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Zn/C-Catalyzed Cycloaddition of Azides and Aryl Alkynes

Xu Meng,[a] Xiaoyun Xu,[a] Tingting Gao,[a] and Baohua Chen*[a]

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Charcoal impregnated with zinc was able to catalyze the cycloaddition of organic azides and alkynes to provide the corresponding 1,4-disubstituted 1,2,3-triazoles and 1,4,5-trisubstituted 1,2,3-triazoles in good to excellent yields. Noteworthy was that the novel and heterogeneous catalyst was successfully applied in this cycloaddition reaction for the first time and could also be easily recycled.

Introduction

"Click chemistry", first defined by Sharpless and co-workers,[1] offers an almost unlimited array of inert triazole-containing architectures resulting from Huisgen [3+2] cycloadditions,[2] in particular between organic azides and alkynes. In the past years, copper catalysts have played an important role in cycloadditions between azides and alkynes,[3] and the developed methods show various applications in organic synthesis, chemical biology, and materials science.[4] Generally, the used copper source comes from direct addition of Cu^{I} species[3b,3c,3h] or reduction of Cu^{II} salts to Cu^{I} salts,[3a,3i] oxidation of copper metal turnings to give Cu^{I} species,[5] copper nanoclusters,[6] copper combined with suitable ligands, and copper complexes.[7] Despite the great advantages of these cases, there remains some drawbacks, such as that oxidative agents are required and a significant amount of catalyst is necessary. As copper(I) salts are quite prone to redox processes, nitrogen- or phosphorus-based ligands must be added to protect and stabilize the active copper catalyst during the cycloaddition reaction. Nevertheless, formation of undesired byproducts, primarily diacetylenes and bistriazoles, was often observed.[3a]

Furthermore, the above approaches are mostly homogeneous in nature and minimal progress has been made in the use of heterogeneous catalysts to perform this kind of cycloaddition. It is acknowledged that homogeneous copper-catalyzed systems have serious shortcomings in the difficulty of catalyst/product separation, reuse of catalysts, and indispensability of additives, such as reducing agents, stabilizing ligands, and bases. By contrast, heterogeneous systems with solid catalysts have significant advantages in catalyst/product(s) separation and reuse of catalysts.[8] These problems and the wide applicability of this reaction led us to explore the possibility of an attractive click-compatible heterogeneous version. To the best of our knowledge, there are a few reports that offer heterogeneous copper catalysts for such a purpose. The Sommer group showed that Cu^{I}–zeolites as a heterogeneous and ligand-free catalyst could be used efficiently for the Huisgen [3+2] cycloaddition.[9] In 2006, the Lipshutz group developed an efficient cycloaddition reaction between organic azides with terminal alkynes in the presence of a heterogeneous recyclable Cu/C catalyst.[10] Recently, Mizuno and co-workers group reported that $Cu(OH)_x/TiO_2$ could act as an efficient heterogeneous catalyst in Huisgen [3+2] cycloadditions.[11] As a complement to the previous methods, we describe a novel and heterogeneous Zn/C (zinc-on-charcoal)-catalyzed cycloaddition of aryl/aliphatic azides and aryl alkynes (including internal alkynes), and this is the first report of zinc being used as a catalyst in [3+2] cycloaddition reactions.

Results and Discussion

Our initial experiments of 4-nitrophenyl azide and phenylacetylene were carried out by using CH_2Cl_2 as the solvent at 50 °C for 15 h in air to better the cycloaddition (Table 1). Firstly, optimization studies revealed that the cycloaddition reaction could perform with moderate yields when using various zinc salts (Table 1, Entries 1–5). When simple Zn powder was used as the catalyst, a reaction was still observed, although the yield of the desired product was poor (Table 1, Entry 6). To our delight, the reaction performed smoothly with the use of Zn/C instead of Zn powder as the catalyst, and it was more effective than other zinc salts (Table 1, Entry 7). It is encouraging that no bases, ligands, or other additives were required for Zn/C to efficiently catalyze the cycloaddition and diacetylene and bistriazole byproducts were not observed. Not surprisingly, the reaction failed when charcoal was used as the catalyst or when no catalyst was used at all. Secondly, to find the most suitable

[a] Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, State Key Laboratory of Applied Organic Chemistry Lanzhou University, Lanzhou University,
Lanzhou 730000, P. R. China
Fax: +86-931-8912582
E-mail: chbh@lzu.edu.cn

