the β-position of the carbonyl group. It is worthy to men-



Scheme 3. Plausible mechanism for the synthesis of 1,4-disubstituted/1,4,5-trisubstituted 1,2,3-triazoles.

tion here that Baohua Chen and co-workers have obtained *N*-2-aryl-substituted 1,2,3-triazole derivatives *via* azide-chalcone oxidative cycloaddition and post-triazole arylation using similar conditions, however they used sodium azide as component.[12a,c]

The plausible mechanism for the formation of 1,4-disubstituted/1,4,5-trisubstituted 1,2,3-triazoles is outlined in Scheme 3.We assume that the reaction of an electron-deficient alkene and azide could initially involve stepwise 1,3-dipolar cycloaddition to produce a triazoline intermediate (**A**). This triazoline intermediate would be oxidzed in the presence of a copper catalyst and molecular oxygen to generate intermediate (**B**). In the further course this intermediate **B** undergoes deprotonation in the presence of base (DIPEA) leading to generation of the desired product. The failure in the production of 1,4-disubstituted 1,2,3-triazole derivatives (**8a**, **9a**) from the reaction of methyl acrylate, and acrylonitrile with benzyl azide can be explained based on the mechanism as methyl acrylate and acrylonitrile are weaker Michael acceptors than methyl/ethyl/phenyl vinyl ketones.[16] Thus, the base-promoted stepwise 1,3-dipolar cycloaddition may not taken place between weak Michael acceptors and benzyl azide. Another reason may be that, even if it forms the triazoline intermediate (**A**), the proton at the α-carbon to ester and cyano functionalities in the triazoline intermediate (**A**) is less acidic compared to that with a keto functionality. Probably, the basicity of DIEPA is not enough for the abstraction of the proton at the α-carbon to ester and cyano functionalities in the triazoline intermediate.

Conclusions

In conclusion, we have successfully developed a novel method for the synthesis of a diverse array of regioselective 1,4-disubstituted/1,4,5-trisubstituted 1,2,3-triazoles through copper(I)-catalyzed aerobic oxidative azide and alkene cycloaddition. This method involves the 1,3-dipolar cycloaddition of alkene and azide followed by aerobic oxidative aromatization in cascade process. A wide range of terminal and internal electron-deficient alkenes and azides were investigated in this reaction. Moderate to excellent yields of 1,2,3-triazole derivatives obtained. We believe this procedure offers an easy and convenient alternative to the existing methodologies for the synthesis of 1,2,3-triazole derivatives.

Experimental Section

General Remarks

Reagents and solvents were purchased from various commercial sources and were used directly without any further purification unless otherwise stated. Column chromatography was performed with Merck silica gel 60 (230–400 mesh). ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million (δ) using TMS and chloroform as an internal standards and coupling constants are expressed in Hz. IR spectra were recorded on an FT-IR spectrometer and are reported in cm^{-1}. Melting points were recorded using an electro thermal capillary melting point apparatus and are uncorrected.

General Experimental Procedure for the Synthesis of 1,4-Disubstituted/1,4,5-Trisubstituted Triazoles

Copper(I) iodide (20 mol%) and *N*,*N*-diisopropylethylamine (1.5 mmol) were added to a stirred solution of azide (1 mmol) and electron-deficient olefin [acrolein or methyl vinyl ketone (3.0 mmol), ethyl vinyl ketone (1.5 mmol), phenyl vinyl ketone/acrylamide/*N*-phenylacrylamide/*N*-butylacrylamide/*S*-phenyl prop-2-enethioate/chalcones (1.0 mmol)] in 1,4-dioxane solvent (5.0 mL) under an oxygen atmosphere. The reaction mixture was then heated to 80 °C and monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and the solvent was removed by vacuum evaporation. The resulting crude product was purified by column chromatography to afford the desired substituted 1,2,3-triazole.

