# COMMUNICATION

### WILEY Applied Organometallic Chemistry

# Claycop/hydrazine: A new and highly efficient recyclable/reusable catalytic system for 1,4-disubstituted-1,2,3-triazole synthesis under solvent-free conditions

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Clay-supported copper(II) nitrate (claycop) has been used as an efficient catalyst for azide–alkyne cycloaddition reactions leading to 1,4-disubstituted 1,2,3-triazoles. The highly efficient claycop/hydrazine hydrate catalytic system affords triazoles in a few minutes (1–20 min) at room temperature, under mild and solvent-free conditions. High regioselectivity, excellent yields, ease of claycop synthesis and recyclability/reusability of the catalyst are considered as practical merits of the protocol.

## **KEYWORDS**

1,2,3-triazoles, alkyne, azide, claycop/hydrazine hydrate, heterogeneous

The 1,3-dipolar cycloaddition reaction between azide and alkyne leading to the formation of disubstituted 1,2,3-triazoles has attracted tremendous interest during the last few decades. Compounds containing the 1,2,3-triazole unit find various applications in medicinal chemistry, organic synthesis, biology and material sciences.<sup>[1-4]</sup> Some of the important properties that the 1,2,3-triazole unit possesses are high chemical stability, generally inert to severe hydrolytic, oxidizing and reducing conditions, even at high temperature, strong dipole moment (4.8–5.6 Debye), aromatic character and hydrogen bond accepting ability.<sup>[5]</sup>

Various synthetic protocols have been developed for the synthesis of 1,2,3-triazole derivatives. Among these methods, the Cu-catalysed azide–alkyne cycloaddition (CuAAC) reaction, discovered independently by the groups of Meldal and Sharpless, is undoubtedly one of the most prominent strategies.<sup>[6,7]</sup> There have been many literature reports of using copper(I) source in regioselective azide–alkyne cycloaddition.<sup>[8]</sup> The copper(I) species is either generated from copper(II) salts with reducing agents (e.g. sodium ascorbate) or added directly as cuprous salts, usually with stabilizing ligands.<sup>[9]</sup> Metallic copper or clusters are also

employed, but these catalytic systems sometimes require oxidative agents.<sup>[10]</sup> The disadvantages of such systems are that the reaction kinetics is relatively slow and a significant amount of catalyst is required. There are also reports indicating the formation of diacetylenes and bistriazoles.<sup>[11]</sup>

In order to overcome the drawbacks associated with homogeneous systems, heterogeneous catalysts have been developed. Along with many other advantages, recyclability and reusability are the key features that heterogeneous catalysts have for application in synthetic chemistry.<sup>[12]</sup> Heterogeneous catalyst systems with Cu catalysts have been successfully used in click reactions. Cu(I) catalysts immobilized on polymers, silica or zeolite, Cu(0) on charcoal, CuO nanostructures, etc., are some examples of heterogeneous systems used in azide– alkyne cycloaddition.<sup>[13]</sup>

To continue our study of 1,2,3-triazole synthesis,<sup>[14]</sup> in the work reported herein we developed a very efficient heterogeneous catalytic system for azide–alkyne cycloaddition reaction. Copper(II) nitrate immobilized on montmorillonite clay (claycop) was used as catalyst and for some substrates the reactions proceeded within 1–5 min affording almost quantitative yields of the desired 1,2,3-triazoles. The highlighting

# 2 of 6 WILEY-Organometallic Chemistry

factors of this novel protocol are that it is a solvent-free approach and the catalytic system is recyclable and reusable.

# **1** | **RESULTS AND DISCUSSION**

Claycop was synthesized following a literature procedure.<sup>[15]</sup> Briefly, it was prepared by adding K10 clay (20 g) to a solution of copper(II) nitrate trihydrate (10 g) in acetone (250 ml). The resulting suspension was placed in a rotary vacuum evaporator and the solvent evaporated under reduced pressure giving claycop as a light blue, free-flowing powder. Powder X-ray diffraction data (Figure 1) indicate the presence of copper in claycop. Brunauer–Emmett–Teller surface area measurements were done to compare the surface area of unmodified K10 clay with that of claycop. Unmodified clay has a surface area of 220 m<sup>2</sup> g<sup>-1</sup> whereas the surface area for claycop is found to be 57 m<sup>2</sup> g<sup>-1</sup> indicating the impregnation of copper on the clay surface.