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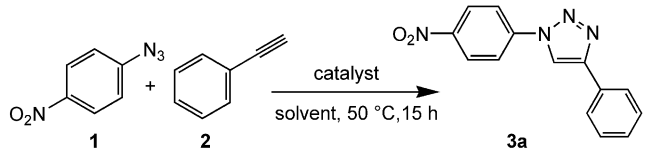
solvent for this catalyst, we used organic solvents, mixed solvents, and H_2O. The results showed that nonpolar and protic solvents were poor, and the polar solvent DMF was the best choice (Table 1, Entries 7 and 10–19). Finally, the reaction temperature and the loading of the catalyst were also examined; the results showed that 50 °C was a suitable temperature and that 0.1 equiv. of Zn/C was the optimum amount of catalyst (Table 1, Entries 7 and 20).

Table 1. Variations in reaction conditions.[a]



Entry	Catalyst	Solvent	Yield [%][b]
1	$ZnCl_2$	DMF	75
2	$ZnBr_2$	DMF	74
3	ZnO	DMF	58
4	$Zn(acac)_2$	DMF	81
5	$ZnOAc{\cdot}2H_2O$	DMF	78
6	Zn powder	DMF	27
7	Zn/C	DMF	91 (90[c], 68[d])
8	none	DMF	0
9	charcoal	DMF	0
10	Zn/C	DMF/H_2O (1:1)	47
11	Zn/C	EtOH	7
12	Zn/C	H_2O	0
13	Zn/C	H_2O/EtOH (1:1)	0
14	Zn/C	acetone	0
15	Zn/C	CH_3CN	0
16	Zn/C	DMSO	56
17	Zn/C	THF	0
18	Zn/C	CH_2Cl_2	0
19	Zn/C	toluene	36
20	Zn/C	DMF	30[e]
21	CuI	DMF	trace
22	$CuSO_4$/C	DMF	0[f]

[a] Reaction conditions: **1** (1.0 equiv.), **2** (1.2 equiv.), catalyst (0.1 equiv.), solvent (1 mL/mmol of **1**), 50 °C, 15 h. [b] Isolated yield. [c] 20 mol-% of Zn/C was used. [d] 5 mol-% of Zn/C was used. [e] At room temperature. [f] Trace amount of $CuSO_4$ (0.0005 mol-%) and C (10 mol-%) were used.

Zinc dust often has trace Cu^{II} impurities (up to 50 mg/kg), whereas charcoal might play a role that could reduce Cu^{II} to Cu^{I}. Therefore, it is wondered whether a trace amount of Cu^{I} generated in situ catalyzed the cycloaddition rather than Zn/C. We used CuI (10 mol-%) as the catalyst instead of Zn/C to carry out the reaction, but the desired product was not obtained (Table 1, Entry 21). Then, a trace quantity of Cu^{II} and charcoal as the catalyst was used instead of Zn/C to perform control experiments (see the Supporting Information). Finally, we did not observe any cycloaddition products, so it is speculated that Zn/C could catalyze the reaction between azides and alkynes.

After optimizing the process, the Zn/C-catalyzed cycloaddition of organic azides with alkynes was performed under the standard conditions: Zn/C (10 mol-%) as the catalyst and DMF as the solvent at 50 °C without exclusion of air. As shown in Table 2, for most of the examined substrates, experiments were performed smoothly and the corresponding triazoles were obtained in good to excellent yields (Table 2, Entries 1, 2, and 4–16). In general, no significant difference in reactivity was observed for the examined reactants with varied electronic properties. Both electron-rich and electron-poor azides as reactants generated good to excellent yields of the products (Table 2, Entries 1, 9, 10, 12, and 14). Moreover, aryl and aliphatic azides could both react with phenylacetylene efficiently (Table 2, Entries 1, 2, and 4–16). Note that low yields were found when the organic azides were hindered (Table 2, Entries 5–8, 11, and 13), and sensitive functional groups like 2-nitrophenyl azide and heterocyclic azide rendered the cycloaddition unresponsive (Table 2, Entries 3 and 17).