Physical and Spectral Data

1-Benzyl-1*H*-1,2,3-triazole-4-carbaldehyde (1a):[17d] Yield: 75%; white dolid; mp 88–89 °C; FT-IR (KBr): ν = 1695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.11 (s, 1H), 7.99 (s, 1H), 7.41–7.39 (m, 3H), 7.31–7.28 (m, 2H), 5.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.2, 148.2, 133.5, 129.6, 129.5, 128.5, 125.3, 54.8; LR-MS (ESI): *m*/*z* (relative intensity) = 210 (M^+ + Na, 48), 199 (12); HR-MS *m*/*z* = 210.0647, calcd. for $C_{10}H_9N_3ONa$ (M^+ + Na): 210.0643.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (2a):[7c,17e] Yield: 87%; white solid; mp 91–92 °C; FT-IR (KBr): ν = 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 1H), 7.39–7.37 (m, 3H), 7.29–7.27 (m, 2H), 5.55 (s, 2H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.0, 148.6, 133.8, 129.5, 129.3, 128.5, 125.4, 54.7, 27.3; LR-MS (EI): *m*/*z* (relative intensity) = 201.1 (M^+, 15), 172.1 (100), 130.1 (26); HR-MS: *m*/*z* = 201.0908, calcd. for $C_{11}H_{11}O_1N_3$ (M^+): 201.0902.

1-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-1-one (3a):[17c] Yield: 82%; white solid; mp 116–117 °C; FT-IR (KBr): ν = 1688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.43–7.40 (m, 3H), 7.35–7.30 (m, 2H), 5.57 (s, 2H), 3.15 (q, *J* = 7.45 Hz, 2H), 1.22 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 148.2, 133.9, 129.5, 129.3, 128.5, 125.3, 54.6, 33.0, 7.94. LR-MS (EI): *m*/*z* (relative intensity) = 215.2 (M^+, 35), 186.1 (98); HR-MS: *m*/*z* = 215.1057. calcd. for $C_{12}H_{13}O_1N_3$ (M^+): 215.1059.

4-Benzoyl-1-benzyl-1*H*-1,2,3-triazole (4a): Yield: 85%; white solid; mp 115–116 °C; FT-IR (KBr): ν = 1635 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42–8.40 (m, 2H), 8.16 (s, 1H), 7.60–7.58 (m, 1H), 7.53–7.41 (m, 2H), 7.41–7.39 (m, 3H), 7.34–7.32 (m, 2H), 5.60 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.8, 148.6, 136.7, 133.9, 133.4, 130.7, 129.5, 129.4, 129.3, 128.5, 128.4, 54.6; LR-MS (EI): *m/z* (relative intensity) = 263 (M^+, 81), 234 (100), 206.(42), 116 (42); HR-MS: *m/z* = 263.1056, calcd. for $C_{16}H_{13}O_1N_3$ (M^+): 263.1059.

1-Benzyl-1*H*-1,2,3-triazole-4-carboxamide (5a): Yield: 65%; white solid; mp 243–244 °C; FT-IR (KBr): ν = 3394, 1701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1H), 7.40–7.38 (m, 3H), 7.30–7.28 (m, 2H), 7.02 (s, 1H), 5.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ and CD_3OD): δ = 162.8, 142.6, 133.8, 129.1, 128.9, 128.0, 126.1, 54.3; LR-MS (ESI): *m/z* (relative intensity) = 203 (M^++H, 31), 225 (M^++Na, 40), 132 (20); HR-MS: *m/z* = 202.0850, calcd. for $C_{10}H_{10}O_1N_4$ (M^+): 202.0855.