FIGURE 1 Powder X-ray diffraction pattern for claycop

The reaction of benzyl azide with phenylacetylene in the presence of 50 mg of claycop and 50 µl of hydrazine hydrate proceeded in less than 1 min affording almost quantitative yield of the desired product. The high activity of the catalyst system is demonstrated by the results in Table 1 (entries 1-5). The yields of desired products of the optimized cycloaddition reaction with different loadings of claycop/hydrazine hydrate catalyst (5-50 mg claycop; 5-50 µl hydrazine hydrate) are between 79 and 98%. The significant acceleration of click reaction using claycop/hydrazine hydrate is related to the reduction of Cu(II) in claycop by hydrazine hydrate. Hydrazine hydrate produces exothermic heating, once it is added to claycop. This heat energy is believed to be the key factor for speeding up the reduction of Cu(II) to Cu (I), as well as the acceleration of the dipolar cycloaddition reaction.

The reaction of benzyl azide and phenylacetylene in the presence of 50 mg of claycop and 50  $\mu$ l of hydrazine hydrate proceeded very fast affording triazole instantaneously (Table 1, entry 1). After a set of experiments (Table 1, entries 1–5), the use of 20 mg of claycop and 10  $\mu$ l of hydrazine hydrate (Table 1, entry 4) was chosen as the optimized reaction conditions for azide–alkyne cycloaddition reaction. In the absence of hydrazine hydrate, the reaction requires more than 12 h with the formation of both 1,5- and 1,4-disubstituted 1,2,3-triazoles.

After optimizing the reaction conditions, the optimal catalytic system for one-pot CuAAC was examined using a series of different azides and alkynes at room temperature under solvent-free conditions.<sup>[16]</sup> The results are summarized in Table 2 (entries 1–13). All reactions proceeded smoothly giving excellent isolated yields of the corresponding triazoles. Both electron-rich and electron-deficient aryl azides showed excellent reactivity and furnished products in excellent yields in short reaction times (Table 2, entries 4, 5, 8–11) at room temperature. Aromatic alkynes show slightly better reactivity towards benzyl or aryl azides as compared to aliphatic alkyne (Table 2, entry 13).

TABLE 1 Optimization of click reaction with various loadings of catalyst (claycop/hydrazine hydrate)<sup>a</sup>

		$+ = - \left\langle \sum_{\text{Clay Cu(II)/NH}_2\text{NH}_2\text{H}_2\text{O}} \right\rangle $	► Bn~N <sup>N</sup> N Ph 3a	
Entry	Claycop (mg)	NH <sub>2</sub> NH <sub>2</sub> ·H <sub>2</sub> O (μl)	Time (min)	Yield (%) <sup>b</sup>
1	50	50 (1 mmol)	1	95
2	50	30 (0.6 mmol)	5	86
3	20	50 (1 mmol)	5	98
4	20	10 (0.2 mmol)	5	98
5	5	5 (0.1 mmol)	10	79

<sup>a</sup>Reagents and reaction conditions: **1a** (1 mmol), **2a** (1.2 mmol), claycop 5–50 mg, hydrazine hydrate (5–50 μl). <sup>b</sup>Isolated yields.

Applied Organometallic-Chemistry TABLE 2 Catalytic system (claycop/hydrazine hydrate) investigated with various azides and alkynes at room temperature under mild conditions<sup>a</sup>

3 of 6

WILEY

	R-N		$\frac{J/NH_2NH_2H_2O}{rt} \sim \frac{R}{\sqrt{2}}$	N_N =√ B'	
Entry	Azide	Alkyne	Product	Time (min)	Yield (%) <sup>b</sup>
1	N <sub>3</sub>		3a	5	98
2	N <sub>3</sub>	=-{	3b	5	98
3	N <sub>3</sub>	MeO	3с	10	92
4	O <sub>2</sub> N N <sub>3</sub>		3d	20	92
5	O <sub>2</sub> N N <sub>3</sub>		3e	30	97
6	N <sub>3</sub>		3f	20	98
7	N <sub>3</sub>		3g	10	98
8	N <sub>3</sub> F		3h	20	97
9	N <sub>3</sub> F		3i	10	98
10	N <sub>3</sub> Br		3j	20	90
11	N <sub>3</sub> OMe		3k	20	92
12	N <sub>3</sub>		31	40	85
13	N <sub>3</sub>	₩~~~~	3m	50	81

<sup>a</sup>All reactions were carried out using azide (1 mmol), alkyne (1.2 mmol) claycop (20 mg) and hydrazine hydrate (10 µl, 0.2 mmol) under solvent-free conditions at room temperature.