Table 2. Zn/C-catalyzed cycloaddition of organic azides with phenylacetylene.[a]

Entry	Azide (R =)	Time [h]	Triazole	Yield [%][b]
1	4-$NO_2C_6H_4$	15	**3a**	91
2	3-$NO_2C_6H_4$	15	**3b**	87
3	2-$NO_2C_6H_4$	15	**3c**	0
4	3-ClC_6H_4	15	**3d**	79
5	2-ClC_6H_4	15	**3e**	66
6	2,5-$Cl_2C_6H_4$	15	**3f**	70
7	2-BrC_6H_4	15	**3g**	65
8	2-IC_6H_4	15	**3h**	64
9	Ph	15	**3i**	93
10	4-$CH_3C_6H_4$	15	**3j**	94
11	2-$CH_3C_6H_4$	15	**3k**	63
12	4-$CH_3OC_6H_4$	15	**3l**	94
13	2-$CH_3OC_6H_4$	15	**3m**	71
14	3,4-$(CH_3)_2C_6H_3$	15	**3n**	95
15	*n*-C_4H_9	20	**3o**	85
16	*n*-C_5H_{11}	20	**3p**	83
17	2-pyridyl	20	**3q**	0

[a] Reaction conditions: **1** (1.0 equiv.), **2** (1.2 equiv.), Zn/C (0.1 equiv.), DMF (1 mL/mmol of **1**), 50 °C, 15 h. [b] Isolated yield.

As shown in Table 3, the cycloaddition of aryl alkynes with benzyl azide performed efficiently to provide the desired products in high yields (Table 3, Entries 1–11). It was concluded that the cycloaddition was slightly influenced by electronic properties. Specifically, electron-rich aryl alkynes gave higher yields of the desired products than electron-poor ones (Table 3, Entries 1–9).

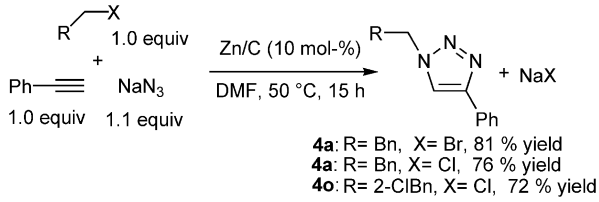
Surprisingly, this cycloaddition also proceeded successfully in the case of heterocyclic alkynes like 2-pyridylacetylene and 3-thienylacetylene, although the yields were lower than other substrates (Table 3, Entries 10 and 11). Disappointedly, the use of aliphatic alkynes as reactants gave no reaction (Table 3, Entries 12–14).

Interestingly, the one-pot synthesis of triazoles from a halide, NaN_3, and an alkyne could be realized (Scheme 1).[12] Triazoles **4a** and **4o** could be obtained by the convenient Zn/C-catalyzed three-component reaction, though the yields were slightly low.

Table 3. Zn/C-catalyzed cycloaddition of benzyl azide with terminal alkynes.[a]

Entry	Alkyne (R =)	Time [h]	Triazole	Yield [%][b]
1	Ph	15	**4a**	90
2	4-$CH_3OC_6H_4$	15	**4b**	95
3	4-*n*-$C_5H_{11}OC_6H_4$	15	**4c**	94
4	3-$CH_3C_6H_4$	15	**4d**	92
5	4-$NO_2C_6H_4$	15	**4e**	91
6	4-BrC_6H_4	15	**4f**	92
7	2-ClC_6H_4	15	**4g**	89
8	4-FC_6H_4	15	**4h**	92
9	3-$NH_2C_6H_4$	15	**4i**	83
10	2-pyridyl	15	**4j**	81
11	3-thienyl	15	**4k**	76
12	*n*-C_4H_9	20	**4l**	0
13	2-OH-propyl	20	**4m**	0
14	$BrCH_2$	20	**4n**	0

[a] Reaction conditions: **1** (1.0 equiv.), **2** (1.2 equiv.), Zn/C (0.1 equiv.), DMF (1 mL/mmol of **1**), 50 °C, 15 h. [b] Isolated yield.

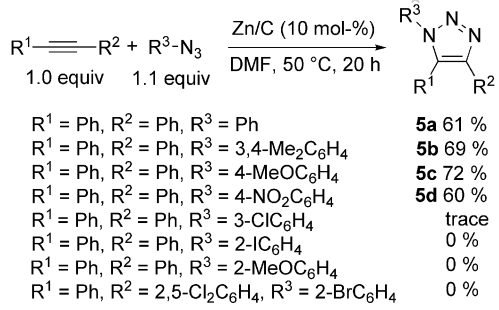


Scheme 1. Three-component reaction.