1-Benzyl-*N*-phenyl-1*H*-1,2,3-triazole-4-carboxamide (6a):[17a] Yield: 75%; white solid; mp 189–190 °C; FT-IR (KBr): ν = 3343, 1662 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.93 (brs, 1H), 8.05 (s, 1H), 7.68–7.66 (m, 2H), 7.42–7.30 (m, 7H), 7.16–7.12 (m, 1H), 5.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 143.9, 137.6, 133.8, 129.5, 129.4, 129.3, 128.5, 125.9, 124.7, 120.0, 54.8; LR-MS (ESI): *m/z* (relative intensity) = 279 (M^++H, 40), 301 (M^++Na, 20); HR-MS: *m/z* = 278.1154, calcd. for $C_{16}H_{14}O_1N_4$ (M^+): 278.1168.

(1-Benzyl-1*H*-1,2,3-triazol-4-yl)(phenylsulfanyl)methanone (7a): Yield: 60%; white solid; mp 143–144 °C; FT-IR (KBr): ν = 1672cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1H), 7.52–7.48 (m, 2H), 7.44–7.43 (m, 3H), 7.40–7.38 (m, 3H), 7.30–7.28 (m, 2H), 5.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.4, 146.5, 135.2, 133.7, 129.8, 129.5, 129.4, 129.4, 128.4, 126.7, 124.4, 54.8; LR-MS (ESI); *m/z* (relative intensity) = 296 (M^++H, 100), 268 (5); HR-MS: *m/z* = 296.0865, calcd. for $C_{16}H_{14}S_1O_1N_3$ (M^++H): 296.0858.

1-{1-[(4-Methoxyphenyl)methyl]-1*H*-1,2,3-triazol-4-yl}-ethan-1-one (10a): Yield: 60%; white solid; mp 111–112 °C; FT-IR (KBr): ν = 1687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1H), 7.26–7.23 (m, 2H), 6.91–6.89 (m, 2H), 5.48 (s, 2H), 3.80 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz $CDCl_3$): δ = 193.1, 160.4, 148.5, 130.1, 125.7, 125.2, 114.9, 55.5, 54.2, 27.3; LR-MS (EI): *m/z* (relative intensity) = 231.1 (M^+, 25), 202.1 (88), 121.1 (100); HR-MS: *m/z* = 231.1007, calcd. for $C_{12}H_{13}O_2N_3$ (M^+): 231.1008.

1-{1-[(4-Methylphenyl)methyl]-1*H*-1,2,3-triazol-4-yl}-ethan-1-one (11a): Yield: 72%; white solid; mp 102–103 °C; FT-IR (KBr): ν = 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1H), 7.18–7.13 (m, 4H), 5.50 (s, 2H), 2.66 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.0, 148.5, 139.4, 130.7, 130.2, 128.6, 125.3, 54.5, 27.3, 21.3; LR-MS (EI): *m/z* (relative intensity) = 215 (M^+, 10), 105 (100), 172 (46); HR-MS: *m/z* = 215.1057, calcd. for $C_{12}H_{13}O_1N_3$ (M^+): 215.1059.

1-{1-[(4-*tert*-Butylphenyl)methyl]-1*H*-1,2,3-triazol-4-yl}-ethan-1-one (12a): Yield: 65%; white solid; mp 117–118 °C; FT-IR (KBr): ν = 1688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (s, 1H), 7.41–7.39 (m, 2H), 7.24–7.22 (m,2H), 5.52 (s, 2H), 2.67 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.1, 152.6, 148.5, 130.7, 128.4, 126.5, 125.4, 54.4, 34.9, 31.4, 27.3; LR-MS (EI): *m/z* (relative intensity) = 257.2 (M^+, 10), 172.1 (100), 147.2 (98); HR-MS: *m/z* = 257.1526, calcd. for $C_{15}H_{19}O_1N_3$ (M^+): 257.1528.

1-{1-[(4-Fluorophenyl)methyl]-1*H*-1,2,3-triazol-4-yl}ethan-1-one (13a): Yield: 70%; brown gummy solid; FT-IR (KBr): ν = 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1H), 7.30–7.27 (m, 2H), 7.09–7.05 (m, 2H), 5.53 (s, 2H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.7, 163 (d, *J* = 247 Hz), 148.4, 130.2 (d, *J* = 8 Hz), 129.5 (d, *J* = 3 Hz), 125.1, 116.3 (d, *J* = 21 Hz), 53.7, 27.0; LR-MS (EI): *m/z* (relative intensity) = 219 (M^+, 5), 190.1 (48), 109.1 (100); HR-MS: *m/z* = 219.0803, calcd. for $C_{11}H_{10}O_1N_3F$ (M^+): 219.0808.