<sup>b</sup>Isolated yields.

TABLE 3 Recyclability of claycop catalytic system<sup>a</sup>

$\bigcirc$	$N_3 + = $	Clay Cu(II)/NH <sub>2</sub> NH <sub>2</sub> H rt	$\xrightarrow{H_2O} \xrightarrow{Bn_N} \xrightarrow{N_N} \xrightarrow{N} \xrightarrow{N}$
1a	2a		За
Entry	Run	Time	Yield (%) <sup>b</sup>
1	First	5	98
2	Second	10	95
3	Third	20	92
4	Fourth	20	90

<sup>a</sup>Reagents and reaction conditions: **1a** (1 mmol), **2a** (1.2 mmol) and claycop catalyst (20 mg), hydrazine hydrate (10  $\mu$ l, 0.2 mmol) under solvent-free conditions and stirred at room temperature.

<sup>b</sup>Isolated yields.



FIGURE 2 Plausible mechanism of formation of 1,2,3-triazoles

In order to demonstrate the practical importance and wide application of this new heterogeneous catalytic system, it is desirable to show that the catalyst is recyclable and reusable. The recycling experiment was performed using the standard reaction of phenylacetylene and benzyl azide in the presence of 20 mg of claycop and 10  $\mu$ l (0.2 mmol) of hydrazine hydrate under solvent-free conditions (Table 3, entry 1). After the completion of the first cycle, the product was extracted by addition of ethyl acetate and the catalyst system consisting of claycop/hydrazine was precipitated from the reaction mixture and separated using a centrifugation system, followed by washing with ethyl acetate three to four times ensuring that no residual product was left with the catalytic system. The catalyst was dried and used for subsequent runs (Table 3, entries 2–4). The experimental results indicate that it is possible to recycle and reuse our catalytic system up to the fourth cycle without loss of any catalytic activity.

The mechanism of CuAAC reaction has been the subject of extensive study and, based on that, a plausible mechanism of the claycop/hydrazine-catalysed azide–alkyne cycloaddition reaction is depicted in Figure 2.

To show the convenient utility of our catalytic system we compare the procedure developed by us with procedures reported earlier for the same purpose. The results are summarized in Table 4. The ease of preparation of the catalyst, easier separation from the reaction mixture and operational simplicity make our protocol superior and easily acceptable.

# **2** | CONCLUSIONS

We have developed a mild and very efficient methodology for azide–alkyne cycloaddition reactions. The clay-supported copper(II) nitrate/hydrazine hydrate catalytic system for the synthesis of 1,4-disubstituted 1,2,3-triazoles is very easy to prepare and has tolerance for a range of azides and alkynes. The CuAAC reactions proceeded very fast under solvent-free conditions at room temperature. This mild methodology is expected to have wide applications.

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TABLE 4	Comparison of	f catalytic efficiency	of claye	op/hydrazine	e hydrate	system with	earlier	reported	catalysts	for synthesis	s of 3a
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Entry	Catalyst	Conditions	Time(h)	Yield (%)	Ref.
1	Cell-CuI NPs 100 mg	70 °C, H <sub>2</sub> O	2	96	[17]
2	Cu-Al <sub>2</sub> O <sub>3</sub> NPs, 10 mg	r.t., H <sub>2</sub> O	3	92	[18]
3	CuI-zeolite (CuI-USY),10 mol%	90 °C, H <sub>2</sub> O	15	90	[19]
4	Cu NPs on charcoal (1 mol%)	100 °C, H <sub>2</sub> O	0.6	91	[20]
5	Silica-immobilized NHC-cu(I), 0.5 mol% cu	80 °C, H <sub>2</sub> O	6	98	[21]
6	CuFe <sub>2</sub> O <sub>4</sub> NPs, 5 mol%	70 °C, H <sub>2</sub> O	3	93	[22]
7	Clay-Cu(II)/NH <sub>2</sub> NH <sub>2</sub> ·H <sub>2</sub> O, 20 mg	Solvent free, r.t.	0.08	98	This work

assistance to the Department of Chemistry, Dibrugarh University.

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### SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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