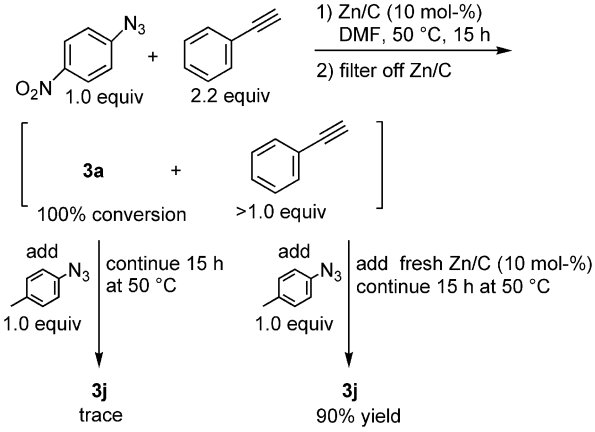
More importantly, some examples of 1,4,5-trisubstituted 1,2,3-triazoles have been obtained in moderate yield by the Zn/C-catalyzed cycloaddition by using internal alkynes as the substrates (Scheme 2), which could not be realized by the Cu-catalyzed system.[13] Because Cu^I acetylides seem to be the bona fide intermediates in copper-assisted azide–alkyne cycloadditions (CuAAC),[3] this transformation is limited to terminal alkynes. The Zn/C-catalyzed system, in fortunate contrast, is active with internal alkynes as well. As shown in Scheme 2, electron-rich and electron-poor azides could react with 1,2-diphenylethyne to provide the desired products in moderate yields. However, steric hindrance affected the reaction obviously and limited the scope of the reaction to some extent.

To confirm that this procedure catalyzed by Zn/C is unambiguously heterogeneous in nature, an additional experiment was carried out (Scheme 3). After filtering a totally converted reaction mixture (4-NO_2PhN_3 as a substrate) to remove the catalyst, 1.0 equiv. of a different azide (4-$MePhN_3$) was added as an additional substrate to the filtrate, and the filtrate was then treated with the remaining amount of phenylacetylene. A trace amount of another triazole, while adding the fresh Zn/C to the filtrate, led to 90% yield of the additional desired product.

Finally, we examined the recovery and reuse of Zn/C. The reuse test of Zn/C was carried out in DMF by using 4-



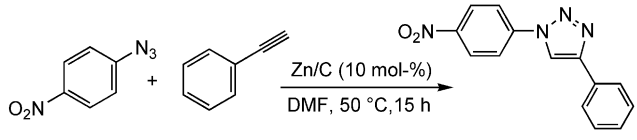
Scheme 2. Synthesis of 1,4,5-trisubstituted 1,2,3-triazoles.



Scheme 3. Testing of the heterogeneous catalyst.

nitrophenyl azide and phenylacetylene as the reaction partners (Table 4). The catalyst was recovered after 15 h, filtered, washed successively with H_2O and CH_2Cl_2, dried, and then subjected to the second run of the same reaction process. After three recycles, the activity of the recovered catalyst decreased gradually to 73%. However, after the fifth time, the catalyst efficiency dramatically decreased (Table 4, run 5 vs. runs 1–4).

Table 4. Recovery and reuse of Zn/C.



Run	Product yield [%][a]	Catalyst recovery [%]
1	91	76
2	88	80
3	85	82
4	73	85
5	45	86

[a] Isolated yield.

The mechanistic underpinnings for this Zn/C-catalyzed synthesis of triazoles need much more studies, but we offer the following tentative hypothesis. As both terminal and internal alkynes participate in the catalyzed reaction, the involvement of zinc acetylides is unlikely. Therefore, a plausible mechanism might involve the oxidative coupling of an

alkyne and an azide onto zinc, which may give a six-membered metallacycle. Then, the six-membered metallacycle would undergo reductive elimination releasing the aromatic triazole product.[13]

Conclusions

In summary, we have shown for the first time that 1,4-disubstituted 1,2,3-triazoles can be constructed from organic azides and aryl alkynes by using Zn/C as an efficient and heterogeneous catalyst. The catalytic system could tolerate a large variety of functional groups, including electron-rich and electron poor substrates and heterocyclic alkynes. Benzyl halides, NaN_3, and alkynes could be converted into 1,4-disubstituted 1,2,3-triazoles by a convenient one-pot three-component reaction. In addition, the preparation of 1,4,5-trisubstituted 1,2,3-triazoles was demonstrated under Zn/C catalysis, but these compounds could not be synthesized under Cu catalysis. Finally, the heterogeneous Zn/C catalyst has significant advantages in catalyst/product separation and reuse.