1-{1-[(4-Chlorophenyl)methyl]-1*H*-1,2,3-triazol-4-yl}ethan-1-one (14a): Yield: 74%; white solid; mp 125–126 °C; FT-IR (KBr): ν = 1684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1H), 7.37–7.35 (m, 2H), 7.26–7.22 (m, 2H), 5.53 (s, 2H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.9, 148.7, 135.5, 132.3, 129.8, 129.7, 125.3, 53.9, 27.3; LR-MS (EI): *m/z* (relative intensity) = 235 (M^+, 5), 125 (100); HR-MS: *m/z* = 235.0515, calcd. for $C_{11}H_{10}O_1N_3Cl_1$ (M^+): 235.0512.

1-(1-Phenyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (15a):[17i] Yield: 80%; white solid; mp 108–109 °C; FT-IR (KBr): ν = 1691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (s, 1H), 7.76–7.74 (m, 2H), 7.58–7.54 (m, 2H), 7.51–7.47 (m, 1H), 2.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.0, 148.7, 136.6, 130.1, 129.7, 123.5, 121.0, 27.4; LR-MS (ESI): *m/z* (relative intensity) = 188 (M^++H, 100), 174 (50), 164 (85); HR-MS: *m/z* = 187.0741, calcd. for $C_{10}H_9O_1N_3$ (M^+): 187.0746.

1-[1-(2-Phenylethyl)-1*H*-1,2,3-triazol-4-yl]ethan-1-one (16a): Yield: 75%; white solid; mp 114–115 °C; FT-IR (KBr): ν = 1683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.31–7.24 (m, 3H), 7.24–7.07 (m, 2H), 4.63 (t, *J* = 7.18 Hz, 2H), 3.23 (t, *J* = 7.18 Hz, 2H), 2.66 (s, 3H); ^{13}C NMR (100 MHz $CDCl_3$): δ = 193.0, 148.0, 136.5, 129.1, 128.7, 127.5, 125.7, 52.1, 36.6, 27.3; LR-MS (EI): *m/z* (relative intensity) = 215.2 (M^+, 4), 104 (100); HR-MS: *m/z* = 215.1059, calcd. for $C_{12}H_{14}O_1N_3$ (M^+): 215.1059.

4-(4-Acetyl-1*H*-1,2,3-triazol-1-yl)butanenitrile (17a): Yield: 75%; white solid; mp 70–71 °C; FT-IR (KBr): ν = 2250, 1679 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 4.57 (t, *J* = 6.56 Hz, 2H), 2.69 (s, 3H), 2.47–2.43 (m, 2H), 2.38–2.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.8, 148.5, 125.9, 118.0, 48.8, 27.3, 26.0, 14.8; LR-MS (EI): *m/z* (relative intensity) = 179 (M^++H,5), 135.1 (100); HR-MS (FAB): *m/z* = 179.0934, calcd. for $C_8H_{11}O_1N_4$ (M^+): 179.0933.

1-(1-Hexyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (18a): Yield: 65%; white solid; mp 63–64 °C; FT-IR (KBr): ν = 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 4.39 (t, *J* = 7.22 Hz, 2H), 2.68 (s, 3H), 1.93–1.89 (m, 2H), 1.33–1.24 (m, 6H), 0.85 (t, *J* = 6.73 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 148.3, 125.2, 50.8, 31.2, 30.2, 27.3, 26.2, 22.5, 14.0; LR-MS (EI): *m/z* (relative intensity) = 195.2 (M^+, 13), 152.2 (76), 124.2 (100); HR-MS: *m/z* = 195.1368, calcd. for $C_{10}H_{17}O_1N_3$ (M^+): 195.1372.

1-{1-[(4-Methoxyphenyl)methyl]-1*H*-1,2,3-triazol-4-yl}propan-1-one (19a): Yield: 72%; brown solid; mp 113–114 °C; FT-IR (KBr): ν = 1692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1H), 7.25–7.23 (m, 2H), 6.91–6.89 (m, 2H), 5.48 (s, 2H), 3.80 (s, 3H), 3.12 (q, *J* = 7.38 Hz, 2H) 1.20 (t, *J* = 7.34 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 160.4, 148.2, 130.1, 125.8, 125.1, 114.9, 55.5, 54.2, 33.0, 7.9; LR-MS (EI): *m/z* (relative intensity) = 245.2 (M^+, 16), 202.1 (45),

121.2 (100); HR-MS: m/z = 245.1166, calcd. for $C_{13}H_{15}O_2N_3$ (M^+): 245.1164.

1-[1-(2-Phenylethyl)-1*H*-1,2,3-triazol-4-yl]propan-1-one (20a): Yield: 65%; brown gummy solid; FT-IR (KBr): ν = 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.77 (s, 1H), 7.29–7.25 (m, 3H), 7.09–7.07 (m, 2H), 4.63 (t, J = 7.22 Hz, 2H), 3.22 (t, J = 7.18 Hz, 2H), 3.13 (q, J = 7.32 Hz, 2H), 1.20 (t, J = 7.32 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 147.7, 136.6, 129.1, 128.7, 127.5, 125.7, 52.1, 36.7, 33.0, 7.9; LR-MS (EI): m/z (relative intensity) = 229 (M^+, 5), 105 (100), 138 (35); HR-MS: m/z = 229.1211, calcd. for $C_{13}H_{15}O_1N_3$ (M^+): 229.1215.

1-(1-Hexyl-1*H*-1,2,3-triazol-4-yl)propan-1-one (21a): Yield: 60%; yellow solid; mp 47–48 °C; FT-IR (KBr): ν = 1679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 4.38 (t, J = 7.24 Hz, 2H), 3.14 (q, J = 7.28 Hz, 2H), 1.95–1.87 (m, 2H), 1.33–1.23 (m, 6H), 1.21 (t, J = 7.38 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 147.9, 125.2, 50.8, 32.9, 31.2, 30.3, 26.2, 22.5, 14.1, 7.9; LR-MS (ESI): m/z (relative intensity) = 232 (M^++Na, 57), 273 (100), 347 (40); HR-MS: m/z = 232.1425, calcd. for $C_{11}H_{19}O_1N_3Na$ (M^++Na): 232.1426.

1-(1-Phenyl-1*H*-1,2,3-triazol-4-yl)propan-1-one (22a): Yield: 72%; white solid; mp 142–143 °C; FT-IR (KBr): ν = 1679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.48 (s, 1H), 7.76–7.74 (m, 2H), 7.58–7.54 (m, 2H), 7.51–7.47 (m, 1H), 3.22 (q, J = 7.34 Hz, 2H), 1.26 (t, J = 7.32 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 148.4, 136.6, 130.1, 129.7, 123.5, 121.0, 33.2, 7.9; LR-MS (ESI): m/z (relative intensity) = 202 (M^++H, 40), 132 (50); HR-MS: m/z = 201.0893, calcd. for $C_{11}H_{11}O_1N_3$ (M^+): 201.0902.