Experimental Section

General Remarks: All reagents were purchased from commercial suppliers and were used with further purification. Zn/C (10%, Alfa Aesar) was commercially available and was used directly. All experiments were carried out in air. Flash chromatography was carried out with Merck silica gel 60 (63–200 mesh). Analytical TLC was performed with Merck silica gel 60 F254 plates, and the products were visualized by UV detection. ^{1}H and ^{13}C NMR (300 or 400 and 75 or 100 MHz, respectively) spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm using TMS as internal standard.

General Procedure for the Zn/C-Catalyzed Cycloaddition Reaction: Zn/C (100 mg, 1.00 mmol/g, ca. 0.1 mmol), azide (1.0 mmol), alkyne (1.2 mmol), and DMF (1 mL) were added to a flask with a stirring bar. The flask was stirred at 50 °C for the indicated time. After cooling to room temperature, the mixture was diluted with ethyl acetate and filtered. The filtrate was concentrated under reduced pressure to afford the crude product, which was further purified by silica gel chromatography (petroleum/ethyl acetate, 5:1) to yield the corresponding product. The identity and purity of the products was confirmed by ^{1}H and ^{13}C NMR spectroscopic analysis.

1-(4-Nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (3a): White solid, isolated yield 91% (Table 2, Entry 1), m.p. 152–154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (s, 2 H), 7.88 (s, 1 H), 7.60–7.57 (m, 2 H), 7.46–7.38 (m, 3 H), 7.26–7.23 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.4, 141.2, 137.9, 134.0, 129.8, 129.2, 128.6, 126.0, 125.2, 124.7 ppm.

1-(3-Nitrophenyl)-4-phenyl-1*H*-1,2,3-triazole (3b): Pale-yellow solid, isolated yield 87% (Table 2, Entry 2), m.p. 192–194 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (s, 2 H), 7.90 (s, 1 H), 7.70 (s, 1 H), 7.65 (s, 1 H), 7.44–7.39 (m, 3 H), 7.26–7.24 (t, J = 4.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.5, 137.4, 130.4, 130.3, 129.9, 129.2, 129.0, 128.6, 125.9, 123.7, 123.1, 120.0 ppm.

1-(3-Chlorophenyl)-4-phenyl-1*H*-1,2,3-triazole (3d): White solid, isolated yield 79% (Table 2, Entry 4), m.p. 167–169 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (s, 1 H), 7.91–7.89 (d, J = 7.2 Hz, 2 H), 7.84 (s, 1 H), 7.72–7.70 (d, J = 8.0 Hz, 1 H), 7.51–7.36 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.6, 137.8, 135.6, 130.8, 129.9, 128.9, 128.8, 128.6, 125.8, 120.7, 118.4, 117.3 ppm.

1-(2-Chlorophenyl)-4-phenyl-1*H*-1,2,3-triazole (3e): Colorless oil, isolated yield 66% (Table 2, Entry 5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 7.93–7.91 (d, J = 7.2 Hz, 2 H), 7.69–7.67 (m, 1 H), 7.61–7.59 (m, 1 H), 7.49–7.46 (m, 4 H), 7.51–7.35 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9, 134.9, 130.8, 130.7, 130.1, 128.9, 128.5, 128.4, 127.9, 127.7, 125.8, 121.6 ppm.

1-(2,5-Dichlorophenyl)-4-phenyl-1*H*-1,2,3-triazole (3f): White solid, isolated yield 70% (Table 2, Entry 6), m.p. 111–113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (s, 1 H), 7.92–7.90 (m, 2 H), 7.74 (s, 1 H), 7.55–7.36 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.8, 135.5, 133.7, 131.6, 130.7, 129.8, 128.9, 128.5, 127.7, 126.6, 125.9, 121.3 ppm.

1-(2-Bromophenyl)-4-phenyl-1*H*-1,2,3-triazole (3g): Colorless oil, isolated yield 65% (Table 2, Entry 7). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (s, 1 H), 7.94–7.79 (t, J = 7.6 Hz, 2 H), 7.78–7.76 (t, J = 6.8 Hz, 1 H), 7.62–7.60 (m, 1 H), 7.53–7.35 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.5, 136.5, 133.9, 131.1, 130.1, 128.9, 128.5, 128.4, 128.1, 125.8, 121.6, 118.5 ppm.