4-Benzoyl-1-[(4-methoxyphenyl)methyl]-1*H*-1,2,3-triazole (23a):[17c] Yield: 70%; white solid; mp 118–119 °C; FT-IR (KBr): ν = 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.41–8.39 (m, 2H), 8.12 (s, 1H), 7.61–7.58 (m, 1H), 7.52–7.48 (m, 2H), 7.29–7.26 (m, 2H), 6.93–6.90 (m, 2H) 5.53 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.9, 160.4, 130.7, 148.4, 136.7, 133.4, 130.7, 130.2, 128.5, 128.2, 125.8, 114.9, 55.5, 54.2; LR-MS (EI): m/z (relative intensity) = 293 (M^+, 6), 121 (100); HR-MS: m/z = 293.1156, calcd. for $C_{17}H_{15}O_2N_3$ (M^+): 293.1164.

4-Benzoyl-1-[(4-methylphenyl)methyl]-1*H*-1,2,3-triazole (24a): Yield: 70%; white solid; mp 113–114 °C; FT-IR (KBr): ν = 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.41–8.40 (m, 2H), 8.12 (s, 1H), 7.60–7.58 (m, 1H), 7.52–7.49 (m, 2H), 7.26–7.24 (m, 1H), 7.22–7.20 (m, 3H), 5.56 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.9, 148.5, 139.4, 136.7, 133.4, 130.8, 130.8, 130.2, 128.6, 128.5, 128.3, 54.5, 21.3; LR-MS (EI): m/z (relative intensity) = 277 (M^+, 62), 248 (45), 105 (100); HR-MS: m/z = 277.1218, calcd. for $C_{17}H_{15}ON_3$ (M^+): 277.1215.

Ethyl 2-(4-benzoyl-1*H*-1,2,3-triazol-1-yl)acetate (25a):[17h] Yield: 65%; yellow solid; mp 125–126 °C; FT-IR (KBr): ν = 1754, 1647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.42–8.40 (m, 3H), 7.63–7.59 (m, 1H), 7.54–7.50 (m, 2H), 5.25 (s, 2H), 4.29 (q, J = 6.14 Hz, 2H), 1.31 (t, J = 7.18 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.6, 165.8, 148.6, 136.6, 133.5, 130.7, 130.0, 128.6, 62.9, 51.2, 14.2; LR-MS (ESI): m/z (relative intensity) = 282 (M^++Na, 45); HR-MS; m/z = 282.0849, calcd. for $C_{13}H_{13}O_1N_3Na$ (M^++Na): 282.0855.

4-(4-Benzoyl-1*H*-1,2,3-triazol-1-yl)butanenitrile (26a): Yield: 70%; white solid; mp 85–86 °C; FT-IR (KBr): ν = 2248, 1651 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.44–8.42 (m, 2H), 8.31 (s, 1H), 7.66–7.62 (m, 1H), 7.56–7.52 (m, 2H) 4.63 (t, J = 6.56 Hz, 2H), 2.52–2.49 (m, 2H), 2.44–2.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.6, 148.6, 136.5, 133.6, 130.8, 128.9, 128.6, 118.0, 48.8, 26.1, 14.9; LR-MS (FAB): m/z (relative intensity) = 241 (M^++H, 35), 105 (100); HR-MS (FAB): calcd. for $C_{13}H_{13}O_1N_4$ (M^++H): 241.1089.

4-Benzoyl-1-hexyl-1*H*-1,2,3-triazole (27a): Yield: 78%; yellow solid; mp 48–49 °C; FT-IR (KBr): ν = 1643 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.44–8.42 (m, 2H), 8.24 (s, 1H), 7.63–7.59 (m, 1H), 7.53–7.49 (m, 2H), 4.44 (t, J = 7.22 Hz, 2H), 2.00–1.92 (m, 2H), 1.37–1.30 (m, 6H), 0.88 (t, J = 7.62 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.9, 148.3, 136.8, 133.4, 130.8, 128.5, 128.3, 50.8, 31.2, 30.3, 26.2, 22.5, 14.1; LR-MS (ESI): m/z (relative intensity) = 258 (M^++H, 3), 280 (M^++Na, 5); HR-MS: m/z = 258.1600, calcd. for $C_{15}H_{20}O_1N_3$ (M^++H): 258.1606.