1-(2-Iodophenyl)-4-phenyl-1*H*-1,2,3-triazole (3h): White solid, isolated yield 64% (Table 2, Entry 8), m.p. 149–151 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (s, 1 H), 8.03–8.00 (d, J = 8.1 Hz, 1 H), 7.93 (t, J = 7.2 Hz, 2 H), 7.55–7.46 (m, 4 H), 7.44–7.27 (m, 1 H), 7.23 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6, 140.2, 140.0, 131.1, 130.2, 129.2, 128.9, 128.4, 127.8, 125.8, 121.5, 93.8 ppm.

1,4-Diphenyl-1*H*-1,2,3-triazole (3i): White solid, isolated yield 93% (Table 2, Entry 9), m.p. 177–179 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (s, 1 H), 7.93–7.90 (d, J = 7.8 Hz, 2 H) 7.81–7.78 (d, J = 8.4 Hz, 2 H) 7.57–7.36 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4, 137.0, 130.2, 129.7, 128.9, 128.7, 128.4, 123.6, 120.5, 117.5 ppm.

1-(4-Methylphenyl)-4-phenyl-1*H*-1,2,3-triazole (3j): White solid, isolated yield 94% (Table 2, Entry 10), m.p. 165–167 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (s, 1 H), 7.92–7.69 (d, J = 6.9 Hz, 2 H), 7.67–7.64 (d, J = 8.1 Hz, 2 H), 7.47–7.42 (t, J = 7.2 Hz, 2 H), 7.38–7.31 (m, 3 H), 2.43 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.2, 138.8, 134.7, 130.3, 130.2, 128.8, 128.3, 125.8, 120.4, 117.6, 21.1 ppm.

1-(2-Methlyphenyl)-4-phenyl-1*H*-1,2,3-triazole (3k): Pale-yellow liquid, isolated yield 63% (Table 2, Entry 11). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95–7.90 (m, 3 H), 7.47–7.34 (m, 7 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.5, 136.4, 133.7, 131.4, 130.3, 129.9, 128.9, 128.2, 126.8, 125.9, 125.7, 121.1, 17.8 ppm.

1-(4-Methoxyphenyl)-4-phenyl-1*H*-1,2,3-triazole (3l): White solid, isolated yield 94% (Table 2, Entry 12), m.p. 160–162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.91–7.89 (d, J = 8.4 Hz, 2 H) 7.69–7.67 (d, J = 8.8 Hz, 2 H), 7.47–7.34 (m, 3 H), 7.04–7.02 (d, J = 8.8 Hz, 2 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 148.2, 130.5, 130.3, 128.8, 128.3, 125.8, 122.1, 117.8, 114.7, 55.6 ppm.

1-(2-Methoxyphenyl)-4-phenyl-1*H*-1,2,3-triazole (3m): Yellow liquid, isolated yield 71% (Table 2, Entry 13). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (s, 1 H), 7.93–7.82 (m, 3 H), 7.46–7.41 (m, 3 H), 7.36–7.32 (m, 1 H), 7.14–7.09 (m, 2 H), 3.90 (s, 3 H) ppm. ^{13}C

NMR (100 MHz, $CDCl_3$): δ = 147.2, 130.6, 130.0, 128.8, 128.0, 126.3, 125.8, 125.4, 121.8, 121.7, 121.2, 112.2, 55.9 ppm.

1-(3,4-Dimethylphenyl)-4-phenyl-1*H*-1,2,3-triazole (3n): White solid, isolated yield 95% (Table 2, Entry 14), m.p. 138–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (s, 1 H), 7.91–7.89 (d, J = 7.2 Hz, 2 H), 7.56 (s, 1 H), 7.48–7.42 (m, 3 H), 7.37–7.27 (m, 1 H), 7.25 (s, 1 H), 2.35–2.32 (d, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 138.3, 137.5, 134.9, 130.6, 130.3, 128.8, 128.2, 125.7, 121.6, 117.7, 117.6, 119.2, 119.8, 119.5, 119.4 ppm.

1-Butyl-4-phenyl-1*H*-1,2,3-triazole (3o): Colorless liquid, isolated yield 85% (Table 2, Entry 15). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (t, J = 7.2 Hz, 2 H), 7.73 (s, 1 H), 7.44–7.32 (m, 3 H), 7.42 (t, J = 6.9 Hz, 2 H), 1.89–1.83 (m, 2 H), 1.44–1.36 (m, 2 H), 0.97 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 130.6, 128.8, 128.0, 125.6, 119.3, 50.1, 32.2, 19.7, 13.4 ppm.

1-Pentyl-4-phenyl-1*H*-1,2,3-triazole (3p): White solid, isolated yield 83% (Table 2, Entry 16), m.p. 75–77 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.82 (m, 2 H), 7.74 (s, 1 H), 7.41 (t, J = 7.6 Hz, 2 H), 7.32 (t, J = 7.2 Hz, 1 H), 4.37 (t, J = 7.2 Hz, 2 H), 1.95–1.92 (m, 2 H), 1.36–1.32 (m, 4 H), 0.90 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6, 130.6, 128.7, 128.0, 125.6, 119.3, 50.3, 30.0, 28.5, 22.0, 13.8 ppm.

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (4a): White solid, isolated yield 90% (Table 3, Entry 1), m.p. 126–128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80–7.88 (m, 2 H), 7.65 (s, 1 H), 7.40–7.36 (m, 5 H), 7.32–7.28 (m, 3 H), 5.55 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.2, 134.7, 130.5, 129.1, 128.7, 128.1, 128.0, 125.6, 119.4, 54.1 ppm.

1-Benzyl-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole (4b): White solid, isolated yield 95% (Table 3, Entry 2), m.p. 116–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.69 (m, 2 H), 7.57 (s, 1 H), 7.38–7.26 (m, 5 H), 6.93–6.91 (d, J = 8.1 Hz, 2 H), 5.55 (s, 2 H), 3.82 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5, 148.0, 134.7, 129.0, 128.6, 128.0, 126.9, 123.2, 118.6, 114.1, 55.2, 54.1 ppm.

1-Benzyl-4-(4-penthoxyphenyl)-1*H*-1,2,3-triazole (4c): White solid, isolated yield 94% (Table 3, Entry 3), m.p. 117–119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.60 (m, 2 H), 7.56 (s, 1 H), 7.37–7.28 (m, 5 H), 6.92–6.89 (m, 2 H), 5.54 (s, 2 H), 3.99–3.94 (m, 2 H), 1.80–1.76 (t, J = 6 Hz, 2 H), 1.44–1.37 (m, 4 H), 0.95–0.90 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 148.1, 134.7, 130.1, 129.0, 128.0, 127.1, 123.1, 118.6, 114.8, 68.1, 54.1, 28.8, 28.1, 22.4, 13.9 ppm.

1-Benzyl-4-(3-methylphenyl)-1*H*-1,2,3-triazole (4d): White solid, isolated yield 92% (Table 3, Entry 4), m.p. 129–131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65–7.55 (m, 3 H), 7.41–7.10 (m, 7 H), 5.54 (s, 2 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.3, 138.4, 134.7, 130.4, 129.1, 128.9, 128.7, 128.1, 127.2, 126.3, 122.7, 119.4, 54.2, 21.3 ppm.

1-Benzyl-4-(4-nitrophenyl)-1*H*-1,2,3-triazole (4e): Pale-yellow solid, isolated yield 91% (Table 3, Entry 5), m.p. 131–133 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26–8.23 (m, 2 H), 7.99–7.95 (m, 2 H), 7.80 (s, 1 H), 7.45–7.28 (m, 5 H), 5.60 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.2, 145.9, 136.7, 134.8, 129.2, 129.0, 128.5, 126.0, 124.2, 120.9, 54.4 ppm.

1-Benzyl-4-(4-bromophenyl)-1*H*-1,2,3-triazole (4f): White solid, isolated yield 92% (Table 3, Entry 6), m.p. 142–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68–7.64 (m, 3 H), 7.53–7.50 (s, 1 H), 7.39–7.30 (m, 5 H), 5.56 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.1, 134.4, 131.9, 129.5, 129.1, 128.8, 128.0, 127.2, 122.0, 119.5, 54.2 ppm.

1-Benzyl-4-(2-chlorophenyl)-1*H*-1,2,3-triazole (4g): White solid, isolated yield 89% (Table 3, Entry 7), m.p. 75–77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25–8.23 (m, 1 H), 8.11 (s, 1 H), 7.43–7.28 (m, 8 H), 5.61 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.4, 134.6, 131.1, 130.1, 129.8, 129.2, 129.1, 129.0, 128.7, 127.9, 127.1, 123.1, 54.2 ppm.