1-Benzyl-*N*-butyl-1*H*-1,2,3-triazole-4-carboxamide (28a): Yield: 65%; white solid; mp 164–165 °C; FT-IR (KBr): ν = 3318, 1647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 1H), 7.38–7.36 (m, 3H), 7.28–7.26 (m, 2H), 7.14 (brs, 1H), 5.53 (s, 2H), 3.42 (q, J = 6.7 Hz, 2H), 1.61–1.54 (m, 2H) 1.44–1.35 (m, 2H), 0.93 (t, J = 7.32 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 144.0, 134.0, 129.4, 129.3, 128.4, 125.3, 54.7, 39.0, 31.8, 20.2, 13.9; LR-MS (ESI): m/z (relative intensity = 259 (M^++H, 100), 233 (15); HR-MS: m/z = 258.1468, calcd. for $C_{14}H_{18}O_1N_4$ (M^+): 258.1481.

(1-Hexyl-1*H*-1,2,3-triazol-4-yl)(phenylsulfanyl)methanone (29a): Yield: 55%; white solid; mp 63–64 °C; FT-IR (KBr): ν = 1672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.54–7.51 (m, 2H), 7.41–7.37 (m, 1H), 7.46–7.43 (m, 2H), 4.41 (t, J = 7.22 Hz, 2H), 1.96–1.89 (m, 2H), 1.34–1.29 (m, 6H), 0.88 (t, J = 6.84 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.6, 146.1, 135.2, 129.8, 129.4, 126.8, 124.3, 51.0, 31.2, 30.3, 26.2, 22.5, 14.1; LR-MS (ESI): m/z (relative intensity) = 290 (M^++H, 100); HR-MS: m/z = 290.1335, calcd. for $C_{15}H_{20}O_1S_1N_3$ (M^++H): 290.1327.

1-(1-Benzyl-5-methyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (30a):[17b] Yield: 65%; white solid; mp 148–149 °C; FT-IR (KBr): ν = 1680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 3H), 7.17–7.16 (m, 2H), 5.51 (s, 2H), 2.69 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.6, 144.2, 137.0, 134.1, 129.3, 128.6, 127.4, 51.9, 27.9, 9.3; LR-MS (EI): m/z (relative intensity) = 215 (M^+, 37), 186 (100); HR-MS: m/z = 215.1054, calcd. for $C_{12}H_{13}O_1N_3$ (M^+): 215.1059.

1-(1-Benzyl-5-phenyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (31a):[17g] Yield: 70%; yellow liquid; FT-IR (KBr): ν = 1689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.39 (m, 3H), 7.26–7.23 (m, 3H), 7.19–7.17 (m, 2H), 7.01–6.99 (m, 2H), 5.40 (s, 2H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.9, 144.0, 139.7, 134.8, 130.3, 129.8, 129.0, 128.8, 128.6, 127.7, 126.2, 52.1, 28.2; LR-MS (ESI): m/z (relative intensity) = 300 (M^++Na, 100), 273 (15), 232 (20); HR-MS: m/z = 300.1115, calcd. for $C_{17}H_{15}O_1N_3Na$ (M^++Na): 300.1113.

4-Benzoyl-1-benzyl-5-phenyl-1*H*-1,2,3-triazole (32a):[17f] Yield: 68%; white solid; mp 114–115 °C; FT-IR (KBr): ν = 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.29–8.27 (m, 2H), 7.59–7.55 (m, 1H), 7.49–7.42 (m, 5H), 7.30–7.25 (m, 5H), 7.07–7.05 (m, 2H), 5.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.5, 144.0, 142.0, 137.3, 134.8, 133.1, 130.8,

130.2, 129.9, 129.0, 128.8, 128.6, 128.4, 127.8, 126.5, 52.2; LR-MS (ESI): *m/z* (relative intensity) = 362 (M^++Na, 45), 340 (25); HR-MS: *m/z* = 362.1271, calcd. for $C_{22}H_{17}Cl_1O_1N_3Na$ (M^++Na): 362.1269.