1-Benzyl-4-(4-fluorophenyl)-1*H*-1,2,3-triazole (4h): White solid, isolated yield 92% (Table 3, Entry 8), m.p. 106–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78–7.73 (m, 2 H), 7.61 (s, 1 H), 7.40–7.25 (m, 5 H), 7.07 (t, J = 8.7 Hz, 2 H), 5.56 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.0, 160.1, 147.3, 134.5, 129.1, 128.8, 128.0, 127.4, 127.3, 119.2, 115.9, 115.5, 54.2 ppm.

1-Benzyl-4-(3-aminophenyl)-1*H*-1,2,3-triazole (4i): White solid, isolated yield 83% (Table 3, Entry 9), m.p. 107–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1 H), 7.61 (s, 1 H), 7.48–7.16 (m, 7 H), 6.62 (s, 1 H), 3.65 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.2, 146.8, 134.7, 133.0, 129.8, 129.0, 128.7, 127.0, 118.7, 115.9, 114.6, 112.2, 54.1 ppm.

1-Benzyl-4-(2-pyridyl)-1*H*-1,2,3-triazole (4j): White solid, isolated yield 81% (Table 3, Entry 10), m.p. 111–113 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.53–8.51 (m, 1 H), 8.18–8.15 (d, J = 7.8 Hz, 1 H), 8.04 (s, 1 H), 7.78–7.72 (m, 1 H), 7.37–7.17 (m, 6 H), 5.57 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.2, 149.2, 148.6, 136.8, 134.3, 129.1, 128.8, 128.2, 122.8, 121.9, 120.2, 54.3 ppm.

1-Benzyl-4-(3-thienyl)-1*H*-1,2,3-triazole (4k): White solid, isolated yield 76% (Table 3, Entry 11), m.p. 92–94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (s, 2 H), 7.41–7.28 (m, 7 H), 5.55 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.4, 134.6, 131.7, 128.9, 127.9, 127.0, 126.2, 125.0, 121.1, 119.2, 54.1 ppm.

1-(2-Chlorobenzyl)-4-phenyl-1*H*-1,2,3-triazole (4o): White solid, isolated yield 72% (Scheme 1), m.p. 79–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.80 (m, 2 H), 7.76 (s, 1 H), 7.45–7.38 (m, 3 H), 7.33–7.20 (4 H), 5.71 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 133.4, 132.5, 130.5, 130.3, 130.2, 129.9, 128.7, 128.1, 127.6, 125.7, 119.7, 51.4 ppm.

1,4,5-Triphenyl-1*H*-1,2,3-triazole (5a): White solid, isolated yield 61% (Scheme 2), m.p. 223–225 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61–7.59 (m, 2 H), 7.40–7.28 (m, 11 H), 7.21–7.19 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 136.5, 133.6, 130.8, 130.1, 129.3, 129.1, 129.0, 128.9, 128.4, 127.8, 127.7, 127.3, 125.1 ppm.

1-(3,4-Dimethylphenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (5b): White solid, isolated yield 69% (Scheme 2), m.p. 157–159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.58 (m, 2 H), 7.39–7.32 (m, 6 H), 7.21–7.18 (m, 2 H), 7.07–7.05 (d, J = 8 Hz, 1 H), 6.92–6.90 (m, 1 H), 2.25 (s, 3 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.6, 137.7, 137.6, 134.3, 133.6, 130.9, 130.2, 129.9, 129.2, 128.9, 128.4, 127.9, 127.7, 127.3, 126.2, 122.3, 19.7, 19.4 ppm.

1-(4-Methoxyphenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (5c): White solid, isolated yield 72% (Scheme 2), m.p. 170–172 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.58 (m, 2 H), 7.41–7.18 (m, 10 H), 6.88–6.94 (m, 2 H), 3.81 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 144.5, 133.7, 130.9, 130.2, 129.6, 129.2, 128.9, 128.4, 127.9, 127.8, 127.3, 126.6, 114.2, 55.4 ppm.

1-(4-Nitrophenyl)-4,5-diphenyl-1*H*-1,2,3-triazole (5d): White solid, isolated yield 60% (Scheme 2), m.p. 238–240 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25–8.23 (m, 2 H), 7.60–7.58 (m, 2 H), 7.54–7.41 (m, 5 H), 7.34–7.31 (m, 3 H), 7.26–7.23 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.3, 145.5, 141.3, 133.5, 130.1, 130.0, 129.5, 128.6, 128.3, 127.3, 127.1, 125.1, 124.6 ppm.

Supporting Information (see footnote on the first page of this article): Experimental procedures, characterization data, and copies of NMR spectra for produces.

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