4-Benzoyl-1-[(4-*tert*-butylphenyl)methyl]-5-phenyl-1*H*-1,2,3-triazole (33a): Yield: 62%; yellow liquid; FT-IR (KBr): ν = 1656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.29–8.27 (m, 2H), 7.58–7.54 (m, 1H), 7.50–7.46 (m, 5H), 7.46–7.43 (m, 4H), 7.03–7.01 (m, 2H), 5.43 (s, 2H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.5, 151.7, 143.9, 141.9, 137.3, 133.1, 131.8, 130.8, 130.1, 130.0, 128.8, 128.3, 127.7, 126.6, 125.9, 51.9, 35.0, 31.4; LR-MS (ESI): *m/z* (relative intensity) = 396 (M^++H, 5), 370 (20); HR-MS: *m/z* = 396.2071, calcd. for $C_{26}H_{26}O_1N_3$ (M^++H): 396.2076.

4-Benzoyl-1-benzyl-5-(4-chlorophenyl)-1*H*-1,2,3-triazole (34a):[12d] Yield: 60%; yellow solid; mp 130–131 °C; FT-IR (KBr): ν = 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.30–8.28 (m, 2H), 7.52–7.45 (m, 5H), 7.29–7.24 (m, 5H), 7.07–7.04 (m, 2H), 5.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.0, 143.7, 142.2, 139.6, 135.6, 134.7, 132.3, 130.3, 129.9, 129.0, 128.9, 128.7, 127.8, 126.4, 52.2; LR-MS (ESI): *m/z* (relative intensity) = 396 (M^++Na, 45), 376 (5), 374 (7); HR-MS: *m/z* = 396.0872, calcd. for $C_{22}H_{16}O_1N_3ClNa$ (M^++Na): 396.0880.

1-Benzyl-5-(4-methoxyphenyl)-4-[(4-methylphenyl)carbonyl]-1*H*-1,2,3-triazole (35a): Yield: 50%; yellow liquid; FT-IR (KBr): ν = 1651 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.21–8.19 (m, 2H), 7.30–7.28 (m, 4H), 7.28–7.26 (m, 1H), 7.21–7.19 (m, 2H), 7.10–7.08 (m, 2H), 6.96–6.94 (m, 2H), 5.46 (s, 2H), 3.85 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.3, 161.0, 144.0, 143.9, 141.7, 135.1, 134.9, 131.5, 131.0, 129.1, 129.0, 128.5, 127.7, 118.3, 114.3, 55.5, 52.0, 21.9; LR-MS (ESI): *m/z* (relative intensity) = 406 (M^++Na, 62), 288 (8), 201 (10); HR-MS: *m/z* = 406.1530, calcd. for $C_{24}H_{21}O_2N_3Na$ (M^++Na): 406.1531.

[1-(4-Methoxybenzyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl]-(phenyl)methanone (36a): Yield: 52%; white solid; mp 153–155 °C; FT-IR (KBr): ν = 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.28–8.26 (m, 2H), 7.58–7.54 (m, 1H), 7.50–7.43 (m, 5H), 7.28–7.26 (m, 2H), 7.01–6.98 (m, 2H), 6.81–6.78 (m, 2H), 5.40 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.5, 159.8, 144.0, 141.7, 137.3, 133.1, 130.8, 130.1, 130.0, 129.4, 128.8, 128.3, 126.8, 126.7, 114.3, 55.4, 51.7; LR-MS (FAB): *m/z* (relative intensity) = 370 (M^++H, 100), 344 (10), 304 (8); HR-MS (FAB): *m/z* = 370.1552, calcd. for $C_{23}H_{20}O_2N_3$ (M^++H): 370.1556.

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[18] CCDC 922118 (**2a**), CCDC 922119 (**6a**), CCDC 922122 (**10a**), and CCDC 922121 (**27a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

